

Workbook for PMOD Version 3.5

Scope and Intended Use

This workbook is a tutorial for novice users of PMOD. It contains a dedicated section for each of the major PMOD tools as well as for database management. The sections provide detailed descriptions of typical tasks accomplished with PMOD plus some additional background information. We recommend the users to start at the beginning of each section and work through the descriptions step-by-step. For more specific information, please refer to the product documentation which is part of any PMOD installation or which is available online at <http://www.pmod.com/technologies/doc/index.html>.

Example Data and PMOD Installation

The example data for the exercises covered by this workbook are distributed as part of any new PMOD installation and are contained in the default database called **Pmod**.

- Users who own a PMOD installation can use that installation to perform the training tasks. To perform tasks with PMOD tools not included in their purchased license, we recommend requesting a trial installation.
- Users working with a trial PMOD installation should download the example database and install it together with the program. Note that the results produced with trial licenses cannot be saved. However, save-enabled trial licenses are available on request.
- For loading the example data, the **Database** data format must be used. To try similar work with your own data, we recommend using the **Autodetect** format and pointing the image loader to the directory containing the data files.
- All example images in the database are in DICOM format, calibrated, decay corrected and with correct timing information. Vector data such as blood activities are text files conforming to the requirements of the PMOD tools. You can export them to the file system for inspection.

Copyright and Disclaimer

The example data provided in the **Pmod** database are by courtesy of the following institutions.

- CFPFX data: Institute of Medicine, Research Centre Jülich, 52425 Jülich, Germany; Dr. A. Bauer.
- DASB data: Molecular Imaging Branch, National Institute of Mental Health, Bethesda, USA; Dr. M. Ichise.
- All other data: Nuclear Medicine, University Hospital, Zürich, Switzerland; Dr. A. Buck.

Note that the original data have been processed and optimized for training purposes.

IMPORTANT:

- The data from the **Pmod** database may only be used for PMOD training purposes. The owners of the original data reserve all rights regarding any type of public use of this data. Particularly, the data may not be used for any kind of publication purposes without getting written consent.
- The content of this workbook is proprietary and may not be reproduced without permission of PMOD Technologies. It corresponds to the functionality of PMOD at the time of writing and can be changed without notice.

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Section 1: PBAS Tool – Image Viewing & Processing





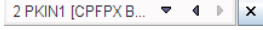
Topics:

- Load/Save Data: Data Formats, Data Transformation during loading.
- Image Viewing: Color tables, Window/Level, Layouts, Reports.
- Image Processing: Filtering, Time Averaging.
- VOI Definitions, Statistics.

Exercises:

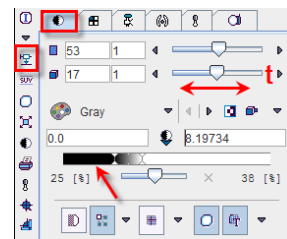
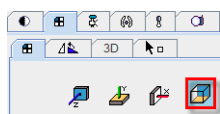
1. Data Loading/Saving


The images in the database are all in DICOM format and contain a complete description including timing. This makes data loading easy. In the following procedure you will load a data set, perform a transformation during loading, and save the same images in the Interfile format. Then the Interfile data are loaded again and compared with the original data.

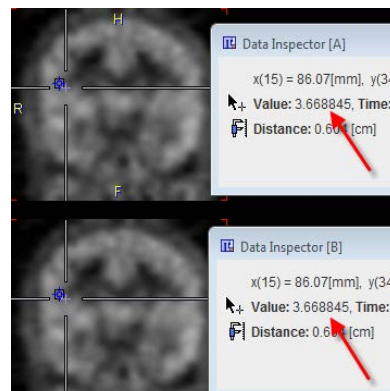
- Open the **PBAS (View)** tool. Initially the **DB Load** page appears, showing the list of patients.
- Select patient **PKIN1**; several series are listed: the two original data sets (Dynamic PET, MR Anatomy) and some derived result series. Select the **Dynamic PET** in the **Series** list. Using **Add** (or by double-clicking) the **Dynamic PET** series can be brought to the **Selected for loading** area.
- Activate the **with Operations** button. An intermediate dialog window appears. It allows selecting a sub-range of slices or frames, and also performing some image processing operations during loading. A visual support tool is available activating the **Assistance** button. It allows bringing into final anatomical orientation the images with inappropriate orientation.
- To apply a smoothing filter during loading select the tab **PREPROCESSING TOOLS**. In the list selection to the left select **3D Gaussian** and define the filter widths for the three directions.
- Load the data with the **Load** button. The smoothed images are shown on the **View** page.
- To save the smoothed data in the **Interfile** format change the **Save** button in the **Save** section to **INTERFILE**. The format is switched and a dialog box is shown allowing several settings. Browse to a local directory activating the selection button . Confirm with the **Select** button. Enable the **Create save name from root** radio button and in the **Save as** section specify the file name **CPFPX-Smoothed**, and **Save**. As there are different types of Interfile formats, a selection list is available in the **Transfer Syntax** section. It allows defining the number format, and whether two files or a combined file are written. Select a **FLOAT** format to avoid rounding errors, the two-file variant, and save. Two files are written, **CPFPX-Smoothed.img** (data) and **CPFPX-Smoothed.hdr** (description, text file). Note that the Interfile data written by PMOD has all relevant information (timing, units) in the header file. This is not the case with some other formats (Analyze, Raw) which require manual specification during loading.
- Before loading the saved Interfile images again set the pushpin in the **Load** area or the sidebar from the “overwrite”  position to the “append”  position.
- Then switch the **Load** button on the **View** page to the **INTERFILE** format. This brings up a file selection dialog box with the suffix filter set to “*.hdr;*.hv”. It should already point to the right directory because PMOD remembers the path of the last successful load or write operation.
- Select the **with Operations** button. Again, the dialog box with the loading options appears. **Note that the last loading configuration is used per default!** In the example the 3D Gaussian filter is still configured. To alert the user a  icon is shown. The best way to get rid of all special settings is to activate the **Reset loading parameters** button (**Alt+R** key). Check the **Select FRAMES** and **Select SLICES** boxes and use the **Select/Edit Time** button to verify the timing. Note the **Units** which are set to **kBq/cc**. This is because PMOD always displays activity values as kBq/cc, and the data were therefore saved with kBq/cc. Use **Load** to finally load the images. There are now two loaded image series in the **View** page, which can be switched using the  selection in the upper right. Depending on the format chosen, the min/max values may differ minimally due to rounding.


- Alternatively, to avoid the steps described above during the loading procedure, activate the **Open** button. The image is directly loaded and no preprocessing is applied.

- To compare the two images switch to the **Compare** page. This page is initially in the “fusion” mode. Hereby it synchronizes the two series in the upper rows and shows their fusion in the third row. Switch the layout to the orthogonal planes and browse through the slices using the mouse wheel or the sliders on the panel.



- To compare the values precisely, open the “data inspector” of both series by selecting  to the upper right of the images. Initially the appearing dialog windows may be at the same location. Move one of them so that both are visible. When the cursor is moved over the images, the corresponding pixel values in both series are displayed and should be identical.





- To see the pixel-wise time-activity curves (TAC) select the  button in the inspector dialog boxes. The boxes are now quite large and have to be arranged so that both curves can be seen simultaneously.

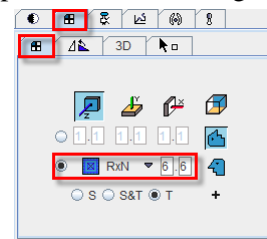
2. Image Viewing



Use the images loaded in PBAS and the **View** page to experiment with image viewing. When images are shown in the PMOD modules, the control elements are available, located to the right of the images. They are organized using tabs.







- **Colors:** switch from **Gray** to **Cold**, then set the lower threshold to 0kBq/cc. This can be done by entering the number of **0** into the text box, or by double-clicking into left part of the color bar. Stepping through the different frames you may notice that the upper and lower thresholds change because they are defined in %. To establish a fix color↔value mapping for the whole study select the **Scale to study minimum: maximum**  . This is particularly important for meaningful movies of dynamic tracer uptake.

- **Layouts:** Prepare a 6x6 layout of a particular time frame with the „layout” tab as illustrated (**Ctrl+6**). Note that for dynamic series the layout can also mix the times and slices (**S&T**), or show a single slice at different times (**T**).




- **Reslicing:** First switch the image display to the orthogonal planes using the “layout” tab  or by clicking into the images and then typing **Ctrl+D**. Then enter **Ctrl+R**, or select the “reslicing” tab . Handles are then shown in the image centers which allow translating (open rectangle) or rotating (closed rectangle) the images. As an alternative, enter discrete numbers for the transformation parameters in the reslicing tab. Note how the anatomical annotations are updated accordingly if you are working with a proper DICOM series.




- **Isocontours:** To see a histogram of the pixel values or get an isocontour overlay, select the  tab and define a threshold by dragging the small rectangle above the histogram or entering a value. To see the isocontour after changing to a different tab, select  before continuing.

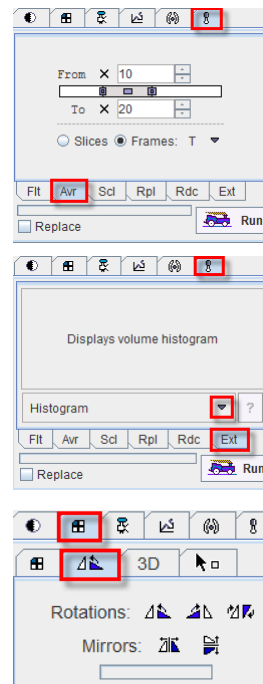
- **Report:** After a suitable layout has been defined, use the  button to start the **Print Preview** window. Adjust the colors appropriately and use  again to refresh. Try adding an annotation and a comment to the images and then save the report in one of the available capture formats.

3. Image Processing

Besides the loading transformations there are several easily available image processing facilities.









- The “tools” tab  offers a selection of handy processing tools. The main tools are immediately shown as sub-tabs. The working principle is always that the user selects a data transformation, and then starts processing with the **Run** button. If the **Replace** box is not checked, a new data set is generated and added to the series list. Otherwise the original data are overwritten.

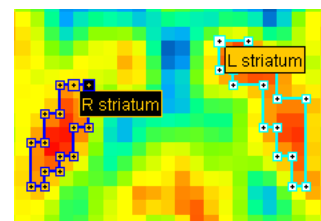
- As the images of dynamic studies are typically noisy, they are often averaged for creating images with sufficient anatomic information. This can quickly be achieved with the average **Avr** sub-tab as illustrated to the right. Select the **Frame** mode, define **From/To** to 10/20 and then select **Run** to average the frames 10 to 20. Spatial filtering can be applied to dynamic series to reduce the noise at the cost of spatial resolution. The **Flt** sub-tab offers two such smoothing filters (**Gaussian**, **Median**), but also an edge enhancement filter (**Canny Deriche**).
- The **Ext** sub-tab is particular. It houses diverse processing routines which can be added by plug-in programming. The functions can be selected from a list with the indicated arrow. Probably the most interesting ones are the **Interpolation** to a different image matrix or resolution, the **Principal Component Analysis PCA**, **Resize** to add a border or extract a sub-volume, the **Segmentation** of structures, the calculation of a **SUV** image, Partial Volume Correction (**PVC**), MR Segmentation and Skull Stripping.
- After creating different processing results, use the study selection  3 [CPFPX-Sm... to switch among them. Unsuccessful results can be closed using the  button.
- A set of helpful reorientation tools is available in the  section of the layout tab. They can be employed to bring the images into a specific orientation. Note that the anatomical annotations are consistently moved during the operations.










4. Volumes-Of-Interest (VOI)

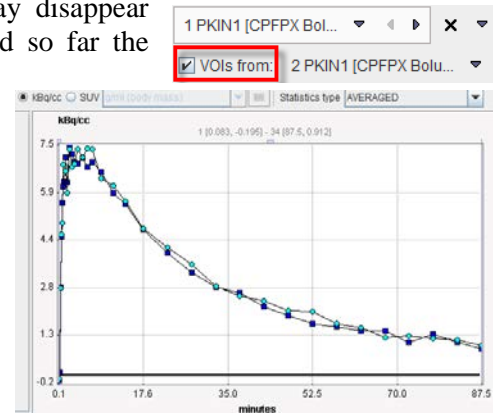
The **VOIs** page of the PBAS tool serves for defining and evaluating “Volumes-of-Interest” (VOIs). VOIs are built from planar polygons called contours (CTR), which can be defined in the axial, coronal or sagittal orientation. All contours belonging to a VOI in a certain plane are called a “Region-of-interest” (ROI). For each level (VOI, ROI, CTR) there is a dedicated toolbar highlighted in different color which houses the applicable tools. These toolbars can be detached by dragging, if needed.


- To start over close all open series using the using  button in the sidebar, or by closing PBAS and starting it again.
- Load just the **Dynamic PET** of patient **PKIN1**. To get an image with enough anatomical information for VOI outlining open the tab  and average the frames 10 to 20.
- Switch to the **VOIs** page, and select the averaged series in the axial orientation. Browse to slice **40** and adjust the image for contrast (eg **Cold** color, **1.0** lower threshold, **7.0** upper threshold).
- Activate the  **New VOI** button below the **VOIs** list to get a new empty VOI, and label the new entry by **R striatum**. Make sure that image **Interpolation** is switched ON . Select the “point-and-click” tool . Outline the first planar CTR of the VOI by clicking along the right striatum. Close the ROI by **double-clicking** or using the “finish” entry  in the context menu (right mouse button). Note the **Z** indication in the **VOIs** list which states that the definition was performed in the axial direction. Enable the fill in checkbox **Fill** to clearly observe the pixels included in the VOI.
- Use the mouse wheel, or the slices slider, to scroll to the axial slices 39 and 38, and outline the right striatum there similarly. The **R striatum** VOI now consists of 3 ROIs, each containing 1 CTR.
- Now use  **New** button to create another empty VOI, label it **L striatum**. This time use the HOT 2D isocontour ROI tool  for outlining. Click at the edge of the left striatum in slice 40. An isocontour is immediately calculated and displayed. It has a step-wise appearance because it follows the pixel boundaries. Click at different seed points until you are satisfied with the calculated result. Repeat the isocontour ROI definition in slices 39 and 38 too. The result in slice 40 might look something like illustrated to the right.

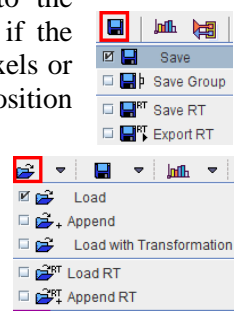



- We are not satisfied with the **R striatum** definition and want to correct. Select that VOI by double-clicking the entry **1** in the **VOI** list. The display will jump to a slice showing a ROI of the selected VOI. Select the  tool and move individual vertices of the ROI polygon. When working with dense polygons it may be helpful using the  tool. Dragging the tool towards a contour will radially push away the vertices.
- Instead of modifying the existing contour it may be better to start over. Use the  button in the **ROI** toolbar to clear the ROI of the current slice (the  button in the **VOI** toolbar will clear the ROIs in all slices!). Then select the drawing tool  and draw along the right striatum holding down the left mouse button.
- After the VOIs have been defined, select the „neutral” mode by the  button. This will avoid creating ROIs when clicking into the images for reviewing the results.
- Now calculate the pixel statistics of the two VOIs using the “statistics” button . The mean and standard deviation of the two VOIs are shown by default in a dialog window. Other statistics values like max, min, volume, etc, are available for selection in the **Selected Statistic(s)** panel. The **Group** entry is the result of the statistics using the pixels contained in the VOIs selected on the **Group** tab. By default, all VOIs are included in the group, but the user may change this definition to group a suitable sub-set of VOIs.
- The statistics operation was applied to the averaged series and thus resulted in individual numbers of the statistical measures. In order to calculate the time-activity curves within the two VOIs they must be projected to the dynamic series, which is still available but currently not shown. When switching to it with the series selection, the VOIs may disappear because each series can have its own set of VOIs, and so far the

dynamic series has no defined VOIs. To disable this synchronization check the box **VOIs from..** while the average series is shown. Now the dynamic images can be selected with the series selection button.

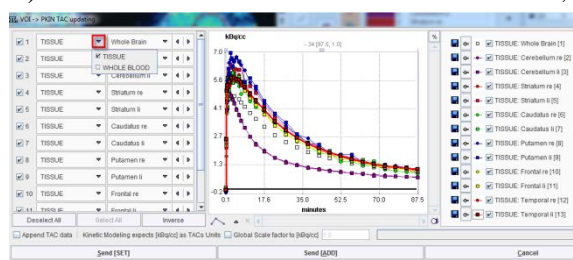


- Activate the statistics  button again. This time the VOIs are evaluated at each time frame and the results are shown as time-activity curves in a dialog box. Note that not only the average can be shown as a TAC, but also the Standard Deviation (SD), the minimum, maximum, etc.
- The TACs can be saved in different formats depending on the future use.
- Once the outlining of VOIs has been completed, the definition can be saved to a “.voi” file using the VOI saving option button. The option button supports saving of all VOIs (**Save**) or only the grouped VOIs (**Save Group**). Note that the VOI definition is relative to the coordinate origin of the current image series, and therefore also applicable if the resolution of the series is changed, for instance by reducing the number of pixels or by interpolation to a different pixel size. However, if the origin changes its position in the data volume the VOIs will be shifted accordingly.



- The VOI definitions can be retrieved by the VOI loading option button. **Load** will first clear the current VOI definitions, while **Append** adds the loaded VOIs to the current list. An example VOI set for the current image series is available in the database. Select the **Load** button. In the appearing DB load dialog box chose the **CPFPX Bolus 13 VOIs** component, then **Retrieve**.
- When TACs are needed for kinetic modeling, it is advised using the general kinetic modeling button **KM**  (the button is grayed for static data) instead of the statistics button. In that case,

the average TACs are prepared and shown in a dialog box. There the user can define what the role of the individual TACs in the subsequent kinetic modeling will be: **TISSUE** (default) or whole blood used for spillover correction (**WHOLE BLOOD**). After the data has been prepared, there are **SEND** buttons to transfer the average TACs to the PKIN tool, either

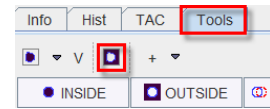


overwriting [SET] its current contents, or adding a new tab to it [ADD].

- Try sending the 13 TACs of the example VOI set. If PKIN is already running the data is loaded, otherwise PKIN will be started and then the data loaded. A warning message will be shown which indicates that kinetic modeling is not yet possible because blood data is missing. Then close PKIN again.

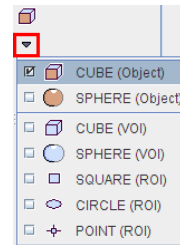
Further VOI Exercises:

- **VOI Masking:** Select the dynamic series, with the example VOIs list active. Select the **Whole Brain** VOI. Then activate the VOI Tools tab which has a **Masking** section. Select the **Mask voxels outside selected VOI** icon. In the dialog window set **Mask by value** to 0, then **Yes**. All pixels which are outside the selected **Whole Brain** VOI are set to the value of 0 at all times. This masked data set could be saved, and used in a pixel-wise data analysis.

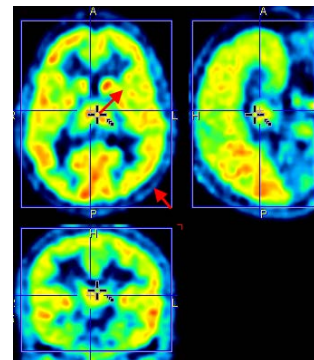


An interactive masking algorithm based on the interactive outlining of a sphere is also available. Its aim is a fast removal of disturbing parts in the image. First, select either inside or outside removal. Locate the center of your anatomic structure. Click and hold the left mouse button until the image area of interest is located within the interactive sphere. Upon the completion of these steps a dialog window appears. Choose an option for masking and enable **Create new study** radio button. Activate **Yes** button to perform removal.

- **VOI Cropping:** The pixels in the masked data set outside the VOI are no longer relevant for the analysis. They can be removed by a cropping operation with the bounding box of the masking VOI. Select the **Whole Brain** again and activate **Crop to VOI Bounding Box** on the VOI Tools tab. Note that the VOIs still fit the structures in the cropped data set because the definitions are relative to the origin which remains at the same anatomical location.

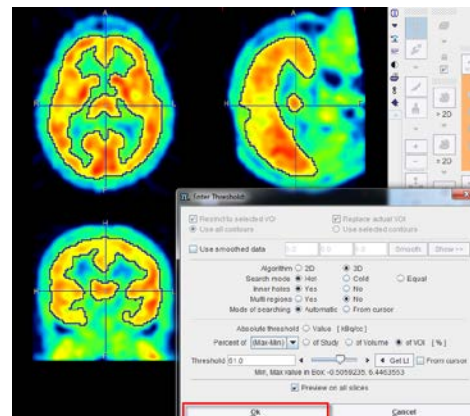


- **Object VOIs:** Standard VOIs are built from planar polygons. This definition is highly flexible because each contour can be individually adjusted. On the other hand, sometimes it is more adequate to change the gross shape of VOIs for roughly encompassing structures. For this purpose, two VOI objects are available with analytically defined boundaries, the **SPHERE** and the **CUBE** object VOIs. Remove the existing VOIs using the “delete all” button ✕ below the VOIs list, then create a new VOI called **Box**. Switch to the averaged series, configure an orthogonal layout, and triangulate the center of the brain. Then select the **CUBE (Object)** from the list of regular objects as illustrated to the right. In the appearing dialog window set the **Size** of the cube to **100mm**, then **Apply**. A box is created and shown in the images, centered at the location you clicked before. This box can be shifted and scaled in all dimensions. To enclose the brain with the box first activate the button to enter the mode for moving/scaling the entire VOI. With the left mouse, shift the box by dragging the handle which has appeared in the center of the box. Move the mouse to any corner of the box and drag, until the brain is entirely enclosed in the box. Similarly, the **SPHERE** object VOI could be applied, which would result in an ellipsoid after scaling.



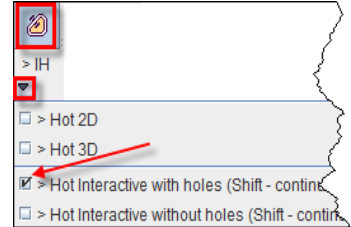
Similarly, the **SPHERE** object VOI could be applied, which would result in an ellipsoid after scaling.

- **Isocontour Auto-VOI:** The “Isocontour Auto-VOI” tool serves for detecting outlines based on a value threshold. It is particularly useful to find organ or lesion boundaries. Let’s find an outline VOI of the brain. The Isocontour Auto-VOI can be confined to a bounding VOI which is replaced by the result. So the first step is to create a copy of the **Box** object VOI: Select the **Box** VOI, activate in the VOI toolbar to copy to the clipboard, create a new VOI and call it **Iso**, then paste using . Select the **Iso** VOI, and then activate the tool. In the appearing dialog window activate the **3D Algorithm**, enable the **HOT Search mode** and the

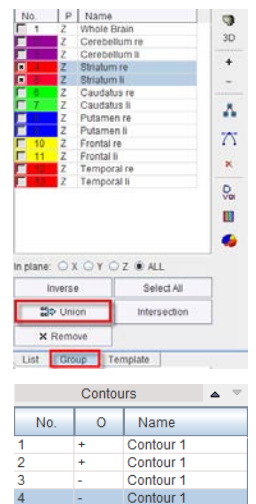



Inner holes radio button. Finally adjust the **Threshold** slider and observe the created isocontour. Check the **Preview on all slices** box, and inspect the contours in different slices using the mouse wheel. Optionally, enable the **Multi regions Yes** radio button for including disconnected parts of the brain. Click **Ok** to accept the result. Often the initial result may not yet be satisfactory because of the image noise level. In this case cancel the operation, smooth the averaged image by using a 6x6x6mm Gaussian filter on the tools tab, and then try the isocontouring with this smoothed data set. This procedure will result in smoother contour outlines.

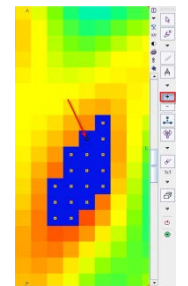
- **Interactive 3D VOI Hot /Cold**: Interactive 3D VOI outlining is based on region growing as long as the mouse button is hold. Create a **New VOI**. Select **Hot interactive with holes** to look for pixels with values above a threshold, allowing inner sparings. Locate the structure in the image you would like to include within the VOI. Click at the edge and hold the mouse button until the outlined VOI completely encompasses the area of interest. After completion of outlining, you can still extend your VOI. There are two options: the first (SHIFT+click+hold) allows continuing the region growing from the original seed, while the second (CTRL+click+hold) allows adding a new seed and continuing region growing from the new point.




- **Merging of VOIs, Exclusion of Pixels**: Sometimes it is useful to combine VOIs to form a new VOI. This can be achieved with the **Union** functionality. Select the **Group** tab, and in the appearing list mark the **Striatum re** and the **Striatum li** VOIs. Then activate **Union** which creates a new VOI called **United**, which can be renamed. Do NOT **Remove the union source VOIs**. Note that the union operation can not only be used to include pixels, but also for more advanced set operations: For example, select the two **Striatum** VOIs and activate the “+” button. Select the two **Caudatus** regions, and then activate the “-“ button to change all its contours on the List panel to “-“. Now select all 4 VOIs and perform the union. (*Note*: it is important to have in the Contour tab as first contours the “+” ones and then the “-“ ones.) The result is a VOI which contains 4 contours per slice, two included and two excluded ones as illustrated to the right. The resulting pixels which will count for the VOI evaluation can be visualized by enabling the **Fill ROI** box. After the union operation make sure to set the **Caudatus** contours back to “+” by selecting the VOIs on the **List** panel and activating the “+” button right to the VOIs list.

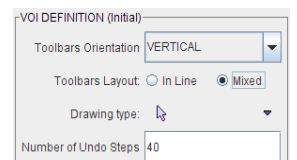


- **VOIs composed of Single Pixels**: When working with small structures it may be preferable to manually define each pixel to be included in the VOI, rather than adjusting contours until these pixels are properly circumscribed. To work precisely switch off the image interpolation,  and zoom the average image by a factor of 4. Remove all VOIs, then create a **New VOI**. Then activate the “+” button in the editing tools and click into the image for adding pixels to the VOI. Make sure that the **Fill ROI** box is checked so that the included pixels are visualized (blue pixels in the image to the right).



- **Removing pixels from VOIs**: The single pixel contour functionality can be used to remove arbitrary pixels from VOIs (except for object VOIs). Outline a contour ROI, then enable **Fill ROI** to see which pixels are included. Select the “-“ button, and then successively click into the area of the ROI. Each time a contour is created with a “-“ sign (exclusion) in the O column, and the selected pixel is not any more among the VOI pixels.

- **Undo/Redo Operations**: Defining VOIs is a time-consuming and iterative procedure. Sometimes unexpected or unwanted effects occur, which destroy all or part of the efforts done so far. To resort from such a situation, the VOI tool maintains a list of historic states of VOI definition. Using the arrow buttons, you can go back in history to undo changes, and then go forward again to redo. The number of undo/redo steps saved can be defined in the settings area of the PBAS tool. Select the “application settings” button  and then the **Display** tab. In the **VOI DEFINITION** area set the **Number of Undo Steps** to a number of your choice.



Section 2: PKIN Tool – Kinetic Modeling



Topics:

- Importing data: TACs from PBAS, blood data from DB files.
- Compartment modeling and graphical plots with tissue time-activity data.
- Reference models for receptor tracers without blood information.
- Assessment of parameter identifiability with Monte Carlo Simulations.

Exercises:

1. Data Import (PBAS, PKIN)

The TACs needed for modeling are calculated using the PBAS tool, and the blood data is added by loading prepared data files in PKIN. (Note: The kinetic modeling data have already been prepared in the database. Instead of the preparation detailed below they can be loaded into new tabs using menu **Kinetic/Add KM File(s)** and then selecting **CPFPX-Bolus-2TC** and **DASB MRTM**, respectively.)

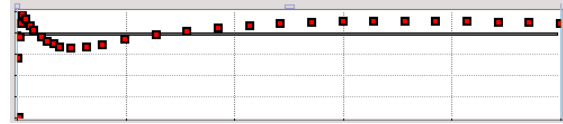
- Start **PBAS (VIEW)**, select **PKIN1** and load all frames of the **Dynamic PET** series.
 - Select the **VOIs** tab. Since there is already a set of VOIs in the database, the VOI drawing step can be skipped. Select the button for VOI loading. In the appearing **DB load** dialog chose the **CPFPX Bolus 13 VOIs** component, then **Retrieve**. A set of 13 VOIs is shown in the overlay.
 - Use the kinetic modeling button  to prepare the TACs, and then **Send[SET]** them to the PKIN tool. **PKIN** is automatically started and the TACs loaded. A notification dialog window appears because no blood data is available yet. It can be closed.
 - Work continues in **PKIN**. To load the blood data open the menu **Kinetic**, item **Load Plasma Activity**, and then the sub-item **Parent**. A dialog box appears showing all blood data in the database. Select **Authentic CPFPX in plasma** of Patient **PKIN1** (plasma activity corrected for metabolites) and **Retrieve**. Confirm the message regarding the missing spillover curve. The loaded plasma data is a simple text file and has the form shown to the right. Such files can be read from disk activating the **Load from File system** button in the above loading dialog.
- | time[seconds] | value[kBq/cc] |
|---------------|---------------|
| 40.2 | 7.61 |
| 60 | 7.75 |
| 120 | 7.46 |
| 180 | 6.32 |
| 240 | 5.02 |
| 300 | 3.55 |
| 360 | 6.54 |
| 420 | 2.78 |
| 480 | 2.26 |
- Similarly load the activity of CPFPX in whole blood using menu **Kinetic/Load Whole Blood** and retrieve **Total CPFPX in blood** of patient **PKIN1**.
 - Now the CPFPX data set is complete and you can save it to the DB or to your local hard disk using menu **Kinetic /Save KM File**. In the **Write as** dialog select **Save to File System** to save outside the **DB** in one of your local directories.
 - Go back to the **PBAS** tool for preparing the second data set similarly. On **DB Load** select patient **PKIN2** and load series **Dynamic DASB PET**. On the **VOIs** tab **Load** the **DASB Regions** component. 11 VOIs are shown. Use the  button to prepare the TACs, and then **Send[ADD]** (*not SET to avoid overwriting*) to the PKIN tool. Note that the data is added as a new page of the **PKIN** tool, which is still open. Since no blood data is available for this study, the data set is already complete.
 - Try to save the data set – it fails with an error message. The reason is that the **1 Tissue Compartment** model was selected per default, and this model requires blood data. So switch the **PKIN Model** of the **thalamus** region to **Ichise NonInvasive MRTM** and set the **Reference** region to **cerebellum**. Then use the button **Model & Par** of the **Copy to All Regions** list selection to propagate the model definition to all regions. Now the data set can be saved without problems.

2. Basic Kinetic Modeling with Blood Data (PKIN)

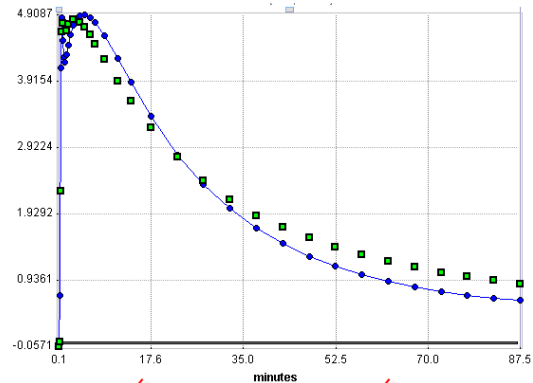
Compartment models of different complexity as well as the Logan graphical plot can be applied to the CPFPX TAC data of PKIN1.

- In **PKIN**, select the tab with the CPFPX data. If the data was prepared as described above all regional TACs will have the **1 Tissue Compartment** model (1TCM) selected, and the default starting parameters. Therefore the blue model curve does not match the green measurement points in the curve area.

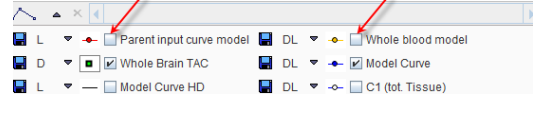
- Select the **Whole Brain Region** and activate **Fit current region**. The optimizer finds the set of model parameters so that the agreement between model and measurement is optimal in a least squares sense. However: note the bias of the residuals which clearly indicates that the 1TCM model is not successful in explaining the CFPFX uptake in Whole Brain (illustration above).



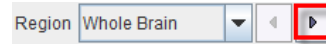
- In the main curve area the agreement cannot be visualized reasonably because the display is scaled relative to the huge initial peak of the blood curves. To focus on the TAC remove the display checks of **Parent input curve model** and **Whole blood model**. The result is illustrated to the right. As alternatives, (1) zoom into a display area using the left mouse button, or (2) select **Range (Zoom)** from the context menu.



- From the mismatch it is clear that model complexity must be increased. Therefore switch the **Model** to **2 Tissue Compartments (2TCM)**. Note that the K_1 and k_2 values are not copied from the 1TCM but set to the model defaults because **Model Conversion** on the **Extras** tab is not enabled. Use **Fit current region** to adjust the K_1 to k_4 parameters of the model. The result shows that the systematic bias in the residuals is almost removed for late data points with a small mismatch remaining at early samples.



- To apply this 2TCM model configuration to all other 12 regional TACs use the button **Model & Par** of the **Copy to All Regions** list selection. It propagates the model definition with the current parameter values to all regions. Then apply **Fit all regions** to adjust the regional parameters.
- The results can be screened by stepping through the regions using the “arrow” button indicated to the right. The agreement between the measurements and the model curve should be ok in all regions.



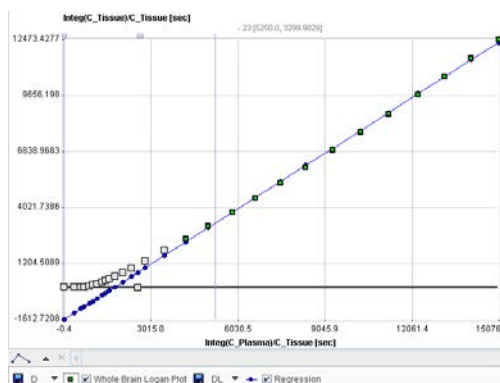
- To get a quick overview of the resulting parameter values a parameter summary can be obtained as follows: in the **Tools** list to the lower right select the entry **View Par**. A dialog box shows all direct model parameters as well as the macro parameters. Note that the smallest and the highest values of each parameter are highlighted in green and red respectively. Note how K_1 is similar in all regions. This summary can be saved using **Copy to Clipboard** and pasting the values into a program such as Excel.

Region	vB	K1	k2	k3	k4	Vs	Vt
Whole Brain	0.05	0.067...	0.125...	0.026...	0.050...	0.288...	0.828...
Cerebellum re	0.05	0.080...	0.227...	0.018...	0.040...	0.167...	0.522...
Cerebellum li	0.05	0.079...	0.225...	0.018...	0.042...	0.156...	0.508...
Striatum re	0.05	0.075...	0.084...	0.003...	0.026...	0.125...	1.012...
Striatum li	0.05	0.082...	0.094...	0.009...	0.040...	0.204...	1.075...
Caudatus re	0.05	0.067...	0.081...	0.003...	0.023...	0.106...	0.937...
Caudatus li	0.05	0.075...	0.090...	0.008...	0.033...	0.211...	1.041...
Putamen re	0.05	0.085...	0.087...	0.003...	0.022...	0.152...	1.125...
Putamen li	0.05	0.087...	0.092...	0.0068...	0.039...	0.165...	1.114...
Frontal re	0.05	0.077...	0.107...	0.015...	0.046...	0.242...	0.964...
Frontal li	0.05	0.078...	0.113...	0.020...	0.054...	0.261...	0.951...
Temporal re	0.05	0.077...	0.109...	0.027...	0.065...	0.300...	1.003...
Temporal li	0.05	0.078...	0.109...	0.024...	0.061...	0.289...	1.009...

Statistics	vB	K1	k2	k3	k4	Vs	Vt
average	0.05	0.077...	0.119...	0.014...	0.041...	0.205...	0.930...
median	0.05	0.078...	0.107...	0.015...	0.040...	0.204...	1.003...
stdv	0.0	0.005...	0.047...	0.008...	0.013...	0.063...	0.192...

- An alternative for saving the parameters is the menu selection **Kinetic/Save KM Parameters File**. Once a model configuration seems meaningful, it is advised to save the full information including data and models using **Kinetic/Save KM File**.
- An important and stable parameter which has been shown to be related to receptor density with CFPFX is the total distribution volume (V_t). This value is a model macro parameter and is also shown in the summary above.
- Because the tracer is reversible ($k_4 > 0$), the Logan plot can be applied for estimating V_t . Switch the **Model** of the **Whole Brain** region to **Logan Plot**. The data is transformed and a linear regression fitted, because theory predicts that after an equilibration time the plot should become linear. To see an explanation of the transformation please use the **?** button. From the equation it becomes clear why the time scale shown is not any more real acquisition time.

- The Logan plot requires an appropriate definition of the time, from when on the transformed samples show a linear behavior. The user can decide intuitively the value (eg. 25). Then they have to enter it into the t^* parameter field. As soon as the value is entered, it is adjusted to match the closest acquisition, the regression is re-calculated and the points before the start are set to gray color (not considered in fit). As an alternative, a criterion **Max Err.** (eg. 10%) can be specified, and **Fit current region** invoked to find the time point from which on all curve points deviate less than the specified percentage from the line. The smaller the criterion, the later the start time found.



- To get V_t by the Logan method fix t^* identified above by removing the check of its fit box, use **Copy Model & Par** to propagate to all regions as before, and **Fit all regions**. Again, display a summary and compare the V_t values with the ones calculated with the 2TCM. The Logan V_t values tend to be higher. This is due to the fact that a 5% blood volume was subtracted in the 2TCM, whereas it is included in the Logan method.
- An essential question to answer for a novel tracer is, which model complexity is needed to describe the kinetic behavior of the tracer. PKIN provides statistical parameters that can be used: the **Schwartz Criterion (SC)**, the **Akaike Information Criterion** and the **Model Selection Criterion (SC, AIC: smaller=better model; MSC: bigger=better model)**. These and other statistical criteria are available on the **Details** tab, and they are also saved with the fit results. Verify with the CPFPX data whether the criteria confirm that a 1-tissue compartment model is not sufficient.

Region	Vt
Whole Brain	0.925...
Cerebellum re	0.637...
Cerebellum li	0.624...
Striatum re	1.065...
Striatum li	1.138...
Caudatus re	0.995...
Caudatus li	1.100...
Putamen re	1.159...
Putamen li	1.169...
Frontal re	1.043...
Frontal li	1.035...
Temporal re	1.089...
Temporal li	1.095...

Statistics	Vt
average	1.006...
median	1.065...
stdv	0.172...

3. Kinetic Modeling with Reference Models

The DASB TAC data of PKIN2 must be analyzed with reference methods, because no blood data is available. Cerebellum is a suitable reference tissue for the DASB tracer.

- In **PKIN**, select the tab with the DASB data. Use the **caudate** region to start with.
- There is a series of different reference models available which all calculate a measure of the binding potential relative to non-displaceable uptake BP_{nd} ($= k_3/k_4$). To see a short model description use **?** to the right of the selected model.
- Note that some of the models require the *prior information of k_2'* , the clearance rate of the reference tissue (**MRTM2, Simplified Reference Tissue Model 2**). These models are aimed at pixel-wise applications where k_2' is common because the same reference is used for all pixels. Such a k_2' can be calculated using the **MRTM** or the **Simplified Reference Tissue Model** models.

- Select the **Ichise NonInvasive MRTM** model, and **cerebellum** in the **Reference** list.

- Note the parameter t^* which describes the equilibration time. Only measurements after this time are considered in the fit. t^* can be fitted according to a **Max Err** criterion. Set **Max Err** to 10% and **Fit current region**. The start time found is 3.5 min. Note the BP_{nd} result in the derived parameters area which has a value of 1.437. To quickly assess the impact of the start time on BP_{nd} select the **Increment** tab. Use the slider or the increment button to steadily increase t^* and observe BP_{nd} which is continually updated. It remains quite stable until about 60 minutes.
- Fit current region** again to switch back to the **Standard** tab and set t^* again to 3.5 min. Remove the fit check of t^* , copy **Model &**

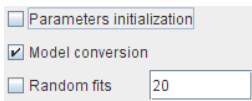


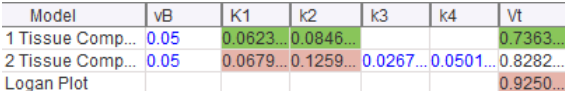
Region	BPnd	BPnd
amygdalae	1.137466	1.134547
basal forebrain	0.968615	0.97164
brainstem	1.017451	1.019726
caudate	1.437198	1.43946
cerebellum	7.072072E-7	1.43946
frontal cortex	0.229283	0.228454
parietal cortex	0.122712	0.124568
putamen	1.656537	1.659632
temporal cortex	0.298599	0.298603
thalamus	2.040828	2.044461
visual cortex	0.390315	0.391275

Par to all regions, and **Fit all regions**. All fits are done with the same starting time and the results can be summarized with **View Par** (left column in illustration above).

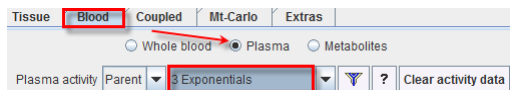
- As an alternative, switch to the **Simplified Reference Tissue Model, Fit current region** (to get reasonable fit starting values for the other regions), copy **Model & Par** to all regions, and **Fit all regions**. The fit fails in cerebellum, which is the reference and thus not relevant. Display the results summary with **View Par** (right column in illustration). The results of both methods are very comparable.
- On the **Extras** pane, enable the **Model Conversion** flag. Note the value of k_2' in the derived parameters section, then switch the model of **caudate** to the **MRTM2** (or **SRTM2**) method. After model switching, k_2' has the value which was determined with **SRTM** (or **MRTM**).
- Recommended procedure for obtaining an average k_2' which can be applied for pixel-wise fitting: Apply **SRTM** or **MRTM** to several regional TACs with high BP_{ND} and average the obtained k_2' values. The averaging should be within the subject and not across a population.

4. Fitting Options in Kinetic Modeling

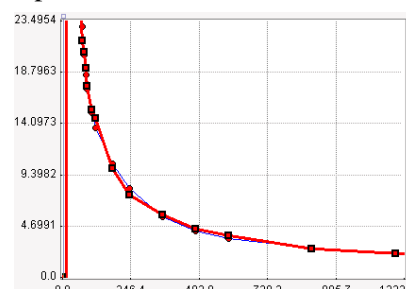
Iterative model fitting is crucially dependent on a set of reasonable initial parameter values. If they are too far from the optimal solution, there is a higher danger of getting stuck in a local minimum.

- One strategy for arriving at suitable initial compartment model parameters is to start with a simple model, and use its result for the more complex model. This can be achieved by enabling **Model Conversion** on the **Extras** pane. Once suitable parameters for the complex model have been found, the function should be disabled again. 
- Another strategy for compartment models is to derive initial parameters by applying a linear least solution. These solutions are known to be susceptible for biased parameter estimates, but most likely they are sufficiently close to serve as initial parameter values. This behavior can be enabled with the **Parameters initialization** flag. Note that with the flag enabled manually entered parameters will not be relevant any more for the fitting outcome.
- A strategy for avoiding local minima is to explore the parameter space from random sets of initial parameters, and to consider the solution with minimal Chi square as the result parameter set. This strategy can be enabled with the **Random fits** flag which applies to all iterative fitting, not just the compartment models. The number of trials per fit can be specified in the number field.
- A **history** functionality is available which records the fitted models. The users can also manually add configurations of interest. Using the arrows they can go through the history, and they can inspect it as a list. Reset the history with . Configure the **2TC** model, then **Fit**, the **1TC** model then **Fit**, **Logan** then **Fit**. Open the history list with . Note that the parameter values are sorted into common columns, so that eg. V_t can be easily compared across models. 

5. Modeling of Blood Data in Kinetic Modeling

The calculation of the model functions requires the interpolation of the blood activity curves. This interpolation is governed by the selected blood model. If no action is performed after loading the blood activity data, simple linear interpolation is applied (“Measured” model). Other behaviors can be configured on the **Blood** pane. 

- Select the tab with the CFPFX data, then the **Blood** tab. For the **Plasma** data set the model from **Measured** to **3 Exponentials**. Keep the default settings. An initial set of parameters is shown with linear interpolation for the first 30 seconds and then interpolation by 3 exponentials. Activate **Fit plasma** to fit the exponential part to the plasma measurements. There is some discrepancy at early times because of the very steep peak.
- Set the **Begin** time to **200** sec and **Fit plasma activity** again –




there is now a good agreement between the Plasma measurement and the **Plasma model** curve at all times.

- If the plasma activity data has not yet been corrected for metabolites, this can be done using the **Metabolites** correction in PKIN. To see an example load **1TCM with Metabolites** from the database and enable the **Metabolites** radio button on the **Blood** tab.

6. Assessing Parameter Identifiability

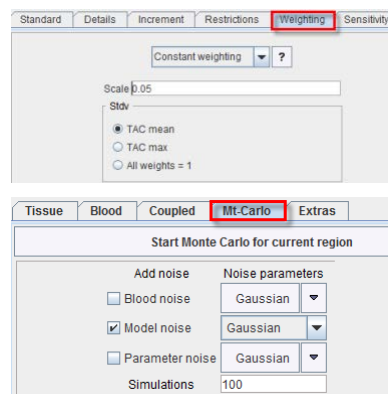
Any fitting procedure will result in parameter values. However, the reliability of these estimates must always be questioned. It is possible that parameters are correlated, so that a change of one parameter can be compensated by the change of a second parameter (correlated parameter). In that case it is not possible to get independent estimates.

- In **PKIN**, select the tab with the CPF PX data. Make sure that the 2TCM model has been selected and fitted in all regions. Note that if the Marquardt fitting method was used, the **%SE** is shown for each fitted parameter. **%SE** is the estimate of the standard error (expressed in percent of the parameter value). It is calculated as the square root of the diagonal elements in the covariance matrix. The macro parameters also show a **%SE** indication which is derived from the standard error of the fitted parameters which are involved in the macro parameter calculation.
- Use the arrow  to step through the regions and look at the **%SE** values. It is obvious that K_1 is the most robust parameter, followed by k_2 . k_3 and k_4 generally show high **%SE** with the maximum in the **Caudatus re** region.
- Subsequently, we perform a **Monte Carlo (MC)** simulation to get a more “experimental” measure of the distribution of the parameter values. The principle of the MC procedure is the following: (1) it assumes the current model represents the truth; (2) then adds realistic noise to the model; (3) fits the model to the noisy curve. MC performs (2) and (3) many times (eg. 1000) and calculates the mean and standard deviation of the (e.g. 1000) parameter results.

- The noise distribution is essential for the simulation. The **Weighting** tab allows defining how the standard deviation in each time point is calculated. The default shown is to use 5% of

the TAC average as the standard deviation of a Gaussian distribution at all times (Constant weighting). There are other settings which add more or less noise depending on the signal value (Calculated weighting).

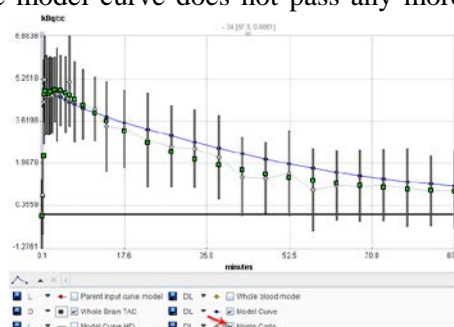
- Switch to the **Mt-Carlo** tab and set the **Model noise** to **Gaussian**. Set the number of **Simulations** to a value of 100 (1000 takes quite long), then activate **Start Monte Carlo for current region**.



The 100 noisy curves are calculated and fitted in the background, while PKIN is locked. After completion, the **Tissue** tab is shown. Now, the parameter values represent the average of the 100 results, and the **%SE** their standard deviation. The **%SE** found are substantially smaller than the **%SE** from the covariance matrix, but the relation between the **%SE** values of K_1 , k_2 , k_3 and k_4 is similar as before.

- Repeat the Monte Carlo simulation with more noise. Set the noise scale factor of the Gaussian distribution to 20% in the **Weighting** tab. Then start the Monte Carlo simulation. The **%SE** of all parameters has clearly been increased. Most probably, the model curve does not pass any more through the measurement points. The reason is that the average parameter results are used for the model calculation, and they can be significantly distorted due to outliers, particularly of k_3 and k_4 .

- To visualize the noisy data used in the Monte Carlo run switch back to the **Mt-Carlo** tab. In the curve display, a new curve **Monte Carlo** appears with vertical bars. The end points of these bars mark the minimal and the maximal value that any of the noisy curves reached at a particular time point.



- Save the parameter values to record the Monte Carlo results.

Section 3: PXMOD Tool – Pixel-Wise Modeling

Topics:

- Step-wise data processing.
- Examples with blood-based and reference models.
- Results exploration.

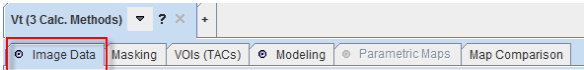


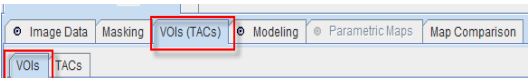
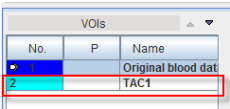
PXMOD Exercises:


1. Step-by-Step Parametric Map Calculation (PXMOD)

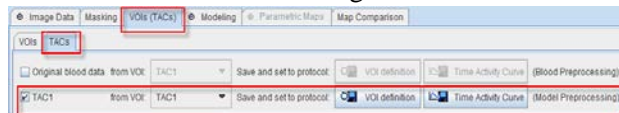
The PXMOD tool implements a step-wise processing strategy: (1) The model is selected so that the program can load the requirements. (2) The image data are defined and loaded. (3) Optionally, a mask can be created to eliminate the background from modeling. (4) Depending on the model, tissue TACs need to be defined. (5) The blood curves are specified, loaded and corrected for some distortions, if necessary. (6) Some model preprocessing is performed for gathering information needed in the pixel-wise calculations. Typically, the regional TACs from (4) are involved. (7) The selected model is applied to the pixel-wise TACs for calculating the parametric maps.

In the program interface, each step is represented by a dedicated panel. During a processing session, the user works from left to right through the panels. Each panel has a red button in the lower right corner to proceed to the next panel. Note that all information created during a processing session, such as masks or VOIs, need to be saved. This has the effect that at the end of a processing session a complete configuration can be saved which allows exactly repeating the analysis.

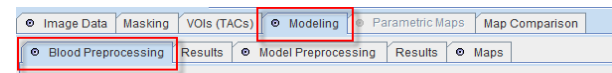
In the following, the step-by-step data analysis procedure will be described.



- Start **PXMOD** to calculate the total distribution volume V_t of the example CFPX bolus study. First, select the **Vt (3 Calc. Methods)** model from menu **Pixel wise/Model** or directly in the model list of the workspace tab. By this model selection the configuration requirements are adjusted accordingly. 
- Define the image data using the **Input Data Settings** button in the **Image Data** tab of the workspace. In the new dialog window make sure the **Input 1** format is **Database**, then use the  button to display the database series selection box. Select the series **Dynamic PET** of patient **PKIN1** and quit the dialog window with **Set series**. Make sure no processing is applied to the data at loading time by activating the **Reset loading parameters** button. Select **OK**. Finally, use the red button to **Load** the image.
- As an optional step generate a mask to restrict modeling only to the brain area and ignore the background. Activate the red **Masking** button in the lower right of the **Image Data** panel to proceed. The program automatically switches to the **Masking** tab. Average 20 frames by entering **10** and **30** into the **From** and **To** fields, and activating **Aver**. With the **Averaged** tab selected, choose the **THRESHOLD** procedure in the **Segmentation** list and set the threshold to **1.0**. Set the color scale for the **Averaged** image to **Gray**. Check the **Ovr** box, so that all pixels fulfilling the criterion are highlighted in red. Activate **Segmentation** to actually create the binary segment image which is shown in the **Current** panel. Configure the **Set to protocol** button to the **Database** format and activate it. In the appearing dialog window use **Edit info** to change the **Series Description** to **Mask thr 1.0**. Close with **OK** then **Save**. The saved mask is automatically used for the **Mask by File** configuration. 
- Proceed with the red **TACs** button to specify TACs for the model preprocessing. The program automatically switches to the **VOIs (TACs)** –  

VOIs tab. In the VOIs list two empty VOI definitions are shown which originate from the model: **Original blood data** and **TAC1**. Select the **TAC1** VOI, navigate to slice 17, select the  button and click into the axial slice in order to generate an iso-contour VOI (e.g. temporal cortex).

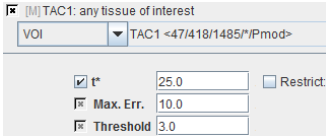





- Proceed with the red **Prepare TACs** button to the **TACs** tab. Since no image-derived input curve is needed, make sure that the **Original blood data** box is not checked. In contrast, enable the **TAC1** box to show the curves from the **TAC1** VOI definition in the curve area. At this point the TAC information must be saved for later use in model preprocessing. There are two possibilities: **Save and set to protocol** saves the **VOI definition** itself (recommended), whereas **Time Activity Curve** saves the TAC resulting from the VOI definition. Activate the **VOI definition** button and save the VOI with **Enter name** set to **TAC1**.

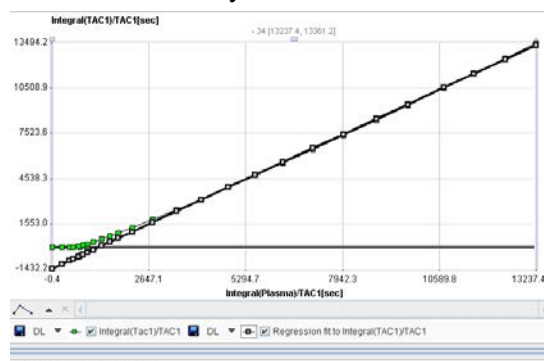


- Select the red **Prepare Model** button to proceed. The program switches to the **Modeling** page, starting with the **Blood Preprocessing** panel. Set the format selection of **Blood data** to **TAC(DB)** to read the prepared blood data from the database. Activate the  button to open the DB selection and reset the filter fields with . The blood curves from all the patients and studies are now listed. Select **Authentic CFPFX in plasma** of **PKIN1** which will serve as the input curve, then **Set selected**. The blood data is already decay corrected, so do not use the available correction.

- The blood pre-processing step is started with the red **Preprocess Blood** button. The blood data is loaded and displayed in the **Results** panel right to **Blood Preprocessing**. For this particular model, no other action is performed during blood preprocessing.

- Proceed to model preprocessing with the red **Set Model Preprocessing Parameters** button. The program switches to the **Model Preprocessing** tab, where the user has to tailor the model calculation. Note that the **TAC1** VOI prepared above is already configured. The section below the **TAC1** specification contains the parameters configuration:  parameters are for input purposes only,  parameters are fitted, and  are parameters which could be fitted but are fixed at the entered value. For the selected model t^* of the Logan plot (start time of the linear section) has to be defined. The Logan plot is therefore applied to the specified tissue TAC. In the example above  next to t^* has the effect that t^* is fitted using the error criterion of **10% Max Err. Threshold** values >0 are useful for background masking in cases where no mask was created and set to the protocol; **3-5%** usually work well. Note that the parameters can be set to recommended default values by the **Set Defaults** button



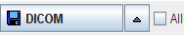





- Start preprocessing with the red **Preprocess Model** button. In the **Results** tab to the right the Logan graphical plot is displayed for visual inspection, and the numerical outcome is available in the **Info** area. The visual inspection should confirm that the regression line is an adequate fit to the late part of the curve.



- Proceed with the **Set Map Parameters** button. Use the checks to specify the parameters for which maps should be generated. In the example below the V_t maps are calculated using two methods: the standard Logan plot (**Vt_logan**), the Logan plot with linear regression based on orthogonal distances (**Vt_perpend**), while the Ichise's MA1 method (**Vt_ma1**) is not active. The **A1** map also belongs to the MA1 method and essentially represents a perfusion map usable for anatomical correlations. Because the analyses with the noisy TACs sometimes result in outliers dominating the image dynamics, the result ranges of the V_t parameters are **Restricted** between a lower value of **0** and an upper value of **20**.

Result of regional Logan Plot:
 t^* = 25.0 [min]
 DV = 1.11751147139668309
 Intercept = -1431.7632713633237

<input checked="" type="checkbox"/> Vt_logan	<input checked="" type="checkbox"/> Restrict: Lower	0.0	Upper	20.0	[ml/ccm]
<input checked="" type="checkbox"/> Vt_perpend	<input checked="" type="checkbox"/> Restrict: Lower	0.0	Upper	20.0	[ml/ccm]
<input type="checkbox"/> Vt_ma1	<input checked="" type="checkbox"/> Restrict: Lower	0.0	Upper	20.0	[ml/ccm]
<input checked="" type="checkbox"/> A1	<input checked="" type="checkbox"/> Restrict: Lower	0.0	Upper	1.0	[ml/ccm/min]
<input type="checkbox"/> Intercept	<input type="checkbox"/> Restrict: Lower	0.0	Upper	0.0	[norm. act]
<input type="checkbox"/> -A2	<input checked="" type="checkbox"/> Restrict: Lower	0.0	Upper	1.0	[1/min]

- At this time the last configuration step has been completed and pixel-wise calculation can be started with the **Pixelwise Calculation** button. The resulting maps are shown on the **Parametric Maps** page.
- When the box in the lateral toolbar is checked, only the parametric maps of the currently shown slice in the **Image Data** tab are calculated. This feature is intended for the prototyping phase of models which take substantial calculation time. 
- The maps can be saved using the  button from the lateral toolbar or using the **Save Maps** button. In the example to the right the format has been configured to **DICOM**. If the **All** box is checked, the maps of all parameters will be saved, otherwise only the current one. To be able to distinguish between the maps, PMOD adds the parameter name to the series description (or the file name for non-DICOM data formats). 
- It is generally recommended to not only save the result images, but also the full processing configuration. This is done with the  button in the **Taskbar** (or from menu **Pixel wise / Save Model Settings**). By loading such a setting later on, all the processing details can be reviewed, edited if necessary, and the processing repeated. Save the configuration of your processing to the database or a directory on your local disk, load it again with , and try running it with the  button.
- Once all the information pieces are available, there is an alternative to the step-wise processing: With the  button a dialog window can be opened which contains the panels of all processing steps, so that the definitions can be changed very quickly. This feature is particularly useful in combination with loading a configuration file and adjusting it for further usage.
- Note that the  button always performs a full processing of all steps, including data loading.

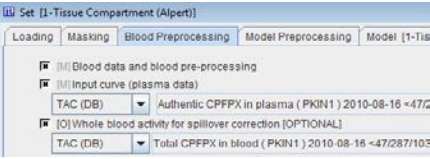


2. Examples with Different Models

This section illustrates the use of various models with different data sets.

1-Tissue Compartment Models:

The CFPFX data of PKIN1 can be fitted with a 1-tissue compartment model. Corresponding settings for testing the different models are available in the database for retrieval.

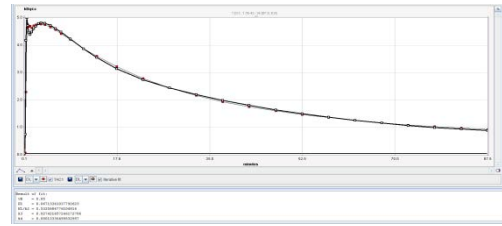
Different Vt Methods	PKIN1
Logan Plot	PKIN1
1-Tissue Ridge Regression	PKIN1
1-Tissue Alpert	PKIN1
2-Tissue, Ridge Regression	PKIN1
2-Tissue, 3 Parameters variable	PKIN1
2-Tissue, 4 Parameters variable	PKIN1

- Select from the **Model list 1-Tissue Compartment (Alpert)**. Define the **Dynamic PET** of PKIN1 as **Loading** data. Go to the **Blood Preprocessing** tab, and in addition to the input curve define also the whole blood activity concentration for spillover correction as illustrated to the right. 
- In **Model Preprocessing**, the blood volume fraction is 5% (0.05) per default, and the lookup table configurations should normally work. Enable the generation of **K1**, **k2** and **Vt** parametric maps in the **Maps** panel, then run the analysis with the  button. Inspect the parametric maps of the 1-tissue compartment model.
- To compare with an alternative model create a new page with menu **Pixel wise/New Workspace** or using the workspace tab with the + button. All configurations are copied from the current workspace to the new one. Switch the model to **1-Tissue Compartment (Zhou GRRSC)**. This is a model with inherent spatial constraints, so that the result will look smoothed. The **Loading** data and the **Blood Preprocessing** configurations are already correct, because they are inherited from the prior model. In the **Model Preprocessing** panel, set the **Filter planar** to **3** pixels because the data set has large pixels, and leave the other parameters as-is. Then activate  and inspect the resulting parametric maps. Compare the values of the two methods by setting the upper thresholds to common values and switching back and forth between the two workspaces.

2-Tissue Compartment Models:

- Create a **New Workspace**. Select from the **Model list 2-Tissue Compartments, K1/k2**. This is a model with K_1/k_2 as a fit parameter instead of k_2 . The K_1/k_2 approach is helpful because often it is reasonable to fix K_1/k_2 (non-displaceable compartment) at a common value for all pixels. Hereby the number of fitted parameters is reduced, making the fit more stable (and faster).

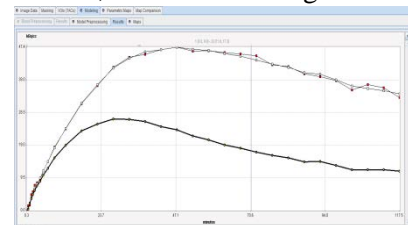
- The **Loading** and the **Blood Preprocessing** configurations are already correct from the 1-Tissue compartment model. In Model **Preprocessing** a tissue TAC is required. Proceed by specifying the **VOI** format and selecting **CPFPX Bolus Whole Brain** from the database. In **Maps** leave the configuration as is. Then make sure that you first only fit the current slice by checking the box from the lateral toolbar.
- Run the processing, which may take several minutes. After fitting, inspect the model preprocessing fitting result of the 2TC model to the whole brain TAC by checking the curves and the parameter values in the **Modeling Results** panel. Inspect the parametric maps. Compare the V_t map with the corresponding maps of the 1TC methods by switching between the different workspaces.
- Now investigate the effect of fixing K_1/k_2 . To this end create a **New Workspace**. There, remove the fit flag of **K1/k2** both in **Model Preprocessing** and **Maps** panels. Then, run the processing again and with the same slice as before, but now with only 3 parameters. Fitting is faster, and the result contains less outliers.
- There is another model for fitting a 2-tissue compartment model: **2-Tissue K_1/k_2 , RR**. It implements a ridge-regression approach, i.e. it imposes spatial constraints on the smoothness of the parameters. After creating a new workspace, load the model setting **2-Tissue, Ridge Regression**, and run the processing. Please check the PXMOD User's Guide to understand the different processing steps and the outcome of this rather complex model.



Reference Tissue Models:

The DASB data of PKIN2 can be fitted with multiple reference models. Corresponding settings for testing the models are available in the database for retrieval.

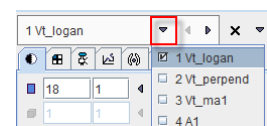
- Create a **New Workspace**. Select from the **Model** list the simplified reference tissue model **BPnd (STRM Ref)**. Activate the configuration button . The **Blood Preprocessing** is not available anymore because no blood data is required. In the **Loading** tab select the **Dynamic DASB PET** of patient **PKIN2**.
- In the **Model Preprocessing** tab define the two TACs needed as illustrated to the right. The **DASB Striatum VOI** represents receptor-rich tissue which is used to test whether the fitting works properly. The **DASB cerebellum VOI** represents the signal from reference tissue without specific binding. The parameters in the lower part are needed for the basis function method which locates the solution in a certain range of the apparent k_2 (k_2a). The default setting should work for the DASB data. In **Maps** check all parameters. This will not have an impact on speed and allows inspecting also secondary information.
- Enable the lateral box from the toolbar to process only one slice, close the configuration window and then run the processing with .
- The **Modeling Results** tab should indicate a good curve fit as illustrated to the right, and the parametric maps show reasonable results. It is important to check that the k_2a values are not truncated by the prescribed range in the relevant parts of the image. This is not the case; the maximal value is only obtained for peripheral pixels.
- Please use the prepared settings in the example database for experimenting with the other reference tissue models (particularly with the **BPnd (Different Methods)** that allows the estimation of the BPnd with SRTM, SRTM2, MRTM0, MRTM, MRTM2, and Logan).





3. Results Exploration (PXMOD, PKIN)



There are several facilities to investigate the PXMOD results.

- To get a data set with multiple parametric maps retrieve the **Different V_t Methods** configuration setting and perform the analysis. The parametric maps are available in the **Parametric Maps** panel in a stacked mode so that only one map is visible. They may be switched using the arrows as illustrated above.

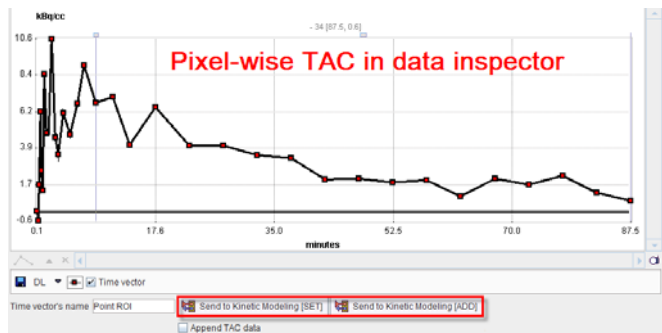


- To probe all calculated parameters of a pixel open the “data inspector” of the maps via the  button in the upper right image corner. Use the  button to extend the information shown. When clicking into a map, the parameter values of the selected pixel are updated in the inspector panel. The example to the right illustrates the known fact that the standard Logan plot tends to underestimate V_t in the presence of noise.

PARAMETER...	
Vt_logan	0.960779
Vt_perpend	0.961743
Vt_ma1	1.005368
A1	0.064363

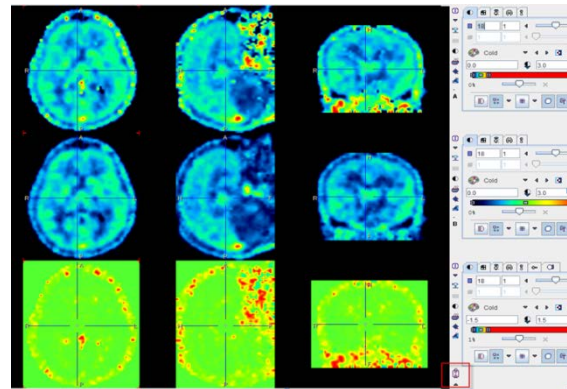
- Select the **Map Comparison** tab to see the image fusion panel. In the first line select the dynamic input image, in the second the Vt_Logan parametric image. Now open the data inspector  for both images, and extend with  for the dynamic image. In the extended area the **pixel-wise TAC** of the current pixel is seen. Navigate through the parametric map and localize points of interest. As soon as you click at them, the TAC and the parameter values are updated in the two inspectors.

- The pixel-wise models are usually simplified and cannot be interactively examined. Therefore, to allow a full analysis, the pixel-wise TACs can be sent to the **PKIN** tool with the **Send to Kinetic Modeling** buttons. If blood data has been loaded by the model, it is also transferred. **SET** replaces the data of the current PKIN tab, while **ADD** creates a new PKIN tab to put the data into. With **SET** and the **Append TAC data** box checked, the TAC is added as a new **Region** to the current PKIN tab. This allows including data from multiple pixels into one PKIN data set.






- As an example, click at a point in the parametric map with both inspectors open. Transfer the TAC of the particular pixel with **Send to Kinetic Modeling** to PKIN. In PKIN, switch the model to **1 Tissue Compartment** model, and **Fit current region**. Now compare the value of V_t shown with the different V_t values in the inspector. It is probably similar but not the same. Now remember that V_t calculated with the Logan plot includes also the blood space. To have the same situation with the 1TCM, set the blood volume **vB** from 0.05 to 0.0 and fit again. You can try the same with the **2 Tissue Compartment** model, but the signal is probably too noisy for 4 fitted parameters. You can also try with the **Logan plot**. Close the inspectors and continue in PXMOD.

- The parametric maps themselves are best compared using the **Map Comparison** panel. Arrange Vt_MA1 in the first row and Vt_Logan in the second row. Set the same lower and upper thresholds to allow for a visual comparison (e.g. 3). Switch to the algebra mode and perform a subtraction of the two maps. The result is shown in the third line as illustrated to the right. From this result it is clear that the MA1 method tends to higher V_t values, and that this effect is depending on the tissue.



Further PXMOD Examples with Prepared Model Settings:

- The **Pmod** database contains the PXMOD configuration settings of several different types of analyses. To try them out we propose the following procedure: (1) Create a new empty workspace. (2) Use  to retrieve a configuration setting. To see all protocols in the DB, activate the  button in the **Read from DB** box. (3) . In this way you will get results on different tabbed pages.
- PKIN3**, setting **FDG Patlak**: Calculates MRGlu maps from dynamic FDG data using the Patlak plot.
- PKIN4**, setting **H2O Perfusion (Alpert)**: Calculates the rCBF perfusion maps from a dynamic $H_2^{15}O$ PET scan with arterial sampling using the Alpert time-weighted integral method.

Section 4: PFUS Tool – Image Registration & Fusion





Topics:

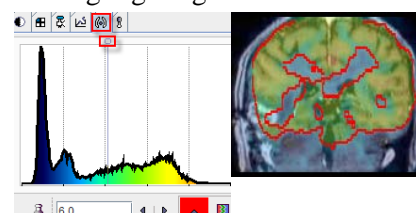
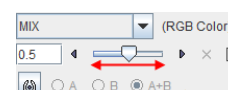
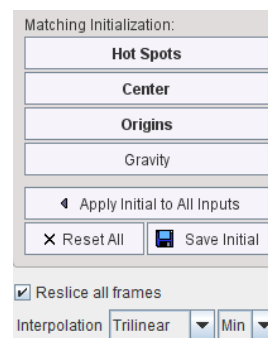
- Interactive and automatic registration of multi-modal brain images.
- Stereotactic normalization of brain PET data and subsequent application of standard VOIs.
- Results saving and documentation.
- Pixel-wise image algebra and scatter plots.



PFUS Exercises:

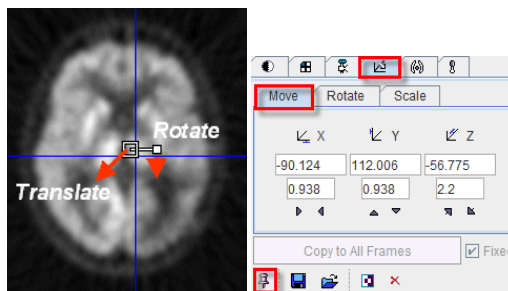
1. Manual Registration of Brain Images



The PFUS tool uses a “Reference” series as the basis for the interpolation of all data sets. Therefore, the best resolved images should in general be used as the Reference.

- Start the **Fusion** tool and switch to the **Initialize/Match** page. Make sure the **Load** buttons are set to the **Database** format. Using **Load Reference**, load the **MRI** series of patient **PFUS1**. Set the layout to the orthogonal planes view and adjust the colors so that the image appears brighter.
- With **Load Input** in the upper right, load the **FDG** PET series. Immediately, the images are interpolated to the resolution of the **Reference**, whereby the program tries to align the two studies. If there are common DICOM landmarks available (**Origins**), they are used, otherwise the center of the two data volumes are aligned. The result of this initial reslicing is shown in the **CoRegistered** area in the lower left fused with the Reference image. Click at different points in the images and note that they are synchronized with the upper reference images (as long as **Synchronization** is checked).
- A reasonable initial alignment should be achieved before continuing, because it will make the manual and the automatic matching easier. The following options are available for improving:
 - Activate the **Origins** button to enforce the alignment of the coordinate origins in the two data sets.
 - Activate the **Center** button to align the center of the two data volumes, which is independent of the pixel slices or slice number.
 - Locate interactively the same anatomical location in the two studies with the triangulation point in the orthogonal views. Then activate the **Hot Spots** button to align the images at this anatomical location.
 - Shift and rotate the Reslice image using the reslice controls  as described below.
 - The fusion image in the lower left can be adjusted using the fusion control button  which allows blending adjustments. Select the FDG series, and shift the blending slider left/right. It is apparent that the FDG series is slightly truncated in sagittal view at the top and tilted relative to the MRI.
- For the precise interactive matching, go to the **Adjust/Compare** page using the tab or  in the toolbar to the right. The first row shows the MRI, the second row the FDG, and the third row their fusion. Make sure that the image layout is set to the orthogonal planes view. Note the synchronized reslicing when you click at points in the image.
- As a first check to inspect the alignment use the “coupled cursor”. Move the cursor cross to distinctive points in one series and observe the position in the other series. Trace the brain contours and try to see the mismatch.
- As an aid for the manual registration, enable the “isocontours” for highlighting the brain contour. It is best defined on the relatively smooth FDG images. As illustrated to the right, define a contour level of **6 kBq/cc** by the marker or by entering the numeric value. Set the color of the contour to red. To see the contours in the fusion display set the radio button to **B** in the control area of the fusion controls.  A B A+B




To start interactive matching, select the “reslicing” tab of the images in the second row (or **Ctrl+R**). Reslicing handles are now shown in the image and allow translating (open rectangle) or rotating (closed rectangle) the images. The handles are hidden when switching to a different tab. To see them permanently, set the  on the tab to the “fixed” mode . As an alternative for interactive dragging, enter discrete numbers for the transformation parameters in the corresponding number fields on the reslicing tab.

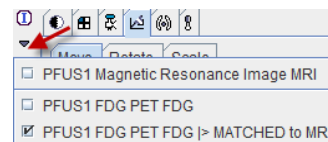
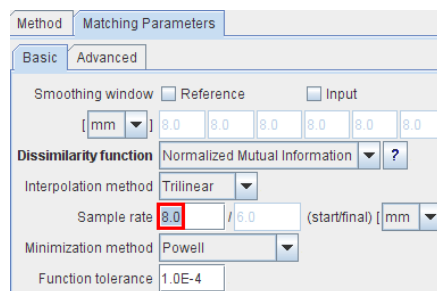
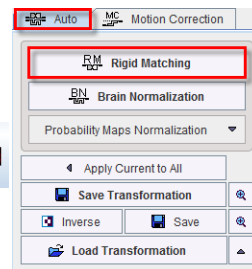


- Try to manually align the FDG images to the MRI. Note that the reslicing controls always remain in the image centre. Click at points located centrally, and then move and rotate the FDG series until the FDG brain contours follow the brain outline in the MRI in all orientations. At this time the transformation parameters can be saved with the  button on the reslicing tab.
- To save the registered images, go back to **Initialize/Match** page. In the fusion panel, the initially resliced FDG images now have been replaced by the result of your interactive reslicing. Use the **CoReg** button and save the images to your database. Alternatively, you can directly use the  button in the toolbar to the right.

2. Automatic Registration of Brain Images

In the following the FDG images are automatically registered to the MRI reference and the result compared with the result of manual coregistration.


- On the page **Initialize/Match** switch **Input** to the “append” mode by enabling the pushpin . Then load the FDG series once more. It is automatically resliced and added as the second series in the list.
- To try the automatic registration, select the **AUTO** tab, and then the **Rigid Matching** button. The **Rigid Matching** configuration dialog box is shown for tailoring the registration. Select the shortcut button for Human MRI/PET matching to initialize suitable registration parameters. These are then shown on the **Matching Parameters** tab of the dialog. Set the **Sample rate** to **8mm** to speed up the registration. Then select **Match Current** to start the registration procedure.
- Calculations take a while. Then the result is shown in the **Fusion** area to the left as the fourth series. The images can be saved with **Save CoReg**, and the transformation with the **Save Transformation** button.
- Switch to the **Adjust/Compare** page to make sure the automatic match is satisfactory. Check that the **PFUS1 FDG >MATCHED to MRI** series is selected in the second row. If necessary, the images resulting from the automatic registration can be further adjusted interactively as described above.
- Finally compare the results from your initial manual registration with the automatic registration result. To this end, configure the first row to the **PFUS1 FDG** image series, and the second row to **PFUS1 FDG >MATCHED to MRI**.
- Try to illustrate the difference by setting the isocontour level to 6 kBq/cc for both studies, and switch the contours radio box to **A+B**. Use a different color for the two contours. Experiment also with different types of layouts (eg 2x6).

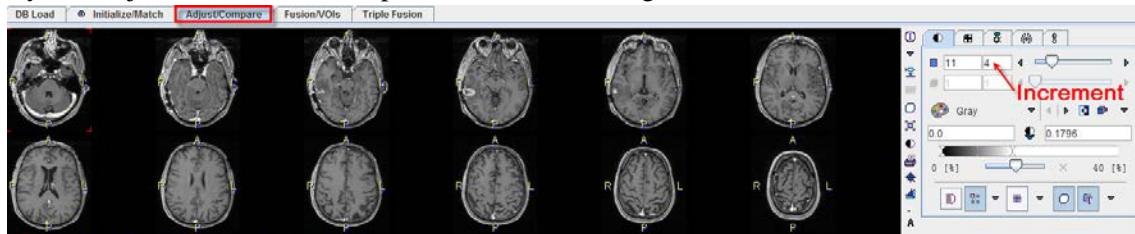


3. Results Documentation

- As described above, the results can be saved by storing the transformation and/or the registered images to disk. An alternative is to save the definition of the current layout to disk. This can be done using the **Save Protocol** button in the status line. Save your current fusion layout, quit PFUS,

start PFUS again, and then retrieve the layout again using **Load Protocol**. (Note that this only works for loaded data, not for data generated using the image algebra.)

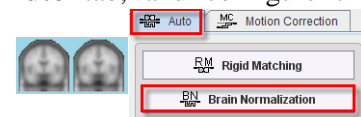
- The “report” button  in the right toolbar allows printing or saving a report. First configure the fusion layout suitably. For example, select the MRI in the first row, and the registered FDG in the second row. Then define a **2x6** layout, and display only every **4th** slice so that the whole brain is covered (arrow in illustration below). The FDG images are automatically shown in the same layout. Adjust the color for an optimal fusion rendering.




4. Spatial Normalization of Brain Images, AAL VOIs

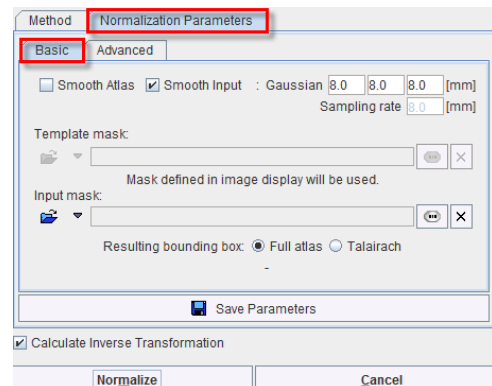
PFUS has MRI and PET brain templates available for the stereotactic normalization. We will spatially normalize the FDG brain images of PFUS1.


- Start PFUS from scratch to avoid mixing with already loaded data, or use **Menu/Close All**.
- From menu **Fusion/File/Load Brain Template** select **PET HFS**. The MNI template (the same as in SPM5) is loaded into the **Reference** area with radiological orientation (**Head First Supine**).
- On the **Initialization/Match** page load the **FDG** series of **PFUS1** with **Input**.
- To stereotactically normalize these patient images select the **Auto** tab, and configure the registration method to **Brain Normalization**.
- A dialog box is shown which allows for some configurations. In **Method** select the **HUMAN** button to apply appropriate

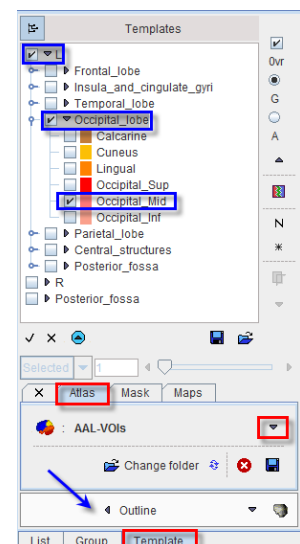


parameters, and then **Normalize**. The calculations are started and after some time the result is shown in the **CoReg** area.

- The transformation can be saved to disk for later use with the **Save Transformation** button. For instance, it could be applied to another study of the same patient which has already been registered to the FDG series (eg. the FET or the FCH series). The **Inverse** transformation can also be **Saved** and used later, e.g. for transforming the standard VOIs from the MNI to the PET space.
- Switch to the **Adjust/Compare** page to verify that the normalization was successful. For instance, enable an isocontour of the smooth template.
- As the normalized patient images are now in the standard MNI space, standard VOIs can be applied for the statistical analysis. Use the “VOIs” button  to enter the VOI analysis dialog window.







- The **AAL** data set is a labeled image file which assigns the individual pixels in the standard space to a set of pre-defined standard VOIs. This definition can be loaded as follows: To the right, in the VOIs list, select the tab **Template** instead of **List** and then the **Atlas** sub-tab. Switch it to **AAL-VOIs** as illustrated to the right.
- Now, the VOIs are shown in the images as grids of different colors. Use the statistics button  to calculate the average VOI values of the standard VOIs.
- You may note that the VOIs do not seem to suit perfectly to the data. To create an adjusted VOI of a structure of interest select only that particular element in the tree list of AAL VOIs, eg the **Occipital_Mid** structure of the **Occipital lobe** in the left hemisphere **L**. Now only **Occipital_Mid** is an overlay in the image. Activate the button **Outline**.

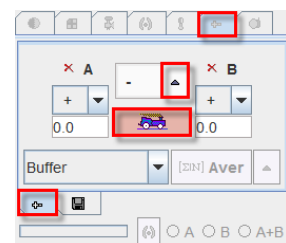
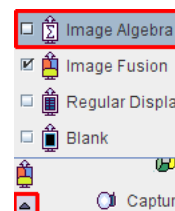


A contour VOI **Occipital_Mid_I_o** is created which encloses all pixels of the standard VOI, and the layout is again switched to **List**. Perform **Statistics** and compare the results of the AAL label VOI and the outline VOI: they should be identical. The advantage of the created outline VOI is that it can be adjusted to the individual brain by scaling, deformations, addition or removal of voxels, and then saved.

5. Image Algebra



A valuable feature of PFUS is pixel-wise algebra, for instance to compare the results of different PXMOD quantification methods.

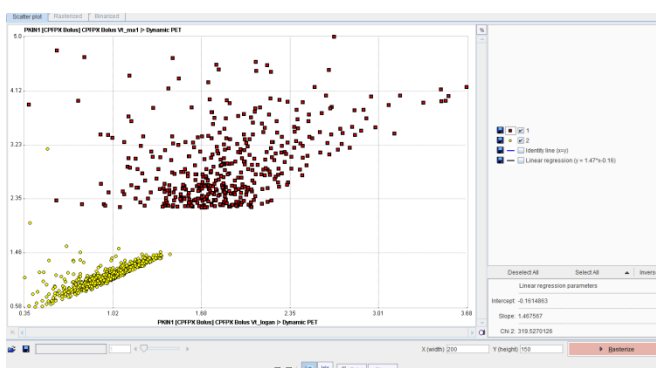
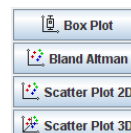
- Re-start PFUS. From the **DB Load** page select patient **PKIN1** and add the three series **Vt_MA1**, **Vt_Logan_perpend**, **Vt_Logan_Open** to load the images.
- In the **Initialize/Match** page select the **Image Algebra** button, or use the  button in the taskbar to the right. The program switches to the **Adjust/Compare** page and sets it to “Image Algebra” mode. (An alternative is to select the **Adjust/Compare** page. There click on the arrow up in the lower right corner of the image area, and then select the **Image Algebra** item.)
- The third row becomes black and a new tab appears. It serves for configuring the arithmetic operations. **A** means the images in the first row, **B** the images in the second row. Arrange the studies such that **Vt_MA1** is in row 1 (A) and **Vt_Logan** in row 2 (B).
- Switch the main operator to the minus sign using the arrow as illustrated. Then click the  button to start the calculation. The subtraction is performed and the result of **Vt_MA1 – Vt_Logan** shown in row 3.
- Perform a quick VOI analysis using the  button in row 3.
- Use the  sub-tab to save the difference series to the database or on your file system.



6. Scatter Plots of VOI Pixel Values

Another possibility for comparing the results of different scans or analysis methods is to produce scatter plots of VOI pixel values.

- In the lower right corner of the **Adjust/Compare** page switch mode to **Regular Display**. All three rows now show synchronized images which can be individually selected from the series list.
- In row 1, use  to start the **VOI construction** dialog box. Define two different, not too large VOIs, called 1 and 2, then quit with **Ok**.
- There are different types of plots available in the lower right. Select the **Scatter Plot 2D** button. The pixel values are evaluated in the series of the upper two rows and plotted in a dialog window. Each VOI is represented as samples in a different color.
- Try the other plot methods. They also take the images in the third row into account.
- Alternative methods to start 3D scatter plotting are the **Menu/Scatter Plot 3D** entry or the  button in the taskbar. If VOIs are already defined, 3D rendering will immediately start, otherwise the user is prompted to outline suitable VOIs.



Further Data Examples for Practicing with PFUS

- **PFUS2:** ^{99m}Tc-tetrofosmin SPECT and ¹³N-NH₃ PET heart images (SPECT Heart & NH₃ Heart).
- **PFUS3:** Dynamic FDG Brain PET scan (FDG Brain) for testing **motion correction**.
- **PFUS4:** MRI and SPM contrast maps for trying the **3 Source Fusion**.

Section 5: P3D Tool – 3D Rendering

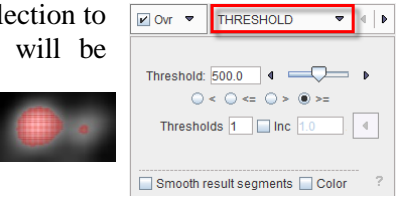
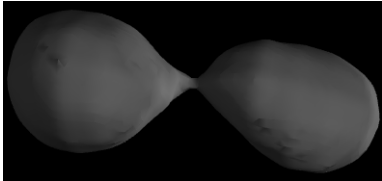






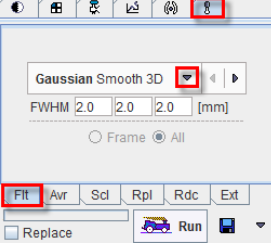
Topics:

- Segmentation of objects by thresholding and region growing.
- Surface and volume rendering of these objects.
- Exploration of the virtual scene.

Exercises:

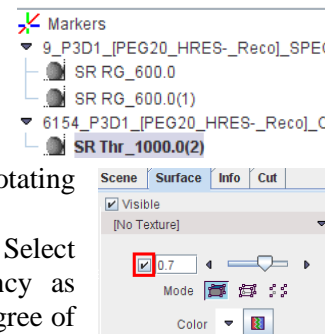
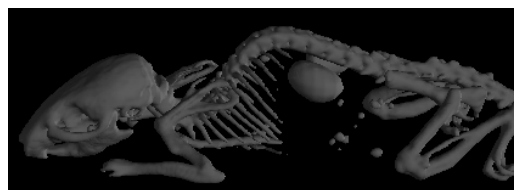
1. Segmentation of Objects

Surface rendering (SR) is based on the segmentation (edge definition) of an object. The surface of the object is then constructed using the marching cubes algorithm and rendered in various styles.

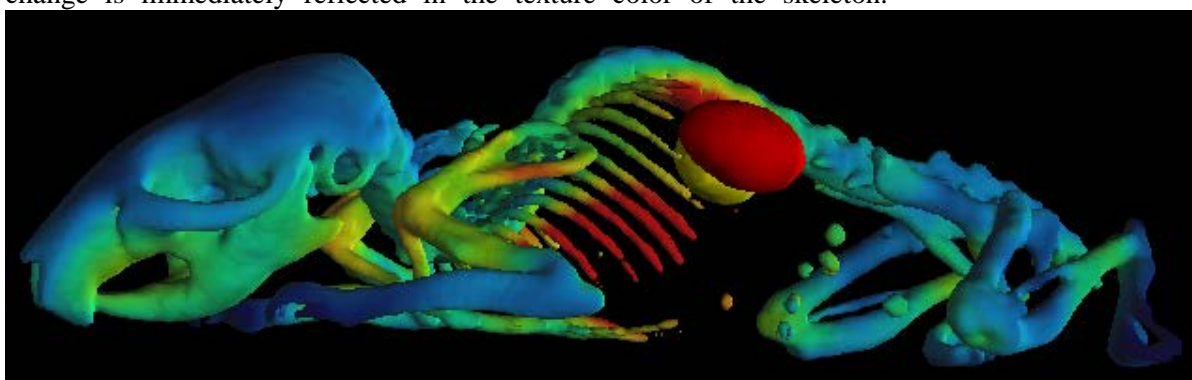
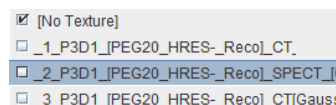
- Start **P3D**. On the **DB Load** tab load the **SPECT** and **CT** series of patient **P3D1**. The loading order is not important.
- In the **Input** tab switch the actual series to **SPECT** using the series selection. To find the slice with **maximal activity** use the button next to the current slice number . You should arrive at slice **113**.
- Define a threshold-based segmentation by setting the method selection to **THRESHOLD**. To see an indication of the pixels which will be included in the segment check the **Ovr** (Overlay) box as illustrated to the right. The color of the overlay is dependent on the color scale. Move the threshold slider and watch the segmentation change. Finally, set the threshold value to **500**. 
- Start object generation by activating the **Surface Rend** button. The segmentation is performed, and two connected spheroids appear. Try manipulating the scene by dragging the mouse buttons in the scene area.
- To get two independent objects switch back to the **Input** tab. Set the segmentation method to **REGION GROWING**, and the threshold value to **600**, with the **>=** criterion selected. Go to slice **103**, click into the center of the hot area to the right, then activate **Surface**. The prior object is removed, and this time only one spheroid is shown. 
- To get the second spheroid switch back to the **Input** tab and click into the center of the left hot area. Before running, set the pushpin to the “append”   **Surface**  mode because otherwise the already existing object will be removed. Then activate **Surface Rend** again. The scene now shows two disconnected objects representing the two mouse kidneys.
- The next step is to construct a skeletal object from the CT image. Switch back to the **Input** tab and select the **CT** image. Note that the segment definition switches to the default **THRESHOLD** setting. This happens because each input data set maintains its own segmentation definition. Since the images are quite dark, adjust the colors. Use the  button in the taskbar to the right of the tool to increase/decrease the image area. As you may notice, the images are quite noisy. Therefore, before starting the segmentation, we will create a smoothed CT data set.
- To determine an appropriate smoothing kernel use the “Study Information” button  to find out the pixel dimension (1x1x1mm). Select the “tools” tab , then the **Filter** sub-tab, and enter **2mm** as the FWHM of the **Gaussian Smooth 3D**. Activate **Run**. A new smoothed CT series is added to the series list as the third entry and automatically selected.
- Select the image presentation tab, lower the upper image threshold and go to slice **136** where the ribs are visible. In the **THRESHOLD** segmentation area try finding a threshold so that only the ribs will be included in the segment, for example **1000**. Make sure the “append” mode is on, and **Surface**. 

2. Surface Rendering (SR)

- The scene now shows 3 objects, the left and right kidneys and the skeleton. All are opaque and shaded in gray.
- Go to the **View** tab to change the appearance of the objects. In the object tree select the object **SR Thr_1000** representing the skeleton. In the **Color** selection on the **Surface** tab choose a lighter gray. Then select the first **SR RG_600** object representing a kidney, and set its **Color** to red. Do the same with the second kidney object **SR RG_600(1)** and set a yellow **Color**.
- Use the **Zoom** slider on the **Scene** tab to enlarge the scene, and try rotating the scene by dragging the left mouse button in the scene area.
- To see the inner structures of the skull make the skeleton transparent. Select the **SR Thr_1000**, and check the box for “blended” transparency as illustrated to the right. The transparency slider allows adjusting the degree of transparency. Note the difference when removing the check. Transparency is set to “screen door” mode with an initial transparency of 0.7. Move the slider and observe the change in transparency which is created by punching holes into the surfaces. Finally set the transparency value back to 0 for getting an **opaque** surface.



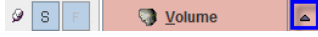

- Next we will add a texture color representing the SPECT uptake value to the skeleton surface. Select the **Input** tab and apply a color table different from **Gray** such as **Cold** to the SPECT series. Switch back to **View**, and highlight the skeleton object **SR Thr_1000** in the tree. In the **Surface** properties area use the arrow to switch the texture from **[No Texture]** to the **SPECT** study as illustrated to the right.
- Initially, the colors applied to the skeleton are probably very dark because of the low uptake in the bone areas. The colors are adjusted as follows: switch back to the **Input** tab and decrease the upper threshold. This change is immediately reflected in the texture color of the skeleton.

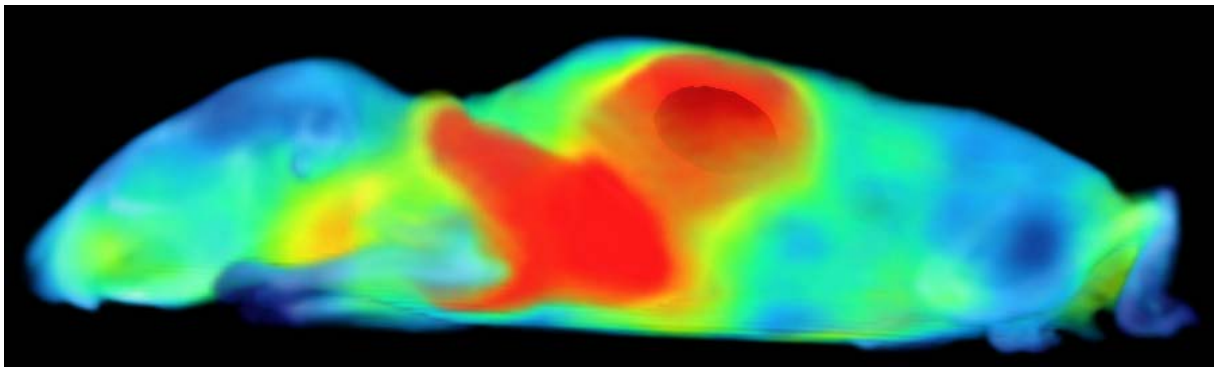


3. Volume Rendering (VR)

Next we will add a VR object of the CT scan to the existing scene of SR objects. As a consequence the blended transparency will not be available any more, only screen-door transparency (punched holes).

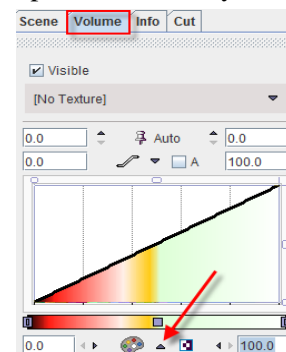
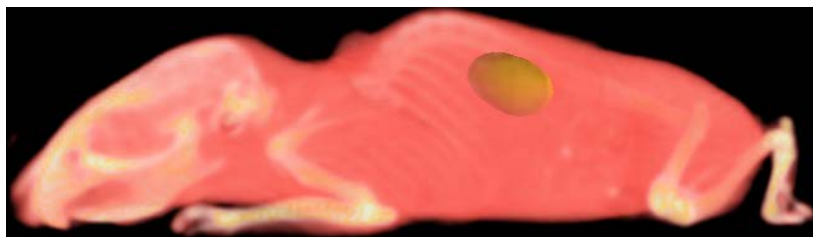
- Switch back to the **Input** tab for creating a new object. Select the smoothed **CT[Gauss]** series, the third in the list. Set the segment method to **THRESHOLD**, and set the threshold value to **400**. As indicated by the segment overlay, the noise pixels will be removed, and practically all body pixels will be included in the segment.

- Make sure the “append” pushpin button is still fixed  and switch the rendering button to **Volume** button. Immediately, the segmentation is performed and a VR object with default properties added to the scene.
- As it is barely visible, remove a part of the other scene information: On the **View** tab, in the tree, select the skeleton object **SR Thr_1000**, and remove the **Visible** check in the **Surface** area.
- Now the skeleton can be seen again, this time in gray from the VR object. The body mass can also be seen as a fine gray mist. The two colored kidneys are visible inside this transparent scene.
- A nice effect can be obtained by adding the SPECT color to the VR object: Select the **VR Thr_400** object in the tree. In the **Volume** tab switch from **[No Texture]** to the **SPECT** series.
- Note the  button which has appeared in the taskbar. This indicates that a scene “refresh” is required. As such a refresh can be quite time-consuming for VR objects, the users have to initiate refreshing after they have completed all desired property changes. Perform a refresh. The scene now shows a semi-transparent mouse in which the SPECT tracer distribution is nicely seen. Note



also the SR objects of the kidneys in the inner of the mouse.

- VR renderings of CT data are often done in a way which provides a sort of anatomic impression. To produce such a rendering with the current data set the texturing of the VR object back to **[No Texture]**. Make sure the **A** (absolute values) box is not checked, meaning that the opacity profile and the colors are defined in percent of the value range. Set the range from **0** to **100**, and select the color table to **Heart VR** using the arrow button below the color bar. Then refresh. The scene should now show the mouse with a white skeleton and semi-transparent red body mass.

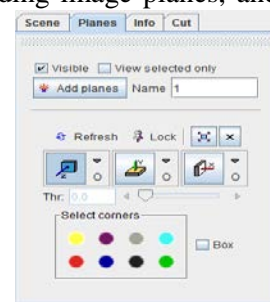


- The lower part of the value range can be removed by changing the lower threshold of the profile range. Enter a value of **5%** into the lower left number field and refresh. The body is still visible, but seems more transparent. With a lower threshold value of **10%**, only the skeleton remains.


4. Virtual Scene Exploration

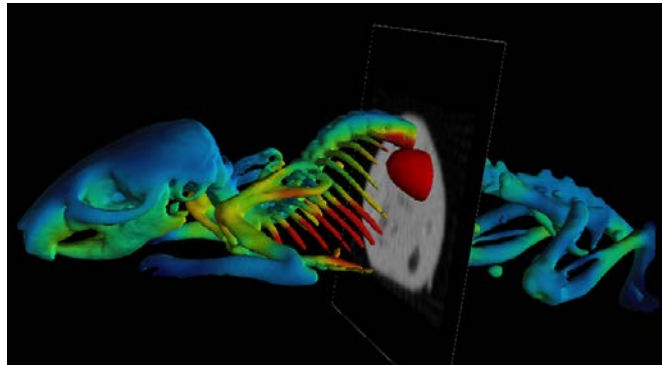
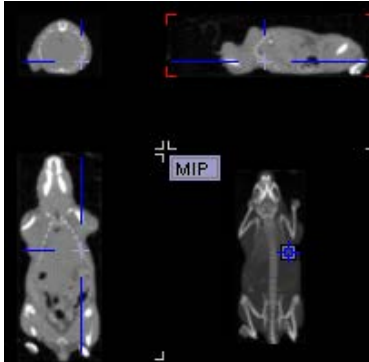
Besides changing the object properties, the scene can be enhanced by adding image planes, and by removing obstructing parts. Furthermore, cines of rotating objects can be created and saved as Quicktime or DICOM movies.

- Hide the VR object from the scene by removing the **Visible** check of **VR Thr_400**. Instead, show the skeleton SR object by enabling the **Visible** check of **SR Thr_1000**.
- Select the **Planes** object in the **Scene** tree, then activate button **Add planes**. Use the **Z**, **Y**, **X** buttons to switch on/off the axial plane images. The **Input** tab allows defining whether the plane images originate from the **CT** or **SPECT** series. In the case illustrated below

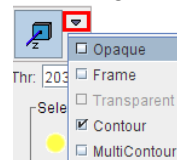


the **Input CT** images are shown, namely the smoothed CT images. To change the slice position, in the **Input** tab, scroll through the slices, or even start a movie running through the axial slices. Changes applied to the presentation of the **Input** images are also immediately reflected in the scene.

- Try also the “navigator” tool for quickly triangulating the planes. It is particularly useful if orthogonal planes are shown in the scene. The navigator is started using the  button in the taskbar. It also has a list selection to define which series is shown.

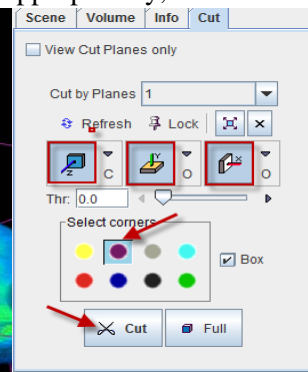
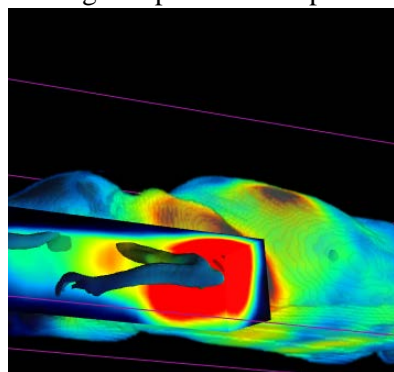




- The planes can be rendered in different styles which can be selected from the list to the right of the plane buttons. **Opaque** planes are shown in the example above. **Transparent** would not obstruct the view, but is not applicable if a VR object has been rendered. **Contour** allows suppressing image information below a threshold which can be defined with the **Thr** slider. Only the biggest connected area will be shown. In contrast, **MultiContour** shows all area above the threshold.




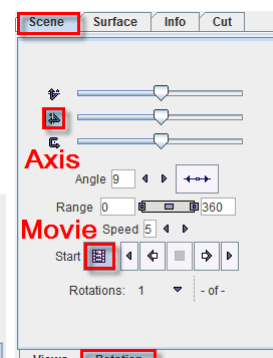
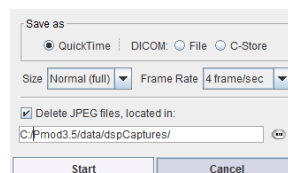
- The planes can also be used for defining quadrants to cut information from objects. Select the **VR Thr_400** VR object in the tree and show it again with the **Visible** check. Then select the **Cut** tab and enable the **Box** check. With the navigator position the planes appropriately, define one or more cutting quadrants by selecting the corresponding color circles in the **Select corners** area. Finally activate the **Cut** button. The scene is updated accordingly.

To cut the same quadrant(s) from other objects **Lock** the planes position, select another object from the tree, and cut in the same way as described above. Also, multiple objects can be selected at the same time in the tree and cut in a single operation.



- In addition to the interactive manipulation of the scene, cines are attractive for getting an overview of the situation, or for creating movies. To start a cine, select the **Rotation** sub-tab on the **Scene** pane, and with the angle sliders find suitable initial angles. Define the rotation axis and start the cine with the  or  button. Note that you can change the rotation smoothness (**Angle**) and the rotation **Speed** during animation. It is also possible to intervene interactively during the animation directly with the mouse button in the scene. Rotation will always continue.

- To save a rotating cine as a movie to disk, enable the “movie” button  before starting the cine. In this case a dialog window pops up for defining the movie quality, a saving directory of the temporary files, and the final output format. After starting, a configured number of rotations are performed and all calculated images saved to disk in JPEG format. Finally the images are combined into the prescribed movie file.



Section 6: PCARD Tool – Cardiac Quantification

Topics:

- Configuration of tracer and workflow.
- Short Axis (SA) reorientation of the images.
- Automatic VOI contouring and manual corrections.
- Kinetic modeling to calculate perfusion values.
- Results inspection and report printing.

Exercises:

1. Configuration Steps

The PCARD tool can be applied for the quantification of different tracers. The configuration of data processing should be adjusted accordingly to make sure the right model is applied and the workflow is as smooth as possible.

- Activate the configuration button in the lower left. In the appearing dialog window select the **HUMAN Heart model type** so that an appropriate heart size is used in the automatic procedures. Select the **NH3** tab and make sure the **Card. NH3 (de Grado)** model is selected. This model is suitable for the analysis of ammonia data dynamically acquired during 4 minutes.
- A preprocessing step consists of generating blood-volume (BV) and myocardium (Myo) images from the dynamic series which contain sufficient anatomical information for the short-axis reorientation procedure and for the polar sampling. These images are simply defined by averaging the dynamic frames between the specified **Start time** and **End time**, and smoothing the result. Enter **0** and **40** into the **Blood Average Parameters** fields to average the first 40 seconds of uptake while blood is still in the ventricles, and apply a **Smoothing** of **6** mm. Enter **120** into the first field of **Myocardium Average Parameters** and select **End of Study** as **End time** for averaging the uptake from 2nd minute until the end of the study. Set also a **Smoothing** of **6** mm. In the **Blood * Factor[1/1]** field enter **0.15** to subtract 15% of the blood activity for making the cavities clearer. Enable the **Calculate Pixelwise Parametrical MBF Map** checkbox.
- In the **Run Automatically** section remove the checks from all boxes to avoid the automatic workflow.
- The sampling and result generation is configured in the **Myocardium TACs Generation & Segments Definition**. Set **Segmentation type** to **Myocardium center line**. Set **Polar sampling** to **Radial Maximum** so that the maximal uptake value in the myocardium during polar sampling from the long axis is used. Set **wall thickness** to **15** mm which restricts the search for the maximum within a 15mm neighborhood of the contour. Select the **AHA(17)** definition for calculating the results in the 17 standard cardiac segments.
- Close the configuration window with **Ok**. The program is now prepared for processing the dynamic ammonia data of the example patient **PCARD1**.
- As an alternative to the described manual configuration you can load the definition from the database using **Menu/Settings/Retrieve**, and then selecting **NH3**. Open the configuration window and remove all checks in the **Run Automatically** section.

2. Data Loading

Typically, two sets of data are acquired, at rest and at stress. These data sets are loaded at once and processed in parallel.

- On the **DB** page, select patient **PCARD1**. In the **Series** list two entries are shown, **NH3, Rest** and **NH3, Stress**. Select the **Add all**



Patient ...	Study date	Time	Study description	Series descripti...
PCARD1	2006.06.07	14:46:47	Patient with reduc...	NH3, Stress
PCARD1	2006.06.07	14:46:47	Patient with reduc...	NH3, Rest

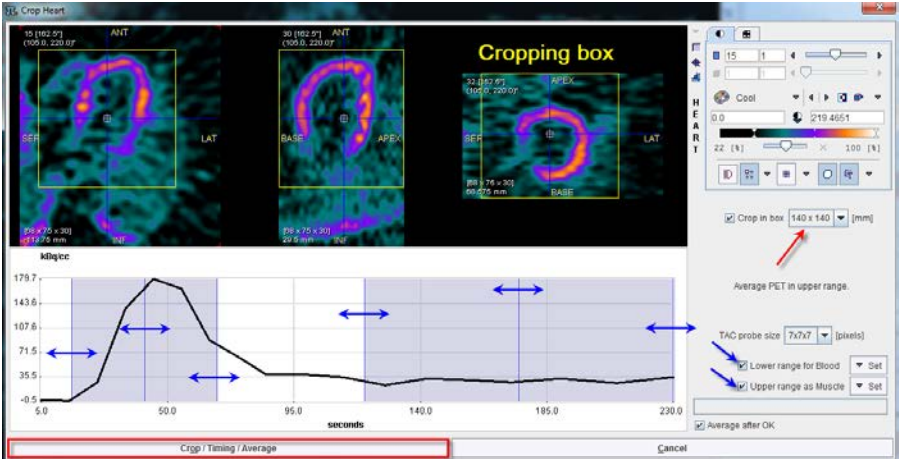
button to get the series to the **Selected for loading** section. Note that the ordering is important: the upper entry in the list should always be the **Stress** series, and **Rest** the lower. By clicking into the column header the sorting order in the list can be changed. Note that another method for list adding/removing is to double-click the list entries.

- Select **Open** for loading the data. The images are loaded on the **Reorientation** page and some automatic processing may run.

3. Short Axis (SA) Reorientation

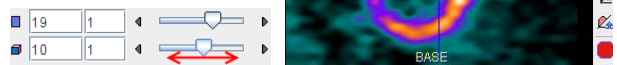
A requirement for the polar sampling of the data is that they are in SA orientation. Based on the default configuration PCARD generates BLOOD and MYOCARDIUM images and applies an automatic procedure for determining the transformations of the SA orientation. With the current data set and configuration the procedure should succeed. However, the manual processing of the **STRESS** data is shown in the following. This procedure is always applicable in the case the automatic steps fail.




- On the **Reorientation** page, in the upper part, remove the checks from all  boxes next to the operation buttons as illustrated to the right. A check means that the automatic processing is started as soon as the preceding step was repeated.
- Select the “Crop/Average” button . A dialog window appears which allows to interactively specify a cropping window as well as the averaging ranges. In the upper part of the window the average images are shown.

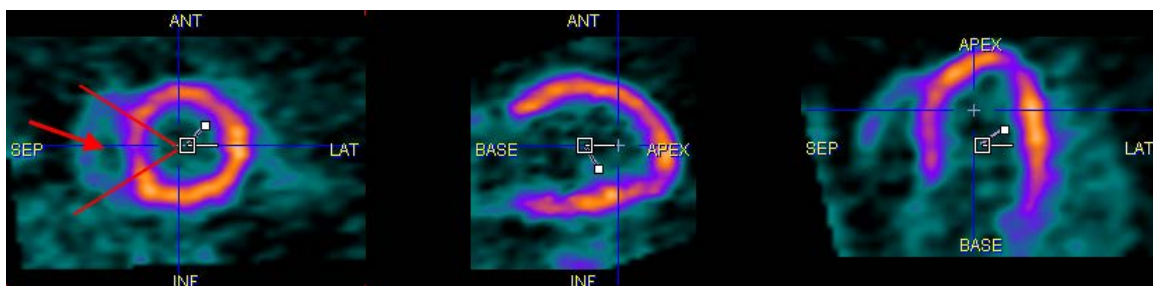
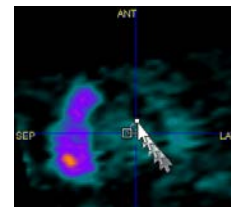
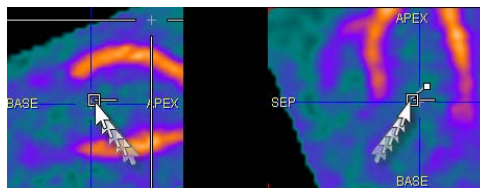




Enable the **Crop in box** checkbox to visualize the cropping volume indicated by yellow rectangles. The center of this box can be placed by clicking into any image plane. Its size can be changed with the list selection. Make sure you place the box such that the whole heart is included in the box as well as enough margins are allowed for the SA reorientation. With each click an average time-activity curve (TAC) is calculated and shown in the lower curve panel. The sampling is performed around the center mark with a configurable **Probe size**. The two shaded areas overlaid on the TAC represent the time ranges for frame averaging. The left area should be adjusted to the blood peak, the right to the myocardium uptake. Finally, click again into the center for placing the crop box properly and start processing with the **Crop /Timing/Average** button. First the cropping has to be confirmed. Then a dialog window shows the frame ranges for the averaging together with the smoothing settings. In order to obtain results compatible with this document, please set frames 1-4 for Blood, and 12-18 for Myocardium. Activate **Yes** to initiate the averaging prescription.

- The created images are now shown in the original orientation, not in SA orientation. Use the indicated arrow button for switching between the MYOCARDIUM and the BLOOD series. Note that in the BLOOD series the right ventricle (RV) is clearly seen, but not the left ventricle (LV). The DYNAMIC images are also of interest. By using the times slider it is easy to find out in which frame the tracer enters the ventricles and when they are again empty.






- The next step is to bring the data into SA orientation. Switch the data to MYOCARDIUM and select the button  to apply an oblique transformation which incorporates a population average of the SA transformation. The angle parameters seem ok, but the images are truncated. Move the images so that the square handle in the image becomes located at the center of the LV. To move the images, click at the rectangle and drag with the left mouse button. Note that the rectangle stays in place, while the images move. Drag the small filled rectangle to rotate the images.
- It is important that the RV is located to the left in the SA images. As the RV location is often not enough clear in the MYOCARDIUM images it is helpful to switch the images to BLOOD and then adjust the rotation in the SA image.
- Note that for orientation adjustments at a later stage the “reslicing” button  should be activated to show the reslicing handles and not , because prior work will be overridden with the latter.
- The final orientation of the images should correspond to the illustration below.

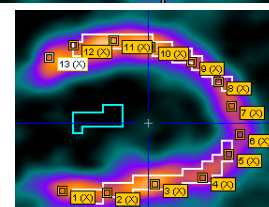
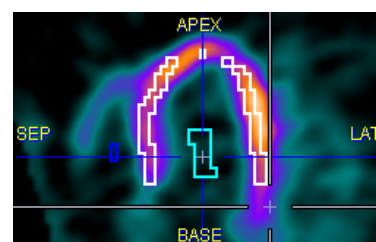


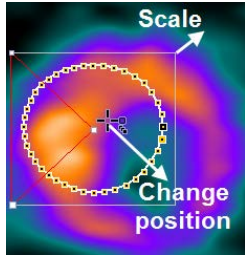




- Often, the orientation of the **Rest** scan is very similar to the **Stress** scan. Therefore, the **Stress** SA orientation is a good starting point for the **Rest** series. It can be easily transferred by the small arrow below the checkbox of the “automatic reorientation” button .
- Fully automatic reorientation is started with . If it fails, two procedures are possible: 1) Try to generate better anatomical images by changing the averaging parameters and start the procedure again. 2) Adjust the orientation manually as described above.

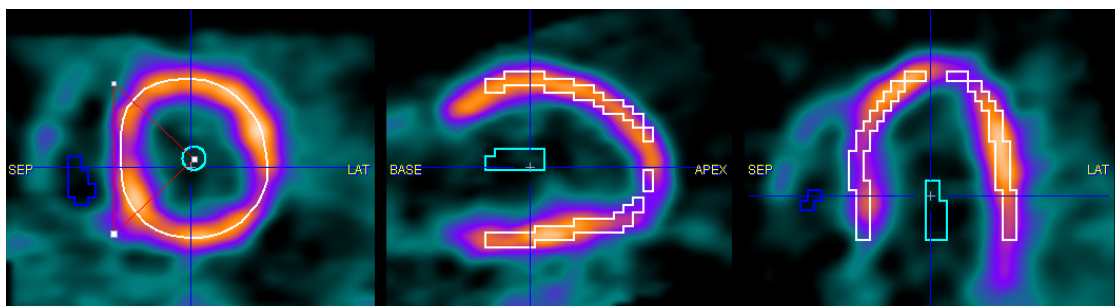
4. Contouring of the Myocardium

For the purpose of polar sampling PCARD constructs a model of the LV myocardium. In principle, the LV model is defined by contour lines of the myocardium center in all SA slices from the apex to the base. There is an automatic procedure for this outlining process which requires a proper SA orientation and sufficient anatomical information in the **MYOCARDIUM** and **BLOOD** images. However, if the procedure fails or provides unsatisfactory results, the user has to open the volume-of-interest (VOI) tool and define/correct the contours. Note that it is not necessary for the contours to *exactly* follow the center *if* the sampling is set to **Radial Maximum**, because the maximal point (normally in the center of the myocardium) should be found on the radial profile. The situation is different if sampling is set to **Model Crossing**. In this case sampling will indeed stick to the contour lines.

- Select the “automatic contouring” button  of the properly oriented **Stress** series. The program creates three VOIs: a LV VOI in the center of the left ventricle which will be used for calculating the input curve, the RV VOI, and the Myocardium VOI shown in white.
- Sometimes the contours are not successfully placed. In this case the user can guide the outlining procedure which in fact fits a model to the data. To this end please select the “markers” button . Then, in any orientation of the plane, click into the image along the myocardium to define markers which should be taken into account while contour fitting. Finally, activate the “contouring” button  again. It is possible that the procedure must be tried several times, until a satisfactory solution is found. To get an overview of the result click at different points so that slice

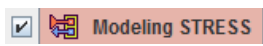
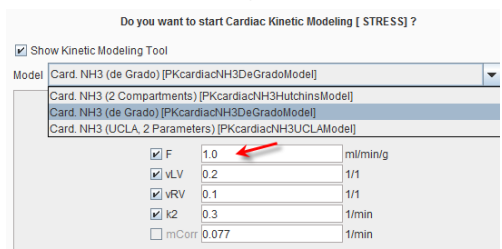
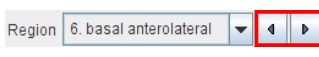


- images with the contours are shown at a range of different anatomical locations.
- If the contouring does not find satisfactory contours, there is no other way than manual work. To open the VOI editor select one of the buttons which represent the different VOIs. While a VOI is undefined the button is red, after definition it turns to green.
 - RV
 - LV
 - Myo
- The **VOI Construction** window opens. Make sure that the third VOI in the VOIs list **Myocard** is selected. Click into the image window and with the mouse wheel scroll through the slices. Locate a slice where the white contour needs an adjustment.
 
- To move or scale the whole contour make sure the  button is selected. In this “ROI editing” mode you only modify the contours in the current slice (as opposed to the  mode which will affect the contours in all slices). Dragging at the edges of the bounding box scales the contour. Dragging the handle in the center moves the contour. Often, these global operations are sufficient for adjusting the automatically generated contours which are more or less elliptical shapes.
- If the shapes need local adjustments, it is recommended to use the “reshaping” tool . Holding the mouse button down and dragging against the contour will drive the contour vertices radially away.
- It is in principle possible to start the VOI definition from scratch without using the result of the automatic outlining. However, this approach has drawbacks in the further processing. Therefore it is highly recommended to try using the automatic approach first and getting at least an approximate solution which can be manually adjusted.
- In difficult cases it may also help to define the VOIs in the better of the Rest/Stress series, and then copy the contour to the other series using the small arrow left to the “contouring” button. This should provide a reasonable starting condition if the SA reorientation was done with a similar transformation.
 
- Finally, both the Rest and the Stress series should be prepared as illustrated below.



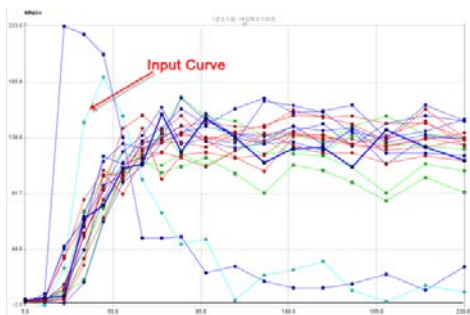
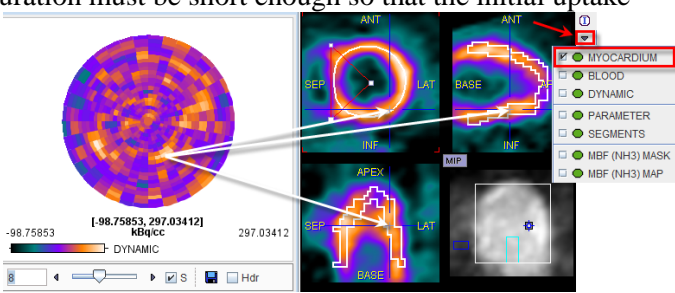
5. Kinetic Modeling

The quantification of cardiac function requires the dynamic tracer uptake in the standard cardiac segments, i.e. the segmental tissue TACs. They are calculated as follows: First, sample points of the myocardium activity are determined. This is done using the **Myocard** contour which provides the long axis of the LV, the location of the base and the apex (first and last contour), as well as the septal angle. The procedure performs a polar sampling of the **MYOCARD** image which uses radial profiles from the LV center all around 360°. Depending on the selected sampling strategy it uses the voxel with the maximal value on the radial profile (**Radial Maximum**), or the voxel at the location of the contour (**Model Crossing**). The values of the samples are then obtained from all frames of the **DYNAMIC** acquisition and arranged in polar plots. Finally, the values in the polar plots are averaged according to the segments to which the sample point belongs. This operation results in TACs which correspond to the tracer uptake in the standard cardiac segments. The next step is the fitting of an appropriate model to the TACs, and arranging the values for inspection and report purposes.




- Select the **Modeling TACs** button to start the TAC generation process. The program switches to the next page **Kinetic Modeling**. If the automatic fitting box has been checked (as illustrated to the right) the configured model will automatically be fitted, otherwise the **Modeling STRESS** and the **Modeling REST** buttons have to be activated to start fitting. 
- Select the **Modeling STRESS** button. A dialog window appears. The box **Show Kinetic Modeling Tool** is active per default. With this setting the PKIN tool is shown with the current cardiac data loaded, and modeling can be performed interactively. Otherwise, fitting will be done in the background and the result parameters returned assuming the fitting was ok. The **Model** selection allows changing among the models appropriate for the loaded data. Below the **Model** the initial model parameters are shown. They can be edited, for instance to set the perfusion value from the default 1 ml/min/g to 2 ml/min/g for the stress study. 
- Select the **Yes** button for starting interactive kinetic modeling. The PKIN dialog window opens, with the model **Card. NH3 (de Grado)** selected. With the **Region** list selection, switch to the **TOTAL MYOCARDIUM** region which represents the average of all sampling points. If it is not available at the end of the list (because it was not configured) use another region, preferably not the apex which is often very noisy. 
- Activate **Fit current region** to fit the model to the measurement. The blue model curve should follow the green measurements reasonably well in the upper curve area. Inspect also the **%SE** column to the right of the parameters which shows their standard error. Use **Fit all regions** for fitting all TACs, and the arrow buttons indicated to the right for browsing through the regions. The agreement between the measurement and the model curve should be satisfactory in all regions. Otherwise, try to improve fitting by interactively changing the initial parameters, or masking outlier measurements.
- Use **Ok** to return to the PCARD program and return the fit parameters. **Cancel** will discard the fitting result.

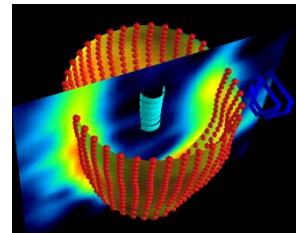
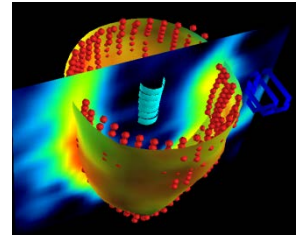
6. Results Inspection

Kinetic modeling returns the final quantification results. Processing in principle is done, and the reports can be shown and printed. However, it is recommended to inspect the results to ensure that all processing steps were successful. All required information is available on the **Kinetic Modeling** page.

- Very important for a correct outcome is the input curve because a reduction of the activity in the input curve automatically increases the calculated perfusion. Therefore, inspect the curves on the **STRESS Input** and **REST Input** tabs. The input curve should be in a reasonable relation to the uptake in the myocardium. The example above illustrates the situation of a stress study. In a rest study, the input curve is typically much higher. Furthermore, it is important that the scan was started early enough so that the entire shape of the input uptake dynamics can be resolved. 
- Also available on the **STRESS Input** and **REST Input** tabs is the result of radial sampling in the form of the raw data polar plots. Use the time slider to inspect the uptake pattern at different acquisition times. Click at different locations into the polar plot. The images to the right are updated to show the corresponding 





sampling point. Note that the image content can be switched with the indicated arrow for assessing different types of information. This mechanism works similarly with the results polar plot on the **Parameters** tab.

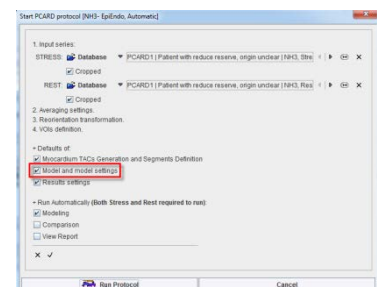
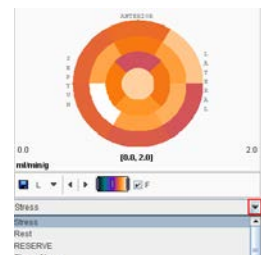
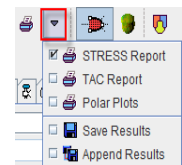
- The locations determined by the radial sampling can be visualized activating the 3D rendering button  (only available if the P3D tool has been licensed) while the  button is enabled. In this case the sampling points are represented by spheres and shown together with the contour model which is rendered as a surface object. Planes with the uptake information can also be shown.
- To see the difference between the different sampling methods activate the “configuration” button  and set **Polar sampling** from **Radial Maximum** to **Model Crossing**, then close the configuration window with **Ok**. Consequently, the **Kinetic Modeling** page is cleared. On the **Reorientation** page outline the VOI automatically. Finally, activate **Modeling TACs** again and look again at the sampling points in 3D. They are now exactly centered on the contour lines. Therefore it is recommended to select **Model Crossing** in cases where the sampling should be manually controlled, for example with perfusion defects in the neighborhood of liver uptake.



7. Reports and Data Saving

After inspection has confirmed that the different processing steps are acceptable, different types of reports can easily be generated. Additionally, data can be saved for processing in external tools, or for exact repeating of the performed processing.

- On the **Kinetic Modeling** page select the **STRESS Report** entry of the  list. It shows a report window with all fit parameter values. The report can be annotated, a **Comment** can be added, and the final version printed with the **Print (Page 1)** button.
- Use the **Save Results** entry of the  list for saving the parameter values numerically to a text file which can easily be loaded in a numerical program such as MS Excel.
- Use the **Compare** button on the **Kinetic Modeling** page for combining the Stress and Rest results and for calculating the reserve outcome. The results are shown on the **Compare** page. The polar plots of the main parameter as well as the reserve are located in the left column.
- In the right part the polar plots can be shown in enlarged form together with the values that they represent. Select the **RESERVE** list selection to switch to the reserve information. Note that it can be calculated in two ways, as the Stress/Rest ratio, or as the Stress-Rest difference. The behavior can be configured with the “configuration” button .
- Select the **Compare Report** button to create the main report which summarizes the Stress and Rest results. It shows a comprehensive report window which can be annotated, printed and saved as usual.
- Select the **Save Results** button to save the numeric data to a text file for external processing purposes.
- The quantification of a cardiac rest/stress study is a complex task which may involve manual adjustments. To ensure the exact reproduction of a PCARD analysis the entire set of definitions can be saved using the **Save Protocol** button which can be found in the lower status line.
- Select the **Save Protocol** button and save your work using the name of your choice, for example **Result of Automatic Procedure**.
- Activate the **Load Protocol** button, and in the appearing window select **Result of Automatic Procedure** protocol, then **Retrieve**. The dialog window illustrated to the right appears. If all options are checked, the analysis will be exactly reproduced. If you would like to test the analysis with a different model, change the model configuration with the  button and remove the check of the **Model and model Settings** box. Activate **Run Protocol** to start processing from scratch.



Section 7: Database Management

Topics:

- Creation of a new database.
- Exchange of data between databases.
- Export of Data from a database.

Exercises:

1. Database Creation and Data Migration


The PMOD software includes the ability to organize all types of data in one or several databases. After installation, a single database called **Pmod** is available which contains the training data sets. In the following a new database is created and some data sets “migrated” between the two databases.

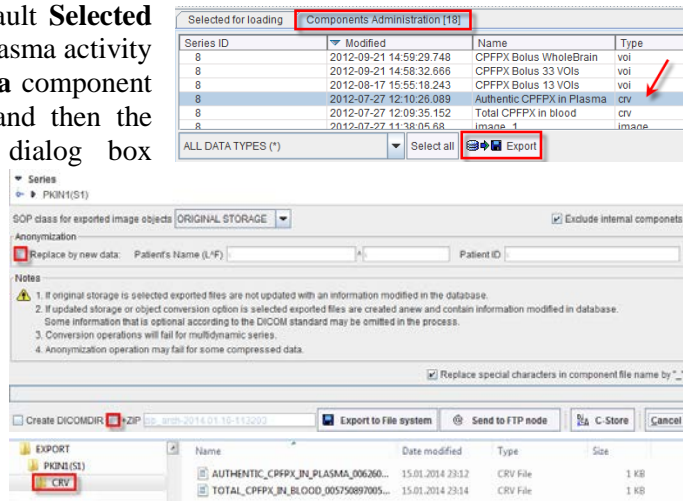
- Select the  **Config** button from the PMOD “ToolBox”. In the appearing **Users configuration** window select the **DATABASE** tab. Activate the button **Add new data source** and enter the **ExampleDB** as its name. Make sure the **Use JDBC connection** button is selected to use the embedded Java database. Defaults are used to fill the entries defining the path for the database files (**Database Path**) and the actual data files (**File Storage Area Path**). Activate **Create Database** to create the database tables. A confirmation message appears stating that the database creation was successful.
 
- The **ExampleDB** is now shown as the visible entry in the data sources list. This means that **ExampleDB** will serve as the default database. To avoid this behavior as long as it is an empty database set the list entry back to **Pmod**.
- PMOD requires a restart to use the new **ExampleDB**. Quit the **Users Configuration** with **Ok**, stop PMOD with the **Exit** button on the ToolBox, and start again.
- Using  **Config** as above and select the **DATABASE** tab. For data migration start the **Database Administration** functionality with the button in the lower left. The appearing window is similar to the window used for image data loading. To migrate data from **Pmod** to **ExampleDB** make sure the **Pmod** database is selected as illustrated to the right.
- To migrate patient PKIN1 (ie copy all of its data) to the new database select **PKIN1** in the **Patients** list and activate **Set as “Selected for Loading”**. If this button cannot be selected because it is gray, first activate the tab **Selected for: replication / export ...** to make it active. The “Add All” operation brings all image series together with all attached data such as VOIs, kinetic modeling files, blood files, into the transport area.
 
- Below the list of selected files there is a configuration button to specify the operation to be done. Select **Replicate to** as illustrated to the right.
- A **Database Replication** window appears. Set the **Replicate to** database to the new **ExampleDB** database and begin data duplication by the **Start Replication** button. At the end of the operation a confirmation appears that the replication was successful, so both DBs contain identical data.
 
- Instead of a replication it is also possible to move the data from one database to the other with the **Move to** operation. In this case, the original data will be removed after replication has succeeded.
- Close the **Database Administration** and the **Users Configuration** window.

2. Data Export from a Database


Sometimes there is a need to export data from a database to process it in a different program. Data export can be done from within the **Database Administration** window, but there is also an export facility in all the windows where data can be loaded from or saved to a database. The example below illustrates how blood files and image files belonging to patient PKIN1 are exported.

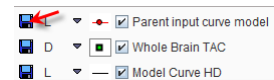
- Start the **PBAS** tool with the **View** button of the ToolBox. On the **DB Load** page switch the database selection to the new **ExampleDB** database which only lists the replicated patient **PKIN1** with its 6 image series.

- In the **Series** list select the **Dynamic PET** series. This series has several different types of data attached as components which can be seen in a list if you select the the **Components Administration** tab instead of the default **Selected for loading**. To selectively export the plasma activity select the **Authentic CFPFX in plasma** component in the list as illustrated to the right and then the  **Export** button. An **EXPORT** dialog box



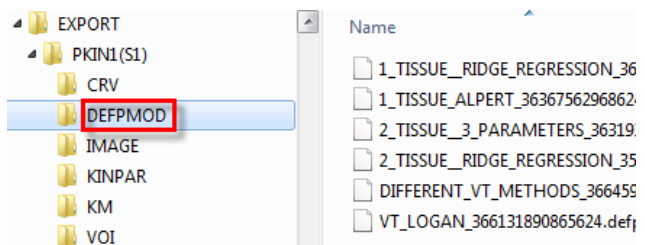
- appears. For image data it is possible to anonymize the data by enabling **Replace by new data** and specifying different name and ID strings. This facility does not apply to the numeric plasma data at hand. Remove the **+ZIP** flag to avoid the creation of a zip archive, and then activate the **Export to File System** button. With the appearing dialog box navigate to the destination directory (**Export** in this example) and then activate **Select**. The data is exported into a directory structure within **Export** as illustrated above right. At the top of the export structure is the patient name **PKIN1(S1)**. Since the blood data is a curve, it can be found in its **CRV** subdirectory. Open the file in a text editor or MS Excel to see how the data is organized.

- Note that curves can be saved into the database from the curve control area. In PKIN for instance, you can save the input curve to the database by the  button left to the **Parent input curve model**.



- Let's continue with the export of the dynamic PET images. Select the **image_1** component in the **Components Administration** tab and repeat the export procedure described above with the same export directory. The image file ends up in a new subdirectory **IMAGE**. You can now read it from any program which is able to import DICOM data.

- There is an alternative to exporting individual components. All data attached to the **Dynamic PET** series can be exported in a single operation from the **Selected for loading** tab. Select **Dynamic PET** and start the **Export** function from the **Selected for loading** tab to the same export directory. This operation creates some additional subdirectories, one for each component type. The different protocols for PXMOD can be found in **DEFPMOD** as illustrated to the right, the PKIN kinetic modeling files in **KM**, and the VOI definitions in **VOI**.



- Note that images received by the DICOM server are saved in original form into the database. The database export function returns these original objects. This is in contrast to the approach of loading the images from that database and then saving to an export directory. In that case new objects are created and a part of the original information (e.g. the private fields of the manufacturers) may be lost. Therefore, the database export is strongly recommended for image data.

Appendix 1: Short Description of Data Sets

- **PKIN1:** Dynamic ^{18}F -CPFPX PET data (90 minutes) using bolus injection, with blood data, and matched MR images. CPFPX is a ligand for assessing the A_1 adenosine receptor in the human brain. There is no tissue without specific binding sites, so reference tissue methods are *not* possible. A two-tissue compartment model is needed for describing the CPFPX kinetics.
- **PKIN2:** Dynamic ^{11}C -DASB PET data and MRI images of the same patient (not matched). Blood data is not available. DASB is a ligand for assessing the serotonin transporter (SERT) in the human brain. The cerebellum can be used as a reference region because there are only few SERT binding sites. The DASB kinetics can be described by a single-tissue compartment model so that the simplified reference tissue model can be applied.
- **PKIN3:** Dynamic FDG brain PET data using bolus injection with whole blood data. The data set can be used for testing the pixel-wise Patlak plot.
- **PKIN4:** Dynamic H_2^{15}O brain PET data at rest, with externally sampled blood data. This example illustrates the usage of delay and dispersion correction which is relevant for online-sampled blood data where the bolus is delayed and dispersed in the blood-drawing catheters.
- **PKIN5:** This patient just contains a single kinetic modeling file for testing the metabolite correction function in the PKIN tool.
- **PFUS1:** Static FDG, FET and FCH Brain PET images as well as a MR image. The images are not matched. They can be used for testing the rigid matching method with different dissimilarity measures, as well as the pixel-wise scatter plots.
- **PFUS2:** Static $^{99\text{m}}\text{Tc}$ -tetrofosmin SPECT and ^{13}N - NH_3 PET heart images. This is an example for the application of matching with heart data.
- **PFUS3:** Dynamic FDG Brain PET data with markers for testing the motion correction in the PFUS tool. This is a data set where motion has been synthetically generated.
- **PFUS4:** MRI and SPM contrast maps for trying the 3 Source Fusion page in the PFUS tool.
- **P3D1:** Matched CT and SPECT images of a hybrid mouse scan for testing the 3D rendering tool. Several rendering protocols are available for demonstration purposes.
- **P3D2:** Matched human CT and SPECT images of the heart. The CT data has been edited to remove the bone parts of the thorax which would be disturbing in the volume rendering.
- **PALZ1:** Highly abnormal FDG scan of an Alzheimer's patient for testing the PALZ tool.
- **PCARD1:** Dynamic images from ammonia heart scans at rest and at pharmacological stress of a patient with reduced perfusion reserve due to unclear origin. This data can be used to test the cardiac kinetic modeling tool PCARD.
- **PCARD2:** Dynamic images from rubidium heart scans at rest and at pharmacological stress of a healthy volunteer. This data can be used to test the cardiac kinetic modeling tool PCARD.
- **Example Brainnorm:** The images (normalization template, mean, standard deviation, mask) of this pseudo-patient constitute an example FDG normal database. This database can be used as an example in the PMOD BrainDB tool. For instance, the FDG images of patient PFUS1 can be compared against this norm.

Appendix 2: Using Keyboard Shortcuts in PMOD

Image-Related Shortcuts

Many of the viewing functions can be activated and are much faster to use by keyboard shortcuts. To direct the keyboard shortcuts to the right images it is essential that they are active. Clicking into an image activates it. To avoid reslicing in the orthogonal viewing mode, please hold down the **Ctrl** key when clicking. In configurations with several viewports it is the image port focus which indicates to which of them the shortcut action is directed to.

LIST of KEYBOARD SHORTCUTS: page 1 of 3 (Focus in the viewport required)

Type	Shortcut	Effect / Test
Data Loading:	<SHIFT + L>	Load image data
	<SHIFT + Q>	Close the currently displayed study
	<Alt + Mouse_Wheel>, <Ctrl + N>	Display next study
	<Alt + Mouse_Wheel>, <Ctrl + P>	Display previous study
Layouts:	<CTRL + X,Y,Z>	Switch to x,y,z-planes (f.e.: <Ctrl+X> = x-plane (sagittal))
	<CTRL + D>	Switch to orthogonal views
	<CTRL + />	Switch to next orthogonal plane
	<CTRL + 1 .. 9>	N x M image display (f.e.: <Ctrl+2> = 2 x 2)
	<CTRL + Click>	Switch 1 x 1 and N x M image display
Reslicing:	<Ctrl+ R>	Enable / disable the oblique image reslicing handles
Slice selection:	<Page Up,Down>	Replace the display by the previous / next page of slices (f.e: <Up> previous page of slices)
	<Arrows>	Increment / decrement the currently shown slices by one (f.e: <Right> next slice)
	<Home,End>	Go to first / last slice (f.e: <Home> first slice)
	<SHIFT + Page Up,Down>	Show the same slices at previous / next page of acquisition times (f.e: <SHIFT + Up> previous page of frames)
	<SHIFT + Arrows>	Show the same slices at incremented / decremented acquisition times (f.e: <SHIFT + Right> next frame)
	<SHIFT + Home,End>	For a dynamic study, go to first / last acquisition (f.e: <SHIFT + Home> first frame)
	<Mouse_Wheel>, <CTRL + Drag>	Scroll through the slices in a movie mode fashion
	<CTRL + M>	Start / Stop movie

LIST of KEYBOARD SHORTCUTS: page 2 of 3 (Focus in the viewport required)

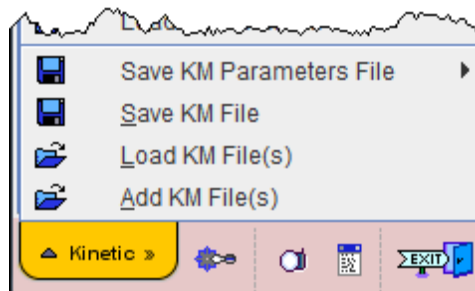
Type	Shortcut	Effect / Test
	Zoom: <CTRL + Mouse_Wheel,+,->	Zoom in / out (f.e: <CTRL + "+"> Zoom in)
Color Table Manipulation:	<SHIFT + Drag>	Modify color table thresholds: horizontal: left = decrease, right = increase lower threshold vertical: down = decrease, up = increase upper threshold
	<CTRL + T>	Invert color map
	<F1>	Switch to next color map
	<CTRL + F1>	Switch to previous color map
	<CTRL + S>	Apply the color table thresholds for each slice individually (slice)
	<CTRL + G>	Apply common color table thresholds over all slices of individual time (frame)
	<CTRL + A>	Apply common color table thresholds over all slices of all times (study)
	<CTRL + F>	Allows for entering absolute values for the upper and lower color table thresholds (fixed)
Contour Overlay:	<CTRL + C>	Enable / Disable showing the contour with currently defined threshold in the overlay
Volume Rendering:	<CTRL + V>	Enable / Disable the volume rendering display (Note that the layout is switched accordingly, as a n*m layout is not reasonable for a volume rendered display)
Reporting:	<CTRL + P>	Print image report
	<CTRL + E>	Capture Display
	<CTRL + O>	Scientific Output

LIST of KEYBOARD SHORTCUTS: page 3 of 3 (Global)

Type	Shortcut	Effect / Test
Screen Capture:	<CTRL + SHIFT + P>	Capture Full Screen to the Console buffer
Save Data:	<SHIFT + S>	Save image data
Keyboard shortcuts help: <CTRL + SHIFT + H>		View this window. Test buttons disabled.
R console	<CTRL + SHIFT + R>	Open R console if not disabled by user settings
Application:	<CTRL + SHIFT + K>	Kinetic Module
	<CTRL + SHIFT + X>	PXMod Module
	<CTRL + SHIFT + V>	View Module
	<CTRL + SHIFT + I>	Fusion Module
	<CTRL + SHIFT + S>	Segment Module
	<CTRL + SHIFT + D>	3D Module
	<CTRL + SHIFT + C>	Cardiac PET Module
	<CTRL + SHIFT + M>	Cardiac MRI Module
	<CTRL + SHIFT + A>	Alzheimer Module
	<CTRL + SHIFT + N>	Neuro Module

Button- and Menu-Related Shortcuts

Functionality implemented as a button or a menu item can often be quickly activated using the keyboard. In these cases, a letter in the item text is underlined. The action item can then be activated by combining the **Alt** key with the underlined letter. For instance when working in PKIN, the **Menu** can be brought up quickly by **Alt+M**. Once the menu is open, an underlined letter is sufficient to activate a menu item. So **Alt+M** and then an “**L**” will quickly perform the **Load KM File(s)** action. In dialog windows **Alt+C** can be used for the *Cancel* action.



Dialog Window Default Action

When a dialog window is opened, the button with the most likely action is usually pre-selected. This default button can be activated with the **SPACE** keyboard key (not with the **ENTER** key) - this is a Java property.