

User's Guide

# PMOD Fuse It Tool (PFUSEIT)

Version 3.6



PMOD Technologies

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## PMOD Fuse It Tool (PFUSEIT)

PFUSIT is PMOD's second-generation image registration and fusion tool. Its purpose is to bring images into a common coordinate space where they can be post-processed in different ways.

Depending on the data to be processed, a user is guided in a workflow through the image registration process, so that the procedure is as convenient as possible and the results reproducible. The following types of image registration are available:

- ▶▶ manual, interactive alignment by shifting and rotating the images;
- ▶▶ automatic alignment using different image comparison methodologies;
- ▶▶ SPM-type elastic deformation to template images;
- ▶▶ motion correction of dynamic series;
- ▶▶ registration based on user-defined anatomical or fiducial landmarks.

Once the images are spatially aligned, there are various ways of post-processing supported:

- ▶▶ different variants of fusing the registered images;
- ▶▶ saving fused images in JPEG/TIFF or as DICOM secondary capture images;
- ▶▶ pixel-wise image algebra of registered images;
- ▶▶ volume-of-interest definition directly in fused images;
- ▶▶ scatter plots of corresponding pixel values in 2 (2D plot) or 3 (3D plot, optional) matched images;
- ▶▶ rotating MIP (Maximum Intensity Projection) images of up to three fused images.

## Operation Principle

The PFUSIT tool regards one image series as the *Reference*. All other series are adjusted in pixel size and slice thickness to the reference. This is done by interpolating their image information within oblique planes across the image volume, a process called *reslicing*. The images to be adjusted are called the *Input* studies in this text. As a result of reslicing, the *Reference* and the *Inputs* have identical resolution, and fusion images can be easily generated by combining the pixel values in the different series. For instance, the pixel colors (RGB values) can be added (*blending mode*), or only one of the image values can be shown depending on a threshold value (*overlay mode*). Furthermore, VOIs can directly be exchanged between all images, and arithmetical operations applied between images.

If the anatomic structures in the *Reference* and the *Input* series are already in spatial agreement, only a mere resolution adjustment of the *Input* series is required, for example to interpolate a 128x128 PET to the 512x512 matrix of the CT (Reference) in a hybrid PET/CT study. In other situations, however, an adjustment of the coordinate system is also required to bring the anatomy in both studies into agreement. For example, in most cases it is required to rotate and shift the images of a brain PET study to match them with the images of an independent MRI study, and interpolate them to the MRI matrix size.

# Spatial Transformations

## Spatial Transformations

PMOD supports two types of spatial transformations:

- 1) **Rigid transformations R** rotate and translate the contents of an image volume, for instance to calculate slices at oblique orientations. Rigid transformations are defined by 6 parameters, the rotation angles and translation distances in the three spatial directions.
- 2) **Elastic transformations E** allow adjusting the shape of the objects in an image volume to objects with a different shape in another image volume (the template). They have an *affine* part and an *elastic* part. The affine part has 12 parameters to account for an overall rotation, translation, scaling and shearing in the three spatial directions. The elastic part consists of a deformation field which performs the local adjustments.

## Combination of Transformations

The PMOD fusion tools support the analytical combination of spatial transformations, avoiding hereby multiple interpolations. For example, when image A is matched to image B by the rigid transformation R1, and B is matched to image C by the rigid transformation R2, A is inherently matched to C by the combination  $R1 \cdot R2$  of the transforms.

In PMOD, an arbitrary number of rigid transformations can be combined, but *only one elastic* transformation at the end of the chain. So for example:

- ▶▶ A CT image from a PET-CT study is matched to MR by R1.
- ▶▶ An MR image is elastically matched to the MNI template by E1.
- ▶▶ Then the CT image is matched to the MNI template by the combined transform  $R1 \cdot E1$ .
- ▶▶ If (and only if) the PET image has the origin at the same anatomical position as the CT, PET can also be matched to the MNI template by  $R1 \cdot E1$ .

## Inverse Transformations

All the automatic methods can not only return the matching transformation, but also the inverse transformation which applies if the role of the *Reference* and the *Input* is reversed. Additionally, PMOD can always calculate the inverse of the current transformation, even if it was created by combining transformations.

## Transformation of VOIs

The spatial transformations can not only be applied to reslice images to reference images, but also to project VOIs from the reference space to the target image space. An application of particular interest is the use of standard VOIs which are defined in the MNI space for the analysis of patient images. This can be achieved with the following steps:

- 1) The patient images are normalized to a MNI template with **Calculate Inverse Transformation** checked.
- 2) The inverse normalization transform is saved.
- 3) The patient images are loaded in the PMOD viewing tool.

4) The MNI VOIs are loaded and the inverse normalization transform applied.

As a result the standard VOIs, adjusted for the particular patient anatomy, are available in the VOI tool as outline contours. The user can adjust them if needed, then save them and calculate image statistics on the unchanged patient data.

## Starting PFUSIT

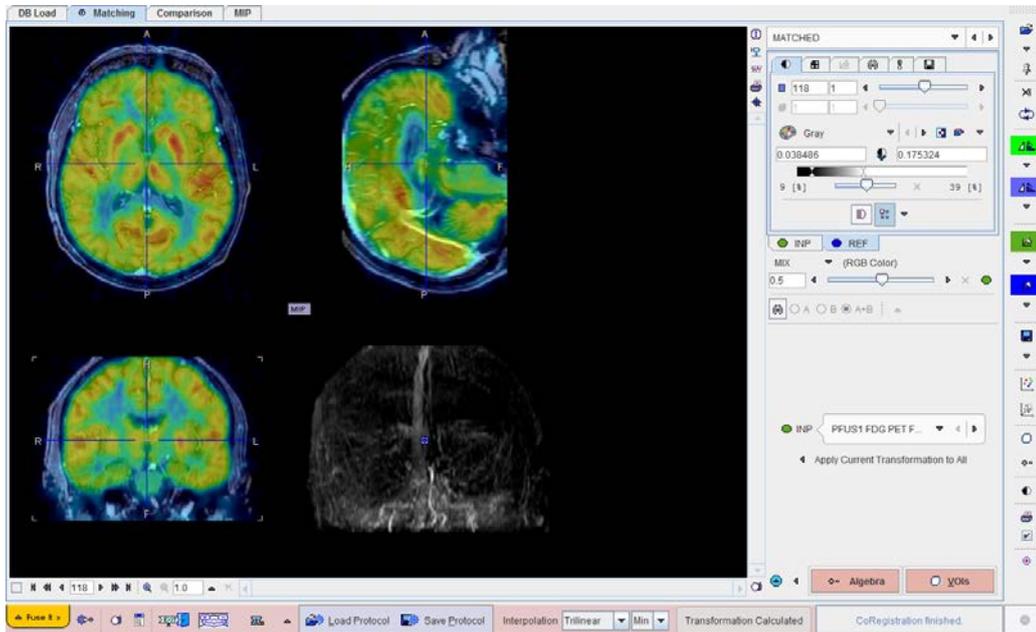
PFUSIT is started with the **Fuse It** button from the PMOD ToolBox



or by directly dragging image files from the desktop onto the above button.

# User Interface

PFUSIT organizes the available tasks on different pages which are explained in the sections below.



Basically, the **DB Load** page serves for image loading from databases, **Matching** for image registration, image algebra and VOI definition, **Comparison** for the parallel visualization of up to six matched images, and **MIP** for the generation of rotating fused MIP images.

## Taskbar

The taskbar on the right side of the application window provides shortcut buttons for frequent tasks. Please note the tooltips for hints regarding the button functionality.

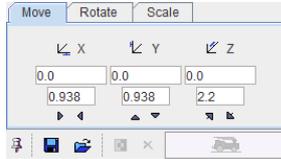
-  **Load images** (on page 30).
-  Toggle button:  Clear the current **INP** list and load as the new **INP** series.  Append the loaded series to the existing **INP** list.
-  Clear all data from PFUSEIT.
-  Swap the role of the **REF** and the current **INP**.
-  Opens saving dialog window.
-  Initial rearrangement of the **INP** images by mirroring and rotations with the panel  


Rotations:   

Mirrors:  

This may be helpful to bring the images into a standard orientation at start.

-  Initial rearrangement of the **REF** images by mirroring and rotations.
-  Initial rearrangement of the **INP** images by arbitrary translations and rotations with the reslicing panel.



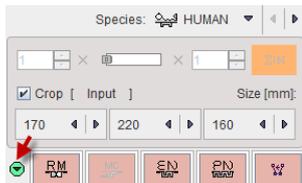
-  Initial rearrangement of the **REF** images by arbitrary translations and rotations with the reslicing panel.
-  Open the **IMAGE ALGEBRA sub-page** (on page 24).
-  Open the **VOIS sub-page** (on page 27).
-  Start the **2D scatter plot** (on page 59) tool.
-  Start the **3D scatter plot** (on page 64) tool.
-  Hide the control area for more image space. Activate again to show controls again.
-  Context-sensitive help, pointing to the html documentation.
-  Reset all configurations to the default values.
-  "Run all" button to start a matching *workflow without interaction* (on page 44).

### Hidden Controls

In several places options are hidden to save screen space. This is indicated by a blue up-arrow as in the example below.



When the button is activated, the area expands, showing all the options.



It can be collapsed again with the green down-arrow.

### Further Information

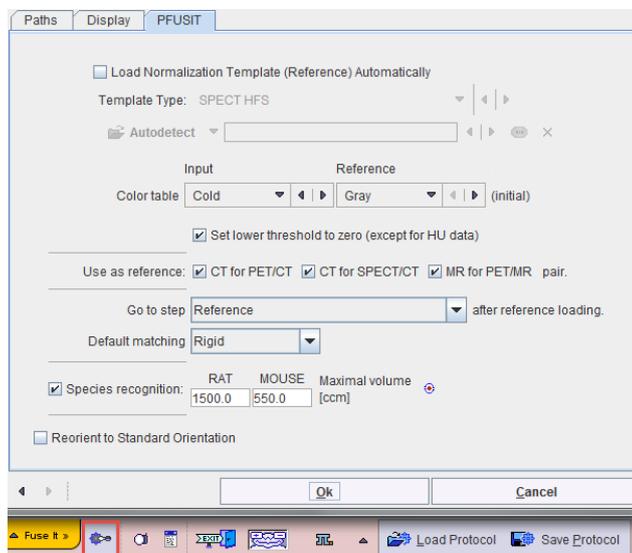
The following description is intended as a reference and not as a tutorial. For practical examples how to work with the PFUSIT software please refer to the overview video and the flipbook explanations which are available in the video and resources area of [www.pmod.com](http://www.pmod.com).

## Recommendations

As the *Reference* determines the final image resolution, it is recommended to use the higher resolved image as the *Reference* for avoiding losses in image quality. The user, however, should be aware that the size of the *Input* series may increase dramatically. For instance, if a dynamic PET study is matched to a 256x256 MRI with thin slices, the size of the resliced PET data can easily grow by a factor of 10. Such big data sets can become a problem for the available RAM, and for subsequent processing steps.

# Configuration Settings

PFUSIT has a set of configuration parameters which can be open with the button next to the **Fuse It** menu button.



The option **Load Normalization Template (Reference) Automatically** is useful if PFUSIT is mostly applied for the normalization of brain images with the same template.

The **Color table** choices allow to establish default colors for the input and reference images. Please not that these defaults are only applied at loading time and can be changed by the user.

**Use as reference** serves for defining the reference image in hybrid situations when more than one image is loaded at once.

**Default matching** sets the registration method which is applied initially. This setting is particularly relevant for the "Run All" operation mode when the images selected in the database interface are directly submitted for registration.

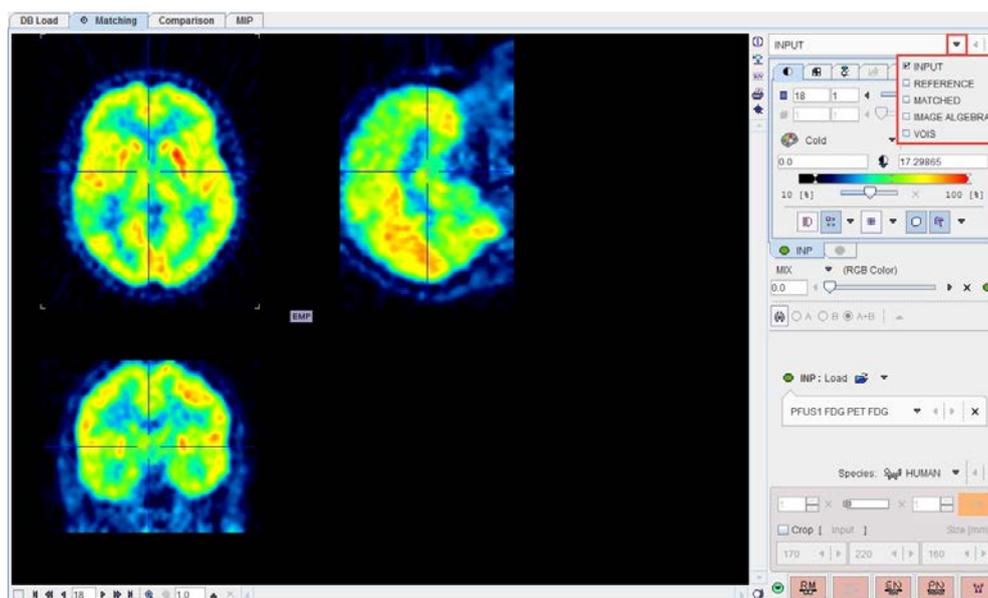
The **Species recognition** option triggers a species selection based on the image volume. If neither the **RAT** nor the **MOUSE** applies, the **HUMAN** default is applied. A correct species setting is important for proper registration defaults.

If **Reorient to Standard Orientation** is enabled, the images are brought into the radiological HFS orientation after loading. A consistent orientation of the alignment is crucial for working with template images and also provides a better initial alignment of multi-modal images.

# Matching Page

## Overview of Matching Sub-Pages

The **Matching** page has five sub-pages, which can be selected with the arrow in the upper right as illustrated below.



Each page consists of an image area to the left, and a control area to the right. The upper part of the control area relates to the image display and fusion, whereas the lower part is highly page-specific. The red action buttons in the lower right are used for starting a processing step or transferring the matched images to a particular post-processing page.

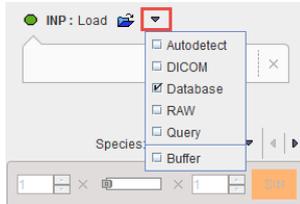
The actual processing works forward through the pages with the red action buttons. After complete processing the pages can be switched without inflicting changes by the selection in the upper right.

## INPUT Sub-Page

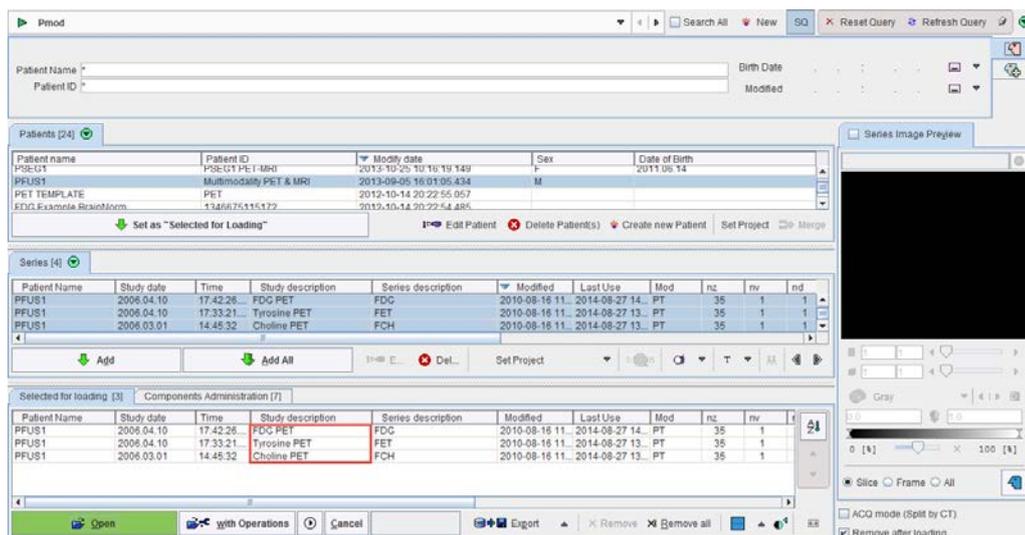
The **INPUT** page is illustrated above. It serves for loading the input images which will be spatially aligned to the reference image.

## Image Loading

Image loading is started with the **INP Load** button, whereby an appropriate file format can be selected using the down arrow.



Note that several input images can be loaded at once as illustrated in the database loading example below.

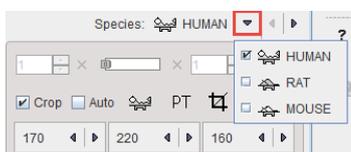


After the images have been loaded, the first in the list is shown in the image area. Please use the list selection illustrated below for switching between the input images. Note the x button for removing the currently selected series.



## Species Selection

In order to apply tailored presets for the automatic procedures, PFUSIT tries to guess the **Species** type from the loaded data according to the criteria in the *configuration* (on page 12). If it is not appropriate, please change the **Species** using the arrow button. The available species are **HUMAN**, **RAT** and **MOUSE**.



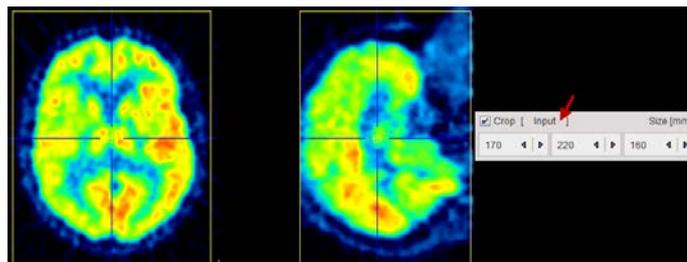
A correct **Species** setting is important for proper registration defaults.

### Image Cropping

Image cropping is often useful for discarding irrelevant information and saving RAM. If the cropping controls are not visible, please activate the blue expansion button.

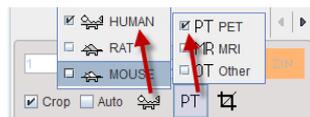


The **Crop** option brings up yellow rectangles in the orthogonal layout. They define the cuboid for the cropping operation.



The edge sizes can be adjusted with the arrow buttons, and the position by clicking at the center of the volume of interest. Cropping is started with the  button.

There is an automatic cropping function available which works for brain images. It is based on the matching of brain templates to the images. To this end the species and the modality have to be set properly by the configuration buttons illustrated below.



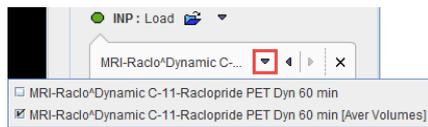
As soon as the **Auto** option is checked, the process is started. It results in the placement of the yellow cropping box, which can be inspected by the user. The actual cropping has to be started explicitly with the  button.

### Averaging of Dynamic Images

If dynamic input images are loaded, a frame averaging option is applicable. In the example below a range between frames 7 and 22 is defined.



As soon as the indicated averaging button is activated, the time-weighted frame average is calculated and the result added to the list of INP images. To label the result the string [Aver Volumes] is appended to the series description.



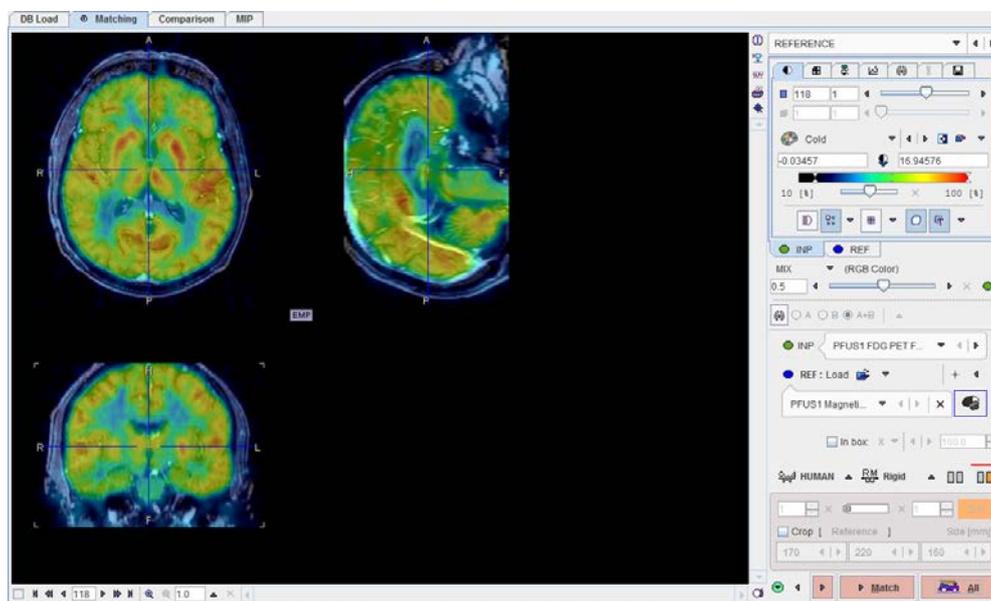
### Action Buttons

After the input images have been loaded and the species selection is appropriate, processing can be moved on by one of the red action buttons. They will open the **REFERENCE** page with an appropriately configured registration method.

-  Rigid matching
-  Motion correction. This option is only available for dynamic **INP** images.
-  Elastic deformation based on a single template reference.
-  Elastic deformation based on a probability maps of grey and white matter, as well as CSF.
-  Matching based on manually defined landmarks.

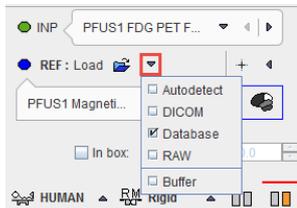
### REFERENCE Sub-Page

The **REFERENCE** page is illustrated below. It serves for loading the reference image and for the configuration of the registration method.

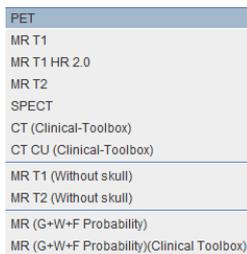


## Reference Image Loading

Typically, anatomical images (MR, CT) will serve as the reference, to which the lower-resolved functional input images are registered. Reference image loading is started with the **REF Load** button, whereby an appropriate file format can be selected using the down arrow.

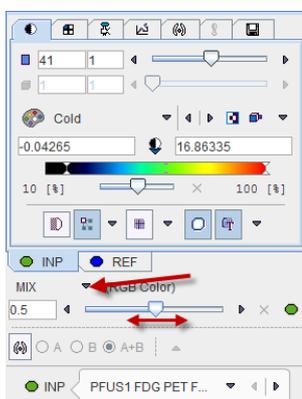


Note the  convenience button for loading brain templates as the reference in deformable registration. The loading is species-sensitive and in the **HUMAN** case shows the available brain template variants.



## Fusion Display

The image display on the **REFERENCE** page shows a fusion of the **REF** image with the currently selected **INP** image. The appearance of the individual images can be adjusted by selecting the corresponding tab and using the image presentation controls, e.g. adjustment of the color thresholds, see *below* (on page 81). In the fusion area below the tabs there is a selection arrow for choosing the fusion method (**MIX** as default), and the slider to change the relative emphasis of the two images in the fusion.

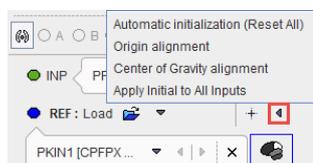


## Initialization of Registration

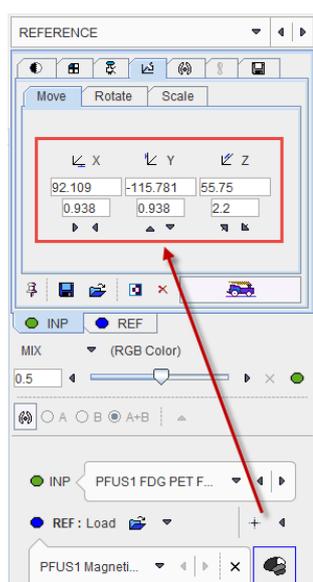
In order to fuse the **INP** and the **REF** images PFUSEIT performs an initial alignment procedure. If the images are from a hybrid acquisition there are good chances, that the

resulting alignment is already final. Otherwise, it is only a preliminary starting point for the registration procedure to follow.

It is important for the automatic registrations that the images on the REFERENCE page show a sufficient overlap. If this is not the case, other initialization types have to be applied which are available to the right of the REF selection:



Note that an initialization results in a translation matrix, which can be inspected on the reslicing tab of the INP series



The initializations behave as follows.



For current **INP**: Alignment of the **INP** and the **REF** image volume center.

**Automatic initialization** Repeats the initial alignment procedure for all loaded **INP** images. This is particularly helpful after unsuccessful matching trials.

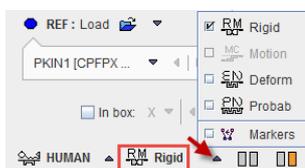
**Origin alignment** For current **INP**: Alignment of the **INP** and **REF** coordinate origins. This works if the two series have the origin at the same anatomical landmark.

**Center of gravity alignment** For current **INP**: Alignment of the **INP** and **REF** gravity centers. This works if the two series have about the same value distribution.

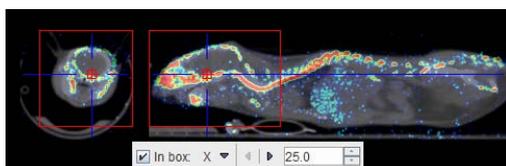
**Apply Initial to All Inputs** Use the current transformation for all **INP** series. This works best if the inputs are already aligned.

## Registration Configuration

The current automatic registration method is shown next to the species label. It can be switched to another method with the selection arrow. The methods and their parameters are described in a separate *section* (on page 29).



Note the **In box** option. It serves for restricting the operation of the automatic registrations to a sub-volume of the reference image. The location of the sub-volume is indicated by the red rectangles. As the crop box, it can be positioned with clicking at the center of the volume of interest, and the edge sizes can be changed with the direction selection and the edge length to the right of **In box**.

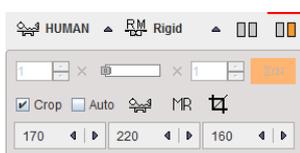


## Reference Image Cropping

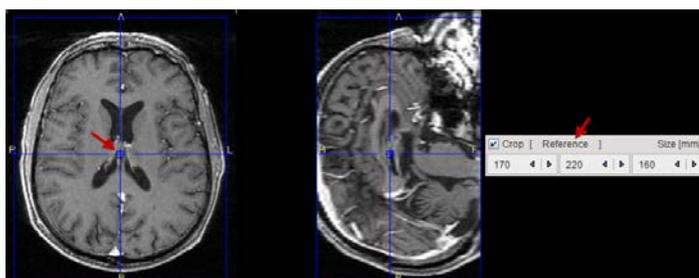
The reference image can be cropped in the same way as the input images. Please shift the fusion slider to the right to only see the reference image



enable the **Crop** option,



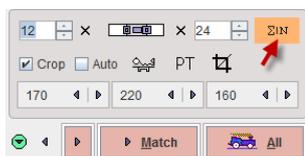
and then adjust the position and size of the blue cropping volume.



The actual cropping has to be started explicitly with the  button. The **Auto** cropping works as described for the *INPUT page* (on page 13).

## Averaging of Dynamic Images

If a dynamic reference image is loaded, a frame averaging option is applicable. In the example below a range between frames **12** and **24** is defined.



As soon as the indicated averaging button is activated, the time-weighted frame average is calculated and the result replaces the reference image.

## Action Buttons

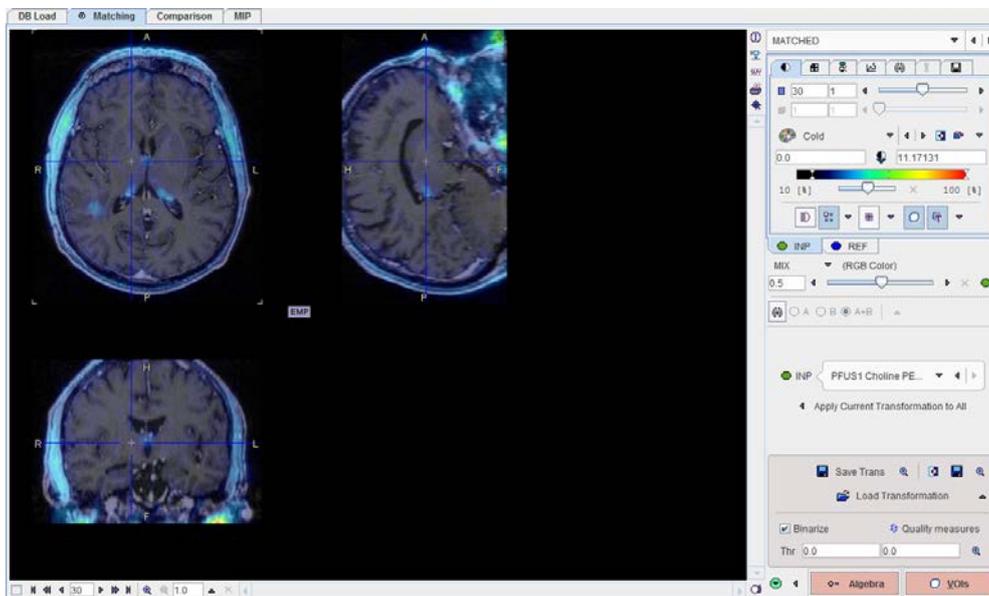
After the reference image has been loaded and prepared by cropping or averaging, the action buttons can be applied.

-  Omits any automatic registration and simply resamples all input images to the reference geometry. For instance, the PET image of a PET/CT hybrid scan will be interpolated to the resolution of the CT image.
-  Starts registration of the selected input image to the reference image using the configured method.
-  Starts registration using the configured method and sequentially registers every input image to the reference image.

At the end of the calculations, the result is shown on the **MATCHED** sub-page.

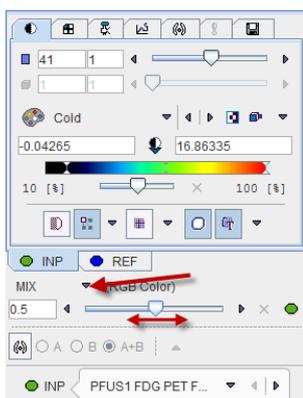
## MATCHED Sub-Page

The **MATCHED** page is illustrated below. It serves for evaluating the matching, manually adjusting the alignment and supports operations with registration transformations.

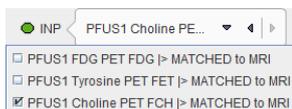


## Fusion Display

The image display on the **MATCHED** page shows a fusion of the **REF** image with the currently selected **INP** image with the usual *image fusion controls* (on page 81).

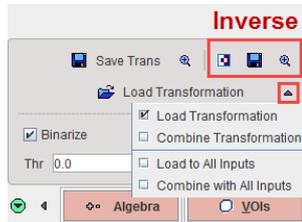


The image used for the fusion display can be selected in the **INP** list.

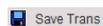


## Transformations

Each of the INP images has its own *spatial transformation* (on page 5) which maps the input image from the original space to the reference space. These transformations as well as their inverse are accessible in the expanded control area at the bottom.



The functionality of these transformation-related elements is as follows:



Save the transformation of the current input image. This includes the automatic registration as well as subsequent manual adjustments.



Show the affine transformation part of the current input image in a dialog window

	X	Y	Z
Translation Parameters [mm]	2.2232	-3.7647	3.8593
Rotation Parameters [°]	-12.8328	1.6259	2.4638

Original reference space stored.

Navigation: Home, Left, Right, Home. Copy to Clipboard



Calculate the inverse of the current transformation.



Save the inverse of the current transformation.



Show the affine part of the inverse transformation in a dialog window.

### Load Transformation

Load a transformation, replacing the transformation of the current input image.

### Combine Transformation

Load a transformation and combine it with the transformation of the current input image. Note that the combined transformation becomes the current one and can be inspected with the

### Load to All Inputs

Load a transformation, replacing the transformation of all input images. This makes sense if all input images are in the same space, for instance for a set of parametric maps generated from a single series.

### Combine with All Inputs

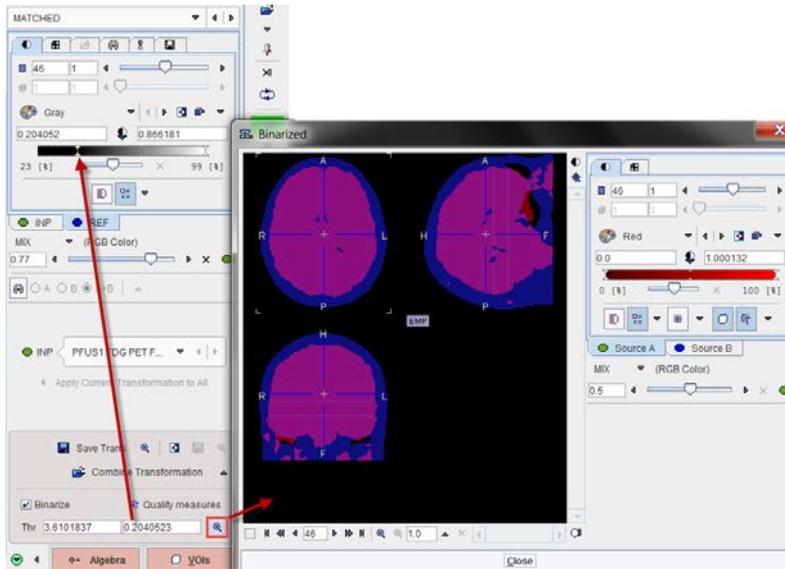
Load a transformation and combine it with the current transformation of each of the input images.

The button **Apply current Transformation to All** allows propagating the current transformation to all input series. This operation is applicable if all input images are in the same space. A typical application case is that the registration calculation has been performed with a frame average of a dynamic series, and the result transformation is now applied to

the dynamic series itself. Another application case is the matching of a set of parametric maps generated from a single series.

### Overlap Indexes

PFUSIT supports the calculation of overlap indexes as follows: In the **Thr** area threshold values can be entered for the registered **INP** and the **REF** image. Alternatively, the lower threshold of the color table can be adjusted, whereby the **Thr** values are modified accordingly. The two binary volumes can then be visualized as a fusion image with the  button.



The overlap criteria are then calculated based on the two masks with the **Quality measures** button.

Binarized [REG = 3.6101837158203125, REF = 0.23320262134075165]

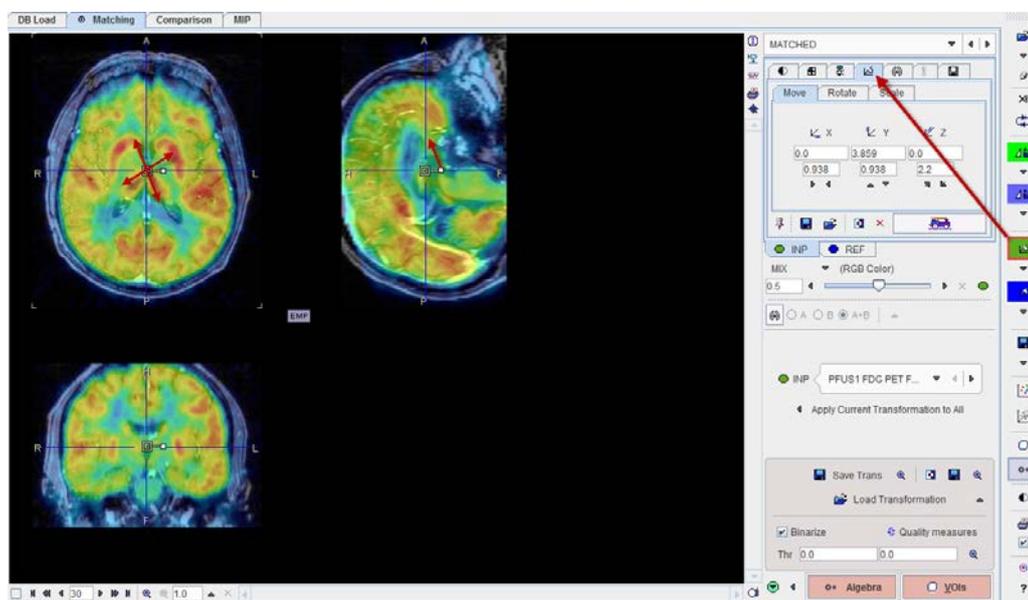
Volume difference:	0.5134	$2 *  A-B  / (A+B)$
Signed volume difference:	0.5134	$2 * (A-B) / (A+B)$
Specificity:	0.98915	$1 - (A - A \cap B) / (A \cup B)$
Sensitivity:	0.5805	$A \cap B / B$
Dice:	0.72951	$2 * A \cap B / (A + B)$
Jaccard:	0.5742	$A \cap B / A \cup B$

 Copy to Clipboard

A - Registered set in binarized or labeled mask  
 B - Reference set in binarized or labeled mask

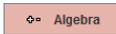
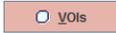
## Manual Adjustments

After automatic registration, the input images can be manually shifted and rotated to improve the alignment, if necessary. The same applies, if automatic registration has been skipped altogether in order to perform a fully manual alignment. Manual adjustment is started with the  button in the lateral taskbar as illustrated below. It opens the reslicing tab of the **INP** images, and shows handles in the image overlay for dragging/rotating the images interactively, as described *below* (on page 33).



## Action Buttons

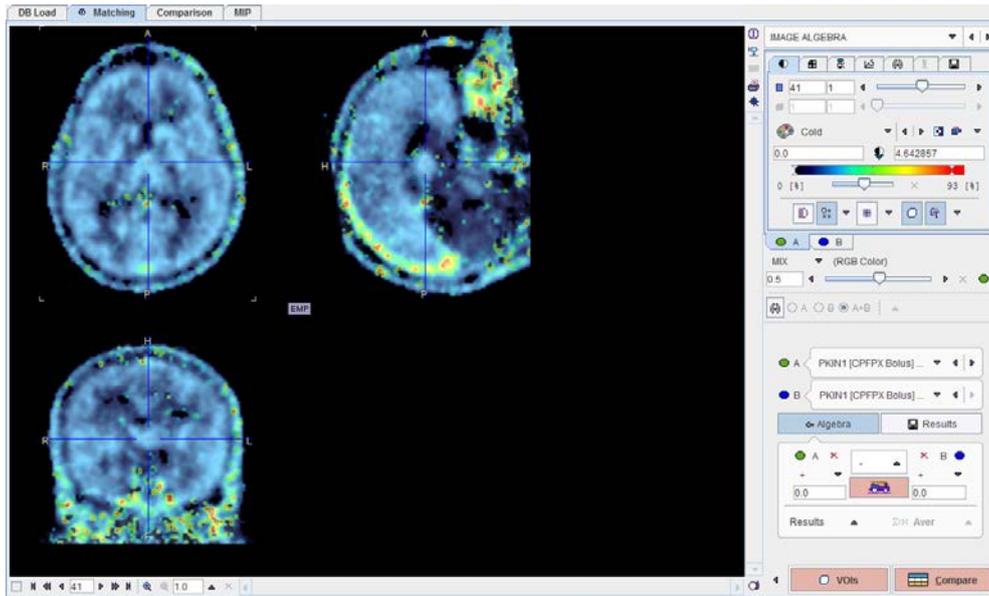
Assuming that all input images have been registered to the reference, the user can proceed to the various post-processing pages with the two action buttons

-  **Algebra** Switches to the **IMAGE ALGEBRA** sub-page for performing pixelwise image arithmetics.
-  **VOIs** Switches to the **VOIS** sub-page for outlining VOIs directly in fused images.

Alternatively the main pages **Comparison** and or **MIP** can be selected.

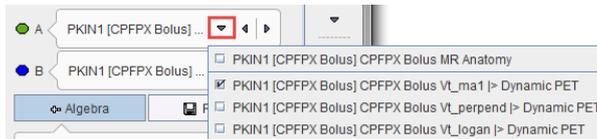
## IMAGE ALGEBRA Sub-Page

The **IMAGE ALGEBRA** page is illustrated below. It serves for applying pixel-wise operations between the registered images. Examples are the calculation of the difference image between two functional maps, or the multiplication of a mask image with a target image.



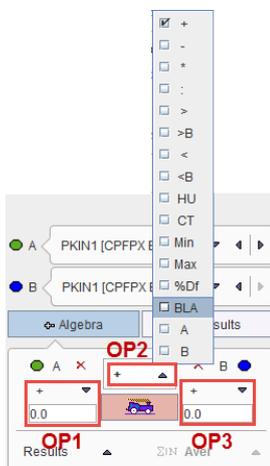
### Operation Principle

The principle is that an algebraic operation is defined between two images, resulting in a new image which can also be used for further operations. The input images are defined via the **A** and **B** list selections



The operation between **A** and **B** is configured with the Algebra area and has the general form

(A OP1 number) OP2 (B OP3 number).



The calculation is then started with the  button and adds the result image to the selection lists.

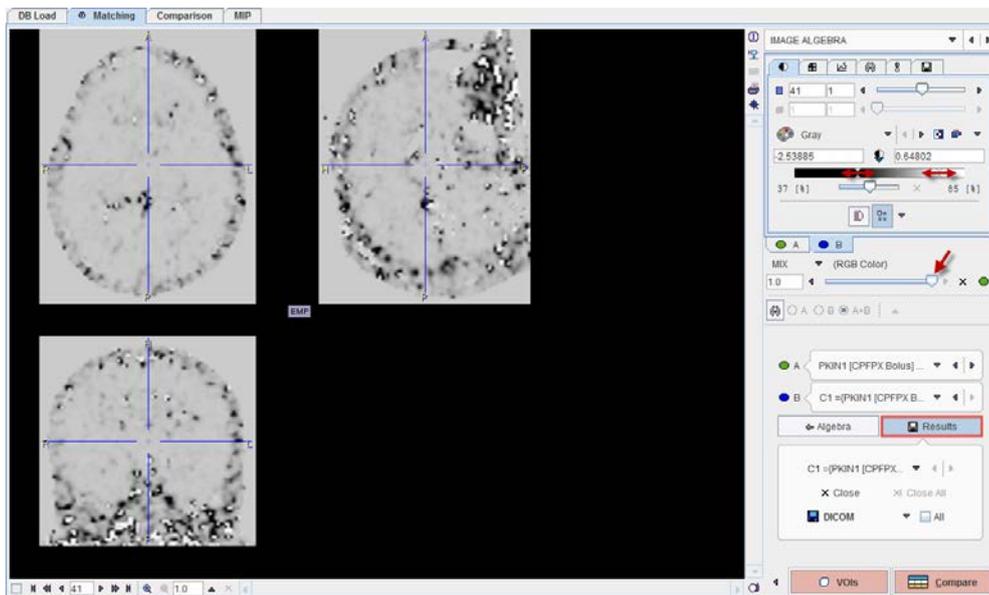
### Available Operations

The following operation can be applied to the individual images (as OP1 or OP3) :



### Results

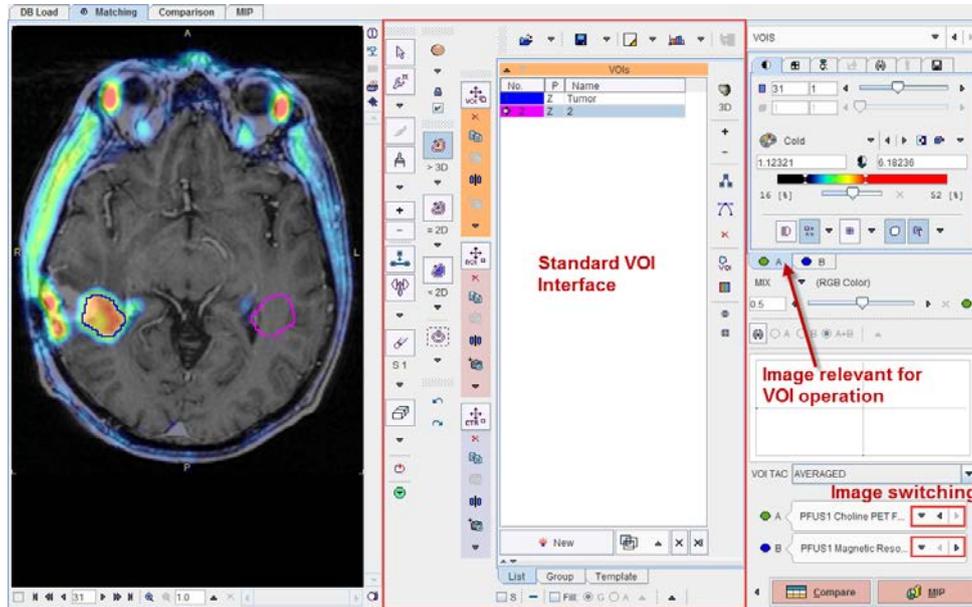
The operation results are automatically selected as the image **B** and shown in the fusion display. The color table may need some adjustments, and to only see the result image the fusion slider should be set to the right. The example below shows the difference between the Vt maps calculated with two different methods.



The **Results** button gives access to the created result images in a dedicated area. There are buttons for selecting among the results, closing or saving a result.

## VOIS Sub-Page

The VOIs page is illustrated below. It serves for outlining volumes-of-interest directly in the fused images.

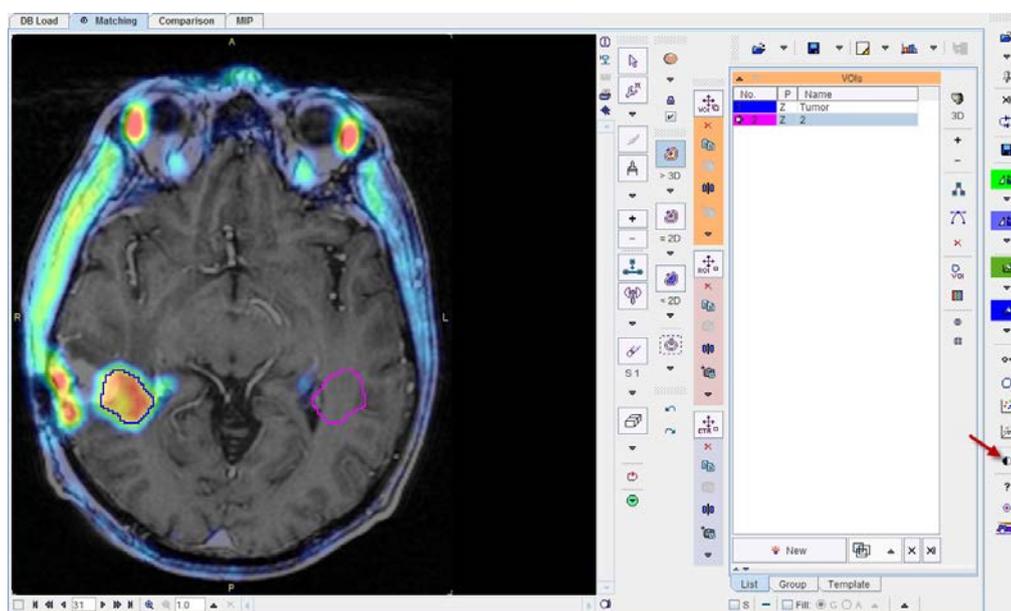


### VOI Definition and Evaluation

The standard VOI options are available for the VOI creation. Please refer to the *PMOD Base Functionality Guide* for explanations of the VOI functionality. The only distinctive thing to consider is, that the series selected on the tab to the right (**A** or **B**) is relevant for VOI definition and evaluation. In the example above, the choline PET series **A** is selected, so that the hot iso-contouring  was successful in detecting the tumor boundary. When the statistics is calculated with the  button, the choline uptake in the tumor uptake is obtained. Otherwise, had the tab **B** been selected, iso-contouring would have operated on the MRI and failed in the tumor outlining task.

## Image Selection

If more than one input series has been processed or image algebra results were generated, there are several candidate images for the VOI statistics. The two selections in the lower right allow freely defining which series is configured on the **A** and **B** tabs. After a suitable configuration of the image presentation and the selection of the appropriate source the image controls can be hidden with the  button to get more image space as illustrated below. They can be brought back using  again.



## Action Buttons

Assuming that all input images have been registered to the reference, the user can proceed to the various post-processing pages with the two action buttons.



Switches to the **Comparison** main *page* (on page 46) for visualizing multiple fused images.



Switches to the **MIP** main *page* (on page 51) for creating rotating fusion MIP renderings.

Alternatively the main pages **Comparison** and or **MIP** can directly be selected with the tabs.

# Matching Workflows

The following sections describe popular matching scenarios. In most cases it is assumed that the input and reference images have been loaded as described *above* (on page 30).

## Recommendations

### Initial Reorientation

Before the actual registration is addressed, the images should be brought into a consistent orientation. If this is not the case after loading, the images may be reoriented. There are shortcut buttons in the lateral taskbar to achieve this conveniently.



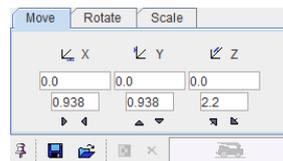
Initial rearrangement of the **INP** images by mirroring and rotations with the panel



Similar for the **REF** images..

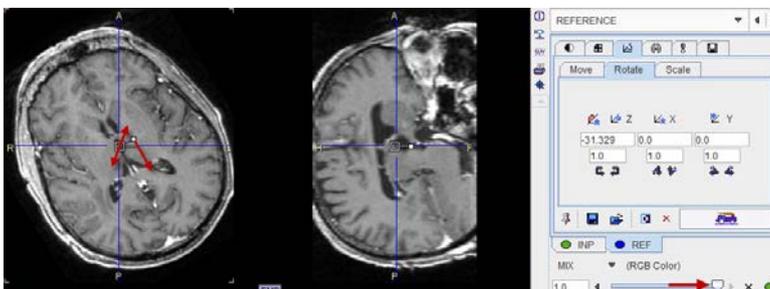


Initial reorientation of the **INP** images by arbitrary translations and rotations with the reslicing panel.



Similar for the **REF** images by arbitrary translations and rotations with the reslicing panel.

In the example below, the reference needs to be straightened. Activate , shift the fusion balance fully to **REF**, and then rotate the axial image.



### Transformation Initialization

The next step is to ensure that the initialization is appropriate. This means that the images are either already aligned on the **REFERENCE** sub-page, or that they are brought into a reasonable overlap as described *above* (on page 16).

## Layout Adjustments

Initially the images will appear in orthogonal layout (Ctrl+D) which allows working easily in all 3 dimensions. For fine adjustments it may be preferable to switch to the axial (Ctrl+Z), coronal (Ctrl+Y) or sagittal (Ctrl+X) single-plane layout.

## Restriction of Matching Volume

In some cases the automatic matching procedure needs to be restricted to a sub-volume of the data. This can be achieved in different ways.

As described *above* (on page 16), the **In box** option allows defining a box in the reference image, top which the registration algorithm will be confined. An alternative is to define a free-form masking volume on the input or reference image using the selections from the lateral taskbar illustrated below.



**Prepare input mask** opens the segmentation tool described in the *PMOD Base Functionality Guide* for generating a mask file. **Mask by file** allows selecting an existing mask file



which can be inspected with the  button. Note that each input file has its own mask definition

## Registering Dynamic Images to a Reference

In the case of a dynamic **INP** series it is recommended to proceed as follows:

- 1) Check whether there is motion in the data. If there is, a *motion correction* (on page 36) should first be applied.
- 2) Calculate an average image from some dynamic frames. Typically, early PET frames will result in a perfusion-related image which provides a good pattern for registration to an MR image.
- 3) Match the average image to the reference.
- 4) Apply the resulting transformation to the dynamic series, as described *above* (on page 21).

## Image Loading

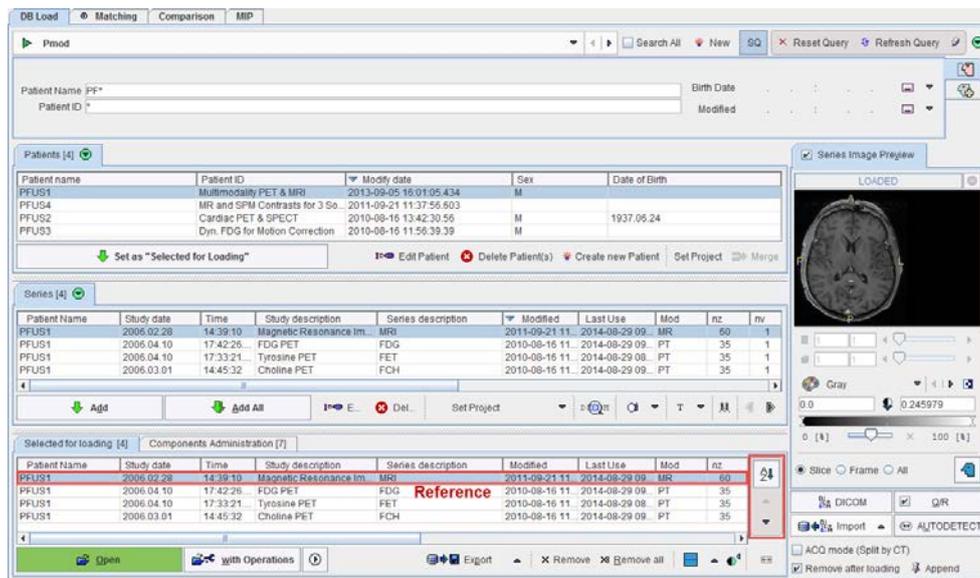
There are several alternatives for loading images in PFUSIT.

### Step-wise Loading

If the user directly starts working on the **Matching** page image loading is straightforward: All images loaded on the **INPUT** sub-page are treated as the input images for registration. The image which is loaded on the **REFERENCE** sub-page serves as the registration reference. Only one reference image is supported, a successive loading will overwrite the current reference.

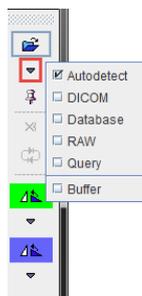
### Loading from DB Load Page

The loading of multiple images is supported when using the **DB Load** page. The basic rule is, that the first entry in the **Selected for loading** list is treated as the reference, all others as input images. Note the arrow to the right of the list for changing the list order, and the button for enabling alphabetical sorting by the column headers.

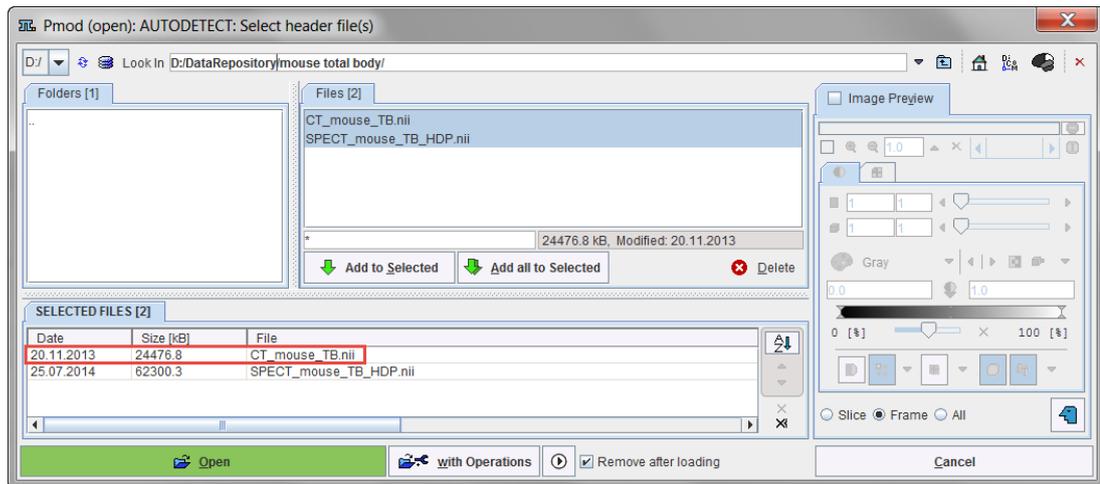


### Loading from Lateral Taskbar

Loading from the taskbar works similarly, but supports different image data formats.



Illustrated below is **Autodetect** format loading. The first entry in **SELECTED FILES** will be loaded as the reference, the following entries as input images.



## Reference Defaults

The *configuration* (on page 12) facility allows establishing convenient defaults for multi-modality situations.

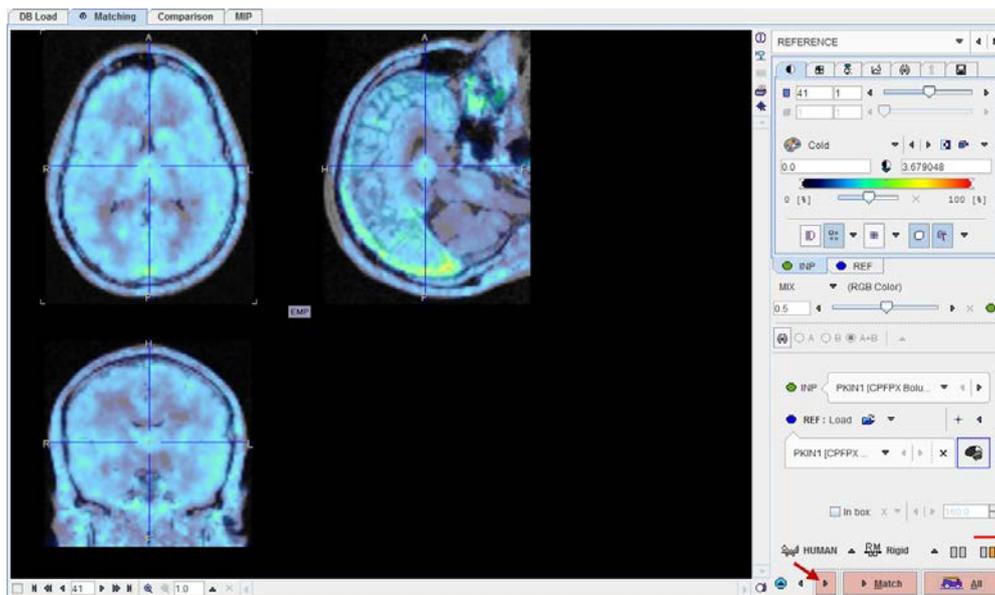
Use as reference:  CT for PET/CT  CT for SPECT/CT  MR for PET/MR pair.

If the modality is encoded in the data format (DICOM, Database), this configuration will take precedence over the order in the loading list and the anatomical image will always appear as the reference. Hence it is not necessary any more to bring the anatomical reference to the first position in the selection list.

## Already-matched Workflow

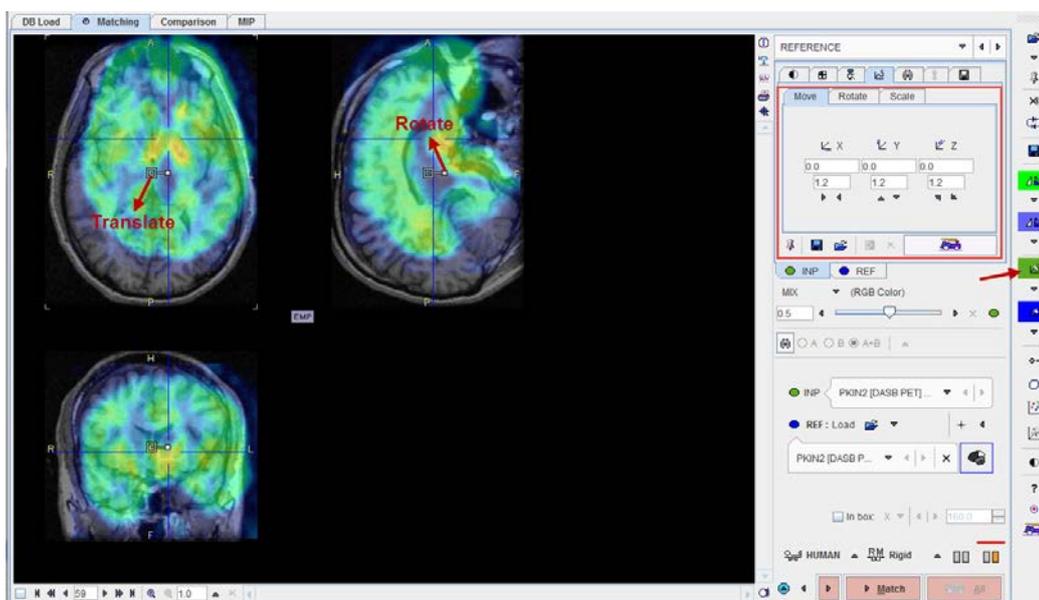
The simplest case is the situation that the input and the reference images are already registered. Examples are images from hybrid acquisitions, images like parametric maps derived from a common data set, or images arising in a standard template space.

In this case, the images should already be aligned on the **REFERENCE** sub-page after loading. Please simply proceed to the post-processing options using the "Already matched" button indicated below.



### Manual Interactive Matching Workflow

If the loaded images don't appear to be aligned on the **REFERENCE** page select the **INP** reslicing shortcut in the lateral taskbar. Then, shift and rotate the **INP** image until it aligns with the **REF**. Shifting can be done by entering offsets in the **Move** panel, or dragging the open rectangle directly in the images. Rotation angles can be numerically entered in the **Rotate** panel, or the image interactively rotated by dragging the small filled rectangle in the image overlay. Adjust the **INP** image position and orientation until the anatomy in both images is aligned.

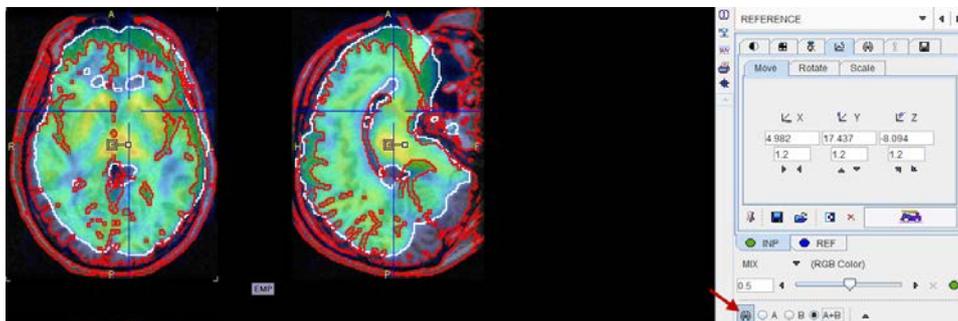


### Evaluating the Alignment

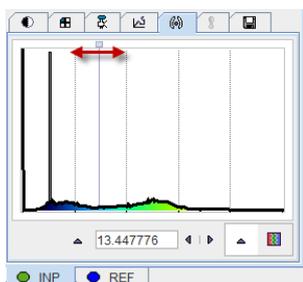
The evaluation of the alignment is a subjective and iterative process. It is recommended verifying the result in all plane orientations and using different fusion techniques such as

iso-contours and overlay windows which are described in more detail *separately* (on page 81).

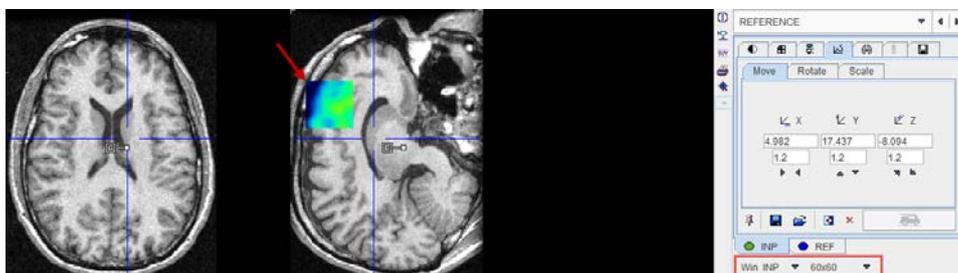
Often the iso-contours are helpful because they highlight boundaries which might be common in both images.



If the contouring level is not appropriated, adjustments can be made on the corresponding panels of the **INP** and **REF**.

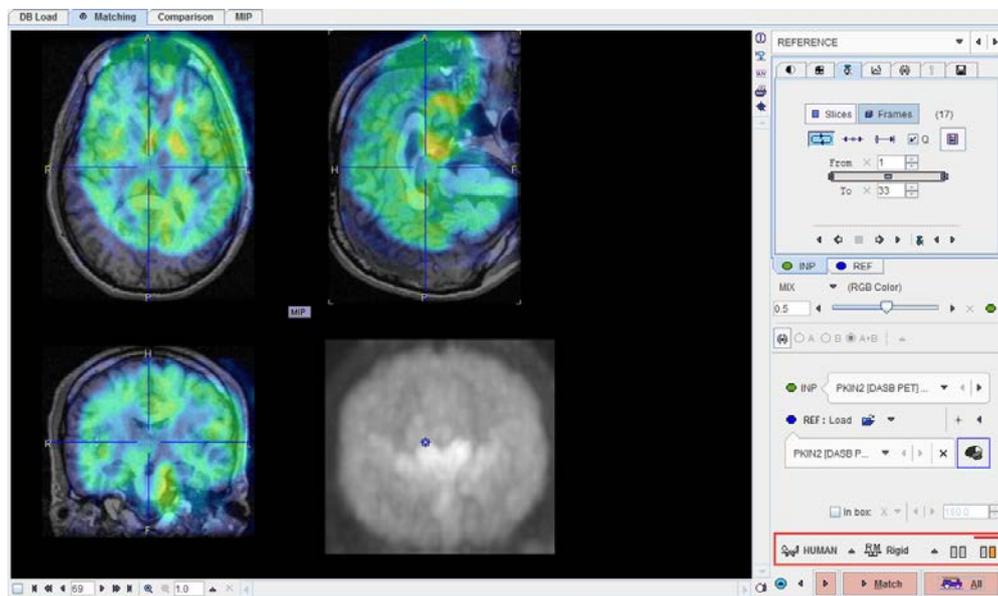


An alternative method for checking the boundaries is with the **Win INP** fusion method. The display only shows the **REF** image, but when the left mouse is clicked in the images the **INP** content at this location is shown in a window of configurable size.



## Rigid Matching Workflow

The rigid matching approach is applicable for images of the same subject if there is no significant deformation in the anatomy of the target tissue. Note that an appropriate initialization is required so that the image volumes overlap sufficiently. Make sure that the proper species is selected (e.g. **HUMAN**), and the registration method is set to **Rigid** as illustrated below.

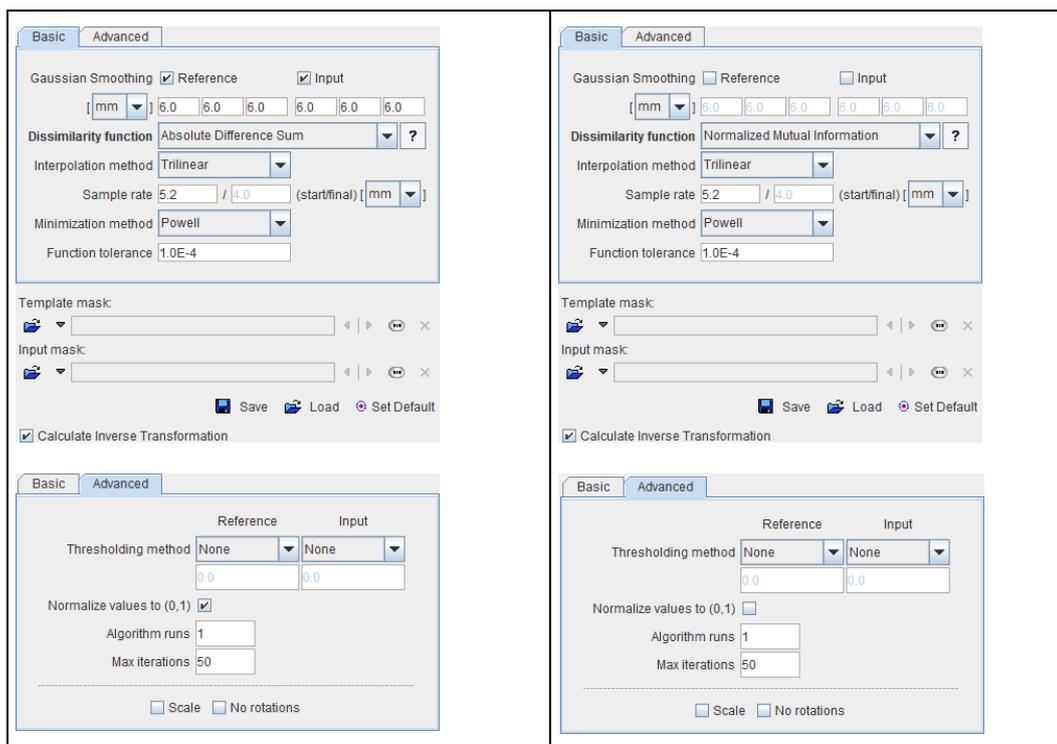


### Rigid Matching Parameters

The **Rigid** matching algorithm uses several parameters, which are hidden from the user interface. There are two presets,  for matching images with similar values (same-modality situation), and  otherwise (cross-modality situation). The red bar above the buttons indicates which preset is active.

To enable a preset and edit the parameters please select one of the two buttons. A dialog window opens and shows the current configuration. The **HUMAN** default settings are shown below and can always be restored with the **Set Default** button.

<input type="checkbox"/>	<input type="checkbox"/>
--------------------------	--------------------------



Note the differences in the **Dissimilarity function**, the **Gaussian Smoothing**, and the **Normalize values**. The parameter details are described in a separate *section* (on page 70).

**Important:** The parameter settings are serialized. The next time **Rigid** matching is selected for the same species, the last parameter configuration will be applied. This is particularly relevant for the *Matching without Interaction* (on page 44) functionality.

### Starting the Registration

Please use the **Match** button to start the registration of the currently selected **INP** series to the **REF** series. In the case of multiple **INP** series the  is also active. It serves for matching each **INP** series to the **REF** applying the same registration parameters. In the case of a dynamic series one would rather perform the registration with a frame average, and use **Apply Current Transformation to All** on the **MATCHED** sub-page to bring the dynamic series also into alignment.

### Motion Correction Workflow

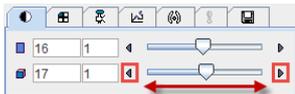
Motion correction can only be applied to a dynamic input series. The aim is to correct for patient motion which is visible in the images and bring the anatomy into agreement across all the dynamic frames. The implementation uses the rigid matching approach, so it is only suitable when the motion doesn't result in deformation of the target tissue. Note that most appropriate way for PET and SPECT data is to correct motion during the image reconstruction, because otherwise the attenuation correction will not be fully accurate.

Please first load the dynamic images on the **INPUT sub-page** (on page 13) and make sure the **Species** setting is correct. Proceed with the motion correction button.

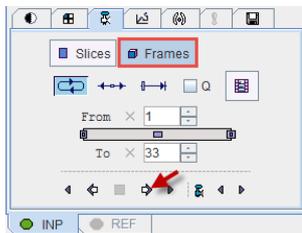


### Image Inspection

On the **REFERENCE sub-page** (on page 16) inspect the motion in the data in order to see where the motion starts. This can be achieved by stepping through the frames using the slider

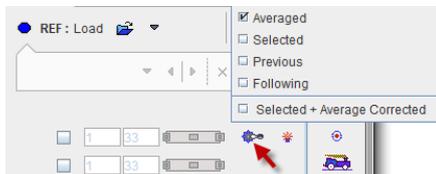


or by playing a cine across time



### Reference Image for Motion Correction

There are various approaches for using rigid matching in the context of motion correction. One approach is to use **REF Load** for loading a suitable image to which the frames of the dynamic series are rigidly matched. Alternatively, a reference can be created out of the series itself in different ways with the button as illustrated below.



The choices work as follows:

**Averaged**  5 10

An average image is calculated from a range of frames and serves as the reference for the correction of the frames. The average is calculated from the sub-range defined by the upper selection range, which should only have negligible patient motion. Use the button for the actual reference creation.

**Selected** [Frame selected in display]

The frame shown in the display will serve as the reference. Please note that if the pattern in the image changes significantly over time it will be difficult to motion correct successfully using a single frame. The use of markers is a way to potentially alleviate this problem. Use the button for the actual reference

creation.

### Previous

[ Previous frame ]

In this mode, motion correction matches each frame to its previous with the advantage that gradual pattern changes are less of a problem. On the other hand, successive matching errors might accumulate with this strategy. The final transformation per frame is obtained by combining the transformation matrices of all preceding frames. In this way multiple interpolations in the final image reslicing are avoided.

### Following

[ Following frame ]

This is the same principle as the **Previous** mode, but the method works from the last frame in the selection through the earliest one.

### Correction Range

Optionally, configure a sub-range, wherein motion correction will be performed.



A reason to exclude a range of frames may be the lack of signal in the initial frames, and/or frames with a short acquisition duration during which patient motion is less likely. Excluded frames will be copied to the corrected series without changes, and the correction matrix of these frames will contain zero for all rotations/translations.

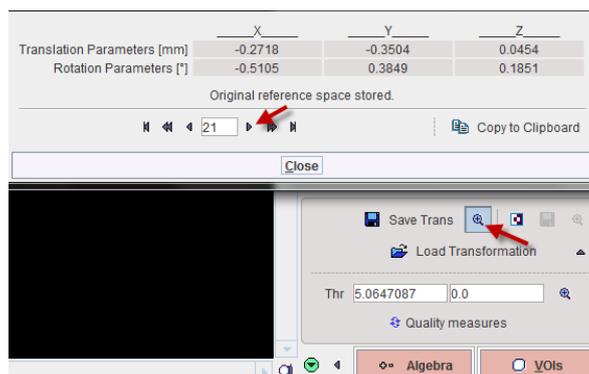
### Matching Parameters

Motion correction uses the rigid matching technology and has the same two parameter presets and (default). The red bar above the buttons indicates which preset is active. As described for *rigid matching* (on page 35), the parameters can be tailored if needed.



### Starting the Motion Correction

Please use the **Motion** button to start the process, and inspect the results which are shown on the **MATCHED** sub-page. The resulting transformation is a sequence of rigid transformations as illustrated below.



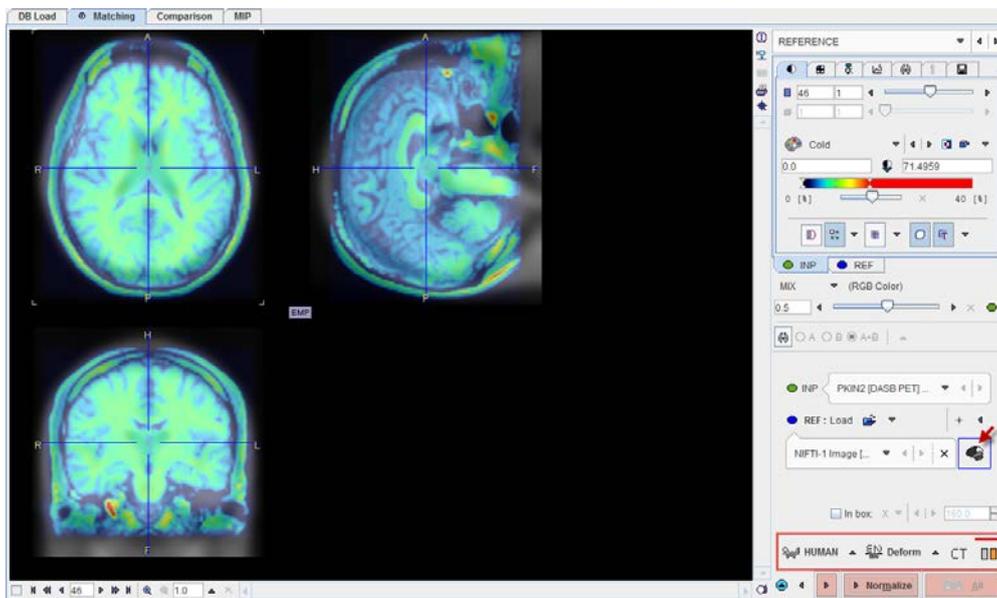
## Elastic Deformation Workflow

The deformable registration approach is mainly suited for the stereotactic normalization of brain images to appropriate template images which can be loaded with the  button. However, application to different scenarios is also possible.

Please first load the input images on the **INPUT sub-page** (on page 13) and make sure the **Species** setting is correct. Proceed with the deformable registration button.



On the **REFERENCE sub-page** (on page 16) load the reference image either with **REF: Load**, or using the shortcut  to load an *in-built template* (on page 73).

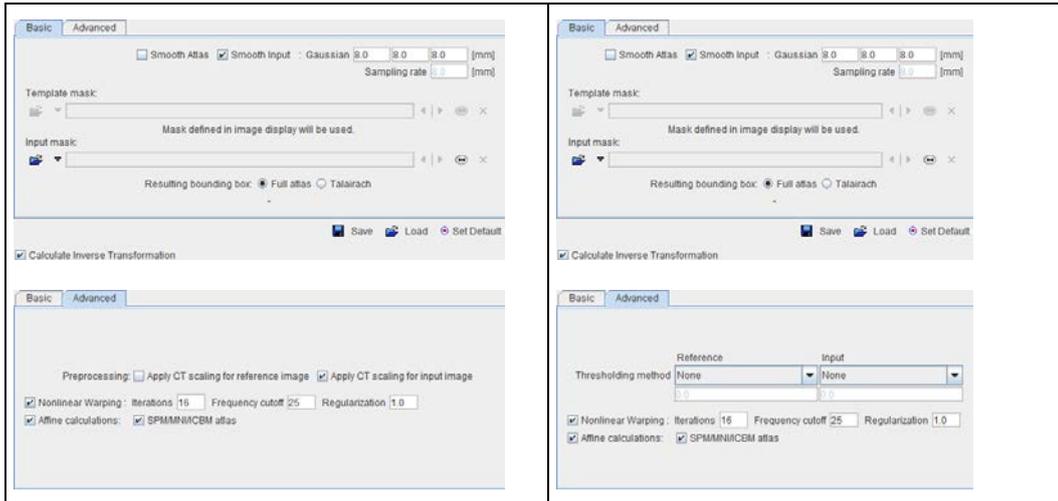


### Deformable Matching Parameters

The **Deformable** matching algorithm uses several parameters, which are hidden from the user interface. There are two presets, **CT** for the normalization of CT brain images, and  otherwise. The red bar above the buttons indicates which preset is active.

To enable a preset and edit the parameters please select one of the buttons. A dialog window opens and shows the current configuration. The **HUMAN** default settings are shown below and can always be restored with the **Set Default** button.

CT	
----	---



Note the **Apply CT scaling** options which transform the values in the CT image such that the contrast between bone and soft tissue is reduced and they are more similar to the usual anatomical images. The parameter details and the deformation method are described in a separate *section* (on page 75).

---

**Important:** The parameter settings are serialized. The next time **Deformable** matching is selected for the same species, the last parameter configuration will be applied. This is particularly relevant for the *Matching without Interaction* (on page 44) functionality.

---

### Starting the Registration

Please use the **Normalize** button to start the registration of the currently selected **INP** series to the **REF** series. In the case of multiple **INP** series the  is also active. It allows matching each **INP** series to the **REF** applying the same registration parameters.

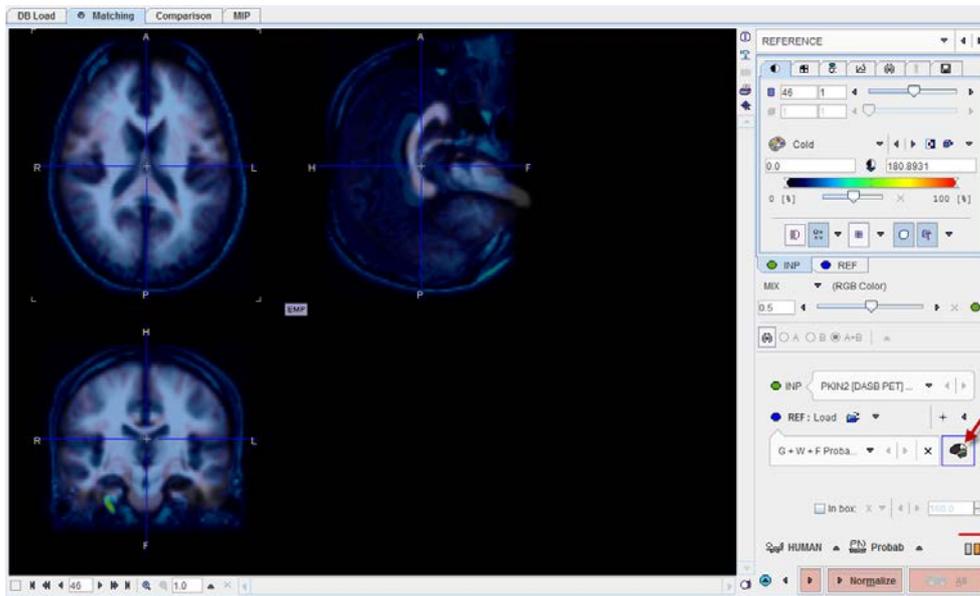
## Probability Maps Normalization

The probability maps normalization approach is an implementation of the Unified Segmentation procedure in SPM8 developed by Ashburner et al [11 <http://dx.doi.org/10.1016/j.neuroimage.2005.02.018>]. It is only applicable for stereotactic normalization of T<sub>1</sub>-MRI brain images to appropriate template images which can be loaded with the  button.

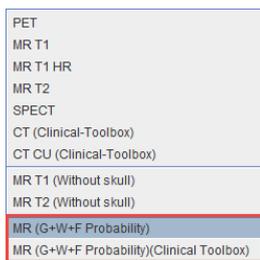
Please first load the T<sub>1</sub>-MRI brain image on the **INPUT sub-page** (on page 13) and make sure the **Species** setting is set to **HUMAN**. Proceed with the probability maps normalization button.



On the REFERENCE *sub-page* (on page 16) load the reference image either with the shortcut  to load an *in-built template* (on page 73).

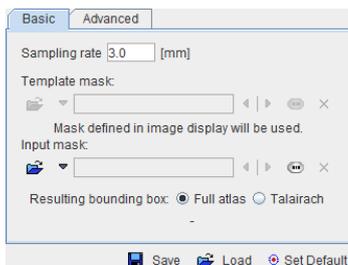


The two relevant templates are the MR (G+W+F Probability) for younger and MR (G+W+F Probability)(Clinical Toolbox) for older subjects.



### Probability Maps Normalization Parameters

The normalization algorithm uses several parameters, which are hidden from the user interface. With the  button they can be shown and edited.



The parameter details and the deformation method are described in a separate *section* (on page 75).

**Important:** The parameter settings are serialized. The next time **Deformable** matching is selected for the same species, the last parameter configuration will be applied. This is particularly relevant for the *Matching without Interaction* (on page 44) functionality.

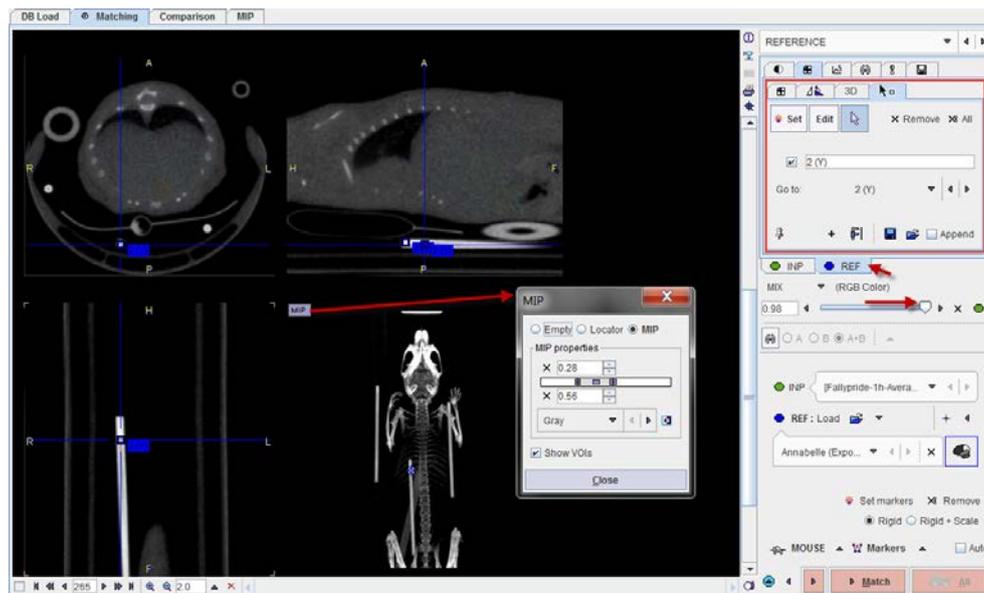
### Starting the Registration

Please use the **Normalize** button to start the registration of the currently selected **INP** series to the **REF** series. In the case of multiple **INP** series the  is also active. It allows matching each **INP** series to the **REF** applying the same registration parameters.

### Marker Matching Workflow

If the automatic matching rigid matching is not working properly for a combination of images, the use of fiducial markers should be considered. In the example below three capillaries filled with activity were attached to the bed of the mouse, and then imaging performed on separate CT and PET systems. The capillaries are clearly visible in the CT, whereas the activity in the inner of the capillaries is picked up by PET. The tubes were plugged by a small plasticine plugs, which can be seen by zooming in on the CT image. Consequently, the end of the capillary activity in PET should correspond to end of the plug in CT.

For marker matching, the user explores the two image sets and marks corresponding locations, i.e. markers. A transformation is then calculated which brings the two spatial arrangements of markers into optimal agreement.

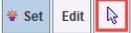


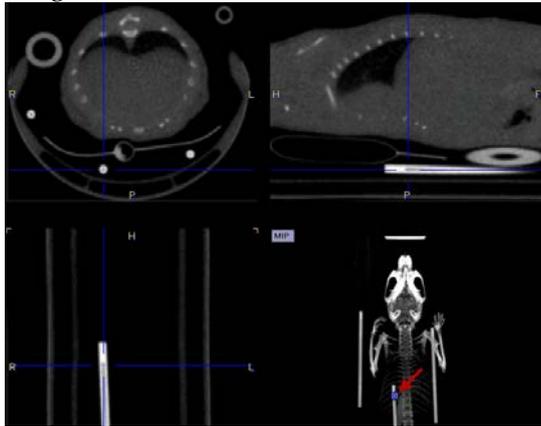
Please first load the input images on the **INPUT sub-page** (on page 13) and make sure the **Species** setting is correct. Proceed with the markers matching button.



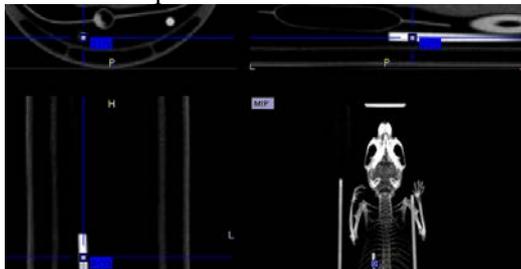
On the **REFERENCE sub-page** (on page 16) load the reference image with the **REF: Load** button. Next start landmark definition with the **Set markers** button.

### Marker Definition for the Reference

- 1) Shift the fusion slider fully to the right, so that only the **REF** image is shown.
- 2) Select the **REF** panel.
- 3) Note the panel for markers definition which is already open. The buttons  define the behavior when clicking into the image. With **Set** active, each click into the image generates a marker. With **Edit** active, markers can be dragged to different locations. The third button is the neutral mode for triangulating the images until the marker position has been found.
- 4) Enable the MIP image in the 4th quadrant with the **MIP** button indicated above and adjust the color thresholds such that the markers are well visible.
- 5) Click at the landmark position in the MIP image and then adjust the plane locations by triangulation or plane scrolling (mouse wheel) until the exact position is seen in the images.



- 6) Enable the **Set** mode and click at the landmark position in one of the plane images. A numbered square indicator of the landmark appears



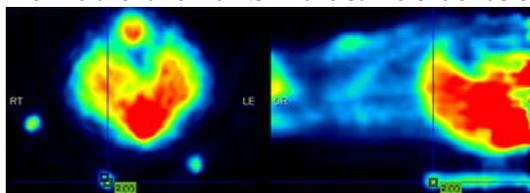
- 7) Switch back to the neutral mode for triangulating the next landmark position, and then define the second landmark in **Set** mode.
- 8) It is recommended to repeat landmark definition for more points in order to improve the accuracy. The landmarks can easily be triangulated later by selecting a marker in the **Go to** list:



## Marker Definition for the Input

The next task is the definition of the corresponding landmarks for the input image.

- 1) Shift the fusion slider fully to the right, so that only the INP image is shown.
- 2) Select the INP panel.
- 3) Define the landmarks in the same order as described above.



## Matching Parameters

As the image content is not used for the registration, only parameter is whether the transformation is strictly rigid, or whether a scaling is allowed (**Rigid + Scale** option). The **Auto** option enables immediate registration as soon as markers are defined.



## Starting Markers Matching

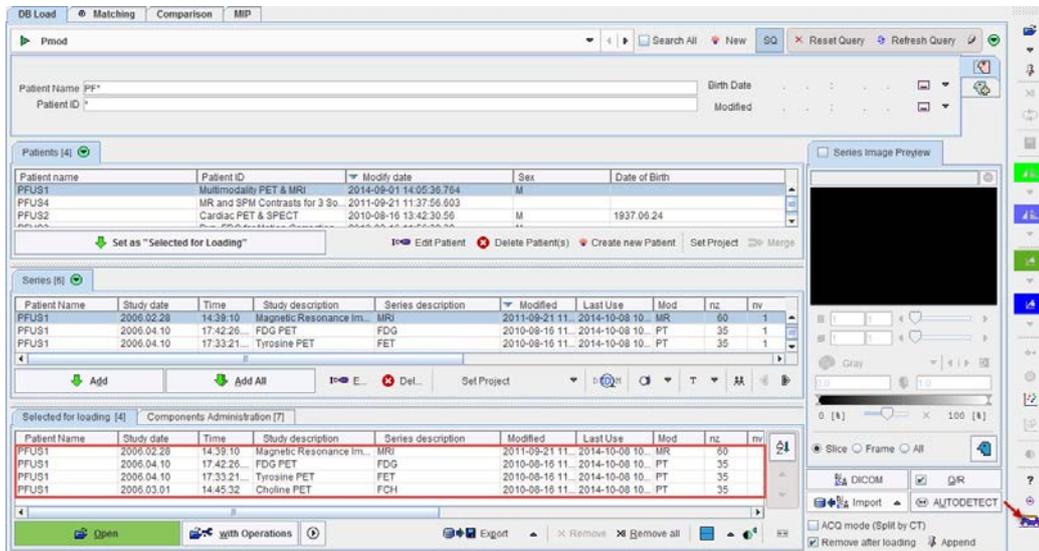
Please use the **Match** button to start the registration of the two sets of landmarks.

## Matching without Interaction

In some situation it is not necessary to step-wise run through the matching. For instance, if a similar matching task is repeated and it doesn't require any interactive adjustments, the data can simply be selected and the processing started.

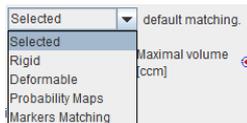
## Data Definition

The automatic approach requires that the images reside in the database. They have to be brought to the **Selected for loading** area, and then the matching can be started with the  button in the lateral taskbar as illustrated below.



## Registration Method

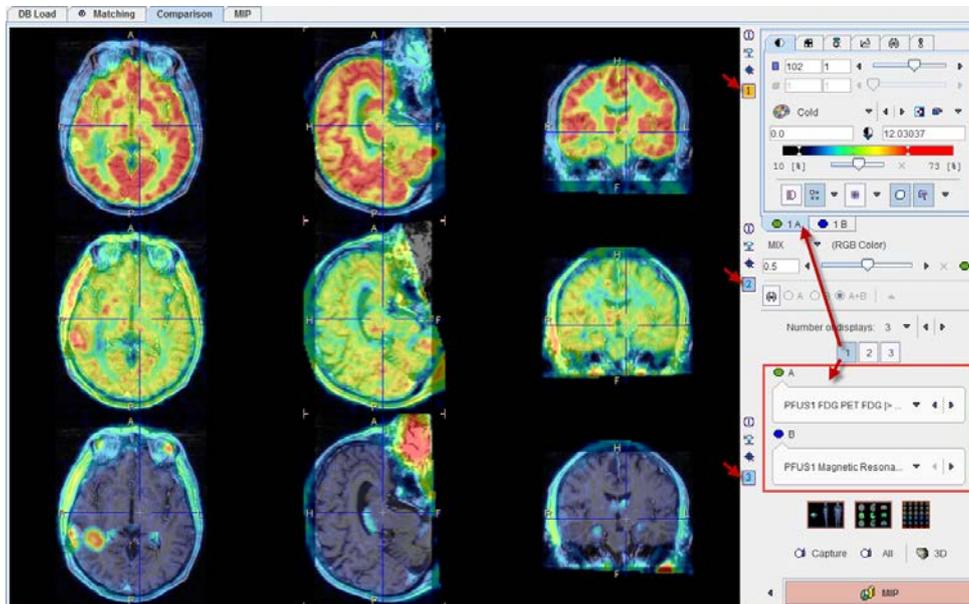
The applied registration depends on **default matching** method specified in the *configuration* (on page 12).



With **Selected** the most recently applied registration is used with all its parameter settings, whereas for the other choices the default species-dependent parameters will be applied.

# Comparison Page

The **Comparison** main page allows to view fused images in varying layouts.



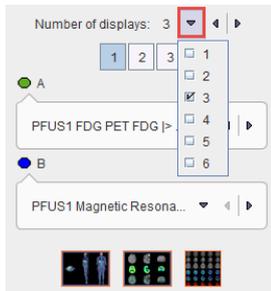
Note the  All button in the lower right for creating a capture of the arrangement in the display area.

## Layouts with Multiple Rows

The image display can be configured for up to 6 rows, each showing a fused image.

### Layout Configuration

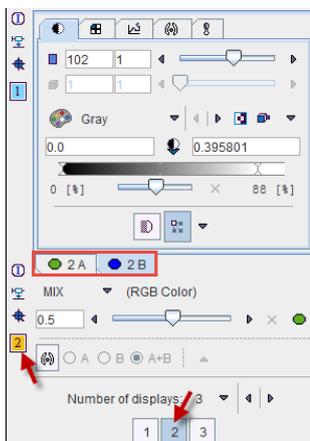
The **Number of displays** selection serves for defining the number of rows into which the display area is split.



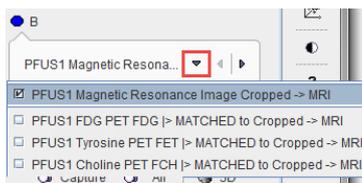
### Image Selection

The fused images shown in a particular row are configured with the **A** and **B** selections. Initially, the reference series is set as **B** series for all rows, although with separate display controls. This means that changing the display characteristics in one row has no effect on the reference display characteristics in the other rows.

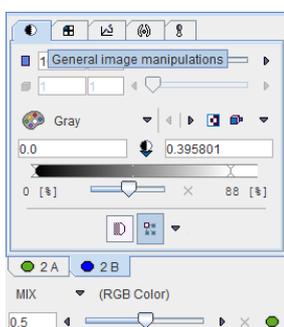
To change the fused images in a row the row has to be activated first. This can be done by clicking the number to the right of the image, or by selecting the number in the button row below **Number of displays** as illustrated below.



The number next to the selected row is highlighted in yellow (e.g. **2**), and the image tabs are labeled accordingly with the number (e.g. **2A** and **2B**). Next, any series can be selected for the **A** and **B** tabs using the corresponding selections.

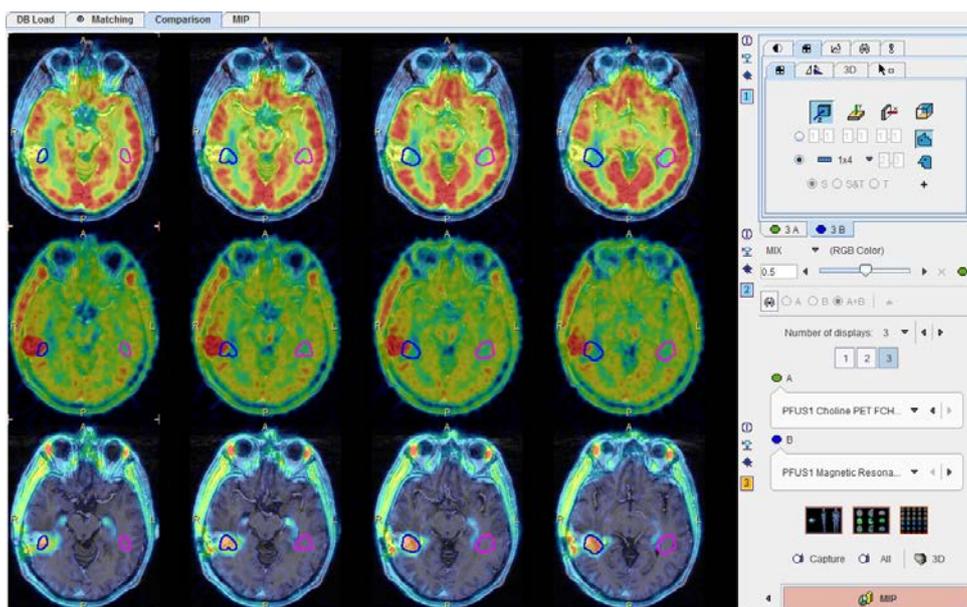


Thereafter, the display characteristics of the two series as well as their fusion can be tailored in the upper right area.



### Layout Changes

While the orthogonal planes are the default layout which is appropriate for approximately cubic data volumes, the layout can be changed to only show a number of axial, coronal or sagittal slices as illustrated below. The layout change to any image will immediately be applied to the images of all rows, since they are always synchronized.



### Layout Presets

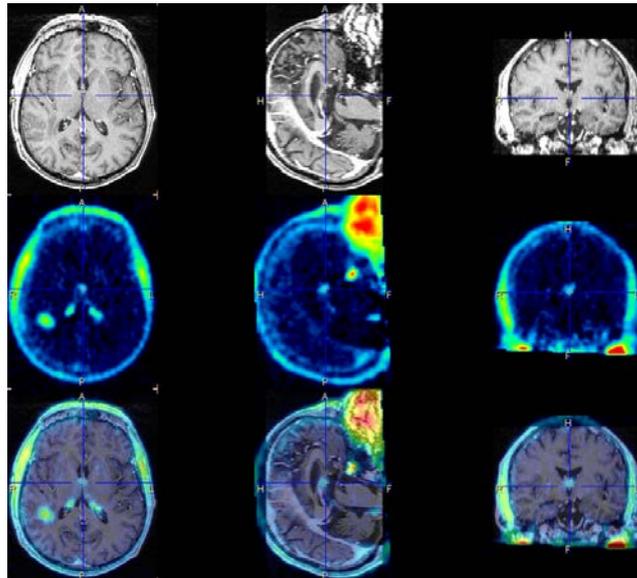
There are presets for some popular layouts in the lower right.



Switches to a single-row whole-body layout as described *below* (on page 50).



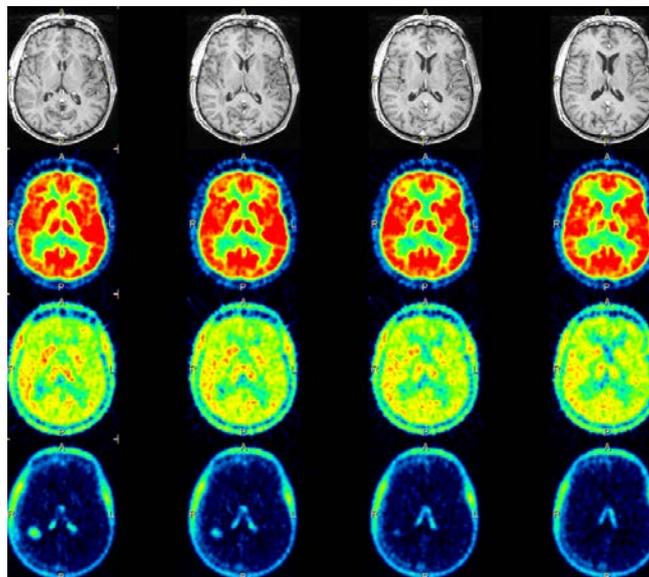
Switches to a three-row layout which mimics the behavior of the legacy fusion tool: Row 1 shows the reference, row 2 the matched input, and row three their fusion.



This appearance is obtained by selecting the matched input and the reference as images **A** and **B**, respectively in all rows. Further, the fusion slider is set to the right, the left and the middle in the rows one, two and three, respectively.



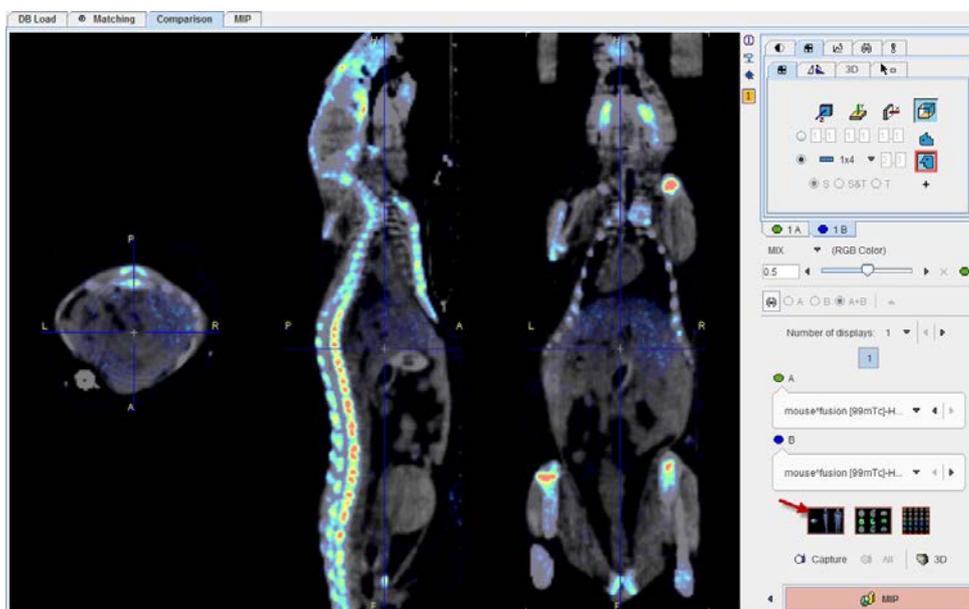
This preset arranges all available images in a separate row and shows them as axial slices. the number of rows therefore depends on the number of loaded and matched images, including the reference.



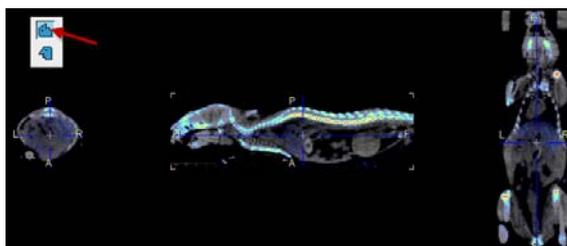
The appearance is obtained by selecting the series sequentially as image **A** in all rows, and setting all fusion sliders to the left.

## Whole-body Layout

The whole-body preset aims at a better use of the display area for non-cubic image volumes which arise in whole-body imaging. It works best in the single-row layout, but can also be used with multiple rows.



Note the non-standard orientation selection in the layout tab which is enabled by the preset. The effect is that the sagittal slice is arranged in parallel to the coronal slice. Otherwise the arrangement would look as illustrated below.



### Action Button

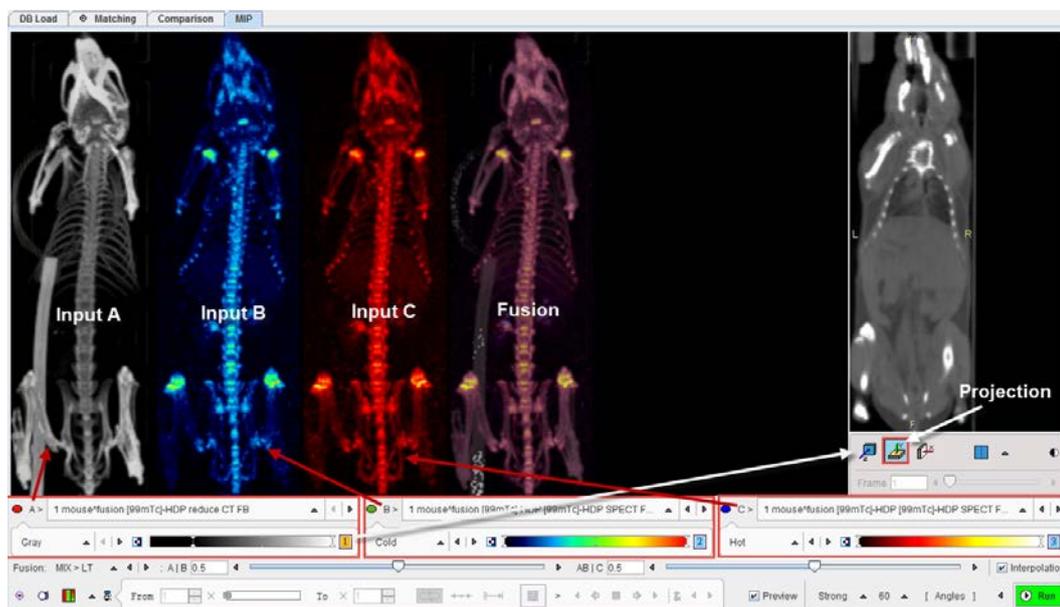
The only action button on the **Comparison** page



transfers the images to the **MIP** main page for creating rotating fusion Maximum Intensity Projection images.

## MIP Page

The MIP main page for generating Maximum Intensity Projection cines has the layout illustrated below.

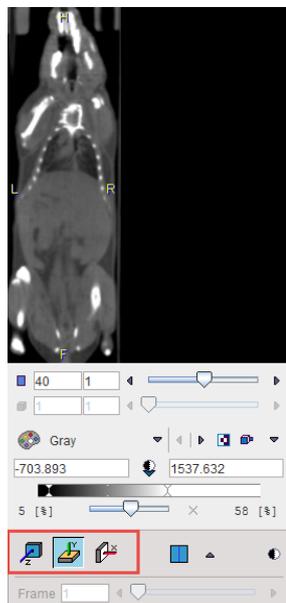


- ▶▶ The upper left image area shows a preview of the input images (**A**, **B**, **C**) and their fusion. Each input image has a color bar associated to adjust the image coloring. The upper right area serves for defining the projection direction, coronal in the example above.
- ▶▶ The fusion image is obtained by first fusing **A** and **B**, and then fusing the result with **C**. The mixing is defined by the two corresponding **Fusion** sliders **A | B** and **AB | C** below the colorbars.
- ▶▶ The control of the MIP characteristics and movie generation is located at the bottom.

Please proceed as described below.

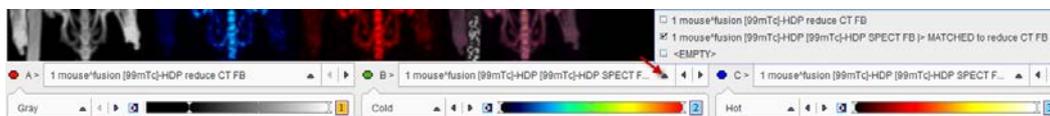
## Projection Direction

The MIP projection direction is set using the plane orientation buttons in the image area to the right. If necessary, the displayed image can be switched as illustrated above.



## Input Image Selection

Per default, the reference image is arranged as series **A**, and the matched input images in sequentially as series **B** and **C**. This arrangement can be changed using the series selection as illustrated below.



Note the EMPTY entries which are only available for **B** and **C** which allow excluding those images from MIP generation.

## Fusion Configuration

Each series has its own colorbar for adjusting the image presentation. The color choices should be such that the different image components can be distinguished in the fusion. As a default *configuration* (on page 12), the reference is shown with **Gray** colors.

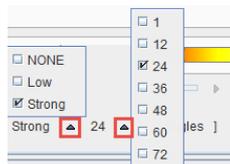


There are three fusion options available:

- MIXING** Simple weighted averaging of the RGB values, whereby the relative contributions are defined by the fusion slider.
- MIX>LT** Weighted RGB averaging considering only pixels which are above the respective lower thresholds, hereby removing the background. The relative contributions are defined by the fusion slider.
- MAXIMAL** With this setting no color averaging of the two inputs is performed. Rather, the bigger of the two contributions is selected.

## MIP Configuration

The **MIP** calculation performs a ray tracing from different angles and selects the maximal value on a ray for display in the MIP image. There are two MIP calculation parameters in the lower right.



- 1) Distance waiting with the settings **NONE** (default), **Low**, **Strong**. This option emphasizes objects closer to the observer by multiplying the value with a factor which decreases with distance.
- 2) Number of projection angles. The selection ranges between **1** and **72** angles. The more angles are chosen, the smoother the rotation cine will appear, however at the cost of longer preparatory calculations.

# Cine Control

## Image Display Selection

Per default, all the input MIPs as well as the fusion MIP are rotated. However, there is a choice in the lower left which allows showing subsets of these images.



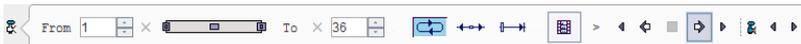
- ABC+F Show the three input MIPs as well as the fusion MIP (default).
- ABC Show only the three input MIPs.
- Fusion Show only the fusion MIP.

## Projection Calculation

Calculation of the configured projections is started with the  button. After the calculation is completed, the rotation cine is immediately started.

## Cine Controls

The direction of the cine, the speed and the behavior after a rotation can be configured with the usual cine control elements.



If any of the image presentation options is activated, the cine stops. However, in most cases a projection recalculation is not required, so the rotation can be simply restarted.

## Maximizing the Display Area

In order to maximize the image area for watching the cine, the controls can be minimized with the show/hide taskbar button indicated below. They are recovered by activating the same button again.



## Movie Generation

In order to create a movie file, the  button has to be activated and then the cine started. A dialog window is shown for configuring the movie format **QuickTime**, **Animate GIF** or **DICOM**.

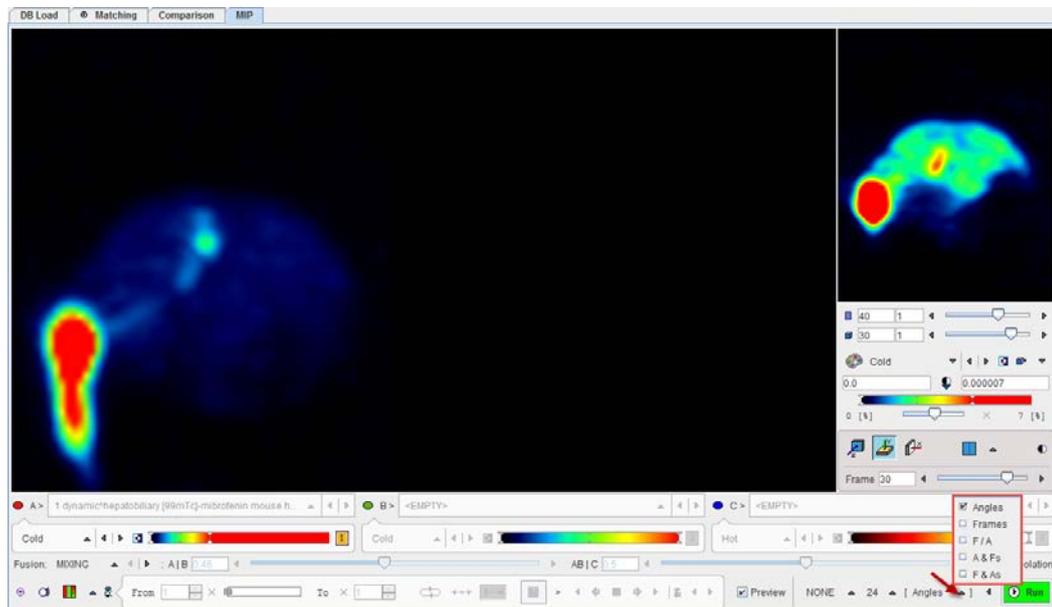


The movie will be assembled from JPEG files which are saved to a folder which is to be configured in the lower part. The JPEG images may be persistent, depending on the **Delete JPEG files** option.

After activating the **Start** button, the JPEG images corresponding to the different angles are written to disk and a dialog window opened defining a location and a name for the movie file.

## MIPs using Dynamic Series

In the special case that an image series is dynamic, there are additional control options.



Angles	Standard rotating MIP cine of the current frame.
Frames	MIP across all dynamic frame in the selected projection direction.
F/A	Mode in which the angle and the frame are simultaneously incremented. As a consequence, the number of angles equals the number of frames. The effect is, that the image changes during the rotation.
A & Fs	In this mode, the projection angle is fixed, while all frames are MIP rendered. This rendering is sequentially performed for all angles.
F & As	In this mode, a full rotation MIP is generated for a fixed frame. This rendering is sequentially performed for all frames.

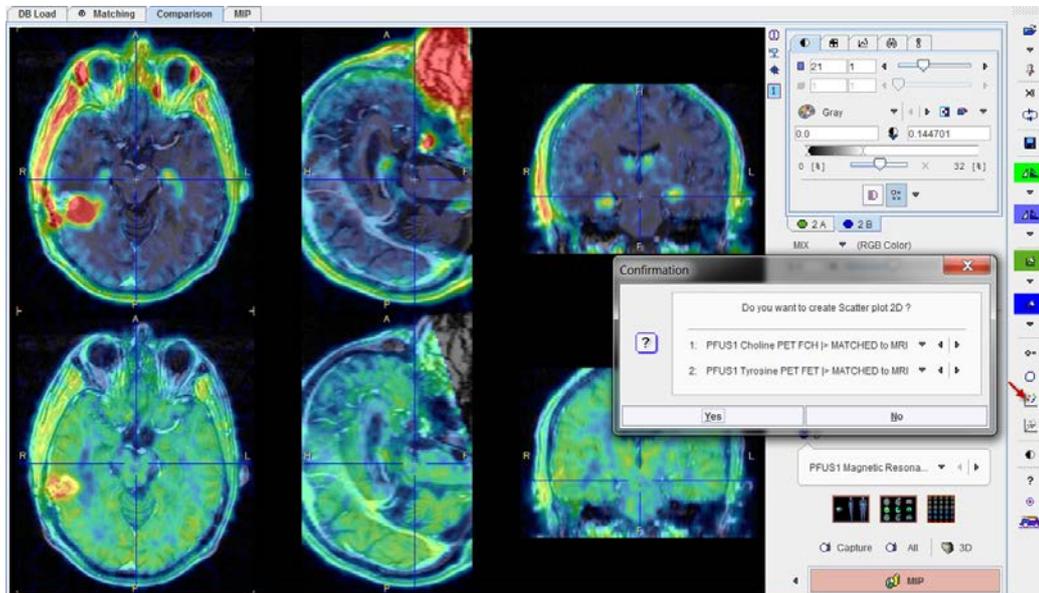
## Scatter Plots in 2D and 3D

The scatter plot functionality allows investigating the values of pixels in two or three image series.

## 2D Scatter Plots

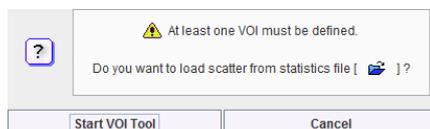
### Scatter Plot Generation

The best way to prepare the data of interest is arranging them on the **Comparison** main page in a two-row layout, and then activating the  button in the lateral taskbar.

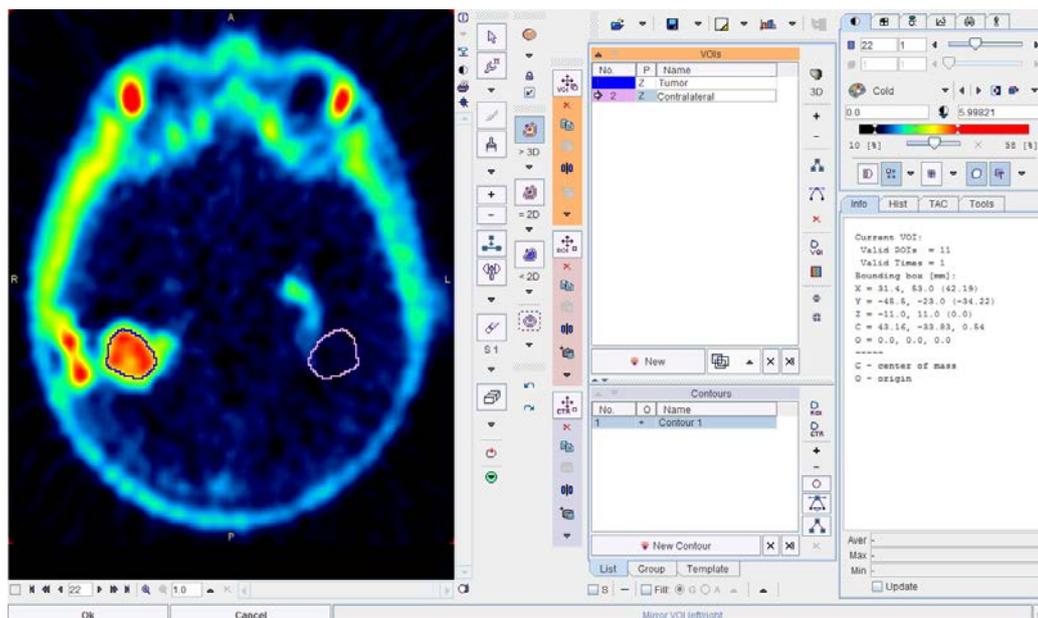


A dialog window is shown for configuring the 2 image series to compare. If the series selection is not yet proper, it can be corrected before proceeding.

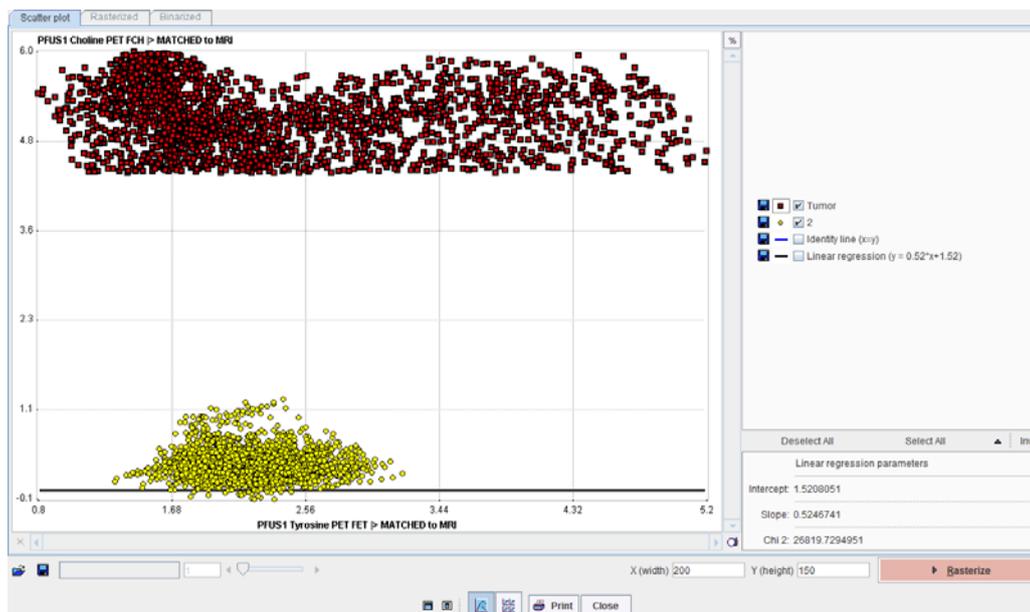
The scatter plot requires VOIs to exist in the first series. If this is not the case, a dialog window appears



and **Start VOI Tool** used to enter VOI definition. The usual PMOD functionality can be applied for defining a list of VOIs.



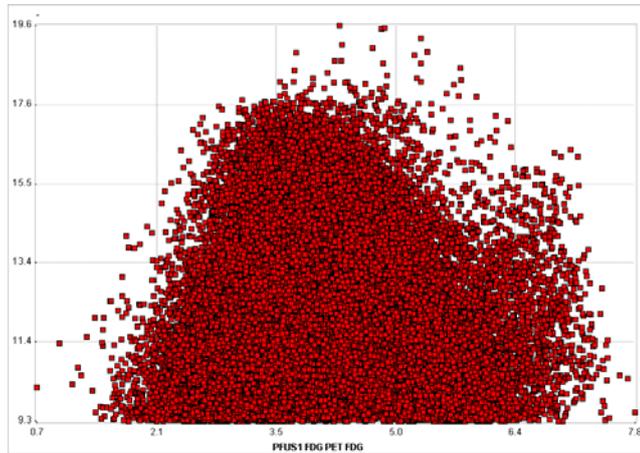
After confirming with **Ok**, the value of each VOI pixel is calculated in both series, and a scatter plot generated.



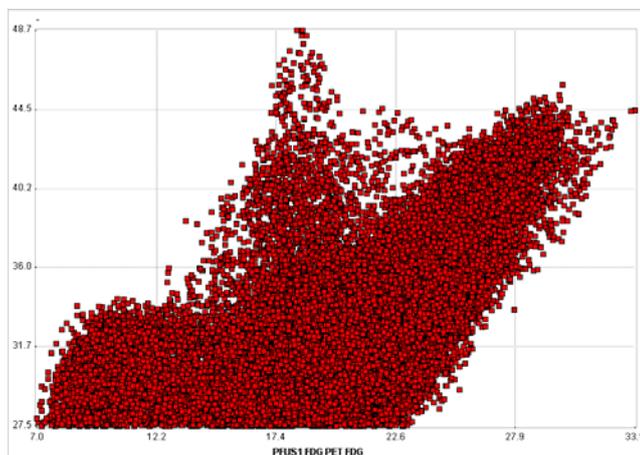
In this scatter plot, each point represents a VOI pixel. The color serves for labeling the different VOIs. The pixel value in the first series is plotted on the vertical axis, and the value in the second series in the horizontal axis. The actual data values can be exported by right-clicking into the plot and selecting **View Values** or **Save all Curves**.

## Shape Analysis of Scatter Plot

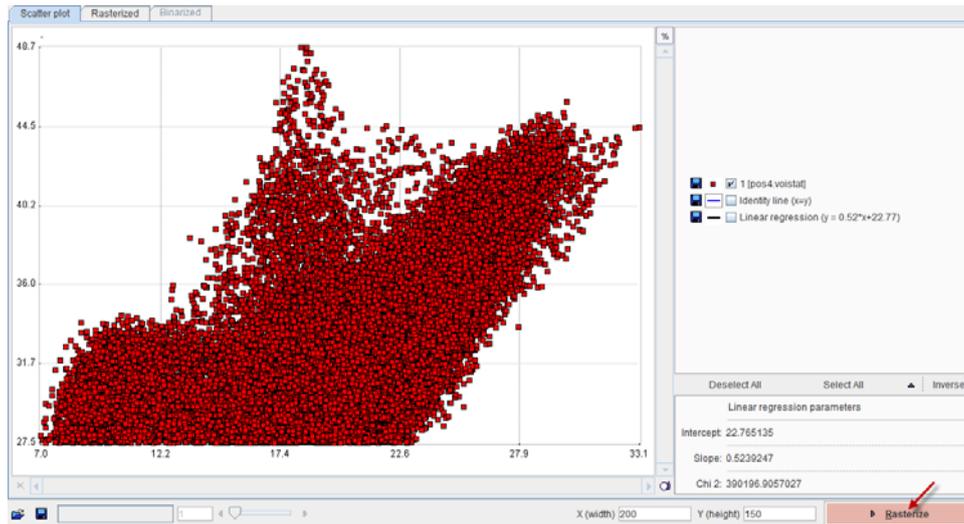
The shape of a scatter plot from a single VOI may contain diagnostic information. As an application example consider the case where the scatter plot of healthy controls is simple and symmetric



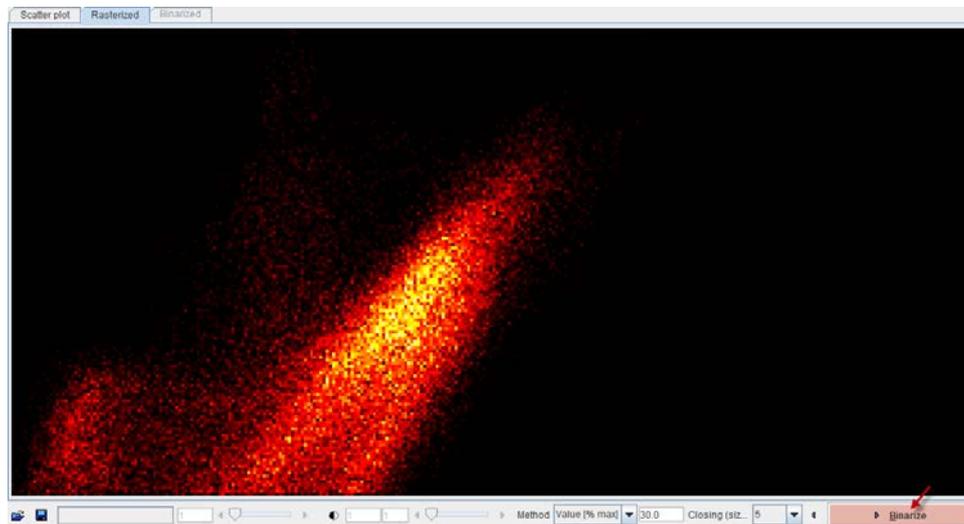
whereas patient scatter plots show distinct irregularities such as



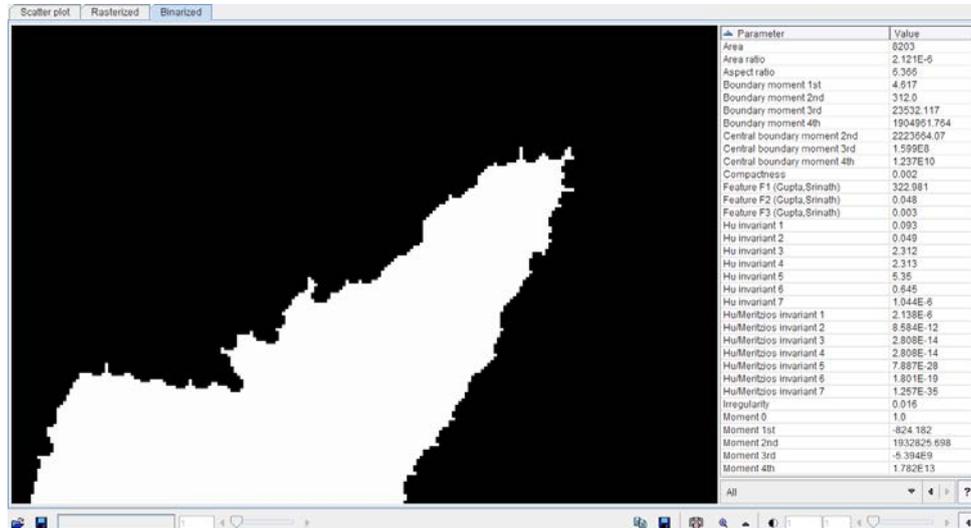
In order to perform the shape analysis, the scatter plot is converted into a binary image in two steps.



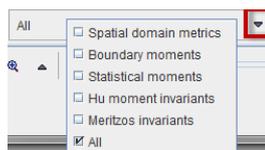
The **Rasterize** step creates an image from the scatter plot with dimensions **X(width)** and **Y(height)**. The value of each pixel in the generated image corresponds to the number of scatter points included in the pixel area.



A threshold value is applied to this image in order to convert it into a binary image. The threshold can be set by choosing one of the **Method** selections: **Optimal**, **Mean**, **Value [%max]**. In order to fill small inner holes, a **Closing** morphologic operation can optionally be set with structure sizes of 5 and 7 pixels. After applying **Binarize**, the result is shown on the **Binarized** panel. Note that the result will depend on the image dimensions as well as the threshold setting.



The binary structure whose shape is analyzed is shown to the left, and the resulting parameters in the list to the right. There are different metric types which can be selected from the list



Please refer to Haidekker [1] for details about the metrics.

As usually in PMOD, these metrics can be saved to the clipboard, to a file, and aggregated for later statistics using the



buttons. By comparing the classification results between populations of controls and patients, it may be possible to develop a criterion of disease.

## Reference

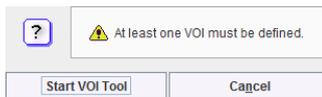
Haidekker, M. A. (2010) Shape Analysis, in Advanced Biomedical Image Analysis, John Wiley & Sons, Inc., Hoboken, NJ, USA.

## 3D Scatter Plots (P3D Option Required)

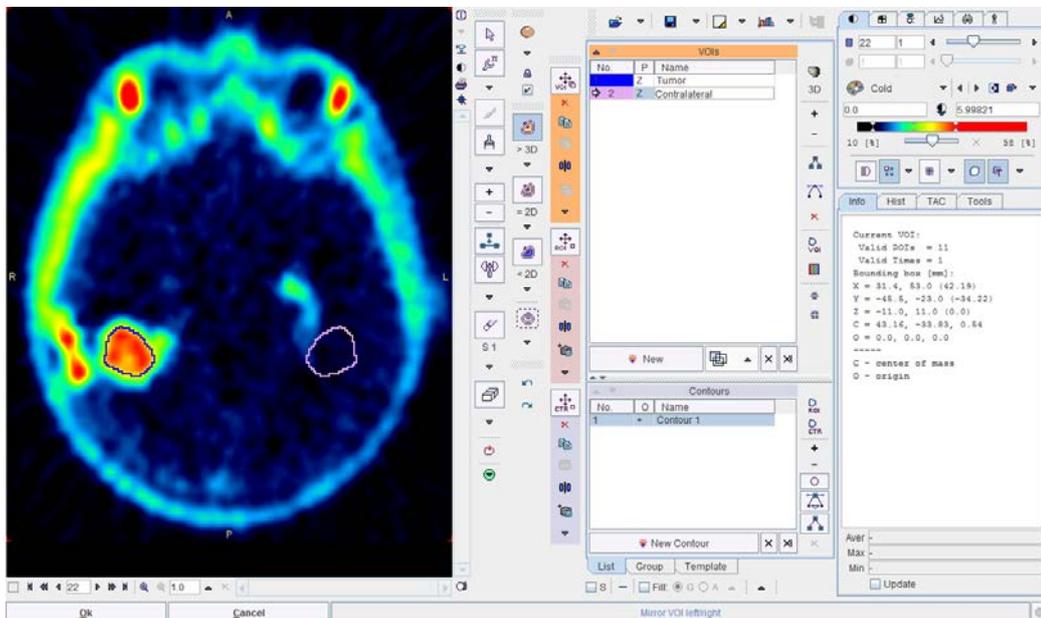
The 3D scatter plot works along the lines of the *2D scatter plot* (on page 59) and requires 3 registered images. After activating  from the lateral taskbar a dialog window appears for configuring the 3 image series to compare.



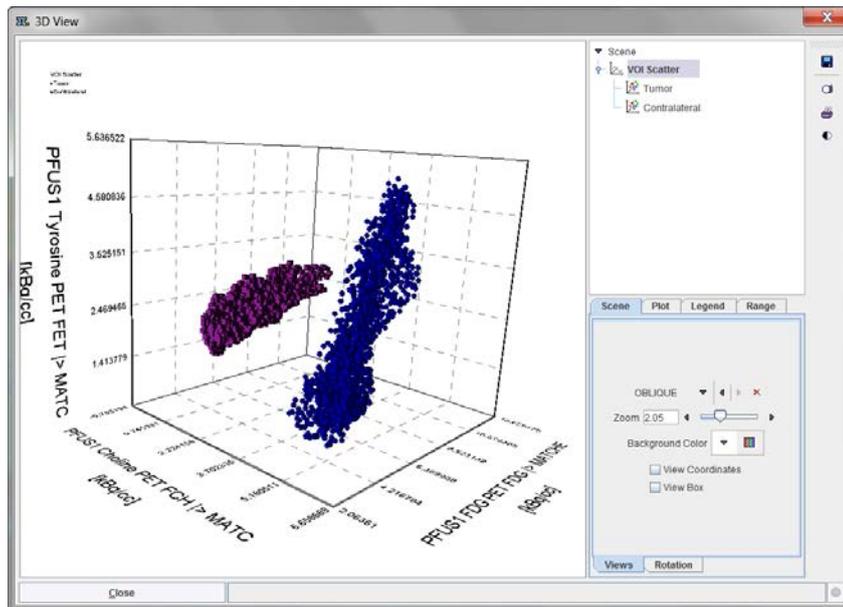
If the series selection is not yet proper, it can be corrected before proceeding. Note that the VOI of the first series will be used. If none exist, the following dialog window shows up.



**Start VOI Tool** starts VOI definition, and the usual functionality can be applied for defining a list of VOIs.



After confirming with **Ok**, the value of each VOI pixel is calculated in all three series, and a 3D plot generated.



In this scatter plot, each point represents a VOI pixel. The color serves for labeling the different VOIs. Please refer to the *P3D Users Guide* for information about the 3D rendering options.

## Results Saving

The actual data values can be exported by the save button in the lateral taskbar.

### Image Saving

### Transformation Saving

### Protocol Saving

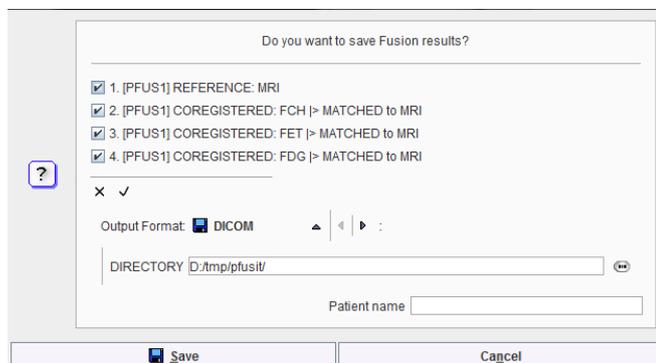
The best way for reproducing a registration result is to save the entire configuration with the **Save Protocol** button in the lower status line.



By simply replaying the registration using **Load Protocol**, the registration is recovered. Note that derived information such as VOIs or image algebra results are not included in the protocol and will be missing.

## Image Saving

Saving of images is started with the  button from the lateral taskbar. A dialog window is shown with the image list in the upper part, and an **Output Format** selection below. Depending on the format chosen, information such as the target directory, a prefix or the transfer syntax have to be specified.

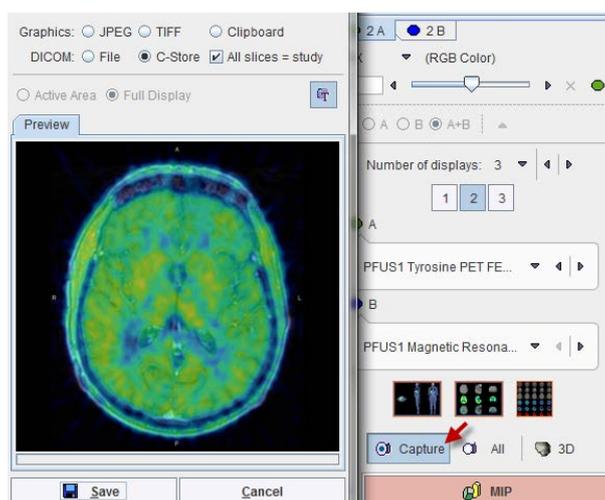


With the **Save** button, the selected images are finally saved.

## Fused Images Saving

In addition to saving the individual images, explicitly fused images can also be saved using the **Capture** button on the **Comparison** page. A dialog window appears for defining the format of the RGB images.

The **DICOM** output is of particular interest because with the **All slices** option it can create a full volume of fused images which can be saved for archival in a PACS system and inspected with any reviewing workstation. With the **File** the DICOM SC images are saved to disk, whereas the **C-Store** option supports direct network transfer to a DICOM server.



## Transformation Saving

The spatial transformations between the reference and the input images are saved from the **MATCHED** *sub-page* (on page 21). Note, however, that reproducing the final state may require the saving of more than a single transformation, because the reference image might have been reoriented as well.

## Registration Reference

## Rigid Registration Parameters

The settings available in the *rigid matching* (on page 35) panels allow fine-tuning the basic procedure in a multitude of ways. While there are successful settings (as the predefined ones), experimenting with these configurations may result in improved or faster matches in specific situations.

### Basic Parameters

<b>Smoothing window</b>	A Gaussian filter with configurable width in mm or pixels can be separately enabled for the <i>Reference</i> and the <i>Reslice</i> study. While this introduces an additional performance burden during start-up, iterations are less likely to get trapped in a local optimum with smoothed images.
<b>Dissimilarity function</b>	<p>This is the main definition of the matching algorithm. Note that a short explanation of the selected dissimilarity function can be shown with the ? button besides the selection. The selections are</p> <ul style="list-style-type: none"> <li>▶▶ <b>Absolute Difference Sum</b>, and</li> <li>▶▶ <b>Squared Difference Sum</b>: These are measures based on image subtraction and therefore require images of the same modality.</li> <li>▶▶ <b>Woods</b>: Partitioned Intensity Uniformity for the registration of MRI-PET images [7], [8].</li> <li>▶▶ <b>Mutual Information, Intra- and Cross-Modality</b>: Mutual information (MI) is a term from information theory [1]-[6]. Mutual information can be expressed as the sum of individual entropy terms of the random variables less their joint entropy. MI normalizes the joint entropy with respect to the partial entropies of the contributing signals. The dissimilarity function value is calculated from joint histogram of resampled reference and input data.</li> <li>▶▶ <b>Mutual Information (PV), Intra- and Cross-Modality</b>: In this MI variant, a partial volume interpolation algorithm is used as a part of the joint histogram construction. The histogram calculations are performed directly on the reference and input data. As a consequence the interpolation method selection in the matching parameters configuration has no relevance for this dissimilarity function.</li> <li>▶▶ <b>Normalized Mutual Information, Intra- and Cross-Modality</b>: The normalized MI variant also uses partial volume interpolation and additionally a normalization scheme proposed by Studholme [5]. This variant has become very popular in the recent years and performs well in many multi-modality situations.</li> </ul>
<b>Interpolation method</b>	Type of interpolation used during reslicing. Has an impact on speed, and may also influence convergence.
<b>Sample rate</b>	Density of resampling the original images during the matching process. Coarse sampling increases speed dramatically, but too coarse images may not allow any more for accurate matching. 6 or 8 mm is often satisfactory for MRI/PET matching.

A strategy with multiple searches can be implemented in combination with the **Algorithm runs** option: the first matching runs are performed at a coarse resolution, but the last one with a fine sampling rate for an accurate final match.

<b>Minimization Method</b>	<b>Powell</b> usually finds the optimal match faster than <b>Downhill Simplex</b> .
<b>Function tolerance</b>	Termination criterion for the iterations.
<b>Reference Mask</b>	Allows defining a mask for the reference image if none was created and/or set to the matching protocol after the reference image was loaded.  To discard the mask activate the <b>Clear file or directory</b> button 
<b>Input Mask</b>	Allows defining a mask for the input image if none was created and/or set to the matching protocol after the input image was loaded.  To discard the mask activate the <b>Clear file or directory</b> button 
<b>Save Parameters</b>	Save the parameter settings for later use.
<b>Calculate Inverse Transformation</b>	If the box is checked, the inverse transformation is also calculated once the matching completed.

### Advanced Parameters

<b>Thresholding method</b>	The image volume considered during matching can be restricted to a sub-volume by thresholding, eg. by excluding the image background. Note: selecting a background separation option reduces the time for dissimilarity function evaluation, but it may also worsen convergence, especially with a poor initial overlap of the segmented objects.  Absolute values can be defined when <b>User defined</b> option is selected as thresholding method.
<b>Normalize values to (0,1)</b>	When this box is checked, the image values are normalized to the numeric range [0,1]. Note that the operation is a scaling, not a binarization of the image. This transformation may be required when applying one of difference criteria, if the dynamic range of the matched images is different for instance because of different administered tracer doses.
<b>Algorithm runs</b>	A value > 1 configures multiple successive matching runs, whereby a run is started with the result parameters of the preceding run.
<b>Max iterations</b>	A maximal number of optimization steps can be configured to avoid "endless" looping.
<b>Scale</b>	If box is checked allows scaling the image during rigid matching

**No rotation**      If box is checked no rotation is performed during the automatic rigid matching.

## Normalization Templates

The normalization templates serve as the reference images for the elastic deformation algorithm. They usually represent the standard anatomy imaged with a certain modality. Currently the following brain templates for different modalities are available via the shortcut



PET
MR T1
MR T1 HR
MR T2
SPECT
CT (Clinical-Toolbox)
CT CU (Clinical-Toolbox)
MR T1 (Without skull)
MR T2 (Without skull)
MR (G+W+F Probability)
MR (G+W+F Probability)(Clinical Toolbox)

- PET** PET template provided with *SPM5*  
<http://www.fil.ion.ucl.ac.uk/spm/software/spm5/> (Statistical Parametric Mapping). It was constructed by Friston et al. at the Wellcome Department of Cognitive Neurology (University College London, UK) using Oxygen-15 water PET images of 12 normal subjects scanned in resting condition with eyes closed. The template is in MNI (Montreal Neurological Institute) coordinates.
- MR T1** T1 template provided with *SPM5*  
<http://www.fil.ion.ucl.ac.uk/spm/software/spm5/>. The image was derived from the ICBM152 image which represents the average of 152 healthy T1 brain images by reducing it to 2mm isotropic resolution and smoothing with an 8mm FWHM Gaussian filter. The original ICBM152 data originates from Alan Evans, MNI, Canada (ICBM, NIH P-20 project, Principal Investigator John Mazziotta).
- MR T1 HR**
- MR T2** The same as the **T1** above, but with the T2 MR images.
- SPECT** T1 template provided with *SPM5*  
<http://www.fil.ion.ucl.ac.uk/spm/software/spm5/>. It was created by Leighton Barnden et al from the Department of Nuclear Medicine at the Queen Elizabeth Hospital in Adelaide 22 normal female subjects. Each was scanned after injection of Tc-99m HMPAO on a triple head camera with ultra-high resolution fanbeam collimators.
- CT (Clinical Toolbox)** CT template for older population created from 30 healthy individuals with ages similar to what is commonly seen in stroke (mean 65 years). Developed for the *SPM8 Clinical Toolbox*  
<http://www.mccauslandcenter.sc.edu/CRNL/clinical-toolbox> by Rorden et al [10 <http://dx.doi.org/10.1016/j.neuroimage.2012.03.020>].

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<b>CT CU (Clinical Toolbox)</b>	<p>CT template as above but with the converted units (CU) which improves the contrast for soft tissue and CSF so that the normalization procedure works better.</p> <p>Conversion procedure : HU values -1000..-100 are mapped to 0..900, values from -99..100 are linearly scaled to the range 911...3100, and values <math>i &gt; 100</math> become <math>[i+3000]</math> [10 <a href="http://dx.doi.org/10.1016/j.neuroimage.2012.03.020">http://dx.doi.org/10.1016/j.neuroimage.2012.03.020</a>].</p> <p>CT images to be normalized with this template must also be converted with the same procedure.</p>
<b>MR T1 (Without skull)</b>	As the <b>T1</b> above, but with the skull part of the image removed.
<b>MR T2 (Without skull)</b>	As the <b>T2</b> above, but with the skull part of the image removed.
<b>MR (G+W+F Probability)</b>	Brain template for the <i>Probability Maps Normalization</i> (on page 40). It consists of probability maps of <i>SPM8</i> <a href="http://www.fil.ion.ucl.ac.uk/spm/software/spm8/">http://www.fil.ion.ucl.ac.uk/spm/software/spm8/</a> for Grey Matter, White Matter and CSF arranged as three frames in a dynamic series.
<b>MR (G+W+F Probability) (Clinical Toolbox)</b>	Brain template for the <i>Probability Maps Normalization</i> (on page 40) of an older population created from 50 healthy individuals (mean 73 years). Developed for the <i>SPM8 Clinical Toolbox</i> <a href="http://www.mccauslandcenter.sc.edu/CRNL/clinical-toolbox">http://www.mccauslandcenter.sc.edu/CRNL/clinical-toolbox</a> by Rorden et al [10 <a href="http://dx.doi.org/10.1016/j.neuroimage.2012.03.020">http://dx.doi.org/10.1016/j.neuroimage.2012.03.020</a> ].

## Brain Normalization Parameters

The settings available in the panels allow fine-tuning the basic procedure.

### Basic Parameters

**Smooth atlas, Smooth input** If either box is checked, an initial **Gaussian** smoothing of the respective data is performed. Both smoothing operations use the same configurable parameters. Usually, the atlas has already been smoothed beforehand so its smoothing is not required for the normalization.

**Calculations sampling rate** The sampling rate of the method is derived from the **Smooth Input** filter size. If no smoothing is applied, the sampling rate needs to be specified by the user.

**Template Mask** This section is needed for defining a mask to be applied during the normalization procedure.

- ▶▶ **MNI brain template (HFS):** a MNI brain template with HFS orientation was loaded. With this selection the standard **Mask** is used, so there is no need to define it.
- ▶▶ **MNI brain template (HFP):** a MNI brain template was loaded as is, appearing as HFP. The corresponding standard mask is used.
- ▶▶ **Other:** Use this selection if you have loaded your own dedicated template using the load **Reference** button, or using the **User defined** File menu entry. In this case, you need to select a file corresponding to the template which restricts normalization to the meaningful area.

**Input Mask** This option allows defining a mask to be applied during the normalization procedure. You need to select a file corresponding to the Input image which restricts normalization to the meaningful area.

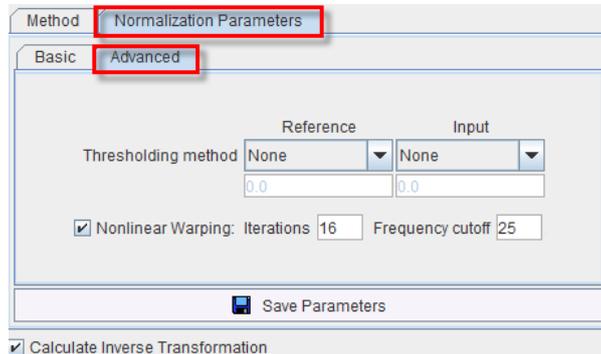
To discard the mask activate the **Clear file or directory** button 

**Resulting bounding box** The radio box selection allows defining the extent (bounding box) of the resulting normalized images.

- ▶▶ **Full atlas:** the result image has the size of the used template.
- ▶▶ **Talairach:** the result image is trimmed to the bounding box of the Talairach brain atlas as in the SPM programs.

## Advanced Parameters

The **Advanced** parameters are usually only changed if a normalization fails or if the user aims at a specific effect.



**Thresholding method** The image volume considered during matching can be restricted to a sub-volume by thresholding, eg. by excluding the image background.

Absolute values can be defined when **User defined** option is selected as thresholding method.

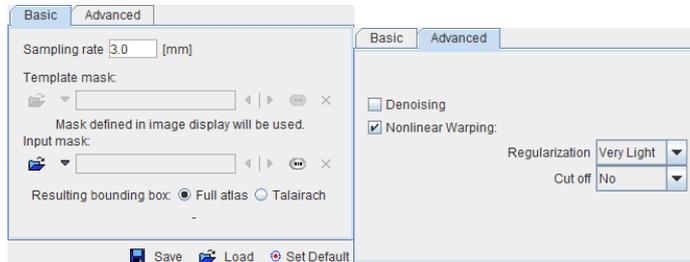
**Nonlinear Warping** If this box is not checked, only the affine (translation, rotation, scaling, shearing) part of the normalization is performed.

**Iterations** Number of nonlinear iterations. The higher the iterations number, the more deformations may occur.

**Frequency cutoff** The specified **Frequency cutoff** (default = 25) is used together with the **Bounding box** size to calculate the number of basis functions. Higher cutoff values result in fewer basis functions.

## Probability Maps Normalization Parameters

The probability maps normalization is based on PMOD's Java implementation of the Unified Segmentation methodology developed by Ashburner et al [11 <http://dx.doi.org/10.1016/j.neuroimage.2005.02.018>]. The following parameters allow fine-tuning the basic procedure.



### Basic Parameters

**Sampling rate** Pixel sampling rate for the calculation.

### Advanced Parameters

The **Advanced** parameters are usually only changed if a normalization fails or if the user aims at a specific effect.

**Denoising** Image denoising prior to the normalization using the fast Non Local Means Analysis method with "low" setting.

**Nonlinear Warping** Enable nonlinear warping in addition to the affine transformation.

**Regularization:** "The objective function for registering the tissue probability maps to the image to process, involves minimising the sum of two terms. One term gives a function of how probable the data is given the warping parameters. The other is a function of how probable the parameters are, and provides a penalty for unlikely deformations. Smoother deformations are deemed to be more probable. The amount of regularisation determines the tradeoff between the terms. Pick a value around one. However, if your normalised images appear distorted, then it may be an idea to increase the amount of regularisation (by an order of magnitude). More regularisation gives smoother deformations, where the smoothness measure is determined by the bending energy of the deformations." Bias regularisation in [12].

**Cut Off:** "Cutoff of DCT bases. Only DCT bases of periods longer than the cutoff are used to describe the warps. The number actually used will depend on the cutoff and the field of view of your image. A smaller cutoff frequency will allow more detailed deformations to be modelled, but unfortunately comes at a cost of greatly increasing the amount of memory needed, and the time taken." Bias cut off in [12]

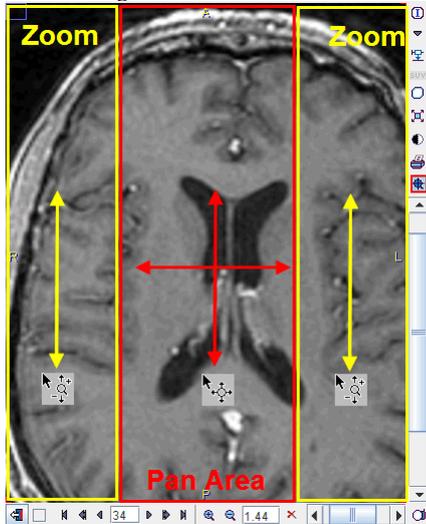
# Image Presentation Hints

During interactive matching and for report generation it is important to configure the displays and the image presentation appropriately. In the following sections the most important features are reviewed, but for a full description please refer to the **PMOD Base Functionality** guide.

## Zooming

For close image exploration zooming is often helpful. There are two modes how this can be done on the **CoRegistration** page:

Activating the  button enables mouse-driven zooming and panning:



To zoom in/out press the left mouse button in the left or right corridor and drag up/down. The center of the image stays in place during zooming. To adjust the visible part of the image (panning) click the left mouse button into the center of the image and drag the image around.

Note that the zoom/pan functions are only working in the active image indicated by the red corner brackets. However, it is easy to change the active image or the active plane in the orthogonal planes mode: just CTRL+Click onto the image that should get the focus and continue.

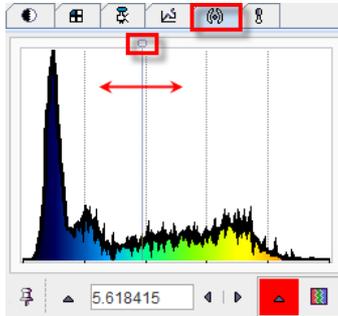
After appropriate zooming, zoom mode should therefore be deactivated by pressing  once more, because some of other mouse-operated functions might not work.

The second mode of zooming is enabled by the  button (only available in the row of the *Reference* image). When active, scroll bars for Zooming/Panning are shown. After the zoom adjustments they can be removed by pressing the button once more.

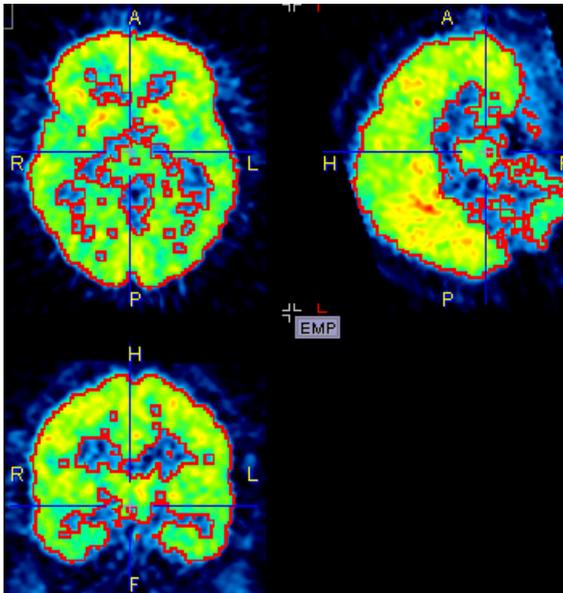
## Iso-contour Lines

Iso-contours are often very helpful to verify that the spatial alignment of studies is acceptable, or to overlay the location of an anatomical structure in the fusion image.

The fourth tab



is used to overlay iso-contour lines onto the images. A histogram of the pixel values is shown, and the value at which the iso-contour lines are drawn can be adjusted by entering a numerical value, or by dragging the marker highlighted in the graphics above. The selection on the right allows to choose among several colors for the contour lines.



Per default, the iso-contour lines are shown as long as the iso-contour tab is selected. If another tab is selected, they disappear. To make them appear permanently in the images the pin button  can be fixed to .

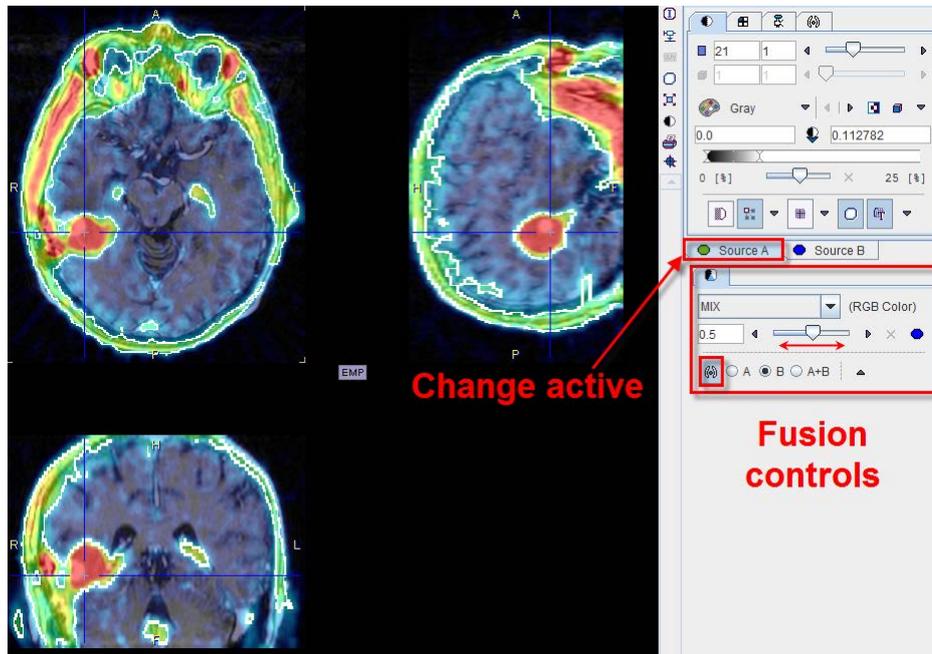
The display of contours in the fusion image is independent of the display in the source image. It is controlled by the the **Contours** radio box.

## Image Fusion Capabilities

There are multiple places in PMOD where two different image sets can be combined into a fused image. Depending on the context, there are two arrangements for performing the image fusion.

### Fusion Images not Visible at the same Time as the Source Images

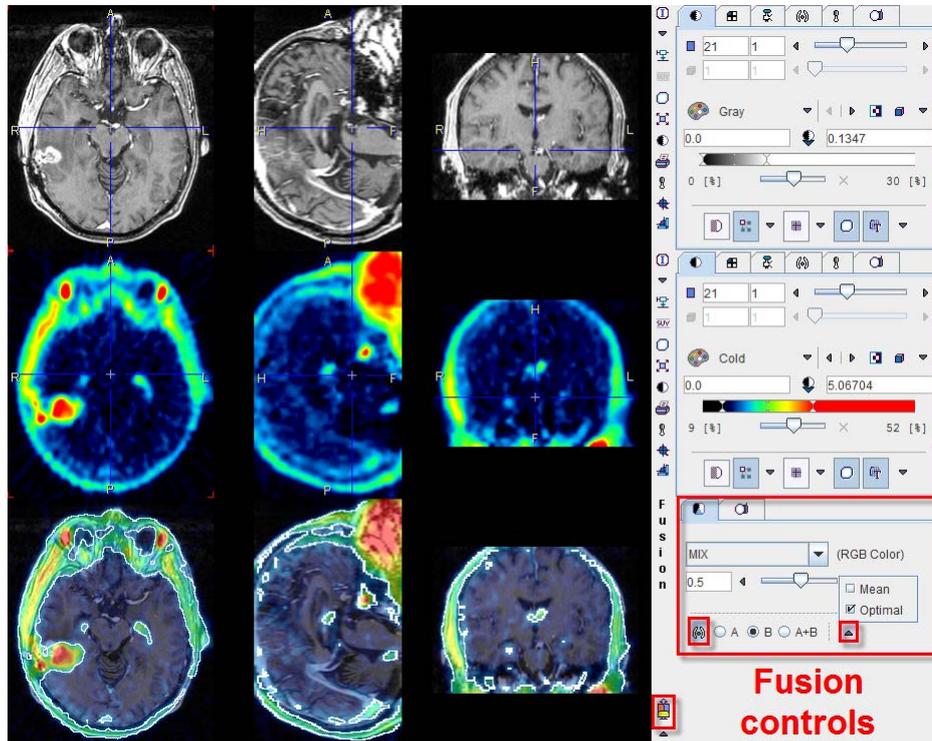
In this layout only the fusion of two source series is shown.



To adjust the presentation of either source image, select the appropriate tab **Source A** or **Source B**, and use the image controls. During such adjustments it will sometimes be helpful to only see the image you are working on, not the fusion. This can easily be achieved by moving the balance slider to one of the end positions left or right.

### Separate Source and Fusion Images

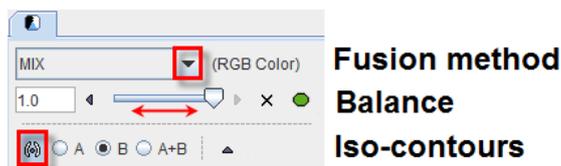
In this layout both the input images and the fusion images are visible at the same time, as in the example shown below.



In this example the first row shows a  $T_1$ -weighted MR image, and the second a matched  $^{18}\text{F}$ -Choline PET image with a highlighted tumor. To the right of the images the controls are available for changing the way how the images are displayed such as the color table, the thresholds, and the layouts. The third row shows the result of the fusion, depending both on the renderings of the source images, and on choice of the fusion controls located to the right.

### Image Fusion Methods

The image fusion control



consists of three rows. The first row contains the selection(s) for choosing between the different fusion renderings, the second row allows enabling the balance to blend the contributions of the two images in the fusion, and the third row allows enabling the iso-contour overlays.

The fusion methods available are:

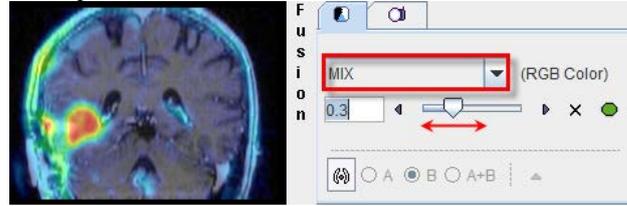
**MIX**      Alpha Blending: weighted addition of the RGB values of both source images according to

$$R_{fusion} = R_A * x + R_b * (1-x)$$

$$G_{fusion} = G_A * x + G_b * (1-x)$$

$$B_{fusion} = B_A * x + B_b * (1-x)$$

Example:



The slider allows defining the relative contributions of the source images. In the example shown image A contributes 30%, and image B 70%.

**MERGE**

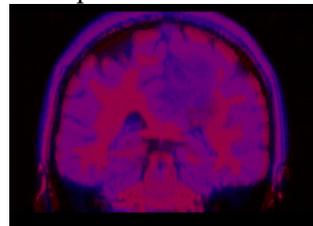
RGB merging uses the maximal RGB value of both source images according to

$$R_{fusion} = \text{Max}(R_A, R_b)$$

$$G_{fusion} = \text{Max}(G_A, G_b)$$

$$B_{fusion} = \text{Max}(B_A, B_b)$$

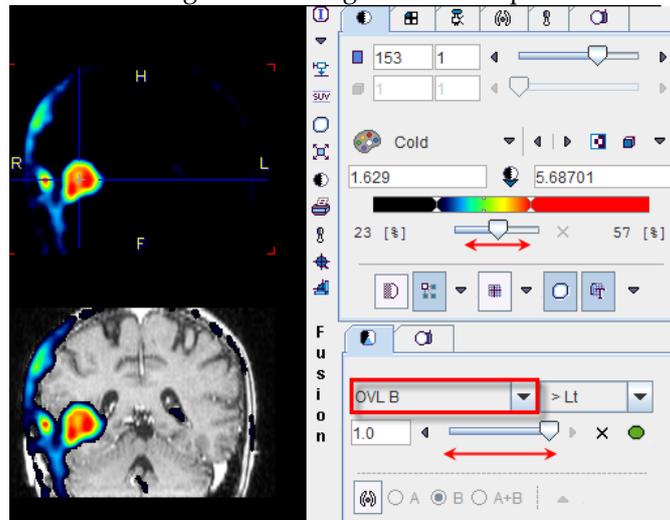
Example:



This fusion mode is most adequate for data arising from RGB sources, or when encoding the images with the [R]ed, [G]reen, [B]lue color tables.

**OVL B**

Shows the images A as background and a part of the images B as the overlay.



With the >Lt setting, all pixels in the PET image (B) below the lower threshold of the color table are replaced by the MR (A) values. Additionally, some transparency is added in the lesion by the balance slider. See below the description of the different threshold options.

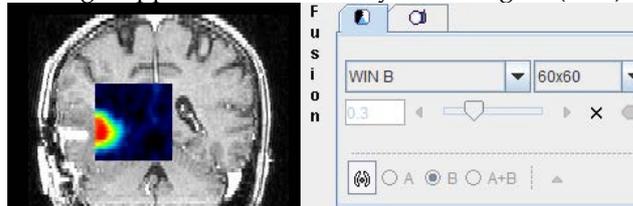
**OVL A**

Is equivalent to OVL B except that the role of the images is reversed.

**WIN A** Shows the images B (PET) as the background. When clicking into an image a rectangle appears which overlays the image A (MR).



**WIN B** Shows the images A (MR) as the background. When clicking into an image a rectangle appears which overlays the image B (PET).



When the **OVL A** or **OVL B** methods are selected, different threshold settings are available in the selection to the right:

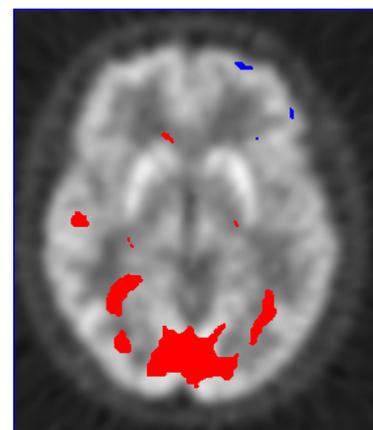
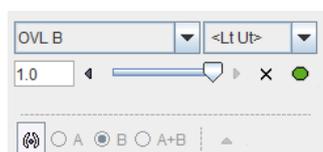
- > Lt Only the pixels (in A for **OVL A** , in B for **OVL B**) with values *above* the lower threshold are displayed. This is the most useful setting when a hot lesion is to be blended into an anatomical image (see example for **OVL B** above).
- < Ut Only the pixels (in A for **OVL A** , in B for **OVL B**) with values *below* the upper threshold are displayed.
- >Lt Ut< Only the pixels (in A for **OVL A** , in B for **OVL B**) with values *between* the lower and upper threshold are displayed.
- <Lt Ut> Only the pixels (in A for **OVL A** , in B for **OVL B**) with values *outside* the lower and upper threshold are displayed. Note that only the first and last color of the selected color table are applied in this setting. A suitable selection in this configuration is the **Split** color table.

An example of the <Lt Ut> method is shown below.

Image A represents normalized patient images, and image B the deviation from the normal pattern expressed as z-score values. The color table configuration of image B is



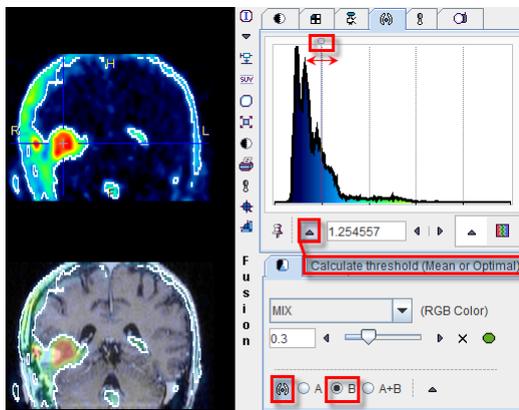
and the fusion settings



Only z-score values  $< -2$  and  $> 2$  are shown, without transparency. Because only the minimal and the maximal colors are used, the result has a binary character. Red are all pixels with an activation of more than two standard deviations, and blue all the pixels with the uptake reduced by at least two standard deviations. This is probably the most useful configuration for exploring the deviations from the standard pattern.

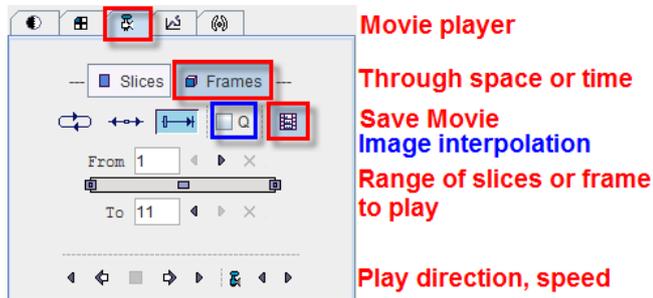
### Iso-contours in Image Fusion

The contours radio box allows overlaying iso-contours derived from the source images **A** or **B** or both onto the fusion result. In the example below an iso-contour circumscribes the lesion clearly delineated in the FCH PET image. The iso-contour for the image **B** can be generated automatically selecting the **Optimal** option in the list in the **Contouring** tab. Setting the radio box **B** displays this contour in the fusion, which has been set to show mainly the MR image (A) by moving the balance slider to the left end. Another helpful application of the contours is in image matching.

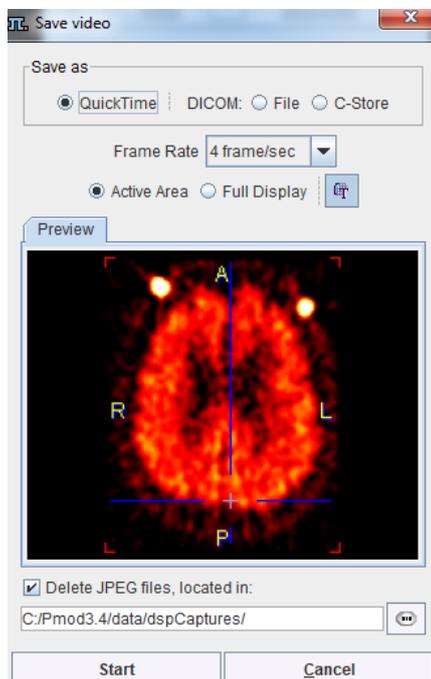


## Movies

The movie player allows showing movies of slice images through the volume or through time (dynamic studies only), as well as rotating MIPs if the 3D button was selected in the layout.



Please use the Q box to enable image interpolation when working with low-resolution images. If the save movie button is activated at the time the user hits the start button, a dialog window appears requesting information for movie generation.



The movie formats include Quicktime or DICOM, and the active image or the entire image viewport can be captured. The movies are generated from intermediate JPEG files, which can optionally be kept for other uses.

A movie of the active image can also be started/stopped with the CTRL+M shortcut without the need to open the movie tab.

Note that when a movie is configured in a fusion display, the images are synchronized in all displayed images during playback.

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[http://www.fil.ion.ucl.ac.uk/spm/doc/spm8\\_manual.pdf](http://www.fil.ion.ucl.ac.uk/spm/doc/spm8_manual.pdf).

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