

# PNEURO Workbook Version 3.9

## Scope and Intended Use

This document is an addition to the PNEURO User's Guide and aims at illustrating PNEURO operation with some application cases. The workbook starts with step-by-step descriptions and progresses towards higher-level outlines. Note that bold face is used for indicating strings corresponding to elements in the user interface of PNEURO.

## Copyright and Disclaimer

The example data for the course demonstrations and exercises are organized in the **Neuro** database. This database is not included in the standard distribution but is available upon request for PNEURO users. The data are by courtesy of the Nuclear Medicine Department, University Hospital, Zürich, Switzerland. Note that the original data have been processed and optimized for training purposes.

### IMPORTANT:

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

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## PNEURO Application Cases

Three example MR and PET data sets are available in the **Neuro** database (DB). In order to reduce the RAM requirements during the PNEURO analyses the MR images have been resampled to 1.2mm isotropic pixel size. This allows running the Maximum Probability Atlas (MPA) analysis with systems having 4GB of RAM, and the T<sub>1</sub>-Parcellation analysis with 8GB RAM.

The following sections describe typical analyses with the example data. It is recommended reading them sequentially, as the level of description detail decreases progressively. The **Neuro** DB is configured in the software environment prepared for PMOD training courses. For independent training use, please request the **Neuro** DB for download and make sure to configure the DB using the **Config** facility as described in the *Readme* which accompanies the data.

### 1. MRI and Dynamic <sup>11</sup>C-Raclopride PET

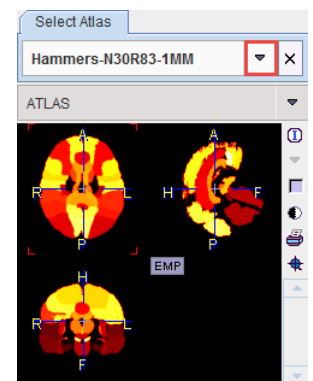
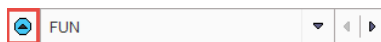
The data set of “patient” **MRI-Raclo Dynamic** includes a dynamic PET acquisition of <sup>11</sup>C-Raclopride during 60 minutes as well as a resampled T<sub>1</sub>-weighted MRI. The brain anatomy in the PET image is not ideal for brain VOI generation, as the initial frames are very noisy and late uptake concentrates in the basal ganglia. Therefore the brain structures will be derived from the MR image and applied to the PET series for regional statistics. The MPA and the T<sub>1</sub>-Parcellation approaches are described in the following.

#### Analysis using the Maximum Probability Atlas Method

Please start the Neuro tool from the PMOD ToolBox and select the **Maximum Probability Atlas** tab.

##### Atlas Selection

As a first step define the brain atlas on which the analysis will be based. The **Select Atlas** panel is located to the left and shows the currently active atlas. If the panel is hidden, activate the show/hide arrow button.

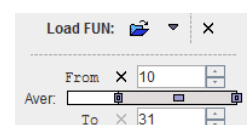



There are two main human atlas choices available: the maximum probability atlas **Hammers N30R83** with 1mm and 2mm resolution, as well as the single-subject atlas variants **AAL-Merged** and **AAL-VOIs**. Note that user-defined atlases will appear in the lower part of the selection together with the animal atlases. Please select the **Hammers-N30R83-1mm** atlas from the list of available atlases.

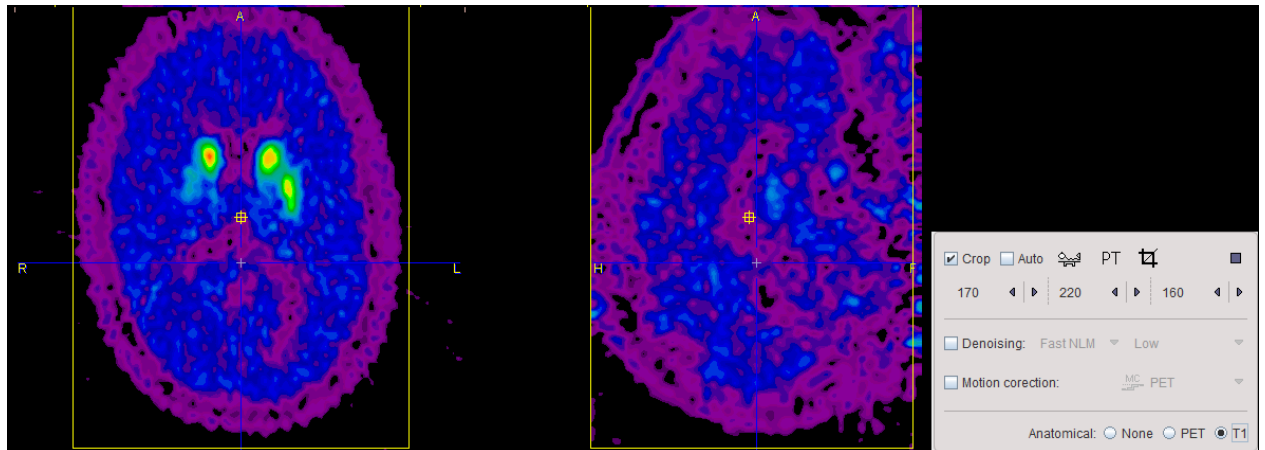
##### PET Image Loading, Averaging and Cropping

Activate the **Load FUN** button with the database format configured. In the appearing DB interface make sure the **Neuro** DB is selected. Seven “patients” are listed in the **Patients** area. Select **MRI-Raclo Dynamic**, and in the updated **Series** list the **Dyn 60 min PET**. Load the data with the **Open** button. The images appear in an orthogonal layout with the default PET color table. Note that the original dynamic PET images are fused with an image calculated from averaging a range of dynamic frames labeled as **FUN AVG**.

The averaged PET will be used for the rigid matching with the MR, so the frame averaging should provide an image containing information about the whole brain with sufficient quality. The optimal averaging range strongly depends on the tracer uptake characteristics. For the present Raclopride PET please define the frame range **From** and **To** as **10** and **31**, respectively. Whenever the range definition is changed, the average image is updated immediately. To only see the average PET drag the fusion slider fully to the right.



For avoiding excessive RAM needs and speeding calculations up, the image is then cropped to the relevant portion of the data. Activate the **Crop** box and place the appearing yellow crop box such that the brain is completely enclosed. The box position can be changed by simply clicking at the brain center in all plane orientations. If needed, the box edge sizes can be adjusted by the three size selection buttons. If the **Auto** box is checked, PNEURO will try to determine the location of the crop box automatically. Activate the  button to execute image cropping. This completes the preparation of the PET image.

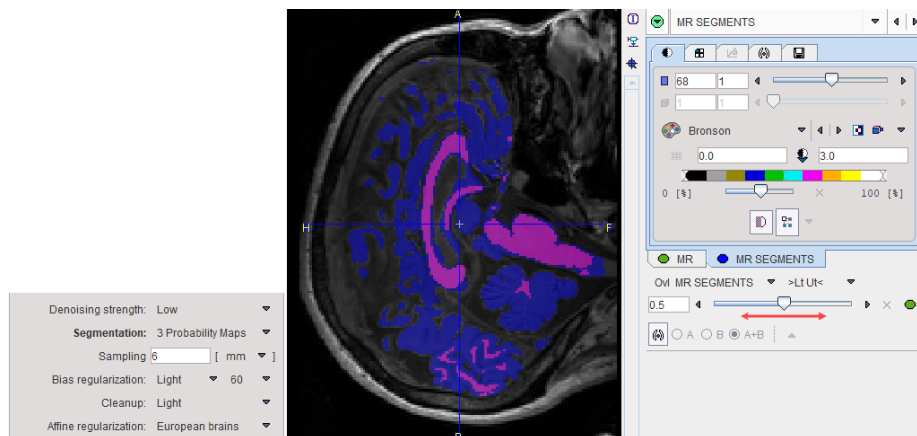


The next step is to load an anatomical image. Ideally, a T<sub>1</sub>-weighed MR image is available which presents the brain anatomy with good resolution in all directions. If this is not the case, an FDG image might be used alternatively. As the MRI is available for this exercise please select the **T1** radio button and activate the **MR** action button in the lower right. Correspondingly, the program switches to the **MR** loading page.

### MR Image Loading and Cropping

Data loading is started using the **Load MR** button. In the DB window select the same patient **MRI-Raclo Dynamic**, and in the **Series** list the **Brain MR**. Load the images with the **Open** button and then define a crop box in the same way as for PET, then crop the data. Note that during loading the MR images are always brought to standard radiological orientation, even if the data was acquired in sagittal orientation.

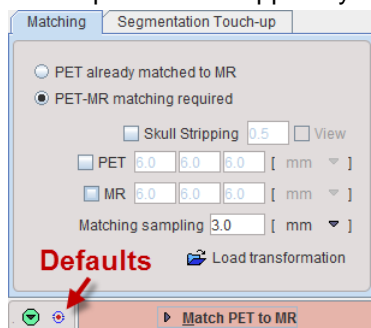
In the next step, probability maps of grey matter (GM), white matter (WM) and cerebrospinal fluid (CSF) will be calculated. This segmentation process is tailored by some parameters above the red action button: **Denoising strength** can be set to different levels. It may improve the image quality and consequently the outcome of segmentation. Please select **Low** as a compromise between quality and processing speed. Set the **Segmentation** method to **3 Probability Maps**, corresponding to the SPM8 unified segmentation. The alternative is **6 Probability Maps**, (SPM12). The **Bias regularization** and **Cleanup threshold** parameters are related to the actual segmentation. Please set both of them to the default value of **Light**. **Sampling** is an important parameter as it determines how much of the data is actually used for segmentation. The smaller the sampling size becomes, the more information is used and the longer the segmentation will take. With the present data, **6mm Sampling** works properly. In other situations, *if the segmentation outcome is unsatisfactory, please try smaller sampling settings.*



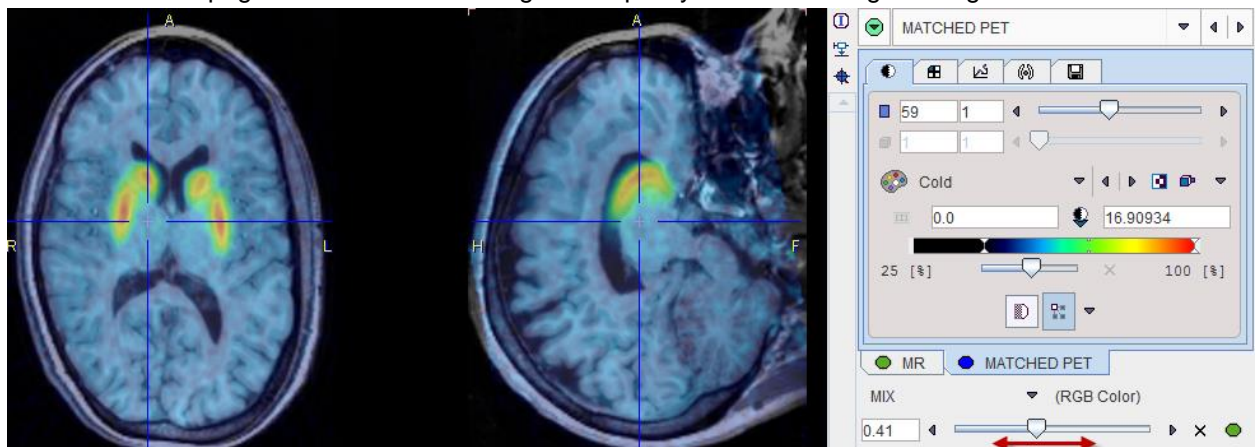
Finally, activate **Segment MR** to start the segmentation process. Calculation time may be around 2.5 minutes on a decent notebook system. The segmentation result is shown on the **MR SEGMENTS** PNEURO page as illustrated above. The **MR SEGMENTS** image tab contains the tissue label image with gray matter (GM), white matter (WM) and CSF represented by the label values 1, 2 and 3, respectively.

### MRI-PET Matching


The next step establishes the mapping between the MR and the PET spaces. To this end the average PET image is rigidly matched to the MR image using the Normalized Mutual Information criterion. There are several available parameter for this procedure. Activating the *default* button as indicated below sets it to **3 pixels**. The **Smoothing** options may help avoiding local minima. If the data were already matched, this step could be skipped by checking the box **PET already matched to MR**.

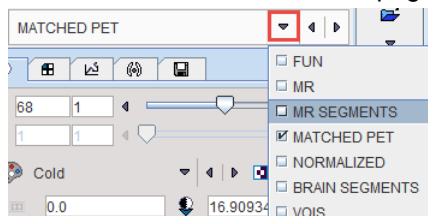


Activate **Match PET to MR** to start rigid matching. The result is shown as a fusion image on the **MATCHED PET** page. Please check the alignment quality of the two images using the fusion slider.



In this exercise the matching outcome is satisfactory. In case of a failure there are three options to try:

1. Interactive correction: activate the **Adjust Matching** button  and drag/tilt the PET images in all directions.
2. Return to the **MR SEGMENTS** page using the list selection illustrated below,

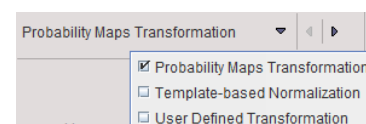


reduce the **Matching sampling** parameter, and start matching again.

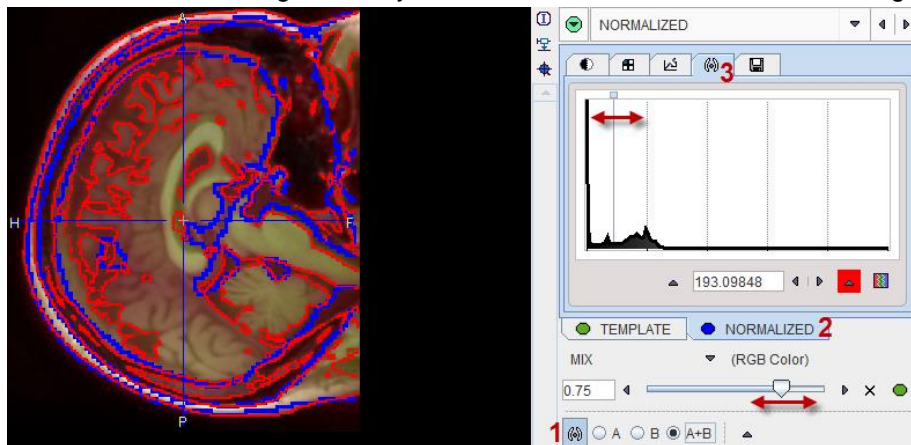
3. Match the PET externally to MR, save it, load the matched PET into PNEURO, and skip matching.

### MR-based Normalization

The next step establishes the stereotactic transformation between the patient brain anatomy and the standard anatomy in the atlas space. There are different options, depending on the atlas selection and the available data. In our example the normalization transformation was already determined. This is configured by the **Probability Maps Transformation** choice. It is applied to the MR image by activating the **Normalize** button.



The result is shown on the **NORMALIZED** page as a fusion of the T<sub>1</sub> MNI **TEMPLATE** with the **NORMALIZED** MR. Shift the fusion slider left/right in order to validate the outcome. Additionally, iso-contours can be introduced into the images for highlighting boundaries in the brain as illustrated below. To arrive at this representation proceed as follows: Enable the iso-contours, select the **NORMALIZED** image tab, activate the iso-contour tab and adjust the iso-contour level. Next, adjust the iso-contour level of the **TEMPLATE** image similarly. Note that the contour color can be changed if necessary.



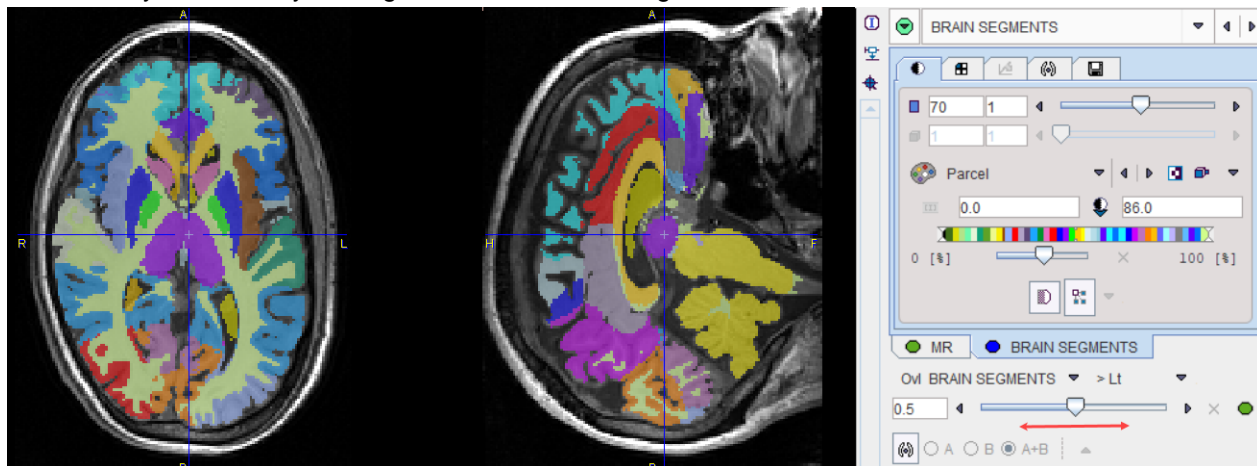
### Atlas Transformation

At this time, the rigid transformation between MR and PET is known as well as the stereotactic transformation between the patient brain and the template. Therefore, all images as well as the atlas regions can be transformed to any involved space: the atlas space, the patient MR space which probably has the highest resolution, and the patient PET space. In the next step, these transformations are applied to the data so that the user can inspect the VOI results on top of the PET and the MR images in any space. Please start the transformation of all data sets with the **Segment Brain** button on the **NORMALIZED** page.

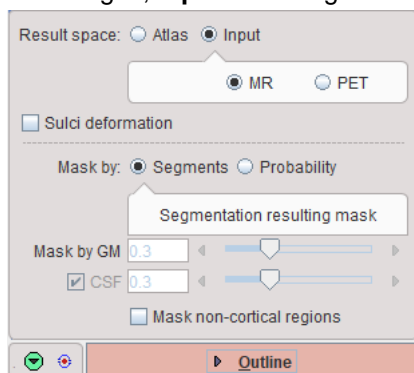


### Volume of Interest Outlining

A fusion of the transformed **MR** image and the atlas segments is shown on the **BRAIN SEGMENTS** page. Please verify that there is a good match of the segments with the anatomy. This is again most conveniently achieved by shifting the fusion slider left/right.



The images are always shown in the **Result space** selected in the configuration area. Please explore the differences in representation when selecting the **Atlas** space, the **Input/MR** and the **Input/PET** space. The image is updated whenever the result space is changed. Because of the superior resolution of the MR images, **Input/MR** brings out most detail.



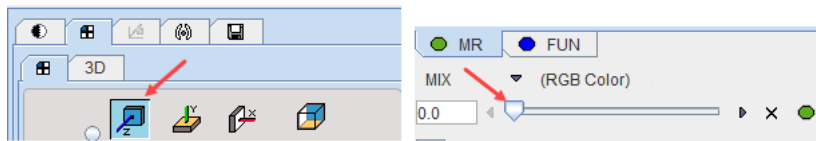
Next, explore the impact of restricting the brain regions to pixels with high grey matter probability. Set the **Mask by** radio button to **Probability/Individual** for using the GM probability map of this particular patient and move the threshold slider left/right. Make sure the CSF box is disabled. The trimmed regions are updated in the display as soon as it is released. The smaller the threshold values are, the larger the regions become. When switched to **Probability/Standard Mask** trimming is based on a population GM map. Because of the lower probabilities the regions grow considerably. With the **Segments** option, the GM label from the individual tissue label map will be used instead of a probability map.

Regions other than cortex structures are usually excluded from this masking operation. To see how GM trimming affects them enable the **Mask non-cortical regions** box. It is evident, that significant parts of the basal nuclei structures become discarded. Therefore, please define the parameters as illustrated above and activate **Outline** to convert the segment image into an outline definition.

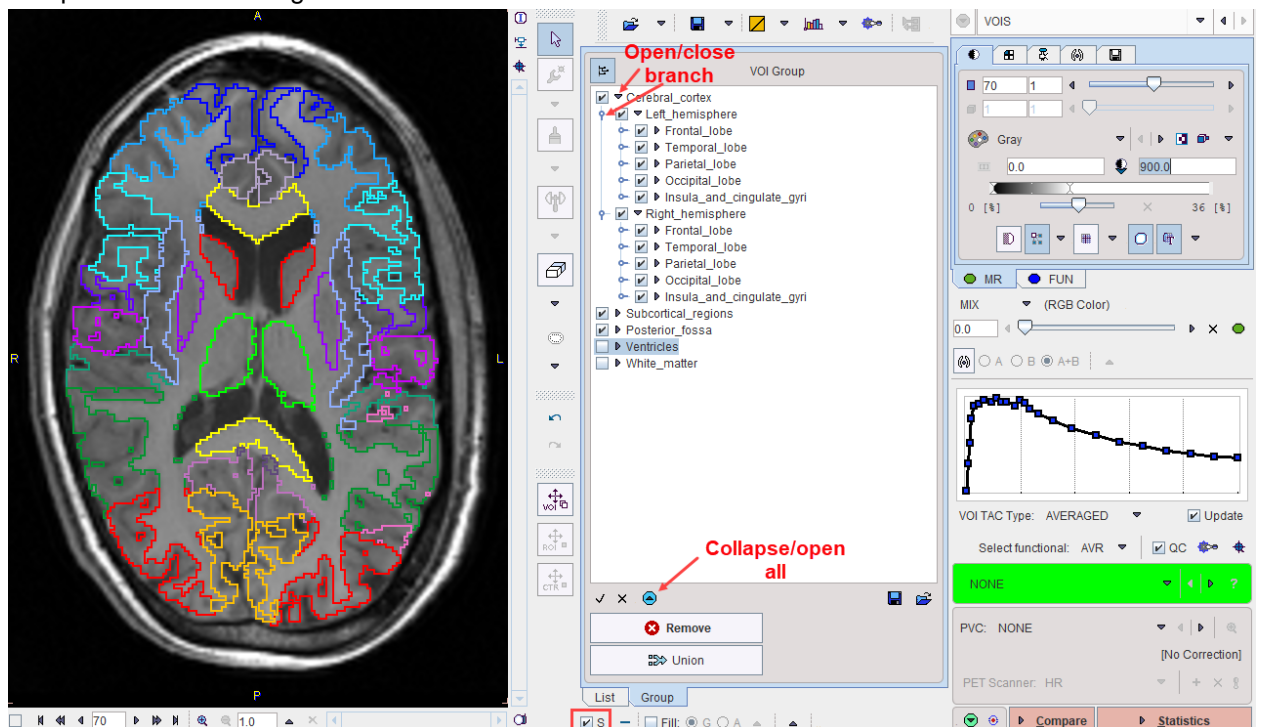
### Volume of Interest Exploration

The resulting VOI outlines are shown on the **VOIS** page together with the tools for manipulating them. Initially, a fusion of the MR and the PET images is shown in the selected result space using an orthogonal

layout. As the images may be small, use the layout tab to change the representation to a single axial slice. Next, bring the fusion balance fully to the left to show the MR image only.

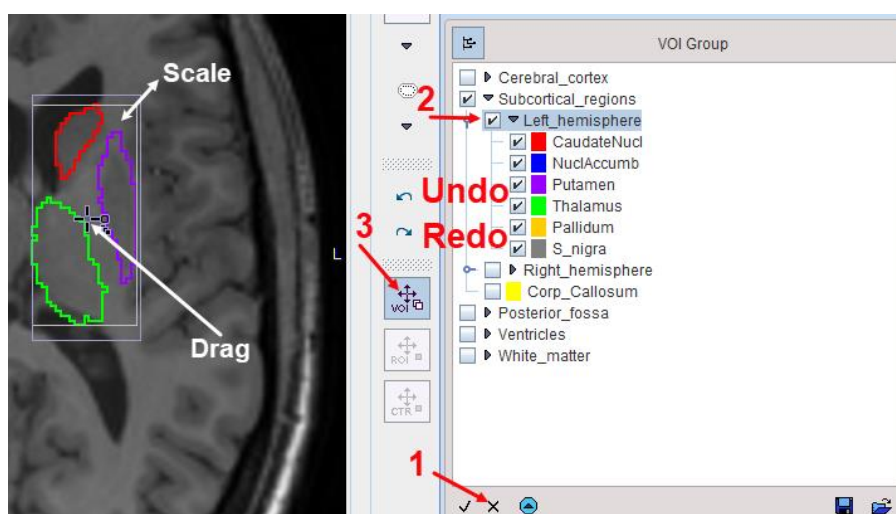


In this representation the region contours can be conveniently explored by scrolling through the slices. It is evident how the cortical VOIs follow the grey matter boundaries. The basal nuclei, however, show some aberration from the anatomy. Initially, most of the VOIs are shown in the image overlay. The tree in the **VOI Group** panel organizes the VOIs hierarchically into **Cerebral\_cortex/ Subcortical\_regions/ Posterior\_fossa/ Ventricles/ White\_matter** branches followed by left/right structure branches. The cortex left/right hemispheres are further organized into lobes. Individual VOIs or whole branches can be hidden or shown by checking the corresponding box as indicated in the illustration below. *Note that the **S** checkbox has to be active for this selective visualization to work.* Otherwise, all VOIs will be shown irrespective of the settings in the tree.



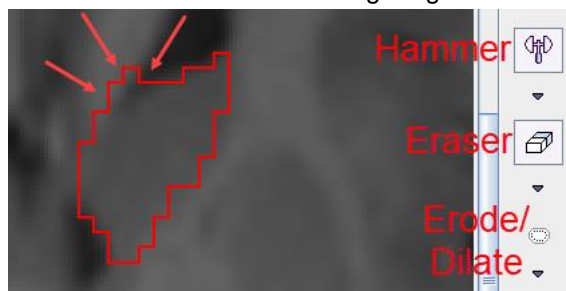
Modifications can be applied to the VOIs in many ways as described in the *PMOD Base User's Guide*. The number of available VOI functions in PNEURO can be defined in the configuration. The example above has all VOI functionality enabled, the example below only a minimal set.

For instance, while the **Group** tab is active, all VOIs selected in the tree can be shifted. As illustrated below, activate the **x** button for disabling all VOIs, then click into the **Left hemisphere** branch of the **Subcortical\_regions**. Only the 6 central structures are shown in the overlay. Next activate the **VOI** operation button. A box appears around the contours with a handle in the middle. Try out how the group of VOIs can be moved by dragging the handle, and scaled by dragging the edges of the bounding box. Finally use the *Undo* button multiple times to bring the VOIs back to the original position.



Note also the **Union** button which combines all VOIs selected in the tree into a single new VOI. To try this out clear all selections with **x**, enable the left and right **Cerebellum** in the **Posterior\_fossa** branch, activate **Union** and enter **Merged\_Cerebellum** as the new VOI name in the confirmation dialog window. As a result, a new VOI branch appears at the end of the VOI tree while the original VOIs disappear at the same time. This is necessary to ensure proper operation of the optional partial-volume correction (PVC). Please return to the original VOI set by activating the *Undo* button.

The editing of single VOIs is done in a different way. First, the **List** tab has to be activated. On this list, the VOI arrangement is linear. Double-click at VOI 57 **CaudateNucl\_I** to select it. It is not clearly seen among all the VOIs. Therefore enable the **S** checkbox which became disabled when switching the panels. Now, only the left caudate VOI is shown. Scroll to slice 63 and note that the VOI seems to be somewhat too large. To trim its size interactively select the *Eraser* tool (Size 1) and drag along the VOI boundaries to wipe away pixels. Alternatively, try out the *Hammer* tool and the tool for the erosion/dilation. Note the small arrows which allow configuring the tool sizes.



Finally reset all changes with the *Undo* button. As an alternative for re-establishing the standard VOI definition, return to the **BRAIN SEGMENTS** page with the selection in the upper right and activate the **Outline** button once again.

### Results Saving

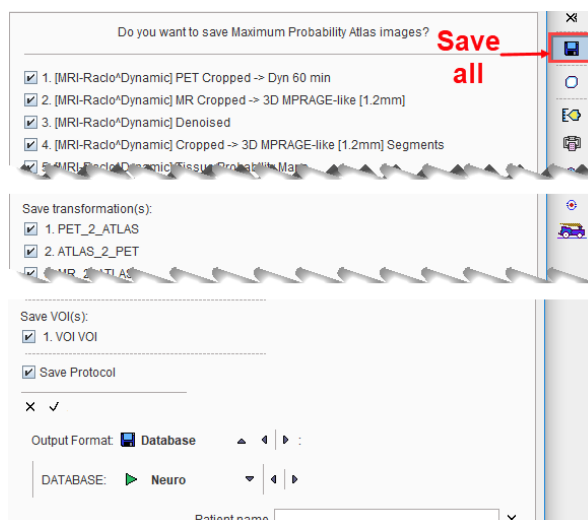
After completion of the VOI adjustments save the VOIs with the corresponding button above the VOI list



and name it **Max Probability MR space**. Any time later, this VOI set can be retrieved and applied to any data in the MR space.



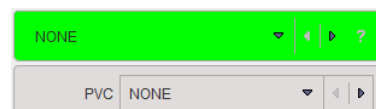
PNEURO offers a convenient facility for saving all generated data at once with the **Save all** button in the lateral taskbar illustration below. As can be seen, the images are available in all spaces, as well as the spatial transformations between all the spaces. Note that the transformations cannot only be applied to the images, but also for transferring the VOIs between the different spaces. Enabling the **Save Protocol** box the whole processing can be saved.



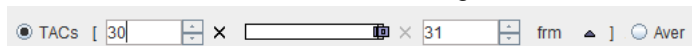
Another way of saving the whole processing is using the **Save Protocol** button in the status line. Activate the button and save the protocol as **MaxProbability-MR-PET**. This saves the processing settings together with the final VOIs.

### Statistics Calculation and TAC Transfer to Kinetic Modeling Tool

To start calculation of the regional PET statistics without partial volume correction and parametric mapping make sure these options are switched off and then activate the **Statistics** button. PNEURO switches to the dedicated **Statistics** page and shows 86 tissue time-activity curves (TAC) representing the regional PET average in the dynamic frames of the Raclopride PET series.

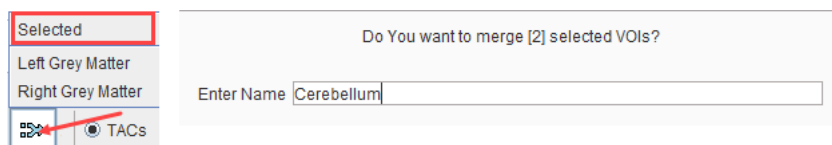


Often, PET scans are static rather than dynamic. To see how the result would look like for an acquisition 50-60 minutes after tracer injection average the last two 5 minutes frames as follows. With the **TACs** radio button enabled set the lower range value to frame **30** (50-55min) and the upper to **31** (55-60min).



Then switch the **Aver** radio button on. Immediately, the TAC curves are replaced by a table which shows the average uptake per region as well as the region volume. To transfer these results activate **Copy to Clipboard**, start a program like Excel and select the *Paste* operation. The full table is pasted and can be further processed.

Return to the TAC display by switching again the **TACs** radio button on. These TACs can be quantified by the *Simplified Reference Tissue* model using cerebellum uptake as the reference. In order to obtain an averaged cerebellum signal from left and right proceed as follows: Use **Deselect All** to switch off all curves. Look for the **Cerebellum\_r** and **Cerebellum\_l** entries towards the end of the list and check both of them. Activate the *Merge* menu as illustrated below, choose the **Selected** entry, and enter **Cerebellum** as the TAC name.



A volume-weighted average of the two curves is calculated and assigned to the TAC **Cerebellum** which appears at the end of the list. Note that opposed to the VOI merging the original curves are still available. Finally, activate the **Kinetic Modeling** button to transfer all curves to the PKIN tool.

## Analysis using the T1-Parcellation Method

When exploring the outcome of the MPA analysis in the exercise above it turned out that the basal nuclei definition - which is most relevant for Raclopride - was not ideal. The following exercise applies the T<sub>1</sub>-based parcellation approach which is specialized for those structures. Many of the processing steps are the same as for the MPA method and will not anymore be described in detail.

Please close and restart PMOD first to free RAM. This is important because the parcellation is challenging for most non-workstation systems.

### *PET Image Loading, Averaging and Cropping*

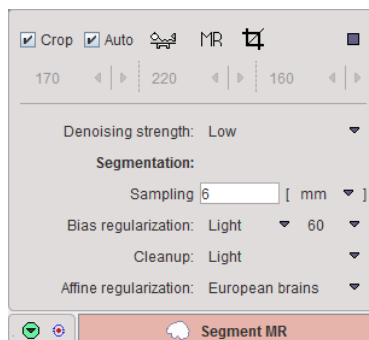
Start the **Neuro** tool and select the **Brain Parcellation** tab. Using the **Load FUN** button, load the **C11-Raclopride PET** series of the **MRI-Raclo Dynamic** patient, average the frame range **10 to 31**, and **Crop** using the automatic procedure. Move on to MR loading with the **MR** action button.

### *MR Image Loading, Averaging and Cropping*

Using the **Load MR** button load the **3D MPRAGE-like [1.2mm]** series and **Auto Crop**.

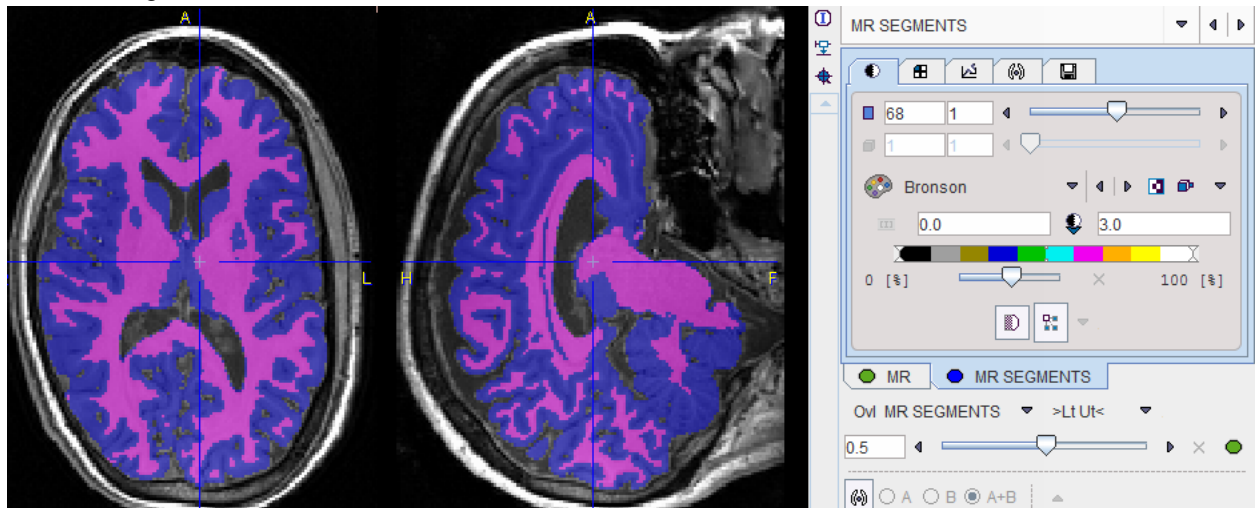
### *MR Image Segmentation*

Still on the **MR** page, set the parameters for the GM/WM/CSF segmentation to the same values as for the MPA method.



Then activate **Segment MR** to proceed.

The segmentation result is shown on the **MR SEGMENTS** page as a fusion of the GM/WM label map with the MR image.

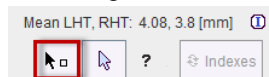


Note that there is a well-defined boundary between the GM (blue) and the WM (pink). It is possible to shift this boundary line towards GM or WM with the tools in the **Segmentation Touch-up** panel, but for this exercise the segmentation is accepted.

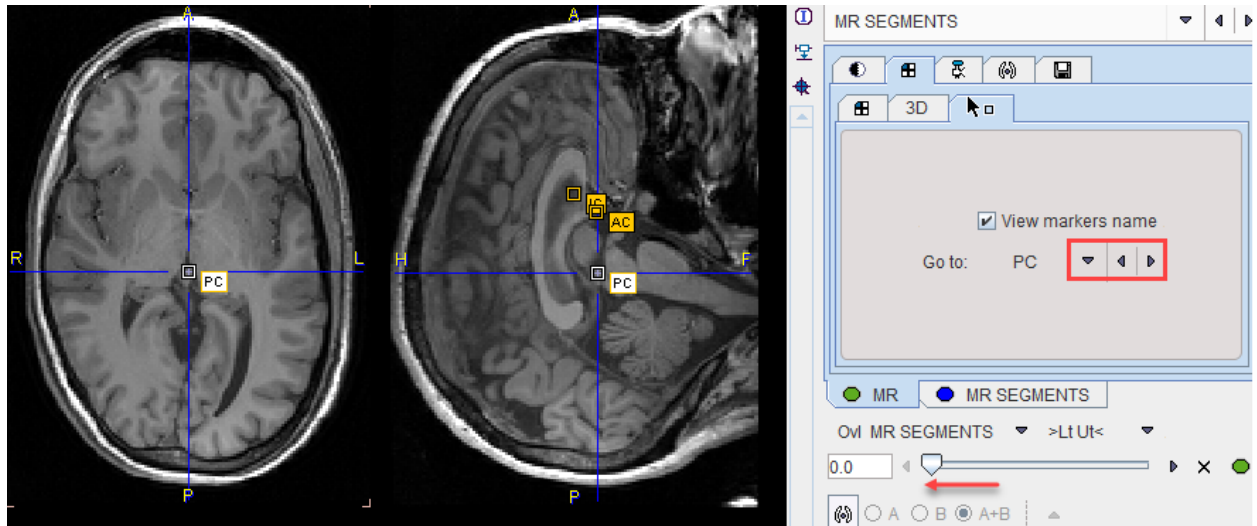
### Landmark Definition

An important difference of the T<sub>1</sub>-parcellation method to the MPA method is that the processing requires four anatomical landmarks. The position of these landmarks is estimated during the segmentation. The user only has to check their accuracy and shift them if necessary.

Shift the fusion slider to the left for a better view of the MR image. Enter the marker adjustment mode by activating the *markers* button indicated below.



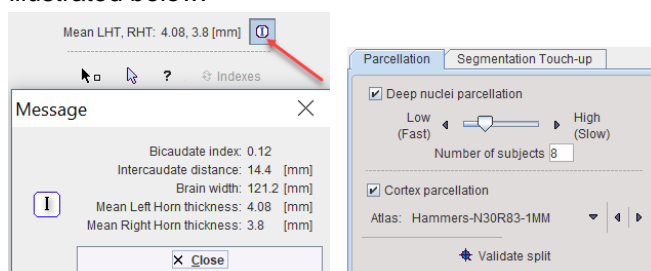
The panel with the marker control elements opens. Use the **Go to** facility for localizing the **IC** (inter-caudate), **AC** (Anterior Commissure), **PC** (Posterior Commissure) and an inter-hemispheric (**IC**) point.



The recommended marker locations can be visualized in a help window by the ? button. If a marker needs adjustment just drag it with the left mouse button in any of the plane orientations. No adjustment is needed for the automatically determined landmarks in this example.

### Parcellation

In the next step, the program will select the most similar hemispheres from the knowledge base (KB) in order to construct a maximum probability atlas of the basal nuclei. This selection is based on a number of indexes which were calculated during the segmentation. They can be inspected by activating the button illustrated below.



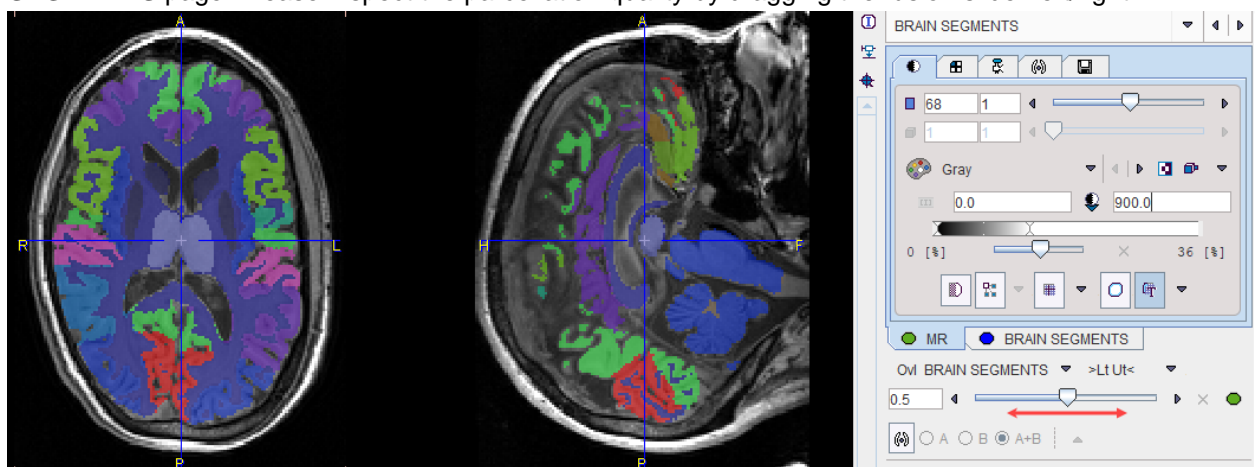
The number of selected references is defined by the **Number of subjects** parameter in the **Parcellation** tab. According to a study the optimal number to use is 8. As the calculation time for the corresponding 16 hemispheres is quite substantial, please set the number of subjects to **2**. Make sure that the **Deep nuclei**

**parcellation** box is checked, as these are the results of interest. Because the derivation of the cortical VOIs doesn't involve major calculations, also check the **Cortex parcellation** box and select the **Hammers-N30R83-1MM** atlas.

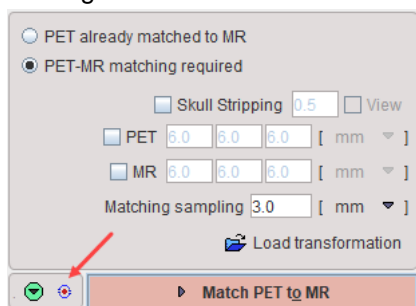
Finally, with the parameters set as illustrated above, initiate **Parcellation** by the corresponding action button. With the setting of 8 subjects the program has to process 16 hemispheres and will try to do this in parallel. Therefore, a system with 4 processing cores will only take 50% calculation time compared to a 2 core system. Most likely, processing will take about 20-30 minutes while you can monitor the progress in the status bar.

### Brain Segments and PET-MR Matching

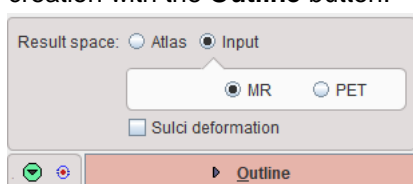
The parcellation results are presented as label map which is fused with the MR image on the **BRAIN SEGMENTS** page. Please inspect the parcellation quality by dragging the fusion slider left/right.



In the next step, PET will be rigidly matched to the MRI. Set the default parameter configuration by clicking the *default* button indicated below. The **Matching sampling** becomes **3mm**.

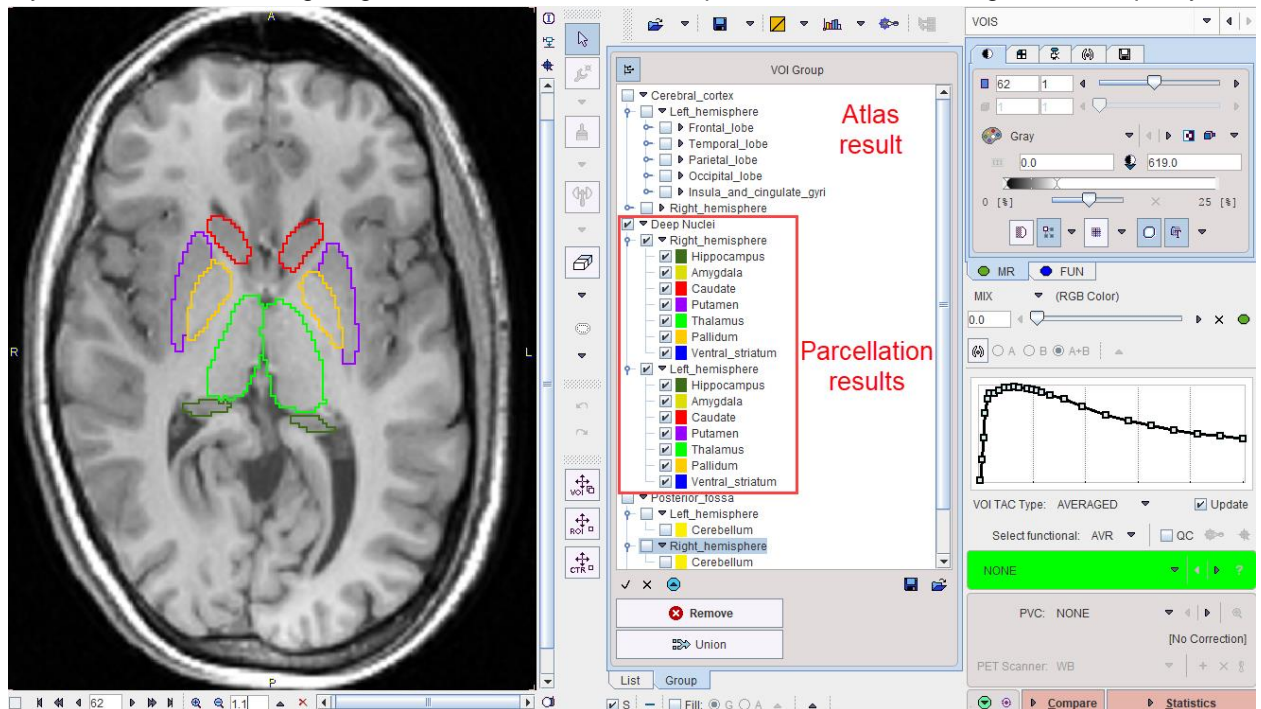


Activate **Match PET to MR** to start rigid matching. The result is shown on the **MATCHED PET** page for inspection and correction. As the result is fine, don't interfere with the matching at this time. In order to compare the parcellation quality with that of the MPA choose **MR** as the **Result space** and start contour creation with the **Outline** button.

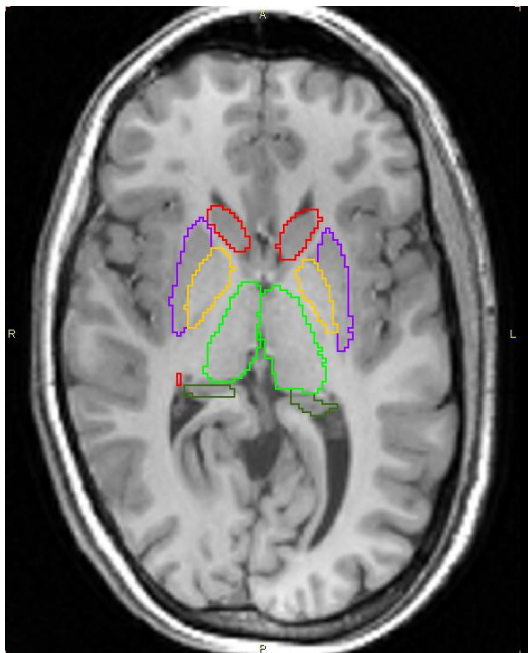


### Volume of Interest Exploration

The resulting VOI outlines are shown on the **VOIs** page. Note that the VOI tree arrangement is somewhat different as for the MPA. The cortical VOIs are derived by intersecting the Maximum Probability Atlas with the GM label segment, the **Deep\_Nuclei** result from the parcellation. Configure the axial single-slice layout, set the fusion weighting to **100% MR**, and then compare the basal nuclei segmentation quality.



It is superior to the MPA result, and it can be further improved by using more than 8 knowledge base subjects. The illustration below demonstrates the difference when using only 2 subjects.



From this stage on processing is identical to that described for the MPA exercise. Please **Save** the **Protocol** under the name **Parcellation-MR-PET (8subj)** and the VOIs under **Parcellation MR space (8 subj)**.

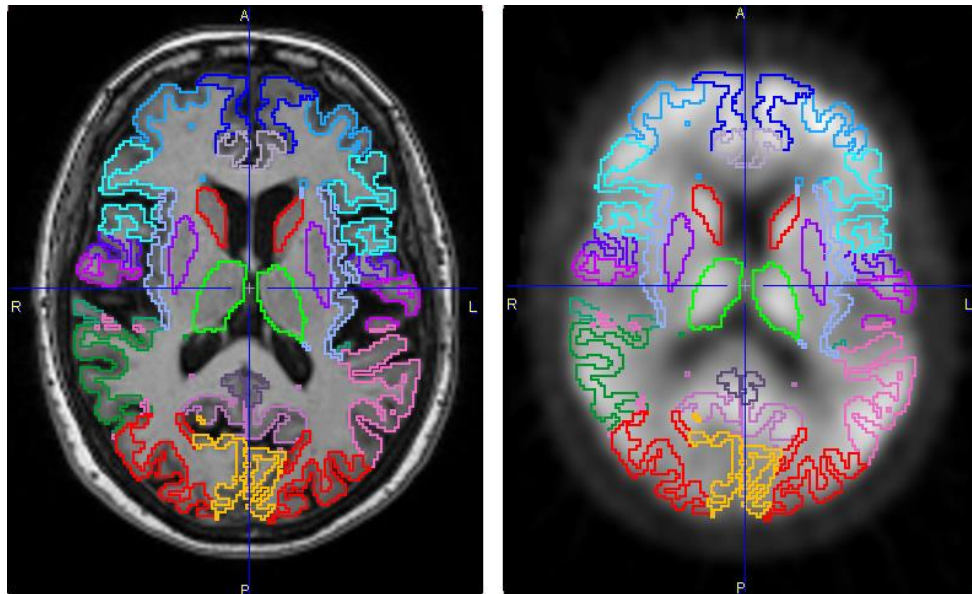


## 2. MRI and Dynamic $^{11}\text{C}$ -PIB PET

The data set of “patient” **MRI-PIB Dynamic** includes a dynamic PET acquisition of  $^{11}\text{C}$ -PIB during 70 minutes as well as a resampled  $T_1$ -weighted MRI. The patient was classified as MCI with MMSE 27 at the time of the PIB scan and had converted to AD one year later.

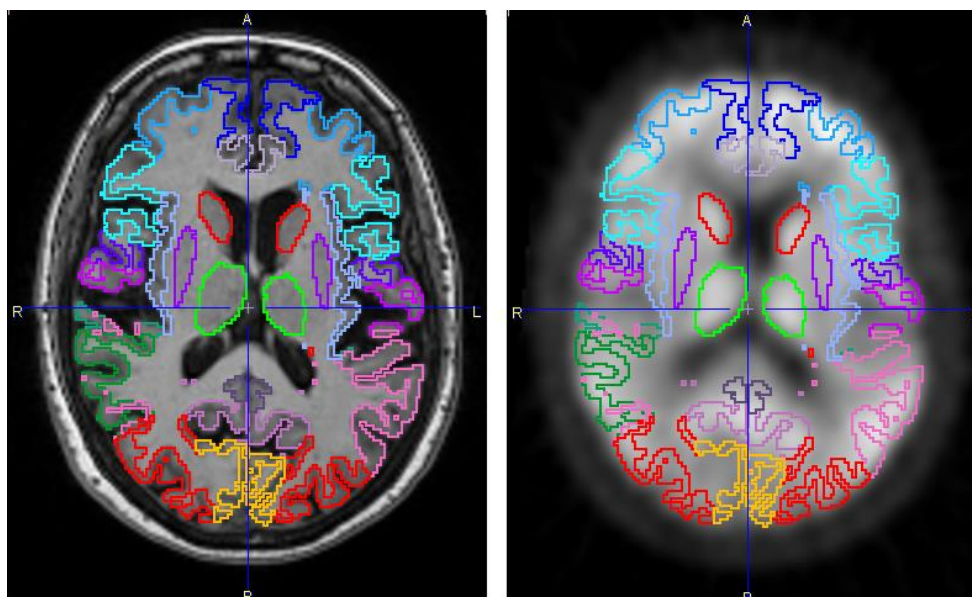
The data can be processed in exactly the same way as described for Raclopride. The only difference is the PET uptake pattern, which however makes no difference for the MR-based VOI-finding. The illustrations below show the VOI outcome in the MR space on slice 73. These results can be reproduced using the protocols available in the **Neuro DB**.

### MR-based Maximum Probability Atlas Result



### $T_1$ -Parcellation Result

Parcellation using 8 knowledge base subjects, with improvement in the basal ganglia and thalamus.



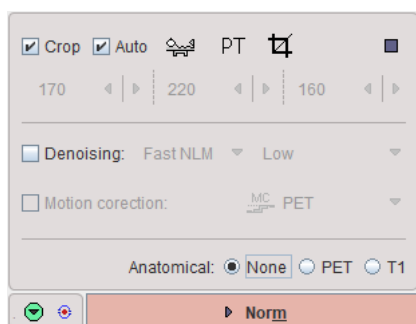
### 3. MRI and Static FDG PET

The data set of “patient” **MRI-FDG Static** includes a static FDG PET acquisition as well as a resampled T<sub>1</sub>-weighted MRI. This data set can be processed using the MRI and PET workflows as described for the Raclopride study above. However, for the exercise described in this section, we will neglect the MRI and directly apply the MPA methodology to the FDG image. This illustrates the PET-only case where the information in the PET image is sufficiently close to the MNI PET template for a direct normalization.

### PET-based Analysis using the Maximum Probability Atlas Method

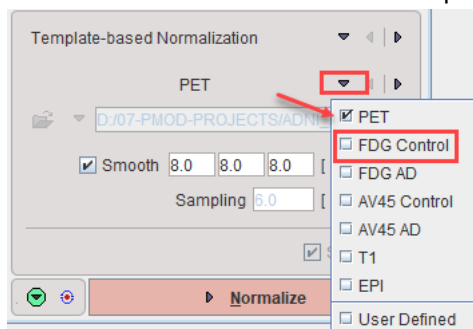
#### PET Image Loading and Cropping

Please restart PMOD, launch the **Neuro** tool from the ToolBox and select the **Maximum Probability Atlas** tab. Activate the **Load FUN** button, select the **MRI-FDG Static** patient, and load the **FDG Brain PET** series. **Crop** the image, set the **Anatomical reference** to **None**, and use the **Norm** action button to start the PET-only workflow.



#### PET Normalization

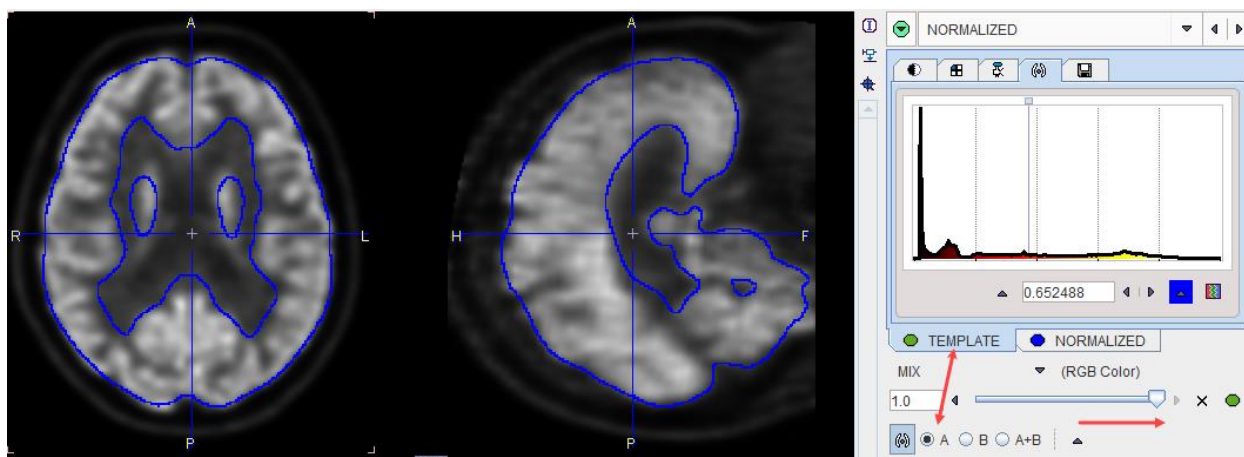
The controls on the **MATCHED PET** page are appropriately set for the PET-based normalization.



Ideally, one would use the **FDG Control** template in the MNI space available in the predefined template selection list. Keep the **8mm** Gaussian filtering definition and proceed with the **Normalize** button to start the calculation of the stereotactic normalization.

#### Normalization Validation

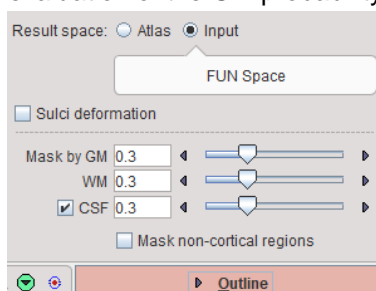
The resulting **NORMALIZED** FDG image is shown together with the PET template. Please use the iso-contours and the fusion slider for verifying that the normalization was indeed successful. The example below shows 100% normalized FDG image (fusion balance fully to the right) with the template iso-contours on top (A radio button).



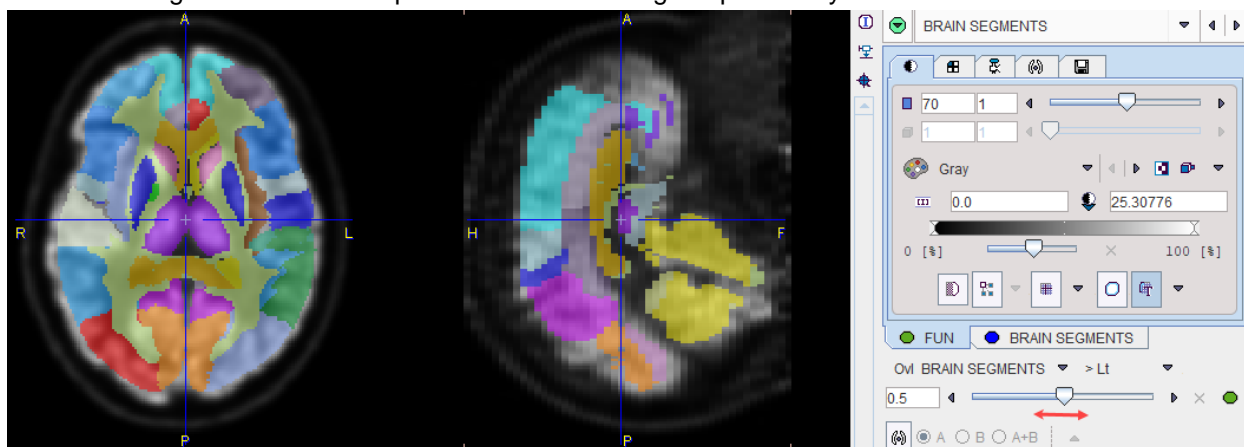
Proceed with the **Segment Brain** button to apply the normalization transform to the Maximum Probability Atlas.

### Brain Segment Validation

The **BRAIN SEGMENTS** page shows the FDG image together with the transformed atlas image in a fusion display. As the PNEURO settings are serialized, the fusion image seen will depend on the last configuration settings of this page. Because the MRI has not been considered for the normalization, the only **Result space** options are **Atlas** and **Input/FUN**, and the GM probability threshold is evaluated using the *a-priori* GM and WM maps. Optionally, the *a-priori* CSF maps can be also considered in the evaluation of the GM probability threshold.



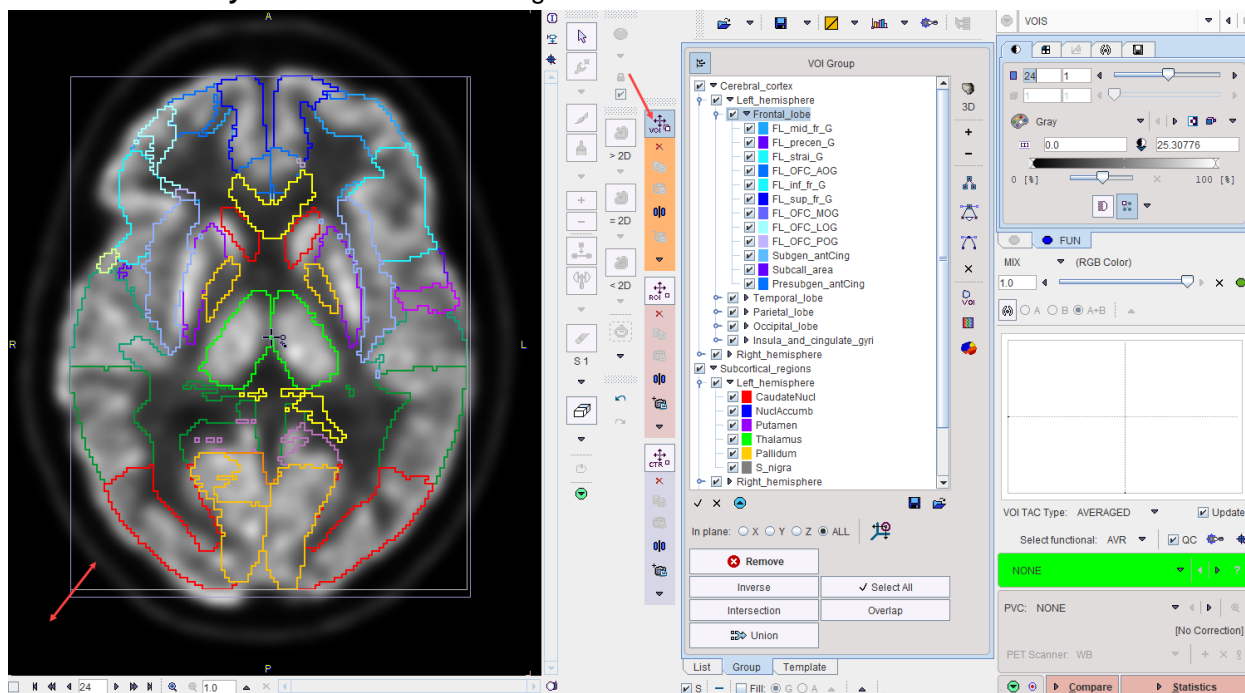
With the configuration settings above the following result is seen. Please try out how the result changes when selecting the **Atlas** result space and when shifting the probability **Mask** thresholds.



Finally, proceed with the **Outline** button to obtain the outline contour definition of the brain structures.

### Volume of Interest Exploration

The resulting VOI outlines are shown on the **VOIS** page. Change the layout to show a single axial slice and select the **Gray** color table. The following result is shown.



Apparently the caudate/putamen VOIs don't fit too well, while the cortical VOIs seem to be positioned too much to the inner of the brain at the left and lower side in the image. A global scaling of all selected VOIs can easily be applied by dragging the left lower corner of the bounding box with the **VOI** action button active.

### Statistics Calculation

Finally, calculate the regional PET uptake with the **Statistics** button. The result on the **Statistics** page shows the average uptake in the structures selected in the VOI tree together with their volumes.

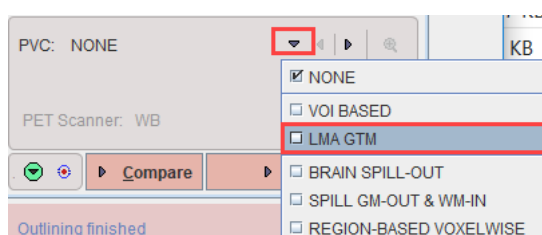
Name	AVERAGED	Volume [ccm]	Unit
FL_mid_fr_G_l	13.284089933798079	24.3753	kBq/cc
FL_mid_fr_G_r	14.337627676489355	25.1297	kBq/cc
FL_prece_n_G_l	12.923596088009601	13.0678	kBq/cc
FL_prece_n_G_r	13.196411002928969	13.1397	kBq/cc
FL_stral_G_l	13.53661920669231	2.3217	kBq/cc
FL_stral_G_r	12.079020868949815	2.2588	kBq/cc
FL_OFC_AOG_l	12.700170861184597	2.874	kBq/cc
FL_OFC_AOG_r	13.465546411374163	2.9953	kBq/cc
FL_inf_fr_G_l	13.17471105827836	11.2042	kBq/cc
FL_inf_fr_G_r	13.741986351711672	10.7911	kBq/cc
FL_sup_fr_G_l	13.559670483651706	26.2299	kBq/cc
FL_sup_fr_G_r	13.868826734836764	27.5098	kBq/cc
FL_OFC_MOG_l	12.765218862908425	3.1075	kBq/cc
FL_OFC_MOG_r	12.094051532745361	2.9189	kBq/cc
FL_OFC_LOG_l	12.065078846469724	1.9849	kBq/cc
FL_OFC_LOG_r	13.444326496591755	1.8322	kBq/cc
FL_OFC_POG_l	11.567384361335108	3.0222	kBq/cc
FL_OFC_POG_r	12.204159977206265	2.9818	kBq/cc
Subgen_antCing_l	10.159475077974035	0.8442	kBq/cc
Subgen_antCing_r	8.336737409881923	0.4131	kBq/cc
Subcall_area_l	9.087901133078116	0.1212	kBq/cc
Subcall_area_r	8.735751021992076	0.0494	kBq/cc

**Copy** the results to the **Clipboard** and paste them to Excel. Return to the **BRAIN SEGMENTS** page, change the **Result Space** to **Atlas**, outline, calculate the statistics and copy them also to the Excel. Compare the results in the **Atlas** and **PET** space by calculating their % difference in Excel.

## Partial Volume Correction

The limited resolution of PET systems causes a blurring of the image. As a result, image areas with high tracer uptake appear decreased but enlarged in size. This partial-volume effect can be corrected for, if the image is decomposed into structures of homogeneous uptake. Assuming that the VOIs created by PNEURO represent homogeneous tissue, partial volume correction algorithms can be applied to recover the true average uptake. In this process, PNEURO not only uses the generated VOIs, but also handle all other parts, like the white-matter and CSF areas.

To enable PVC, return to the **VOIS** page and set the **PVC** method to LMA GTM (Local Means Analysis, Geometric Transfer Matrix) method, with a percentage of **Voxels to be kept** of **15%**. This method estimates the average in the inner of the VOI, where the partial volume effect is minimal.



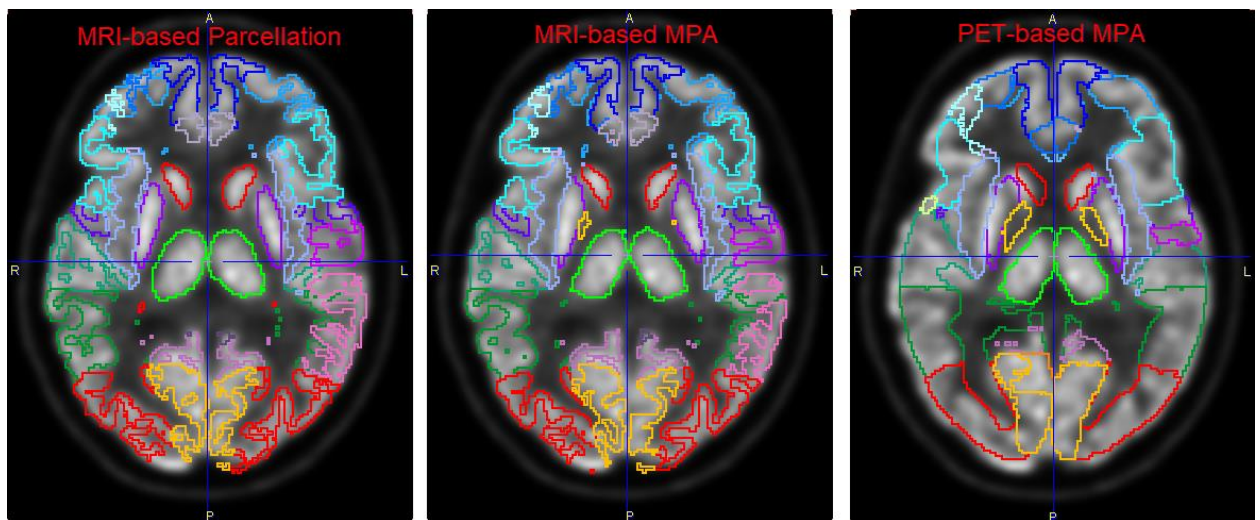
The calculation is started with the **Statistics** button, resulting in a table with not only the VOI averages, but also the PVC corrected average values. The percentage difference (%Diff) between the non-corrected and PVC corrected average value is also estimated and shown.

DB Load    Maximum Probability Atlas    Brain Parcellation    Mapping    Compare to Norm    Statistics						
Name	AVERAGED	PVC	% Diff [(A-P)/A*100]	Volume [ccm]	Unit	
FL_mid_fr_G_l	13.278810231771697	12.534064292907715	5.609	26.4994	kBq/cc	
FL_mid_fr_G_r	13.808280391359542	14.270893096923828	-3.35	27.2179	kBq/cc	
FL_prece_n_G_l	12.597226616385036	14.127612113952637	-12.149	16.6918	kBq/cc	
FL_prece_n_G_r	12.650832233181589	14.035948753356934	-10.949	16.2741	kBq/cc	
FL_strai_G_l	12.660846667781843	14.306248664855957	-12.996	2.5238	kBq/cc	
FL_strai_G_r	12.992472735120028	15.995325088500977	-23.112	2.9459	kBq/cc	
FL_OFC_AOG_l	13.333183232579744	15.140924453735352	-13.558	3.6329	kBq/cc	
FL_OFC_AOG_r	11.726531154538955	9.253676414489746	21.088	3.6599	kBq/cc	
FL_inf_fr_G_l	13.162734061105303	13.09738826751709	0.496	12.5155	kBq/cc	
FL_inf_fr_G_r	13.31917162426984	11.134138107299805	16.405	12.1742	kBq/cc	
FL_sup_fr_G_l	13.206098298194773	13.54365062713623	-2.556	31.3583	kBq/cc	
FL_sup_fr_G_r	13.071214411739696	13.125398635864258	-0.414	31.8972	kBq/cc	
FL_OFC_MOG_l	12.534872564037194	11.930252075195312	4.824	3.9967	kBq/cc	
FL_OFC_MOG_r	12.38577123293801	14.465893745422363	-16.794	3.9608	kBq/cc	
FL_OFC_LOG_l	12.483727159426193	9.695940017700195	22.331	2.3172	kBq/cc	
FL_OFC_LOG_r	12.80906686834667	11.804396629333496	7.843	2.4788	kBq/cc	
FL_OFC_POG_l	12.061244476188733	13.519245147705078	-12.088	3.7003	kBq/cc	
FL_OFC_POG_r	11.418762026183561	11.038591789245605	3.321	3.4219	kBq/cc	

## Comparison of the Outcome using Different Methodologies

For your convenience the VOIs resulting from the MR-based approaches were also calculated. The illustration below shows a side-by-side comparison of slice 24 in the PET space. The left outlines were obtained with the T<sub>1</sub>-parcellation using 8 subjects, the middle outlines with the MPA method applied to the MRI, and the right outlines with the MPA method directly applied to the FDG PET as described above.





The quality of the VOI definition seems to decrease from left to right. This is in line with the recommendation of employing the anatomical MRI whenever it is available, and applying the T<sub>1</sub>-parcellation if the basal nuclei are relevant.

Note that protocols for reproducing these results are available in the **Neuro** database.

## PNEURO Hints

### **Computer System:**

For the effective use of PNEURO with original high-resolution data workstation systems with 8 cores and 16GB RAM (or better) are highly recommended. The availability of multiple cores will speed up denoising as well as parcellation, because all hemisphere s of the subjects selected in the knowledge base can potentially be processed in parallel. Note that the number of cores can effectively be doubled by enabling hyper-threading on some processor chips like the Intel core i7.

### **When to Apply Parcellation:**

The T<sub>1</sub>-MR-based parcellation is preferable for questions related to the deep nuclei and thalamus because of the construction of an individual maximum probability atlas in this area. If only cortical structures are relevant, the Maximum Probability Atlas might be preferable because the cortical outcome is very similar for both methods, but it is faster.


### **Waiting Time Reduction:**

While the step-wise workflow with inspection of intermediate results is aimed at robust results, it involves some waiting time during the different processing steps. One approach to partially circumvent this problem is using the *Run all* button in the lateral taskbar:



The procedure for the MPA and the T<sub>1</sub>-parcellation is:


- Load PET image and Crop
- Load MR image and Crop
- Set the parameters on the different pages, if there is any change to the settings of the prior analysis,
- Start Run all

Note the  button in the lateral taskbar which establishes the parameter defaults on all pages.

### **Batch Mode:**

A convenient way for the T<sub>1</sub>-parcellation of multiple data sets non-interactively is as follows: Load a data set (PET and/or MR), define the bounding boxes, adjust the parameters on the different pages without calling the actual processes, save the protocol. Repeat for all data sets. Start the batch mode from the menu, select all protocol files, and run the processing. While PMOD will be busy, other work can be completed. For data residing in databases batch setup is much easier, as described in the documentation.

### **Saving of Information:**

There are different ways of saving the intermediate and final results of PNEURO. Generally it is recommended saving a protocol, so that any time later the details of the analysis configuration as well as the manually edited VOIs may be inspected. If you would like to re-use intermediate results such as spatial transformations and/or transformed images, the most convenient procedure is to open the *Save all* window with the lateral  button, check all items of interest and save, optionally with replacing the patient name by a new string.