Centiloid Analysis

PMOD APPLICATION NOTE
Version 3.9

PMOD is a software
FOR RESEARCH USE ONLY (RUO)
and must not be used for diagnosis or treatment of patients.

1 Rationale of Centiloid Analysis

"Centiloid" was introduced as a "standard" method for the analysis of PiB PET data, and scaling of any "non-standard" method of PiB PET analysis (or any other amyloid tracer), by Klunk et al. in 2014. In their paper, Klunk et al. highlight the need for standardization in amyloid PET, citing the range of tracers used, acquisition duration, scanner model, reconstruction parameters, method of attenuation correction, method of analysis, choice of regions for analysis and inclusion/exclusion of partial volume correction as sources of variability.

The Centiloid concept is that comparable results can be achieved by linearly scaling the outcome data of any amyloid PET method to an average value of zero in "high-certainty" amyloid-negative subjects (0-anchor) and to an average value of 100 in "typical" Alzheimer's disease patients (100-anchor). In their 2014 paper, Klunk et al. use 34 "young control 0-anchor" (YC-0) and 45 "AD 100-anchor" (AD-100) subjects with [C-11]Pittsburgh Compound-B (PiB) PET and T1-weighted MRI.

The approach is based on PiB PET tissue ratios gathered 50- to 70-minute post-injection and standardized cortical/reference regions (cerebellum/brainstem). Suggestions for other sites to validate their workflow and derive scaling for use with other tracers, including F-18 tracers, are provided.

The data expected for standard Centiloid analysis (detailed description below) are a 3D T1-weighted MRI and PiB amyloid PET (e.g. static PiB PET for 50-70 minutes after tracer injection). These data can come from a combined PET/MR scanner or be acquired independently, and either combination is ideally suited to the Maximum Probability Atlas workflow in PNEURO. In the standard case, the SUVr tissue ratio between a standardized cortex VOI and whole cerebellum reference VOI is directly calculated in PNEURO, and converted into Centiloid (CL) based on the following equation from Klunk et al. 2014:

$$CL = 100(^{PiB}SUVr_{IND} - 1.009) / 1.067$$

The derivation of this equation, and its adaptation to non-standard analysis is discussed below.

The scan data (34 YC-0 and 45 AD-100) used in the 2014 publication are made available on the Global Alzheimer's Association Information Network website (GAAIN, http://www.gaain.org), and the standardized regions can be requested (included from PMOD version 3.9 build 6).

2 Summarized Workflow from Klunk et al., 2014

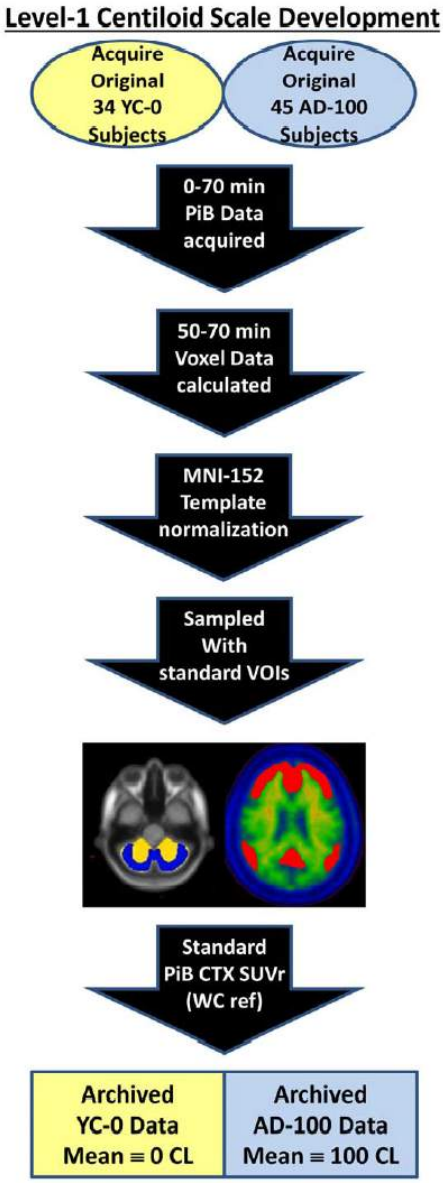
There are three “levels” to the Centiloid process. The purpose of “level-1” was to define the 0- and 100-anchor SUVr points for “standard” PiB data acquisition/analysis. This process utilized the 34 YC-0 and 45 AD-100 subjects. Klunk et al., state that it should not be necessary for other groups to repeat their “level-1” analysis to use the Centiloid scale (sites using “standard” PiB PET should validate their analysis pipeline using “level-3” analysis, described below).

The purpose of “level-2” is to calculate the scaling for individual sites to convert their non-standard PiB, or surrogate tracer, PET data (i.e. including site-specific scanner, reconstruction, attenuation, imaging protocol) to the Centiloid scale.

The purpose of level-3 is to verify that an individual site’s analysis pipeline does not introduce errors when a previously described image acquisition/reconstruction protocol is exactly reproduced. For example, a site wishing to use 50-70 minute PiB PET data with corresponding T1-weighted MRI may directly use equation 1.3b from Klunk et al., 2014. To verify that the analysis pipeline produces comparable Centiloid values the site should reanalyze the YC-0 and AD-100 reference data from the GAAIN website, and produce a scatterplot with regression slope/intercept/R^2 confirming close reproduction of the values from Klunk et al. 2014 Supplementary Table 1. This process is essentially identical to the first half of the “level-2” workflow shown below. The results obtained using PNEURO and the GAAIN reference data shown later in this application note represent “level-3” validation of the PNEURO analysis pipeline.

2.1 Level-1: Standard PiB 0- and 100-anchor points

The level-1 workflow is summarized in the figure below, reproduced from Klunk et al., 2014 (Supplementary Flowchart 1):

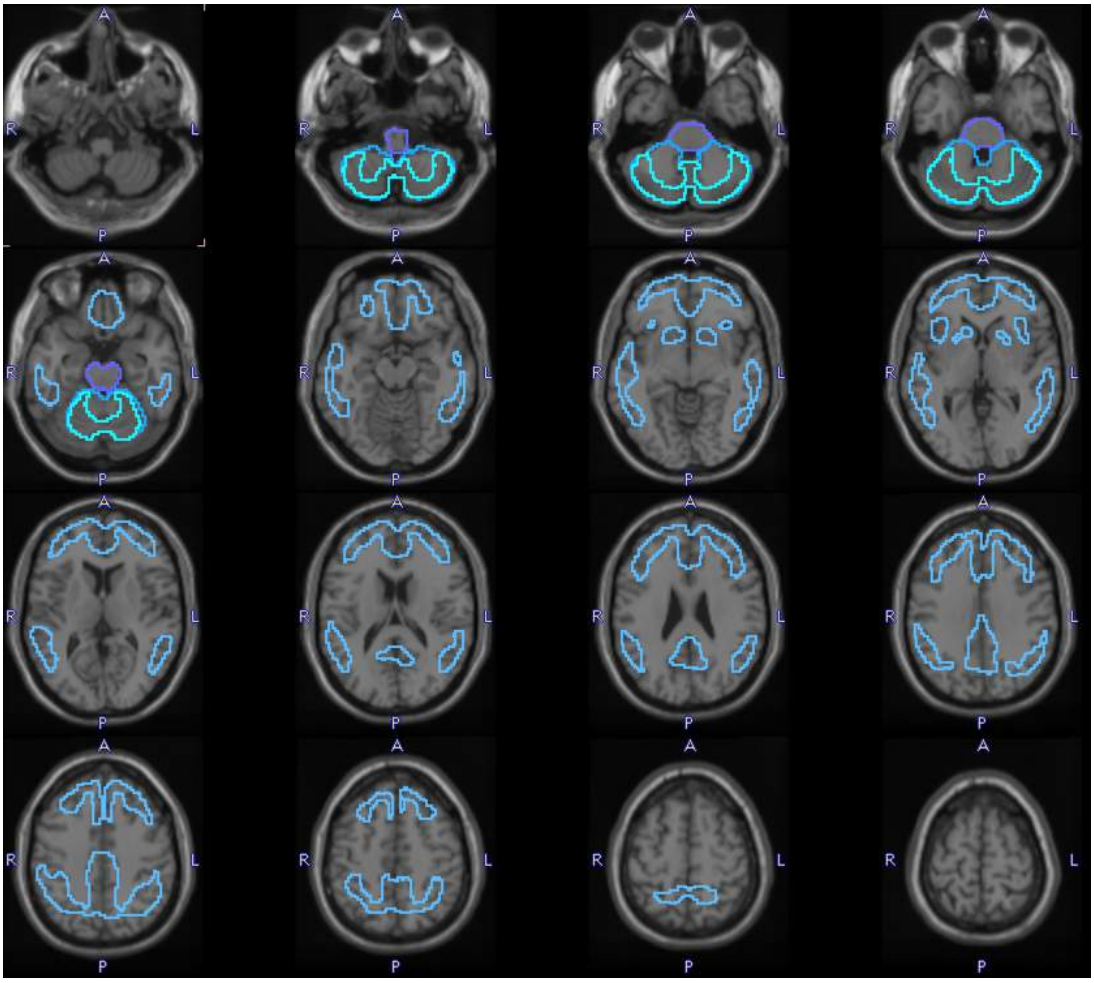


Following the selection of YC-0 and AD-100 subjects, including outlier removal, a separate set of AD and older control subjects were used to define the "global cortical target region" (CTX). The Statistical Parametric Mapping version 8 (SPM8) normalization process was specifically recommended for normalization of individual subject PET and MRI to the Montreal Neurological Institute (MNI)-152 T1-weighted template (2 mm resolution). The "elastic deformation based on tissue probability maps" workflow using 3-probability maps in PFUS and PNEURO is directly equivalent to the SPM8 method.

Four reference volumes-of-interest (VOIs) were defined for Centiloid level-1. These were whole cerebellum (WC) and Pons VOIs based on the previously defined International Consortium for Brain Mapping (ICBM) Single Subject MRI Anatomical Template (Mazziotta et al., 2001), a cerebellar grey (CG) matter VOI and a whole cerebellum plus brainstem (WC+B) VOI.

The CTX VOI was data-driven and based on averaged PiB PET 50-70 minute SUVr parametric images. Briefly, the average parametric SUVr image for older controls was subtracted from that for Alzheimer's subjects, the result smoothed with a 3D-Gaussian filter, then thresholded at 1.05 SUVr units. When overlaid on the SPM single subject T1 MRI in MNI-152 space, left/right asymmetry and a minor "shrinkage" are apparent. Left/right orientation has been confirmed with the authors, and the minor "shrinkage" likely results from thresholding after Gaussian smoothing.

An atlas including the CTX and WC VOIs has been included in PMOD from version 3.9 build 6 onwards, and VOIs (CTX, WC, CG, Pons, WC+Brainstem; allowing overlapping) in MNI-152 space are additionally provided in the resources/templates/voitemplates/Centiloid folder. The resulting VOIs, overlaid on the SPM single subject T1 in MNI-152 space, are illustrated below:



A 50-70 minute CTX SUVr was calculated using each reference region, and the reference region that resulted in the lowest variance and largest effect size between YC-0 and AD-100 was selected for further use. This was the WC VOI.

The standard Centiloid value for an individual subject is then defined as:

$$CL = 100(^{PiB}SUVr_{IND} - ^{PiB}SUVr_{YC\text{-}0}) / (^{PiB}SUVr_{AD\text{-}100} - ^{PiB}SUVr_{YC\text{-}0})$$

Where:

$^{PiB}SUVr_{IND}$ is an individual's SUVr value

$^{PiB}SUVr_{AD\text{-}100}$ is the mean SUVr of the AD-100 subjects

$^{PiB}SUVr_{YC\text{-}0}$ is the mean SUVr of the YC-0 subjects

Using the Klunk et al. level-1 results, the above equation simplifies to:

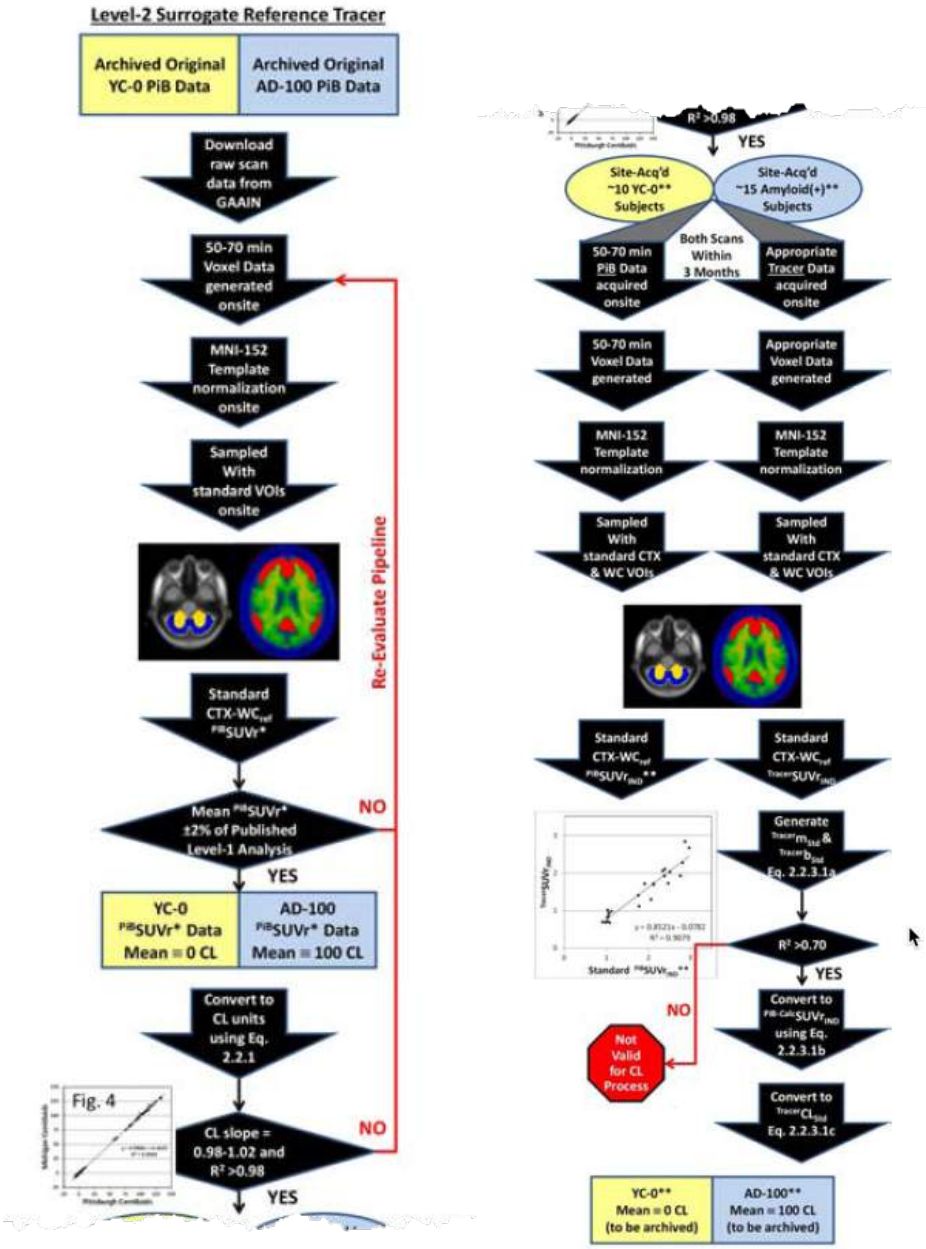
$$CL = 100(^{PiB}SUVr_{IND} - 1.009) / 1.067$$

Note: this is Klunk et al. equation 1.3b, referred to later for level-3 analysis with the GAAIN reference data.

2.2 Level 2: Calibration of a surrogate tracer

The level-2 workflow is the process that independent groups should use to calibrate their surrogate/alternative (to PiB) tracer, or specific analysis pipeline, to CL units. Klunk et al. state that the level-2 process should be performed whenever a procedure other than the "Standard PiB Method" (PiB 50-70 minute SUVr, PET and MRI analysed using SPM8, using the standard CTX and WC VOIs) is to be calibrated to the CL scale. They specifically include methods utilizing atrophy-correction, alternative cortical or reference region VOIs, direct PET to MNI normalization without T1-weighted MRI, or tracers other than PiB. Therefore the use of PNEURO with Centiloid atlas, 50-70 minute PiB PET, T_1-weighted MRI, and SPM8 normalization does not require level-2 "calibration". Use of the Hammers atlas, SPM12 normalization, or inclusion of partial volume correction would represent significant deviations from the "standard" workflow, and thus require level-2 "calibration".

The level-2 workflow is summarized in the figure below, reproduced from Klunk et al., 2014 (Supplementary Flowchart 2):



2.3 Level-2 Part One: analysis pipeline validation

As illustrated, each independent group should first download and analyse the archived original YC-0 and AD-100 PiB data from the GAAIN website and verify that their analysis tools/processing pipeline are able to closely reproduce the mean SUVr for each group based on the Klunk et al. reported results, within +/- 2 %, and correlate the resulting CL values per subject to the original data with 0.98<slope<1.02, -2<intercept<2 and R2 > 0.98. The MRI normalization step is noted as a particular source of error.

The site-specific CL for each of the YC-0/AD-100 subjects is calculated using Klunk et al. equation 2.2.1:

$$CL = 100(^{PiB}SUVr_{IND*} - {}^{PiB}SUVr_{YC\text{-}0*}) / (^{PiB}SUVrAD\text{-}100* - {}^{PiB}SUVr_{YC\text{-}0*})$$

Where * denotes the site-specific result for the GAAIN reference data.

The workflow in PNEURO, including recommended configuration/settings, for this Level-2 Part One analysis will be described in detail below. The user should download the GAAIN reference data, then process the data for all subjects according to the workflow in PNEURO as described below to obtain SUVR. Batch processing may be used to process the YC-0 and AD-100 groups efficiently. The SUVR statistics can then be exported to an editor such as Microsoft Excel, where CL and the group means can be calculated. The regression slope and intercept for the site-calculated CL vs. GAAIN CL can then be assessed.

2.4 Level-2 Part Two: Calibration of amyloid PET with a surrogate tracer to CL

Following validation of the analysis pipeline in level-2 part one, The first step in calibration of a surrogate tracer is to acquire both “standard” (50-70 minute SUVr using CTX and WC VOIs) PiB and surrogate tracer PET data in at least 25 new subjects (10 YC-0, 15 AD-100). Their recommendation is that these two independent PET scans are acquired within 3 months of each other, based on the assumption that the amyloid load will not change significantly over such a duration. This requirement for imaging with both PiB and the surrogate tracer thus means that the site’s radiopharmacy should be prepared to produce PiB, in addition to their surrogate tracer. SUVr using CTX and WC VOIs should be calculated for both PiB and surrogate tracer, allowing a linear conversion between PiB SUVr and “tracer” SUVr to be derived. Note that SUVr for the surrogate tracer should be calculated at an appropriate time window for the tracer if that differs from the 50-70 minute PiB norm. From a linear regression analysis between the new subject (site-specific) 50-70 minute PiB SUVr ($^{PiB}SUVr_{IND**}$) (** denotes new subject in Klunk et al. notation) values and SUVr for the surrogate tracer ($^{Tracer}SUVr_{IND}$, note that Klunk et al. do not use the ** notation for this value in equations 2.2.3.1a/b, although the same ‘new subject’ is implied) the relationship (i.e. slope and intercept) between the tracers can be determined (Klunk et al. 2014 equation 2.2.3.1a):

$$^{Tracer}SUVr_{IND} = TracermStd(^{PiB}SUVr_{IND**}) + TracerbStd$$

This relationship can then be used to convert subsequent $^{Tracer}SUVr_{IND}$ values from new subjects (for whom PiB PET was not acquired) into “calculated PiB” SUVr values for use in Centiloid scaling (Klunk et al. 2014 equation 2.2.3.1b):

$$^{PiB\text{-}Calc}SUVr_{IND} = (^{Tracer}SUVr_{IND} - TracerbStd) / TracermStd$$

These $^{Tracer}SUVr_{IND}$ values can then be used to calculate surrogate tracer CL, in combination with the site-specific 0- and 100-anchor points (Klunk et al. 2014 equation 2.2.3.1c):

$$TracerCLStd = 100(^{PiB\text{-}Calc}SUVr_{IND*}* - {}^{PiB}SUVr_{YC\text{-}0*}) / (^{PiB}SUVr_{AD\text{-}100*} - {}^{PiB}SUVr_{YC\text{-}0*})$$

where “Std” denotes that “standard” CTX and WC VOIs were used.

The reliability of the alternative tracer calibration should be evaluated by calculation of the correlation coefficient R^2 for the linear regression between the site-acquired standard PiB SUVr, $^{PiB}SUVr_{IND**}$, and alternative tracer SUVr, $^{Tracer}SUVr_{IND}$. Klunk et al. suggest that R^2 should be greater than 0.7 for a well-correlated tracer.

Calibration of a site-specific method using alternative cortical and reference VOIs, and/or a metric other than SUVr, is similarly described by Klunk et al. However, as we believe most users will want to use the standardized CTX and WC Centiloid VOIs, this is not discussed in detail here.

2.5 Level-3: Analysis pipeline validation for direct CL calculation

This level of the Centiloid process is intended for sites that wish to express their data in CL, using the standard PiB method (or another previously calibrated method) without modification.

No new data is required for calibration, but the site should download the previously calibrated dataset. i.e. for standard 50-70 minute PiB PET with T1-weighted MRI the 34 YC-0 and 45 AD-100 GAAIN/Klunk et al. 2014 reference data should be downloaded.

The site should demonstrate that their analysis pipeline does not introduce errors by calculating CL for the reference dataset using the standard CTX and WC VOIs, and comparing their results to those published for the reference data (i.e. for standard PiB PET, Klunk et al., 2014, equation 1.3b for CL calculation, compare to reference CL values in Supplementary Table 1). As before, a scatterplot and regression analysis should be used. The slope should be between 0.98 and 1.02, the intercept between -2 and 2, and R2 should be greater than 0.98.

The use of PMOD in this analysis pipeline verification part of the workflow has already been reported (Battle et al., 2016), showing PiB PET SUVr values within the recommended range, correlation slope of 0.9992, intercept of 0.0399 and R^2 of 0.9982. A tested workflow in PNEURO will be described below.

3 Workflow in PNEURO

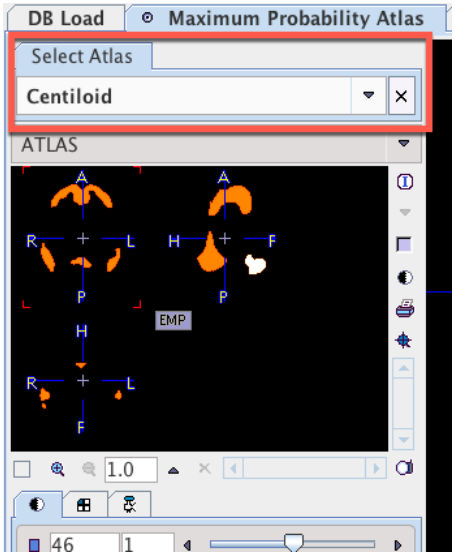
The data expected for standard Centiloid analysis (level-1, level-2 reproduction of level-1 results, level-3) are a 3D T1-weighted MRI and amyloid PET (e.g. dynamic PiB PET of at least 70 minutes, or static PiB PET for 50-70 minutes after tracer injection). These data can come from a combined PET/MR scanner or be acquired independently, and either combination is ideally suited to the Maximum Probability Atlas workflow in PNEURO. Rather than the Hammers N30R84 atlas, an atlas comprising the Centiloid CTX and WC VOIs will be used, and calculation of statistics in template space is required (also facilitating loading of the full Centiloid VOI set including WC+brainstem, cerebellar gray, pons).

The workflow for an individual subject with static 50-70 minute PET is described below. This workflow (including use in batch processing) has been validated using the GAAIN reference data (45 AD-100, 34 YC-0; level-3 regression results shown after description of the workflow). The GAAIN reference data was imported into a PMOD database for ease of processing, and all PET/MR pairs were associated. This PMOD database will also be available for download from the GAAIN website.

The screen captures represent Pmod3.9, but the procedure is similar in later versions.

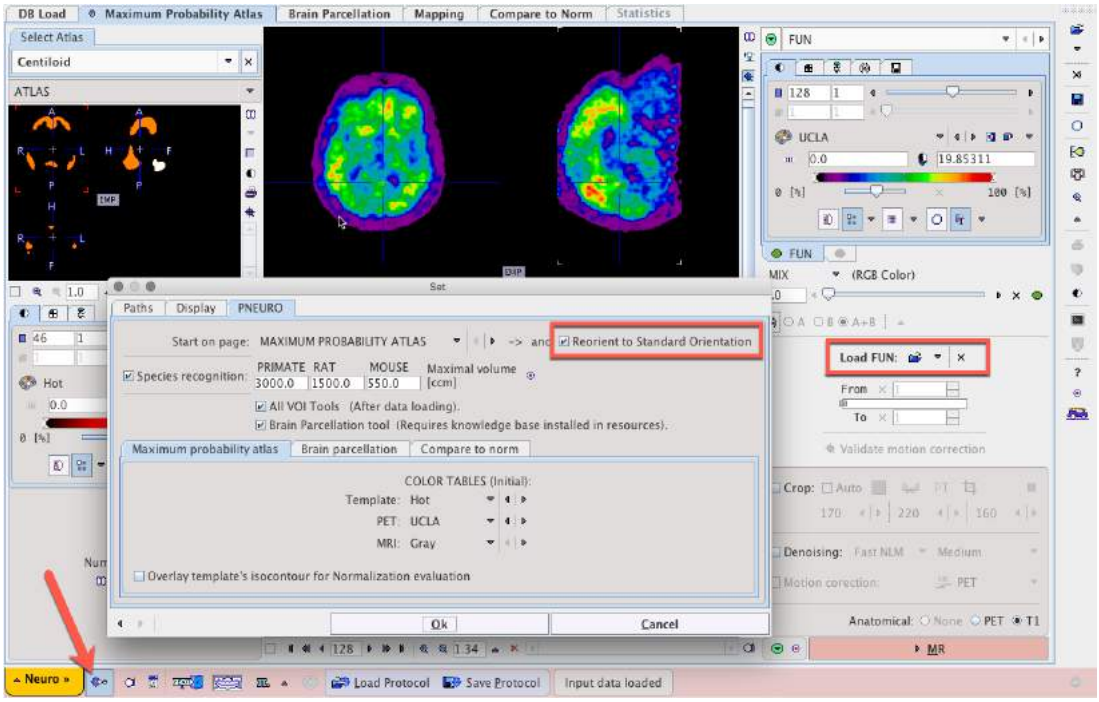
3.1 Step-wise Maximum Probability Atlas workflow

Following opening of PNEURO, the user should select the **Centiloid** atlas from the drop down list at the top left.

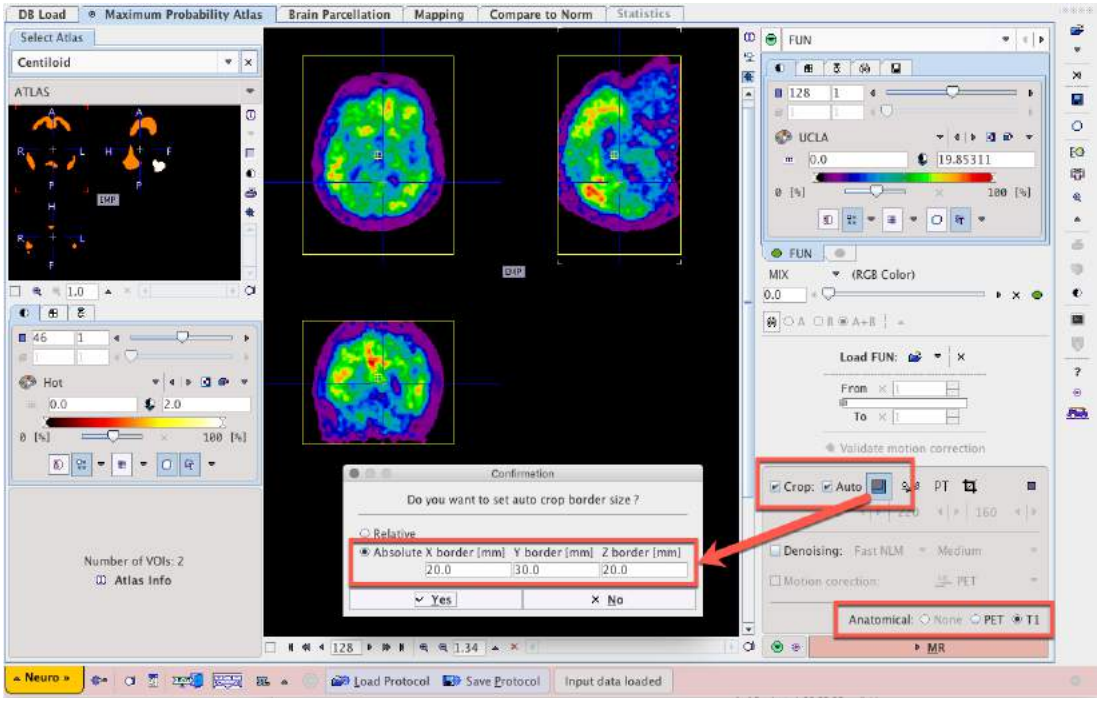


Additional information about the atlas is available via the Atlas Info button, lower left.

The PET data is loaded as usual (a single PET field-of-view targeting the head/brain is assumed). Use of PMOD's automatic reorientation to standard orientation is recommended:



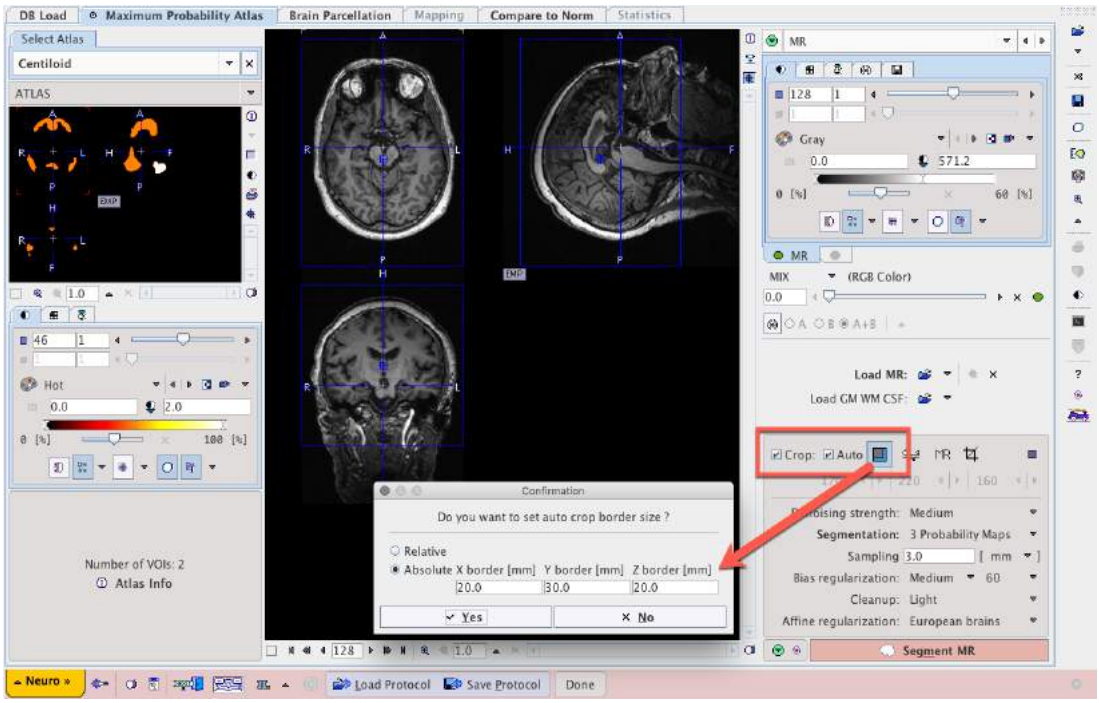
Automatic cropping should be applied to remove unnecessary data. Non-specific tracer uptake outside the brain itself can still be of use in rigid matching to the MRI, particularly the nose area. For this reason the bounding box used for auto-cropping should be extended by 20 x 30 x 20 mm. The box-shaped icon to the right of the Auto checkbox opens a dialog for definition of the auto crop border size. The **Absolute** method allows precise mm extension in x/y/z:

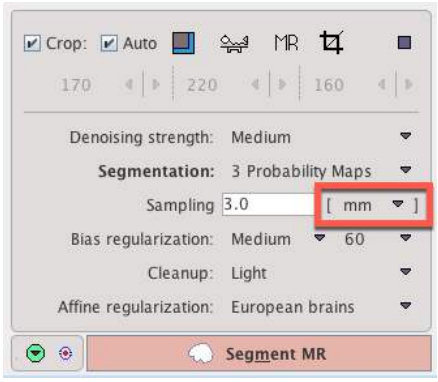


Denoising of the PET is not required. The radiobutton for **T1** MRI anatomical reference should be selected, then the **MR** workflow button activated, taking the user to the MR page.

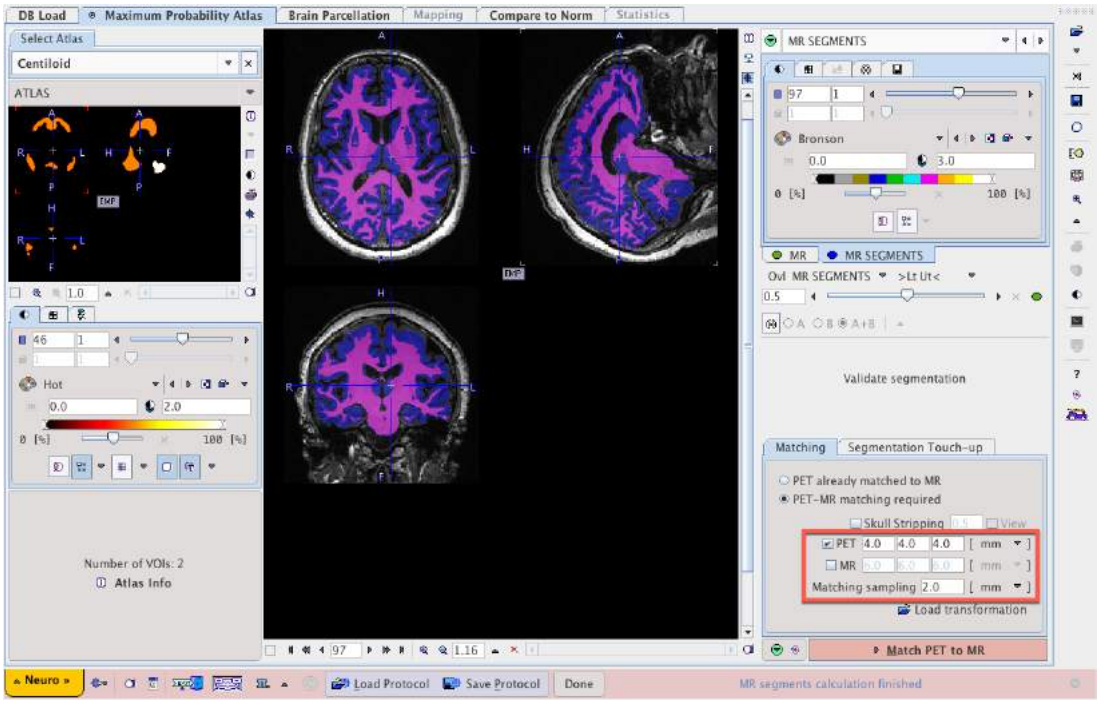
Confirm that the loaded 3D T1-weighted MRI is in the PMOD standard template orientation (i.e. automatic reorientation to standard orientation in general PNEURO settings is recommended, and essential for batch processing if the MR data is not preprocessed). Automatic cropping (**Crop**, **Auto**) should be applied with an extended bounding box (20 x 30 x 20 mm). **Denoising strength Medium** should be applied. To ensure the use of the SPM8 normalization procedures in

accordance with the Centiloid recommendations the **3 Probability Maps Segmentation** method should be selected. Ensure that **Sampling** is set to 3 mm. **Bias regularization** with **Medium** setting and **kernel** = 60 should be applied. **Cleanup** with **Light** setting is sufficient and affine regularization for **European brains** should be selected (validated for GAAIN reference data. Individual sites using Asian subjects should revalidate with the Asian brains setting). Proceed using the **Segment MR** workflow button:

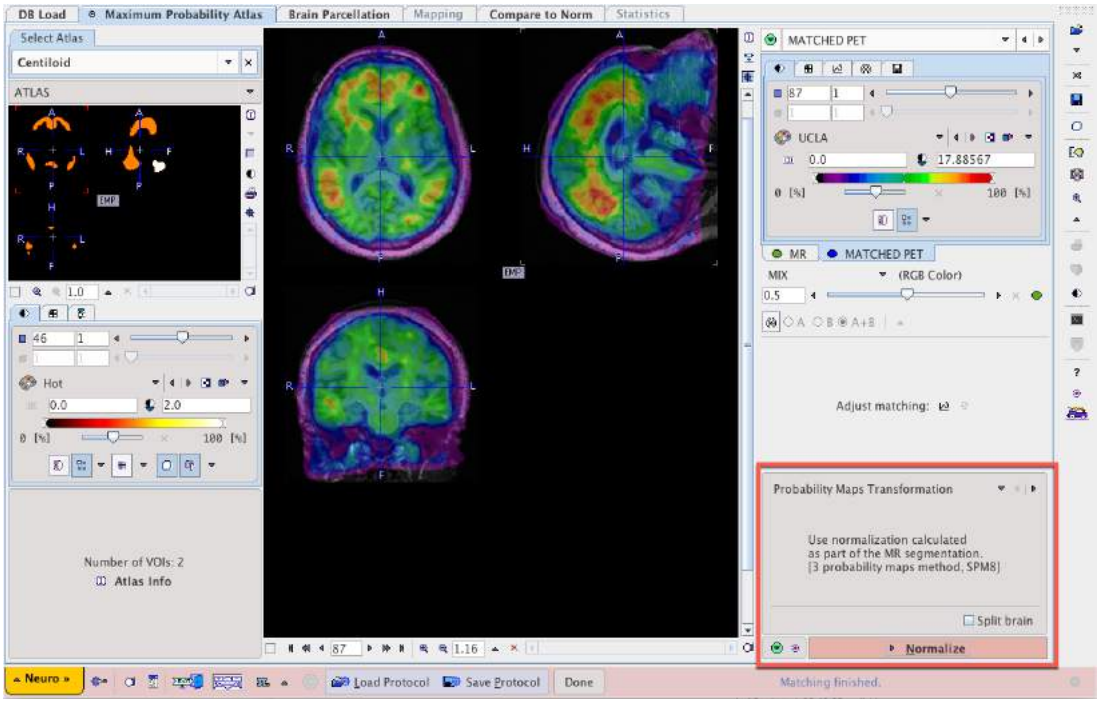




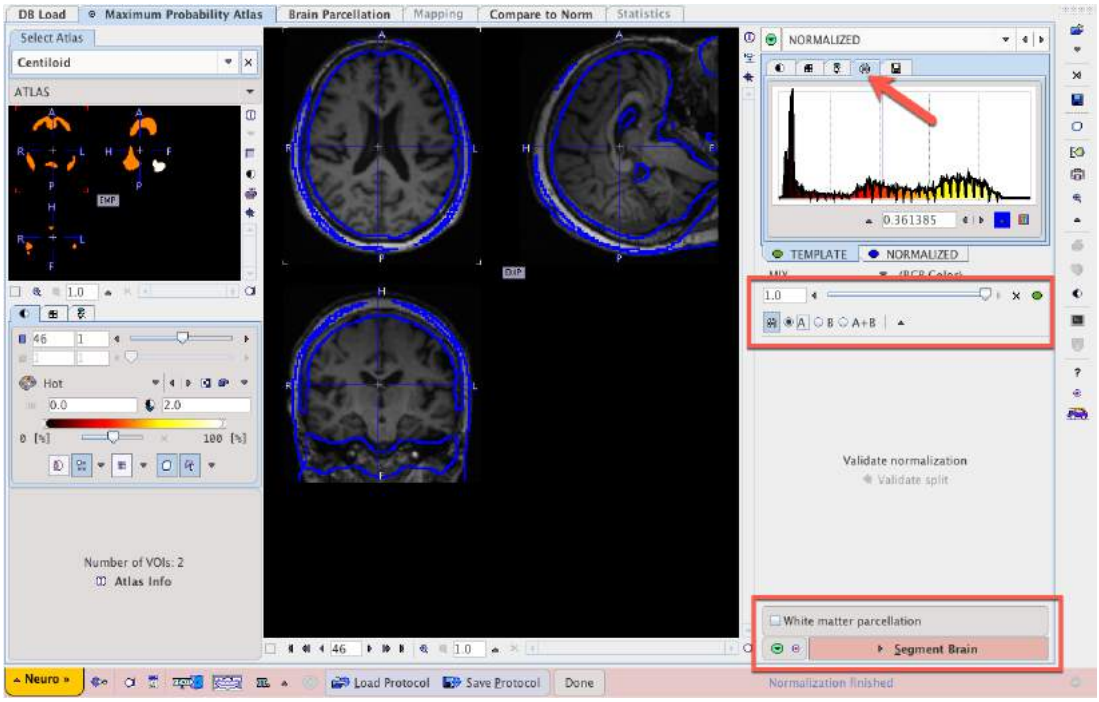
The resulting segmentation of grey and white matter is not necessary for standard Centiloid analysis, but an accurate segmentation result helps to confirm the success of normalization. **Smoothing** of the PET data with a 4 x 4 x 4 mm Gaussian should be applied, with 2.0 mm **Matching sampling**. Proceed using the “Match PET to MR” workflow button:



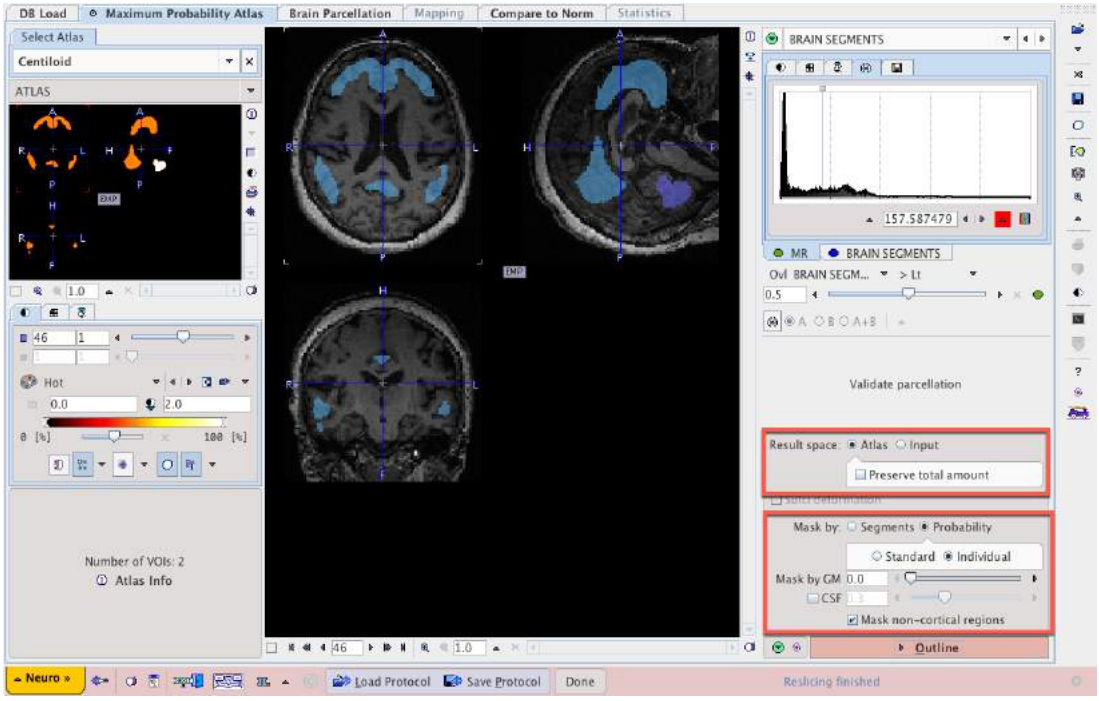
The rigid-matching result of PET to MR can be validated visually and using the usual PMOD fusion controls. The **Split Brain** setting is not required for Centiloid analysis. The general result of MR normalization can then be inspected using the **Normalize** workflow button:



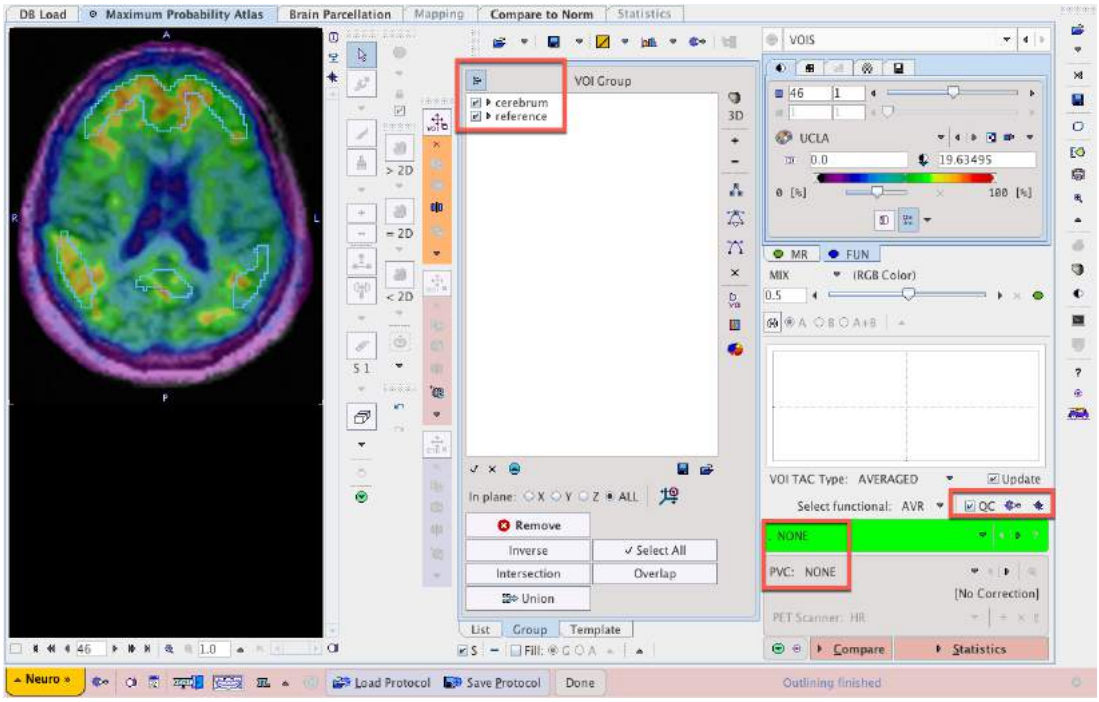
The MR normalization result can be validated visually and using the fusion controls, such as contouring of the template brain outline and alpha-blending to display only the normalized individual MR. **White matter parcellation** is not required for Centiloid analysis. Proceed using the **Segment Brain** workflow button:



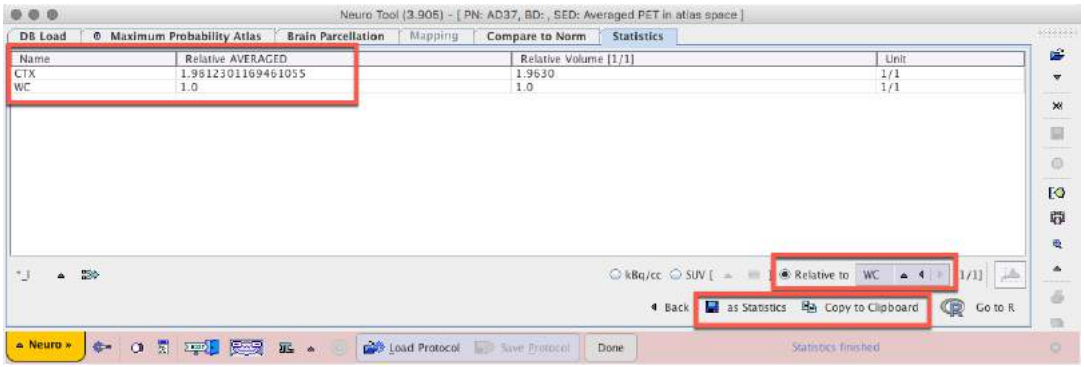
The visualization of the atlas and white matter segments is not important in the Centiloid analysis, but the selection of **Atlas** result space and negation of grey matter masking (Mask by GM: 0.0) are critical. **Masking of non-cortical regions** should be activated to remove the automatically generated white matter VOI. Proceed using the "Outline" workflow button:



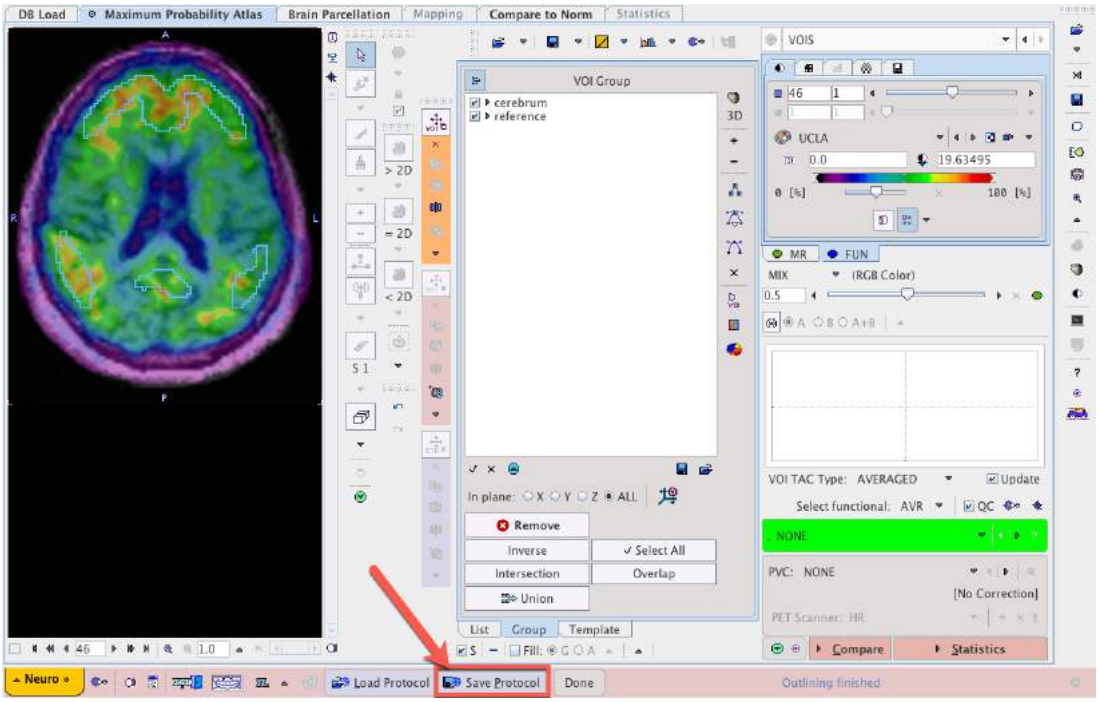
VOIs are created from the atlas segments and displayed on the PET/MR fusion image. Using the Centiloid atlas we utilize only the CTX and WC VOIs. (The full Centiloid VOI set including all reference regions can be loaded from the /Pmod3.9/resources/templates/voitemplates/Centiloid folder using the usual Load VOIs button if another reference region will be used.) Activate the **QC** checkbox to ensure that a quality control jpeg capture of the VOI overlay on PET in Atlas space is saved for batch processing QC. For standard Centiloid analysis the None selection for Parametric Mapping and Partial Volume Correction (**PVC**) should be active. Finally, the statistics are calculated using the **Statistics** button:



On the resulting Statistics tab SUVr(whole cerebellum) for the CTX region can be directly calculated by selecting the **Relative To**: **WC** option. The SUVr statistics can be saved in PMOD voistat format for aggregation and group analysis, or Copied To Clipboard for external analysis:



Return to the **Maximum Probability Atlas** tab to **Save Protocol** (thus including calculation of SUVr(WC)):



The outcome measure of processing in PNEURO is therefore an SUVr for the selected subject. Using either Klunk et al. equation 1.3b, or similar equation with slope and intercept derived from newly-acquired [11C]-PiB PET, this SUVr should be converted to CL in a program such as R or Microsoft Excel.

$$CL = 100(^{PiB}SUVr_{IND} - {}^{PiB}SUVr_{YC\text{-}0}) / (^{PiB}SUVr_{AD\text{-}100} - {}^{PiB}SUVr_{YC\text{-}0})$$

Where:

$^{PiB}SUVr_{IND}$ is an individual's SUVr value,

$^{PiB}SUVr_{AD\text{-}100}$ is the mean SUVr of the AD-100 subjects

$^{PiB}SUVr_{YC\text{-}0}$ is the mean SUVr of the YC-0 subjects

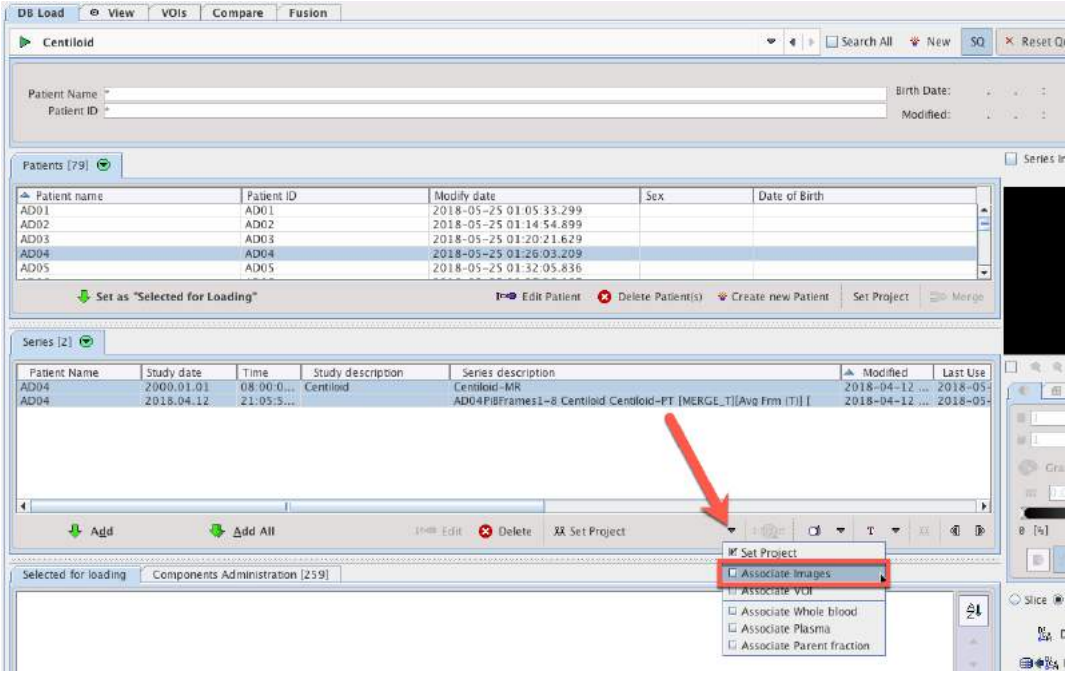
Using the Klunk et al. level-1 results, the above equation simplifies to:

$$CL = 100(^{PiB}SUVr_{IND} - 1.009) / 1.067$$

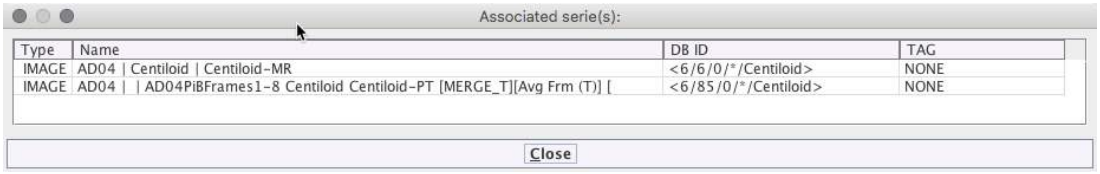
Note: this is Klunk et al. equation 1.3b.

3.2 Batch Processing: Image Series Association

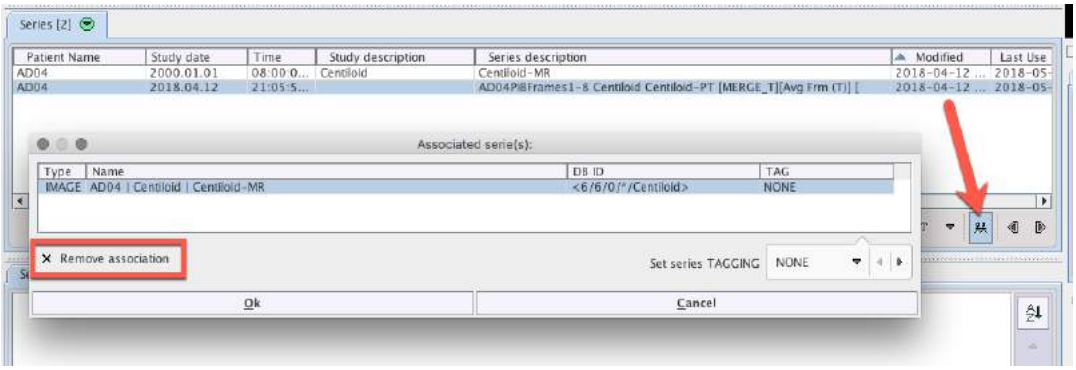
The protocol saved can be used to initiate Batch Processing of several subjects. For example, the entire 79 subject (34 YC-0 and 45 AD-100) GAAIN PiB reference dataset may be processed in a single batch process. A single saved protocol can be Cloned for use on subsequent datasets. Association of the PET and MR series in a database is essential for cloning of PNEURO protocols (otherwise the user must manually define each PET/MR pair). Association is achieved via the DB Load tab in any tool. In the case of the GAAIN reference data, the PET and MR series to be associated for a given subject should both be selected (SHIFT+Left Click, or CTRL+Left Click), and **Associate Images** selected from the drop-down menu below:



A dialog window confirming the association is displayed:

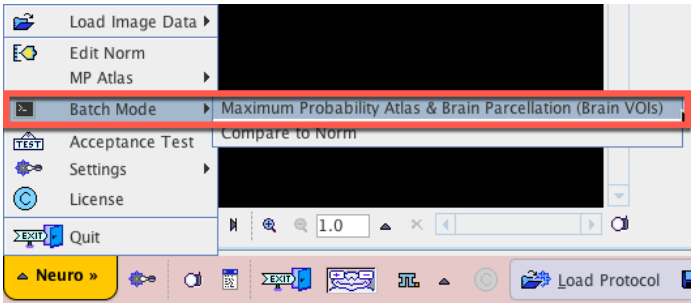


In the event of incorrect association (i.e. when more than two series are present for a given subject), the associations for a single series can be viewed, and associations removed:

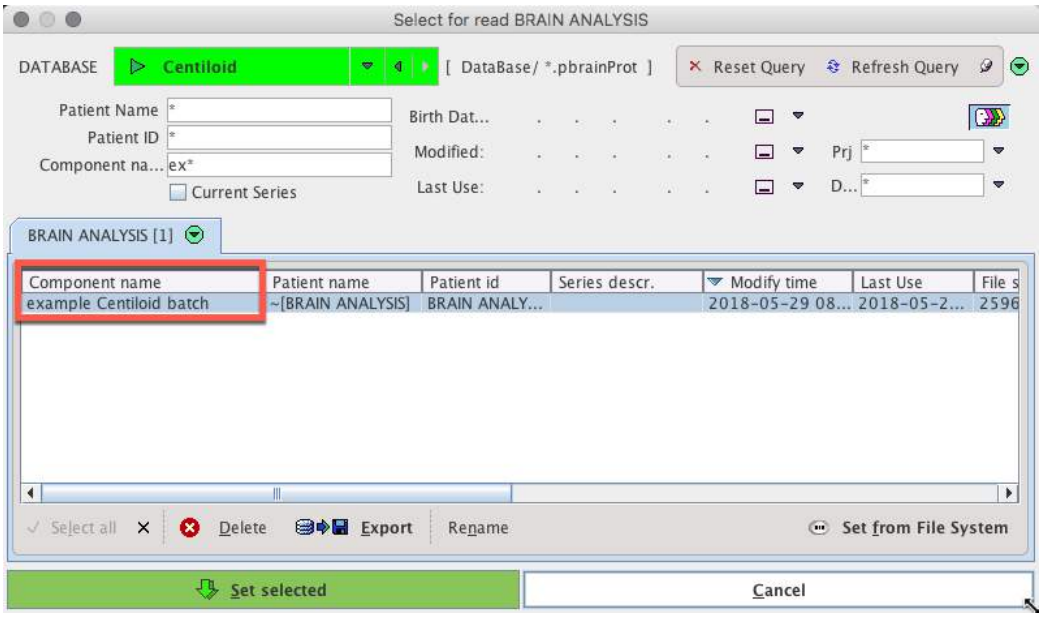


3.3 Batch Processing: Workflow

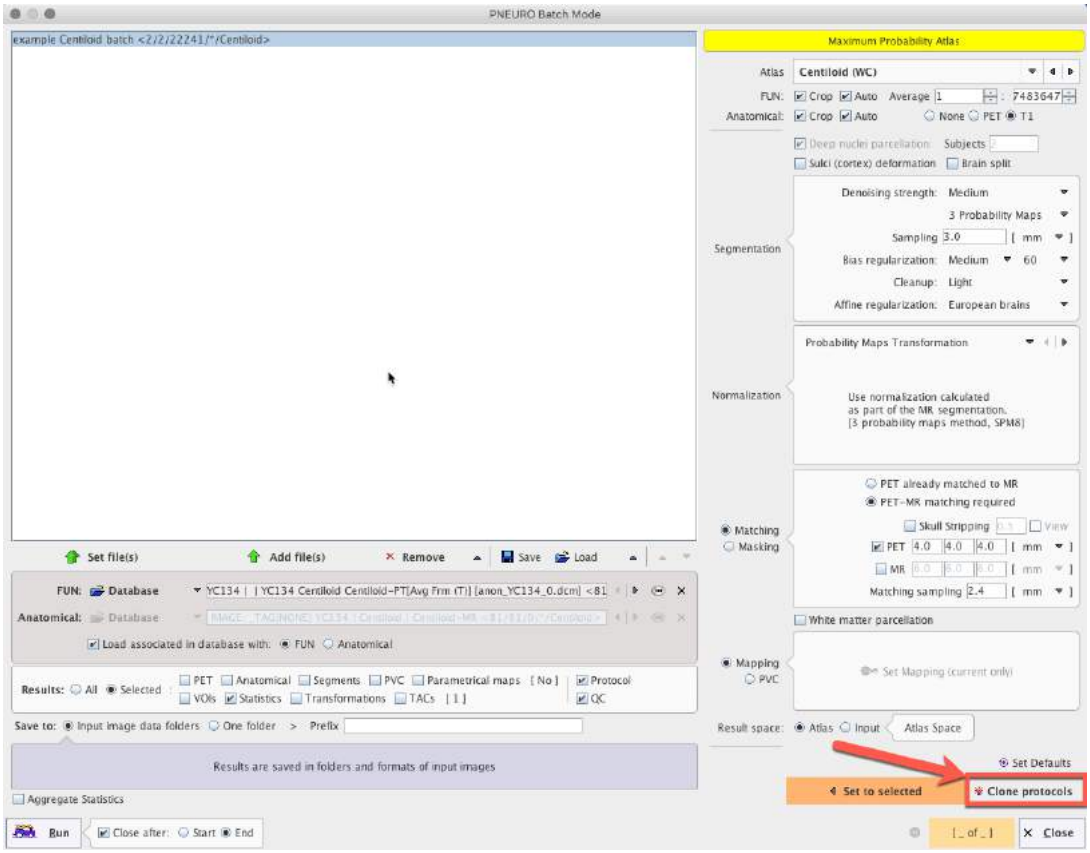
For Batch Processing the above workflow should be completed for a single subject, and the protocol saved. All subject PET and MR pairs should be associated in a database. The protocol will be cloned for all other subjects. Batch processing can be configured as follows:



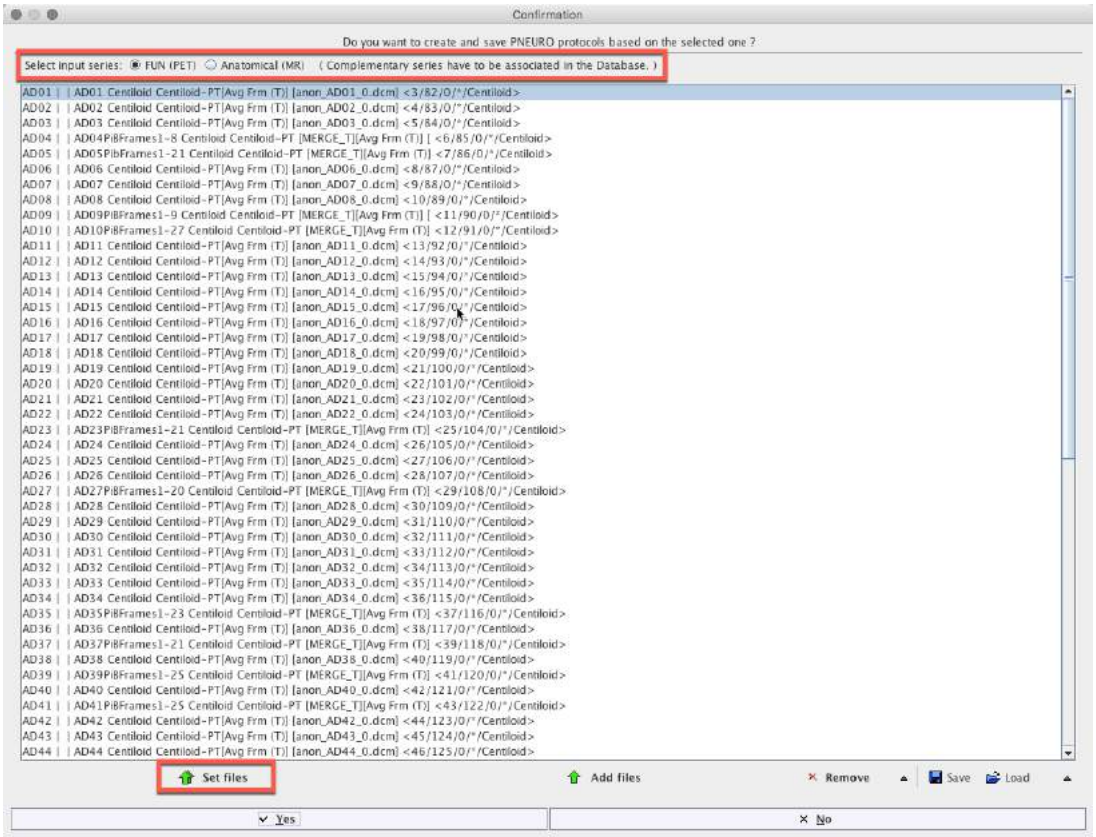
The saved protocol should then be selected:



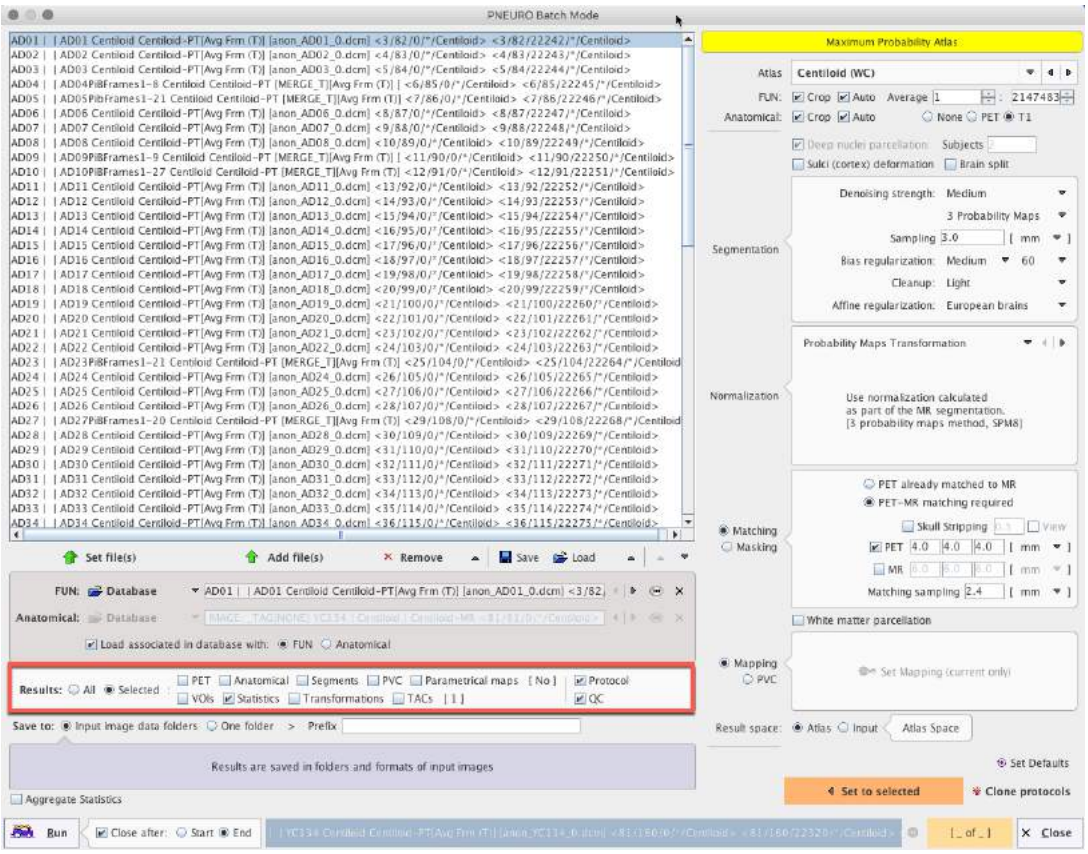
The PNEURO Batch Mode dialog is then opened, and the settings found within the selected protocol displayed on the right. These settings can be propagated to the full list of Centiloid reference subjects using the Clone Protocols function:



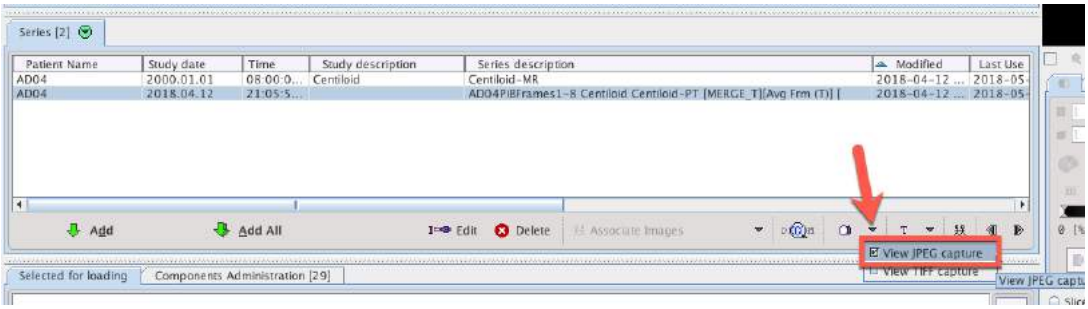
The **Set Files** button opens a database query dialog, from which all PET images can be selected (i.e. advanced database query, modality filter). During batch processing the corresponding MR images will be identified by Association in the database:

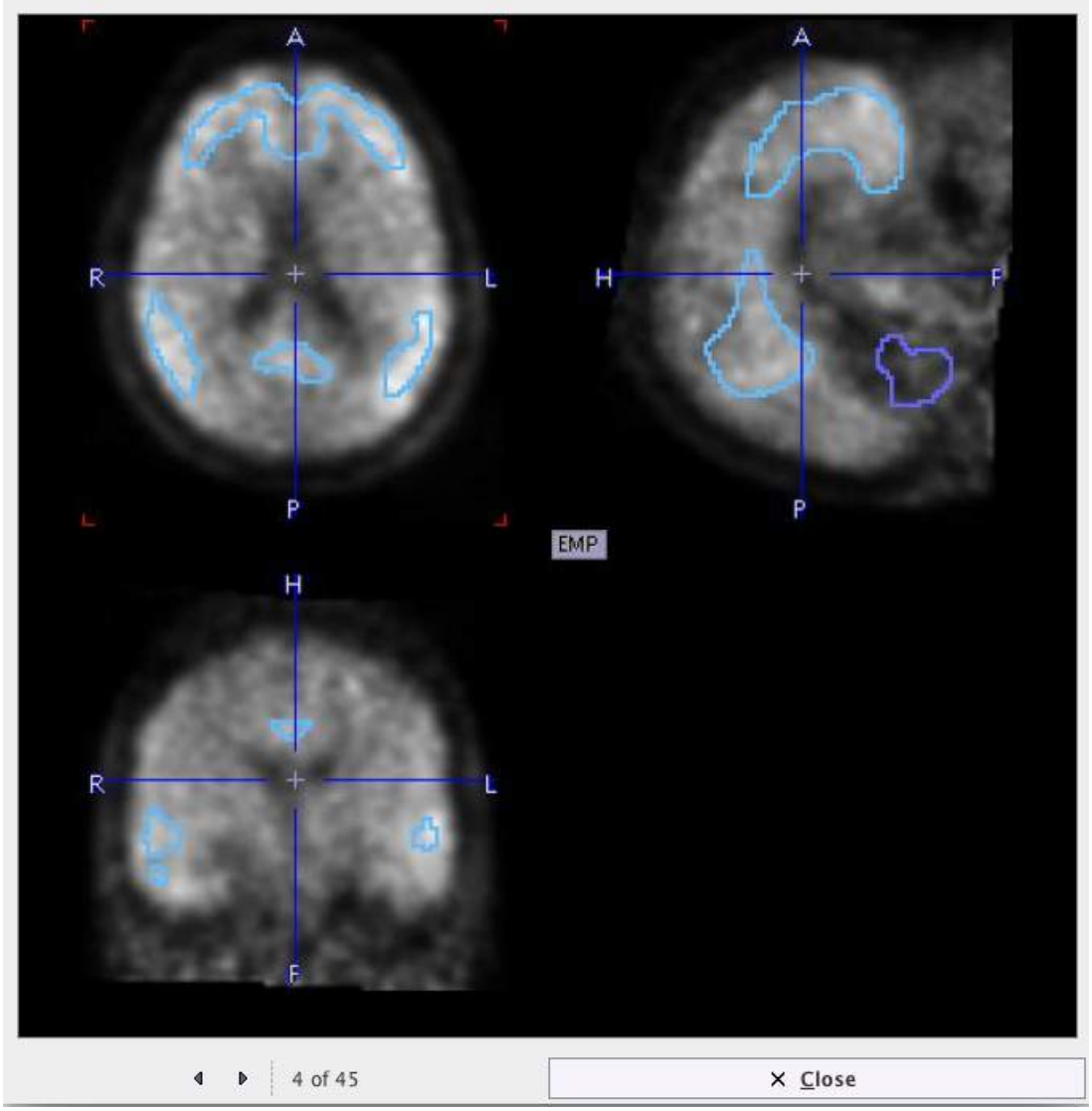


Once the list of protocols has been generated for all subjects, the results to be saved can be selected in the **Results** panel. **Statistics**, **Protocol** and **QC** are the minimum recommended. Saving of the PET in Template space may additionally be useful if a comparison of reference regions is desired (further post-processing required). Processing is then started with the **Run** button:



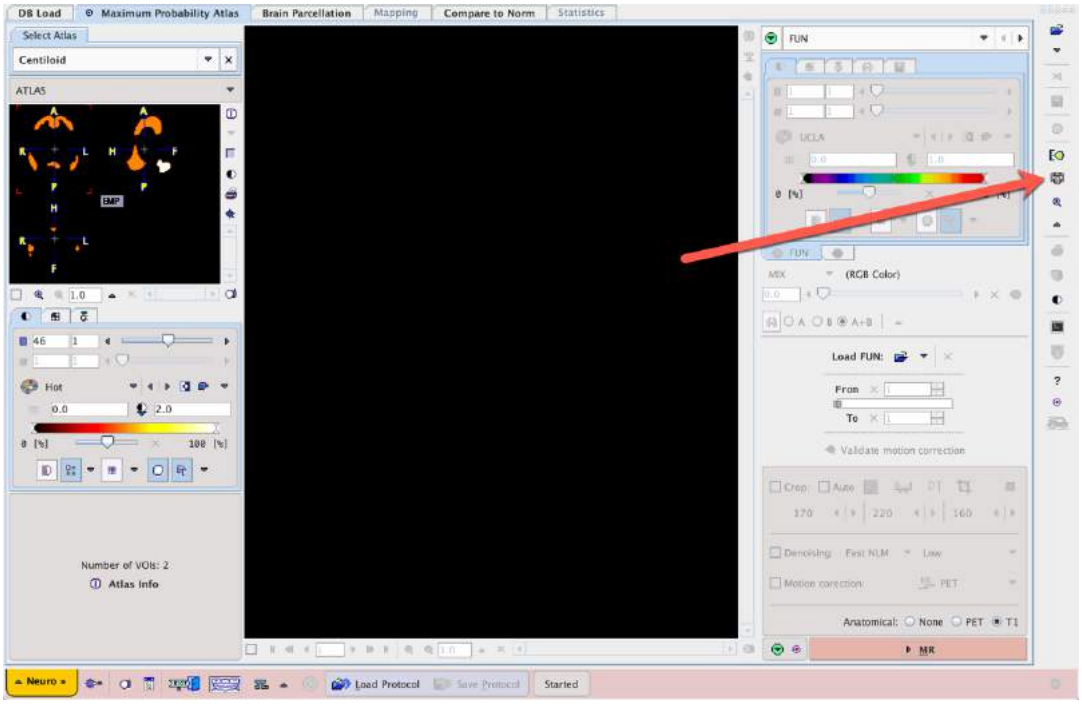
The QC jpeg captures should be reviewed to confirm that processing was successful in all cases. The QC captures can be accessed using the **View JPEG Capture** button on the DB Load page (n.b. multiple JPEG Captures may be selected for rapid viewing):



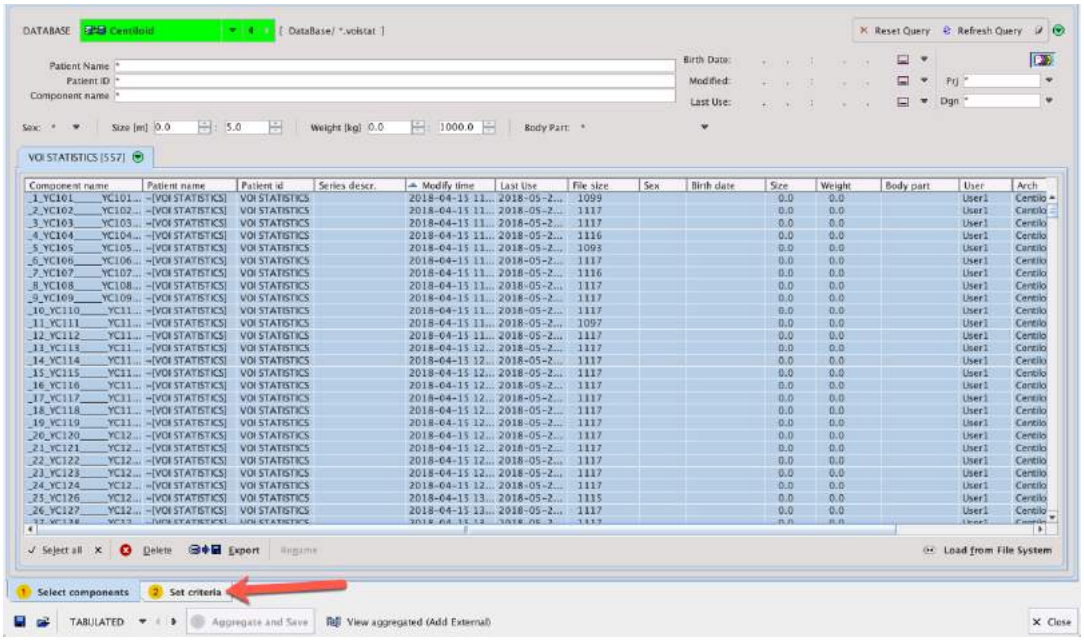


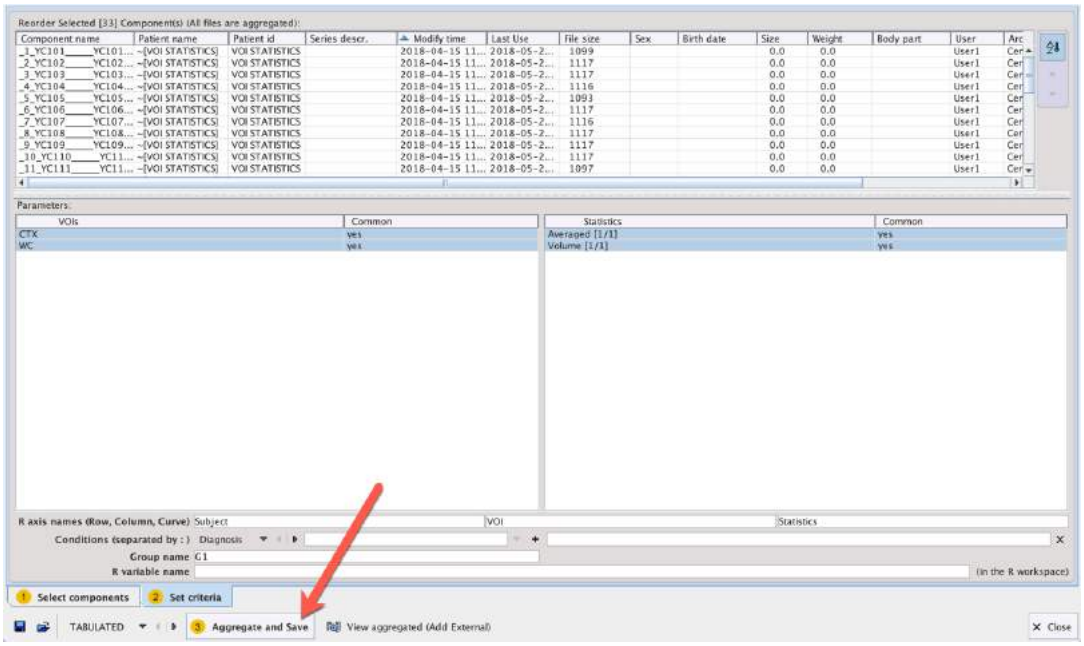
The results from PNEURO batch processing are a set of *.voistat format results files. The SUVr results can be readily extracted for regression analysis by aggregating all results (45 AD, 34 YC) and loading in the **R Console**. From there the tabulated data can be conveniently Copied To Clipboard.

The **Aggregate Statistics** tool is accessed from the right lateral taskbar:

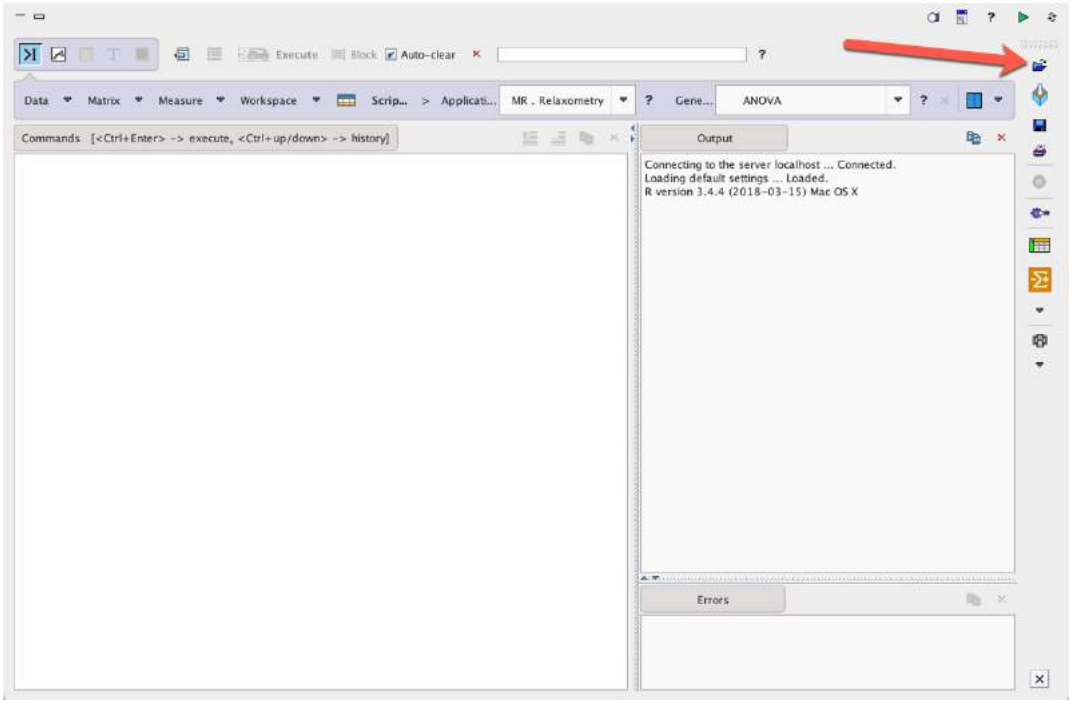


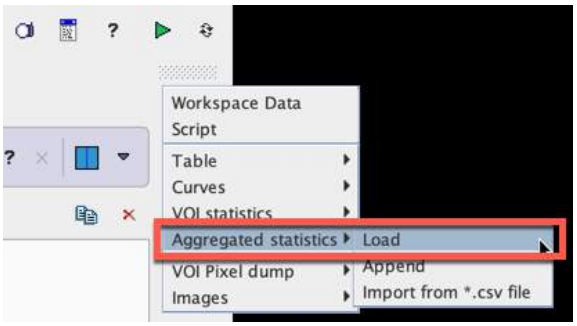
Where all results for a given group (e.g. all YC-0) can be selected, and an aggregate file saved:

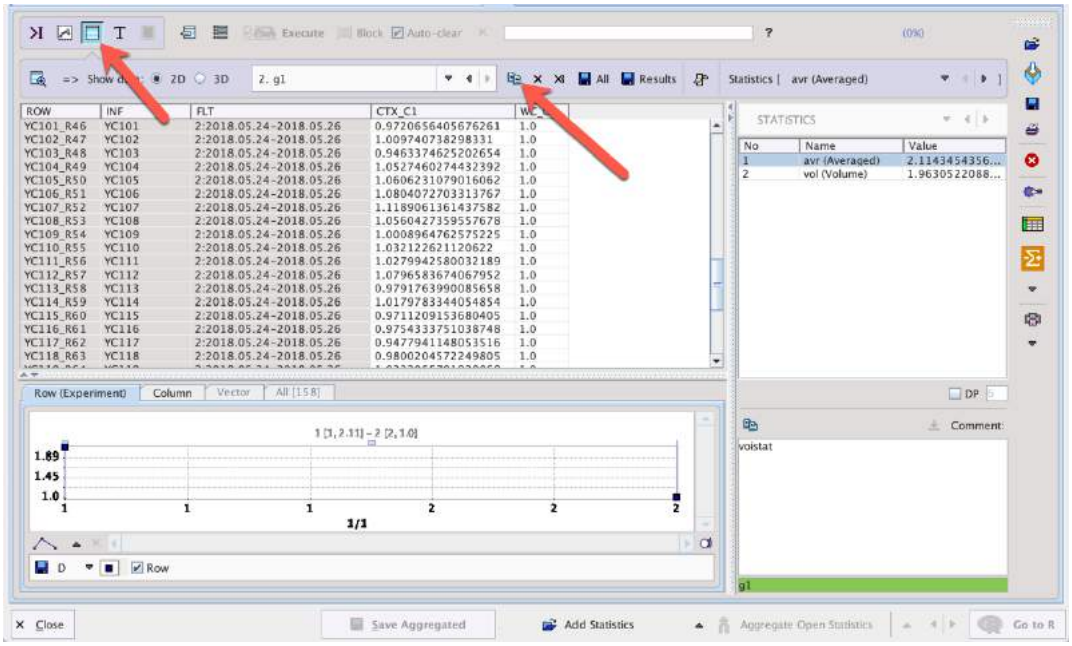


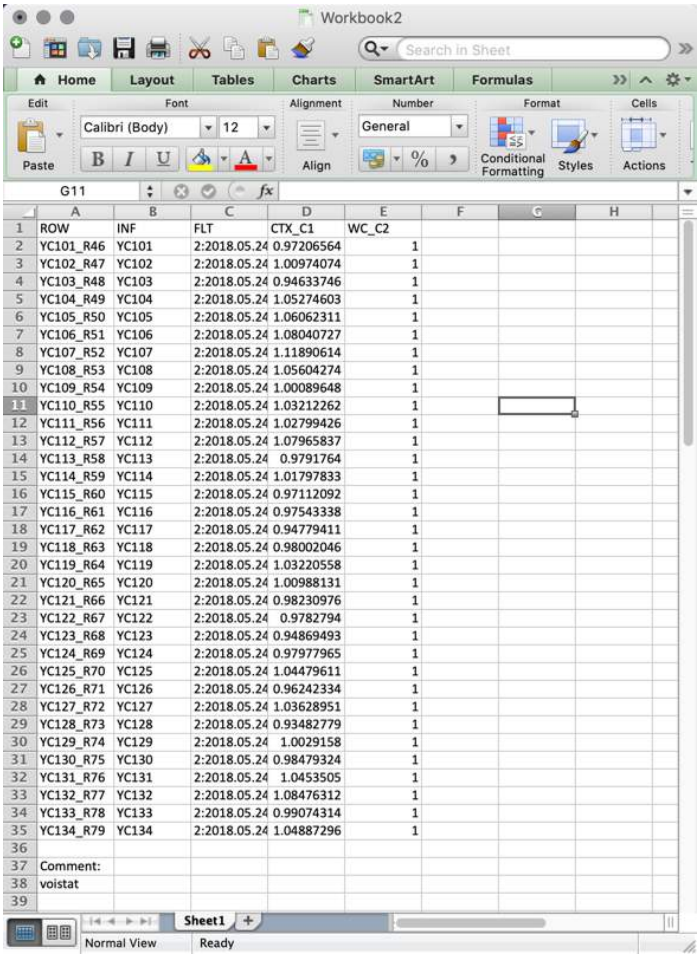


This aggregate file may be processed using external software such as R or Excel, or if the PMOD R Console has been configured, the aggregated results may be opened and the tabulated results Copied To Clipboard for paste into a spreadsheet editor:

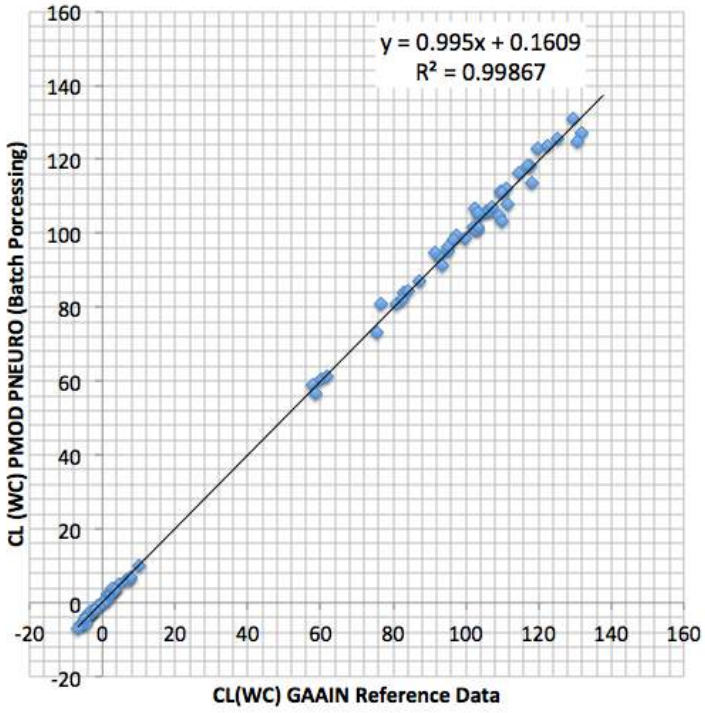






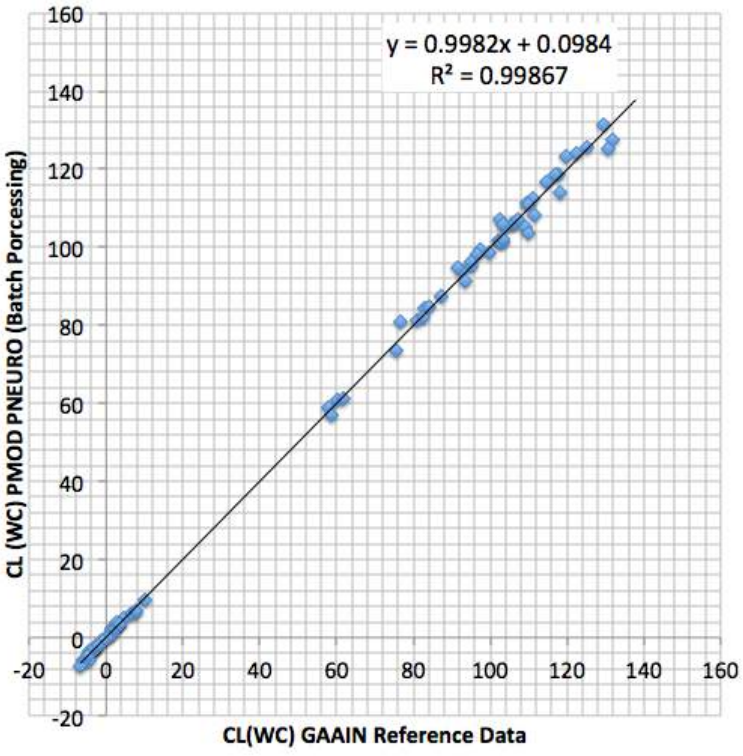


Following the processing of the complete GAAIN reference dataset using the workflow described above, in a single batch process, the results of regression against the Klunk et al. 2014 results (Supplementary Table 1), using their equation 1.3b to calculate CL from PMOD SUVr ($^{PiB}SUVr_{IND}$) are:



The resulting mean SUVr(WC) for the YC-0 group ($^{PiB}SUVr_{YC\text{-}0^*}$) for PNEURO processing is 1.0102, well within the stipulated 2 % variation from the mean calculated from GAAIN Centiloid reference data Table 1 (1.0095; actual difference: 0.07 %). The mean SUVr(WC) for the AD-100 group ($^{PiB}SUVr_{AD\text{-}100^*}$) is 2.073, also well within the 2 % specification (Table 1 AD-100(WC) mean: 2.0761; actual difference: -0.13 %).

When CL is recalculated using $^{PiB}SUVr_{YC\text{-}0^*}$ and $^{PiB}SUVr_{AD\text{-}100^*}$ in Klunk et al. equation 2.2.1 ($^{PiB}SUVr_{YC\text{-}0^*}$ and $^{PiB}SUVr_{AD\text{-}100^*}$ replace the values in equation 1.3b), the results of regression against the Klunk et al. 2014 results (Supplementary Table 1) are:

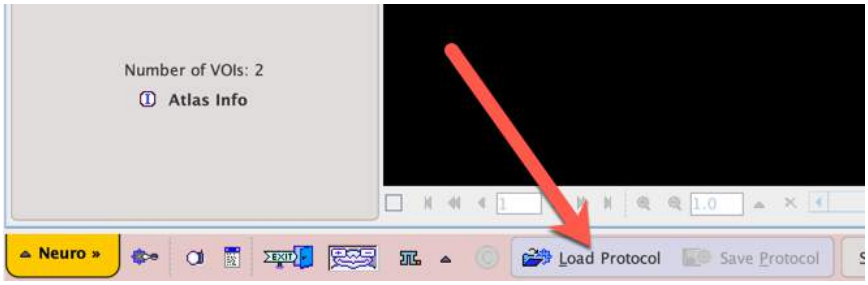


The results of either regression analysis are well within the specifications described by Klunk et al.: slope between 0.98 and 1.02, intercept between -2 and 2 CL, R2 > 0.98.

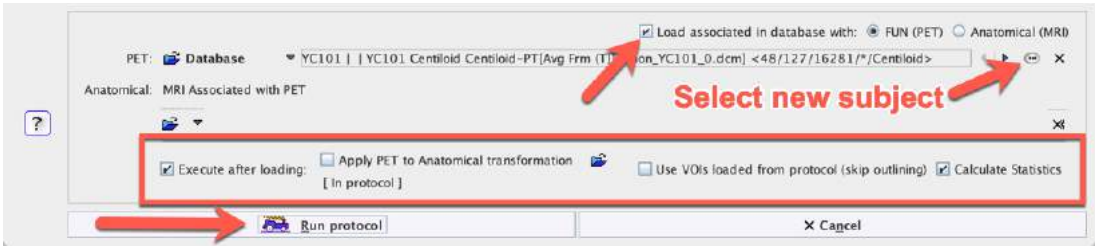
4 Analysis of New Data

The workflow and settings described above can thus be considered validated for the Centiloid processing of subsequent [11C]-PiB PET data between 50-70 minutes, with corresponding T1-weighted MRI. The saved protocol may be used, with selection of the new dataset instead of that initially used, or PNEURO can be used step-wise while confirming the settings described above.

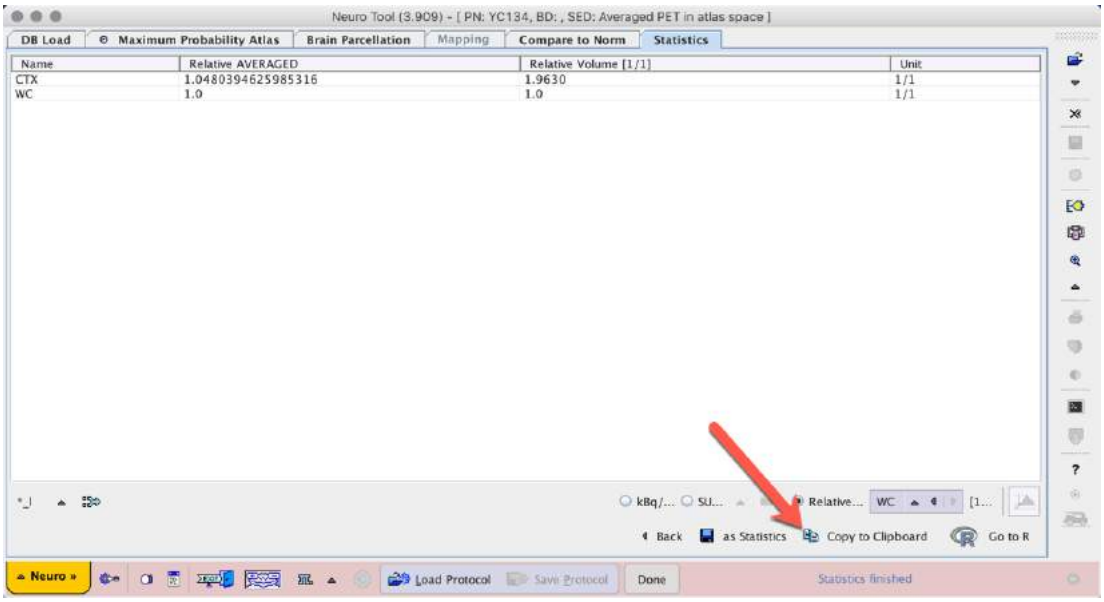
Thus, having processed their [11C]-PiB PET dataset according to the workflow described above (individual analysis, or batch processing), the user can process any new subject as follows:

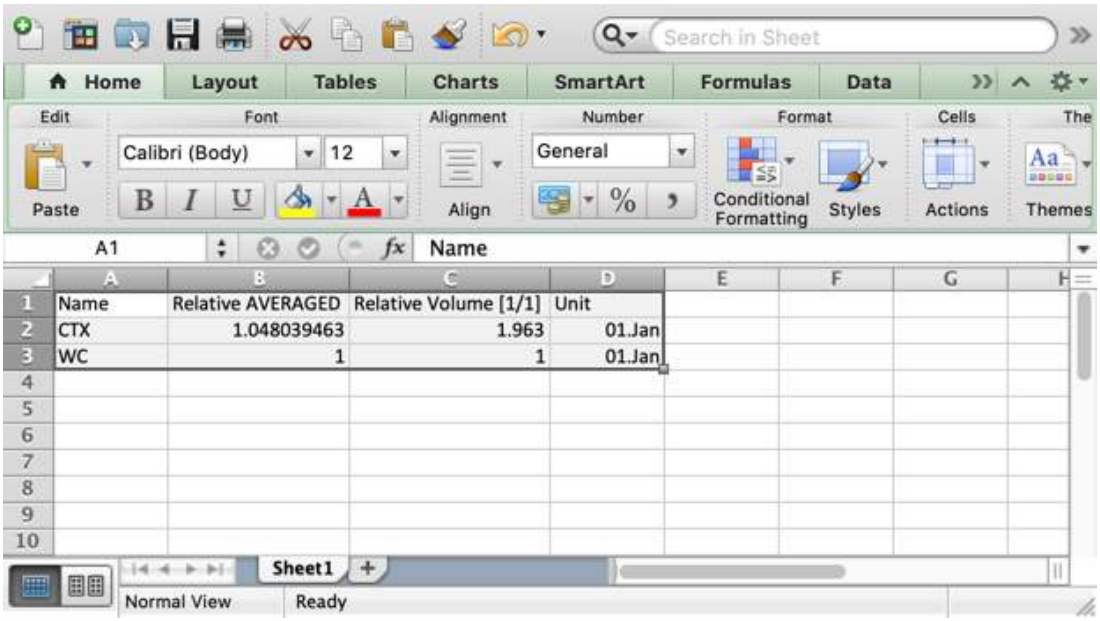


The new subject to be processed should be selected (screenshot assuming that Association between PET and MR series has been made):

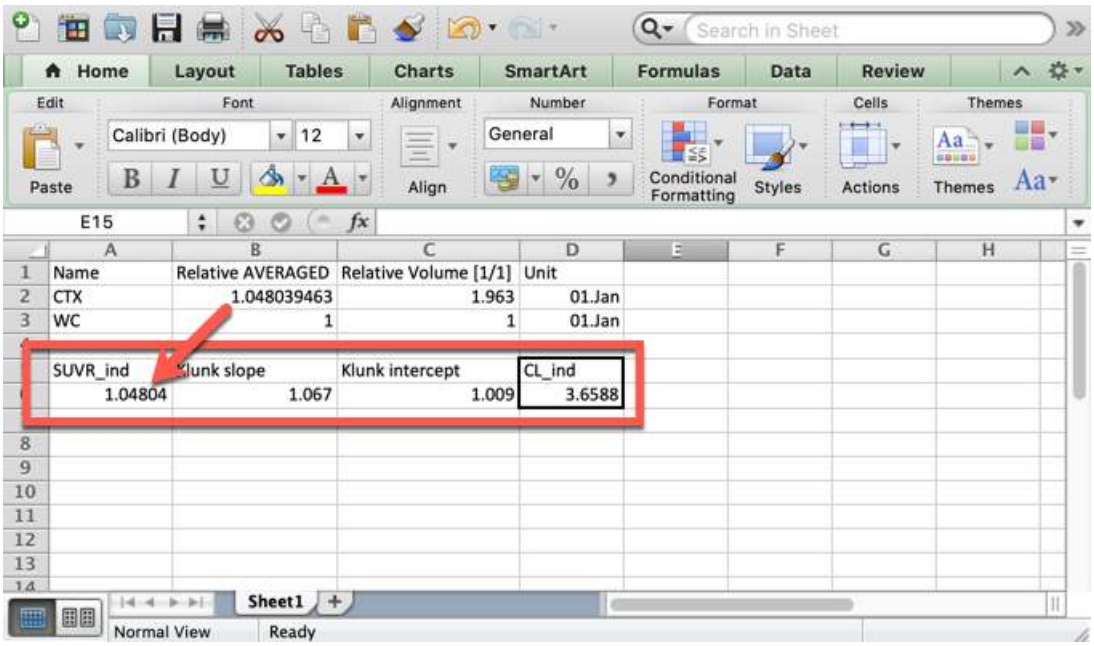


Once the protocol has run completely, the resulting SUVR statistics (Relative to: WC) can be Copied To Clipboard, and the results pasted into a spreadsheet program:





In which CL can be calculated from SUVR according to Klunk et al. equation 1.3b:



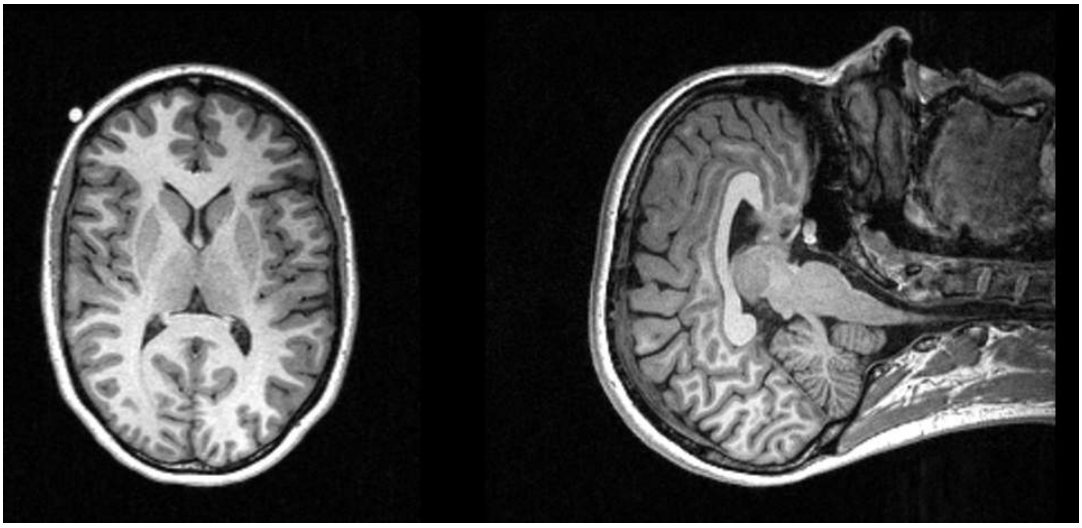
In the event that a tracer other than [11C]-PiB will be used, the procedure for calibration of another tracer described by Klunk et al., 2014, should be followed (section 2.2.2.3).

5 Notes on image quality and suitability for processing in PNEURO

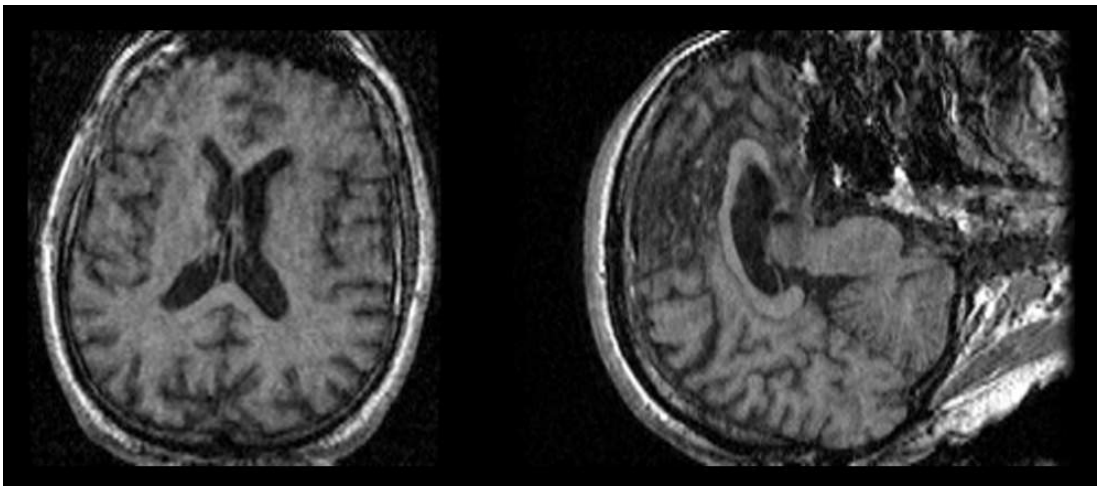
The success of, and processing time required for, MRI-based normalization (SPM8 methods) and PET to MRI rigid registration in PNEURO is dependent on image quality, contrast and cropping.

A T1-weighted MRI covering the entire brain is required for SPM8 normalization and segmentation (grey/white matter, cerebrospinal fluid). An isotropic high resolution in the order of 1 mm is strongly recommended. The contrast between grey and white matter should be optimized by adjusting MR acquisition parameters such as inversion time and flip angle. Examples of good, and poor, grey/white matter contrast are shown below.

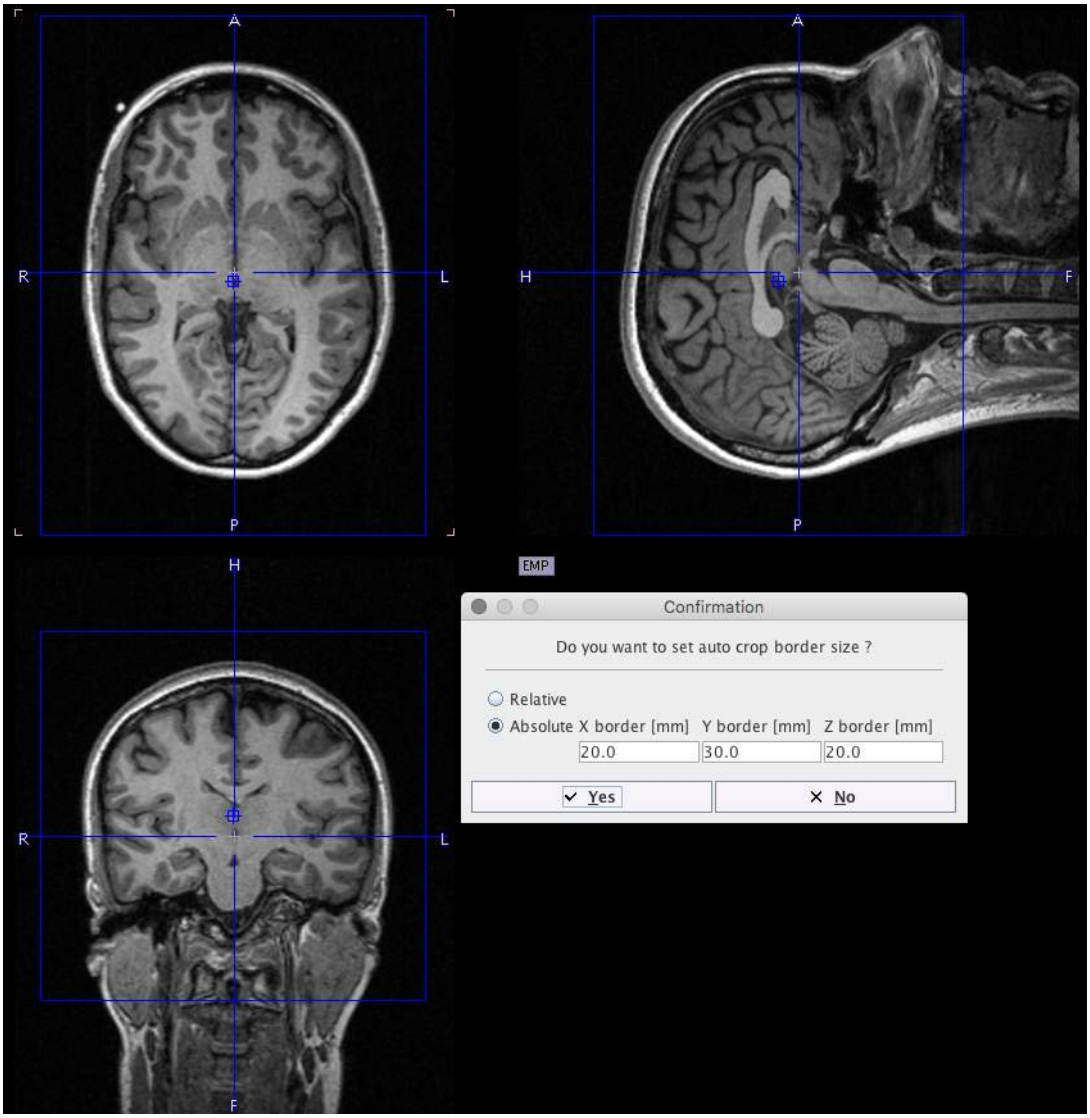
High grey/white matter contrast T1-weighted MRI:



Poor grey/white matter contrast T1-weighted MRI:



Additionally, cropping of both PET and MRI input series to remove unnecessary space in the reconstructed bounded box and/or anatomical features outside the brain is recommended. However, the inclusion of the nose in the cropped image may be beneficial during rigid matching of PET to MRI, where it can contribute to calculation of rotation around the (subject) L-R axis. Thus, when defining the field-of-view for T1-weighted MRI acquisition, inclusion of the nose may be of benefit in later post-processing. When using PNEURO's automatic cropping feature the bounding box may be extended by a fixed distance in mm in x, y and z dimensions. The recommended cropping of an MRI (automatic cropping, with bounding box extension by x=20, y=30, z=20 mm) is illustrated below.


A
R
L
P
H
F
EMP
Confirmation
Do you want to set auto crop border size ?
Relative
Absolute X border [mm] Y border [mm] Z border [mm]
20.0
30.0
20.0
Yes
No

6 References

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