

User's Guide

PMOD Alzheimer's Discrimination Analysis (PALZ)

Version 3.3



PMOD Technologies

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PMOD Alzheimer's Discrimination Tool

Introduction

The PMOD Alzheimer's Discrimination Tool (PALZ) supports the fully automatic analysis of FDG brain PET scan acquired from patients with clinical symptoms of Alzheimer's Dementia (AD). It is based on the data of a large multi-center trial and implements the proven discrimination methodology developed by Prof. K. Herholz et al. [1].

Methodology

It is a prerequisite for the applicability of the analysis that the patient suffers from clinical symptoms of AD. Assuming that this is the case, the PALZ tool performs the following processing steps with a loaded FDG brain PET scan:

- ▶▶ The image is first stereotactically normalized using the methodology and the anatomical PET template of SPM99 [2].
- ▶▶ The resulting image is then smoothed by a 12 mm Gaussian filter to minimize side-effects of varying scanner resolutions.
- ▶▶ The image voxel values are divided by the voxel mean value, averaged within a mask representing voxels with AD-preserved activity. This operation results in normalized voxel values which are comparable across patients.
- ▶▶ In each image voxel the activity expected at the patient's age is calculated using voxel-wise age regression parameters.
- ▶▶ The difference between the measured and the expected voxel values are transformed into t-values, resulting in a t-map [3].
- ▶▶ The t-values of all abnormal voxels within an predefined AD-mask are summed, yielding a criterion related to AD-severity called *AD t-sum*. The AD mask represents all voxels that had shown a close correlation (at $p < 0.01$ uncorrected) with the Mini Mental Status Examination (MMSE) in patients with probable AD (see [1], Fig. 1). It includes major parts of the temporal and parietal association cortices (including the precuneus and posterior cingulate), as well as some lateral prefrontal areas.
- ▶▶ The AD t-sum is compared with the 95% prediction limit (11089) established in the NEST-DD multi-center trial, and tested for significance of abnormality. The result of this test is the main outcome of the present AD discrimination.
- ▶▶ The *PET Score* is calculated from the AD t-sum by reference to the upper normal limit and log transformation to approach a normal distribution: $PET\ Score = \log_2(AD\ t-sum/11089 + 1)$ [4].
- ▶▶ For interactive reviewing, the t-maps can be displayed and fused with the normalized patient images. They can also be saved for use in an external analysis.
- ▶▶ Additionally, a cluster analysis is performed for grouping of voxels with significantly reduced uptake [1]. Clusters of at least 216 contiguous voxels with $p < 0.05$ (not corrected for multiple comparisons) are determined, ordered by their size in a table, and also made available as images.

For a thorough understanding of the discrimination analysis please refer to the *NeuroImage* article which exactly describes how the method was derived and validated [1].

Results

AD t-sum [1]: The discrimination analysis described above provides the basis for a statistical test with null hypothesis "*The AD t-sum is normal*". As the distribution of the AD t-sum has been assessed in the control group, a 95% prediction limit and error probabilities were calculated. In the evaluation, the AD t-sum was shown to be a highly sensitive indicator of scan abnormality [1]. Therefore, if the AD t-sum is within the normal range it is unlikely that a tested individual has AD. Otherwise, if the AD t-sum is outside the 95% prediction limit, the null hypothesis is rejected ("*AD t-sum within AD regions is abnormal*"), and the error probability is stated (eg. "*Error probability < 0.0001*"). Such a finding, always in conjunction with clinical symptoms, supports a diagnosis of AD.

PET Score [4]: The PET Score was shown to be a valid imaging biomarker for monitoring the progression of mild cognitive impairment (MCI) to Alzheimer's disease (AD). Its excellent test-retest reliability and signal strength is expected to allow substantially reducing the number of subjects or shortening of study duration in clinical trials.

Clusters: The outcome of the cluster analysis is not quantitative and solely intended for the visualization of concentrated area of abnormal voxels. Note that even in perfectly normal individuals up to 5% of all voxels may appear abnormal, and the appearance of a few abnormal clusters does not indicate any abnormality.

Validation

In 2009 the performance of the PALZ tool was assessed with a large number of cases from two independent databases (ADNI and NEST-DD) [5]. The databases differ regarding the demographics and the acquisition protocols as summarized below. The data sets were processed with PALZ, and the AD t-sum outcome used to calculate sensitivity and specificity.

	Controls	Mild AD-patients	Protocol	Results
ADNI	102 controls, age 76 \pm 4.9, MMSE 28.9 \pm 1.1	89 patients, age 75.7 \pm 7.6 MMSE 23.5 \pm 2.1	Eyes open, quiet darkened room, 3D	Sensitivity: 83% Specificity: 78%
NEST-DD	36 controls, age 62 \pm 45; MMSE 29.6 \pm 0.7	237 patients, age 70.8 \pm 8, MMSE 20.9 \pm 4.4	Eyes closed	Sensitivity: 78% Specificity: 94%

The main outcome of the study is the confirmation of the high accuracy of FDG PET with PALZ for the discrimination between AD patients and normal controls. Furthermore it was demonstrated that although the eyes open condition results in higher occipital glucose consumption, there is no relevant effect on the AD t-sum. Therefore, PALZ can be equally applied to studies with eyes open or closed during the uptake phase. Only 7 out of 464 images had to be excluded from the analysis due to a failure of the normalization procedure.

Applicability

The PALZ tool may only be used to analyze FDG brain scans of patients with suspected AD. Note that the following guidelines must be observed to avoid invalid results:

- ▶ A patient must not be younger than 49 years. For such patients, the linear age regression might result in a (most probably too) high expected uptake in the frontal cortex. The consequence of such a situation would be a false positive finding.
- ▶ PET images must be reconstructed with attenuation and scatter correction.
- ▶ The stereotactic normalization may fail. In that case the subsequent discrimination calculations will be invalid. Therefore, the user is required to verify the outcome of stereotactic normalization.

Failure of normalization has been observed in the presence of severe brain atrophy. There are two indications of such a situation:

1. A shell-like distribution of the pathological voxels along the boundary cortex/external liquor space.
2. Concentration of the pathological voxels in the cingulate gyrus and the basal ganglia as a consequence of the severe widening of the inner liquor space.

CAUTION: The PALZ tool is not a general brain FDG analysis tool and thus not suited to search for non AD-related defects in FDG brain scans. Any other disease that also affects the association brain areas, which are abnormal in AD, may also lead to a significantly abnormal result. Scientific evidence is not yet sufficient for the interpretation of an abnormal AD t-sum in subjects without clinical symptoms of AD.

Disclaimer


THE PMOD ALZHEIMER'S DISCRIMINATION ANALYSIS (PALZ) TOOL HAS NO APPROVAL FOR CLINICAL USE. THEREFORE, THE PALZ TOOL MAY ONLY BE USED FOR RESEARCH OR INVESTIGATIONAL PURPOSES.

PALZ Operation Modes and Configuration

The PALZ tool can has two modes of operation:

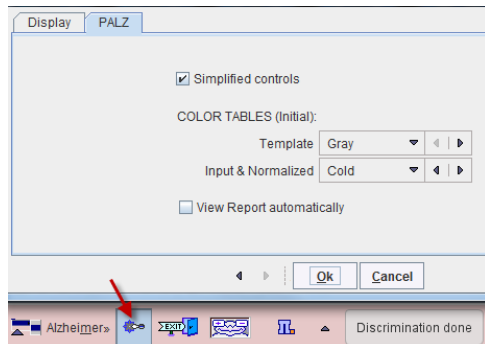
- » **Simplified mode:** In this mode the user interface elements are reduced to the essential minimum for minimizing user interaction and avoiding errors. This mode should be used for routine analyses.
- » **Extended mode:** This mode provides all user interface elements available in PMOD, as well as additional features dedicated to the PALZ analysis. For instance, the original patient images can be viewed, and the t-maps can be saved. This operation mode is recommended for experienced PMOD users and research purposes.

Configuration

The PALZ configuration panel can be shown by activating the  button in the left part of the status line. The contents of the **PALZ** panel differs on the mode the program is operating in.

Configuration Panel in Simplified Mode

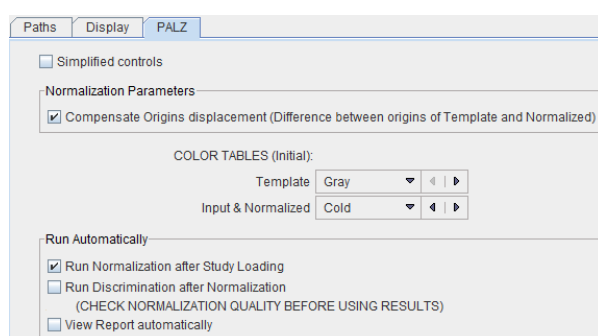
In this mode there configuration panel only contains the elements illustrated below.



Simplified controls allows switching between the two processing modes. In the **COLOR TABLES** section the default color tables of the stereotactic **Template** and the patient images (**Input & Normalized**) can be defined. If the **View Report automatically** box is checked, the report viewer will be started each time a discrimination analysis is completed.

Configuration Panel in Extended Mode

Additional elements are shown on the configuration panel in the extended mode.

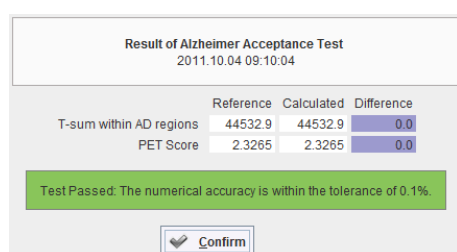


Compensate Origins displacement implements a logic to establish a suitable initial situation for the stereotactic normalization. It allows normalizing some cases which would otherwise fail, and therefore should be on per default. The main purpose for switching it off is to maintain exact compatibility with PALZ versions before 3.3.

The Alzheimer's discrimination analysis in the extended mode requires only a few button clicks. However, it is possible to reduce the amount of user interaction further by setting appropriate flags in the **Run Automatically** section. They represent trigger flags, so that for instance after loading the images all processing steps are run sequentially (all checks enabled). However, it is strongly recommended that the normalization result is inspected before trusting the analysis outcome.

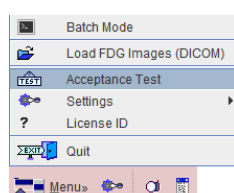
Acceptance Test

The first time PALZ is started after an installation an **Acceptance Test** is automatically run. It performs all processing steps using a test image and compares the outcome with the stored values. The result is presented as a confirmation dialog window as illustrated below.



If the result is beyond the acceptance criterion of 0.1%, there is a problem with the installation which has to be fixed before proceeding with the analysis of patient data.

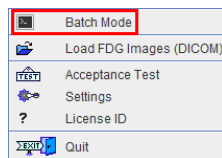
To verify an installation the **Acceptance Test** can be initiated at any time from the **Menu**.



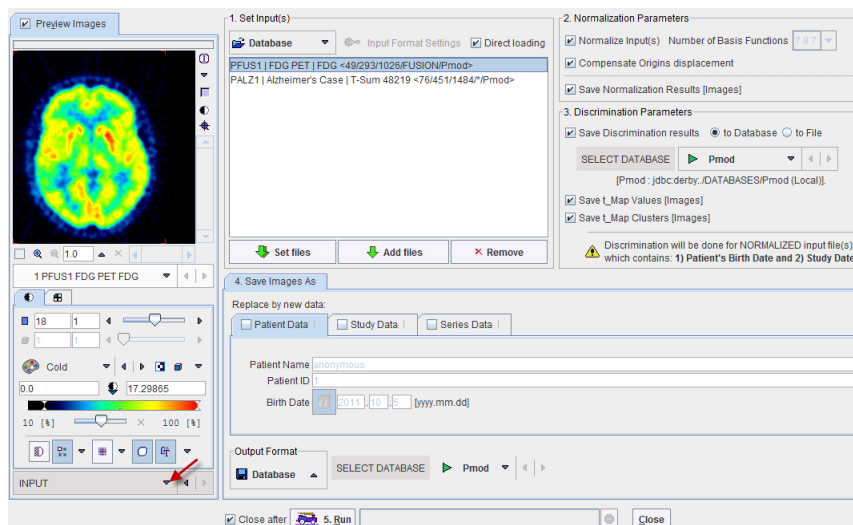
Batch Mode

The PALZ tool offers a batch facility which is useful when several studies need to be analyzed. The batch mode allows performing the spatial normalization - which is the time-consuming processing step of the whole analysis - for a list of FDG studies and save the normalized images for a later, interactive discrimination analysis. It is also possible to perform the discrimination analysis at the same time and save its results, but this unsupervised mode is *not* recommended due to the potential failure of spatial normalization.

Batch mode is started using the corresponding **Batch Mode** menu entry



and displays the following dialog window.



There are numbered sections in the dialog which must be configured appropriately:

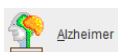
- 1. Set Input(s)** In this section the studies to be normalized are defined. Please first select the data format (in the example **Data Base**) and then add the files to the list to be processed using the **Set files** button. Note the button **Input Format Settings** which allows to configure optional pre-processing steps, such as A-P mirroring, smoothing, time-averaging, etc.
- 2. Normalization Parameters** The **Normalize Input** check defines whether the input images need to be spatially normalized (this is not necessary if previously normalized images are selected), and the check **Save Normalization** whether the resulting images are saved. The number of basis functions used in the elastic part of matching is currently fixed, but may become relevant in future enhancements.
- 3. Discrimination** This section is only relevant if the user wants to perform the discrimination analysis in unsupervised mode, which is *not recommended*.

Parameters	All the discrimination results can be saved for post-batch reviewing.
4. Save Images As	If result images have been configured to be saved, the format defined in this section will be applied. First select the data format (recommended is the database), then configure additional parameters of that format. As an additional option, the Patient , Study or Series Data can be replaced.

After the configuration is complete, the **5. Run** button can be activated to initiate batch processing.

Performing an Alzheimer's Discrimination Analysis with the PALZ Tool

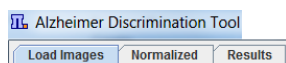
The PALZ tool is started using the



button in the PMOD ToolBox. Depending on the operation mode it organizes the processing steps on three or four pages as explained below.

Processing in Simplified Mode

The processing sequence in simplified mode consists of 3 steps, each represented by a page.



First, the FDG images of the patient have to be loaded on the **Load Images** page. Then, on the **Normalized** page, the spatial normalization has to be verified and the discrimination analysis started. Finally, on the **Results** page, the analysis outcome can be inspected and documented.

Loading the Patient Images

PMOD includes a DICOM database, to which users can directly transfer their images from the PET system. As an alternative, users can load DICOM images from anywhere in the file system or from a CD/DVD.

The DICOM format has the advantage that patient, acquisition and reconstruction related information is included in the image header. Therefore the images can be displayed with consistent orientation (Left/Right, Anterior/Posterior, Inferior/Superior), and the patient's age can be determined which is crucial for the discrimination analysis.

Loading Images from the Database

The **Load Images** page shows all the studies stored in the PMOD database.

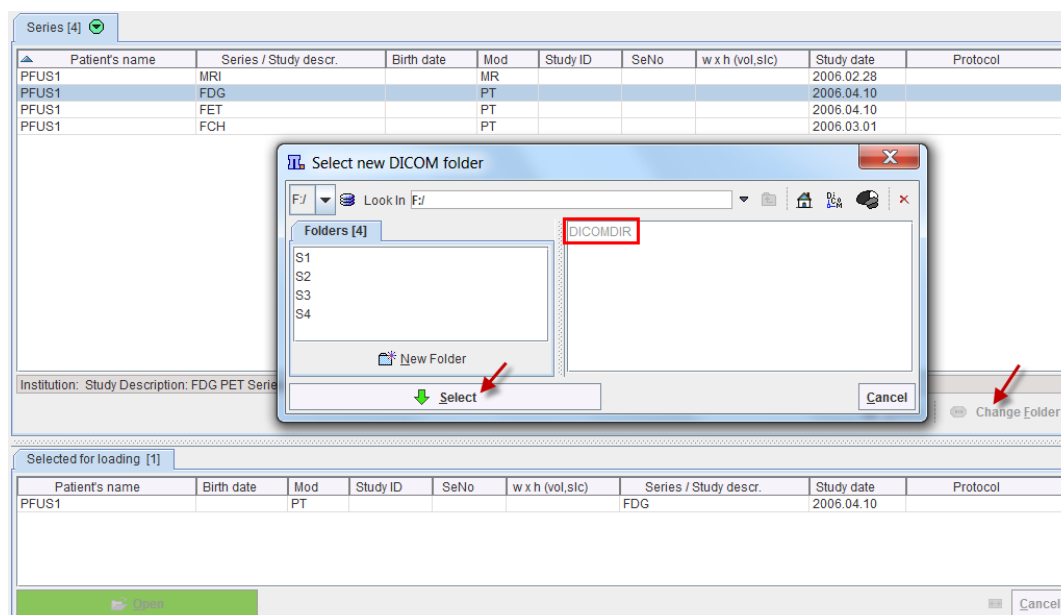
The screenshot shows the 'Load Images' window of the PALZ Tool. It features a 'Patients' list and a 'Series' list. The 'Patients' list contains 177 entries, with 'PALZ1' selected. The 'Series' list contains 1 entry, 'PALZ1', which is also selected. The 'Open' button is highlighted in green, and the 'DICOM' button is visible at the bottom right. Red arrows indicate the selection of the patient, the series, the 'Open' button, and the 'DICOM' button.

To load the FDG images of a patient with clinical symptoms of AD, first select the patient in the **Patients** list, then the appropriate image series in the **Series** list. Finally activate the **Open** button.

Loading Images from a CD or from File System

If there is a need to load the FDG images from outside of the database please start the DICOM loader with the **DICOM** button. In the appearing dialog window the contents of the directory from which images were loaded the last time is initially shown. Use the **Change Folder** button to bring up a navigator window which allows changing the current folder.

There are two cases for the path selection: if a **DICOMDIR** file exists such as in the example below, don't navigate to a subdirectory, but activate **Select**. PMOD will read the information in DICOMDIR and list all image series contained in any subdirectory. Select the appropriate FDG series in the list and activate the **Open** button for loading.



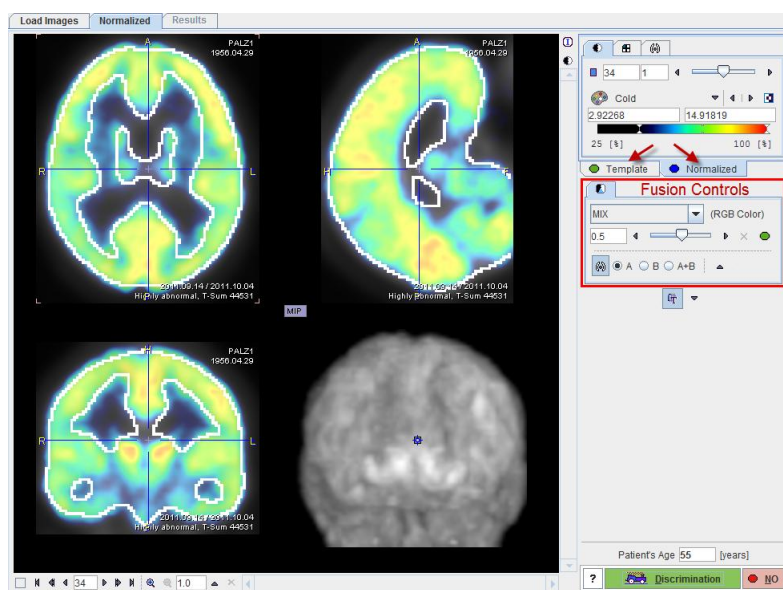
If there is no DICOMDIR please navigate into the folder with the image files and **Select**. In this case PMOD will scan all the files in the folder and list the available images series. Proceed by selecting the appropriate FDG series activate the **Open** button for loading.

Processing of the Loaded Images

After the images have been loaded the stereotactic normalization is immediately started, and the result shown on the **Normalized** page.

Verifying the Normalized Images

The normalization step results in a new image set which represents the patient images in the stereotactic space of the template. This image set has the resolution of the PET template, so that the images can be fused. The fusion result is shown in the large image area.



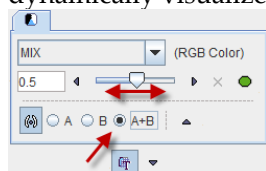
Initially, the color tables are applied which were defined in the *configuration* (on page 6) panel. To change the color tables or the thresholds please activate either the **Template** or the **Normalized** tab, and adjust the settings according to your preference.

CAUTION: The spatial normalization is expected to succeed in most of the cases. However, the user is strongly recommended to verify that the normalization was accurate by examining the alignment of the resulting brain shape with the template.

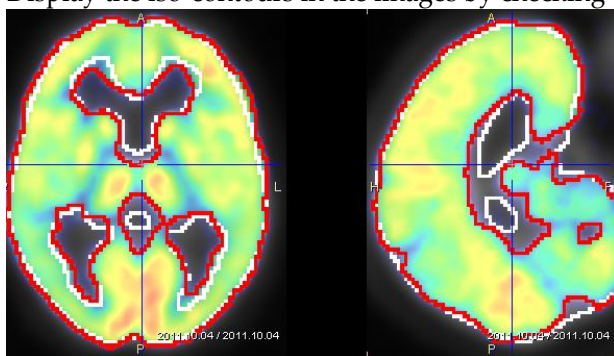
Verification of the Normalization Result

There are different features available for checking the normalization result:

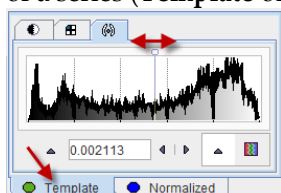
- Shift the fusion slider left/right to change the mixing of the two image sets and dynamically visualize the correspondence.



- » Display the iso-contours in the images by checking the **A+B** radio box.



Note that the level of the iso-contouring can be adjusted by selecting the contouring tab of a series (**Template** or **Normalized**) and changing the threshold level.



- » Click at different points across the brain to verify the alignment for all relevant anatomical structures.

There are additional fusion options available, which are described in the guide for the PMOD image fusion tool and briefly summarized *below* (on page 44).

Starting the Discrimination Analysis

The **Patient's Age** is essential for the age regression. If it can be derived from the input data, the age is shown in the number field (and can be edited if required), otherwise the user is prompted to enter the age interactively. If the age is correct and the normalization accuracy has been found to be acceptable, the Alzheimer's discrimination analysis can be started with the **Discrimination** button. Otherwise, processing should be stopped with the **NO** button.

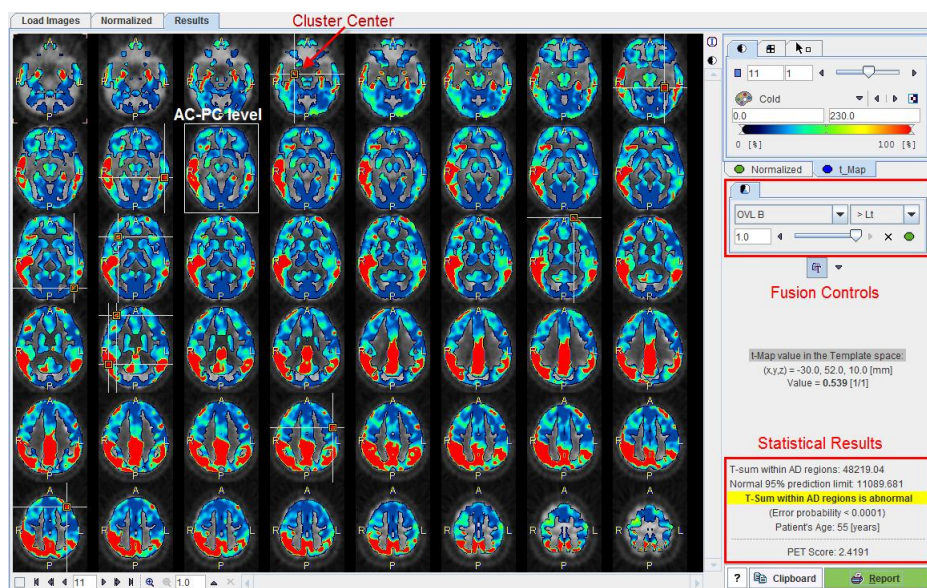
Results of the AD Discrimination Analysis

The outcome of the discrimination analysis is available on the **Results** page.

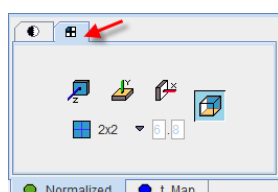
Result Images

The large image display shows a fusion of the clustered t-maps with the normalized patient images.

Note: The cluster images are a synthetic compilation of information with values in the range from 0 to 230. The value of 230 corresponds to abnormal voxels and is shown in red using the default color table.

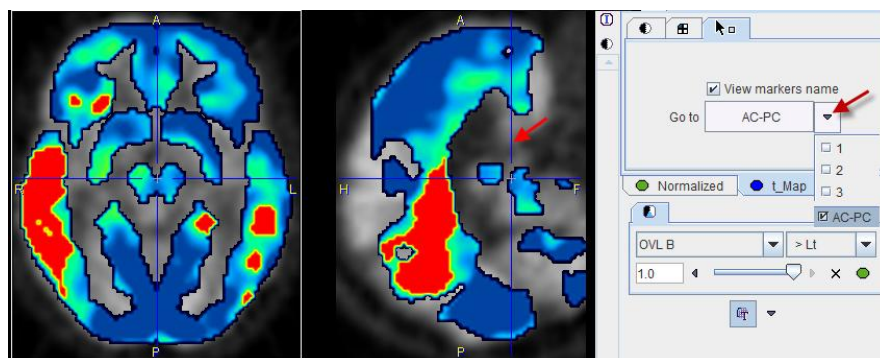


Initially, 2 mm thick slices parallel to the AC-PC line are shown in a 6x8 layout as illustrated above, but the arrangement can be changed as usual using the layout tab.



Using the fusion slider the mixture between the normalized patient images (fully to the left) and the cluster t-maps (fully to the right). There are many other fusion options available to closely examine the data, as described in the PMOD image fusion tool guide.

The image at the AC-PC level is enclosed in a white rectangle. The cluster maxima are indicated in the images by markers and crossing lines. With the **Go to** button in the markers panel of the **t_Map** it is possible to directly jump to these markers, and also to the **AC-PC** plane.



By enabling the **View markers name** box, the cluster numbers can additionally be shown in the image overlay.

The **Template space** section allows localizing the points of interest in the MNI template space. As soon as the cursor is moved over the images, the voxel coordinate is reported together with the t-value.

Note: The MNI template coordinate system is a right-handed patient-oriented system (like the Talairach system). Therefore, the x-coordinate is increasing from the right side of the image (patient left) towards the left side, which might be somewhat unexpected in the beginning.

Statistical Results

The numeric results are summarized in the lower right corner. The **AD t-sum** calculated for the patient (example below: 48219) is shown together with the upper normal limit (always 11089). If it is above 11089 the finding is abnormal, and the error probability is stated ($p < 0.0001$).

T-sum within AD regions: 48219.04
 Normal 95% prediction limit: 11089.681
T-Sum within AD regions is abnormal
 (Error probability < 0.0001)
 Patient's Age: 55 [years]

PET Score: 2.4191

? Clipboard
Report

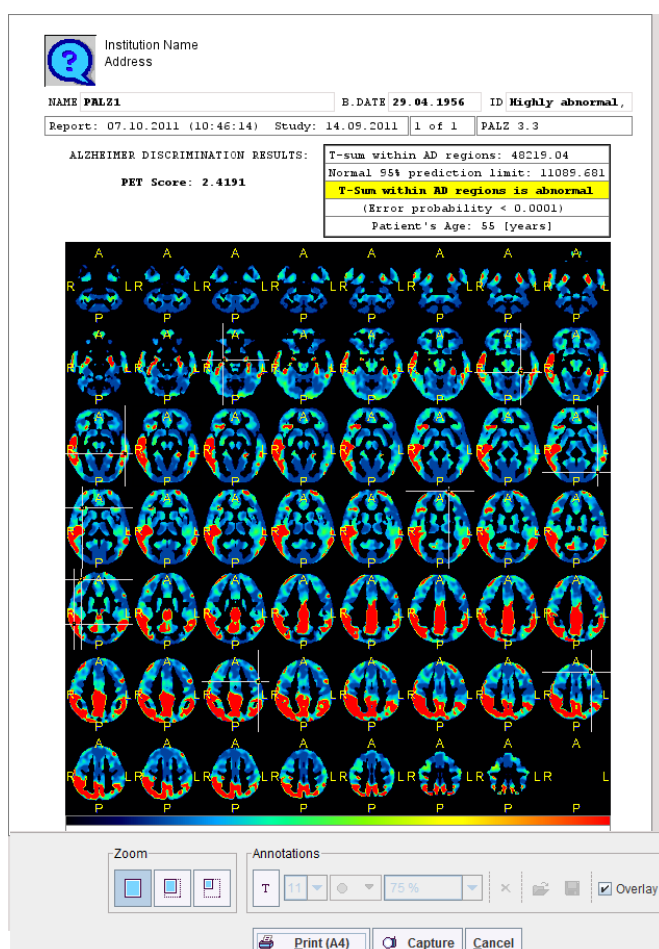
The **PET score** has a value of 1 for an AD t-sum equal to the normal limit, and >1 for abnormal t-sums. It has been shown to be closely related to the stage of AD, providing a measure of cognitive impairment. As it has a high test-retest reliability, it can be used as an imaging biomarker for clinical trials aiming at preventing dementia in MCI patients.

The results can be saved via the **Clipboard** button, and then pasting into a suitable program such as MS Excel, as illustrated below.

Alzheimer Discrimination Results:					
Evaluation Date: 2011.10.04					
Evaluation Time: 15:11:38					
[PATIENT INFO]					
Patient Name: PALZ1					
Birth Date: 1956.04.29					
PET Study Date: 2011.09.14					
[CLUSTERS TABLE]					
No.	Size	Max	X	Y	Z
-	[pix]	[t_Value]	[mm]	[mm]	[mm]
1	22844	4.92582	58	-52	30
2	650	3.52901	-30	-36	-6
3	591	4.02966	42	52	30
4	595	2.89921	-60	-36	-2
5	584	2.67745	38	28	14
6	350	3.23179	28	-8	-14
7	272	3.1008	-20	68	24
8	237	2.94186	-54	4	50
9	221	2.59095	-34	26	60
10	219	2.40292	-50	-80	12
[ALZHEIMER DISCRIMINATION RESULTS]					
T-sum within AD regions: 48219.04					
Normal 95% prediction limit: 11089.681					
T-Sum within AD regions is abnormal					
(Error probability < 0.0001)					
Patient's Age: 55 [years]					
PET Score: 2.4191					

Results Documentation

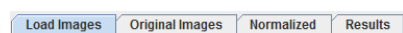
When the **Report** button is activated a report dialog window appears. It contains the numeric outcome as well as the cluster images from inferior to superior, including markers at the cluster centers. The images are helpful for documenting left/right asymmetries.



General information how to annotate and print report pages is available in a dedicated *section* (on page 35).

Processing in Extended Mode

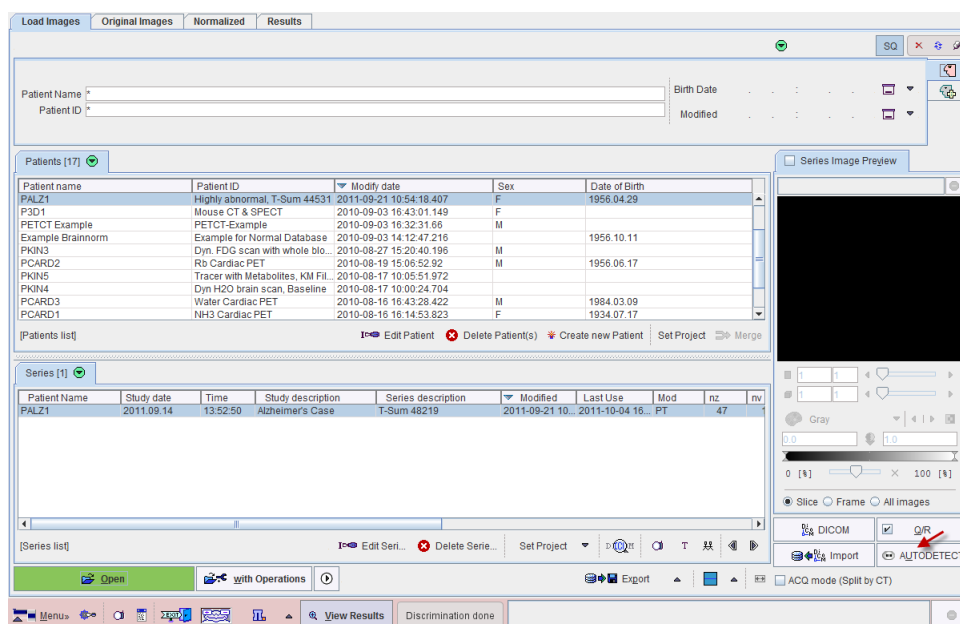
The extended mode offers additional functionality at different places. Most notably an additional page **Original Images** appears in the tool. Its purpose is to inspect the raw patient images before the normalization transform has been applied.



In the following the same data set used for the description of the simplified mode is processed. Assuming that the reader is familiar with the simplified PALZ processing as well as PMOD image processing in general, the discussion is focused on the functional additions of the extended mode.

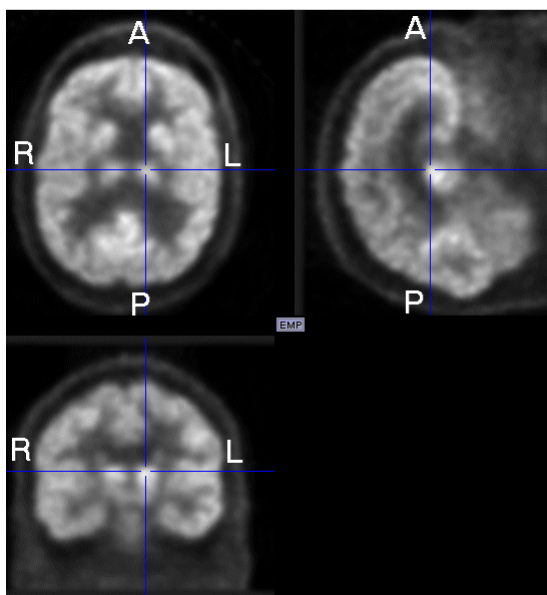
Loading the Patient Images

In the extended mode the **Load Images** page shows the full interface to in the PMOD database.



The most notable functional addition in the current context is the **AUTODETECT** button which allows loading images in other formats than DICOM, for instance ECAT, Nifti, Interfile and others.

CAUTION: Images loaded in formats other than DICOM must be checked for correct HFS display orientation. Please load an image of this particular format wherein all three orientations can be unambiguously identified. Then, in the orthogonal planes view, the patient coordinates must match the radiological convention as illustrated below.



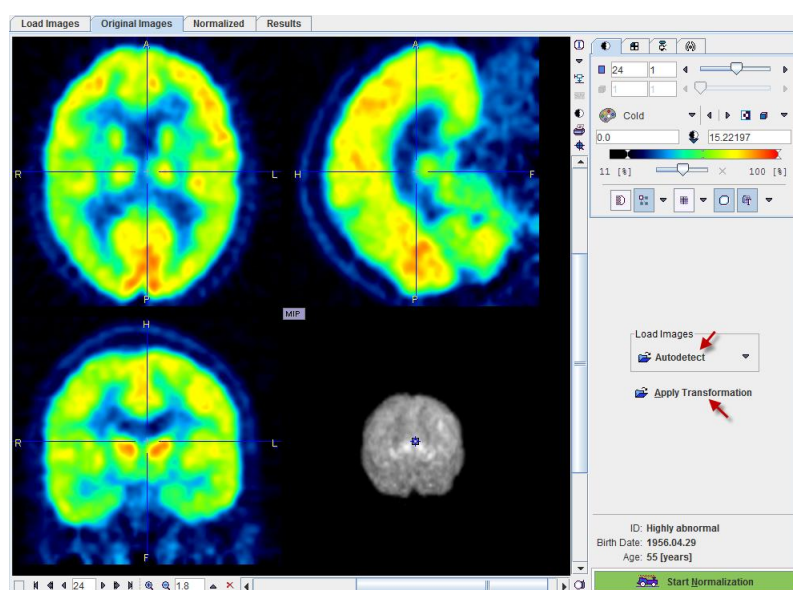
Reviewing the Original Images

Non-DICOM Images

The **Original Images** page also contains a **Load Images** button for loading images in different formats.

Image Reviewing

The original patient images can be reviewed on this page. Please refer to the PMOD base documentation to find out how to change layouts, colors, print reports, etc. The example below shows the orthogonal layout, but tiling arrangements are also possible.



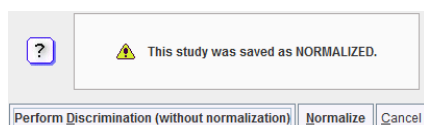
Applying Transformations

In the extended mode it is possible to save the stereotactic normalization transform (on the **Normalized** page). In case the analysis of the image series needs to be repeated, this transform can be loaded with the **Apply Transformation** button and applied to the images. As soon as the transform has been retrieved, it is applied to the patient's FDG images and the result shown on the **Normalized** page.

Starting Spatial Normalization

The stereotactic normalization is started with the **Start Normalization** button and may take up to 2 minutes.

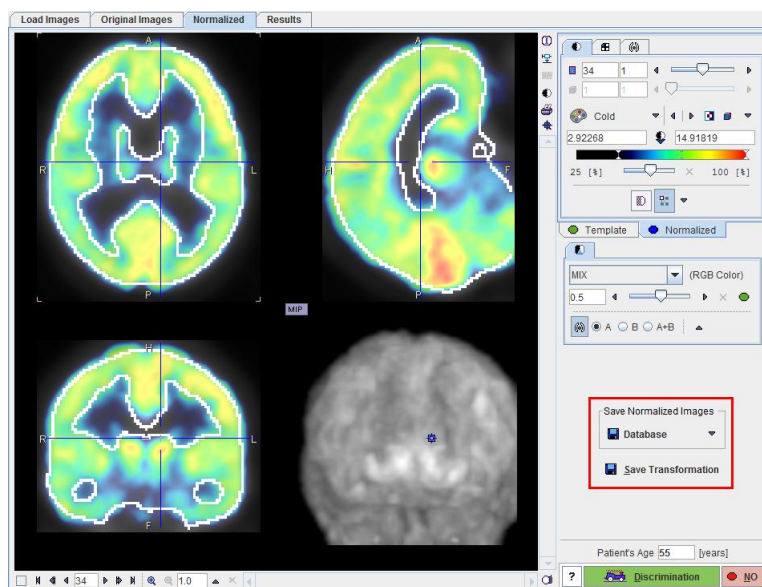
In the extended mode it is possible to save the normalized patient images (on the **Normalized** page). These images contain the term **NORMALIZED** in the series description. The normalization of such images is not required, therefore a confirmation dialog window is shown when the user starts the processing:



The user has to confirm with **Perform Discrimination (without normalization)** that the images are indeed the normalization result of an earlier PALZ analysis. In this case the spatial normalization step is skipped. Otherwise, the standard procedure can be continued with the **Normalize** button.

Reviewing the Normalized Images

There are two additional features on the **Normalized** page.

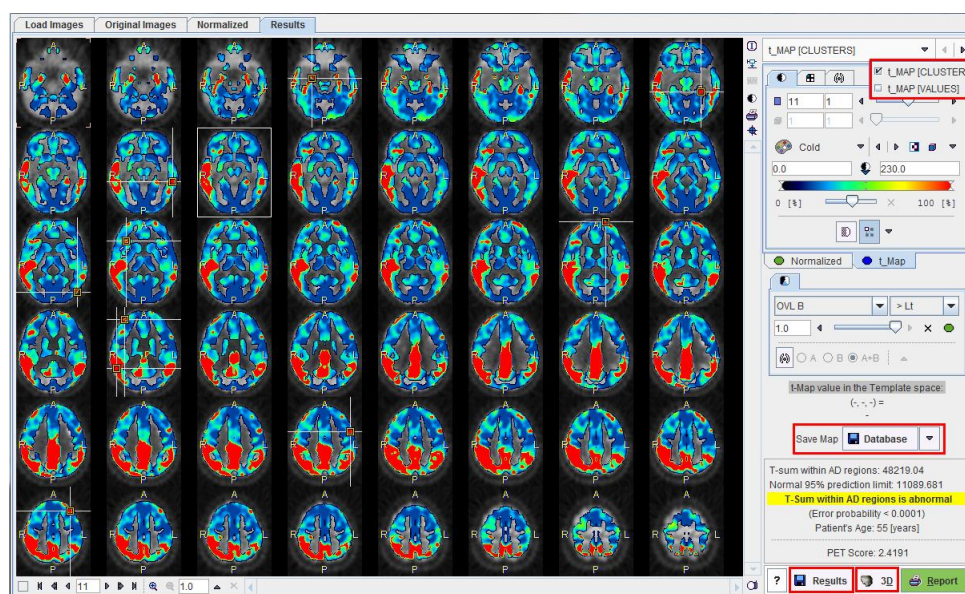


The normalized images can be saved for later referral in the **Save Normalized Images** section. As an indicator that they are the result of a spatial normalization they will contain the term **NORMALIZED** in the series description.

Additionally, the SPM-compliant transformation matrix can also be saved using the **Save Transformation** button. It allows directly recalculating the normalized images from the original images without repeating the normalization calculation.

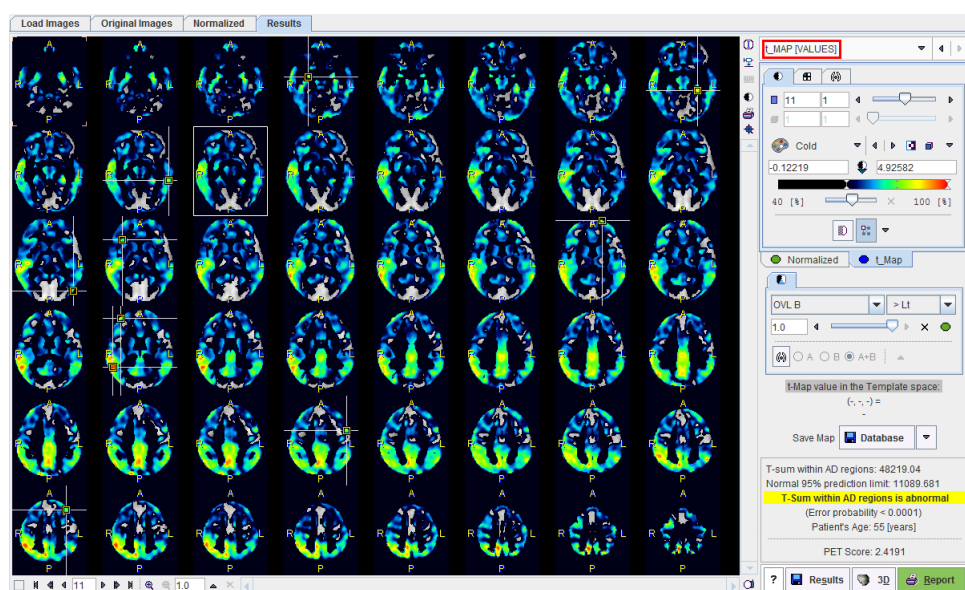
Results of the AD Discrimination Analysis

The extended mode provides four additional features on the **Results** page.



Maps Selection

After selecting the **t_Map** panel, the user can select between the clustered t-values (**t_MAP [CLUSTERS]**) which is the default, and the raw t-values (**t_MAP [VALUES]**) as illustrated below. The selected data set can be exported for external processing or visualization using the **Save Map** button.



Numeric Results Comparison

The result of the discrimination analysis is text information, which can be saved using the **Results** button. This file can either be opened in a general editor (eg. Wordpad, Excel), or using the **View Results** button in the status line of PALZ.

The PALZ result viewer has two windows, into which PALZ results can be loaded and compared side by side as illustrated below.

Alzheimer Discrimination Results:

Evaluation Date: 2011.10.04
Evaluation Time: 17:37:45

[PATIENT INFO]
Patient Name: PALZ1
Birth Date: 1956.04.29
PET Study Date: 2011.09.14

[CLUSTERS TABLE]

No.	Size	Max	X	Y	Z
-	[pix]	[L_Value]	[mm]	[mm]	[mm]
1	22844	4.92582	58.0	-52.0	30.0
2	650	3.52901	-30.0	-36.0	-6.0
3	591	4.02966	42.0	52.0	30.0
4	595	2.89921	-60.0	-36.0	-2.0
5	584	2.67745	38.0	28.0	14.0
6	350	3.23179	28.0	-8.0	-14.0
7	272	3.10080	-20.0	68.0	24.0
8	237	2.94186	-54.0	4.0	50.0
9	221	2.59095	-34.0	26.0	60.0
10	219	2.40292	-50.0	-80.0	12.0

[ALZHEIMER DISCRIMINATION RESULTS]
T-sum within AD regions: 48219.04
Normal 95% prediction limit: 11089.681
T-Sum within AD regions is abnormal
(Error probability < 0.0001)
Patient's Age: 55 [years]
PET Score: 2.4191

Load [ALZHEIMER DISCRIMINATION RESULTS]

Alzheimer Discrimination Results:

Evaluation Date: 2011.10.04
Evaluation Time: 17:30:07

[PATIENT INFO]
Patient Name: PALZ1
Birth Date: 1956.04.29
PET Study Date: 2011.09.14

[CLUSTERS TABLE]

No.	Size	Max	X	Y	Z
-	[pix]	[L_Value]	[mm]	[mm]	[mm]
1	22844	4.92582	58.0	-52.0	30.0
2	650	3.52901	-30.0	-36.0	-6.0
3	591	4.02966	42.0	52.0	30.0
4	595	2.89921	-60.0	-36.0	-2.0
5	584	2.67745	38.0	28.0	14.0
6	350	3.23179	28.0	-8.0	-14.0
7	272	3.10080	-20.0	68.0	24.0
8	237	2.94186	-54.0	4.0	50.0
9	221	2.59095	-34.0	26.0	60.0
10	219	2.40292	-50.0	-80.0	12.0

[ALZHEIMER DISCRIMINATION RESULTS]
T-sum within AD regions: 48219.04
Normal 95% prediction limit: 11089.681
T-Sum within AD regions is abnormal
(Error probability < 0.0001)
Patient's Age: 55 [years]
PET Score: 2.4191

Load [ALZHEIMER DISCRIMINATION RESULTS]

Report Pages

The illustration below shows the overview of the three available pages. To edit, save or print a page select it in the **Pages** section.

1

2

3

CLUSTERS TABLE:

No.	Size	Max	X	Y	Z
1	22844	4.92582	58.0	-52.0	30.0
2	650	3.52901	-30.0	-36.0	-6.0
3	591	4.02966	42.0	52.0	30.0
4	595	2.89921	-60.0	-36.0	-2.0
5	584	2.67745	38.0	28.0	14.0
6	350	3.23179	28.0	-8.0	-14.0
7	272	3.10080	-20.0	68.0	24.0
8	237	2.94186	-54.0	4.0	50.0
9	221	2.59095	-34.0	26.0	60.0
10	219	2.40292	-50.0	-80.0	12.0

Cluster table

Images at cluster centers

Annotations

Zoom

Pages

Print (All pages) **Save As 1238 x 1580 pixels** **Cancel**

As described above, the first report page contains the discrimination result and slice images of the clustered t-map.

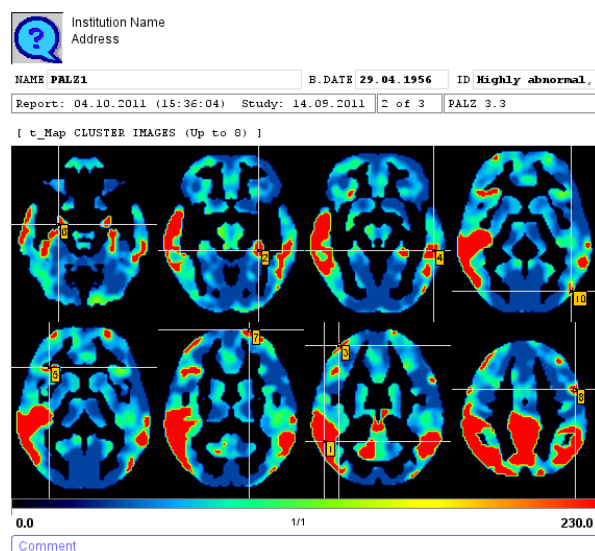
The second report page lists the clusters indicating the cluster size in number of contained pixels, the maximal t-value in the cluster, and the location of the cluster maximum in template coordinates. The list is sorted according to the cluster size.

CLUSTERS TABLE:

No.	Size	Max	X	Y	Z
-	[pix]	[t Value]	[mm]	[mm]	[mm]
1	22844	4.92582	58.0	-52.0	30.0
2	650	3.52901	-30.0	-36.0	-6.0
3	591	4.02966	42.0	52.0	30.0
4	595	2.89921	-60.0	-36.0	-2.0
5	584	2.67745	38.0	28.0	14.0
6	350	3.23179	28.0	-8.0	-14.0
7	272	3.10080	-20.0	68.0	24.0
8	237	2.94186	-54.0	4.0	50.0
9	221	2.59095	-34.0	26.0	60.0
10	219	2.40292	-50.0	-80.0	12.0

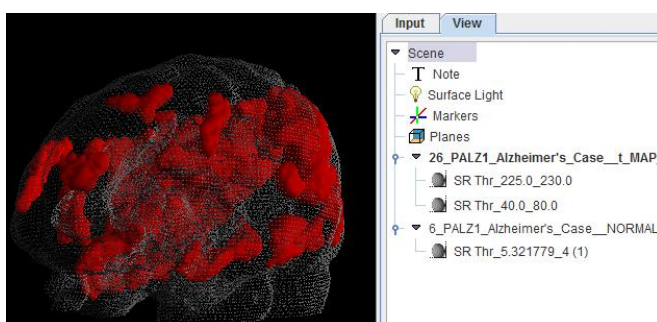
Comment

The third report page contains the slice images located at the cluster centers, ordered by slice location.

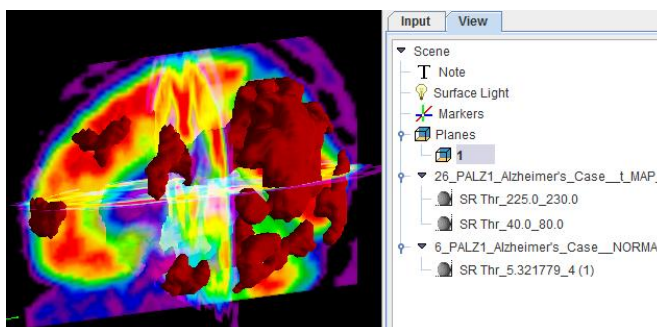


3D Rendering (Separate Option)

If the PMOD 3D option is included in the PMOD license, the result of the analysis can directly be transferred with the **3D** button and a default rendering will be applied. In the example case the 3D tool will show an image similar to the one shown below.



This scene can interactively be examined and the rendering changed in a multitude of ways.

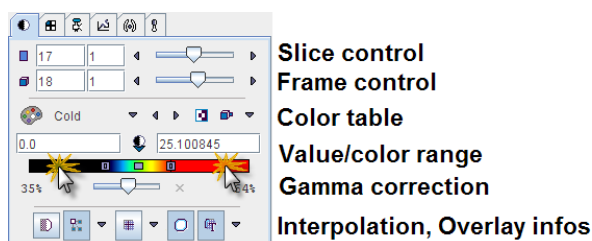


Summary of PMOD Image Display Functionality

For your convenience, this section contains a summary of the methods which can be used for image viewing in PALZ. For a complete review please refer to the *PMOD Base Functionality User's 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.

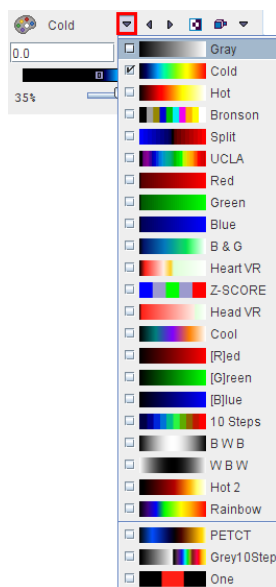
Instead of selecting slices using the controls, the user can also scroll slices by dragging the left mouse button over the image holding the **CTRL** key in the Up/Down direction (see the summary of shortcuts below), or with the mouse wheel.

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.

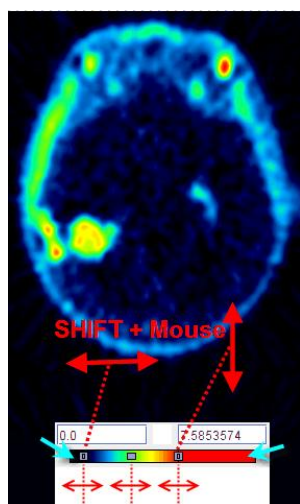
Color Tables

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.

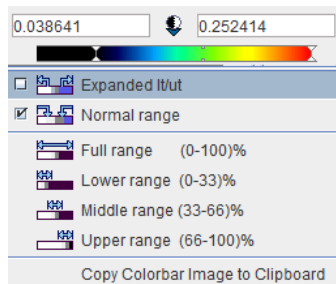
A minimal/maximal threshold value defines the range of displayed values. The thresholds can be entered numerically, or the handles in the color bar can be dragged with the mouse. Additionally, the user can modify them by dragging the left mouse button over the image holding the **SHIFT** key. Left/Right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



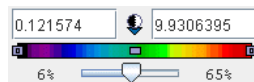
Note: Double-clicking into the lower end of the color bar sets the lower threshold to zero. Double-clicking into the upper end of the color bar sets the upper threshold to the maximum.

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



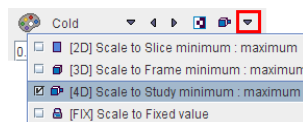
The first menu entry **Expand It/ut** then performs the desired task and makes the color bar change to



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.




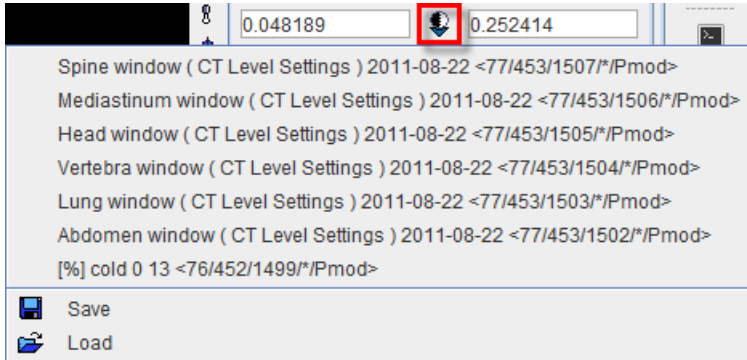
Color Table Modes

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



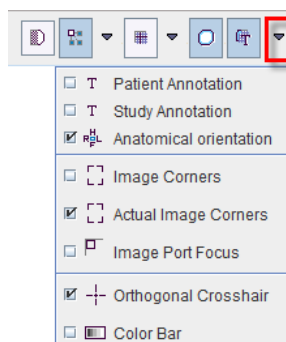
The different modes are:

	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.
	<p>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.</p> 

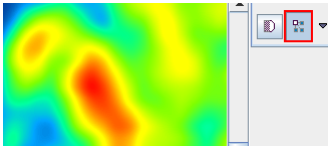
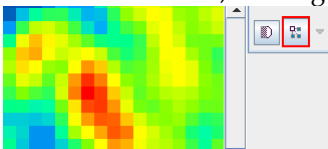




Information Overlays and Image Smoothing

The lowest row contains several control buttons.



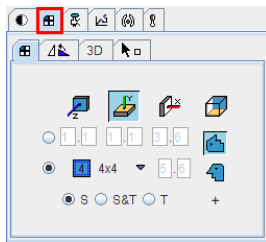
All of the buttons can be on or off, and some might have some configuration options attached. Their functionality is:

	Smoothing: Enables a temporary 9-point smoothing filter. The smoothing is only for display
---	---

	purposes and does not affect calculations.
	<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>  <p>If this button is off, the original rectangular pixels are shown.</p>  <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>
	<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).</p>
	<p>VOIs: Enables the displays of VOI contours, if there have any been defined for the current series.</p>
	<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>: 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>




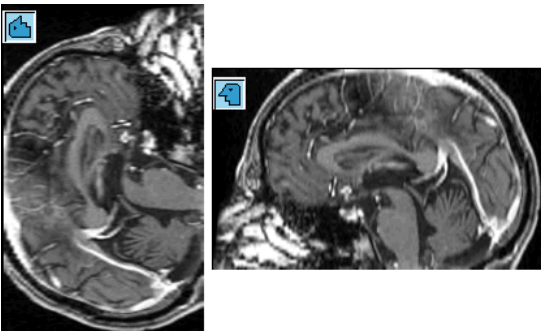

Configuring the Layout

Volumetric images can be displayed in many different ways in the PMOD tools. The layouts are accessible by the second control tab, on the first sub-tab **Layout**.



Slice Orientation

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

	z-Plane: Corresponding to the major slice orientation of the loaded data. Usually <i>axial</i> images. Keyboard shortcut: CTRL+Z.
	y-Plane: Usually the <i>coronal</i> images. Keyboard shortcut: CTRL+Y.
	x-Plane: Usually the <i>sagittal</i> images. Keyboard shortcut: CTRL+X. The x-plane image can be shown in two different ways depending on the modifier buttons. 
	Orthogonal Planes: Layout showing three orthogonal slice images. The intersection point can be moved by clicking into the images.

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


The direction z, y or x indicates the normal to the shown plane shown. The y-, x- and orthogonal buttons are not active if the study is planar only and can thus not be resliced in an other than the original direction.

Tiling Layouts

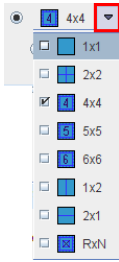
The second and third rows allow configuring the number of images shown concurrently.

If the radio button in the second row is enabled, a dedicated row x column layout is used 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. The definition of the layout per plane orientation is done in the particular tool configuration .

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

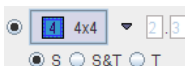


Keyboard shortcuts allow to quickly switch arrangements. After clicking into an image enter

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

To change from a tiling layout 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 and click once more.

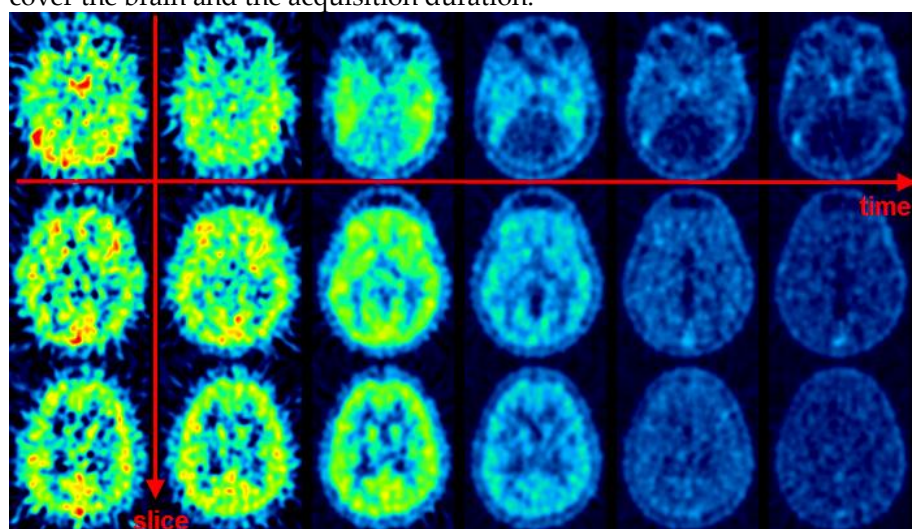
The radio button in the fourth row is only applicable for image tiling with dynamic studies.



If the radio button is in the position of

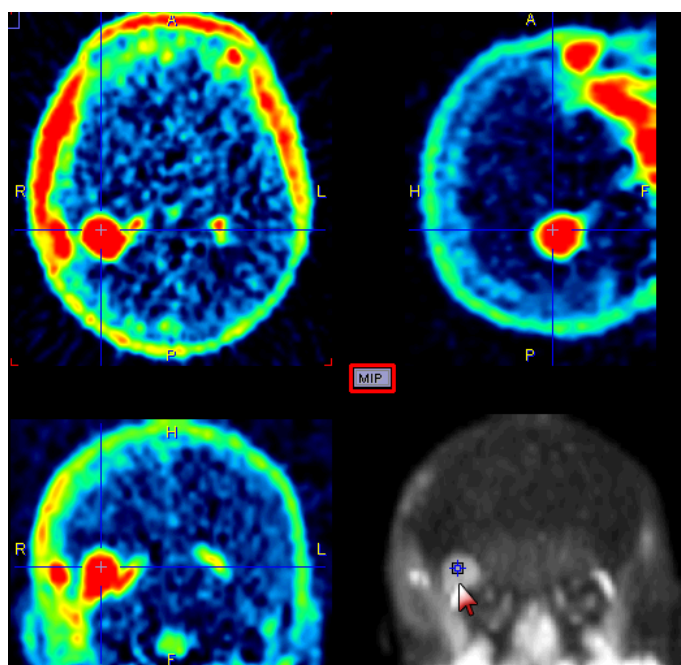
- » **S**: only slices acquired in a single time frame are shown in the image window.
- » **T**: only the images of a single slice are shown at different acquisition times.
- » **S&T**: the images are sorted by slice (vertically) and time (horizontally). Consequently each row corresponds to a slice at different times, and each column to the slices of an acquisition. An example is shown below. Note that increments $\gg 1$ have been set to

cover the brain and the acquisition duration.

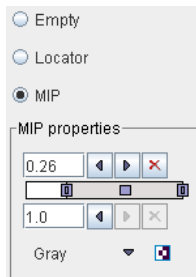


Orthogonal Layout

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 (triangulation point). As soon as the user clicks into an image, the images are updated by the slices intersecting at that new point.



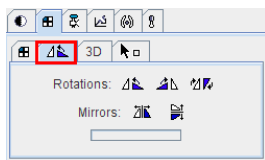
The fourth quadrant is available for different information. It can be configured by activating the button located in the upper left corner of that quadrant, indicated in red in the screen capture above. A dialog appears



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.

Rotations and Mirroring

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




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.

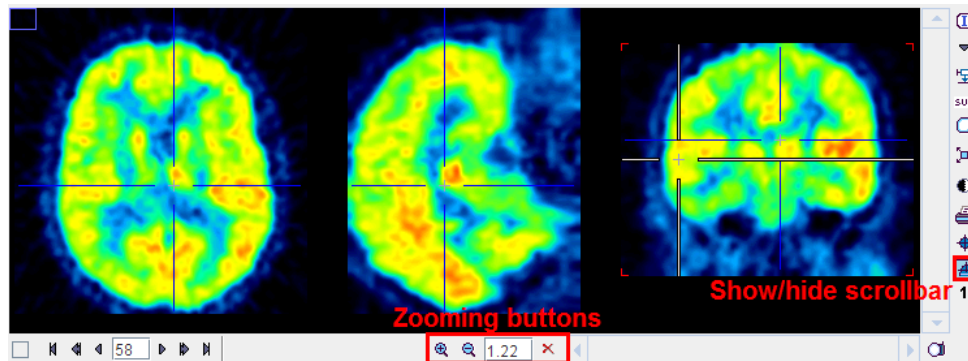
Note: For data with enough information about patient positioning PMOD will keep track of patient orientation and update the annotations accordingly.

Image Zooming

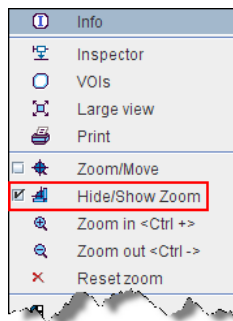
Sometimes it will be helpful to zoom the shown images, for instance during VOI outlining. Image zooming can be operated in different ways

Scrollbar Zooming

Often images ports have a scrollbar area around them. Then the zoom buttons can be used for zooming/shrinking, or a zooming factor can directly be entered.  resets zooming. If the scrollbar is not visible, it can be shown by the indicated button to the image right.




If there is no such button, the image context menu (click right mouse button in image area) can be used instead.





The visible part of the image can be adjusted using the scrollbars around the image which appear as soon as the full image is not visible any more.

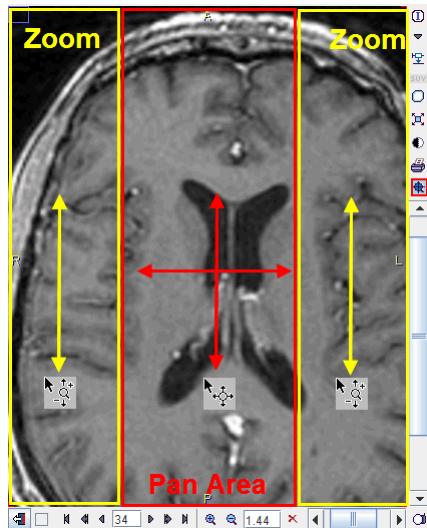
Mouse-driven Zooming


There is also a mode for mouse-driving zooming which can be entered by the  button from the image border or the context menu.

When the cursor is moved over the image, it changes its shape:

- 1) In left and right border area (zooming area) it has a  shape. To zoom in/out click the left mouse button and drag up/down.

- 2) In the central area (panning area) it has a  shape. To adjust the visible part of the image click the left mouse button into the center of the image and drag the image around




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


Zooming with Mouse-Wheel


Similar to the zooming mode in other programs PMOD supports zooming with the mouse wheel while holding down the CTRL key. Note that in the orthogonal mode the triangulation point will be kept within the visible area.

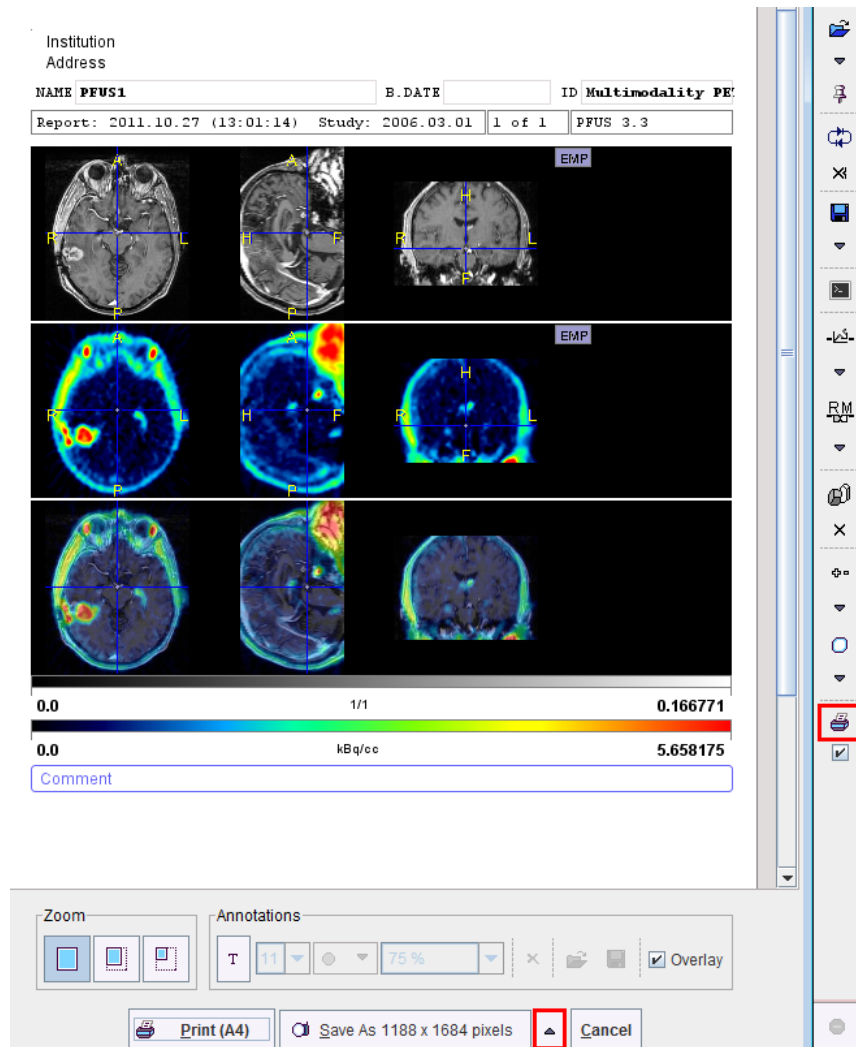
Reports

Reports of the current configuration in a single image display can always be generated using the report button  next to the image. In more complex configurations such as image fusion (PFUS) or image comparison (PVIEW) a dedicated report button is available which creates a composite report.

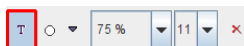
The report button opens a dialog window consisting of a header part, the image area, a comment field, and control buttons for adding annotations, saving and printing.

The logo and the institution address of the header can be configured using the  Config button in the PMOD ToolBox. The patient demographic information is extracted from the image header. It can only be changed by changing the image information itself with the **Edit Patient/Study Info** function.

The central part contains the image(s) in the layout and color as on the image viewing port(s). As long as the presentation is not fully satisfactory, the user can change it in the application and then activating the  button again.

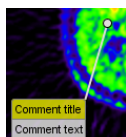


In addition to the provided content the user may add annotations. This can be achieved by enabling the **T** toggle button in the **Annotations** area



and then clicking into the report. A dialog window opens for entering a comment title and body.

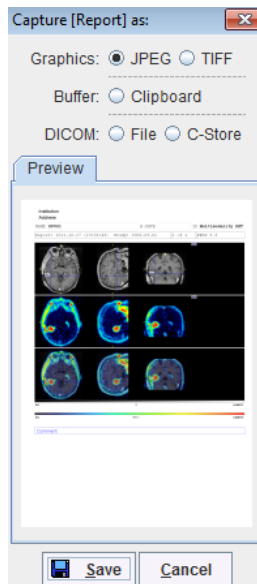
After closing with **Ok**, the comment text is shown together with a circular marker, connected by a line.



Both the text and the marker can be dragged around so as to properly label a point of interest without obstructing the view on relevant information. By changing the opacity and font size in the **Annotations** area, the comment appearance can be adjusted appropriately. To stop adding annotations, the **T** toggle button must be set to off by clicking it again.

When the report contents is satisfactory, the page can be sent to a printer using the **Print** button. Alternatively it can be saved in different graphic formats using the **Save as** option button. Note that there are two resolutions available: **1188x1684** and **594x842**. With **1188x1684**, the generated graphic files have notable better quality (particularly the text), but are considerably larger in size.

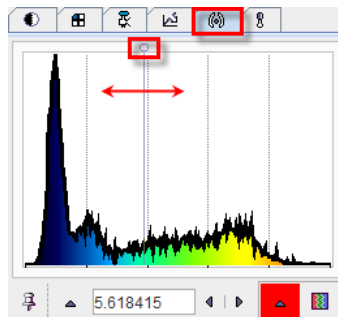
Several saving formats are available in the appearing dialog:



The report page can be saved as a graphic file (**JPEG** or **TIFF**) or copied to the **Clipboard** (for pasting it into a different application). Another alternative is to create a DICOM Secondary Capture object which can be saved to disk (**DICOM File**) or directly sent to a DICOM server (**DICOM C-Store**).

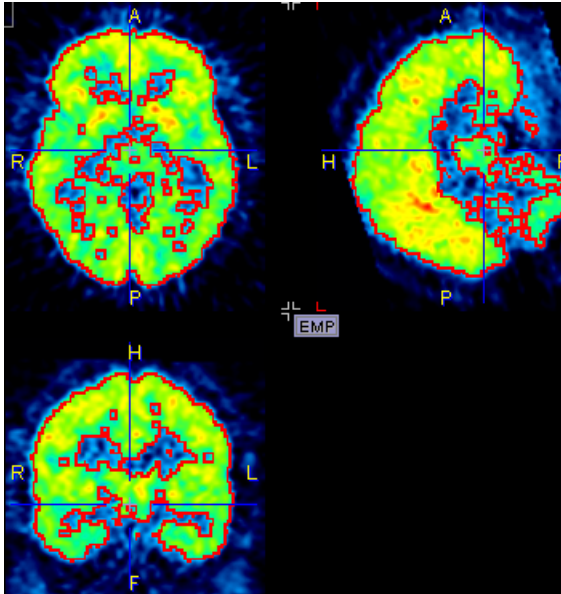
Adding Iso-Contour Lines to Images



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.



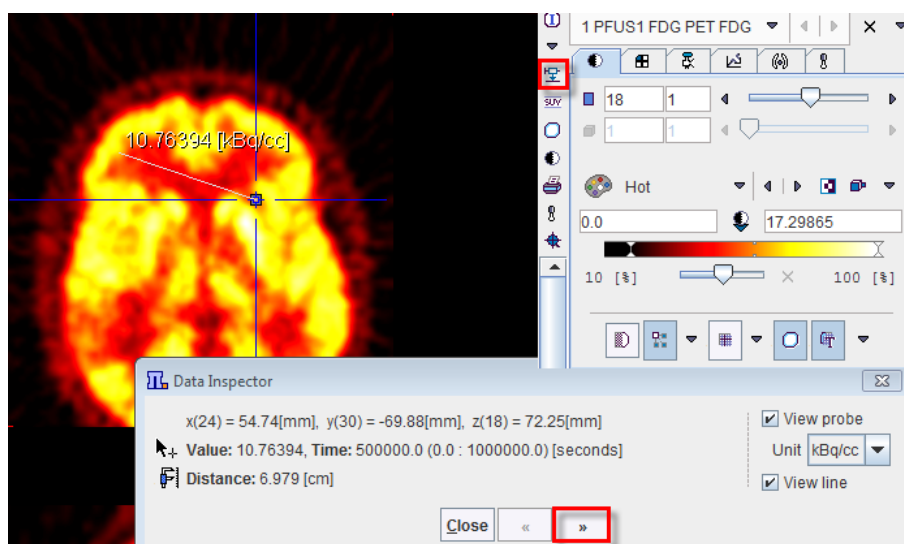
Per default, the iso-contour lines are shown as long as the iso-contour tab is selected. If another tab is selected, they disappear. To make them appear permanently in the images the pin button  can be fixed to .

Data Inspector

The data inspector tool is opened using the button



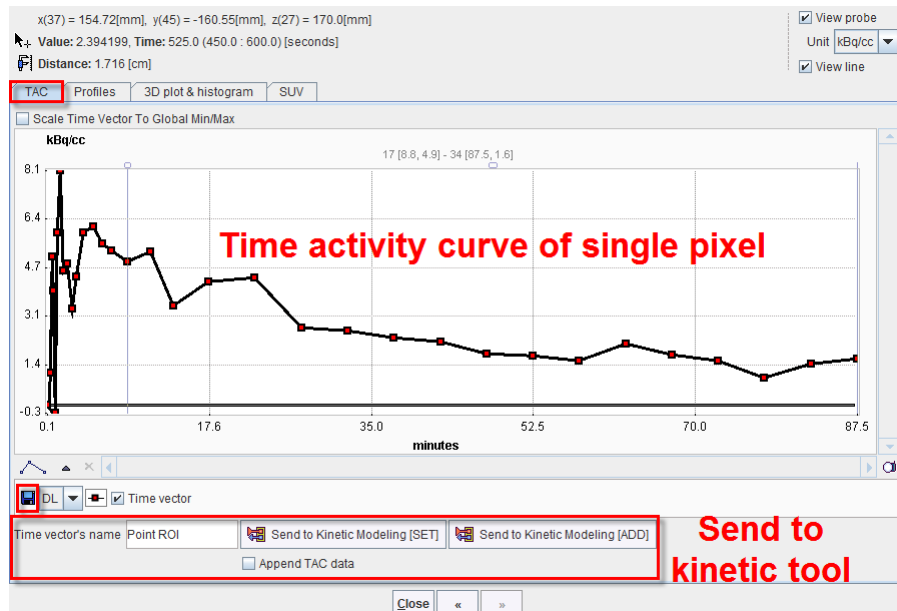
and initially shows the dialog window illustrated below.



When the cursor is moved over the images, the information about the cursor location (in pixels, and mm from the coordinate system origin) and the pixel value at that location is

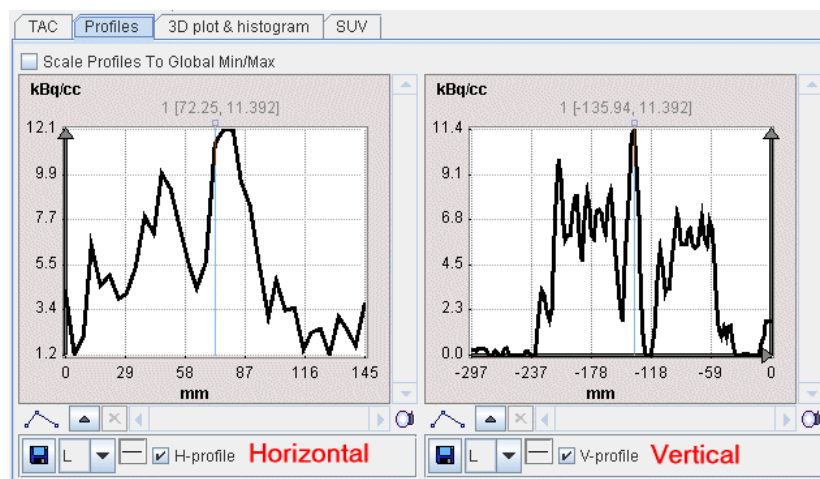
continuously updated. A locator is shown in the image, marking the last position where the left mouse button was clicked into the image. The distance from the locator to the current cursor position is continuously updated. If the **View line** box is checked, a line indicates the measured distance. If the **View probe** box is checked, the pixel value is also shown close to the cursor and the units displayed. If the **SUV** option is selected in the **Unit** list while **View probe** box is enabled, the **SUV [g/ml]** is automatically calculated and displayed for each pixel. Note that in order to calculate the SUV, the patient weight and size as well as the injected dose are requested.

The >> button extends the dialog window to show more information



Using the **TAC** tab the time-activity curve of single pixels can be inspected (for dynamic studies only) and sent to the kinetic modeling tool. It gets updated as soon as the user clicks at a pixel.

The **Profiles** tab displays the horizontal and vertical profiles at the current location of the locator.



On the **3D plot & histogram** tab a 3D plot and the histogram of the slice values are shown, whereas the **SUV** tab allows to inspect the pixel values in SUV rather than kBq/cc, provided that all activity information is available. The **SUV** tab is explained in the next section.

SUV Value Inspection and Statistics

Standard Uptake Values (SUV)

The information contained in PET and SPECT images is related to the physical concentration of tracer in tissue. If all images distortions are corrected by the reconstruction procedure, the value units are activity concentrations, for instance Bq/ml. The uptake in tissue is dependent on many factors. It is directly proportional to the injected activity, and inversely related to the mass within the tracer can distribute. To calculate a measure of tracer uptake which is better comparable among patients (therefore Standard Uptake Value) the measured activities are therefore divided by the injected dose and multiplied by the (mean) body mass. PMOD supports three variants of this calculation:

- 1) SUV Body mass [g/ml]: Directly uses the patient weight entered in the demographic patient information. This is the mostly used SUV.
- 2) SUV Lean Body Mass [g/ml]: First calculates a mean body mass from the patient weight, the height and the gender, which is used in the actual SUV calculation.
- 3) SUV Body Surface Area [cm²/ml]: In this case the uptake is normalized to the body surface area, which is calculated from the weight, the height and the gender.
- 4) Injected dose per cc measured [%ID/ml]: The uptake is normalized to the injected dose and then multiply with 100.

In addition to the patient weight (and size) the SUV calculation has to know the injected dose. For correcting the physical radioactive decay of all activities to the same time the program also requires information about radionuclide, the time of dose calibration, time of injection, the activity remaining in the syringe and when it was measured. Also required is the acquisition start time, because the PET measurements are decay-corrected to the acquisition start.

If all information has been entered by the technicians during the acquisitions, it is directly extracted from the DICOM header. Otherwise, the information has to be completed in a dialog window before the SUV can be calculated.

SUV Value Inspection

The **SUV** (Standard Uptake Value) button



below the data inspector button is a shortcut for opening the data inspector with the SUV tab selected:

$x(37) = 153.09[\text{mm}]$, $y(21) = -87.85[\text{mm}]$, $z(27) = 170.0[\text{mm}]$
 Value: 6.343531, Time: 525.0 (450.0 : 600.0) [seconds]
 Distance: 0.207 [cm]

☒ View probe
 Unit: kBq/cc
☒ View line

TAC Profiles 3D plot & histogram **SUV**

SUV (body mass) ☒ 1.6992 [g/ml]
 SUV (lean body mass) ☐ 1.3599 [g/ml] (LBM estimated by James method)
 SUV (body surface area) ☐ 0.4383 [cm2/ml]
 Injected Doser per cc measured ☐ 0.0023 [%ID/ml]

Patient weight [kg] 75.0
 Patient height [m] 1.79
 Patient sex M

Scan Date and Time:
 (☐ Series ☒ Acquisition ☐ GE Scan) 2006 .3 .1 13 :26 :760

Radionuclide half-life [sec] 6586.2 18 F (109.77 m)

Pre-injected tracer activity [MBq] 280.0
 Tracer measured Date and Time 2006 .3 .1 13 :26 :760
 Admin Date and Time 2006 .3 .1 13 :26 :760

Post-injected tracer activity [MBq] 0.0
 Post-injection Date and Time 2006 .3 .1 13 :26 :760

The times of tracer calibration and / or post-injection were missing.
 They were replaced by the Administration time.

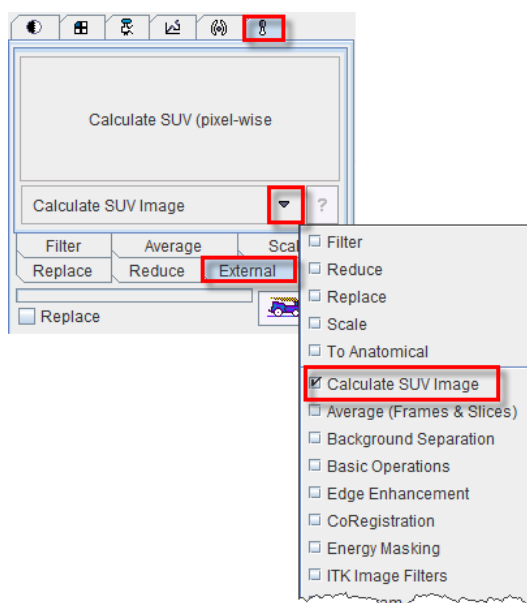
The upper part serves for showing the SUVs of the current pixel. The SUV changes when the cursor is moved over the image. Note that the three different types of SUV and the image normalization value respect to the injected dose are displayed simultaneously.

The lower part shows the information which is involved in the calculation of the SUV. It requires that the image units are kBq/cc, and that all information fields in the dialog are filled in. Per default, the scan start time is read from the acquisition time field of DICOM. However, as situations have been met where this information was wrong whereas the series time was correct, the **Scan Date and Time** radio button allows switching to the series time.

Note that using the **Copy to Study Info** button the information can be saved for later use, and for saving together with the data.

SUV Statistics and Image Calculation


The calculation of statistics in SUV units is directly supported on the original image by the VOI functionality, provided that all required information is available. Explicit SUV images can be calculated with the **Calculate SUV Image** entry of the external tools as shown below.

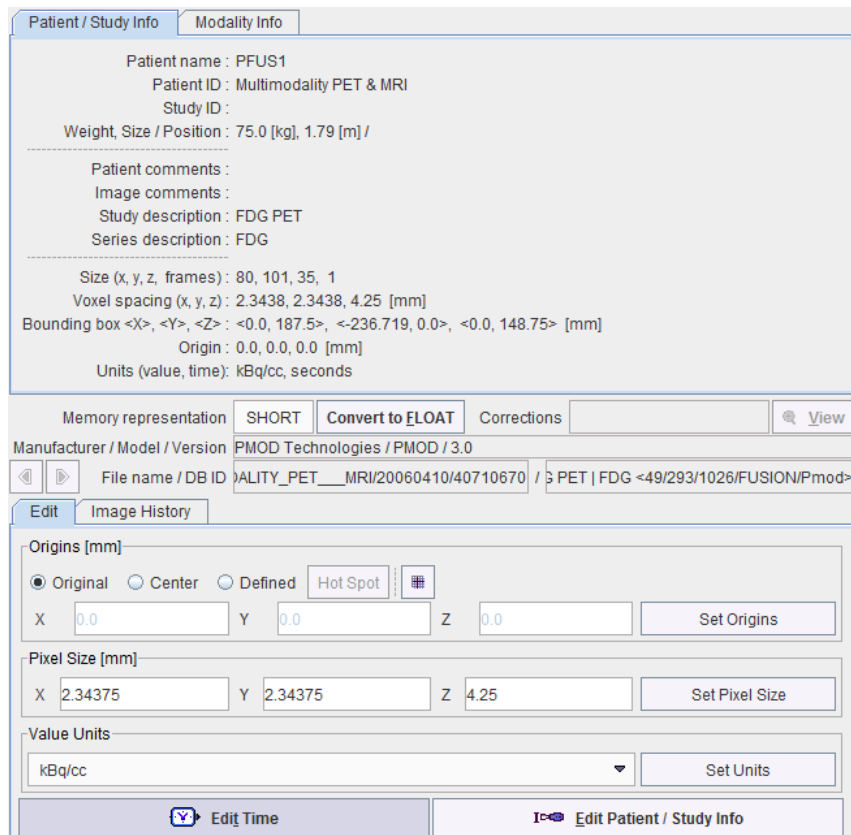


The SUV tool shows a dialog window similar to the one shown above, but it has an additional **SUV** selection which determines the SUV type to be calculated.

The **Ok** button starts the calculation. A new image series with changed units ([g/ml], [cm²/ml] or [%ID/ml]) is created if the **Replace** box is unchecked, otherwise the original series is overwritten.

Viewing and Changing Study Information

In PMOD, each loaded image series has a set of attributes. Depending on the loaded image format they may be partly empty. Using the  button, the information can be shown in a dialog window as illustrated below, and edited.



Patient / Study Info Modality Info

Patient name : PFUS1
 Patient ID : Multimodality PET & MRI
 Study ID :
 Weight, Size / Position : 75.0 [kg], 1.79 [m] /

 Patient comments :
 Image comments :
 Study description : FDG PET
 Series description : FDG


Size (x, y, z, frames) : 80, 101, 35, 1
 Voxel spacing (x, y, z) : 2.3438, 2.3438, 4.25 [mm]
 Bounding box <X>, <Y>, <Z> : <0.0, 187.5>, <-236.719, 0.0>, <0.0, 148.75> [mm]
 Origin : 0.0, 0.0, 0.0 [mm]
 Units (value, time): kBq/cc, seconds

Memory representation SHORT Convert to FLOAT Corrections View

Manufacturer / Model / Version PMOD Technologies / PMOD / 3.0

File name / DB ID ALITY_PET___MRI/20060410/40710670 / PET | FDG <49/293/1026/FUSION/Pmod>

Edit Image History

Origins [mm]
☒ Original ☐ Center ☐ Defined Hot Spot 
 X 0.0 Y 0.0 Z 0.0 Set Origins

Pixel Size [mm]
 X 2.34375 Y 2.34375 Z 4.25 Set Pixel Size

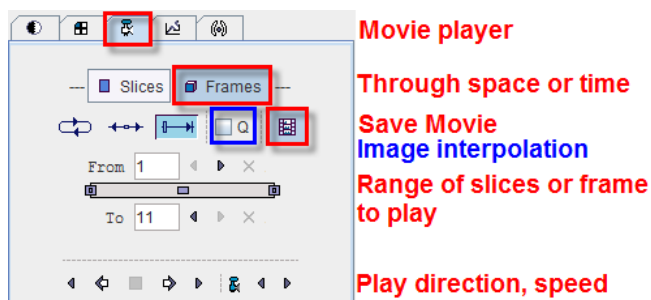
Value Units
 kBq/cc Set Units

Edit Time Edit Patient / Study Info

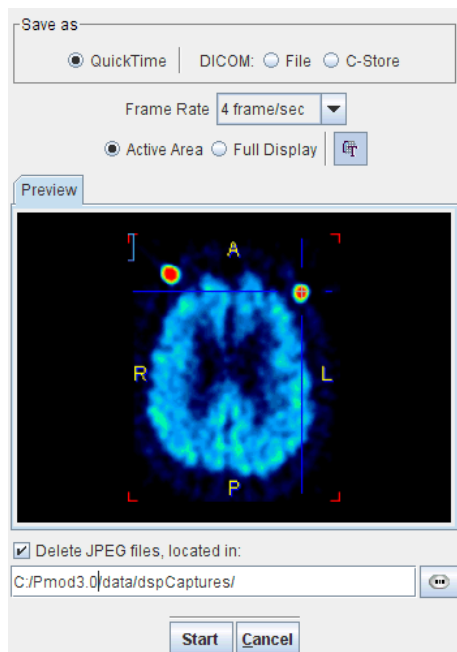
Note that after changing information the data set needs to be saved to make the changes permanent.

Showing and Saving 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.

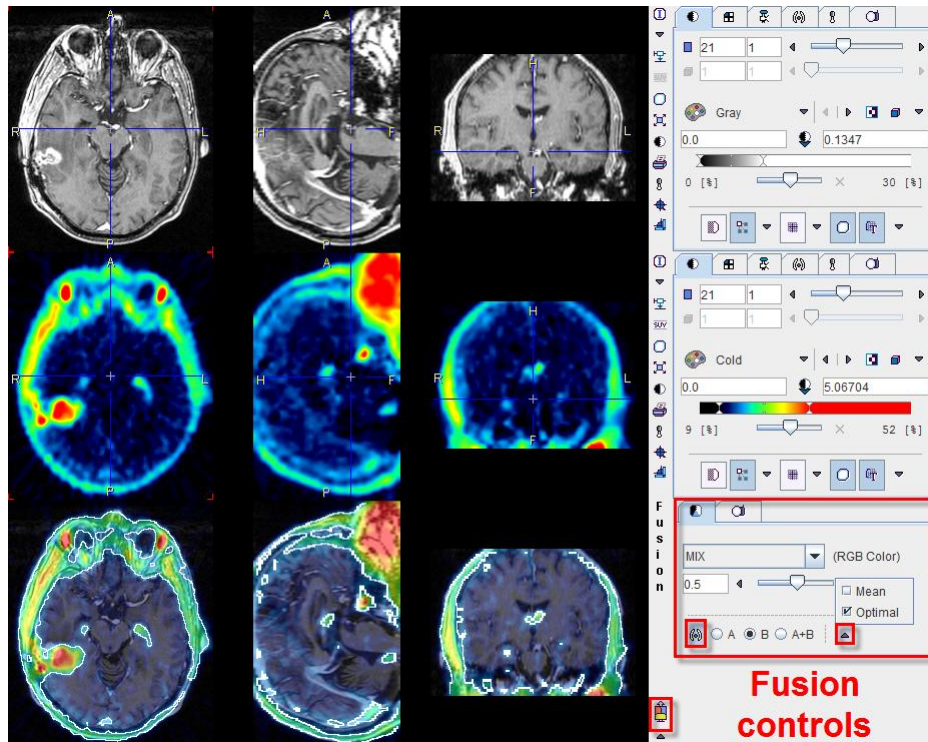
A movie of the active image can also be started/stopped with the **CTRL+M** shortcut without the need to open the movie tab.

Presentation of Fused Images

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

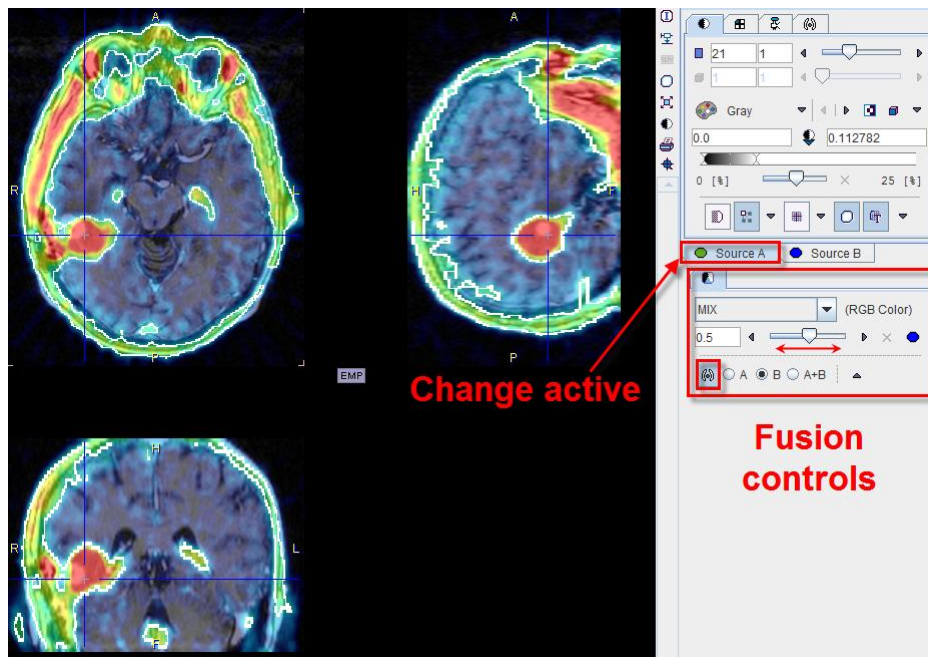
In this layout both the input images and the fusion images are visible at the same time, as in the example shown below.



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.

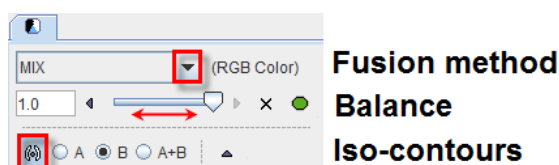
Fusion Images not Visible at the same Time as the Source Images

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:

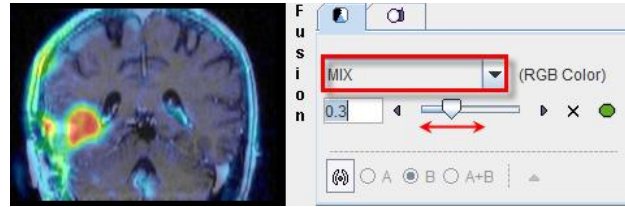
MIX Alpha Blending: weighted addition of the RGB values of both source images according to

$$R_{\text{fusion}} = R_A * x + R_B * (1-x)$$

$$G_{\text{fusion}} = G_A * x + G_B * (1-x)$$

$$B_{\text{fusion}} = B_A * x + B_B * (1-x)$$

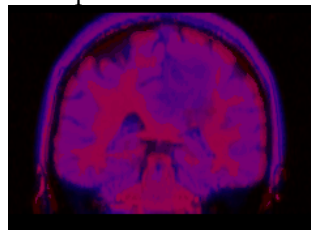
Example:



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

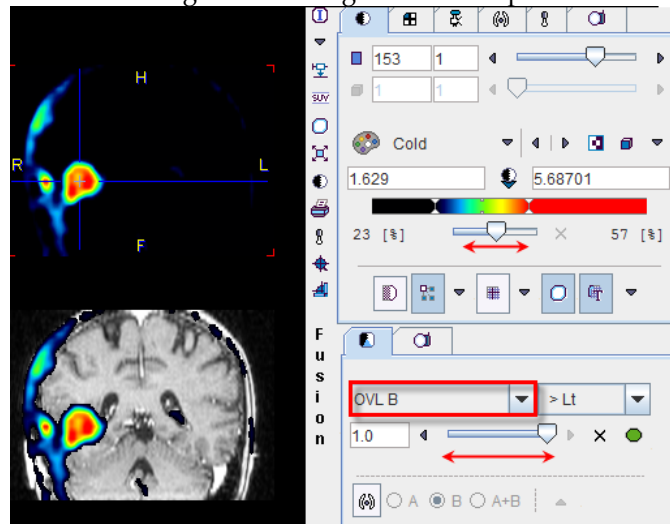
MERGE RGB merging uses the maximal RGB value of both source images according to
 $R_{\text{fusion}} = \text{Max}(R_A, R_B)$
 $G_{\text{fusion}} = \text{Max}(G_A, G_B)$
 $B_{\text{fusion}} = \text{Max}(B_A, B_B)$

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.

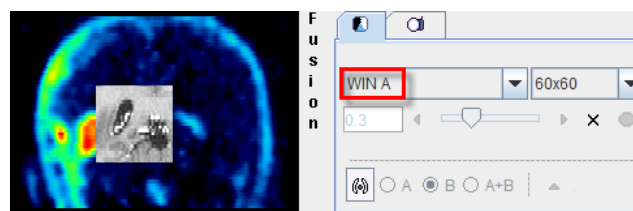
OVL B Shows the images A as background and a part of the images B as the overlay.



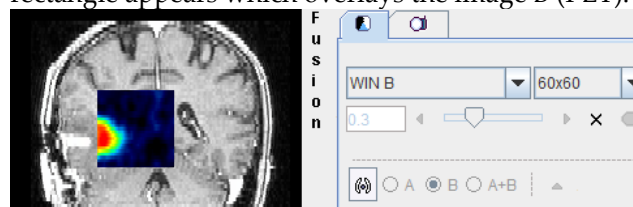
With the >Lt setting, all pixels in the PET image (B) below the lower threshold of the color table are replaced by the MR (A) values. Additionally, some transparency is added in the lesion by the balance slider. See below the description of the different threshold options.

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).

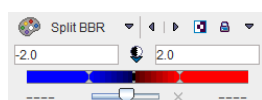


When the **OVL A** or **OVL B** methods are selected, different threshold settings are available in the selection to the right:

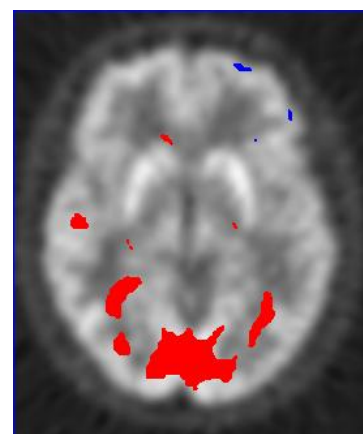
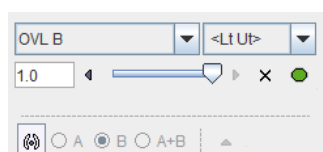
- > Lt Only the pixels (in A for **OVL A** , in B for **OVL B**) with values *above* the lower threshold are displayed. This is the most useful setting when a hot lesion is to be blended into an anatomical image (see example for **OVL B** above).
- < Ut Only the pixels (in A for **OVL A** , in B for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

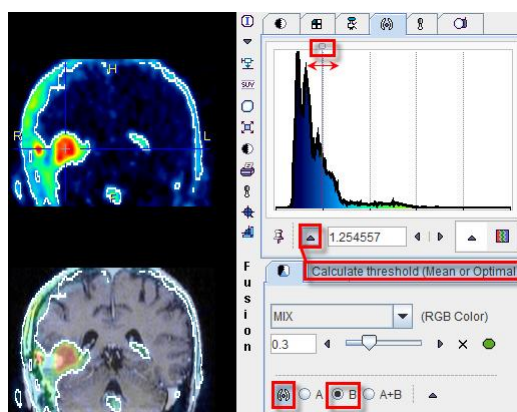


Only z-score values < -2 and > 2 are shown, without transparency. Because only the minimal and the maximal

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.

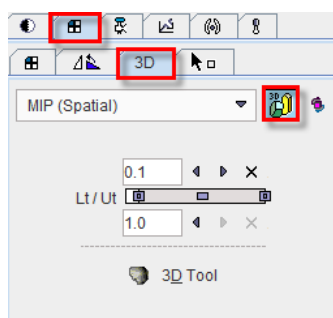
Iso-contours in Image Fusion

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.



3D Volume Rendering, Rotating MIP Images

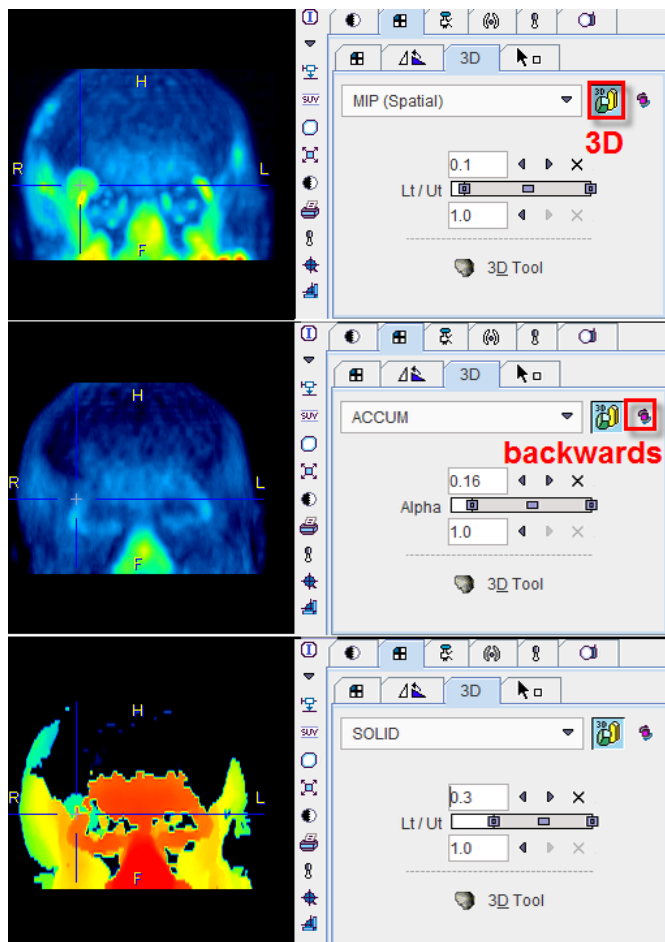
Instead of showing individual slice images, a volumetric data set can be volume rendered. Simple volume rendering can be enabled in the **3D** sub-pane



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.

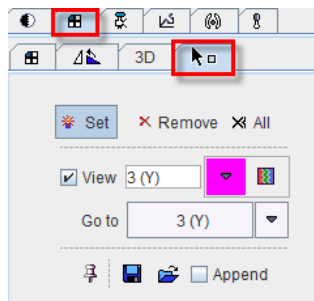
MIP images will be calculated from different viewpoints and displayed as a rotating cine. If you would like to save a movie, enable the saving button as explained in *Showing and Saving Movies* (on page 43).

Transfer to Full 3D Rendering

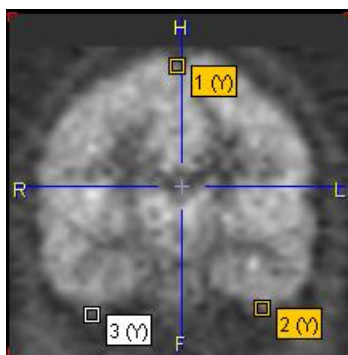
The  button in the 3D pane is only functional if the PMOD 3D option is installed. When this button is activated, the current data set is loaded into the full 3D rendering tool for advanced processing.

Markers



The **Markers** sub-pane



is used in combination with landmark-based image matching. The best way to define landmarks is to operate in the orthogonal layout.



If the **Set** button is active the user may click into an image to define anatomical landmarks which are shown in the image. To avoid marker generation, hold CTRL+SHIFT when clicking. The slices can be scrolled by the mouse wheel or by CTRL+DRAG.

The spatial arrangement of landmarks can be saved for later use with . If the pushpin button is enabled , the clicks into the image will still produce markers even when the **Markers** pane is closed.

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