

Workbook for Instructional Videos - Human Examples

PMOD Workbook Using Pmod4.1

PMOD is a software
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and must not be used for diagnosis or treatment of patients.

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1 Scope and Intended Use: VIDEOS Human Examples

The instructional videos and this workbook are intended as a tutorial for novice users of PMOD. Exercises are organized into sections for each of the major PMOD tools as well as for database management. The exercises (video plus workbook section) provide detailed descriptions of typical tasks accomplished with PMOD, including additional background information where possible.

We recommend that users watch the videos in consecutive order, then try to reproduce the workflows step-by-step using the data provided in the databases. For more specific information, please refer to the product documentation which is part of any PMOD installation or which is available online: www.pmod.com > Support > Documentation (and doc.pmod.com).

2 *Example Data and PMOD Installation*

The example data for the exercises covered by these workbooks (i.e. human and animal data examples) are distributed as an optional part of any new PMOD installation and are contained in the databases called Demo and BrukerPCI.

Users who own a PMOD installation can use that installation to perform the training tasks, as long as the training databases were installed (contact us on support@pmod.com for assistance adding the training databases to your installation later). To perform tasks with PMOD tools not included in their purchased license, we recommend requesting a trial installation.

Users working with a trial PMOD installation should download the example databases and install them together with the program. Note that the results produced with trial licenses cannot be saved. However, save-enabled trial licenses are available on request.

For loading the example data, the Database data format must be used. To try similar work with your own data, we recommend using the processes described for DICOM and other image formats in Section 1 below.

All example images in the database are in DICOM format, calibrated, decay corrected and with correct timing information.

NOTE: For some exercises the timing/SUV information has deliberately been removed to illustrate how this may be corrected with older data.

Vector data such as blood activities are text files that conform to the requirements of the PMOD tools. You can export them to the file system for inspection.

3 *Copyright and Disclaimer*

The example data provided in the **Demo** database are by courtesy of the following institutions.

CPFPX data: Institute of Medicine, Research Centre Jülich, 52425 Jülich, Germany; Dr. A. Bauer.

DASB data: Molecular Imaging Branch, National Institute of Mental Health, Bethesda, USA;

Dr. M. Ichise.

Mouse FDG PET and MR data was provided courtesy of the Werner Siemens Imaging Center, University of Tübingen, Tübingen, Germany; Dr. K. Herfert.

All other data: Nuclear Medicine, University Hospital, Zürich, Switzerland; Dr. A. Buck.

Note that the original data have been processed and optimized for training purposes.

The example data provided in the **BrukerPCI** database are from Bruker demo sites. Three additional external datasets are included in the BrukerPCI database. These datasets were provided courtesy of the Werner Siemens Imaging Center, University of Tübingen, Tübingen, Germany; Dr. K. Herfert.

IMPORTANT:

The data from the Demo/BrukerPCI databases may only be used for PMOD/Bruker 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 workbook 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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4 Section 1: Image Viewing, Processing and Basic Analysis (PVIEW)

4.1 Image loading

PMOD will load all widely used image formats (e.g. DICOM, nifti, interfile, analyze). DICOM data is best loaded using the dedicated DICOM loader, while the AUTODETECT loader is designed for other formats. Additionally, image data may be saved to PMOD's built-in DICOM Database. DICOM image files can be directly imported into a PMOD Database, and other formats will be converted to DICOM when saved to a Database. The Pmod Database is created by default in all PMOD installations, and a Demo database is created when the demo data is included during installation. Creation of new databases is described later in this workbook.

4.2 S1-exercise 1: Loading images from the database

1. Image series stored in the Database can be directly selected via the interface on the DB Load tab.
2. It is displayed by default when each tool is started.
3. The active database can be selected via the DB Name panel at the top of screen.
4. The Subject is selected on the Subjects tab, and Series available for that subject are displayed on the Series tab.
5. Each column can be sorted by clicking on the title bar, and search queries can be entered at the top of the screen.
6. Select the Demo database, then subject PFUS1 (Multimodality PET & MRI).
7. Select the FDG series and Add it to the Selected for Loading tab.
8. The PET series is loaded on the View tab, and displayed in the 3 Orthogonal Planes layout.
9. Clicking on any of the planes displayed triangulates that position in the other planes.
10. Try loading multiple images at the same time (for example the FDG, FET and FCH series). The images open will be listed in the top right.

4.3 S1-exercise 2: Loading DICOM images

1. New datasets can be loaded without having to clear the existing data.
2. On the DB Load tab there is a dedicated DICOM button in the lower right.
3. This opens the DICOM loader, which scans the currently selected folder for DICOM files.
4. The folder can be changed using the orange Change Folder button at the top of the dialog.
5. Select the folder USBdrive:/Pmod-Trial/Pmod/data/DICOM-human-example.
6. The DICOM loader scans the folder and displays any series available for loading. Note that PMOD can read DICOMDIR files as a table of contents to DICOM subfolders.
7. Select the PET-FET series and Load.

4.4 S1-exercise 3: Loading images using format AUTODETECT

1. As a final comparison, we can load a nifti format image using the AUTODETECT load button in the lower right of the DB Load tab. Nifti is common from SPM and custom routines in Python.
2. Use the interface to select the folder USBdrive:/Pmod-Trial/Pmod/data/Nifti-human-example.
3. PMOD automatically detects the format during loading, so this method can be used for most common non-DICOM formats.
4. Select PET-FCH.nii and Load.
5. Compare the Gray, Cold and Hot color tables.

4.5 S1-exercise 4: Image display and capture

Creating pleasing captures for presentation and publication is an essential part of imaging research. PMOD provides convenient tools for image and movie capture throughout the software. The functions introduced in the View tool here are conserved across all of the PMOD tools.

1. Select PFUS1 from the Demo database.
2. Select the MRI series, Load.
3. On the Layouts tab, change from Orthogonal Planes to Z.
4. Change from 1x1 to 4x4.
5. Switch back to the General Image Manipulation tab and check the effect of moving the Slice Selection slider.
6. Make the display skip 2 slices between displayed slices by setting the Slice Step to 3.
7. Use the mouse wheel or Slice Selection slider to adjust the display until the complete brain is covered in the display.
8. Using the Capture icon at the lower right corner of the image display, select Capture Display (note there is also a keyboard shortcut CTRL+E).
9. Select the Clipboard format and Full Display.
10. The Set button saves the capture to the OS clipboard, ready for paste into other programs such as MS Powerpoint.
11. To include a color bar, select Scientific Output from the Capture menu (note keyboard shortcut CTRL+O).
12. Activate Color Bar, choose Vertical, and Annotated.
13. Select 768 pixel Output Width.
14. Confirmation opens the Scientific Output Dialog, and the color bar can be seen on the right-hand side.
15. Capture opens a similar format selection, where again Clipboard can be selected.

4.6 S1-exercise 5: Dynamic images and capturing tracer kinetics

PMOD automatically distinguishes between static and dynamic data, providing the tools necessary to process either type. Movies and GIFs can be a great way to illustrate tracer kinetics for presentations. For publication a 2D grid showing several time frames can be useful.

1. Select subject PKIN1 (Dynamic CFPX bolus & MRI) from the Demo database.
2. Select the Dynamic PET series, Load.
3. Right click in the Image Display Area, then select Layout > Orthogonal.
4. Set the lower/upper color table thresholds to 0/30.
5. On the General Image Manipulation tab, reset the Slice Step to 1.
6. Use the Time Frame slider to move through the available time frames.
7. This can be automated, and a movie created, on the Movies tab.
8. Select Frames, and start the movie using the white arrow pointing right.
9. It is still possible to triangulate new positions in the Image Display Area, and adjust the movie speed using the smaller black arrows in the Movies tab.
10. Activating the Filmstrip icon in the Movies tab changes the play mode to once-through, and will produce a Save Video dialog when the movie is next started.
11. Start the movie again, and view the Save Video dialog.
12. Select Animated GIF (which is convenient for embedding into MS Powerpoint), 8 frames/sec, GIF continuous loop, Active area (e.g. axial plane), then Start.
13. After playing/creating the movie, the Database Save dialog appears.
14. To save the GIF in a folder for use in MS Powerpoint, select Save To File System.
15. Navigate to a suitable folder, enter a file name, and Save.
16. Additionally, the multi-slice layout can be converted to multi-frame.
17. On the Layouts tab, select Y, then choose the multi-slice layout RxN and set 1x8.
18. The slice and time radio buttons then become active. Select T.
19. Once again, a gap between displayed time frames can be configured. On the General Image Manipulations tab, enter a value of 2 in the Frame Step box, then use the mouse wheel or time frame slider to adjust the display on screen.
20. The 2D illustration of the time series can be captured using the Capture icon at the lower right of the Image Display area as before.

4.7 S1-exercise 6: Image cropping and saving

In this exercise we will demonstrate cropping of the brain from a whole body PET examination. Such a workflow is common when using existing patient data for a retrospective study. In PMOD version 4.1 cropping has been incorporated as part of the workflow in the View tool. Cropping using VOIs, such as cubes, is also convenient.

1. Clear the workspace in the View tool.
2. Return to the DB Load tab and select PSEG2 PET/CT (Whole body tumor), PET WB. Load.
3. If necessary, return to the Orthogonal planes display.

4. There is a dedicated workflow for image cropping in the lower right of the View tab.
5. We will crop the brain from the image so that it could be used more effectively in batch processing later.
6. Check the Crop checkbox and check that the Species selection is set to Human. An appropriate size crop box is displayed in yellow, centered on the cursor. The center point can be adjusted by triangulating a new point in the Image Display, and the box size adjusted using the arrows in the Crop workflow dialog.
7. Center the box on the brain, and adjust the box to 200 / 250 / 200 mm.
8. Cropping will be performed when the workflow is followed to VOIs (Volume-Of-Interest analysis), or it can also be applied using the Crop icon.
9. Apply cropping using the Crop icon.
10. Reset the color table upper threshold to 30 if necessary.
11. Turn off the Cropping workflow checkbox.
12. The cropped image can be saved in any supported format.
13. Select Save: Database.
14. A Save dialog opens, in which the database can be selected and parts of the DICOM header edited using Edit Info.
15. Select Edit Info.
16. Editing the Series Description is a useful way to add information to entries in the database. Add [brain crop] to the Series Description, confirm and Save.
17. Go to the DB Load tab and view the new entry for PSEG2 PET/CT.
18. The Save menu allows several other formats to be selected.
19. Select Save: Nifti.
20. A different save dialog is opened. The folder in which to save the data can be defined in a file browser opened using the Save Path icon.
21. The Transfer Syntax is important for non-DICOM formats. PMOD tests the data to determine whether pixel values will lose precision using particular syntax. A yellow warning icon is displayed if precision will be lost, otherwise [transfer syntax validated] is displayed. If in doubt, use the Float (LE) option!
22. Save the image in Nifti format to an appropriate folder.

4.8 Volumes-of-Interest (VOI)

The extraction of information from our images relies on volumes-of-interest (VOIs). The drawing/definition of VOIs constitutes segmentation of regions/organs within the subject. This process may be driven by tracer uptake, or by anatomical information where available (see Fusion workflows later). VOIs are built from planar polygons called “contours” (CTR). Contours can be defined in coronal, sagittal and horizontal planes. All contours from a given VOI in a single plane are grouped and considered as region-of-interest (ROI). Many VOI drawing/definition tools are available in PMOD. Where possible, (semi-) automated methods are favored, including methods with careful control of segmentation thresholds. Fully manual methods are always available as backup, for example where image contrast is poor and automatic methods fail. A number of examples are demonstrated below, and further examples will follow in the Fusion and Automated Segmentation sections.

4.9 S1-exercise 7: VOI analysis

1. Load the original PSEG2 PET/CT, PET WB, from the Demo database again.
2. In this case, the organs with most prominent FDG uptake are the brain, bladder, heart left ventricle and a number of tumors. We will use some of the tumors as examples for VOI drawing and extraction of statistics.
3. Activate the 2D MIP display in the Image Display area, and invert the Gray color table.
4. Set the lower/upper color bar thresholds to 0/30, highlighting the activity in the brain, tumors and bladder.
5. Go to the VOIs page using the workflow button in the lower right.
6. As we are working with 3D data we will start with simple 3D VOIs.
7. Use the MIP image as navigator, and click on the large tumor near the heart. Zoom in to see what you are working on more clearly. Create a 3D sphere object to approximately enclose the tumor with minimal background. A 15 mm radius works well here.
8. The sphere can be interactively expanded in $x/y/z$ direction to create an ellipsoid, and rotated around each axis if necessary.
9. Rename the VOI lesion-1.
10. A number of keyboard-shortcut VOIs are available for human oncology analysis. These can be found in the general list of shortcuts, via a right-click in the image display, and on the VOI configuration tab where the dimensions and threshold can be set.
11. Select the lesion in the liver, and zoom into the image display. Note that the MIP does not zoom and can be used as a navigator.
12. Use CTRL+L to create an automatic iso-contour VOI around the lesion.
13. Return to the lesion near the heart and use CTRL+Q to create an automatic SUVpeak VOI. We can compare this to the results from the sphere later.
14. Note that some VOI statistics can be overlaid on the image for convenience and quick captures. The units can also be directly switched to SUV.
15. Turn on Peak, select a VOI and use CTRL+E to make a capture. Captures can be appended to the Console to be saved together later.
16. Select the lesions in the right armpit.
17. Iso-contouring is also possible with adjustable thresholds.
18. Create a sphere around the lesion as starting boundary, then open the iso-contouring tool.
19. The default is a percentage-based threshold, but a precise SUV can also be used. This will be seen in Exercise 9.
20. For now, use Default settings and a threshold of 45% to be comparable with the CTRL+L method.
21. One-click 3D iso-contouring is less reproducible, but useful for quick exploration of the data. Create a New VOI and try the tool on another lesion.
22. We can now calculate the Statistics for these VOIs. Use the Selected Statistics configuration to select the options needed for your study.
23. The Statistics Viewer is opened, and basic statistics for the VOIs shown.
24. These results can be saved in PMOD's *.voistat format, or Copied To Clipboard for easier transfer into programs like MS Excel.

25. In fact, the default mode for calculation of Statistics is Selected Statistics. Expand the Statistics menu to see the other available options. The statistics included in Selected Statistics match the configuration seen a moment ago.
26. Close the Statistics dialog.

4.10 S1-exercise 8: VOI-based masking for improved 3D rendering with CT data

A common use of VOIs is VOI-based masking, which can be used to prepare images for presentation. This is common for most modalities. In the case of PET, high activity in areas that are not of interest may be masked to allow presentation of the image with more appropriate focus on tumor uptake. For CT, a common task is removal of the bed and associated hardware, improving MIP and 3D rendering. We will use such CT “clean-up” as an example.

1. Load the CT from Subject PSEG2 PET/CT (Whole Body Tumor).
2. The MIP shows that the teeth and a ring are the densest parts of the image, followed by the bones, meaning that rendering of the skeleton alone could be quite effective without masking. However, the bed materials have a similar density to the soft tissues, which will make whole body rendering less attractive (e.g. volume rendering).
3. When there is some separation between the subject and the bed materials (e.g. when the bed is topped with foam padding) separation with regular VOIs can be straightforward. It is helpful when the surfaces of the bed are exactly parallel to the reconstructed image planes, but PMOD’s reslicing tools can be used if this was not the case.
4. Proceed to the VOIs tab.
5. Explore the image to understand the location of the arms.
6. The subject is widest from left-right at the level of the elbows. A custom VOI shape will help to avoid cropping of the arms during masking.
7. Use the Vertex Paintbrush tool to draw a 2D ROI around the body on the axial plane, wide enough to include the arms. It may be useful to change the Image Display to show only the axial slice (z) for this operation.
8. From the ROI tools, select ROI Apply to All.
9. Switch back to the Orthogonal Planes display.
10. Select the VOI tools Neutral Mode, and explore the image to see the now 3D VOI.
11. On the VOI Tools tab, select Mask voxels outside selected VOI.
12. As we are masking CT data, the background value for air is -1000 HU.
13. This assumption can be tested using the Data Inspector.
14. Enter -1000 in the Mask outside VOI(s): by value box. Do not check Mask inside.
15. Allow a new image to be created, so that we can compare the masked to the original.
16. Save the masking VOI to the database.
17. Use the workflow button in the lower right to proceed to the Compare tab.
18. The third row can be switched off, and the MIP for both series activated.
19. The effect of masking is clear.
20. The process could be repeated to remove the head support in a similar way.

21. Save the masked version of the image to the database for later rendering (edit the Series Description to help identify the masked series later).

4.11 S1-exercise 9: Isocontouring using a defined SUV threshold

Iso-contouring is a very useful VOI definition technique as it allows careful control of the voxel inclusion threshold, and the search area can be confined to a user-defined boundary. It is particularly useful for PET/SPECT data where there is high tracer uptake in a given region/organ, but it can also be used to segment bone, lungs, or contrast-enhanced-lesions in CT or clear contrast and enhanced areas in MR.

1. Load PSEG2 PET/CT, PET 3D, from the Demo database.
2. Activate the MIP display, and use an inverse Gray color table.
3. The MIP reveals that FDG uptake is most evident in brain, heart, bladder and a number of lesions. We will use isocontouring to segment the lesion near to the heart, using a directly controlled SUV threshold.
4. When SUV information is included in the image header working with SUV units can be very easy.
5. Open the Series Information and Editing Window, then select Edit Subject / Study Info.
6. The timing and dose information important for SUV can be found on the SUV Parameters tab.
7. For SUV body weight we need at least the body weight, acquisition time, isotope, dose and administration time. PMOD automatically calculates the dose at the Image Decay Correction Time to use for SUV.
8. We have the necessary information, so we can directly switch between kBq/cc and SUV units when necessary.
9. Proceed to the VOIs tab.
10. Triangulate the lesion near the heart in the display and zoom to factor 4.
11. To create a boundary for the isocontouring search algorithm, create a Sphere object VOI around the lesion. A radius of 25 mm is effective. Reposition the sphere interactively if necessary.
12. The active units can be set using the shortcut to the left of the color table lower threshold box. Keep Original for now.
13. Open the isocontouring dialog.
14. Click the Set Defaults button
15. An exact value threshold can be used instead of a percentage. At the moment the units kBq/cc are shown.
16. Change the units to SUV body weight and see the change in the iso-contouring dialog.
17. Now a fixed SUV threshold such as 5 g/ml can be used.
18. Click OK, then calculate Statistics for this VOI.
19. The Statistics Viewer also allows a direct switch between kBq/cc and SUV units when the SUV information is complete.

5 Section 2: Image Registration and Fusion (PFUS)

Fused image display is not only interesting for image presentation, but can also be valuable during segmentation. Anatomical CT or MR images can be complementary to PET or SPECT, aiding in organ/lesion delineation. Hybrid scanners may provide directly coregistered PET/SPECT and CT or PET and MR images, removing the need for calculated coregistration. Nevertheless, in neurology studies spatial normalization of the brain to VOI atlases may be desirable. Whether this is achieved directly from PET/SPECT data, or using the anatomical MR or CT, PMOD's fusion functionality is required and allows the normalization result to be properly inspected. In longitudinal studies each subsequent scan may be registered to the individual baseline, and PMOD supports "image algebra" between such studies to aid in visualization of differences over time (Note: longitudinal image registration is most successful for brain studies, while reproducible body/limb positioning is a major hurdle in whole body matching).

5.1 S2-exercise 1: Fusion display of hybrid data and simple VOI analysis

In the case of data from a hybrid scanner, the fusion workflow is reduced to fused display of each modality, bringing the user efficiently to the VOI analysis step.

1. The Matching workflow in the Fuse It tool is broken down into five major steps: Loading of the Input Image(s), Loading of a Reference Image and Matching of Input to Reference, Inspection of the Matching Result, Image Algebra, and finally VOI Analysis.
2. When you are analyzing hybrid data, it is useful to set the Hybrid workflow as Default. This is performed in the Fuse It Configuration.
3. Note that default color tables, and the volumes used for species recognition, are also configured here.
4. With the Hybrid workflow set as Default, both Input and Reference image can be loaded together. This is most effective from Database, or DICOM, where the series modality is clearly identified.
5. Select PSEG2 PET/CT from the Demo database, and Add the PET 3D and CT series to the Selected for Loading list. As you saw in the Configuration dialog, the CT is automatically loaded as Reference for a PET/CT pair.
6. When you click Open, Fuse It loads the images, selects the Hybrid workflow, reslices the PET to the resolution of the CT and jumps to the Comparison tab to display the alpha-blended fusion of the series in whole body layout.
7. In the top right the image controls are identical to the View tool as seen in the previous Section. When fusion functionality is available, there are two copies of the image controls, and an additional set of fusion controls immediately below.
8. The image controls labeled with a green spot correspond to the Input image, and green labeling is used elsewhere to highlight controls for the Input image. Blue is used for the Reference image.
9. The new slider below the image controls adjusts the alpha blending between Input and Reference images, and shortcuts for 0/50/100% are color-coded green/blue to the right of the slider.
10. Additional controls for choice of displayed images (when more than two are available), layout shortcuts, and Capture shortcut are available on the right of the Image Display.
11. To perform VOI analysis in fusion mode, use the shortcut to the VOIs page of the Matching tab on the right lateral toolbar.

12. Note that here there are also two sets of image controls in the top right. When using threshold-based VOI tools it is essential that the appropriate set of controls is active (i.e. to use the Hot 3D one-click iso-contouring tool on a hot-spot of activity in the PET image, make sure that the Input image controls are active).
13. The MIP display can be configured for Input and Reference separately.
14. We will use the oncology hot-key VOI methods to create some VOIs.
15. Use the Input MIP to find the lesion near the heart, then zoom in by factor 4.
16. Use the Fusion Slider to see how the FDG uptake in the lesion corresponds to the anatomy on the CT.
17. Use CTRL+L to create standard iso-contour VOIs on some of the lesions seen in the PET.
18. Use the Fusion Slider again to see how the VOI corresponds to the CT anatomy.

5.2 S2-exercise 2: Registration of images from different scans and scanners

When functional and anatomical data from the same subject is not already coregistered, rigid matching methods can be used. This normally means rotations and translations, followed by reslicing to the same image matrix as the reference. This is common when PET data is acquired on a PET/CT and anatomical MRI is acquired separately.

1. Load the MRI and FCH series for PFUS1 from the Demo database.
2. Once the Hybrid workflow has completed, it is clear that the PET and MR are not properly coregistered.
3. Select the Matching tab, then the Reference & Matching page from the menu in the top right.
4. Select the Input Reslicing shortcut. Manually translating the PET into approximate alignment with the MR is easy for the user and provides a better starting point for the automatic rigid matching algorithm. Drag the PET into approximate alignment with the MR using the central white square of the reslicing controls. Rotations are not necessary.
5. Check that the Species is set to Human, and the matching method to Rigid. The colored icons to the right of matching method indicate same-modality or different-modality matching. Clicking on them opens the Matching Settings dialog.
6. Click Match Current.
7. Explore the coregistration result using the Image Display and Fusion Controls.
8. Using the Save icon on the right lateral toolbar, save the coregistered PET back to the database.
9. Proceed to the VOIs page using the workflow button in the lower right.
10. The MIP for the PET reveals a lesion in the right temporal lobe.
11. It can be outlined using the CTRL+L hot-key oncology VOI.
12. Compare the VOI outline between PET and MR, then calculate Statistics for the VOI.
13. As the PET contains the necessary SUV information you can easily switch between kBq/cc and SUV body weight.

5.3 S2-exercise 3: Template-based brain spatial normalization and VOI atlases

In human neurology research the use of standardized brain atlases is common. Application of these VOI atlases relies on matching of images from an individual to a template image that has the same “image space” as the VOI atlas. Ideally, individual and template images should be from the same modality, for same tracer/sequence. Many templates and atlases are already available and shared online. T1- and T2-weighted MRI templates are common, as are PET/SPECT templates for blood flow tracers and FDG. Note that many brain templates, whether PET or MR, are averages of spatially normalized images from several subjects. This can help to remove minor regional variations and left/right asymmetry, but obviously requires researchers to have images from several normal subjects (ideally outside of the study population), and a template/VOI atlas that these subjects can be registered to. Fuse It provides several brain normalization approaches and atlases with templates.

1. The FDG PET data from PFUS1 in the Demo database will be used to demonstrate spatial normalization to an FDG PET template.
2. Clear all data in Fuse It.
3. Open the Fuse It Configuration and set the Default Matching to Deformable.
4. On the DB Load tab, select only the FDG PET and Open. When a single series is selected for loading it will automatically be assigned to Input Image.
5. Averaging of time frames, or cropping, are unnecessary in this case, so Proceed using the Deform workflow button.
6. Load a Reference image using the Templates shortcut.
7. Select the PET template at the top of the list.
8. Use the Fusion controls to see the differences between the individual and the template.
9. A manual translation using the Input reslicing tools can help the matching algorithm.
10. Start the spatial normalization using the Match Current workflow button.
11. On the Matching Result page the result can be readily assessed by displaying contours for the template. Activate Contours in the fusion controls and select B. Move the Fusion Slider to the right to see how the contours correspond to the brain outline in the template image. Then move the Fusion Slider to the left to compare the brain outline in the transformed Input Image to the contours.
12. Save the transformation to the database for later recalculation.
13. Proceed using the VOIs workflow button.
14. Rather than using the VOI definition tools seen so far, we will now load the pre-defined Automatic Anatomical Labeling, AAL, atlas.
15. From the Template tab, select Atlas, then AAL Merged from the list of atlases. A preview of the atlas VOIs is shown in the Image Display. In order to use the VOIs for quantification, they should be Outlined onto the images. The atlas VOIs are organized in a tree structure, and a subset of VOIs to suit a specific study goal can be selected for outlining, rather than automatically using all available regions.
16. For now, Outline all available VOIs, then inspect the result by moving the Fusion Slider to show only the PET, and deactivate the contours from the Reference.
17. Atlas VOIs are generalized, but can be applied reproducibly. Users can modify atlases in PMOD and introduce their own if they are not fully satisfied with those available as standard.
18. Using Selected Statistics, calculate the Average and SD for all of the atlas VOIs.

6 Section 3: 3D Rendering (P3D)

3D rendering can yield eye-catching presentation images. PMOD's 3D tool allows surface and volume rendering of data from all modalities, as well as rendering of VOIs. A dedicated segmentation interface allows particular tissues to be extracted and the segments to be organized before rendering. Multimodality data from the same subject can be combined, including application of 4D textures to show tracer kinetics. Many data types require some preprocessing to improve the 3D rendering outcome. CT data benefits from masking of the imaging bed and tubes used for tracer injection/monitoring. PET data (including hybrid data) should be resliced to the same matrix as an anatomical reference (CT/MR). This is readily achieved using the Fuse It tool. Protocols can be saved so that rendering projects can be restored for further work and adjustments.

6.1 S3-exercise 1: Simple CT surface/volume rendering with VOIs

1. The basic principles of the 3D tool are easiest understood using a single input image. We will combine surface and volume renderings from the same CT dataset and add a VOI to highlight an organ.
2. Open the 3D tool and select PSEG2 PET/CT from the Demo database.
3. The PET 3D and CT series are the original data from the scanner. We have prepared masked and resliced versions of the data to improve the 3D rendering result (i.e. removal of the CT bed, reslicing of the PET to match the CT image matrix). These steps are omitted here to save time.
4. Select and load the CT [Masked] series.
5. After loading, processing starts on the Segmentation page. The image is displayed in the Input tab, top left. In the lower section, thresholding and other segmentation methods are available on the left, and either the image histogram or a list of segments prepared are shown on the right. The histogram can be used as part of threshold definition (as can the Data Inspector in the Input Image Display).
6. CT is useful for an initial demonstration as certain tissues can be readily segmented by finding voxels with values above a particular HU threshold.
7. Enter a threshold of 500 HU and click the orange Segmentation button.
8. The voxels above the threshold are displayed in the Current tab, top right. Turn on the MIP for the Current tab Image Display. If the threshold was correct for detection of the bones, the MIP should closely resemble the skeleton.
9. Save this voxel selection for rendering using the Add Segment button (green). The selection is added to the Segments tab in the lower right.
10. Select the entry in the list on the Segments tab, then click Set Segments 3D Rendering Properties.
11. In the Edit Segment dialog, the rendering type can be set using the radio buttons, the color set for surface renderings, and a name defined. The skeleton will be rendered as a surface, in white, and the name "skeleton" can be entered.
12. Click OK to close the Edit Segments dialog, then click the Render Selected workflow button in the lower right.
13. The resulting rendering can be rotated using the mouse (left click, drag) and zoomed using the mouse wheel or dedicated slider on the Scene, Views, tab.
14. On the Scene tab, Views sub-tab, the Background Color can be adjusted.

15. On the Scene tab, Rotation sub-tab, rotating movies can be started, and saved by activating the Filmstrip icon as seen in Section 1. During movie recording the scene can be interactively rotated and zoomed.
16. The Capture icon on the right lateral toolbar allows 2D captures to be saved in a range of formats.
17. Additional renderings can be appended to the overall scene.
18. Return to the Segmentation tab.
19. Change the segmentation mode to In Range and enter lower/upper thresholds of 0/500 HU to segment soft tissue. Click Segmentation.
20. Add Segment to the Segments list, then set its Rendering Properties to Volume HD, Color: Gray, named soft_tissue.
21. Activate the Append pin immediately left of the Render Selected workflow button, then Render Selected.
22. The rendering is updated and shows the surface rendered skeleton and new soft tissue volume. The entries for the two segments are listed in the View tab in the top right.
23. Select VR soft_tissue. The color transfer function is shown in the lower right. Enter a value of 0.02 to increase the opacity of the volume segment.
24. We can highlight additional features by rendering a VOI previously defined in the View tool using the PET information.
25. Select the Input tab in the top right.
26. Select the PET-derived-heart VOI from the Demo database using the Browse icon right of the text No VOLUME OF INTEREST.
27. Using the menu arrow to the right of the workflow button, select VOIs [Surface], then confirm rendering.
28. The VOI is rendered and displayed.
29. Explore the overall rendering using the mouse and try capturing a rotating movie.
30. Save the Protocol for the rendering project to the Demo database.
31. Suggestion: See how the saved Protocol can be used to restore the project after clearing all data from the 3D tool.

6.2 S3-exercise 2: Fused PET/CT rendering

1. A combination of surface rendered skeleton from CT with volume rendered PET is pleasing for PET/CT data. VOIs can still be added as in the previous exercise, and elements of the skeleton can be trimmed away to reveal details from the PET. For example, the top of the skull can be trimmed to reveal tracer uptake in the brain.
2. Clear the previous data in the 3D Rendering tool.
3. Open both PSEG2 PET/CT CT [Masked] and PET 3D [Resliced to CT]. Note – this version of the PET was loaded together with the CT WB in Fuse It and the resliced version, thus with the same matrix dimensions as the CT, saved.
4. On the Segmentation tab, select the CT, then Segment voxels above a Threshold of 500 HU.
5. Add Segment to the Segments list, and set its 3D Rendering Properties to Surface, Color: White, Name: skeleton.
6. Render the skeleton.

7. Next, return to the Segmentation tab and select the PET using the menu arrow below the Image Info for the Input tab.
8. Change the Segmentation mode to Range, then Segment all voxels between 1 and 30 kBq/cc. This will avoid having the high activity in the bladder dominate the rendering. The Data Inspector can be used to explore the values in the image to find this range.
9. Add this general body segment to the Segments list, and set its 3D Rendering Properties to Volume HD, Color: Cold, Name: PET-1to30.
10. Make sure that Append mode is active, and Render the PET volume.
11. Select VR PET, then the Volume tab.
12. The prominence of the lesions can be improved by setting the top of the profile range to approx. 50%. Observe the effect of these changes on the PET rendering (allow some processing time).
13. Change to the Input tab and select the heart VOI available in the database.
14. Switch on Append mode, and Append a surface rendering of the VOI to emphasize the heart.
15. Finally, we will trim the top of the skull to reveal the PET tracer uptake in the brain.
16. Select Planes, and Add an Oblique plane.
17. Click and hold the tail of the arrow through the oblique plane and drag it to an angle that will trim the top of the skull – this could be an iterative process!
18. Next, click and hold the plane to move it until it transects the top of the skull.
19. Select the skeleton SR in the Scene panel, then the Cut tab.
20. Uncheck Arrow Side, then select Cut (allow some processing time for this step).
21. Select Plane 1 in the Scene list and uncheck Visible to reveal the trimmed rendering.
22. Explore the scene and capture a rotating movie.
23. Save the Protocol for the rendering project to the Demo database.
24. Suggestion: See how the saved Protocol can be used to restore the project after clearing all data from the 3D tool.

7 Section 4: Kinetic Modeling (PKIN)

7.1 S4-exercise 1: Gold-standard two-tissue-compartment PET kinetic modeling with an arterial input function – full-quantification of receptor binding

1. Clear all the images in the View tool workspace and go to the DB Load tab. Select the Demo database, and load the Dynamic PET series for subject PKIN1.
2. Adjust the color table thresholds to 0/30, and select the last frame. Create an averaged image using all frames (do not Replace). This average could help to create VOIs, or in this case make it easier to check loaded VOIs.
3. Proceed to the VOIs tab, then load the CPFPX Bolus 13 VOIs from the Demo database. Their anatomical positions are easily checked on the average image.
4. Now that we have used the average image to check the VOIs, we can switch to the dynamic image to extract time activity curves.
5. Use the PKIN export button to prepare time-activity curves for the 13 VOIs, then Send[SET] to transfer the curves to the PKIN tool.
6. A warning message tells us that blood data must still be loaded to fit the default compartment model. The TACs are organized according to a list in the top right. The model can be configured independently per region, or applied to all regions simultaneously. The next step is to load the blood data that we need for the 2-tissue compartment model.
7. Load the whole blood Total CPFPX in blood curve from the main Kinetic menu > Load Whole Blood Activity.
8. In this example we also have data for the concentration of authentic CPFPX in arterial plasma, which is the gold standard for PET modeling input function. Load it from the Kinetic menu > Load Plasma Activity > Parent. The whole blood data is useful even though we have this gold standard plasma data. It allows the fraction of activity from the blood in each time activity curve to be estimated in the model. Since the plasma data already accounts for metabolism of the tracer in the body, we don't need to load a Parent Fraction.
9. An important concept in studies with external measurement of the tracer activity in blood is a difference in timing between the PET data and blood data. This is known as the Delay. This represents the time it takes the blood to leave the body along the catheter used, before activity reaches the detector. We can enter a reasonable starting value for the Delay on the Whole Blood tab. Enter a value of 5 s. Zooming in on the peak lets us see how this shifts the blood model curve left. The goal is to find the best alignment with the PET time activity curve, and this can be done as part of the modeling process.
10. Now that we have the necessary blood data, we can perform modeling with a first representative TAC. Although the whole brain could be a good average of all the curves, it might also mix grey and white matter. We can select another large, but more homogeneous region from the list of regions, such as the right frontal VOI, and select the 2-Tissue Compartments model.
11. A first model fit can then be tested by clicking Fit Current Region. Using iterative methods, PMOD finds rate constants for the model that produce the best agreement between the blue model curve and the measured PET data. Relative error in these estimates is shown to the right of the resulting rate constants, and the residuals between model and PET curves are shown in the lower plot window.

12. The Delay can also be included in model fitting. This may improve the reliability of the model results. From the menu below Fit Region, Fit Region & Blood can be selected. After fitting, a blood delay of nearly 10 s is estimated. This value can be inspected on the Blood tab.
13. The changes of the parameters using the different fitting options are best inspected using the Show History button. Mathematical criteria such as the Akaike Information Criterion (AIC) and Schwartz Criterion (SC) can be used to identify the best model. These indices are available on the Tissue Details tab. Small values indicate a better fit.
14. The modeling results can be summarized using the View Parameters button. From this dialog the results table can be Copied To Clipboard for use elsewhere.
15. Finally, the entire PKIN analysis can be saved via the Kinetic menu > Save KM File in order to resume analysis later.

7.2 S4-exercise 2: Reference-tissue-based kinetic modeling – receptor density with the non-displaceable binding potential (BP_{nd})

Reference-tissue kinetic models were developed to avoid the complexities of collecting blood data for classical compartmental models. However, there are critical assumptions that must be carefully considered. The reference tissue must be completely devoid of the tracer target, yet have very similar tracer delivery and washout to the target region. In this way the reference tissue TAC provides the information about tracer delivery to the target tissue that would otherwise be provided by the blood data, allowing the two-tissue compartment model to be simplified.

1. Start in the View tool and select Subject PKIN2. Load the Dynamic DASB PET series.
2. Once again we have pre-prepared simple VOIs for this example. They are available in the Demo database. In a full study you would normally take more time to use atlas VOIs with or without an MRI for anatomical reference.
3. Calculate the time activity curves for transfer, and set the Model Selection to Reference.
4. Use Send[Add] to transfer the TACs to PKIN and simultaneously create a new workspace.
5. The Ref radio button on the right lateral task bar is automatically used to set the filtering of the Model list to reference tissue-based models.
6. Select Simplified Ref. Tissue SRTM from the Model List. The documentation for each model in the list can be called up using the question mark icon next to the model name.
7. On the Tissue tab, select the thalamus as first target Region, and select cerebellum as the Reference region.
8. Click Fit Current Region.
9. The blue model curve is updated and the fit results shown on the right.
10. If the model fit is satisfactory, the Model and Parameters can be Copied to All Regions, then the model Fit in All Regions automatically.
11. With reference tissue models an error about failed fitting in one region is common. This is the reference region.

12. Inspect the model fit and results in other regions, then the tabulated results using View Parameters. Although cerebellum is included, the very high chi-squared value indicates the failed fit. Chi-squared is low in all fitted regions, indicating a good fit.
13. The project can be saved as a KM File so that it is easy to go back to the analysis later.

8 Section 5: Parametric Mapping (PXMOD)

8.1 S5-exercise 1: Maps of serotonin transporter density using reference-tissue-based modeling

Parametric mapping is the application of kinetic modeling in every image voxel of a dynamic PET series. This creates new 3D images in which the voxel values directly represent a quantitative parameter from the model. For example, instead of kBq/cc or SUV per voxel in an FDG PET, the result of parametric mapping could be an image with quantified glucose metabolism ($\mu\text{mol_glucose/ml_tissue/min}$) per voxel. Beyond interesting image presentation, parametric mapping allows image-wise averaging, subtraction, etc. within study groups or for longitudinal measurements for single subjects. This allows clear visual representation of treatment/pathology effects and supports statistical parametric mapping (voxelwise statistics in the same style as functional MRI). In this exercise the calculation of parametric maps of serotonin transporter density (binding potential, BPnd) will be described. The BPnd (Logan Reference) method in PXMOD will be used. This method applies the Logan Graphical Analysis with Reference Tissue in all voxels.

1. Start PXMOD and select the BPnd (Logan Ref) model in the workspace tab list. By selecting this model, the configuration requirements are adjusted accordingly.
2. Additional information about this model and its implementation can be found in our online Documentation (see Section 9).
3. Define the image data using the Input Data Settings button in the Image Data tab of the workspace. In the new dialog window make sure that Input1 format is Database then use the file browser button to select the Dynamic DASB PET series from PKIN2 in the Demo database for loading. Use the Reset loading parameters button to make sure that no pre-processing will be applied. Select OK to open the image. (The Load button is used when working with pre-saved protocols).
4. Use the Masking workflow button to proceed. In the next step we will define a mask of the brain in order to limit the modeling calculations to the voxels we are interested in (i.e. within the brain).
5. Creation of an average image that resembles the whole brain can aid threshold-based masking. Such an average can be created from a time range where tracer concentration is high throughout the entire brain. This is often the first minutes after tracer injection when the concentration in the blood pool is high. For tracers with a low extraction fraction it may also be a middle time range, while for trapped tracers like FDG it could be a late average.
6. Average frames 10-20 for this DASB example.
7. Enter a Threshold of 10 kBq/cc. The histogram illustrates how this threshold separates high and low activity in the image. Check that the greater-than-or-equal-to (\geq) radio button is selected, then create a preview of the mask using the Segmentation button.
8. The resulting mask has some holes, which can be reduced using the morphological closing tool. Use Morphological Closing with 3 pixels and Segment again. The holes are substantially reduced. The mask should be saved to the database for later use in the Protocol.
9. Proceed using the TACs workflow button. TACs (particularly the Reference tissue TAC) are used for the model preprocessing and eventual application in all voxels. The program automatically switches to VOI (TACs) – VOIs tab. In the VOIs List three empty VOI definitions are shown, which originate from the model: Target tissue VOI, Reference tissue VOI and a VOI in which k_2' is determined from an SRTM k_2' map as an alternative to TAC1 - a VOI defining voxels in which the reference tissue washout rate (k_2') will be calculated. VOIs can be drawn, or Loaded. The reference tissue VOI is important, as the reference curve will be used for modeling in all voxels. A target tissue VOI is not always necessary.

Instead, a VOI defining voxels in which k_2' will be calculated can be provided, or k_2' can be fixed based on prior knowledge from kinetic modeling.

10. Select Load VOIs and locate the DASB-Regions VOI file from the Demo database.
11. Cerebellum will be our reference region.
12. We can create a VOI for k_2' calculation by averaging all of the other VOIs.
13. Use the Union tool on VOI Group tab.
14. Proceed using the red Prepare TACs button to the TACs tab. Deactivate Target Tissue and select cerebellum as Reference Tissue. Select the Union VOI just created as VOI in which k_2' is determined. We have to save either a VOI or a TAC before proceeding, so that they are identified for the Protocol. We will save the VOIs. Save the VOIs using the names DASB-Cerebellum and DASB- k_2' prime.
15. Proceed using the Modeling workflow button. The program switches to the Modeling/Model Preprocessing panel. Note that the Reference Tissue and VOI in which k_2' is determined VOIs previously prepared are already configured in this panel (assuming that the VOIs were saved in the previous step of the workflow). Deactivate Target Tissue if necessary.
16. The t^* parameter represents the start time of the data segment used for the estimation of BPnd in the Logan Reference model. A fixed value will be used when we don't use a Target Tissue.
17. The k_2' parameter (washout rate constant) of the reference tissue will be calculated as the median k_2' of VOI pixels within a specified BPnd range. SRTM mapping will be performed in the Union VOI, providing the k_2' values for median calculation. This value will then be used for BPnd calculation in all voxels.
18. All the parameters can be set to recommended default values using the Set Defaults button in the lower left. The t^* can be fixed to 10 min based on prior knowledge (that we provide) for this example.
19. Start preprocessing using the Preprocess workflow button. In the Results tab the reference tissue TAC is displayed for visual inspection, and the t^* is available in the Info area. The SRTM maps used to calculate the median k_2' can be inspected on the SRTM Maps tab.
20. Proceed using the Set Map Configuration workflow button. The check boxes indicate which maps will be calculated.
21. The last configuration step is now completed and the pixel-wise calculation can be started using the Start Pixelwise Calculation workflow button.
22. The resulting parametric map is shown in the Parametric Maps panel. The Data Inspector can be used to quickly inspect the BPnd values.
23. The maps can be saved in one of the available formats (e.g. back to the Database for best study organization) using the Save icon on the right lateral taskbar, or using the Save Maps button in the Parametric Maps panel. During the saving process, PXM0D adds the parameter name to the series description or to the specified file name, depending on the output format.
24. We highly recommended saving the full processing configuration in order to retrieve all the processing details later, edit the settings if necessary, and then repeat the processing. Save the configuration using the Save Protocol button in the status line.
25. To test the configuration, open a new PXM0D workspace, load the configuration settings using Load Protocol and Run Protocol.

9 Section 6: Automated Image Segmentation (PSEG)

9.1 S6-exercise 1: PERCIST oncology workflow with PET/CT data

PERCIST (PET Response Criteria in Solid Tumors) defines an objective method to assess the tumor burden and treatment response for FDG PET images. PMOD supports semi-automated PERCIST processing of whole body PET data in the Segment tool. A simplified outline of the main steps is:

1. A 3cm diameter reference sphere is manually placed in the right side of the liver. If the liver is diseased, the blood pool of the descending aorta is used as an alternative.
2. The threshold for tumor uptake is calculated from the average and the standard deviation of the activity in the reference region.
3. An iso-contouring segmentation is performed at the calculated threshold, resulting in a list of lesion VOIs.
4. The lesions are sorted according to their peak uptake.
5. The lesion with highest peak uptake is considered the target lesion at baseline and after treatment.

Although only a single target lesion is used for assessing treatment response in PERCIST, using additional exploratory data is recommended, particularly from the 5 hottest lesions.

1. Open the Segment tool and immediately select the Segment tab. We will follow each step of the workflow for clarity. The initial steps are organized in pages of the Segment tab. A list of the steps is available in the top right.
2. The first step is to Load the PET data using the recognizable tools on the right of screen.
3. Load the PET 3D from Subject PSEG2 PET/CT in the Demo database.
4. The processing steps follow the workflow presented by the pink buttons in the lower right.
5. Since an anatomical CT is available, we can Load that next. Set the Masking method to CT, then use the Load CT button to proceed.
6. Select the PSEG2 CT from the Demo database.
7. The Whole Body method should generate a suitable mask.
8. On the MASK page we see the whole body mask based on the CT overlaid in red.
9. It allows us to exclude unimportant voxels from the rest of the analysis.
10. Next we choose PERCIST from the list of segmentation methods in the orange-labeled menu.
11. A hint is displayed to remind us of the CTRL+SHIFT+U shortcut to define the reference sphere in the liver.
12. We can proceed using the Segmentation button.
13. On the Segments page we see our familiar VOI controls, and specific settings for PERCIST in the lower right.
14. First we should set the units to SUV lean body mass. This requires the subject height and weight in the image header.
15. Next we identify the right side of the liver between the dome and inferior margin, then place the reference sphere.
16. We can use the MIP to navigate, then zoom in to help us place the sphere.
17. Use CTRL+SHIFT+U to place it.

18. The SUV lean body mass threshold for lesion identification is displayed on the right.
19. The PERCIST VOIs button starts the iso-contouring algorithm to find all potential lesions above the calculated threshold and within the volume restrictions.
20. Several VOIs are detected, and the list sorted from high to low SUV peak. The sorting criteria can be adjusted at the top of the list. Selecting SUV peak reapplies the criteria and moves the liver reference VOI to the end of the list.
21. On the VOI Settings tab we can turn on display of the SUV peak value for the selected VOI.
22. Next we should check the image and MIP for VOIs that do not appear to be lesions.
23. The high activity in the bladder is a common source of a false positive. Note that the brain has not been detected since the volume would have been above the restriction.
24. As we select VOIs in the list they are triangulated in the image and labeled on the MIP.
25. The first VOI is the bladder, so we can remove it.
26. This process would be repeated for any VOIs that do not represent lesions.
27. The VOIs can be renamed using predefined lists. This is described in detail in our Documentation.
28. A report can then be generated using the PERCIST workflow button. By default it will report the five VOIs with highest SUV peak, and the reference.
29. The report for a given image can be saved, as well as used in a formatted report.
30. The Comparison button reveals a dialog to load previous, or Baseline, results for a direct comparison.
31. There are additional features that are not covered in this video, such as radiomics measures. More information is available in the Documentation.

10 Section 7: Human Brain Image Analysis (PNEURO)

10.1 S7-exercise 1: Automatic brain VOIs for human PET/MR

Precise definition of functional brain areas in the individual patient is crucial for the accurate quantitative analysis of brain PET images and meaningful interpretation of the results. The Neuro tool provides this objective region outlining with easy step-by-step procedures. The tool includes three main workflows: 1) Automatic brain region definition using MR anatomy and an atlas based on the probability of a voxel belonging to a certain region; 2) Automatic brain region definition through parcellation of T1-MR images; 3) Comparison of individual data to databases of normal subject PET images. In this demonstration we will go through the first workflow, using data from an experimental tracer targeting an enzyme involved in tau protein tangling. Extra, more advanced, exercises using this data for kinetic modeling and parametric mapping are available. Ask the PMOD team for more information.

1. Open the Neuro tool and go to the tool Configuration. The default workflow can be defined, and automatic reorientation to what PMOD considers the Standard Orientation (to suit PMOD's built-in atlases and templates) can be activated.
2. With experience, the PET and MR data can be selected together. But if cropping or processing of the PET is required, individual loading of the PET data can be more convenient.
3. Select the Maximum Probability Atlas workflow tab.
4. The atlas can be selected on the Select Atlas tab in the top left. Information specific to the selected atlas can be opened using the Atlas Info button. We will use the Hammers atlas for this demonstration.
5. Load a functional image from Database. Use the Demo database and search for Subject PKIN6. Select the Dynamic PET baseline – motion corrected Series.
6. An average image is created automatically. The frames used for the average are controlled by the selector center-right of screen.
7. An average of early frames can produce a better outline of the brain for matching to the MRI than any individual time frame. Use frames 10-20 for this example.
8. The average can be examined using the fusion controls.
9. The image can be cropped quite tightly around the brain. Auto-cropping can be useful in Batch Processing, but you should test it first.
10. Since we have an MR available we can select MR for Anatomical reference.
11. The 3D T1-weighted MRI can then be used for grey matter segmentation. Again, Cropping is recommended for large FOV images like this. The segmentation settings required are heavily dependent on the MR quality/contrast. With high-quality MR (clear GM/WM contrast, no motion artefacts, low noise, low bias due to head coil inhomogeneity) no/low denoising and bias regularization can be sufficient, along with coarse Resampling (3 or even 6 mm). The 3 Probability Maps method is equivalent to SPM8, while the 6 Maps method is equivalent to SPM12. The 6 Maps method has proven useful in successful segmentation of poor-contrast MR.
12. Start Segmentation using the Segment T1 MR workflow button. The segmentation process includes elastic normalization to the template space. It will take some minutes depending on the power of your computer and data resolution and quality.
13. The resulting identification of grey and white matter should be inspected, and adjusted if necessary. Note that Segmentation Touch-up can only apply global adjustments. In case of a very poor result you should return to the MR page and re-run the segmentation with improved settings. The degree of accuracy required is dependent on the desired result space and whether the tissue probability maps will be used elsewhere. For example, small

clusters of voxels identified as GM that fall outside the brain will likely also fall outside the VOI atlas regions and be ignored. Additionally, if the desired result space is PET or Template, the low resolution may also make the influence of small inaccuracies negligible. Proceed using the Match PET to MR workflow button.

14. The result of rigid matching between the averaged PET and cropped MR should then be assessed, and the MR-to-Template normalization method selected. The standard PMOD fusion controls are available to inspect the matching result. Adjustments are only possible using manual translations and rotations. Alternatively you can return to the MR Segments page and adjust the Smoothing or Matching sampling settings. When MR segmentation was used, the use of the Probability Maps Transformation is strongly recommended. The Split Brain option is useful if you also want detailed WM VOIs. Continue using the Normalize workflow button.
15. Again, the general normalization result can be assessed using the fusion controls. The normalized MR is shown in fusion mode with the MR template. Creating a general brain outline from the template image using the controls to contour A is useful. The Segment Brain workflow button takes you to the next processing step, where the result space can be selected.
16. The intersection of the VOI atlas and tissue probability maps is shown in fusion mode on the MR. For a PET/MR workflow three results space options are available. Atlas space, in which PET and MR are transformed to match the SPM template space and resolution/bounding box, and Input space, within which either the original (cropped) MR space or PET space can be chosen. By default, masking of GM by the individual grey matter probability is used. Mask non-cortical regions allows trimming of sub-cortical VOIs by the GM mask. This means regions such as the basal ganglia, thalamus, brainstem. Finally, the segments are Outlined into VOIs. This step can also take some time depending on the number of VOIs and the processing power of your computer.
17. The resulting VOIs are shown on a fusion of the MR and average PET in the chosen result space. You can choose to display the dynamic PET by adjusting the Select functional option below the time-activity curve preview. The tree-structure of the VOIs can be expanded to see the full list. If you want to use batch processing later, activating the QC capture checkbox is highly recommended, as is Saving the Protocol. Mapping can be activated using the green box and partial volume correction methods are also available.
18. Standard statistics can be calculated as part of the workflow. Use the Statistics workflow button.
19. The time-activity curves are displayed for all selected VOIs, and a number of post-processing options are provided.
20. For example, image frames 33-35 can be selected, to calculate Average values for 120-130 minutes post-injection. .
21. The full time-activity curves also be sent to the Kinetic Modeling tool directly.

11 Section 8: PMOD Database Management

11.1 S8-exercise 1: Creating a new database for a new project

As illustrated by all of the exercises in this workbook, PMOD includes the ability to organize all types of data into databases. Images in the databases are stored as DICOM, and components of processing, such as VOIs, TACs, protocols, are saved using our formats. The database functionality is available in all PMOD installations at no extra cost. Databases allow data to be clearly organized by studies/projects, and annotation within the database interface can help with treatment group labeling. Additionally, data within the database can be associated to greatly facilitate batch processing (e.g. association of PET/MR pairs for automated brain analysis). The database storage structure in the PMOD file system also makes backup and archiving of data and processing results convenient. After standard installation, two databases (Pmod and Demo) are available. In the following exercise a new database is created and some data sets “Replicated” between the Demo database and the new database.

1. Open the Users Configuration from the main PMOD toolbar.
2. Select the DATABASE tab, then select Add new data source (it may be necessary to use the menu drop down from Duplicate data source).
3. Use the name ExampleDB.
4. Make sure that Use Direct Connection is selected to use the embedded Java database. Defaults are used to fill in the entries defining the path for the database files (Database Path) and the actual data files (File Storage Area Path). These default locations are within the PMOD installation folder, however you can also separate the database location from the installation folder to allow easier version updates and backup schemes.
5. Activate Create Database to create the database tables. A confirmation message appears, stating that the database creation was successful (note – on Mac and Linux creation can be blocked due to folder access permissions. Contact us for Support in such cases).
6. The ExampleDB is now shown as the visible entry in the data sources list.
7. PMOD requires a restart to make the new ExampleDB available in all tools. Quit the Users Configuration with Ok. In the Save Configuration dialog window enable Quit Pmod to restart, then wait for PMOD to restart.
8. Open the View tool, and select the new ExampleDB entry in the database selection. Naturally it is empty.
9. Data can be directly transferred from one database to another using Replication. In this way an Import database and separate databases for Projects could be used.
10. Select the Demo database, then select the PET 3D series for PSEG2 PET/CT. Add it to the Selected For Loading list.
11. Expand the Export menu in the lower left and select Replicate.
12. In the green colored database selection menu, select the new ExampleDB, then Start Replication.
13. A confirmation message confirms whether Replication was successful.
14. Accept the message, then switch to the ExampleDB. The PSEG2 PET/CT PET 3D is now visible.
15. Alternatively, new data can be directly imported from DICOM or other image formats, or can be loaded for quality control before saving to Database in the usual way.

12 Section 9: Online Documentation of PMOD and Requesting Support

Beyond this workbook, comprehensive documentation for all of the PMOD tools is available via our website. The list of documentation can be found via the Resources > Documentation menu. For each part there is a choice between HTML structure, which includes navigation on the left-hand side and many links between items, and a downloadable PDF. The PDF can also provide access to simple searching using your own PDF reader software.

Support from our Application team is also available for your specific questions. Your support requests can be submitted through the interface within the PMOD software, or via our website.

Via the Support > Support Request menu on our website you will find instructions for direct support via the software Console interface, as well as a form to submit your request if email via the software is blocked by your institution.

12.1 S9-exercise 1: Access to further Documentation and Support

Please see www.pmod.com

Resources > Documentation

Support > Support Request