

User's Guide

PMOD Image Fusion (PFUS)

Version 3.3



PMOD Technologies

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PMOD Image Matching and Fusion Tool Introduction

The PMOD image registration and fusion tool (PFUS) supports a large range of tasks related to image matching and fusion such as

- ▶▶ the manual realignment of volumetric image sets,
- ▶▶ automatic image registration using different methodologies,
- ▶▶ SPM-type spatial normalization (e.g. to stereotactic template images),
- ▶▶ motion correction of dynamic series,
- ▶▶ a multitude of fused renderings of registered images,
- ▶▶ saving of fused representations in JPEG/TIFF or as DICOM secondary capture images,
- ▶▶ pixel-wise image algebra on registered images,
- ▶▶ scatter plots of VOI pixel values in 2 (2D plot) or 3 (3D plot, optional) matched studies,
- ▶▶ volume-of-interest definition directly in the fused image display.

Overview of the PFUS Operation Principle

The PFUS tool regards one study as the *Reference*. All other studies are adjusted in pixel size and slice thickness to the reference study. This is done by interpolating their image information within oblique planes across the image volume, a process called *reslicing*. Hence the images to be adjusted are called the *Reslice* studies in this text. As a result of reslicing, the *Reference* and the *Reslice* studies have identical resolution, and fusion images can be easily generated by combining the pixel values in the different series. For instance, the color values can be added (*blending mode*), or only one of the image values can be shown depending on a threshold value (*overlay mode*).

If the anatomic structures in the *Reference* and the *Reslice* studies are already in spatial agreement, only a mere resolution adjustment of the *Reslice* study is required, for example to interpolate a 128x128 PET to the 512x512 matrix of the CT (*Reference*) in a combined PET/CT study. In other situations, however, an adjustment of the geometry 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 a MRI study, and interpolate them to the 256 x256 MRI matrix.

After the reslicing/matching step, all image sets have the same resolution. As a consequence, all of them can be used for fusion purposes, pixel-wise arithmetics as with a "hand-held calculator", and also for the evaluation of VOI pixel values with scatter plots.

Data Size Considerations

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 *Reslice* study 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.

Starting the Fusion Tool

The image fusion tool PFUS is started with the **Fusion** button from the PMOD ToolBox



or by directly dragging image files from the desktop onto the above button. PFUS organizes the available tasks on different pages which are explained below.



Basically, one page is for database loading only, two pages are for matching purposes, while the last two provide advanced fusion displays.

Taskbar

The taskbar on the right side of the application window provides a quick shortcut for several frequent tasks. Please note the tooltips which provide short explanation of the button functionality.

Further Information

Please note that the following description is intended as a reference and not as a tutorial. For practical examples how to work with the PFUS software please refer to the **PMOD Workbook**, which is also distributed as part of the PMOD documentation.

Spatial Transformations in PMOD

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 PFUS tool supports 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 provide the facility to not only return the matching transformation, but also the inverse transformation which can be applied if the role of the *Reference* and the *Input* is reversed. Additionally, PFUS 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 VOI 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.

The **DB Load** page appears only if the use of the database within PMOD has been enabled by checking the box **Use database (General Activation)** in the global **Config** pane. The summary below explains the database loading interface. Note that when loading multiple series at once, the *first* series in the **Selected for loading** list becomes the *Reference*, while all subsequent series become the *Reslice* studies.

Patient Name	Study date	Time	[Study description]	[Series description]
PFUS1	2002.02.28	14:39:10		MRI Reference
PFUS1	2003.04.11	14:45:32		FCH for Reslice
PFUS1	2006.04.10	17:33:21....		FET
PFUS1	2006.04.10	17:42:26....		FDG

Summary of Image Loading from the Database

When loading images from the database the interface shown below allows searching for studies according to different criteria such as patient demographics, study date, modality, a project name or diagnosis. There is a basic filtering mode as illustrated bellow, and an advanced filtering mode illustrated later.

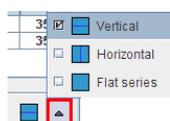
The screenshot shows the 'DB Load' interface with several key sections:

- Database selection:** Located at the top right, it includes a search bar and options to 'Reset Query' and 'Refresh Query'.
- Basic filtering criteria:** A section for entering search parameters like Patient Name, Patient ID, Birth Date, and Modified.
- Patients [5]:** A table listing patient information:

Patient name	PatientID	Modify date	Sex	Date of Birth
PKIN1	Dyn. CPFPX bolus & MRI	2011-10-16 13:00:24.51	M	1981.01.01
PKIN2	Dyn. DASB without blood & MRI	2011-09-13 09:44:09.891	M	
PKIN3	Dyn. FDG scan with whole blood data	2010-08-27 15:20:40.196	M	
PKIN5	Tracer with Metabolites, KM File only	2010-08-17 10:05:51.972		
PKIN4	Dyn H2O brain scan, Baseline	2010-08-17 10:00:24.704		
- Image series of selected patient:** A table showing series details for patient PKIN2:

Patient Name	Study date	Time	Study description	Series description	Modified	Last Use	Mod	nz	nv	nd	nx	ny
PKIN2	2006.03.21	15:15:09	DASB SERT	MR Anatomy	2011-09-13 09:...	2011-09-13 09:...	MR	124	1	1	137	17
PKIN2	2006.03.21	15:15:07	DASB SERT	Dynamic DASB PET	2010-09-03 16:...	2011-10-18 12:...	PT	32	33	1	59	7
PKIN2	2006.03.21	15:15:09	DASB SERT	MR Anatomy	2010-08-16 10:...	2011-10-06 08:...	MR	124	1	1	137	17
- Series in the loading list:** A table at the bottom showing the 'Selected for loading' list, which currently contains one entry: PKIN2.
- Series Image Preview:** A window on the right showing a loaded axial MRI slice of a brain with various controls for zooming and windowing.

The layout can be organized vertically (as illustrated above), or horizontally with the **Series** tab stacked behind the **Patients** tab. This may be an advantage if patients tend to have many image series. The layout is switched by the option button



The **Flat series** is another arrangement which lists all image series in a single list.

Loading Overview

The uppermost section represents the filtering options. The use of filtering is recommended in large databases, because it substantially reduces the response time. Below the filters, the list of **Patients** is shown which match the current selection criteria. When one of these patients is selected, his image series available in the database are updated in the **Series** list section.

One or several image series can be selected and brought into the **Selected for loading** area by the **Add** button or by a double-click at the series entry. On the right side there is a preview window to verify the image contents before actually loading the whole data set. If the **Series Image preview** box is checked, an image is displayed as soon as a series is selected.

Finally, by activating the **Open** button, all series in the **Selected for loading** area are loaded into the PMOD tool. **Append** pushpin button is important for the outcome of the loading operation: with the appending setting  the images are added, while with the overwriting setting  any already loaded images will be discarded.

Note that multi-series selection depends on the context. If only a single series is expected by the program, double-clicking at the series will immediately start image loading.

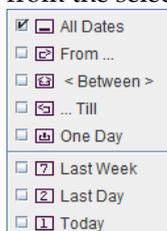
User Interface Elements for Filtering

First of all the database to be searched must be selected with the selection in uppermost section, **Pmod** in the example above. The basic filtering options include the following elements.

Name Patient name, starting with the last name. The wildcard * can be used as a replacement for arbitrary sub-strings.

Patient ID The patient ID filter, also supporting wildcards.

Birth Date The filters for the birth date include an exact date, or a date range available from the selection list.



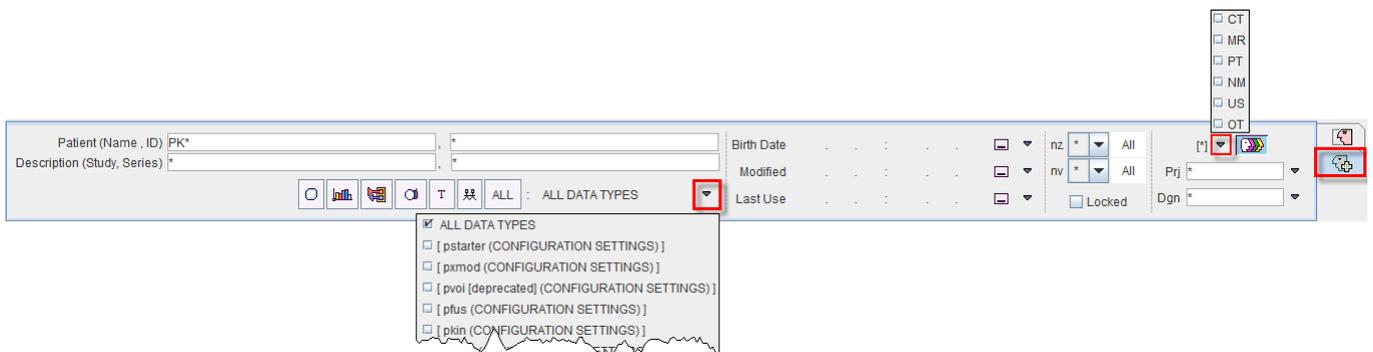
These specifications apply for all other filter dates.

Modified A date/time is maintained in the database recording when the data of the patients was modified the last time by adding an image series or by changing the patient information. For example, setting the field to **Last Week** only shows patients modified in the last seven days.

SQ Means *Save Query*. If this button is enabled, the same filter settings will be applied when the database window is opened again.

-  **Reset Query** This button resets the filter settings by removing all specifications.
-  **Refresh Query** The refresh button to apply the query to the database potentially updated in the meantime, or after changing the filter and disabled automatic refreshing.
-  **Toggle button** to enable/disable automatic refreshing after changing a filter element

There is an extended filtering capability available on the second sub-tab which is illustrated below.



It contains several new elements:

Study Description Filtering of text appearing in the study description. The * wildcard is supported.

Series Description Filtering of text appearing in the series description. The * wildcard is supported.

ALL DATA TYPES This selection lists all available data types in PMOD such as images, VOIs, etc. Setting this field to *VOI Templates* for example will only list patients who have a VOI definition attached to one of the image series.



These shortcut buttons allow filtering for frequently used data types such as VOIs, statistics, kinetic modeling files, comment texts, paired series. **ALL** resets all filter setting.

Last Use A date/time is maintained in the database when data of the patients was accessed the last time. This information is listed for each database object. Selecting a date range allows browsing the database content based on a *least recently used* criterion.

nz Filter to search for studies with a certain number of slices, including the criteria



For instance, planar only studies could be looked for by setting $nz = 1$.

nv Filter to search for studies with a certain number of dynamic frames. For

instance $nv > 1$ will only list dynamic series.

- Locked** If the box is checked, only patients who have a *Locked* flag are listed.
- Modality** A selection to restrict the search to a specific modality, e.g. to *PT* (PET) as in the example. Multiple modalities can be searched for at once.
- Prj** Patients can be assigned to a **Project**. The selection allows choosing from the list of available project names.
- Dgn** Similarly, patients can be given a **Diagnosis**. The selection allows choosing from the list of available diagnosis names.
-  or  Every time data is saved in the database, the PMOD name of the user who saved is recorded together with the data. This button allows restricting the search to the PMOD user currently logged in (button out), or to show data of all users (button in).

The green button  allows hiding the filter section. Upon activation the filter area collapses and the button appearance changes . This new button allows showing the hidden filtering settings.

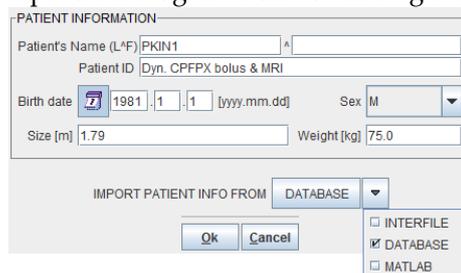
Patient Operations

When a patient has been selected from the list, a row of buttons becomes active.

Set as "Selected for loading" Moves all series of the patient to the **Selected for loading** area.

Edit Patient

Opens a dialog window for editing the patient demographic data.



The **IMPORT PATIENT INFO FROM** button allows importing this information from a file in the Interfile format, from an existing **DATABASE** patient, or from a **MATLAB** file. Note that the information in the DICOM object is not modified, just the database entries. However, when loading the images, the information in the database overrides the DICOM information, and when the data is saved or exported, it will contain the changed information in the file.

Set Project | Locked

Allows defining three attributes for a patient:



A **Project** name can be entered, or if it already exists, selected from a list. Similarly, a **Diagnosis** can be specified, and the patient can be **Locked** to

prevent erroneous deleting.

- Delete Patient(s)** Delete the patients selected in the list.
- Create new Patient** Create a new patient in the database, to whom information can be attached if there is no image series in the database.
- Merge** Sometimes several entries are created for a single patient because of a mismatch in the name/ID information. To merge such entries, select all of them in the **Patients** list (with **CTRL+Click**) and activate the **Merge** button. As a result all series end up under a single patient entry.

The /  buttons allow hiding/showing the patient list controls.

Series Operations

When a series of the current patient is selected, the row of buttons below the list becomes active.

- Add** Moves the selected series of the patient to the **Selected for loading** area.
- Add All** Moves all series of the patient to the **Selected for loading** area.
- Edit Series** Opens a dialog window for editing the series information

- Set Project | Locked** Brings up the same dialog window as on the patient level to define project, diagnosis and locking on the series level.
- Pair Images** This option in the selection list serves for associating two (or more) series. This association is used in processing tools which require the information of two image series.
- Pair VOIs** This option in the selection list allows associating a VOI file to image series.
- Delete Serie(s)** Delete the series selected in the list.
- DICOM** Inspect the attributes of the selected series in a DICOM browser.
-  Search JPEG or TIFF captures stored in the database. They can be opened in a

viewer.



Comment editor. Allows creating a comment for the selected image series. Existing comments can be edited or read.



Search for a study which is associated to the selected series.



Buttons allowing to step from patient to patient

The / buttons allow hiding/showing the series list controls.

Selected for Loading Area

In most situations more than one series (from the same or different patients) can be added to the loading area, but there are exceptions when only a single series is allowed. The *order* in the list is relevant for the loading order. This is most important for the fusion tool because the first series will serve as the reference. To change the sorting order just click one of the column headers.

As soon as there are series in this area, the row of buttons below the list becomes active.

Open Starts loading the image series directly. The images are loaded without intervening dialog, and without any operations. Otherwise the dialog for specifying pre-processing options is shown. If the **Append** flag is on (), the selected series will be loaded as *additional* images to the tool, otherwise the tool will be cleared before loading.

with Operations Starts loading the image series. The dialog for specifying pre-processing options is shown. If the **Append** flag is on (), the selected series will be loaded as *additional* images to the tool, otherwise the tool will be cleared before loading.



This button serves for loading the selected data with a macro.

Replicate Copy the selected series including components to another database which can be selected in the appearing dialog window.

Export Export the series in the list from the database to a directory located on the file system or directly to an FTP node. The export dialog window

optionally allows anonymizing the images, generating a **DICOMDIR** file and compressing the whole data into a **ZIP** archive. The action can be aborted with the **Cancel** button.

C-Store This button allows sending the selected series directly to a DICOM server without first loading them into an image area. This has the advantage that *no modifications are done to the original DICOM objects*. In contrast, when loading the images and sending them to a DICOM server, some changes are applied to the DICOM attributes.

Remove Removes the selected series from the selected for loading area, but does not delete from the database.

Remove All Clears the **Selected for loading** area.



This button allows setting defaults column order and width.



This button allows sorting the images **Selected for loading** by the selected column.



This buttons allow changing the images order in the list.

DICOM Query/Retrieve

Q/R This button underneath the image display area starts the dialog window for the DICOM Query/Retrieve functionality. If the box left to Q/R is checked the demographic patient information is copied to the Q/R dialog window.

Loading Images from the File System

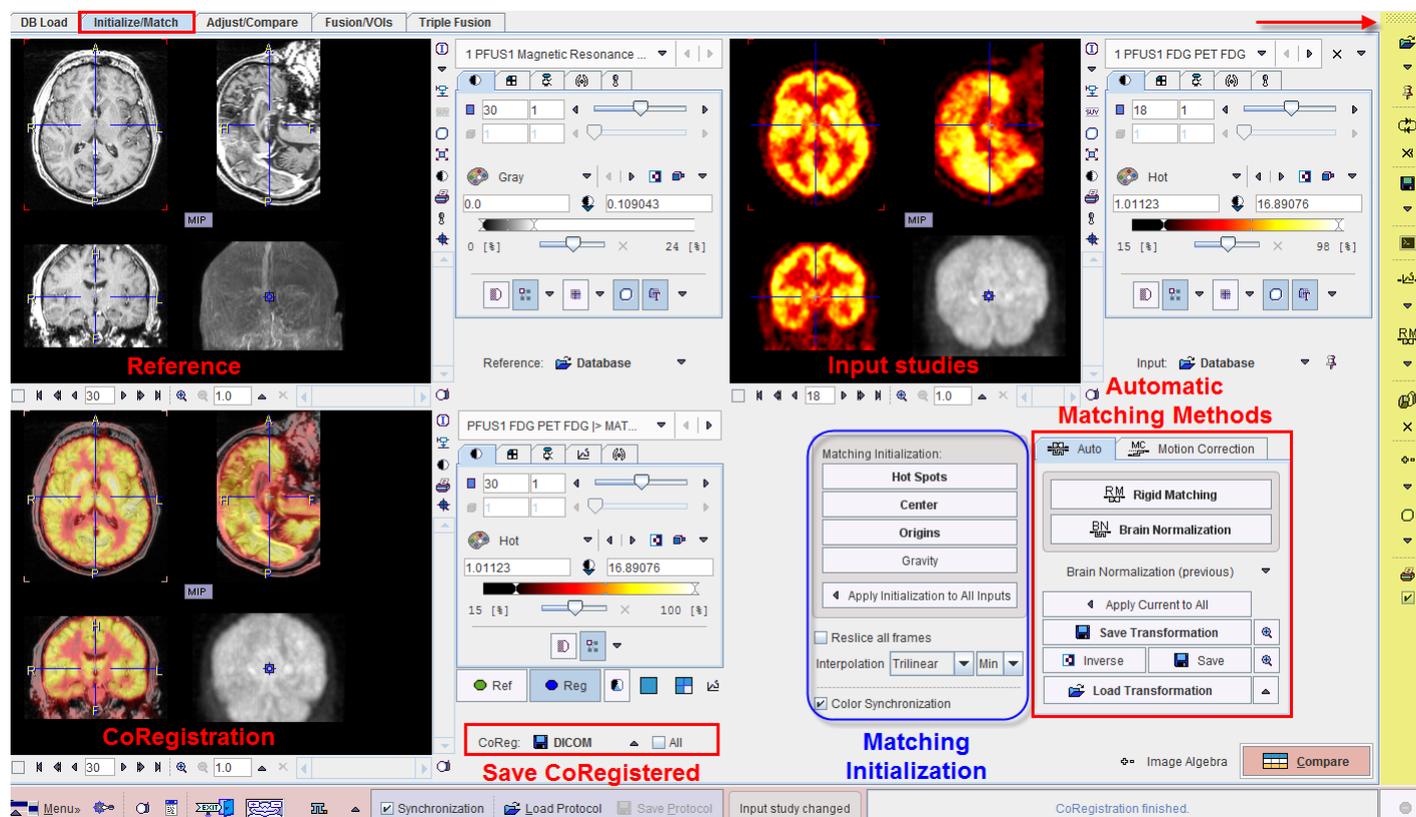
AUTODETECT T This button allows loading image data from outside the database. Basically, it is an **Autodetect** loading, so the user can just browse to any directory and select any type of image file. PMOD will detect its file format and perform the image loading operation, if possible.

DICOM This button serves loading DICOM part 10 images. The difference with the **Autodetect** loading is that the user has to select a directory, not a file.

Import This buttons allows direct importing of Dicom files to the current database.

Initialize/Match Page

The **Initialize/Match** page serves for image loading in different formats, initial reslicing as a preparation step for manual matching, automatic matching, for motion correction of dynamic studies, and for saving the matched images. The page layout is illustrated below, and the functionality described in the following sections



Note the action buttons in the lower right workspace corner which allow moving to the next step in the matching process.

 **Image Algebra** If this button is activated the program automatically switches to the **Adjust/Compare** page which is displayed in **Algebra** mode.

 **Compare** If this button is activated the program automatically switches to the **Adjust/Compare** page which is displayed in the **Fusion** mode.

Processing Overview

Working in the PFUS tool typically has the following workflow.

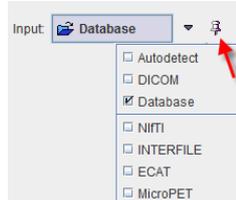
1. Data Loading	<ul style="list-style-type: none"> » Load the reference images. They define the final resolution of the matched images. » Load one or more input image series. These series are automatically resliced to the reference using information in the image headers.
2. Matching Initialization	<ul style="list-style-type: none"> » Improve the initial alignment of the images before starting one of the automatic matching methods. » Test the different available initializations such as aligning the data set origins, the image volume centers, and the center of gravity. » Shift and rotate the input images manually to come into a reasonable alignment.
3. Automatic Matching	<ul style="list-style-type: none"> » Select an appropriate matching method, rigid or elastic. » Initialize the matching parameters by selecting one of the presets reflecting different situations (human ↔ animal, intra-modality ↔ multi-modality). » Start the matching algorithm.
4. Results Inspection and Adjustment	<ul style="list-style-type: none"> » Visually check the alignment, either on the Initialize/Match page, or on the Adjust/Compare page. » Perform the check in different parts of the volume and with different fusion renderings. » In the case of rigid matching the result can be fine tuned interactively, preferably on the Adjust/Compare page.
5. Results Saving	<ul style="list-style-type: none"> » Save the matched images for further analysis on the Initialize/Match page. » Save the transformation and its inverse in order to re-apply them to the original images or to VOIs at a later time.
6. Image Analysis and Results Documentation	<ul style="list-style-type: none"> » With the resulting images perform the different types of analysis which are possible in the PFUS tool. » Save these results and create reports

Data Loading

Data Loading and Closing

As an alternative to loading from the database in the **DB Load** page the **Initialize/Match** page provides two loading buttons.

- ▶▶ The *Reference* MRI series is loaded into the image tool in the upper left corner by the load **Reference** button.
- ▶▶ The *Reslice* (or input) series (or several series at once, here FDG, FET and FCH) to be registered are loaded to the upper right image tool by the load **Input** button. At later times, additional studies can be incrementally loaded if the need arises. To avoid overwriting of previously loaded input studies, the pushpin button next to the **Input** button must be activated.



Note the study selection top right which allows switching between different input series.

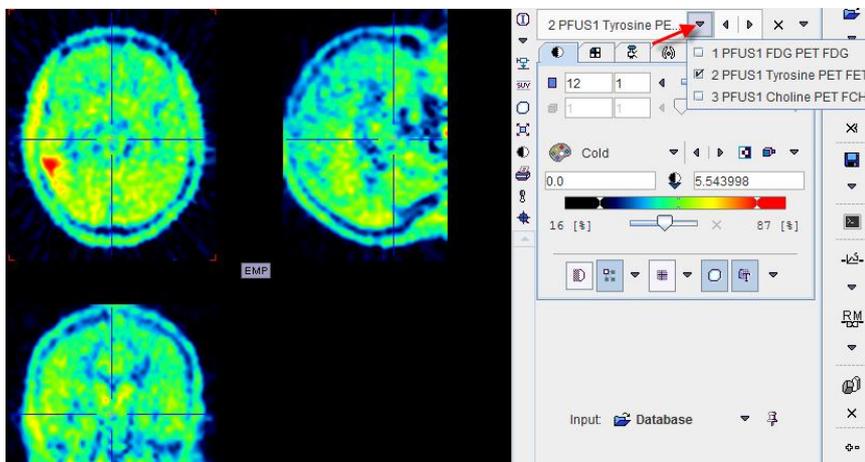
Image loading and data management can also be done with the taskbar.



-  Load reference and input images. The format can be selected with the small arrow below the button. The  button serves for enabling the input image appending mode.
-  Interchange the role of the reference and the current input image. All images will be resliced to the new reference after the interchange.
-  Close all image series in the PFUS tool, including any image algebra results.

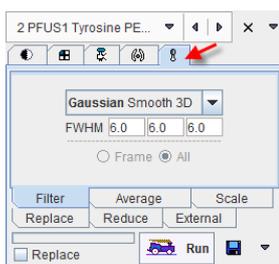
Input Data Selection

When loading several images at once or appending input images, the PFUS tool has to handle multiple reslice series. On the **Initialize/Match** page it arranges them in a stacked arrangement as illustrated below. Please use the indicated buttons to switch between the different series. Note that the series switching in the **Input** and in the **CoReg** area are synchronized.



Input Data Processing

In some cases it is helpful to process the raw input images before starting the actual matching using the image processing tools illustrated below.



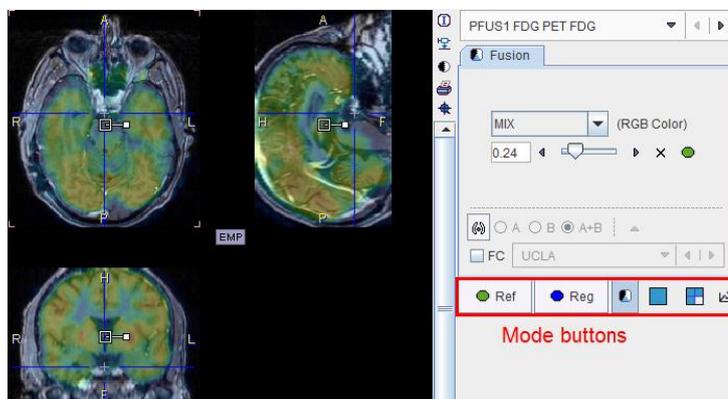
If the **Replace** box is not checked, and additional image series is created which is exactly aligned with the original data. Once a matching transformation has been determined with the secondary image series, it can be easily applied to the original raw data.

Typical applications are the smoothing of noisy images or the time averaging of a part of a dynamic series.

Resliced and Result Images

CoReg Image Panel

As soon as input images have been loaded and resliced, they are fused with the reference images and shown in the lower left image area.



Note the row of mode buttons to quickly change the upper part of the control area.

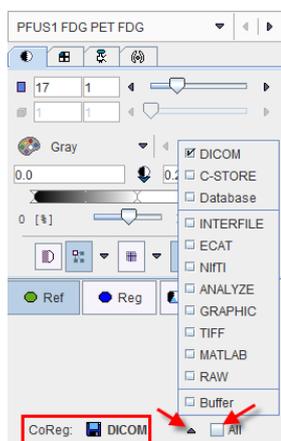
-  **Ref** Button to show the image controls of the reference images. Then the color or the image layout can be adjusted.
-  **Reg** Button to show the image controls of the currently selected reslice images.
-  Show the image fusion controls as in the example above, so that the fusion rendering can be adjusted.
-  Switch to single plane layout.
-  Switch to orthogonal planes layout.
-  Button to activate the reslice panel on the input images. At the same time the reslicing controls are also shown, allowing to interactively move/rotate the images.

The available methods for image fusion are explained in detail *below* (on page 76).

All matching activities will update the images in the **CoReg** area. So if an automatic matching is applied starting from a certain initialization, and then the outcome is manually refined, the result images are available in **CoReg**.

Result Image Saving

To save the matching result images, use the saving button indicated below. Note the **All** check box. If it is enabled at the time of saving, all reslice series will be saved at once. The saving format can be adjusted using the usual arrow button. An alternative for saving the currently selected reslice images is using the save button in the taskbar.



Matching Initialization

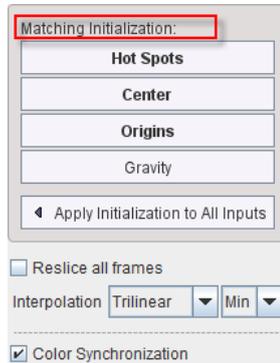
Reslicing after Loading

When loading an input study, the images automatically get resliced to the *Reference* resolution, whereby the program tries to align the two studies. If there are common DICOM landmarks available (**Origins**), they are aligned, otherwise the centers of the two data volumes are aligned. The result of this initial reslicing is shown in the *CoReg* area in the lower left fused with the *Reference* image. If multiple studies are loaded, this procedure is performed for each input independently.

The results of the matching initialization can be inspected in the *CoReg* panel by clicking at different points in the images. Note that they are synchronized with the upper reference images (as long as **Synchronization** box from the bottom status line is checked). The **Color Synchronization** check box allows linking the color tables of the fused images in the *CoReg* area with that of the original the *Reference* and *Input* images.

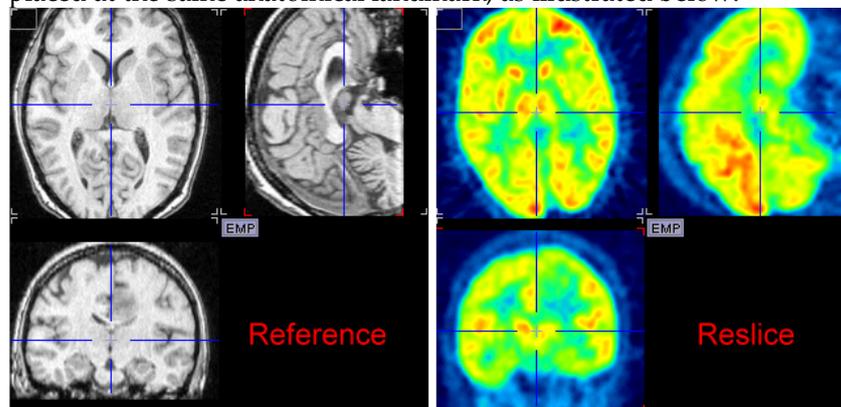
Automatic Initialization Variants

The **Matching Initialization** panel provides options to easily modify the properties of initial reslicing.



The following buttons are available. If the initial alignment is poor, please try them out to get a better result to start with.

Hot Spots This button needs to be used in combination with the orthogonal views of the *Reference* and the *Reslice* studies. The cross indicating the hot spot should be placed at the same anatomical landmark, as illustrated below.



The **Hot Spots** button will then perform the alignment of the two locations.

Center This button brings the centers of both data volumes into agreement. It is the preferred mode if the coordinate origins are distinct, but the studies cover (about) the same anatomical volume.

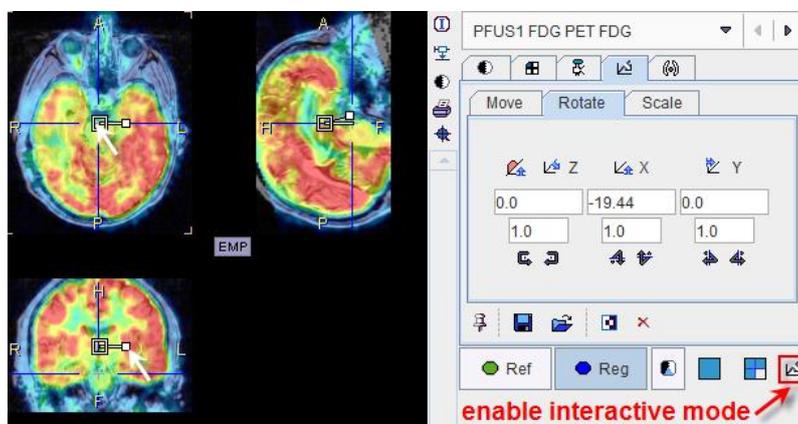
Origins This button brings the origin of the coordinate system in both data sets into agreement. It works successfully if the same origin based on a common landmark has been defined in both studies, e.g. in a hybrid PET/CT study.

Gravity This button brings the origin of the centers of mass in both data sets into agreement.

All of these initialization buttons calculate and apply an initial **Move** transformation, which can be inspected in the panel.

Interactive Adjustments of Initialization

If none of the automatic initializations provides a reasonable starting point for the automatic procedure, the alignment can easily be manually adjusted. To this end activate the button in the **CoReg** image area illustrated below.



Now the selected reslice series can be shifted and rotated using the corresponding handles, as explained in more detail *below* (on page 38).

Manual Initialization

The reslicing panel of the **Reg** image illustrated above shows the result of the initialization operation. However, the transformation parameters can also be set manually, for instance if the images to be registered always have the same constant offset. In these cases the initialization can be saved using the **Save** icon  once, and then retrieved using the **Load**  buttons the next time images have to be matched. Note that these settings can be applied to all loaded images with the **Apply Initialization to All Inputs** button.

Dynamic Image Series

Dynamic series may become huge when resliced to anatomical reference images with high resolution. Therefore, with the **Reslice all frames** box, the reslicing behavior can be modified. If the box is checked, all frames of the dynamic input series will be resliced to the reference, creating again a dynamic series. If the box is not checked, only the frame currently selected in the **Input** area is resliced, resulting in a static series. This is the recommended mode at least for the initialization phase.

Results Interpolation

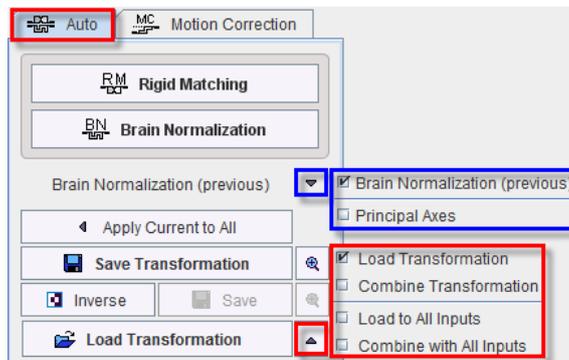
The **Interpolation** method choice lets the user define how image values are interpolated from the original pixel values when new slices are calculated. Default is **Trilinear** which is a simple and fast interpolation using all 8 enclosing pixel values. The truncated sinc interpolations **Sinc (Window 5)** and **Sinc (Window 7)** are more accurate, but considerably slower. **Nearest** neighbor interpolation just uses the value of the closest pixel, so it is very fast but in most cases does not provide satisfactory quality. However, it is the method of choice if an object map image containing integer values needs to be resliced.

The appropriate interpolation value for pixels which were outside the original field-of-view is unknown. Per default a value of 0 is applied, but the behavior can be changed to use the minimum of the data set (**Min** selection) which is more adequate for CT data.

Note that the interpolation choice has an impact on all calculations in the fusion tool.

Automatic Matching

In order to use the automatic matching methods, the **Auto** tab must be brought to the foreground after loading the images. The following interface appears



which contains a series of user interface elements:

Rigid Matching Allows accessing different types of rigid matching methods.

Brain Normalization Allows performing procedures for transforming individual brain images into a standard anatomical coordinate space. They require a suitable template image which is already in the standard space, and an elastic matching procedure for warping the images appropriately. (Formerly called Brain Normalization II)

Option Button 1 Contains the historic **Brain Normalization (previous)** and **Principal Axes**. Activating either of these buttons pops up a corresponding dialog window as described below for the different methods.

Apply Current to All Copies the transform of the current **Input** series to all, overwriting the prior transforms.

 Shows the parameters of the current transform (as a result of transformation loading, automatic matching or calculation of the inverse). Only the affine component is shown, not the elastic part of the normalizations.

Save Transformation Allows saving the final transformation obtained from initialization, automatic matching, manual adjustments as well as the result of a transformation combination.

- Inverse** Allows calculating the inverse of the current transformation. Note that this applies also if the current transformation has been calculated by the combination of multiple transformation.
- Save** Allows saving the inverse transformation.
- Option Button 2** Allows loading a transformation which has been saved to disk after a manual or automatic matching process. The following is done with the loaded transformation:
- ▶▶ **Load Transformation:** The transformation is loaded to the series shown in the **Input** window. A prior transformation is overwritten.
 - ▶▶ **Combine Transformation:** The transformation is combined with the prior transformation of the series shown in the **Input** window.
 - ▶▶ **Load to All Inputs:** The transformation is loaded to all **Input** series. Prior transformations are overwritten.
 - ▶▶ **Combine with All Inputs:** The transformation is combined with the prior transformation of all **Input** series.

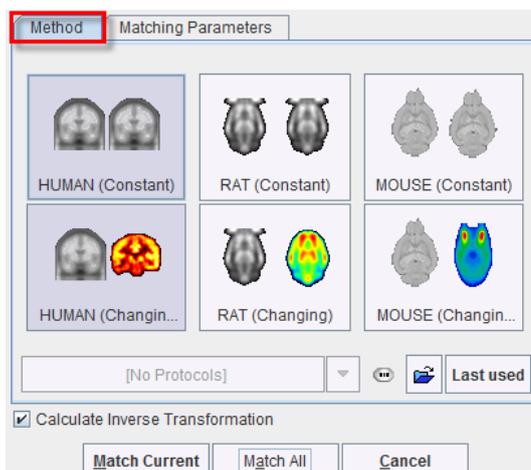
Each time after loading or combining transformations the images are resliced automatically. See the comment *above* (on page 4) regarding the effect and the allowed combination of transforms.

The matching methods are described in the following sections.

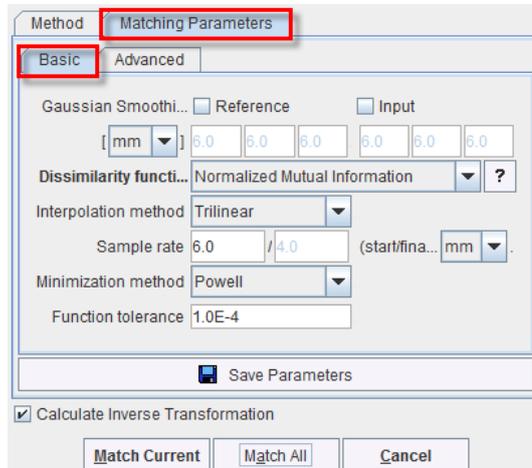
Note: The performance of the automatic registration methods is highly dependent on the actual images to match!

Rigid Matching

The **Rigid Matching** button provides access to the different types of rigid matching methods. An interface dialog window appears with two tabs. The first one serves to quickly retrieve pre-defined or saved configurations of the iterative matching settings, the second one gives access to all parameters.



There are predefined methods for intra-modality matching (MRI-MRI, PET-PET), and cross-modality matching. Activating the corresponding buttons displays the **Matching Parameters** pane with appropriately configured settings. There are **Basic** and **Advanced** parameters on separate tabs.



The settings available in the 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

Smoothing window

A Gaussian filter with configurable width in mm or pixels can be separately enabled for the *Reference* and the *Reslice* 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.

Dissimilarity function

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

- ▶▶ **Absolute Difference Sum**, and
- ▶▶ **Squared Difference Sum**: These are measures based on image subtraction and therefore require images of the same modality.
- ▶▶ **Woods**: Partitioned Intensity Uniformity for the registration of MRI-PET images [7], [8].
- ▶▶ **Mutual Information, Intra- and Cross-Modality**: 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 a reference and input data. The inherent part of implemented joint histogram creation method is a process of a partial volume interpolation. As a result, the interpolation method has no relevance for the MI method.
- ▶▶ **Mutual Information (PV), Intra- and Cross-Modality**: In this MI variant,

a partial volume interpolation algorithm is used as a part of the joint histogram construction.

- » **Normalized Mutual Information, Intra- and Cross-Modality:** 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.

Interpolation method Type of interpolation used during reslicing. Has an impact on speed, and may also influence convergence.

Sample rate 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.

Minimization Method **Powell** usually finds the optimal match faster than **Downhill Simplex**.

Function tolerance Termination criterion for the iterations.

Save Parameters Save the parameter settings for later use.

Calculate Inverse Transformation If the box is checked, the inverse transformation is also calculated once the matching completed.

Advanced Parameters

Thresholding method 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 **User defined** option is selected as

thresholding method.

Normalize values to (0,1)	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.
Algorithm runs	A value > 1 configures multiple successive matching runs, whereby a run is started with the result parameters of the preceding run.
Max iterations	A maximal number of optimization steps can be configured to avoid "endless" looping.
Scale	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.

Starting Rigid Matching

The **Match Current** button starts the matching process of the current input series with the given settings. A bar will appear in the status line which is incremented for each function evaluation. With **Match all**, all *Reslice* series are sequentially matched.

The principle of iterative rigid matching

- 1) An initial set of translation and rotation parameters is assumed or derived.
- 2) The *Reslice* study is transformed with these parameters.
- 3) The match between the *Reference* and the transformed *Reslice* study is evaluated according to the given matching criterion (**Dissimilarity function**).
- 4) Based on the criterion before and after transformation (better?, worse?), the parameters are modified according to an improvement strategy. The updated parameters are expected to yield a better match.

The steps 2 – 4 are repeated until the improvement drops below a given threshold, the function tolerance.

Brain Normalization

Brain normalization methods are procedures for transforming individual brain images into a standard anatomical coordinate space. They require a suitable template image which is already in the standard space, and an elastic matching procedure for warping the images appropriately. The **Brain Normalization (previous)** (BN I, Deprecated) and **Brain Normalization** (formerly BN II) methods have been implemented according to the methodologies used in SPM99 [9] and *SPM5* www.fil.ion.ucl.ac.uk/spm, respectively.

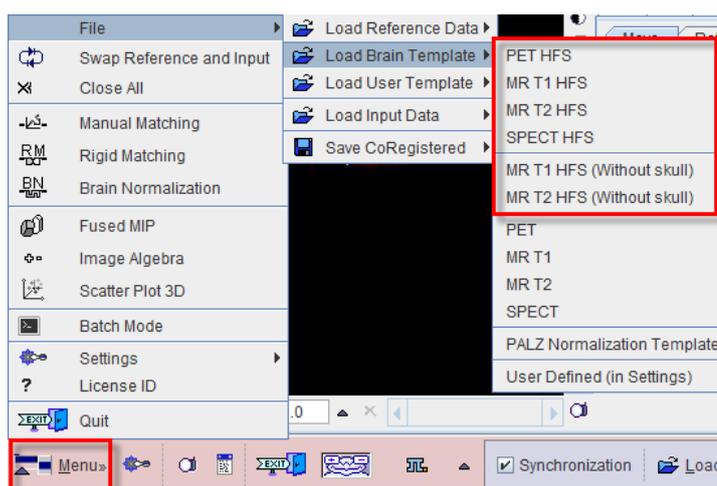
Brain Normalization (previous) uses a fixed sampling scheme, whereas **Brain Normalization** derives the sampling density from the smoothing parameter. Another

difference is that **Brain Normalization** derives the number of basis functions from the specified **Frequency cutoff** (default = 25) and the **Bounding box** size. Higher cutoff values result in fewer basis functions.

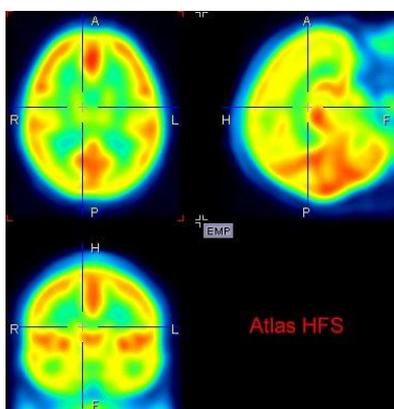
Note: For work with small animal data only the **Brain Normalization** method should be applied.

Available Templates (Atlases)

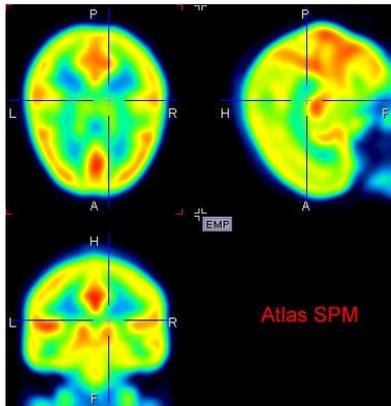
Template (or *Atlas*) images represent a "standard" anatomy imaged with a certain modality. For the spatial normalization of human brain images the MNI (Montreal Neurological Institute) templates are commonly used. In **PFUS**, they have been prepared for easy loading as the *Reference* by the **Menu** as illustrated below.



It is important to note that the anatomic orientation in the images after loading depends on the menu entry. If a menu entry with **HFS** (Head First Supine) is selected, the loaded image appears in *radiological* convention, which is the default for PMOD. For example, loading **PET HFS** results in the following orientation.



When loading the same images without the HFS arrangement, the result is in HFP (Head First Prone), ie the images are rotated about the z-axis and the face is pointing down as illustrated below.



The available brain templates:

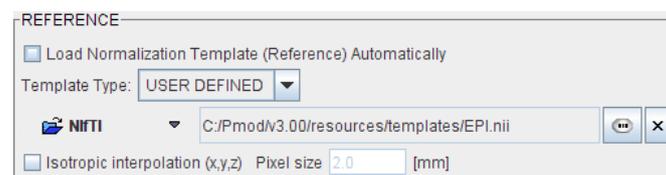
PET / PET HFS PET template provided with *SPM5* www.fil.ion.ucl.ac.uk/spm (Statistical Parametric Mapping). It was constructed by Friston et al. at the Wellcome Department of Cognitive Neurology (University College London, UK) using Oxygen-15 water PET images of 12 normal subjects scanned in resting condition with eyes closed. The template is in MNI (Montreal Neurological Institute) coordinates.

MR T1 / MR T1 HFS / Skull removed T1 template provided with *SPM5* www.fil.ion.ucl.ac.uk/spm. 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).

The T1 HFS image is also available with the skull removed.

MR T2 / MR T2 HFS / Skull removed The same as above, but with the T2 MR images.

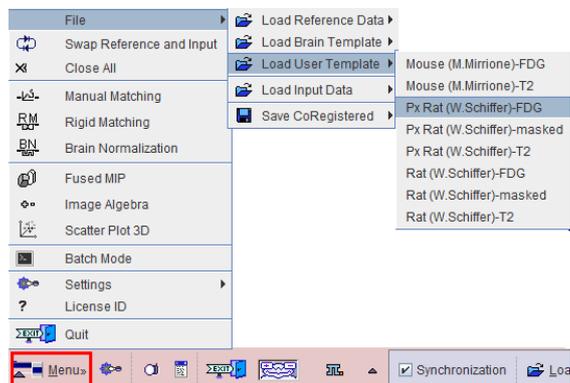
User defined Allows loading a template which is configured in the settings of the PFUS tool as illustrated below.



The user can set up additional template images for quick loading with the **Load User Template** menu entry. Such template images must be in NIfTI format and placed in the

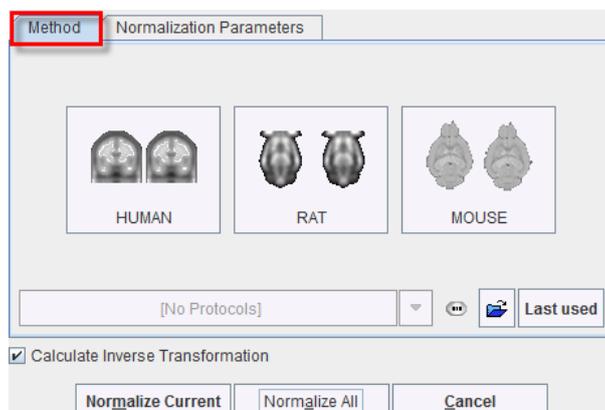
`Pmod3.3/resources/templates/usertemplates` directory. Their proper orientation is up to the user. Note that the menu entry only appears if there are valid templates available.

The PMOD distribution already includes some templates which are described in the **PMOD Base Functionality Guide**.



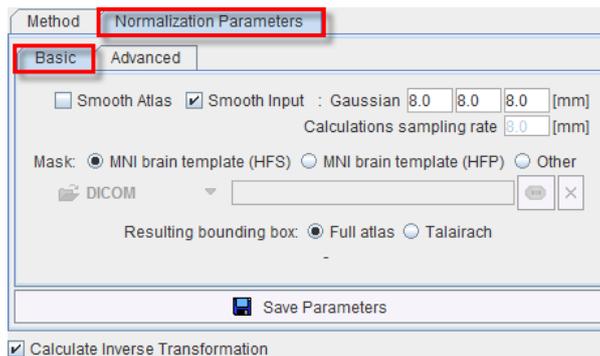
Brain Normalization Method

After the template has been loaded as the *Reference* and the study to be spatially normalized as the *Reslice*, activate the **Brain Normalization** button. A dialog window appears for configuring the processing.



There are buttons in the **Method** pane to establish proper parameter presets for certain tasks, particularly for processing **HUMAN**, **RAT** or **MOUSE** data. Activating one of the buttons displays the **Normalization Parameters** pane with appropriately configured settings. The **Last used** button restores the parameter configuration of the latest **Brain Normalization** invocation, and the list selection allows retrieving special purpose parameter sets.

There are **Basic** and **Advanced** parameters on separate tabs.



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.

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

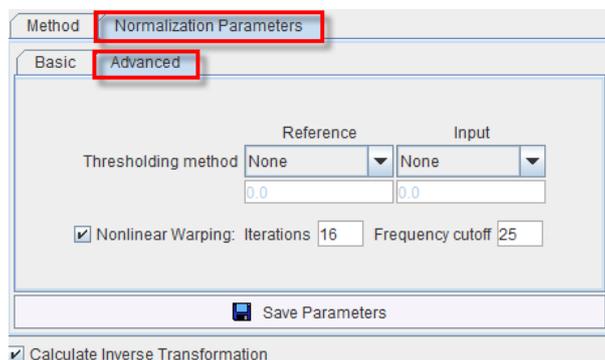
- ▶▶ **MNI brain template (HFS):** a MNI brain template with HFS orientation was loaded. With this selection the standard **Mask** is used, so there is no need to define it.
- ▶▶ **MNI brain template (HFP):** a MNI brain template was loaded as is, appearing as HFP. The corresponding standard mask is 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.

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.

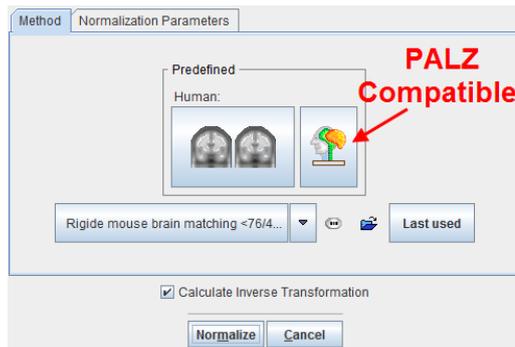
Frequency cutoff The specified **Frequency cutoff** (default = 25) is used together with the **Bounding box** size to calculate the number of basis functions. Higher cutoff values result in fewer basis functions.

Starting the Normalization

The **Normalize Current** button (or **Normalize** if only one *Reslice* series was loaded) starts the normalization process of the current *Reslice* series with the given settings. A bar will appear in the status line which indicates the normalization progress. With **Normalize All** all *Reslice* series are sequentially normalized.

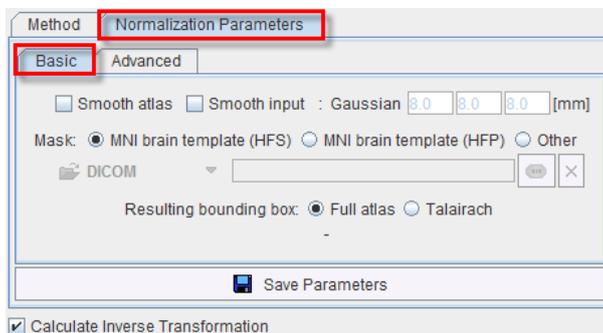
Brain Normalization (previous) Method (Deprecated)

After the template has been loaded as the *Reference* and the study to be spatially normalized as the *Reslice*, activate the **Brain Normalization I** option button. A dialog window appears for configuring the processing.



Since the **Brain Normalization (previous)** method is not supported for animal data, only human preset buttons appear. The button to the right serves for configuring the normalization in a way which is compatible to the normalization used in the PMOD Alzheimer's Discrimination tool PALZ.

Activating either of the buttons displays the **Normalization Parameters** pane with appropriately configured settings. There are **Basic** and **Advanced** parameters on separate tabs.



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.

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

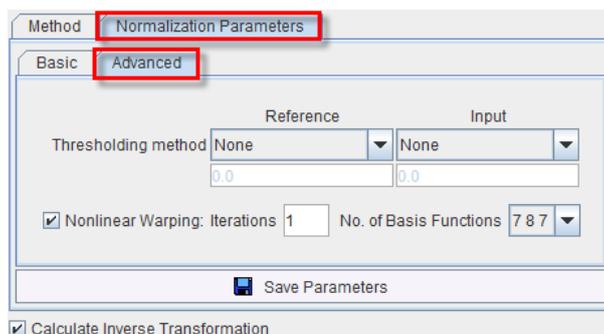
- ▶ **MNI brain template (HFS):** a MNI brain template with HFS orientation was loaded. With this selection the standard **Mask** is used, so there is no need to define it.
- ▶ **MNI brain template (HFP):** a MNI brain template was loaded as is, appearing as HFP. The corresponding standard mask is used.
- ▶ **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.

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.

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

No. of Basis Functions Number of basis functions from the cosine transformation in each direction.

Starting the Normalization

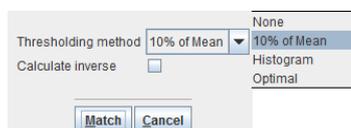
The **Normalize Current** button (or **Normalize** if only one *Reslice* series was loaded) starts the normalization process of the current *Reslice* series with the given settings. A bar will appear in the status line which indicates the normalization progress. With **Normalize All** all *Reslice* series are sequentially normalized.

CAUTION: This method exists for compatibility reasons only and is not further developed. Please use the Brain Normalization method for your work.

Principal Axes Matching

The **Principal Axes** method is an analytical matching method yielding the rigid transformation parameters in one calculation step. It interprets the image volumes as a mass distribution and aligns the principal axes of the two objects.

The presence of a background signal is crucial for the performance of the algorithm. Therefore several approaches for thresholding are offered in a selection.



Note that in practice principal axes matching rarely provides a satisfactory final match.

Motion Correction

The purpose of motion correction is to correct the image time frames of a dynamic study for relocations due to patient motion.

To start motion correction please begin by first selecting the **MOotion Correction** tab or the  button in the taskbar. As a consequence, the load **Input** button of the *Reslice* images gets active as shown below, and the study to be motion corrected can be loaded.

1. Select Mode

2. Load dynamic

3. Define reference

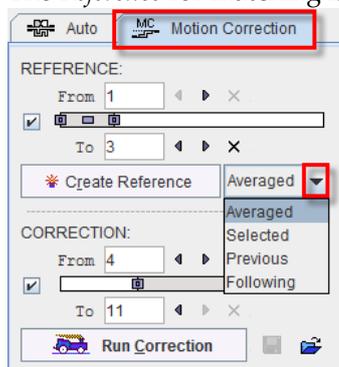
4. Define correction range

5. Run

The next step is to configure the different elements of motion correction using the interface elements which have now become active.

Reference image for Motion Correction

The *Reference* for matching is defined with the upper part of the panel:



The following options can be selected from the list:

- Averaged** An average image is calculated from a range of frames and serves as a static *Reference* for the correction of the frames. The average can be calculated from all frames, or from a sub-range as defined by the upper **From To** range. For finding out a range of frames with negligible patient motion it is recommended to review the frames beforehand in the movie mode (see below).
- Selected** The frame shown in the upper right image window will serve as the *Reference*. Please note that if the tracer distribution 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.
- Previous** In this mode, motion correction matches each frame to its previous with the advantage that the changes in spatial tracer distribution 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** This is the same principle as the **Previous** mode, but the method works from the latest frame in the selection through the earliest one.

After the *Reference* configuration has been completed, please activate the **Create Reference** button to initiate creation of the *Reference* image, which is then shown in the upper left image section. Creation of the *Reference* can be repeated until a satisfactory *Reference* has been found.

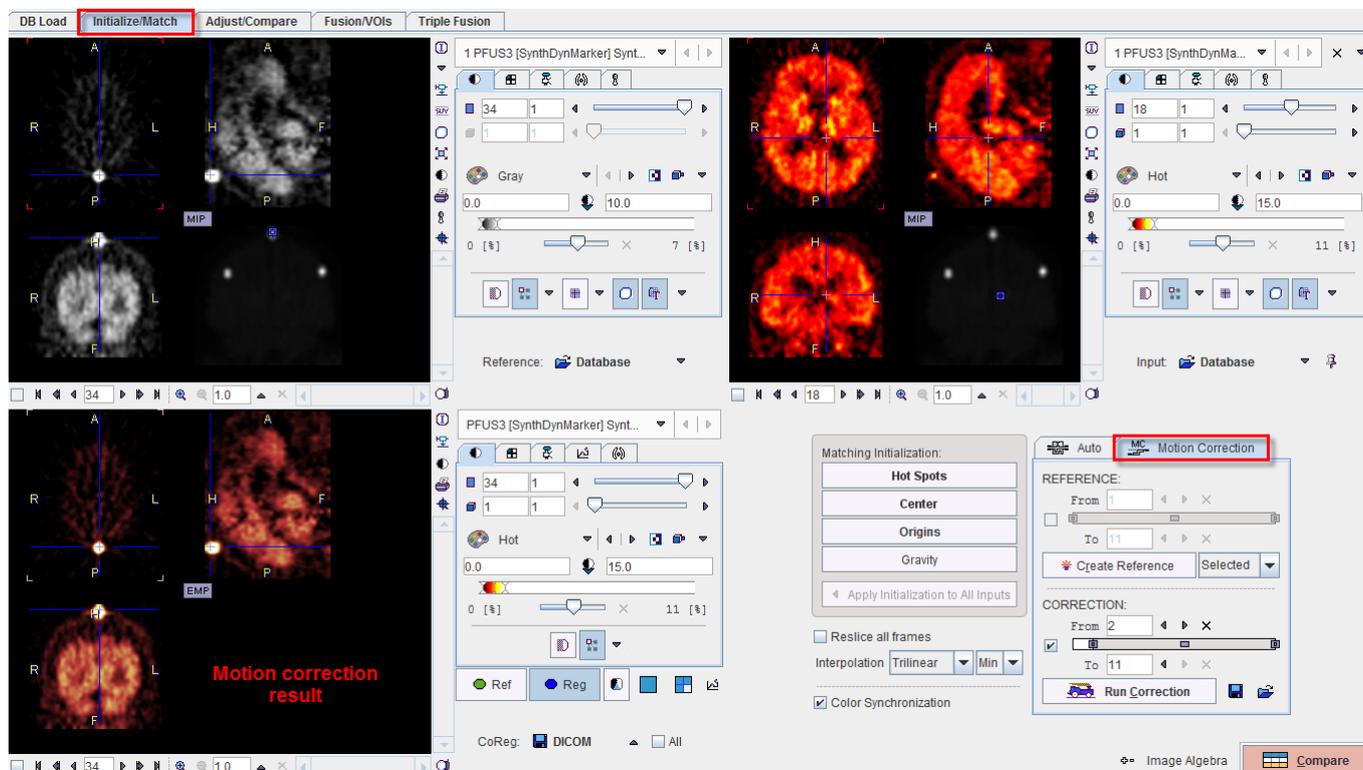
Correction Range

Next configure the 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. If adequate, check the second **From .. To** range box and define the correction sub-range.

Starting Motion Correction

To start motion correction, activate the **Run Correction** button which becomes active as soon as a *Reference* has been created. It brings up the rigid matching dialog, allowing to modify the matching parameters. All rigid matching methods are available. When the **Match** button is activated, motion correction starts, and the result is shown in the lower left section. Shown below is the result of motion correction with the demonstration study (containing markers).



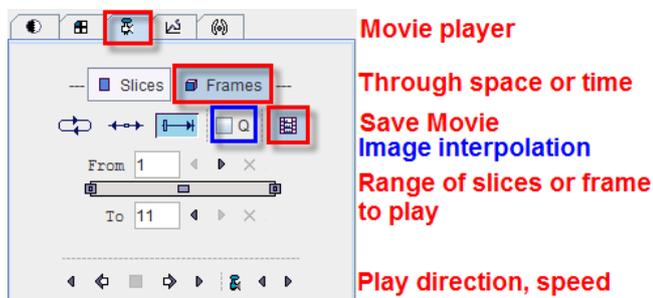
The motion corrected study can be saved in a format of your choice using the **CoReg** button. The motion correction transformations can be saved/retrieved using the corresponding buttons on the **Motion Correction** pane.

Control of Motion Correction Quality

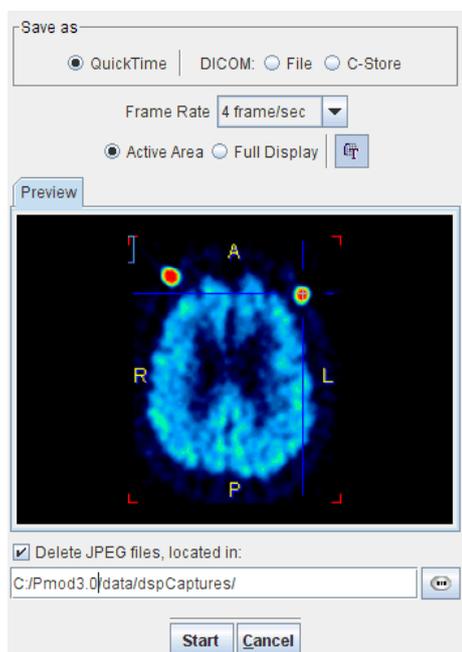
To check the quality of the applied motion correction we propose the following procedure:

- ▶ use a fixed range of the color table and set the minimum/maximum value to a globally reasonable value;
- ▶ select the movie tab, enable **Frames** looping, and start the movie. If necessary, use the reduce speed / single step buttons to examine the corrected study.

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.

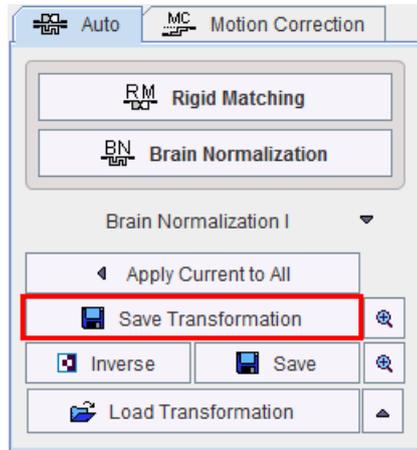


The movie formats include Quicktime or DICOM, and the active image or the entire image viewport can be captured. The movies are generated from intermediate JPEG files, which can optionally be kept for other uses.

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

Saving of Transformations

The transformations are saved from the **Auto** panel on the **Initialize/Match** page.



To save a transformation please proceed as follows:

- 1) Select the appropriate reslice series in the **CoReg** area.
- 2) Use the Save Transformation button and save the transformation matrix

Motion Correction

The transformation for **Motion Correction** are saved using the **Save** icon  and can be

Adjust/Compare Page

retrieved using the **Load**  icon available on the **Motion Correction** pane.

All the studies shown on the **Adjust/Compare** page have run through the reslicing process and hence have the same resolution as the *Reference* study. As a consequence, there is a one-to-one relationship between the pixels in all studies. This allows several tasks to be performed easily:

- ▶ The pixel values in two or three studies can be combined (for instance by adding the RGB colors) to calculate a "fusion" value. All fusion pixels together form a fusion image.
- ▶ Image algebra can be performed with the pixel values, for instance to calculate a pixel-wise difference image.
- ▶ VOIs can be applied to several studies, and the values of the VOI pixels shown in scatter plots (2D or 3D).
- ▶ Reports can be generated and saved as JPG/TIFF, or as a DICOM Secondary Capture object.

If the after automatic matching or initial reslicing is not yet satisfactory, there are two methods to adjust the alignment with the *Reference*:

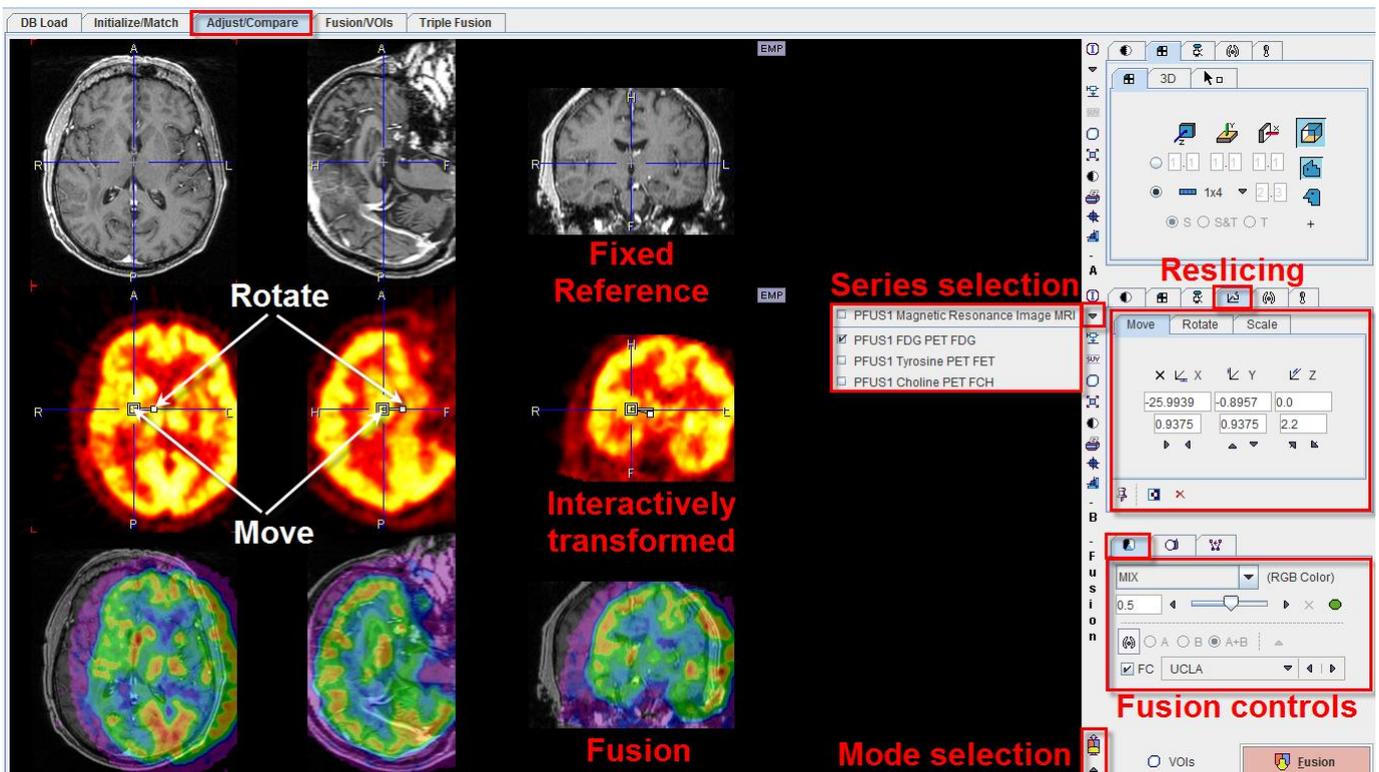
- ▶ Manual Matching, or
- ▶ Markers Matching

Note: Images matched manually or with the markers method can be saved with the  button in the taskbar, or using the **CoReg** button on the **Initialize/Match** page.

The different registration modes and processing tasks are described in the following sections.

Manual Matching and Fusion

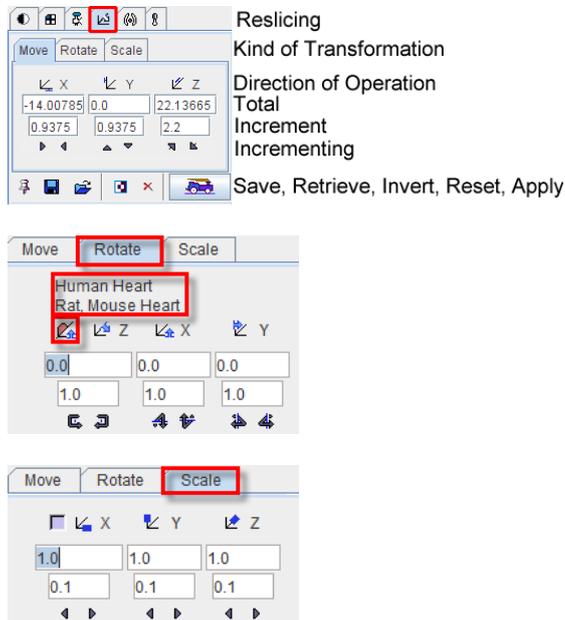
Start manual matching using the  button from the taskbar, the **Manual Matching** entry in the **Menu** or activating the **Compare** button in the lower right corner. The **Adjust/Compare** page appears as a three-row layout in the fusion mode as shown below. The first row contains the *Reference*, the second row a *Input* series, and the third row the fusion of the two. Note the selection for switching among the *Input* series. Each of them has its own transformation matrix associated.



The principle of manual matching is to shift and rotate the *Input* study in all three directions, until it gets into spatial alignment with the *Reference*. It is recommended to operate in the orthogonal planes mode (CTRL+D after clicking onto the *Reference* study, or the corresponding icon in the layout section). To be able to transform the *Input* study, the reslice mode must be active in the second row. It is enabled by selecting the corresponding  tab in the controls area of the *Input* study (see above), or pressing CTRL+R after clicking onto the *Input* study.

Summary of Interactive Reslicing

To calculate slices at oblique orientations or rotate images the reslicing pane must be activated. Reslicing is defined by a transformation consisting of translations in all directions, rotations about all axes, and potentially scaling along the axes. Each of these transformation components has its own sub-pane.



Note that **Scale** values of 1 indicate that the pixels sizes read from the image header are correct. Any other number will scale the pixel size accordingly.

The transformation parameters can be specified in different ways, on the corresponding sub-panes **Move**, **Rotate**, **Scale**:

- ▶ by entering values for the shifts or rotations in the number fields, or
- ▶ by clicking on one of the arrows to increase/decrease the values by the shown increments.

In the **Rotate** tab a help re-orientation button is available for heart studies . This option button allows re-orienting the heart data such that is closest to the short axis orientation (SA). The heart type can be selected when the button is activated. Two options are available: **Human Heart** and **Rat Mouse Heart**.

After changing the transformation, new slice images are immediately calculated and shown. However, the entire data set is only generated when needed, for instance to save the images. The  button serves for enforcing the reslicing process for the whole data volume.

The  button resets the transformation parameters. A transformation can be saved to disk using , and later retrieved with  if needed.

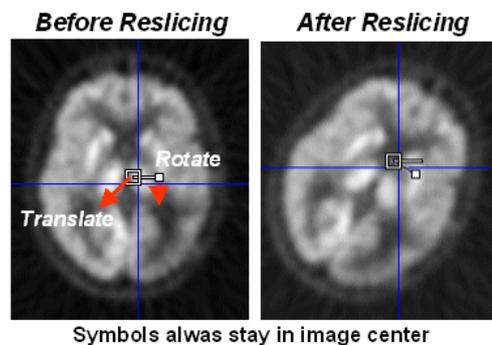
Important Notes:

1. The facility buttons in the reslicing panel for **Save**, **Retrieve** and **Apply** transformation are not always available.
-

2. The manual transformations are not fully equivalent with the automatic rigid matching transforms of the fusion tool. Manual transformation can be used in PFUS activating the **Load Transformation** button in the **Auto** panel available on the **Initialize/Match** page. In PFUS, the **Inverse** transformation is possible to calculate for any type of transformation activating the dedicated button  **Inverse** .

Mouse-driven Reslicing

As soon as the reslicing pane is activated, handles appear in the image overlay. They allow for interactive, mouse-driven reslicing.



Translation: Move the mouse pointer to the open white rectangle. The cursor changes to  . Click the left mouse button down, and then drag along the direction you want to move the image to.

Rotation: Move the mouse pointer to the filled small white rectangle. The cursor changes to  . Click the left mouse button down, and then drag while the image gets rotated. To get finer control of rotation, the rectangle can first be dragged radially outward, so that the handle distance from center increases.

Per default, the reslicing handles are shown as long as the reslicing tab is selected. If another tab is selected, they disappear. To make them appear permanently in the images and enable mouse-driven reslicing at all times, the pin button  can be fixed to  . A quick alternative to show/hide the reslicing controls in the active image is the **CTRL+R** shortcut.

In the fusion mode combined information of the upper two rows is shown in the third row. This fusion information should allow the user to check the alignment during interactive matching, so that in the end he can be confident that the found match is satisfactory. There are several ways of fused image rendering, which are explained a *lower section* (on page 52).

Selective Frame Alignment of Dynamic Series

Static image series naturally have only one transformation associated with them. For dynamic series, however, PFUS supports one transformation per frame. The automatic **Motion correction** calculates one transformation per frame with the aim of compensating rigid patient movements throughout the acquisition.

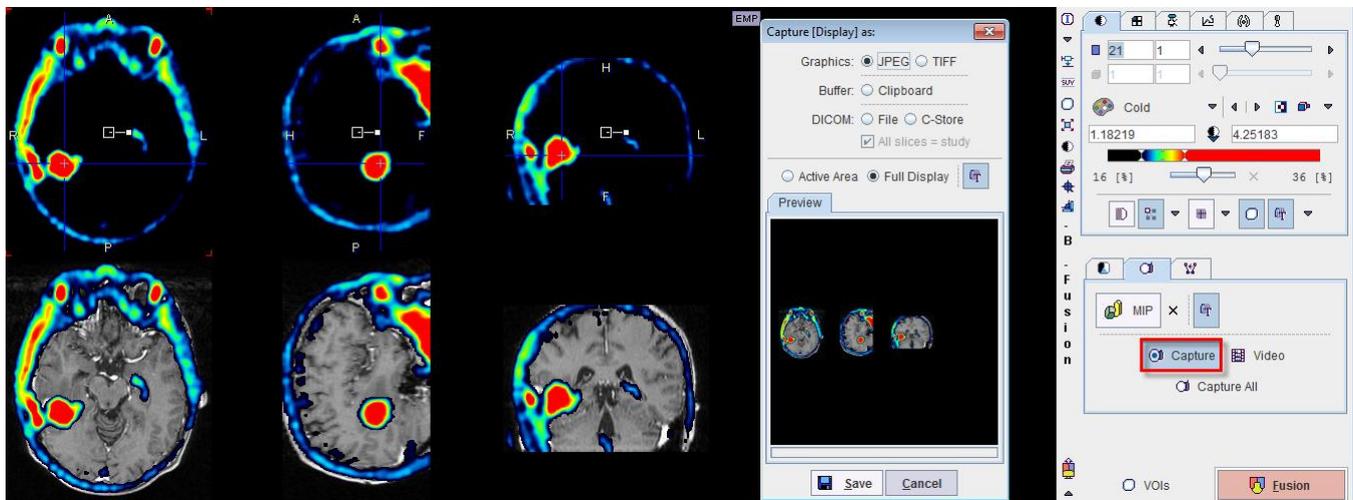
In manual coregistration, the user can chose to transform all frames at once, or to operate on individual frames. This behavior is controlled by the **Reslice all frames** box on **Matching Initialization** pane, in the **Initialize/Match** page. If the box is checked, all frames share the

same transformation. If **Reslice all frames** is not checked, the user only works with the current frame. When selecting a new frame, he can adjust the transformation without changing that of the prior frame.

When a successful automatic transformation is performed for one frame, the transformation matrix can be saved. To apply the same transformation to all frames the **Reslice to all frames** box needs to be enabled. The **Load Transformation** button allows loading and applying the individual transformation to all frames of the series. This function could be used to initially establish an "average" correction of all frames, and then apply fine-tuning for the individual frames.

Secondary Capture Image Generation of Fusion Images

In the manual matching and fusion mode there is  tab with a **Capture** button. It serves for saving the fused images in different formats. It displays a dialog window as illustrated in the example below.

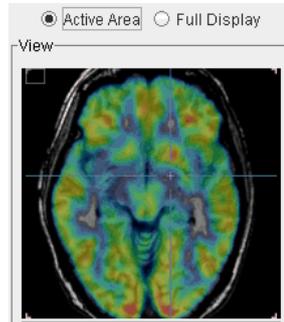


Note that the **Active Area** (image with red corners), or the whole row (**Full Display**) can be captured. Similarly, the **Capture All** button creates a capture of all three rows.

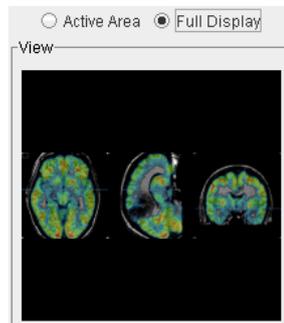
The output format can be chosen as follows.

JPEG, TIFF The generated images are saved in the corresponding graphic format to a disk location. With these selections an additional radio box becomes active:

Active Area: uses just the active slice in the current presentation, eg.



Full Display: uses the whole row, eg.



Clipboard As above, but copies the graphic to the clipboard. After that, it can be pasted into a different program such as MS Word or MS Powerpoint.

DICOM File With this selection, the images are turned into DICOM Secondary Capture objects, and can be saved to disk. In this case, zooming is not considered, but the full images are used.

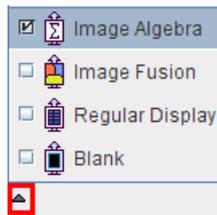
The DICOM output has an additional box **All Slices**. If it is checked, a fusion object is generated from all slices in the study, otherwise only from the currently active slice.

DICOM C-Store As above, but the generated DICOM objects can directly be sent to a DICOM server which can be selected from the list of configured DICOM nodes.

Image Algebra

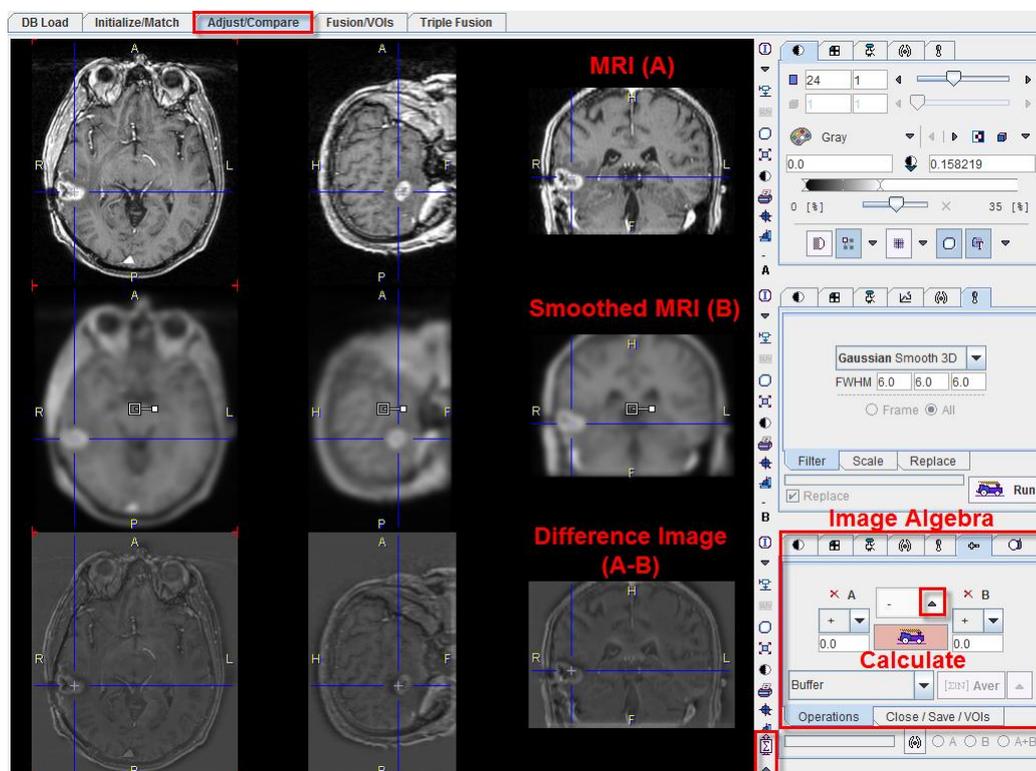
The image algebra functionality in PFUS allows pixel-wise calculations with two studies, yielding a new result study. For instance, a baseline perfusion study can be subtracted from a stress study, and the result divided by the baseline to calculate a percent perfusion increase image.

Image algebra is entered by the  button in the taskbar, the **Image Algebra** entry in the **Menu**, by the mode selection in the lower right corner or activating the **Image Algebra** button in the lower right corner in the Initialize/Match page.



As a result, a new tab \pm appears to the right of the third image row which gives access to a panel containing arithmetic tools.

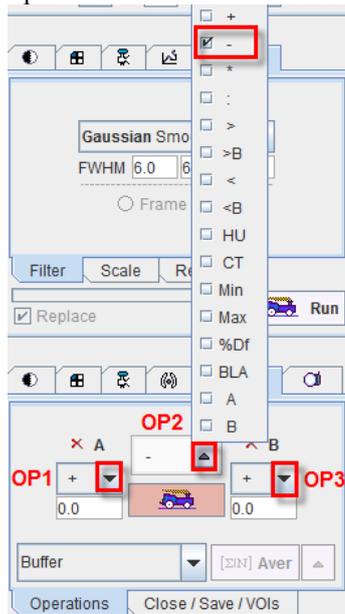
The example below illustrates image arithmetics by "unsharp masking". A MRI study has been loaded twice, as the *Reference* and also as a *Input* study. One of the image sets is displayed in the first row (**A**), the other one in the second row (**B**). The images in **B** are first smoothed with a 6 mm **Gaussian** filter available on the tools tab. Then the operation in the third row is configured to the - sign, and the  button is activated. The difference image *Reference* (A) - *Reslice* (B) is calculated and shown in the third row, demonstrating enhanced edges.



Operation Configuration

In general, operations of the form
 (A OP1 number) OP2 (B OP3 number)
 can be configured. This is achieved by setting the three operators OP1, OP2, OP3 with the

option buttons illustrated below.



The calculations are started by activating the  button. Besides the standard operations there are the $>$, and $<$ operators which perform comparisons and return the value itself if it satisfies the criterion, otherwise zero. The variants $>B$ (binary) and $<B$ return a binary mask image. For instance, the configuration



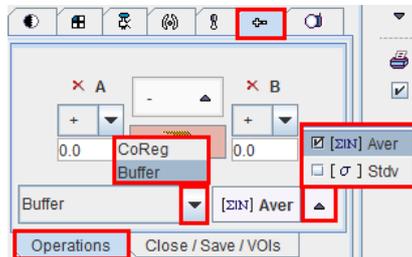
results in a binary mask with 1 in all pixels where study $A > 10.0$, and 0 elsewhere.

Min (Max) returns in each pixel the smaller (larger) value of both data sets. **%Df** calculates the percent difference by $(A-B)/A*100$, and similarly **BLA** calculates the percent difference by $(A-B)/(A+B)/2*100$. Note that the **A** and **B** operators allow restricting operations to only one image source. A tooltip of the functionality is obtained by moving the cursor after the configuration over the operator.

Important Note: In case the images are SHORT, any mathematical operation introduces a rounding error starting on 5th position after dot. If such error is not acceptable for processing, the solution is to convert the images to FLOAT representation. This can be easily achieved after loading in the **Info** dialog window activating **Convert to Float**. Please consider that when converting to FLOAT format the required memory size is doubled.

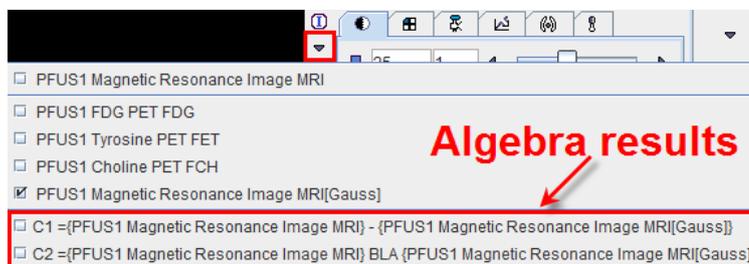
Mean and Standard Deviation of Images

Image algebra also provides a means to calculate the pixel-wise mean or standard deviation of a set of (matched) images. To this end load the images as *Input* images, set **CoReg** as the data range and activate the **Aver** or **Stdv** button. If the data range is set to **Buffer**, the average or standard deviation of all the image algebra results will be calculated.



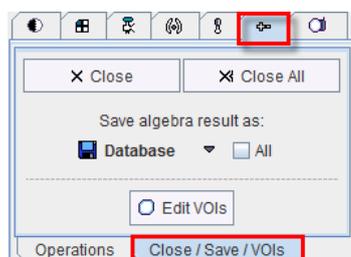
Using Algebra Results in further Calculations

The result studies of image algebra operations are displayed in the third row per default. However, they are also appended to the list of available studies, and they can be selected in the upper two rows as illustrated below. In this way, intermediate results can be made available for further calculations until the final result has been determined.



Saving and Closing Algebra Results

The images resulting from image algebra can be saved from the +- panel, after activating the corresponding **Close/Save/VOIs** sub-tab. On the same panel, results can be closed if they are no longer needed.



Markers Matching

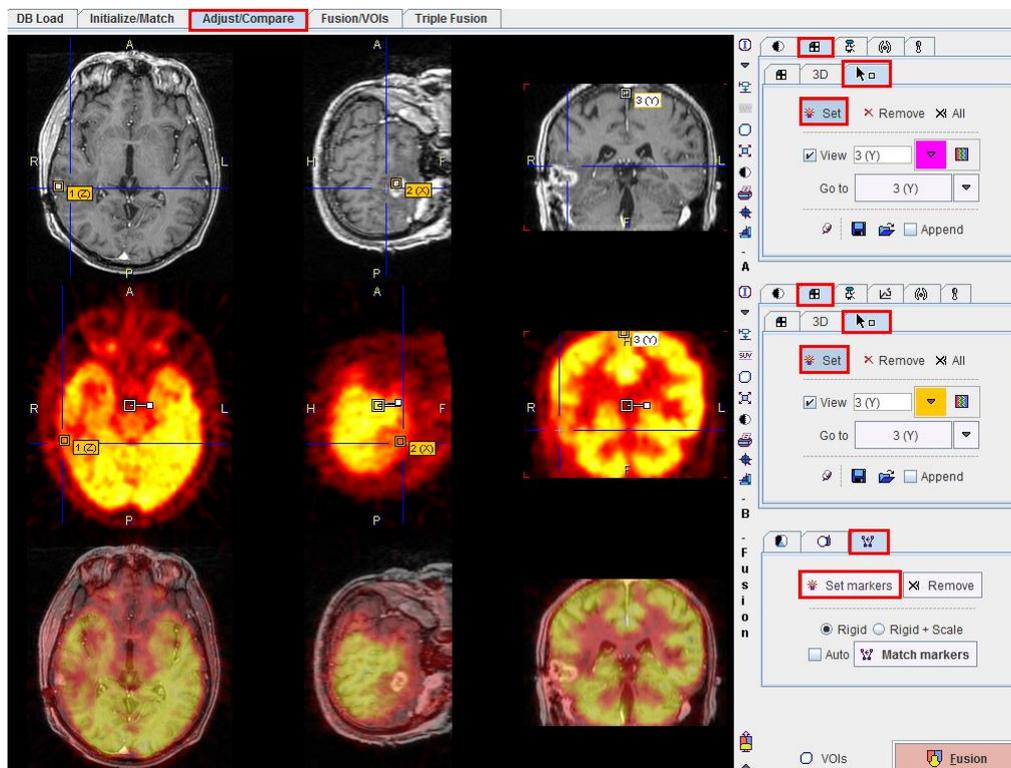
With this technique, the user explores the two image sets and marks corresponding anatomical locations, i.e. markers. A transformation is then calculated which brings the two spatial arrangements of markers into optimal agreement. In PFUS this operation is performed as follows.

Markers Matching Procedure

- 1) Start marker matching using the  button from the taskbar. The **Markers** panel is shown both for the *Reference* and the *Input* studies.
- 2) The **Set** button on the **Markers** panes is central for landmark setting: as long as it is not active (bright), mouse clicks into the image just cause reslicing. This is the mode to navigate to an anatomical landmark. When **Set** is active, any mouse click into the image defines a new landmark which is entered into the list. In this mode, multiple landmarks can quickly be set. The mouse wheel can be used to scroll slices in order to avoid the generation of landmarks by navigating, and CTRL+Click to change the active slice orientation.

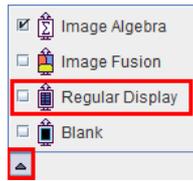
Note that you can jump to one of the landmarks, move it, remove it, save/retrieve a set of landmarks.

- 3) The user has to define at least three corresponding landmarks in either image study in this way. Only then, the **Match markers** button becomes active. When it is activated, an iterative optimization is performed to find a rigid transformation which brings the landmark sets into optimal agreement. This transformation is then applied to the *Input* study as well as its markers, and the result is shown.
- 4) To save the transformation or adjust the match manually, please select the  tab of the *Input* study and then use the  button.



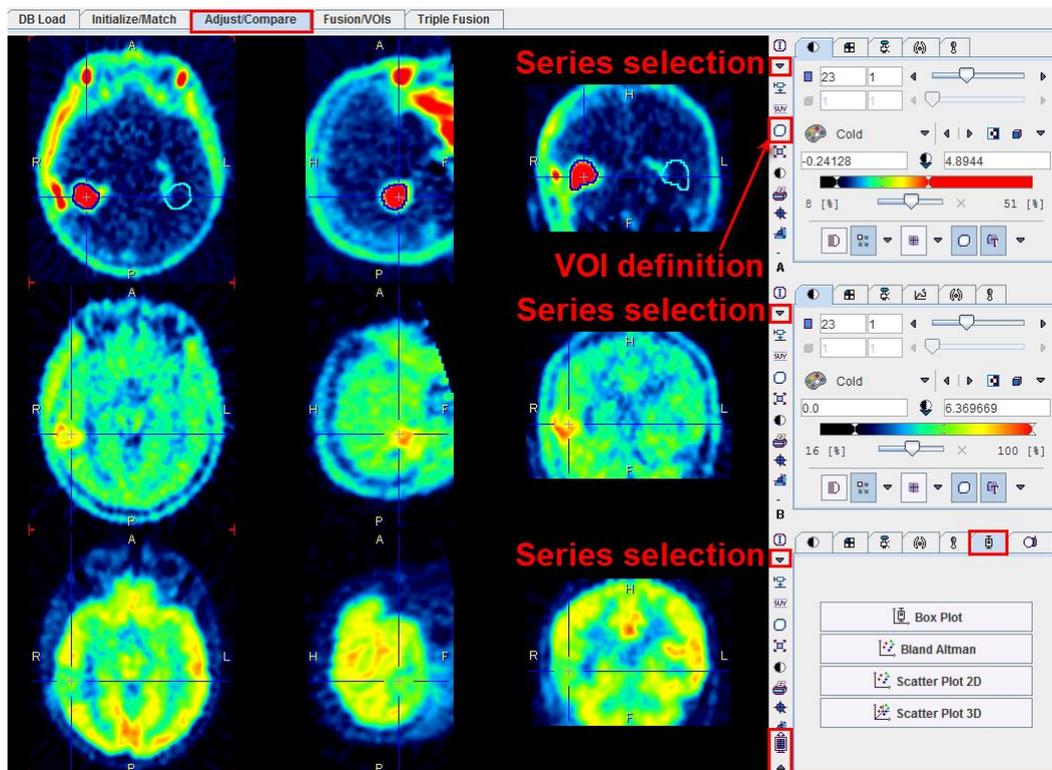
Regular Display, Scatter Plots

The **Regular Display** functionality in PFUS allows reviewing three matched studies in parallel. Furthermore, VOIs defined in the first row can be applied to the studies for generating 2D and 3D scatter plots. The **Regular Display** mode can be selected in the lower right



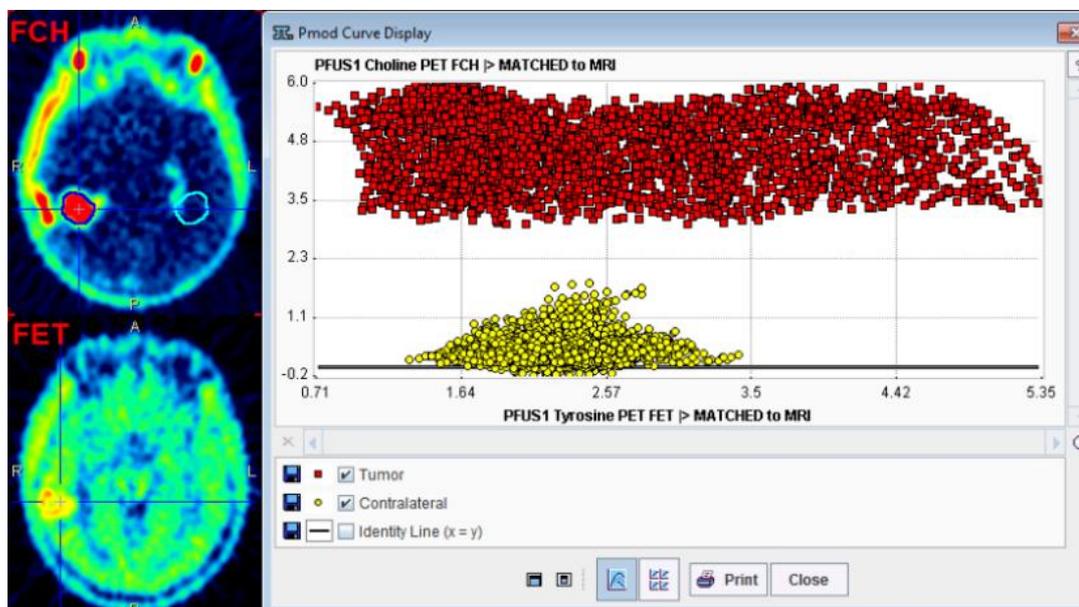
by selecting  in the taskbar, or by the **Scatter Plot 3D** in the **Menu**. The latter two methods will also prompt for VOIs for scatter plots.

The study selection allows in each row to select among all loaded studies. When reviewing, the three studies shown will always be synchronized.

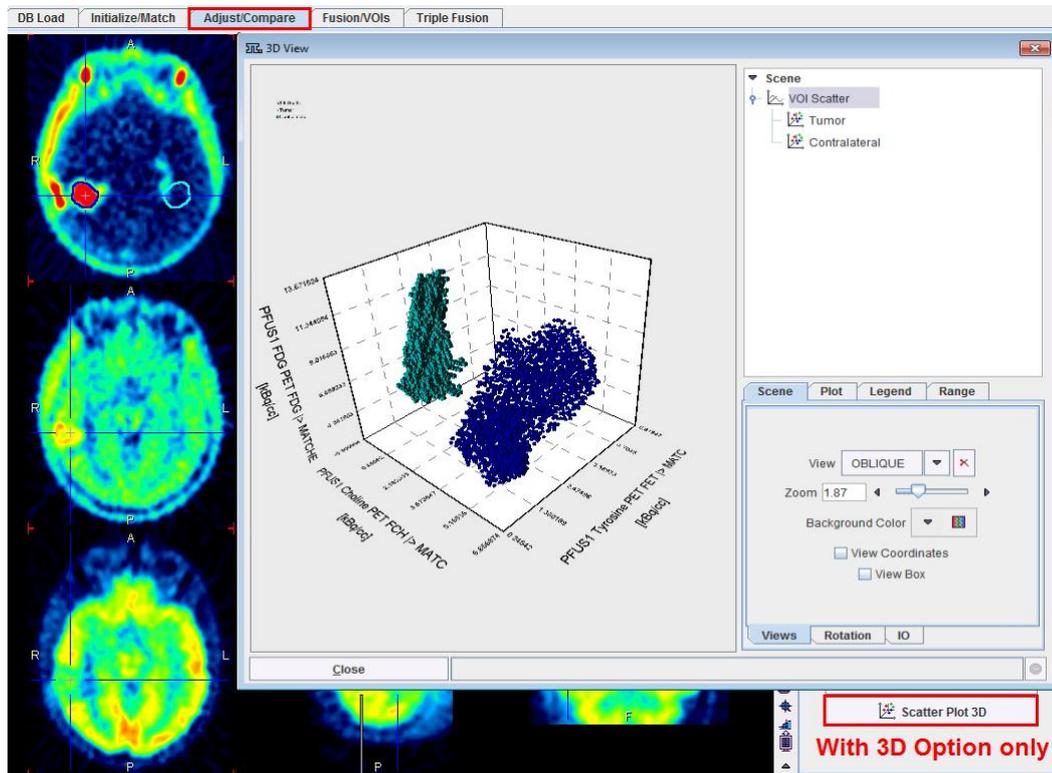


Scatter Plots

Scatter plots are a means to visualize the value of a pixel in different image series. The VOI(s) must be defined in the uppermost image row. There, the VOI tool can be started as indicated and an arbitrary number of VOIs can be outlined. Using the buttons in the lower right scatter plot generation can be started. With **Scatter Plot 2D** the pixel values are evaluated in all the VOIs of the upper two rows and shown in a scatter plot.

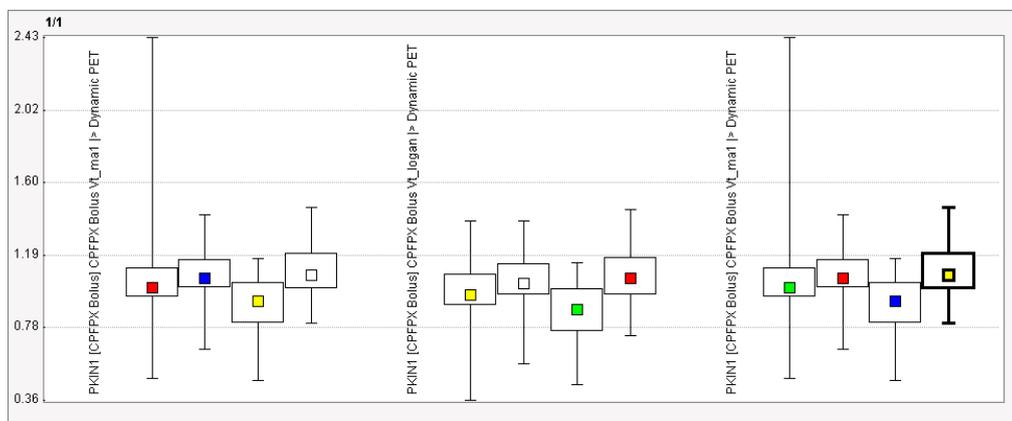


If the P3D option has been purchased, there is also a **Scatter Plot 3D** button available. When it is selected, the VOIs in the studies of all three rows are evaluated, and a 3D scatter plot generated, for example

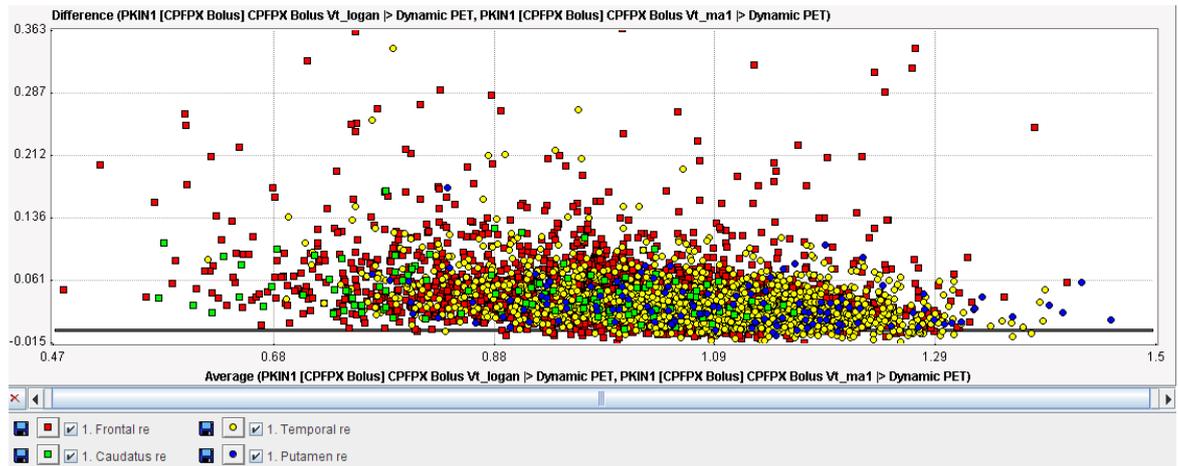


Note: In P3D, the numeric scatter data can be saved as a text file using the **Save** button on the **IO** sub-panel.

The **Box Plot** calculates a box plot representation of the VOI pixel values for all three image sets.

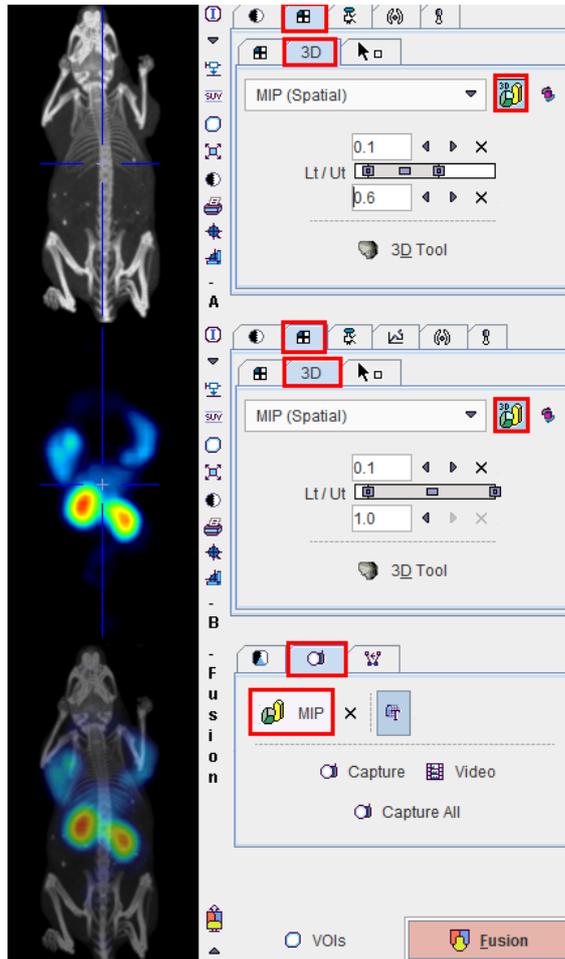


The **Bland Altman** plot can be used for a quick method comparison. For each VOI pixel it calculates the average and the difference across the images in the upper two rows, and plots the result (average on horizontal axis, difference on vertical axis).



Rotating Fusion MIPs

Use the  button on the taskbar to enter the MIP display mode. The **MIP** and **Video** buttons on the  tab of the third row can be used for creating movies of rotating scenes wherein the MIPs of the *Reference* and the *Input* are fused. Activating the **MIP** button switches both the first and the second row into MIP mode and shows the corresponding layout tabs. Use the lower threshold to remove low-intensity components, change the upper threshold to adjust the brightness, and pick a suitable color table for a convincing representation.



Then select a plane which is appropriate for the rotation (most likely the coronal or sagittal image) by clicking into the image. Start movie generation by selecting the **Video** button . Note how the control tab in the first row is switched to  as illustrated below. This tab has a list selection for defining the number of rotation angles, set to **40** per default. Setting more angles results in smoother rotations.

A **Save video** dialog window appears for defining the movie output. Note that the reference image is shown in the preview, but that a movie of both the reference and the fusion will be generated. After **Start** has been activated, the images in the different projection angles are calculated, saved as intermediate jpeg images, and then combined into the movies according the specified format. Please note that the calculations may require substantial time,

depending on the size of the data. For saving the result in Quicktime, the user is prompted for a movie name.



The  button next to MIP serves for quitting the MIP mode in all image rows.

Fusion Report Printing and Saving

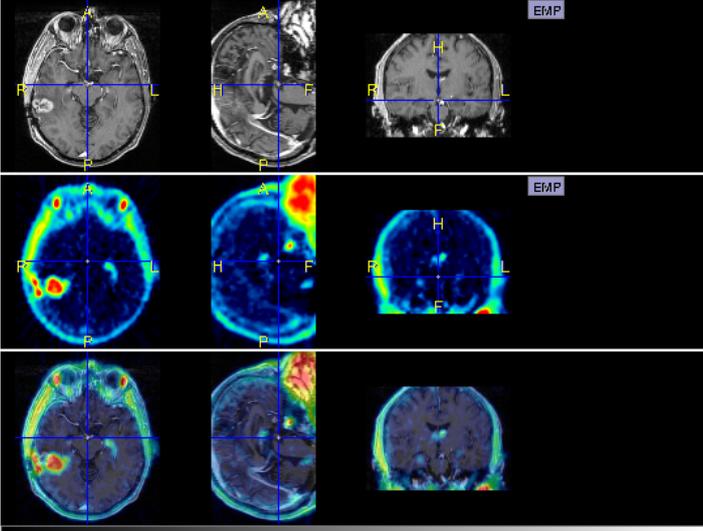
To document the current fusion arrangement, the user can select the report button  in the taskbar. Note that the orientation of the color bars (horizontal, vertical) can be configured in the application settings configuration , while the hospital logo and address can be defined with the  Config facility.

The **Report** button brings up a dialog swindow howing a preview of the report, such as

Institution
Address

NAME **PFUS1** B. DATE ID **Multimodality PE**

Report: 2011.10.27 (13:01:14) Study: 2006.03.01 1 of 1 PFUS 3.3



0.0 1/1 0.166771

0.0 kBq/cc 5.658175

Comment

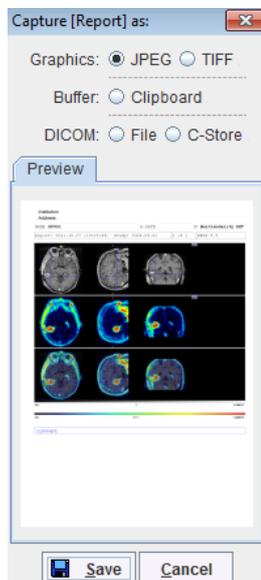
Zoom Annotations

T 11 75 % Overlay

Print (A4) Save As 1188 x 1684 pixels Cancel



After annotations have been added as a **Comment** or an overlay in the images, the page can be printed using the **Print** button, or saved in different formats using the **Save as** button. For producing a lower quality output the save button can be switched to **Save as** with a reduced number of pixels in the report image. As usually in PMOD, the page can be saved as a graphic file, copied to the clipboard, or converted into a DICOM Secondary Capture object. The DICOM object can be saved to disk or sent to a DICOM server.



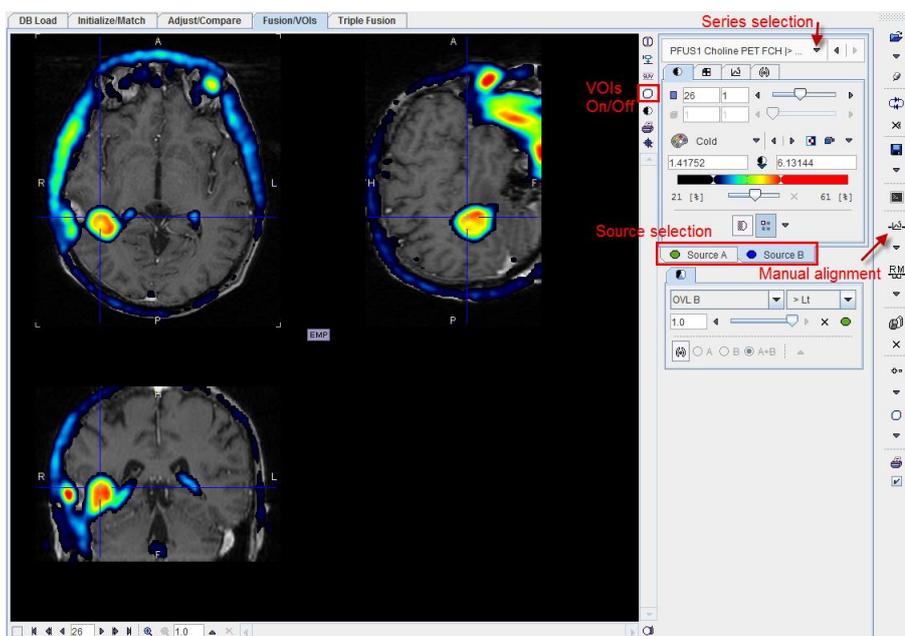
Fusion/VOIs Page

The **Fusion /VOIs** page has three functionalities.

- 1) Reviewing the fused images in a larger display window, not just in the third row.
- 2) Adjusting the alignment manually.
- 3) Definition of volumes-of-interest directly in the fused images.

Fusion Image Reviewing

The **Fusion/VOIs** page in reviewing mode has the layout as illustrated below.



The two tabs **Source A** and **Source B** provide the access to the two image components constituting the fusion. So if you would like to adjust the colors, define iso-contours, etc., first select the tab corresponding to the appropriate image, and then use the image controls as usual. The image which is shown as **Source A** or **B** can be selected with the upper study switching controls.

The image fusion controls are always available to change among the available fusion methods. To see only one of the images, the fusion balance slider can be moved to the left or the right in the mixing mode. Note: the balance slider can also be moved with **SHIFT+drag** the left mouse button *right/left*.

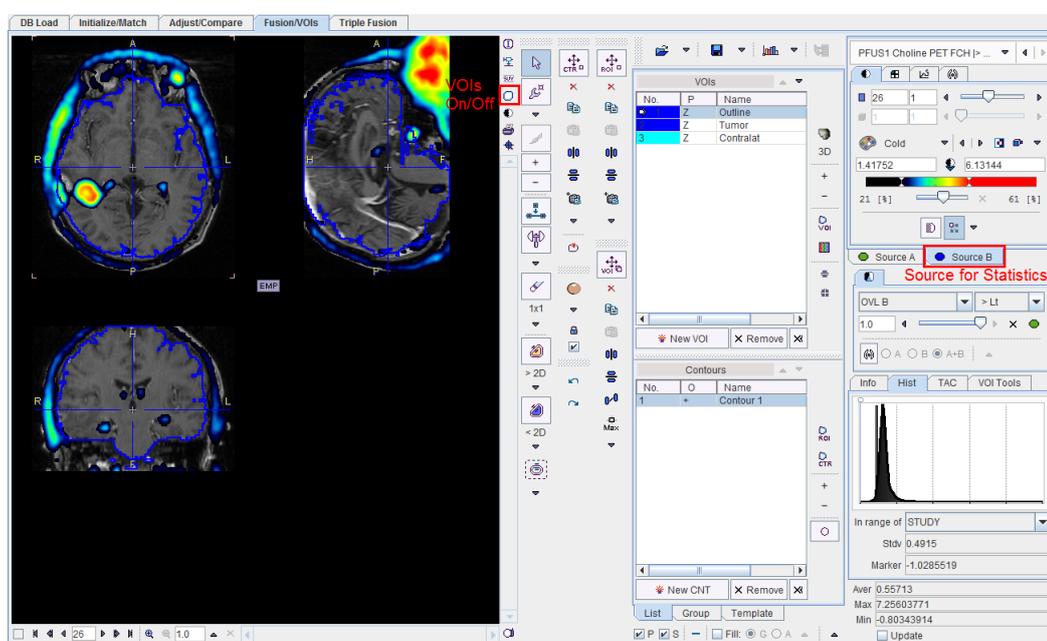
Switching Modes between Reviewing and VOI Definition

For switching to the VOI definition mode (and back from it), select the indicated VOI button. The VOI definition controls appear, and allow the outlining and evaluation of volumes-of-interest.

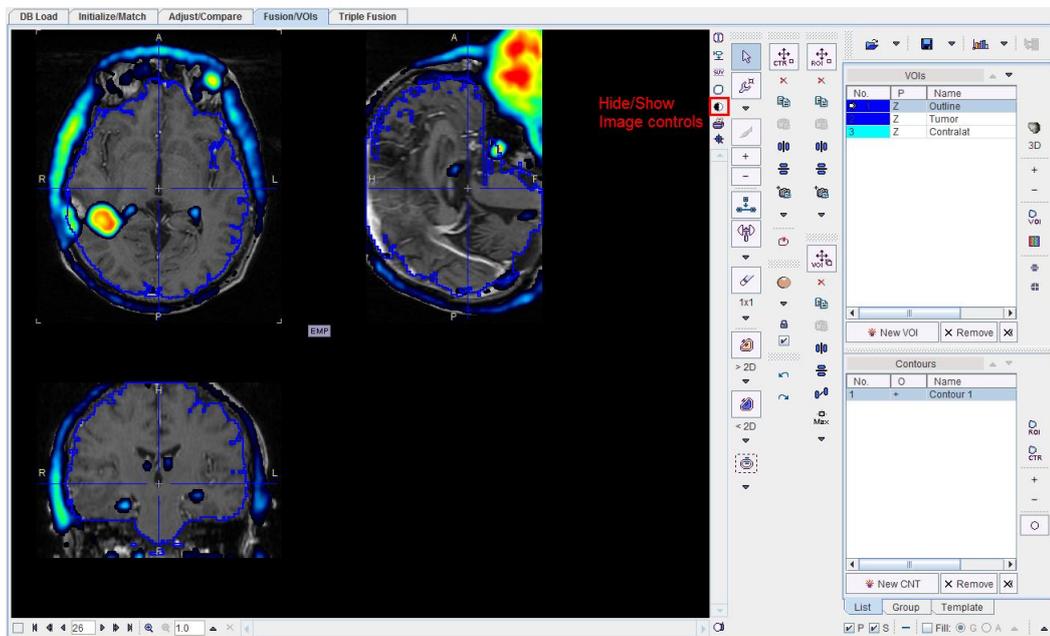
VOI Definition with Fused Images

The indicated VOI button besides the image toggles between the VOI definition mode and the reviewing mode. In principle, VOI definition works exactly as described in the PMOD Base Functionality Guide. The only thing one has to care about is, that the selected **Source** study (**A** or **B**) is relevant for VOI definition and evaluation. So before using one of the iso-contouring or region-growing tools please select the relevant source.

The example below shows the fusion of a MRI and a Choline PET in the VOI mode, with Choline (**Source B**) selected as the active study. The tumor VOI is obtained by defining a bounding box VOI and using the iso-contour auto-voi. When the **Statistics** button is selected, it starts the statistics calculations with the Choline study. To evaluate the statistics of the MRI, first select **Source A**, and then **Statistics**.

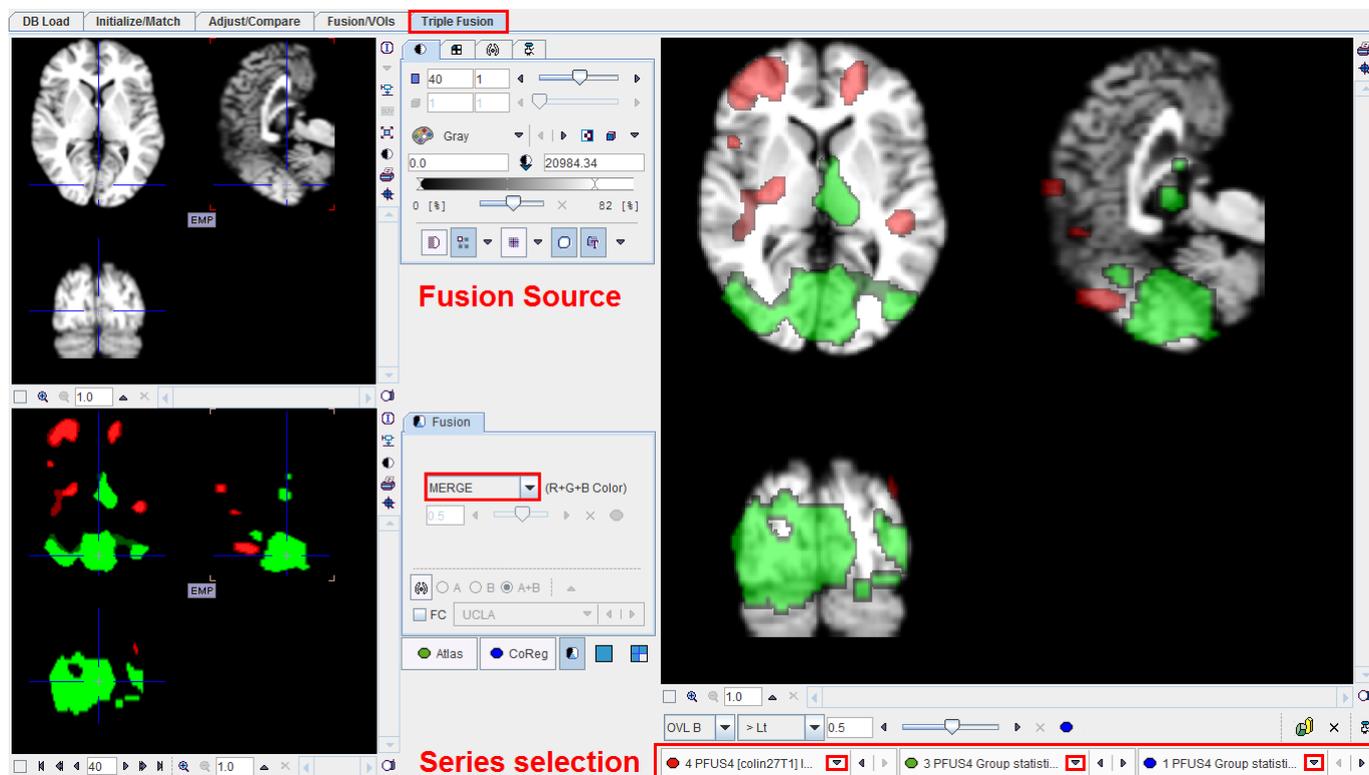


After a suitable configuration of the image presentation and the selection of the appropriate source the image controls can be hidden with the  button to get more image space as illustrated below. They can be brought back using  again.



Triple Fusion Page

In some situations it may be helpful to compile the information of three images into one fused rendering. This can be done on the **Triple Fusion** page as illustrated below with a functional MRI study. Three studies were loaded, an anatomical data set and two contrasts. The series selection can be performed as indicated below.



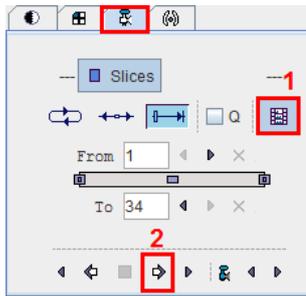
The image selection ● corresponds to the fusion source panel in the upper left. The next selections correspond to the **Atlas** and **CoReg** and are displayed in the **CoReg** panel in the lower left.

The anatomical MRI image was selected as fusion source. One contrast was selected as **Atlas** and the color table set to **Red**. The other contrast was selected as **CoReg** and the color table set to **Green**. The **CoReg** panel shows the fusion of the two image contrast, **Atlas** and **CoReg** using the **MERGE** mode.

The large image display to the right always shows the fusion of the image selected as fusion source with the image shown in the lower left part. So if the images are selected as in the example, the 3 source fusion shows the two contrasts on the anatomical image. In this configuration, the **OVL B** method was used to clearly see the anatomy outside the contrast area.

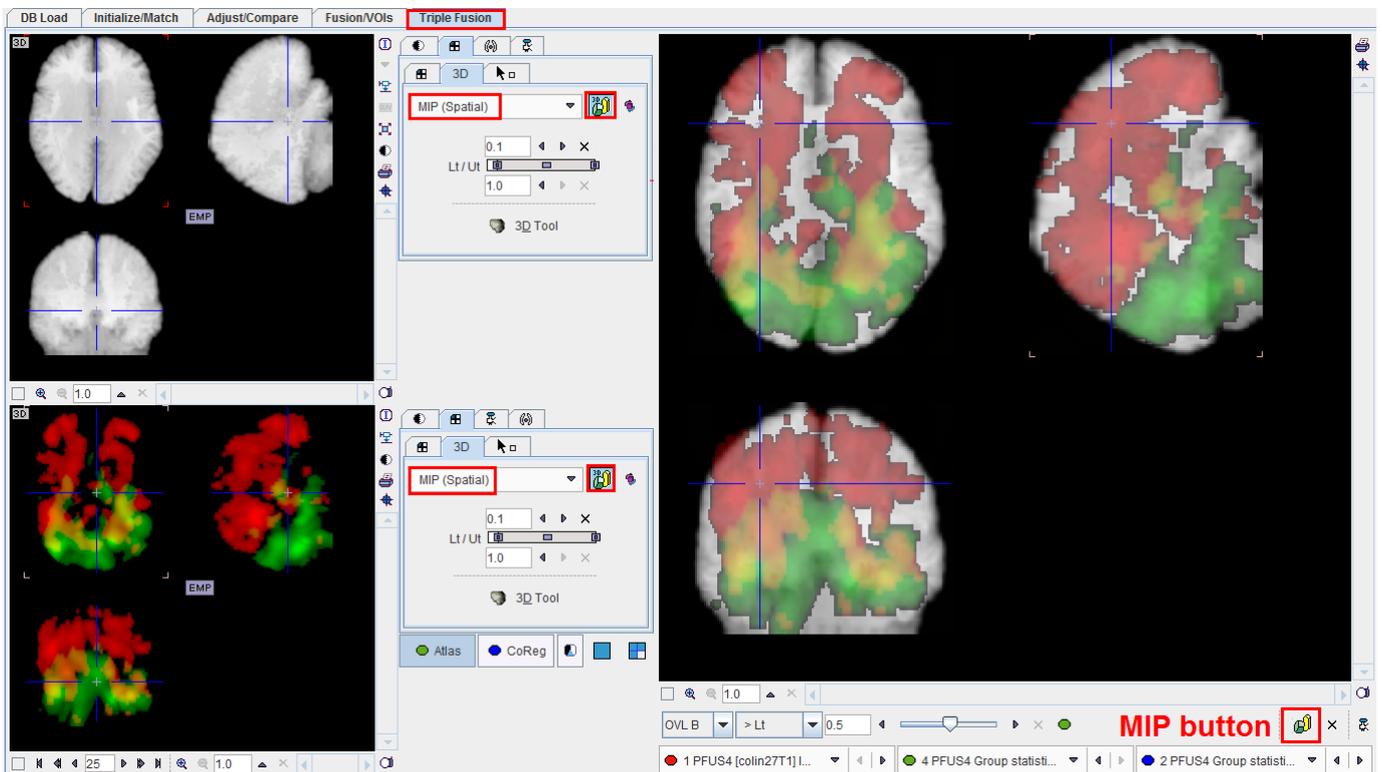
An additional helpful feature is the ability to capture the images in the right display into a sequence of JPEG files and to generate a movie. As soon as the **Movie** control button  in the lower right corner is activated all studies are switched into the **Movie** mode. Activate the

Save video capture button 1 and starts with button 2 stepping the fusion images through all the slices of the currently selected plane. At the end the program prompts for a movie file name.



Select the plane around the vertical axis of which the projection should be rotated, and then start processing.

As soon as the MIP button is selected, all studies are switched into MIP mode:



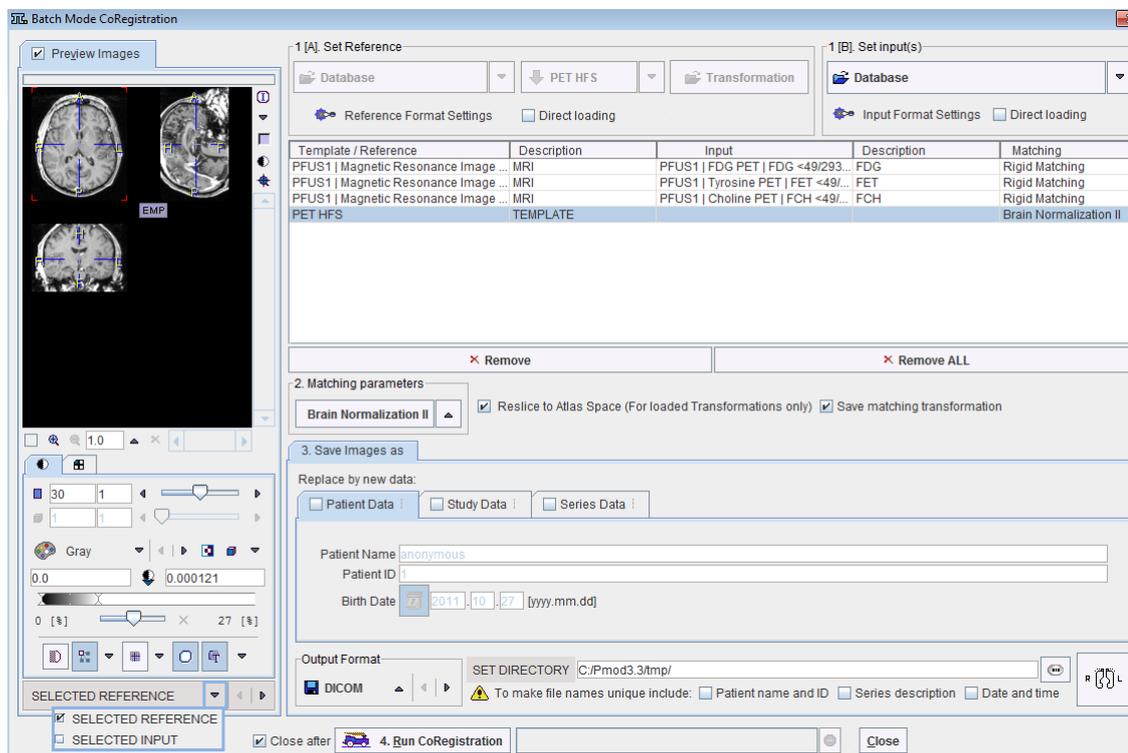
Use the  button to switch off the MIP mode.

Matching and Reslicing in Batch Mode

The PFUS tool offers a batch matching facility which is useful if several studies are to be matched to a single *Reference*. Spatial normalization to an atlas template is a typical situation

of this kind. For example, all images of a clinical trial could be normalized by batch matching to a common template.

Batch matching is started using the  button from the taskbar or **Menu/Batch Mode** and displays the dialog window illustrated below.



The following configuration tasks must first be completed for running matching in a batch procedure.

- 1) Selection of the matching method in the **Matching parameters** section. In the appearing configuration dialog the **Matching parameters** can be adjusted as discussed above for the different methods. If the **Save matching transformation** box is checked, the resulting transformation parameters will be saved in addition to the resliced images.
- 2) Definition of the job(s) which are Reference/Input pairs. As a first step select the data formats correctly, in the example above **Database**. Then proceed by selecting a reference data set using the **Database** button, and subsequently the input data set(s) to be matched to this reference. The result is a job entry in the list as illustrated above. Continue these configuration steps until all matching pairs are listed.

Note that only a single data format is supported for a batch procedure. For normalization procedures a template can easily be configured using a dedicated button, here labeled **PET HFS**. If there are pre-processing transformations which should be applied during loading, these can be configured using the **Input Format Settings** buttons. Note that, in this case, the **Direct loading** box have to be unchecked.

- 3) The matching method can be selectively adjusted for each job in the list by clicking at it and then changing the **Matching parameters** selection.
- 4) **Save Images as**: Specification of the output. First select the data format, and then configure the parameters of that format. Finally, specify the output path (or the target database). As an option, the **Patient Data**, **Study Data**, **Series Data** information can be

replaced by an arbitrary string to create anonymous data sets in the corresponding sub-tabs.

Finally, the **Run CoRegistration** button can be activated to initiate batch processing. The matching jobs are processed one after the other and the results saved according to the specification.

Batch Reslicing

In addition to matching the batch mode can also be used to apply previously calculated transforms to a series of data sets as illustrated below. In this case **Transformation** is used to select a transformation instead of a reference.

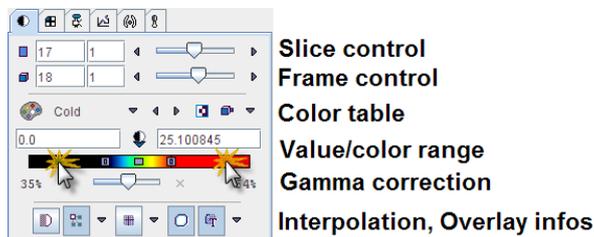


Image Presentation Hints

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.

Changing the Image Presentation

The first tab in the main controls contains most functions to modify the way how the images and the overlay information look like.



Control of Slice(s)

The slice control section allows to scroll through the images using the increment buttons, the slider, or directly by entering a slice number. The value right to the number of the active slice controls incrementing. This is particularly relevant in multi-image layouts. For example, if the increment value is set to 2, only every second image will be displayed.

Instead of selecting slices using the controls, the user can also scroll slices by dragging the left mouse button over the image holding the **CTRL** key in the **Up/Down** direction (see the summary of shortcuts below), or with the mouse wheel.

The frame control section only becomes active for dynamic studies with multiple time frames and behaves the same way as the slice control. To allow for mouse-operated scrolling over time, the time box on the left side below the image must first be checked.  

Note: There is a quick way for jumping to the particular slice/frame containing the maximal pixels value: just click the buttons   next to the slice/frame selection.

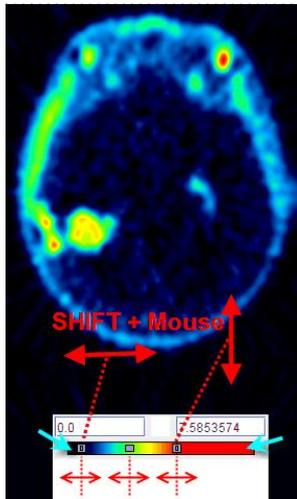
Color Tables

There is a selection of pre-defined gray and color tables which can be chosen with the list selection.



Note: A new user defined color table can be simply be added. Create a 3-column text file with the RGB values and saving it to the sub-directory *resources/colortables* (see the examples there). They are appended to the lower section of the color table list such as **PETCT** in the example above.

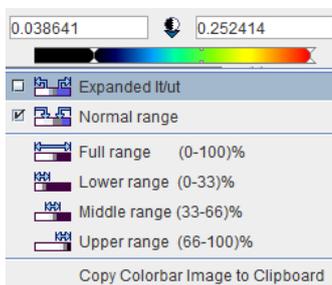
A minimal/maximal threshold value defines the range of displayed values. The thresholds can be entered numerically, or the handles in the color bar can be dragged with the mouse. Additionally, the user can modify them by dragging the left mouse button over the image holding the **SHIFT** key. Left/Right movements modify the lower threshold, while Up/Down movements modify the upper window.



Note: Double-clicking into the lower end of the color bar sets the lower threshold to zero. Double-clicking into the upper end of the color bar sets the upper threshold to the maximum.

Zooming into Color Table

In some cases, the range of image values of interest only covers a small part of the color bar which makes it difficult to adjust the brightness precisely. In this situation, the user can zoom the color bar into the current sub-range of values. Clicking the right mouse button into the color bar pops up the context menu



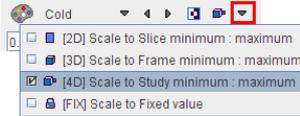
The first menu entry **Expand It/ut** then performs the desired task and makes the color bar change to



The second entry performs the reverse operation, and the other entries are just shortcuts which may be helpful. The last option in the list allows copying the colorbar image to clipboard.

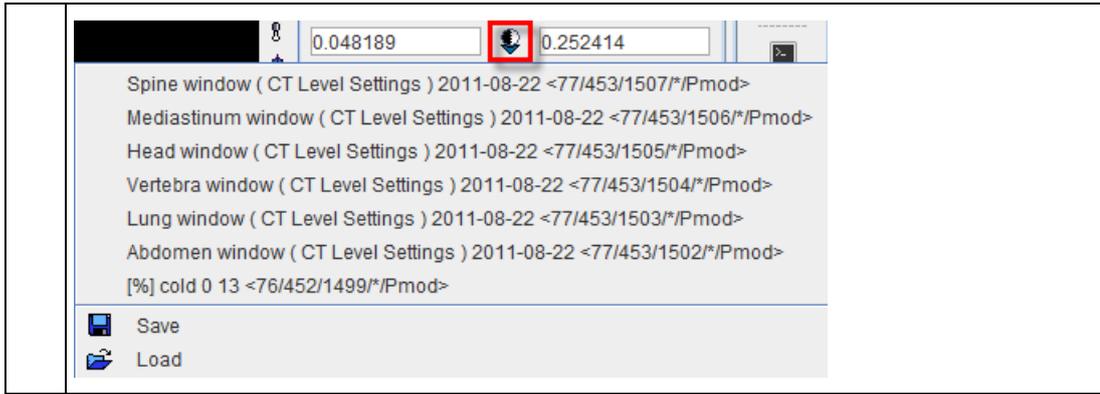
Color Table Modes

Several modes are available for the color table application. They can be selected using the option button



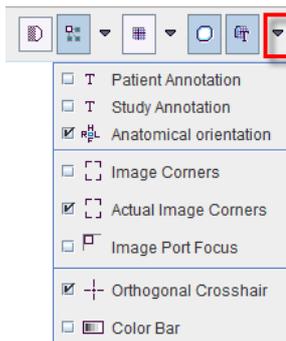
The different modes are:

	Inversion of the color table order.
	Slice mode: The same % threshold is applied to each individual slice. Hereby the dynamic color range is fully exploited per slice. However, <i>the same color will represent a different value in different slices</i> . Therefore, this mode is not recommended in most cases.
	Frame mode: With this setting, the minimal/maximal value in an entire frame is determined, and the % threshold applied to them. As a consequence, the colors represent fixed values when inspecting the slices of a frame. However, as the absolute minimal/maximal value will vary at different times of a dynamic acquisition, the <i>same color will most likely represent different values when comparing different frames</i> . This setting is recommended for static studies.
	Study mode: With this setting, the minimal/maximal value in the entire series is determined, and the % threshold applied to them. This setting is recommended for dynamic series and movies because the same color represents the same value at all times and in all slices.
	Fixed mode: This setting allows the user entering arbitrary minimal/maximal values which need not belong to the data range.
	This button allows saving or retrieving a color table configuration. During saving a dialog windows appears allowing to choose the thresholding save option: % Maximum-Minimum or Absolute values . Finally activate OK to save the level settings. Different level settings can be define and saved in the database as Absolute values for CT images and used for CT image presentations. These settings are available on the list when the button is selected. Alternatively, the predefined color properties can be retrieved from the file system selecting the Load button.

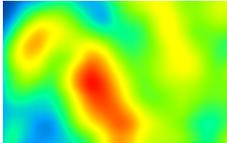
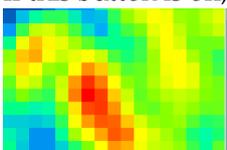


Information Overlays and Image Smoothing

The lowest row contains several control buttons.



All of the buttons can be on or off, and some might have some configuration options attached. Their functionality is:

	<p>Smoothing: Enables a temporary 9-point smoothing filter. The smoothing is only for display purposes and does not affect calculations.</p>
	<p>Interpolation: Enables image interpolation. Interpolation is needed because in most situations the resolution of the display viewport differs from the original image matrix.</p> <div data-bbox="373 1442 703 1585" style="border: 1px solid gray; padding: 2px;">  </div> <p>If this button is off, the original rectangular pixels are shown.</p> <div data-bbox="373 1644 703 1794" style="border: 1px solid gray; padding: 2px;">  </div> <p>The three interpolation options are Triangle, BSpline, Mitchell (Default).</p> <p>Note: the smoothing/interpolation functions serve only for image display enhancement. Statistical analyses are always performed with the original pixel values.</p>

	Grid: Enables a grid centered at the origin of the data set. Bold lines indicate the location of the image origin. The grid size can be defined by the option (50,20,10,5,1mm or from 1 pixel to 10 pixels with 1 pixel increment).
	VOIs: Enables the displays of VOI contours, if there have any been defined for the current series.
	<p>Overlay: A toggle to switch off all overlay information at once.</p> <p>Its option menu allows defining the level of information included in the overlay display as illustrated above.</p> <p><input checked="" type="checkbox"/> REL: This option enables Display of the anatomical annotations in the images: H - head, F - feet, A - anterior, P - posterior, R - right, L - left For oblique orientations the letters are combined whereby the first letter indicates the direction closest to the current row/column direction.</p> <p>Allows displaying the colorbar selected for the image.</p>

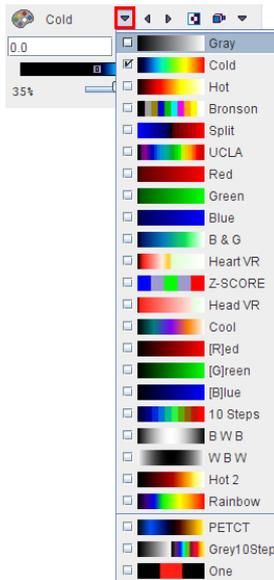
Color Table and Image Selection

The slice control section allows scrolling through the images using the increment buttons, the slider, or directly by entering a slice number. The value next to the number of the active slice controls incrementing. This is particularly relevant in multi-image layouts. For example, if the increment value is set to 2, only every second image will be displayed. Please note that there is a quick way for jumping to the particular slice/frame containing the maximal pixels value: just click the button next to the slice/frame selection. Instead of selecting slices using the controls, the user can also scroll slices by dragging the left mouse button over the image holding the CTRL key in the Up/Down direction (see the summary of shortcuts below).

The time control section only becomes active for dynamic studies and behaves the same way as the slice control. To allow for mouse-operated scrolling over time, the time box on the left side below the image must first be checked.



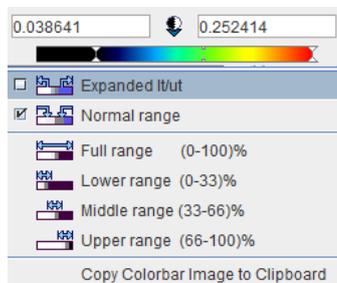
There is a selection of pre-defined gray and color tables which can be chosen with the list selection



Note: User defined color tables can be added by creating a 3-column text file with the RGB values and saving it to the sub-directory *resources/colortables* (see the examples there). They are appended to the lower section of the list.

A minimal/maximal threshold value defines what the range of displayed values is. The thresholds can be entered numerically, or the handles in the color bar can be dragged with the mouse. Additionally, the user can modify them by dragging the left mouse button over the image holding the SHIFT key. Left/Right movements modify the lower threshold, while Up/Down movements modify the upper window.

In some cases, the range of image values of interest only covers a small part of the color bar which makes it difficult to adjust the brightness precisely. In this situation, the user can zoom the color bar into the current sub-range of values. Clicking the right mouse button into the color bar pops up the context menu



The first menu entry **Expand It/ut** then performs the desired task and makes the color bar change to



The second entry performs the reverse operation, and the other entries are just shortcuts which may be helpful. If a window/level setting has been defined in a DICOM data set, this definition is added to the list using a specific name, or **W1** if such a name was not available as in the example.

The following modes are available for the color table application:

	Inversion of the color table.
	Slice mode: The same % threshold is applied to each individual slice. Hereby the dynamic color range is fully exploited. However, <i>the same color will represent a different value in different slices</i> . Therefore, this mode is not recommended in most cases.
	Volume mode: With this setting, the minimal/maximal value in an entire volume is determined, and the % threshold applied to them. As a consequence, the colors represent fixed values when inspecting the slices of a volume. However, as the absolute minimal/maximal value will vary at different times of a dynamic acquisition, <i>the same color will most likely represent different values when comparing different frames</i> . This setting is recommended for static studies.
	Fixed mode: This setting requires the user to enter the minimal/maximal value. The same absolute threshold will be applied for all slices and times. This is the recommended setting for dynamic studies and when running movies over time frames.

Interpolation and Overlays

The control buttons in the lowest row define image interpolation and the degree of overlay information are

	Activates a temporary 9-point smoothing filter for display purposes.
	Enables/disables smooth image interpolation. Interpolation is needed because in most situations the resolution of the display viewport differs from the original image matrix. If this button is not active, the original rectangular pixels are shown.
	Defines the image interpolation method (Trilinear, B-Spline, Mitchell = <i>Default</i>).
	Displays a 20mm grid centered at the origin of the data set. Bold lines indicate the location of the image origin.
	Displays patient/study information such as patient name, id, study date, etc as an image overlay.
	Displays anatomical information. The annotations are the same as used in DICOM: H - head, F - feet, A - anterior, P - posterior, R - right, L - left For oblique orientations the letters are combined whereby the first letter indicates the

	direction closest to the current row/column direction.
	Displays VOIs which have been defined for the current study.
	A toggle to switch on/off all overlay information at once.

Note: the smoothing/interpolation functions serve only for image display enhancement. Statistical analyses are always performed with the original pixel values.

Layout Definition

Images can be shown in different layouts such as tiling modes or the orthogonal mode, as summarized in the next sections.

Note that the PFUS tool assumes that after the **Initialize/Match** processing the images are aligned. Therefore, the layouts in the different rows are always synchronized and images corresponding to the same coordinate location are shown.

Layouts and Reorientations

The buttons in the first row allow defining the orientation of the displayed images.



Note: The direction z, y or x indicates the normal to the plane shown. The z-plane denotes the orientation of the images after loading (assuming axial slices). The y-, x- and orthogonal buttons are not active if the study is planar only and can thus not be resliced in other directions.

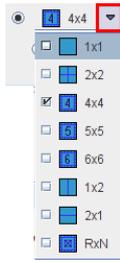
The plane orientation can rapidly be switched by first activating an image (click into image), and then entering

- ▶▶ CTRL+Z for axial plane
- ▶▶ CTRL+Y for coronal plane
- ▶▶ CTRL+X for sagittal plane
- ▶▶ CTRL+D for the layout showing three orthogonal planes

The second and third rows allow configuring the number of images shown concurrently. If the radio button in the second row is enabled, a dedicated row x column layout can be defined for the different orientations. This is particularly helpful for a whole-body study where the coverage in z is much larger than in the other directions.



Otherwise, if the radio button of the third row is enabled, the same layout is applied for all orientations and the arrangements are accessible through the selection



Keyboard shortcuts allow to quickly switch arrangements. After activating the image enter

- ▶▶ CTRL+1 for 1x1
- ▶▶ CTRL+2 for 2x2
- ▶▶ CTRL+3 for 3x3
- ▶▶ etc.

To change from a RxN arrangement to 1x1 just click on the image to be enlarged holding down the CTRL key. To change back to the multi-image layout just CTRL+ click once more.

The radio button in the fourth row is only applicable for image tiling with dynamic studies. If the radio button is in the position of

- ▶▶ **S**: only slices acquired in a single time frame are shown in the image window.
- ▶▶ **T**: only the images of a single slice are shown at different acquisition times.
- ▶▶ **S&T**: the images are sorted by slice (vertically) and time (horizontally). Consequently each row corresponds to a slice at different times, and each column to the slices of an acquisition.

Image reorientation operations such as mirroring and rotations can be done using the buttons in the bottom row.

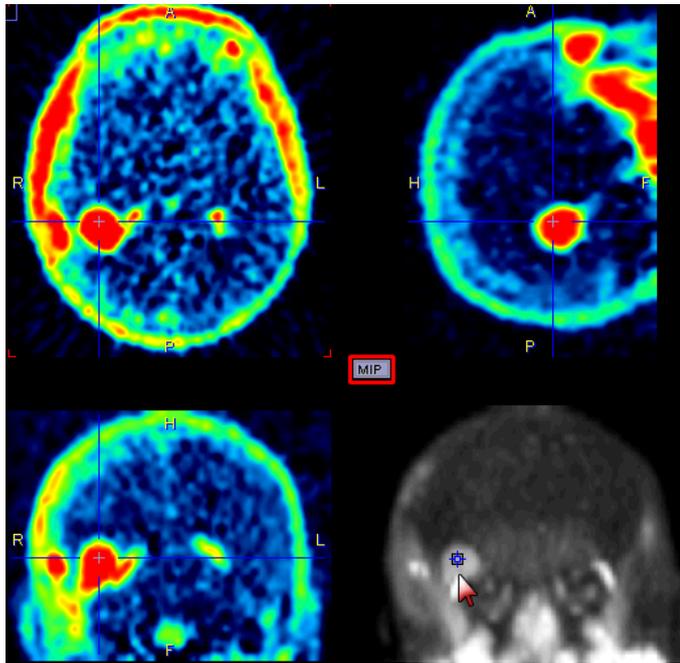


If the display is in the orthogonal viewing mode, first activate the appropriate plane by clicking onto the corresponding image (holding down the CTRL key avoids new reslicing), and then activate the appropriate button. For data with enough information about patient positioning PMOD will keep track of patient orientation and update the annotations accordingly.

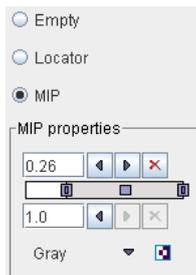
Sagittal images can be shown in two ways, either horizontally (laying on back), or vertically (standing). The user can set his preference by means of the two buttons on the right of the pane.



If the orthogonal layout is selected, three quadrants show the orthogonal slice images intersecting at the point indicated by the cross centered in the blue slice indication lines. As soon as the user clicks into an image, the images are updated by the slices intersecting at that new point.



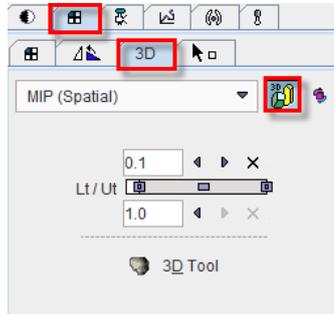
The fourth quadrant is available for different information. It can be configured by activating the button located in the upper left corner of that quadrant, indicated in red in the screen capture above. A dialog appears



which lets choose between an **Empty** quadrant, a **Locator** display showing the slices location schematically, and a **MIP** (Maximum Intensity projection). Note that there is a marker in the MIP image, which indicates the current slices intersection. It can be moved, and the slice images will follow. This function may be helpful to track vessels showing up highlighted in the MIP.

3D Volume Rendering, Rotating MIP Images

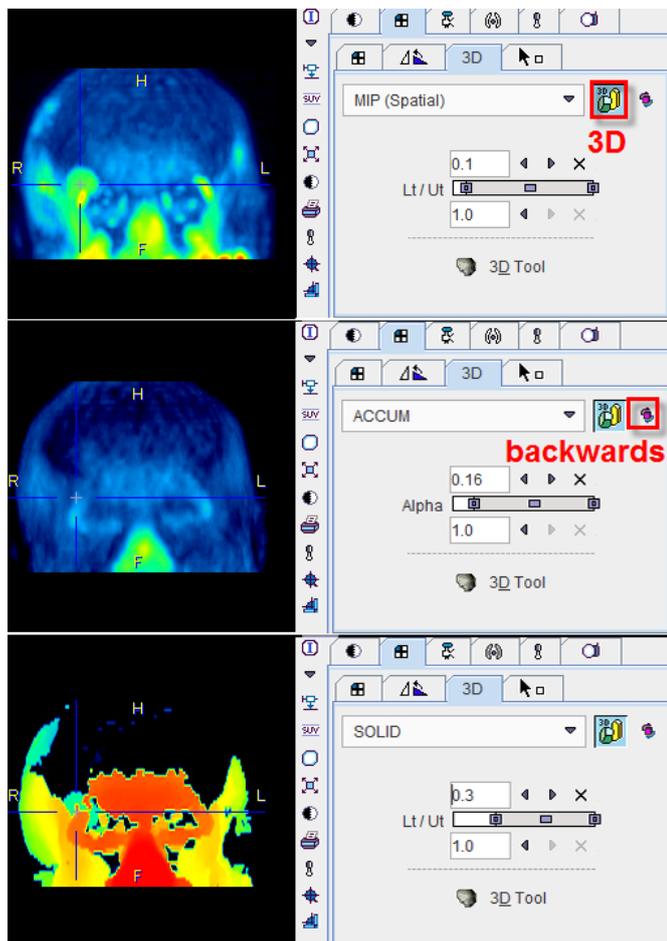
Instead of showing individual slice images, a volumetric data set can be volume rendered. Simple volume rendering can be enabled in the 3D sub-pane



There are four methods to choose from the selection

- ▶▶ MIP (Maximum Intensity Projection) being the most known one
- ▶▶ MinIP (Minimal Intensity Projection)
- ▶▶ ACCUM (Accumulation of color and opacity)
- ▶▶ SOLID

As soon as the rendering button indicated in red is activated (or CTRL+V on the image) the image display switches from slice display to volumetric display, with the projection direction orthogonal to the image plane. Three renderings of an example PET using the same color table are shown below. Note that the value range considered in the renderings is somewhat different.



The button to the right of the 3D selection is a toggle to perform the 3D operation from backwards, which will result in a different image in the case of a depth-dependent weighting function.

Note that image scrolling is still enabled in 3D mode. When CTRL+Drag the left mouse button over the image, the 3D rendering disappears and the slice images are shown until the mouse button is released.

Rotating MIP

To create a rotating coronal MIP movie please proceed as follows:

- ▶▶ In the **Layout** pane select the **Coronal** orientation (or CTRL+Y in the image).
- ▶▶ In the **3D** pane enable MIP and 3D, then adjust the upper/lower thresholds.
- ▶▶ In the **Movie** pane the number of slices has been replaced by the number of projections with a default value of 40 angles. Increase the number to get smoother rotations. Start playing.

MIP images will be calculated from different viewpoints and displayed as a rotating cine. If you would like to save a movie, enable the saving button as explained in Showing and Saving Movies.

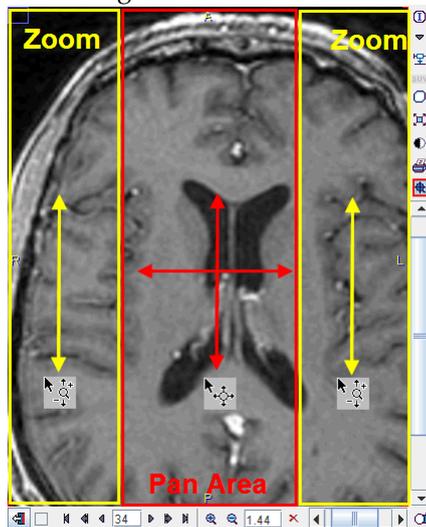
Transfer to Full 3D Rendering

The  button in the 3D pane is only functional if the PMOD 3D option is installed. When this button is activated, the current data set is loaded into the full 3D rendering tool for advanced processing.

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.

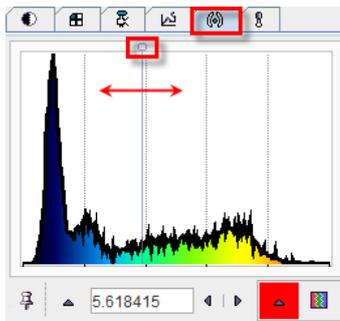
After appropriate zooming, zoom mode should therefore be deactivated by pressing  once more, because some of other mouse-operated functions might not work.

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.

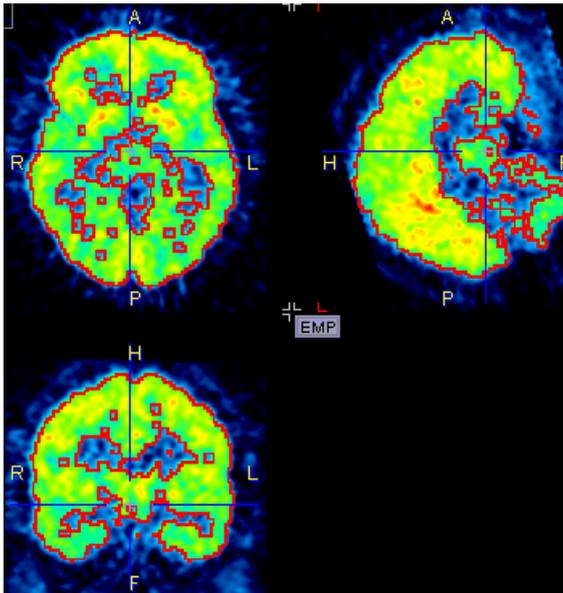
Iso-contour Lines

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 .

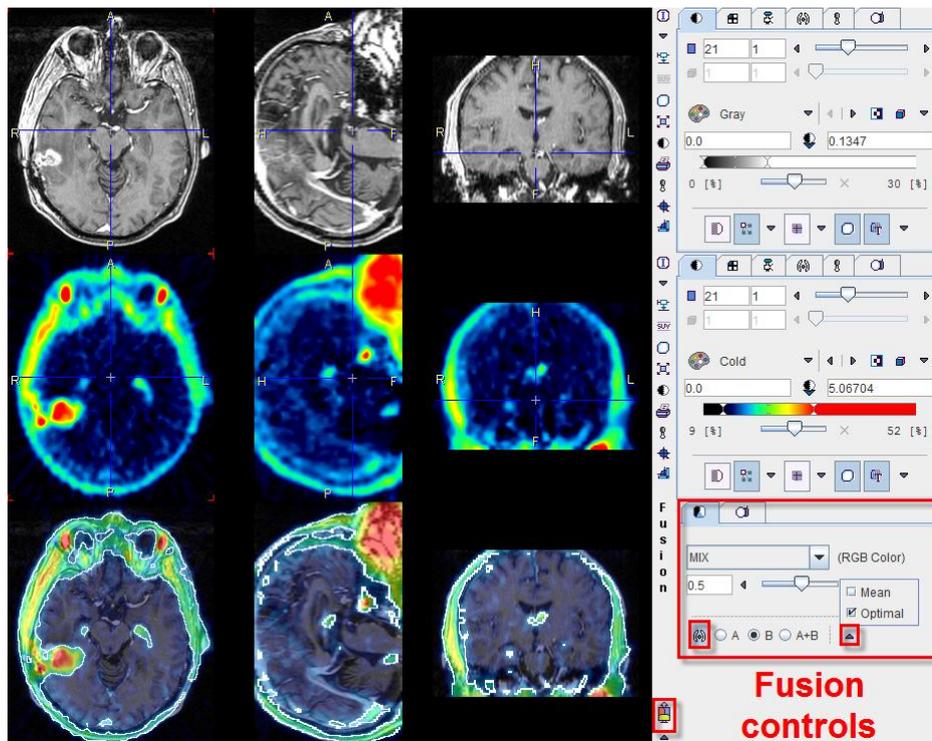
The display of contours in the fusion image is independent of the display in the source image. It is controlled by the the **Contours** radio box.

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.

Separate Source and Fusion Images

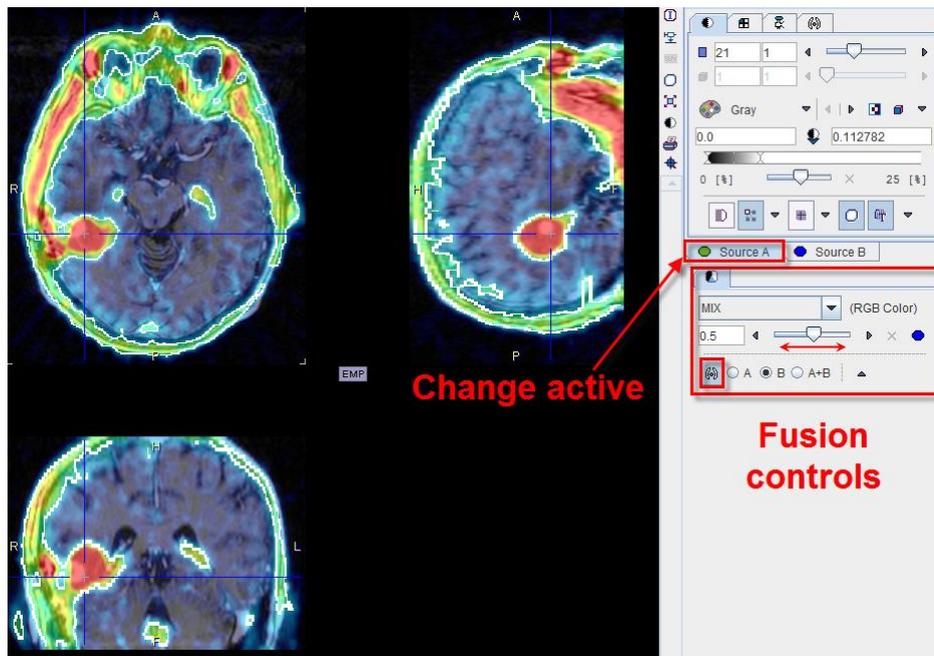
In this layout both the input images and the fusion images are visible at the same time, as in the example shown below.



In this example the first row shows a T₁-weighted MR image, and the second a matched ¹⁸F-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.

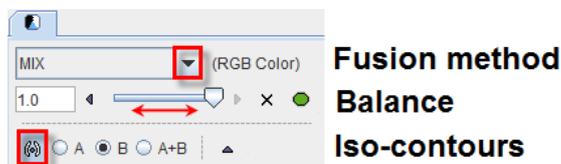
Fusion Images not Visible at the same Time as the Source Images

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.

The image fusion control



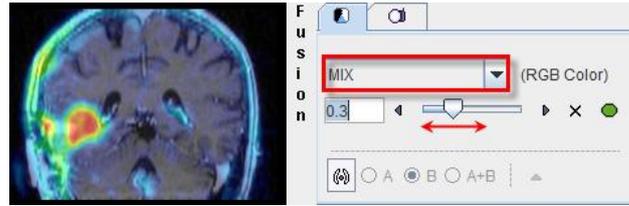
consists of three rows. The first row contains the selection(s) for choosing between the different fusion renderings, the second row allows enabling the balance to blend the contributions of the two images in the fusion, and the third row allows enabling the iso-contour overlays.

Image Fusion Methods

The fusion methods available are:

MIX Alpha Blending: weighted addition of the RGB values of both source images according to
 $R_{fusion} = R_A * x + R_b * (1-x)$
 $G_{fusion} = G_A * x + G_b * (1-x)$
 $B_{fusion} = B_A * x + B_b * (1-x)$

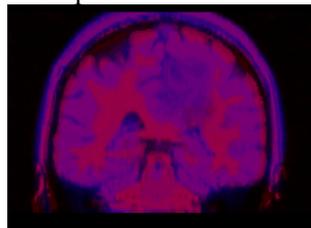
Example:



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

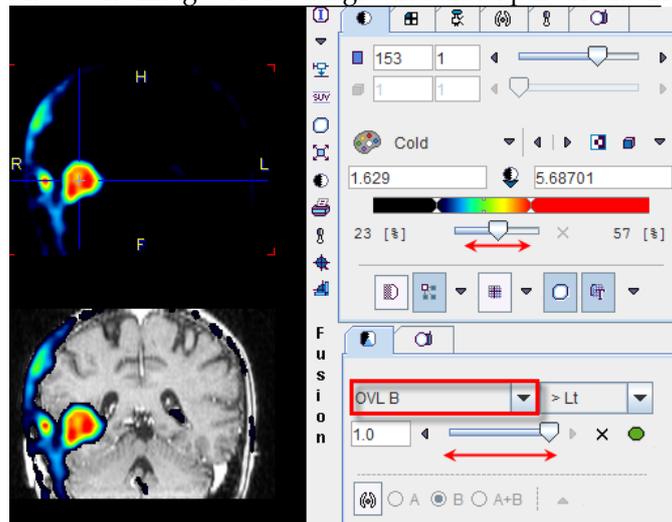
MERGE RGB merging uses the maximal RGB value of both source images according to
 $R_{\text{fusion}} = \text{Max}(R_A, R_b)$
 $G_{\text{fusion}} = \text{Max}(G_A, G_b)$
 $B_{\text{fusion}} = \text{Max}(B_A, B_b)$

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.

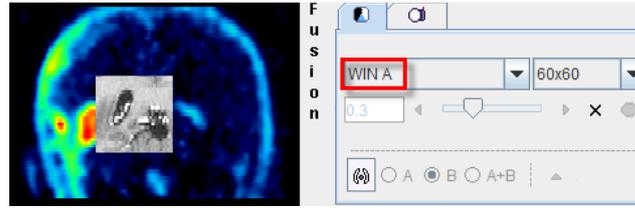
OVL B Shows the images A as background and a part of the images B as the overlay.



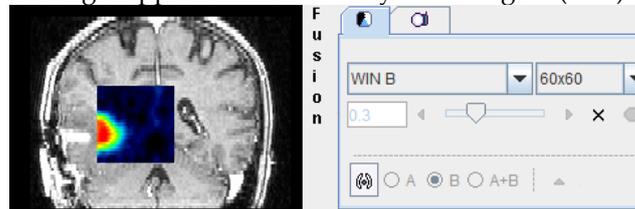
With the >Lt setting, all pixels in the PET image (B) below the lower threshold of the color table are replaced by the MR (A) values. Additionally, some transparency is added in the lesion by the balance slider. See below the description of the different threshold options.

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:

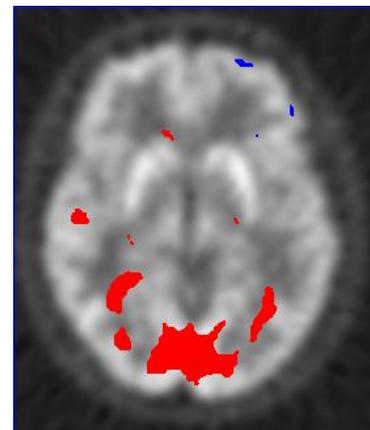
- > Lt Only the pixels (in A for **OVL A** , in B for **OVL B**) with values *above* the lower threshold are displayed. This is the most useful setting when a hot lesion is to be blended into an anatomical image (see example for **OVL B** above).
- < Ut Only the pixels (in A for **OVL A** , in B for **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

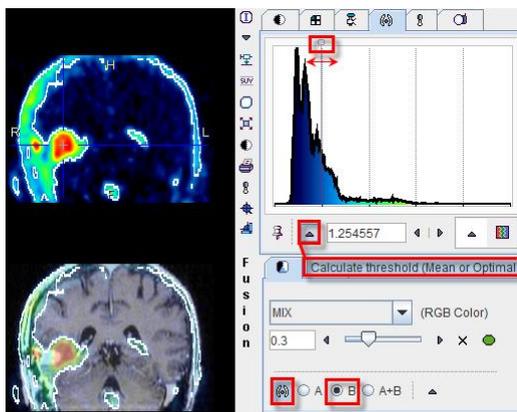


Only z-score values < -2 and > 2 are shown, without transparency. Because only the minimal and the maximal

colors are use, 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.

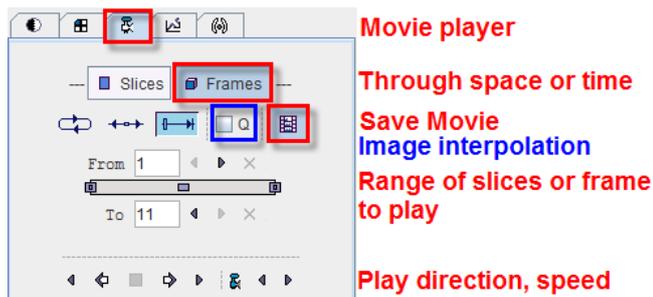
Iso-contours in Image Fusion

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.

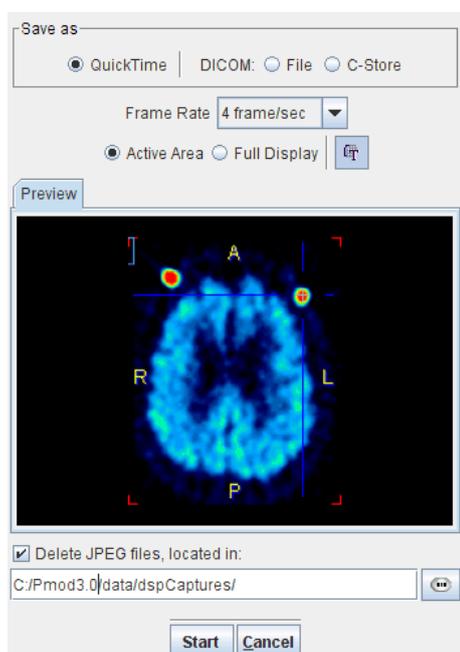


Movies

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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