Cardiac PET Guidelines Version 3.4

Scope and Intended Use

This document has been prepared for the Cardiac Quantification Course in Zürich, Sept. 19, 2012. It is an addition to the User's Guide and section 6 of the general PMOD workbook which describes the basic steps for the quantification of well-behaved cardiac PET data. The main purpose of the current document is to give the users some additional guidelines and hints for processing clinical cardiac PET data with reliable outcome.

Copyright and Disclaimer

The example data which are provided for the course demonstrations and exercises are organized in the **Cardiac** database. The data are by courtesy of the following institutions:

- Nuclear Medicine, University of Florence, Italy; Prof. Dr. R. Sciagrà.
- Nuclear Medicine, University Hospital, Zürich, Switzerland; Prof. Dr. Ph. Kaufmann.
- Note that the original data have been processed and optimized for training purposes.

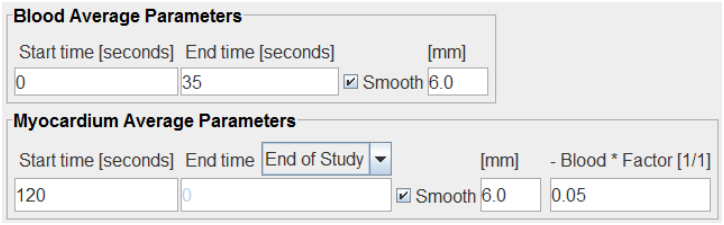
PCARDP Processing Recommendations

1. Automatic Processing

The recommended way of using PCARDP is to first optimize the frame averaging and then try using the automatic processing of the following two steps. If one of the steps fails to provide a good result, the subsequent steps are also invalid. The user has to manually correct the failing step, and from there on work interactively through the subsequent steps.

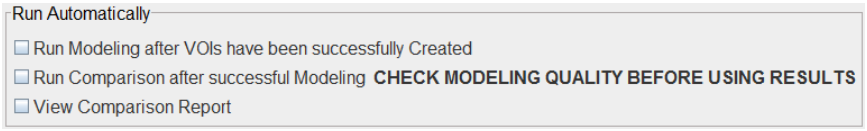
The following configuration of the cardiac tool options is recommended.

1. In the configuration panel, which is opened with the button, the correct tracer must be selected, and the averaging parameters should be reasonable for the acquisition protocol.



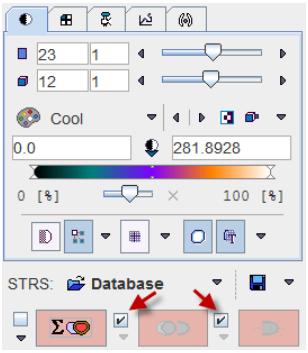
Note that the **End of Study** averaging is only suitable, if the modeling also uses all data to the end of the scan. If only the initial part is used, averaging should be restricted to the same frame range.

In the workflow area it is recommended to remove the checks of all boxes because the fully automatic procedure works only for few well-behaved data sets.



With these settings the TACs are only calculated and modeled when the user activates the **Modeling TACs** button.

2. On the **Reorientation** page of PCARDP enable all the two check boxes which correspond to the automatic processing steps as illustrated below.



The check boxes are located to the left of the red action buttons:

: Button to start the cropping/averaging process for calculating the BLOOD (average of some early frames while the tracer arrives in the left and right ventricle) and the MYOCARDIUM images.

: Button to start detection of the Short Axis (SA) orientation based on the BLOOD and the MYOCARDIUM images.

: Button to start detection of the myocardial centerline or the epi/endo boundaries. This is done by fitting a smooth model of the left ventricle (LV) shape to the MYOCARDIUM image and adjusting locally to the uptake pattern. The results are shown as contour lines in the SA images.

2. Cropping and Revision of Frame Averaging

Depending on the field-of-view of the scanner and the reconstruction settings, the heart may only cover a small fraction of the image volume. In order to ease processing it is recommended using apply a cropping procedure for restricting the image volume to the heart. Ideally, cardiac PET images should already be reconstructed with limited field-of-view centered at the heart, and with pixel sizes in the order of 2 mm.

The purpose of averaging the early (BLOOD) and the late frames (MYOCARDIUM) is to obtain images with optimal anatomical information to be used for the SA reorientation and myocardium detection. Their quality has a direct impact on the automatic procedures, and manual adjustments are also easier with clear images.
There are various reasons why the images calculated with the default averaging settings may not be optimal:

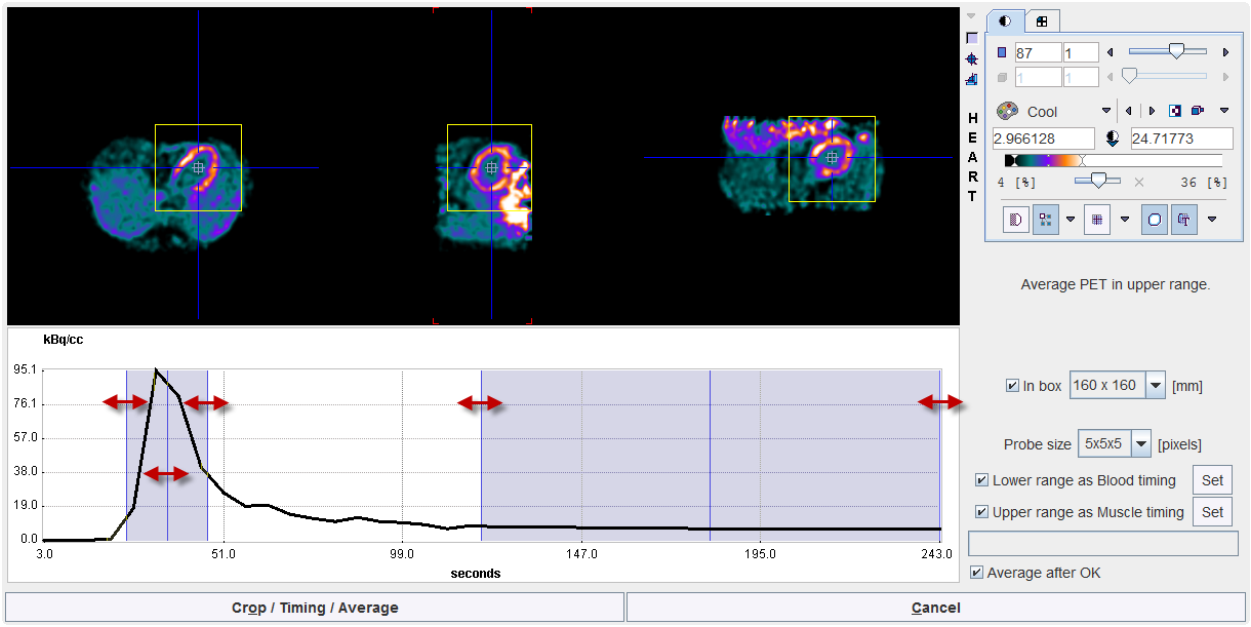
- Low injected activity, resulting in noisy images. Because of the dilution effect the tracer is not well seen in the cavity of the left ventricle (LV).
- Delayed appearance of the bolus so that too much background is included in the calculation of the BLOOD images.
- Poor tissue perfusion making the LV anatomy unclear. There is no real solution to overcome the problem. A workaround is using the BLOOD image as an additional guidance in outlining.
- Patient or heart motion causing a blurring of the MYOCARDIUM image.

The following procedure is recommended to generate optimal BLOOD and MYOCARDIUM images:

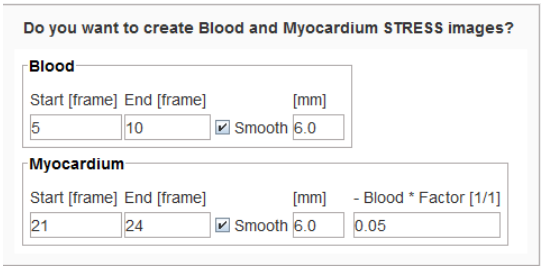
- Compare the Stress and Rest series and decide, which images have better quality. Work on these images towards a satisfactory solution.
- Select the button for the averaging process.

  A dialog window appears which allows to interactively specify a cropping window as well as the averaging ranges. The upper part of the window shows the average images. If the **In Box** check is enabled, a cropping volume is also indicated by yellow rectangles. The center of this box can be placed by clicking into any image plane. Before proceeding the box should be placed such that the whole heart is included in the box as well as enough margin is allowed for the SA reorientation.
  With each click an average time-activity curve (TAC) is calculated and shown in the lower curve panel. The sampling is performed averaged around the center mark with a configurable **Probe size**.
  The two shaded area overlaid on the TAC represent the time ranges for frame averaging. First click into the blood pool of the LV. The TAC curve should show a clear initial peak. Adjust the left area by dragging with the mouse so that the peak is enclosed. Next click into the LV wall to generate a myocardium TAC. Adjust the right shaded area to cover the relevant portion of the late uptake. If modeling only uses 4 min of the data, the myocardium averaging should ideally not extend past 4 min to avoid motion mismatch. Finally click again into the center for placing the crop box properly.

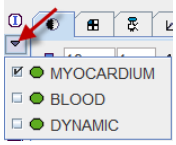


The operation button to continue is located in the lower left. It changes the naming according to the enabled options. With all options enabled (recommended) the button is labeled **Crop/Timing/Averaging**. When it is activated, the images are cropped and a dialog window is shown



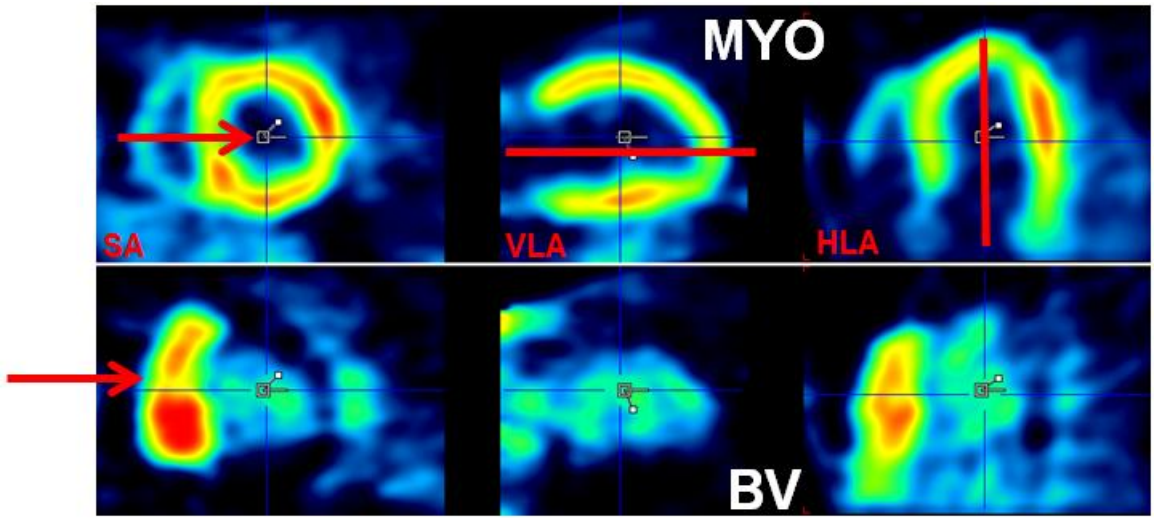
with the settings for the averaging operation corresponding to the shaded ranges. Upon confirmation, the averaging performed as prescribed.

- Because the “automatic” checks for the SA reorientation and contouring are on, those two steps are also immediately performed.
- The BLOOD images can be inspected by switching the series as illustrated below.



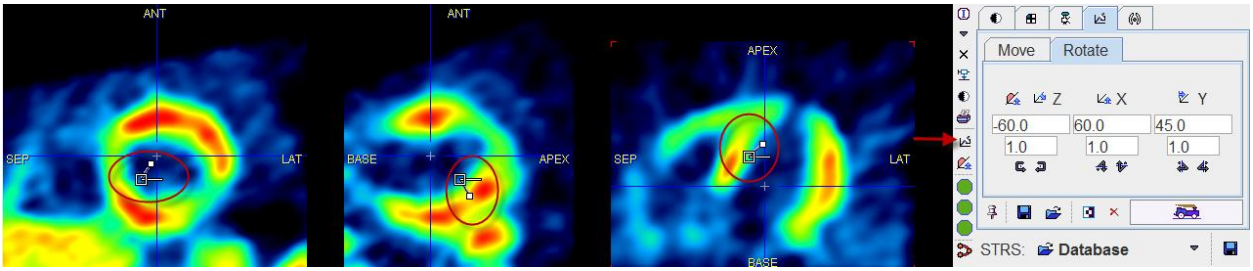
3. Revision of the Short Axis (SA) Reorientation

The aim of the SA reorientation is to bring the anatomical images into the well-defined LV position illustrated below. It is important that the right ventricle (RV) RV is to the left in the axial SA images, the axes are horizontal and vertical, and the rectangle is centered in the left ventricle (LV).



The following procedure is recommended if the automatic reorientation result is not satisfactory:

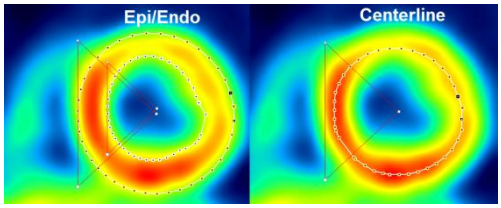
- If the orientation is quite reasonable, start manual reslicing with the button. Adjust the rotation angles and bring the rectangle into the LV center using the reslicing handles. Drag the filled white square for rotations, and the open rectangle for translations.



- If the orientation is completely off, use the button to initialize the reorientation. This operation corresponds to bringing a heart with “average” rotation angles relative to the patient axis into SA orientation. Then finalize the reorientation interactively as described above.

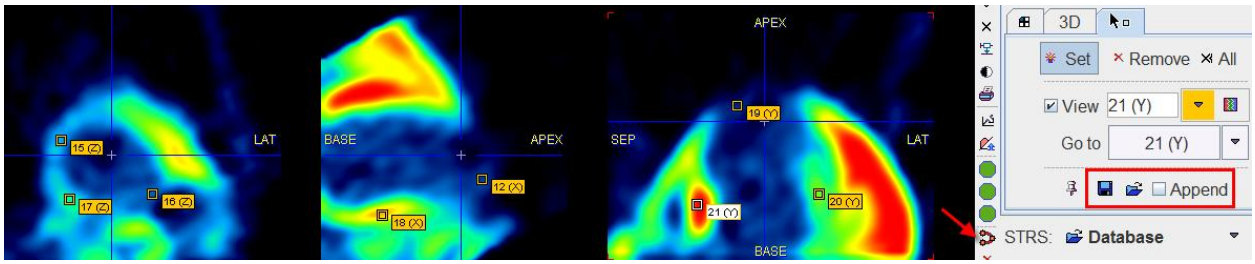
4. Revision of Myocardial Definition

After the images have been reoriented to correct SA orientation, try again the automatic myocardium definition by activating the button. The program will try fitting an analytical LV model to the MYOCARDIUM images and then adjust it locally according to the tracer uptake pattern. This procedure should work reasonably with images showing most parts of the myocardium, but may result in a distorted shape in the case of severe defects or activity close to myocardium. Generally, it is recommended to try improving the automatic result interactively, rather than outlining the contours in a fully manual fashion.
There are two types of LV definitions, either by the myocardial centerline or by the epi/endo boundaries. The preferred method can be set in the configuration of the PCARDP tool. Representative results after some interactive adjustments are illustrated below.



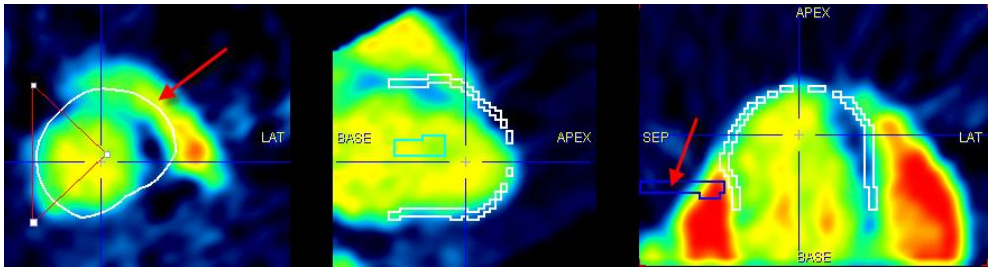
The following hints should help improving the automatic centerline definition. A similar approach is applicable for the epi/endo definition.

- Use the markers button to guide the LV model fitting procedure. As soon as the **Set** button on the markers panel is enabled, each click into the images will place a marker which is considered being located in myocardium. Try to place such markers in different planes and at different portions of the LV. Misplaced markers can be dragged with the mouse or deleted with the **Remove** button. The easiest way to triangulate the images at different locations without placing markers is to hold down the **`Ctrl+Shift`** keys while clicking. Another way of changing the anatomical location is to place the cursor over an image (SA, VLA, or HLA) and scroll slices using the mouse wheel.



  After placing enough markers retry the outlining with the button. It should result in contours closer to the markers.

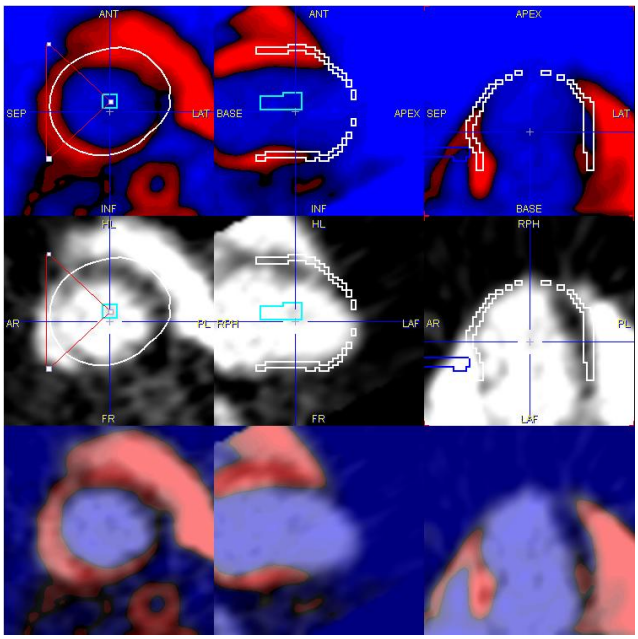
- To verify the outlining switch the images also to BLOOD. In this way locations of the contours can be detected which reach into the blood volume. Furthermore, locations can be found where the contours probably include neighboring activity, because they deviate too much from the boundary of the LV blood pool. An example of this problem is shown below.



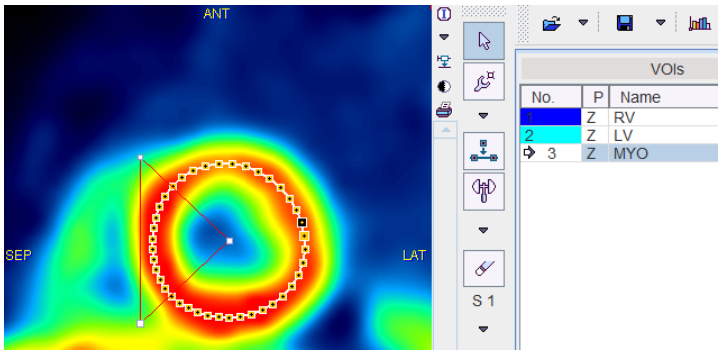
  In such a case the first action is to place new markers, focusing where the deviations occurred. An alternative to starting markers definition each time from scratch is saving the markers cloud before outlining, retrieving them, modifying their location and adding some new ones. This can be achieved using the Append buttons in the markers panel.

- Note, however, that potentially the BLOOD and the MYOCARDIUM images may not be exactly aligned, since they are offset in time and the heart or patient may have moved. The alignment of the two images can be inspected with the button. It opens a fusion tool with the MYOCARDIUM loaded in the first row, BLOOD in the second row, and their fusion in the third row. In the example below the

alignment seems quite good.

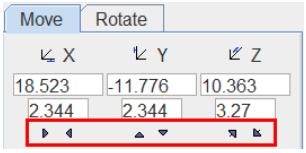


- If it is not possible to find a solution with an appropriate centerline in all SA slices, the contours can be interactively edited. To this end select the button  which opens the VOI tool with the Myocardium VOI selected.



Note that initially the SA slice images are shown, and the “VOI action” mode is active. This means that you can grab any edge of the enclosing bounding box and drag to scale the whole VOI. To change only the contour of the current slice, select the “ROI action” . VOI scaling followed by ROI scaling is often sufficient to rectify the contour, particularly if the **Radial Maximum** sampling is used. Alternatives for changing the contour shape are using the tool and shifting individual vertices by mouse dragging, or using the “hammering” tool and dragging against the contour. It is *not* recommended to delete the contour and draw it from scratch, but this would also work. If something goes wrong, remember that there is an **Undo** history available via the button to go back to earlier states of VOI definition.

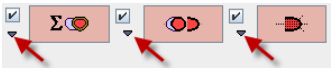
- The definition of the apex is often relatively difficult. In some cases the contours are quite reasonable, but in the HLA and VLA views they seem shifted slightly towards the base. A solution which can be tried in such a situation is to shift the *images*, rather than the contours. To do so, enable reslicing with the button and drag the images until the contours fit. Take care to avoid rotations by only dragging the open rectangle or using the increment buttons in the **Move** panel.



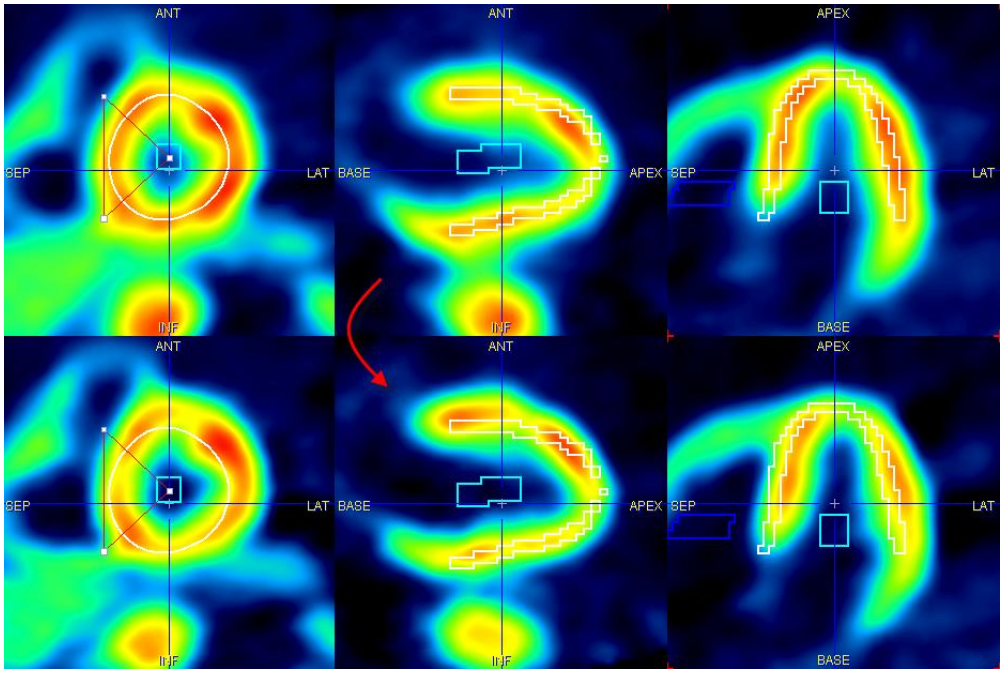
At the end of these operations there should be sufficient confidence that the contours describe the LV myocardium centerline appropriately.

5. Propagation of the Results between Stress and Rest

The similarity of the anatomy in the Rest/Stress studies depends on the acquisition protocol as well as the physiologic conditions. Often, there is enough similarity to use the information obtained with the above approaches in one of the series for the other series.
Illustrated below are the arrows which allow propagating Stress definitions to Rest. The first arrow copies the time averaging definitions, the second arrow the SA transformation, and the third arrow the myocardial definition.

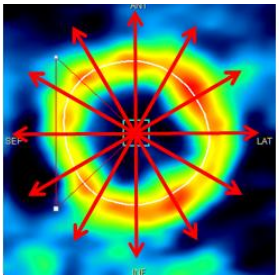


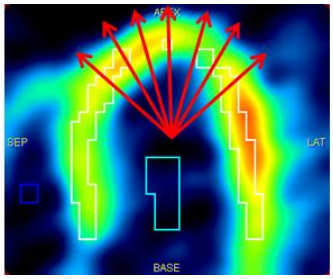
As sometimes the Rest data is better suited for the processing there are similar arrows for Rest to Stress propagation.
After propagation, some adjustment may be needed. In the example below the transformation and the contours were copied from Stress to Rest. A slight shift between the Stress images and the contours is notable. The recommended adjustment procedure is to try shifting the images (rather than the contours).



6. Selection of the Sampling Mode

For the quantification of myocardial function the PET signal of different area of the heart (the *segments*) is averaged. The calculation of these averages is called **Polar Sampling**, and its result are the segmental tissue time-activity curves (TAC). The polar sampling is detecting the myocardial activity by using radial profiles as illustrated below:

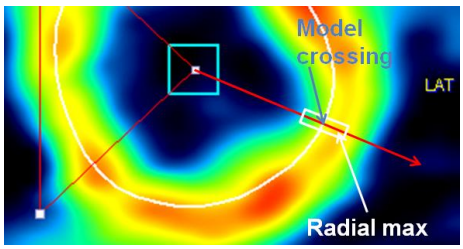




In the base and apical ranges profiles orthogonal to the long axis of the heart are applied, whereas rays on conical directions are applied in the apical part.

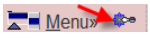
The myocardial centerlines or the epi/endo contours serve as a means for determining the location of the myocardium along the sampling profiles. There are essentially two different modes:

1. **Radial Maximum**: In this mode the maximum value of the MYOCARDIUM image along the profile determines the sampling location. Note that the maximum is searched within a window around the centerline which represents the expected wall thickness. This is for avoiding sampling outside the myocardium in cases without uptake in the myocardium. Maximum determination is limited in a similar fashion by the epi/endo contours.

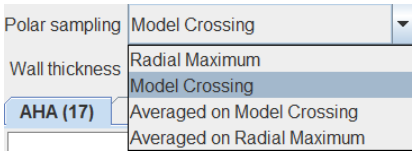


2. **Model Crossing**: In this model, the intersection of the profile with the centerline defines the sampling location. With the epi/endo definition, the center between the contours is regarded as the “model location”.

Note that the locations found are not strict pixel locations, but geometrical coordinates. Correspondingly, the program will calculate the image values at the sampling points by interpolation from the neighboring pixels. Radial Maximum is recommended if there is reasonable uptake in tissue, while Model Crossing allows the user to tightly control the sampling, at the cost of having to exactly define the contours.

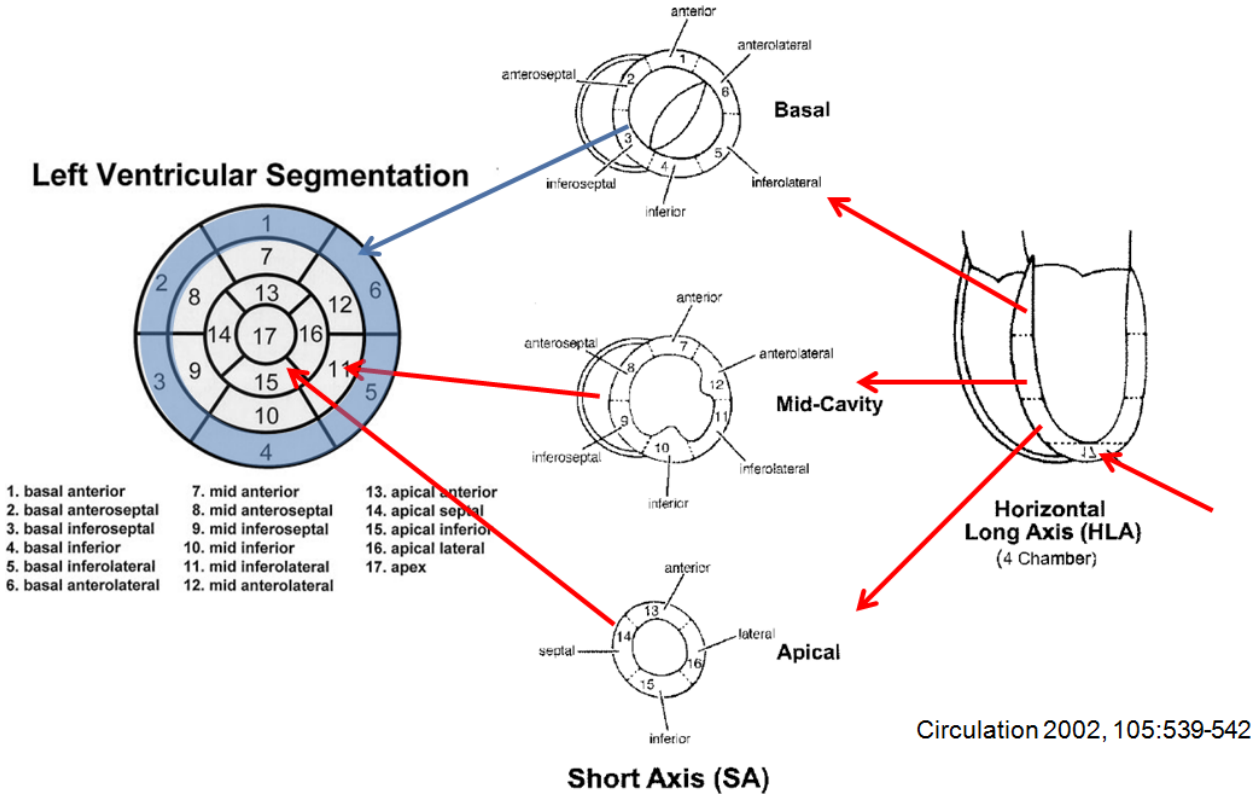
The sampling mode is defined in the configuration window which can be opened by the configuration button in the lower left 

. There are in fact four polar sampling choices as illustrated below.



With the “**Averaged on** ..” variants more than a single sampling point is determined: the left/right and the inner/outer neighbors will also be included. Note that the suitability of averaging is very depending on the pixel size: if the pixel size is large, the outer/inner samples might add information which is actually outside the myocardium. Therefore, averaging should only be applied with pixel sizes in the range of 2mm.

For the creation of the segmental TACs the subdivision of the heart area into tissue patches is relevant. Usually, the 17-segment AHA definition is applied as illustrated below.

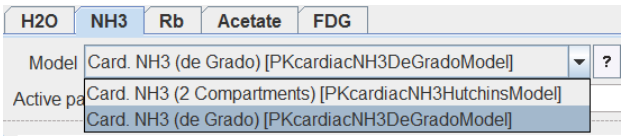


Correspondingly, every sampling point determined by Polar Sampling is sorted into one of the 17 segments, and the signals of all sampling points in a segment are averaged.

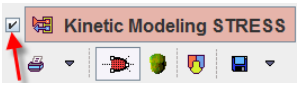
The sampling in the apex is quite delicate because often no clear uptake is seen in the image. A likely reason for this effect is the reduced wall thickness of the tissue from 8-15mm down to 2mm, combined with the motion due to contraction and breathing.

7. Quantification by Kinetic Modeling

Once the contours, the polar sampling and the segmentation have been defined, the segmental TACs can be calculated and quantified. To this end, an appropriate model has to be defined in the configuration. Our recommendation is to use models with a small number of parameters to be fitted, so rather 1- than 2-compartment models. Otherwise the identifiability of the parameters may be low, resulting in an excessive variation of the quantity of interest.



From a workflow perspective it is recommended to enable the automatic background fitting of the models by checking the corresponding boxes on the **Kinetic Modeling** page.



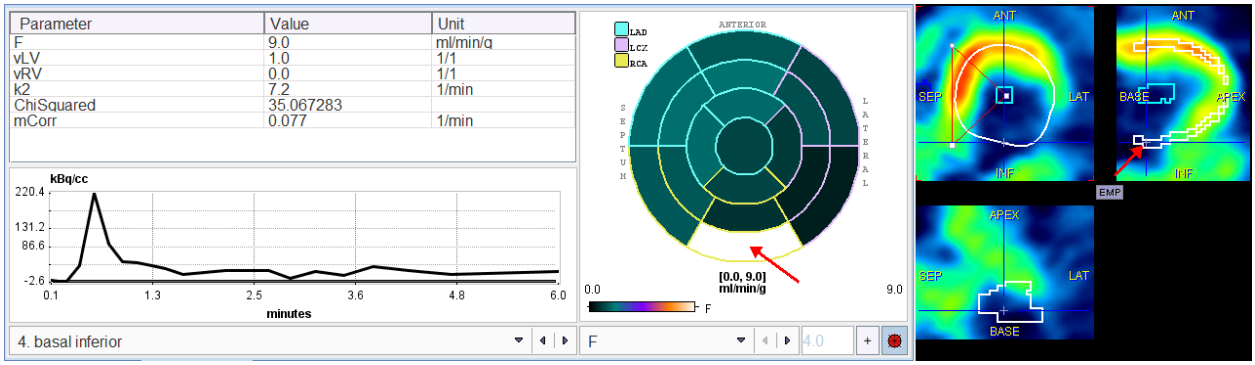
With this setting the kinetic models are fitted to the segmental TACs in the background each time they are calculated, and the results are immediately available.

Inspection of the Modeling Results

Careful preparation steps with the structured approaches described above will most likely result in stable and reproducible results. Nevertheless it is recommended to thoroughly inspect the quantification outcome.

1. Flow Outlier Analysis

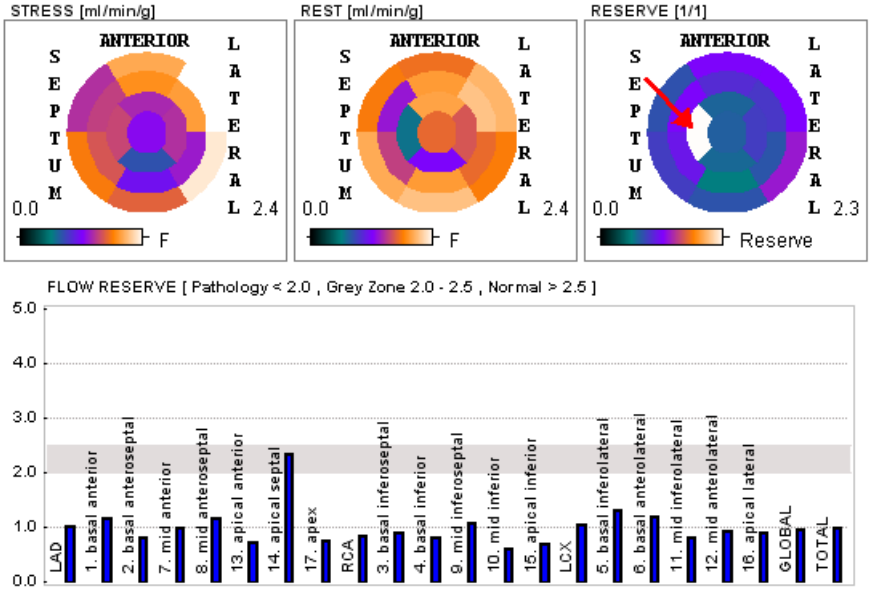
The polar plots provide a good overview of the results. In the example below it is obvious that in segment 4 (basal inferior) the determined flow value is beyond any other value. By clicking at the segment in the polar plot, the corresponding TAC and its quantification result is brought to the left panel, while the images in the display to the right are triangulated by the blue lines.



In the example above this evaluation clarifies the problem immediately: from the triangulation point in the images it is clear that there is no significant tissue uptake. Correspondingly, most of the signal is due to spill-over from blood in the LV cavity. This can be seen in the curve panel by the predominance of the initial peak, and from the value of the LV fraction in the TAC (vLV=1). As the tissue fraction (=1-vLV) is essentially zero, the flow value can have any arbitrary value without changing the model function.

2. Reserve Outlier Analysis

The reserve is best inspected in the **Compare Report** on the **Compare** page. It provides the three polar plots and a bar plot which make it easy to detect outliers. In the example below the CFR of segment 14 stands clearly out, most likely because of the small Rest value.

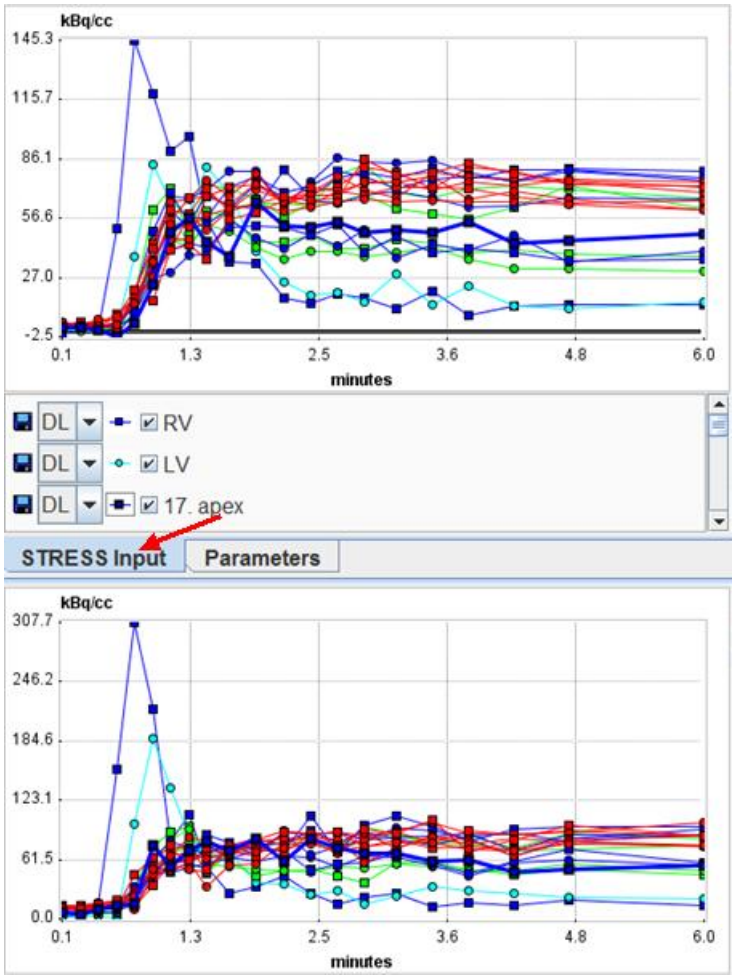


In this case the sampling for TAC 14 should be investigated in the Rest study, because the flow at Stress is not suspicious.

3. Common Scaling of Flow Values

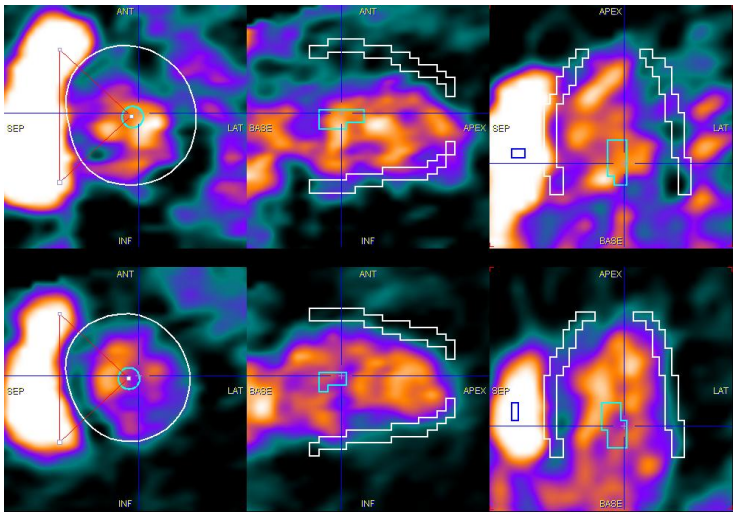
It is important to remember that the result of perfusion quantification by kinetic modeling is crucially dependent on the input curve, i.e. the LV TAC. If the input curve is scaled, all resulting flow values will be scaled in inverse proportion. As a consequence, scaling the Rest or Stress input curve evenly scales the CFR in all segments.

Therefore, inspection of the LV curves is important. This can be easily done by selecting the **STRESS Input** and **REST Input** tabs on the **Modeling** page. In the example below it is obvious that the LV curve (light blue) in Stress (upper plots) is much smaller relative to the segmental TACs compared to Rest (lower plots). Consequently, Stress flow must be significantly higher than rest flow, resulting in a substantial overall CFR value.



An input curve will be scaled towards lower values, if its LV VOI is not placed completely within the blood volume. The LV VOI is automatically placed as a function of the LV model: it consists of circle ROIs which are centered within the basal part of the LV model. If this is not adequate for some reason, the input curve will be wrong. In this case the LV VOI should be manually edited. The VOI editor for this purpose is started with the middle VOI button.

The example below illustrates a case where the LV blood pool is not very well delineated because of streak artifacts from reconstruction by filtered back-projection. However, the LV VOI location is quite comparable at rest and stress and thus not suspicious.



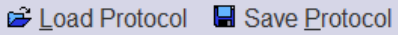
Note, however, that the BLOOD image only represents the initial part of the input curve, so that shifting the LV VOI based on this information alone may also lead to wrong conclusions.

Concluding Remarks

The quantification of dynamic cardiac PET data is a complex task with several potential pitfalls. Accurate results can only be obtained, if the heart did not move “too much” during the acquisition. This should always be inspected using the dynamic images in SA orientation. Only under this premise should the methodology in PCARDP be applied.

Although PCARDP embodies automatic approaches, the outcome always has to be carefully inspected and corrections applied if necessary. This will require understanding of the principles and mastering the tools of PCARDP, but with growing experience the processing will deliver reliable results as documented in several publications.

Because the processing of a data set in PCARDP is quite involved and later inspection may be required, it is highly recommended to save not only the quantifications results, but also all auxiliary information such as the SA transformation and the VOI definitions. This can most easily be achieved by saving the processing state as a “protocol” with the **Save Protocol** button.



When loading such a protocol with the **Load Protocol** button, all processing steps are replayed and they are then available for inspection.