User's Guide

PMOD Cardiac MR ModelingTool (PCARDM)

Version 3.5

PMOD Technologies

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PMOD Cardiac MR Modeling Tool

Cardiac Perfusion MR

Perfusion assessment by cardiac magnetic resonance (CMR) is clinically applied for the detection of coronary artery disease. The standard method uses the injection of a contrast agent bolus and dynamic imaging while the bolus passes the myocardium. The contrast agent enhances the MR signal of blood so that tissue with reduced perfusion appears darker than well-perfused tissue. Today's analysis of first-pass CMR images is a manual, interactive process resulting in relative scores such as "normal", "probably normal", "probably abnormal" or "abnormal". An overall perfusion score and scores related to the vascular territories are derived from the scores assigned to 16 standard segments. Although the use of such scores is a proven clinical method, CMR image analysis is time-consuming, not fully objective, and definitely requires expert readers.

Quantification of Cardiac Perfusion MR

The principle of CMR is similar to the use of tracers in PET, but involves complications due to the facts that the MRI signal is not always proportional to the contrast agent concentration, and that the MR acquisition is not volumetric. For more than a decade, researchers have worked on solving these problems and have recently approached truly quantitative, high-resolution perfusion CMR. These new solutions will broaden the applicability of CMR and bring added value to patients with globally reduced perfusion by multi-vessel obstruction or micro-vascular disease, which cannot be detected by a qualitative evaluation.

Cardiac MR Modeling with PCARDM

PMOD's PCARDM tool is a joint development by PMOD Technologies and the CMR research group of ETH Zurich, Switzerland. It combines PMOD's long-standing modeling expertise with ETH's leading-edge MR methodology in a comprehensive package for qualitative and quantitative CMR image analysis. Using PCARDM, researchers in the field of CMR may apply the state-of-the art perfusion quantification approaches to their data and compare them with the standard qualitative outcome or an external gold standard. The PCARDM tool is most useful when bundled with accelerated MR acquisition sequences, whereby the full extent of the heart can be imaged in a single breath hold [1]. Currently, such a unique bundle is offered by GyroTools LLC for Philips MR research sites.

Requirements

The PCARDM tool requires gadolinium first-pass CMR images. As of now, full quantification is only supported for specific Philips MR acquisition sequences and dedicated reconstructions, which can be obtained from GyroTools (www.gyrotools.com). The MR acquisitions required for fully quantitative CMR include:

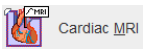
- Dynamic gadolinium first-pass scan: A 3D k-t PCA sequence which is able to acquire volumetric contrast images covering the entire left ventricle within a breath hold of 20 seconds. Taking into account ECG triggers, contrast images can be reconstructed which are practically devoid of motion. It is recommended setting ECG-triggering to end-systole. This minimizes heart motion and the myocardium is thickest due to the contraction. The images should be acquired in short axis orientation and loaded such that the apex appears to the left (first slice).
- B1 scan (COCA): A volumetric sequence allowing the assessment of the B1 field inhomogeneity of the surface coils. This scan can be omitted if the B1 field across the heart is sufficiently homogeneous.
- T1 scan: A single-slice sequence measuring the global T_1 relaxation time in the blood pool and the myocardium in a mid-ventricular slice using four time points. It is applied for converting the MR signal to contrast agent concentration. This scan can be omitted if the relation between contrast agent concentration and MR signal is linear.

Only a partial analysis can be performed with the images from classic gadolinium first-pass CMR sequences available on current clinical scanners. These acquisitions are longer, subject to breathing motion, and provide only 3 slice images at representative levels of the left ventricle.

User Interface

Starting the PCARDM Tool

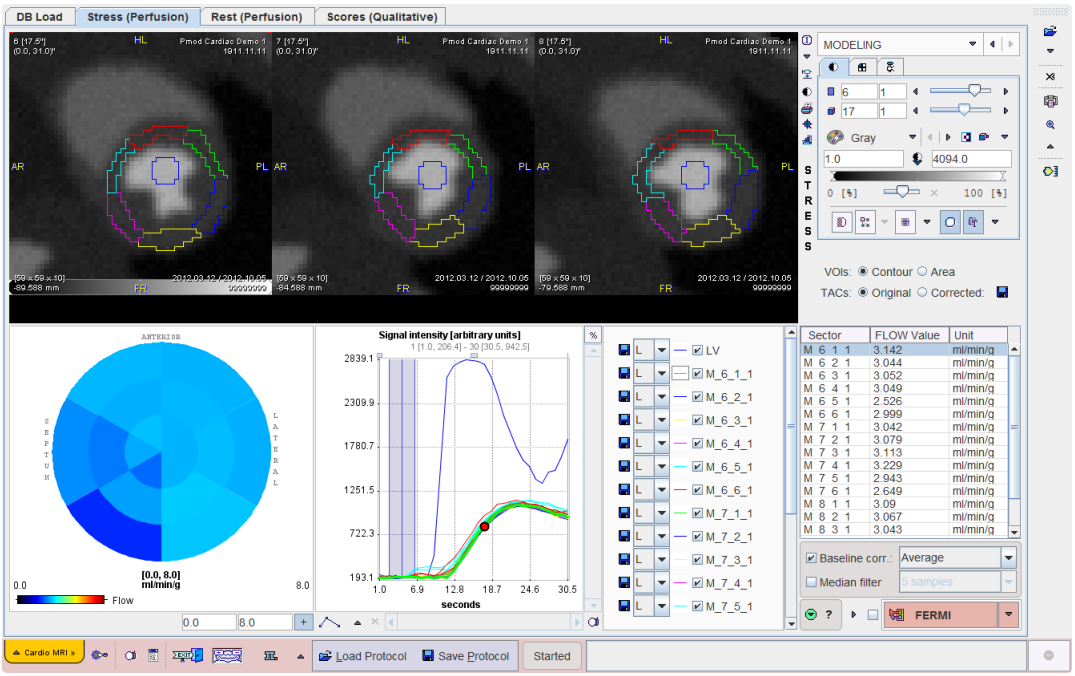
The PCARDM tool is started with the **Cardiac MRI** button from the PMOD ToolBox



or by directly dragging image files onto the above button.

The user interface of PCARDM consists of four pages which can be selected by tabs:

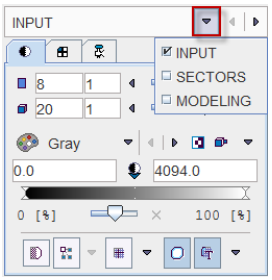
1) **DB Load** page: This page is only available when using PMOD databases.
2) **Stress (Perfusion)** page: Page for the step-wise analysis of the stress scan.
3) **Rest (Perfusion)** page: Same page as for the stress scan, but for analyzing the rest scan. Definitions resulting from the stress analysis can be used as initial settings to be improved.
4) **Scores (Qualitative)** page: Page for interactively assigning visual scores to the heart sectors.



These pages is described in separate sections of this guide.

Step-Wise Processing

Flow quantification on the **Stress (Perfusion)** and **Rest (Perfusion)** pages is organized by a stepwise progression towards the end result. On each processing stage the user has to take some action such as data loading, heart sector definition, or kinetic modeling and then start the next processing step with the red action button located in the lower right. As soon as the result is calculated, it will be shown on the next page representing the new processing stage. The cascade of stages is available by the selection area in the upper right.



It conveniently allows inspecting the results of prior stages without initiating any calculations. To repeat a calculation with modified parameters, the action button in the lower right has to be activated again. The idea is to first fully process stress data, and then the rest data.

Convenience Buttons

Next to the action button is an area with two or three buttons

offering the following functions:

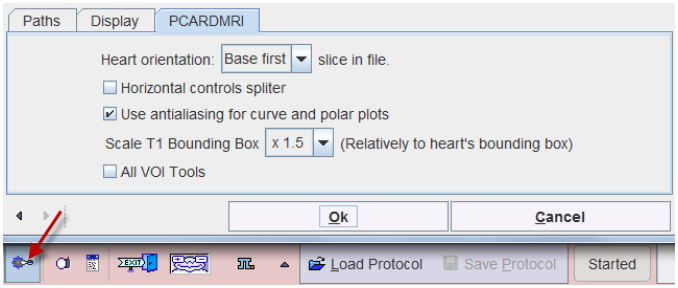
- Hide the parameters panel to free some space in the user interface. With the panel hidden, the icon changes to . When this button is activated, the panel is shown again.
- Button to copy the definitions specified on the **Stress (Perfusion)** page to the **Rest (Perfusion)** page. The idea is that the analysis is first performed with the stress data, and then the stress definitions are adjusted to the rest images.
- ? Display help information for the current page.

Protocols

PCARDM allows saving the final processing configuration as a protocol. Such a protocol includes definition of the input data as well as the parameters of the different processing stages. It is advised saving a protocol after every completed data processing, so that at any later time the configuration can be retrieved, verified and modified to try variations of the processing parameters.

Configurations

The PCARDMR tool can be configured according to user preferences in a dialog window as illustrated below.



The **Heart orientation** configuration is important. It should be configured in such a way, that the apex appears as the first slice after loading, i.e. as the leftmost image in the display. Please make sure that when loading images of a new study type that this requirement is met.

Documentation

The PCARDM tool is based on a range of functionality from the PMOD environment which are not explained in this documentation. Please refer to the

- *PMOD Base Functionality Guide* for information related to data loading, image viewing, volume-of-interest (VOI) definition, statistics, results aggregation, and the
- *PMOD Kinetic Modeling Tool Guide* for information regarding the fitting of models to measured time-concentration curves.

Methodology Overview

In PCARDM, left ventricular perfusion is quantified by the following steps:

- Loading of the dynamic perfusion series. Here it is important that the acquisition timing information is correctly interpreted, because otherwise modeling will not provide correct results.
- Interactive cropping of the heart volume from the surrounding tissue.
- Loading of the B_1 correction map (COCA) and correction of the perfusion signal (optional).
- Interactive definition of the left ventricle segments in all slices of the left ventricle.
- Interactive definition of a representative blood volume in the center of the left ventricular (LV) cavity.
- Calculation of the average MR signal curves in the LV segments and the LV cavity.
- Loading of the T_1 series and geometric interpolation to the perfusion scan (optional).
  - Calculation of the average T_1 in the LV segments and the cavity.
  - Conversion of the signal curves to contrast concentration.
  - Optional concentration curve filtering and baseline correction.
- Quantification of the segmental concentration curves by one of the available methods, using the LV cavity contrast concentration as the arterial input function. The result is a segmental perfusion value in [ml/min/g] per segment.
- Calculation of the segmental coronary perfusion reserves.
- Documentation of the outcome in comprehensive reports.
- Saving of all configurations in a protocol so that the data analysis can be exactly reproduced and examined any time later.

Data Processing

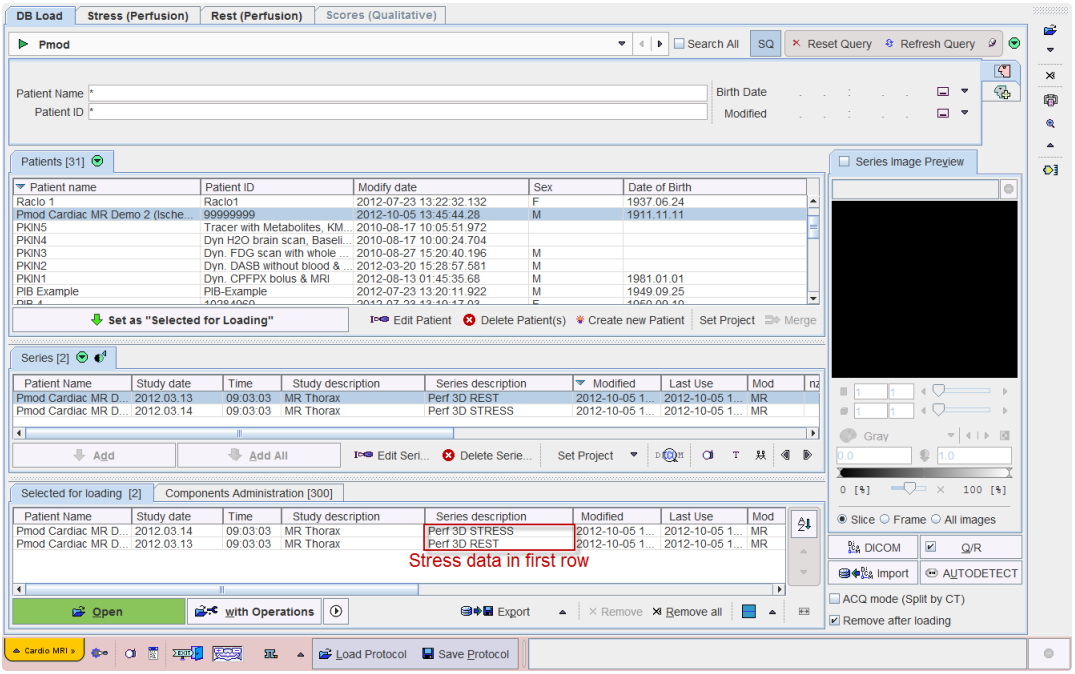
Stress and rest studies are processed sequentially on different pages, whereby the user is guided in a step-by-step manner. Please start on the **Stress (Perfusion)** page to first

completely process the stress scan. The rest scan will subsequently be processed in exactly the same way.

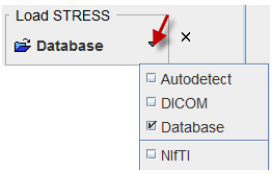
Input Data

Image Loading

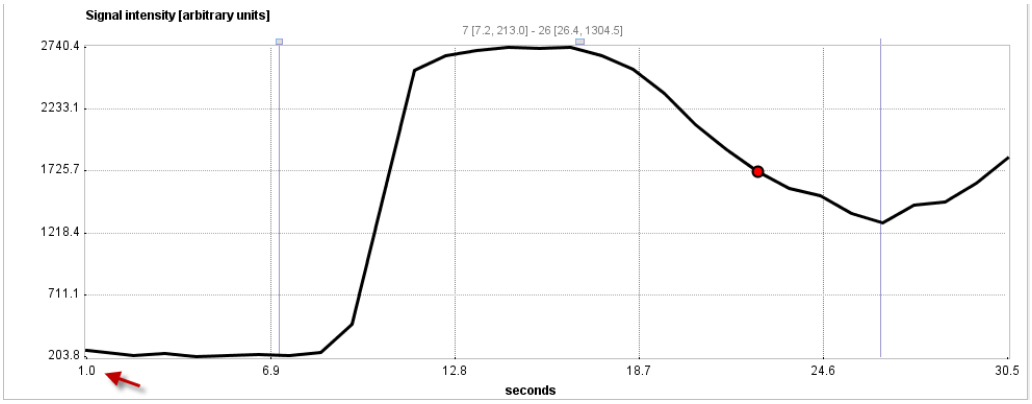
If the MR perfusion data resides in a PMOD database, it can be loaded from the **DB Load** page as illustrated below. It is important that the stress scan is in the first row of the **Selected for loading** area so that the images end up on the proper page.



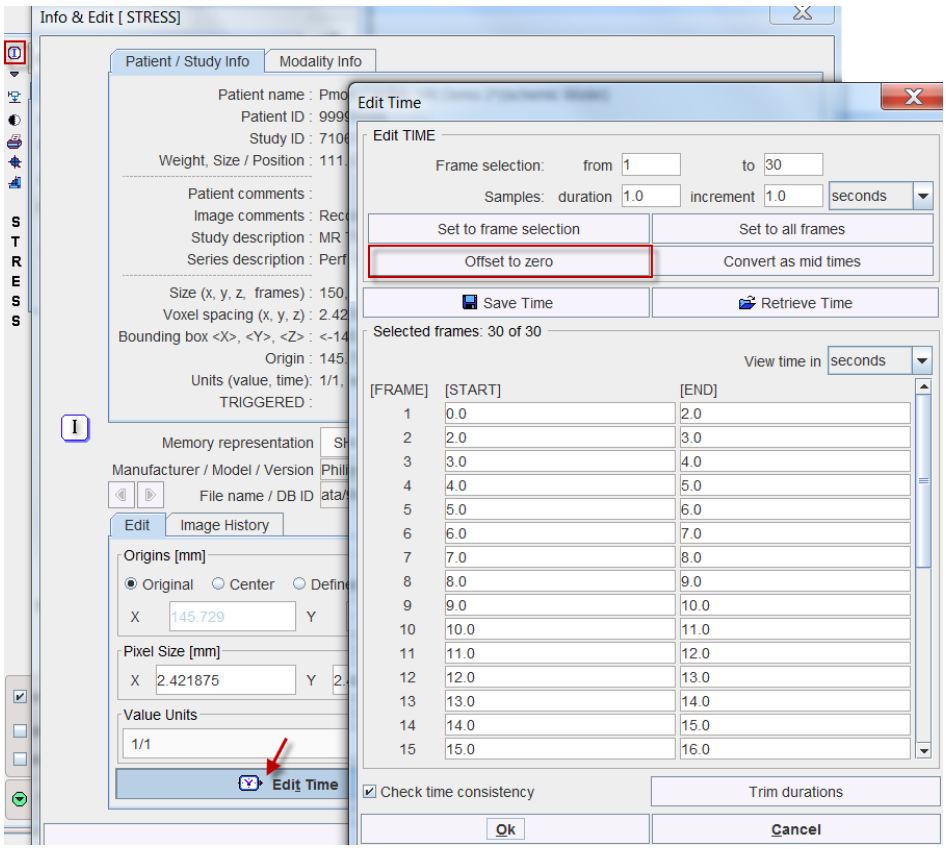
Alternatively, the images can be loaded directly from the **Stress (Perfusion)** page using the **Load** button which can be configured to the appropriate format using the arrow button indicated below.



It is important that the timing of the sequence is correctly interpreted and that the first scan starts at time zero. Therefore, please inspect the time axis of curve area which should start with a value close to zero. It is not exactly zero, because the signal curve is plotted using the mid-time of the scans. The value of 1 sec in the illustration below is the mid-time of the first acquisition starting at time zero end ending after 2 seconds.



The timing can be inspected and corrected in the **Edit Time** window. To this end use the information button and in the appearing information window activate the **Edit Time** button.



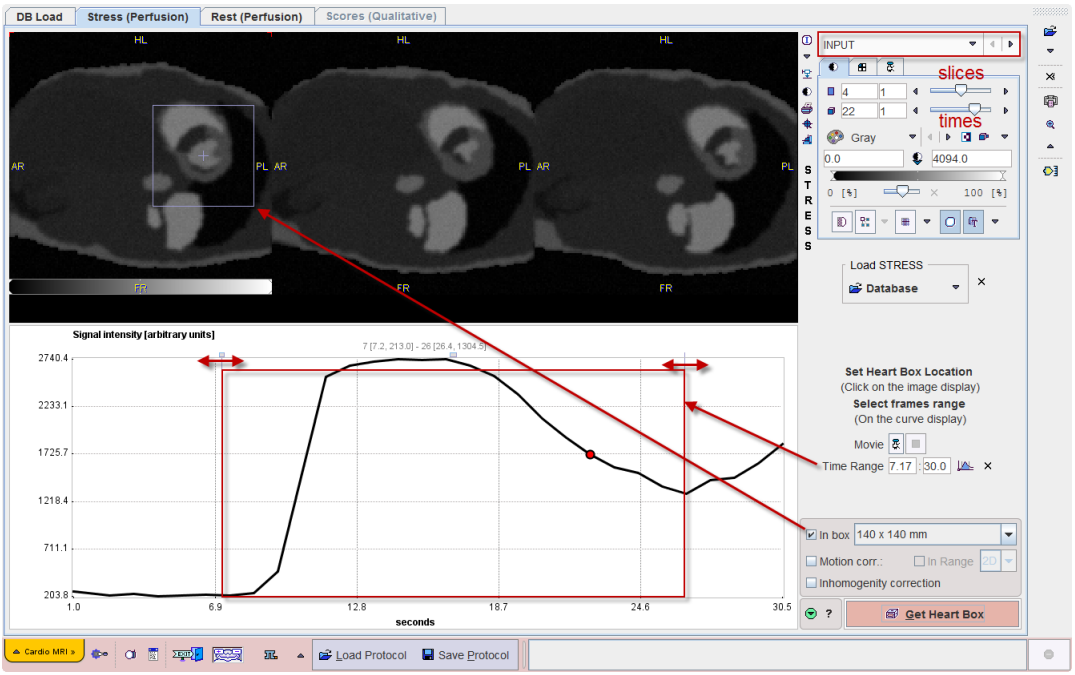
Note the **Offset to zero** button for correcting a constant time offset. Alternatively, the times can be manually edited or loaded from a file with **Retrieve Time**.

Data Cropping

The data should be cropped in two ways:

1) spatially, to remove signal remote to the heart, and

2) in the time domain, to only include proper first-pass signal.



Heart Cropping

If the **In box** is checked, a square is shown in the images which should be centered on the left ventricle. To do so, just click into the center of the cavity. Verify that all slices of the LV are within the box by moving the slices slider left/right. If the box is too tight, a bigger size can be selected from the size list. Note that the motion of the heart during the acquisition can be inspected by moving the times slider. Ideally, motion due to respiration is only minimal.

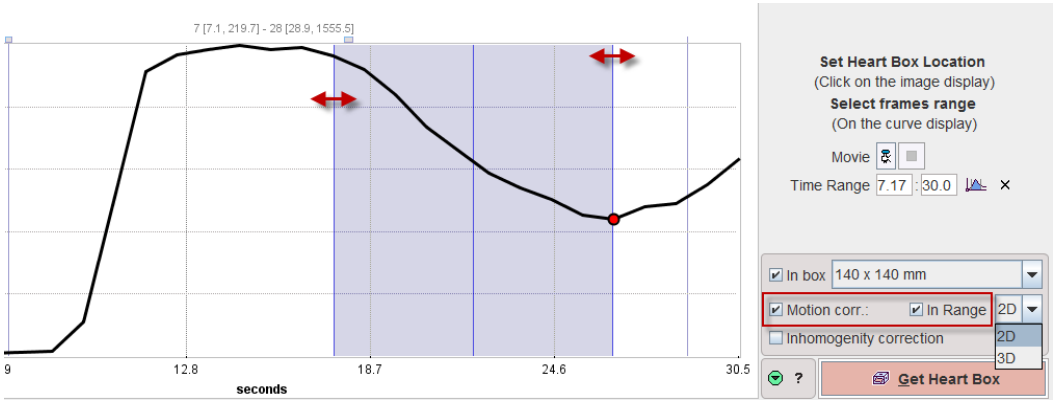
Time Range

The time range of the data used for the perfusion quantification should be restricted to the first-pass phase. The initial part is removed to avoid a signal bump or other erroneous signal contributions specifically for kt-PCA reconstructed data due to the temporal correlations included in the reconstruction process. It is particularly important to avoid late signal with recirculating contrast agent. The start and end times can be specified numerically in the **Time range** section. Alternatively, corresponding markers can be dragged directly in the curve area as indicated above.

Data Correction

Motion Correction

Cardiac MRI data are acquired with ECG-gating and ideally during a single breath hold. In this case motion should only be minimal. However, if the user detects that the heart is not still, then he can try correcting it. To this end the **Motion corr** box needs to be checked.



Motion correction can be restricted to a part of the sequence (e.g. the late part) by the **In Range** box. With this box a blue shaded range appears in the curve area which can be adjusted to the affected acquisition phase by dragging the edges. The motion correction algorithm operates in **2D** or **3D** mode. **2D** will only look for in-plane motion, while **3D** also allows vertical motion.

Inhomogeneity Correction (COCA)

Ideally, the scan sequence includes an acquisition for measuring the B_1-field inhomogeneity in the area of the heart. With the dedicated scan sequence provided by Gyrotools this scan is called **3D COCA**. In this case the **Inhomogeneity correction** box should be enabled.

Please activate the **Get Heart Box** action button to start the corrections. If **Inhomogeneity correction** is enabled, a window will open in the course of the processing to select the COCA scan.

Heart Segment Definition

The corrected data are shown on the **SECTORS** page. The task on this page is to define on each acquired slice the sectors of the myocardium. The MR signal will be averaged in each segment and used for the quantification of perfusion.

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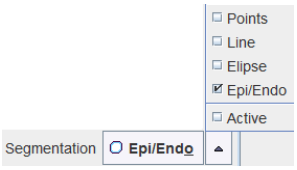
Overview of Myocardium Segmentations

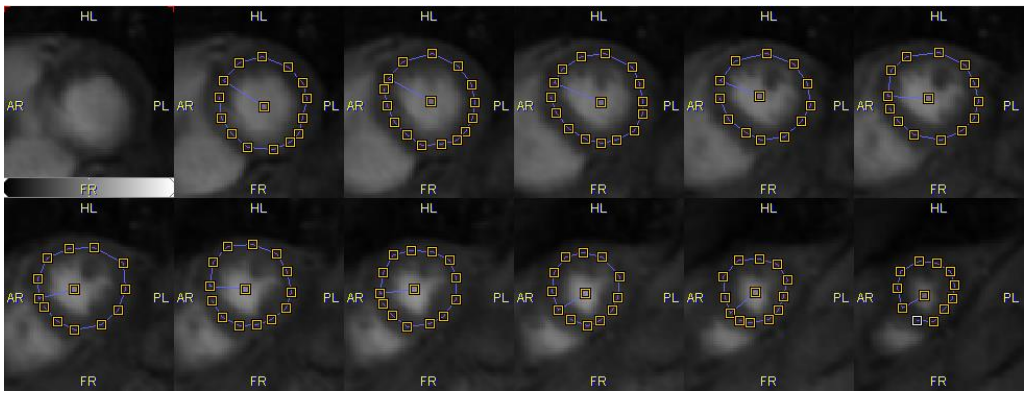
There are several segmentation methods available in the **Segmentation** list:



Basically, three categories of segmentations can be distinguished.

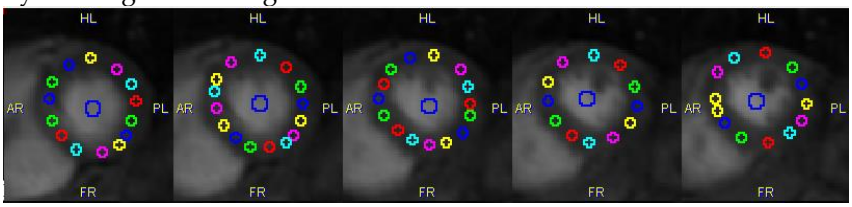
Manual Segmentations with Marker Points along Myocardium Centerline

With these methods the user first has to manually place markers along the myocardium centerline in all slices covering the left ventricular wall. The example below shows a volumetric acquisition with 11 relevant slice images together with the defined markers.

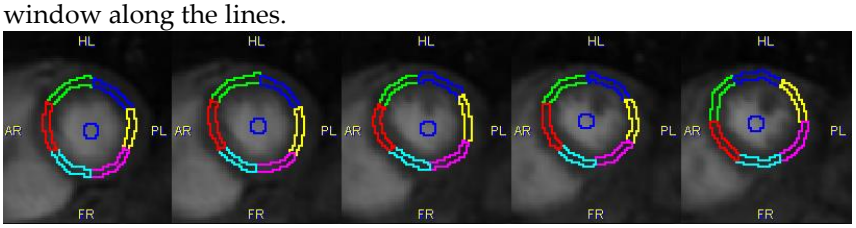


Based on these markers the segments for averaging the MR signal are derived as follows:

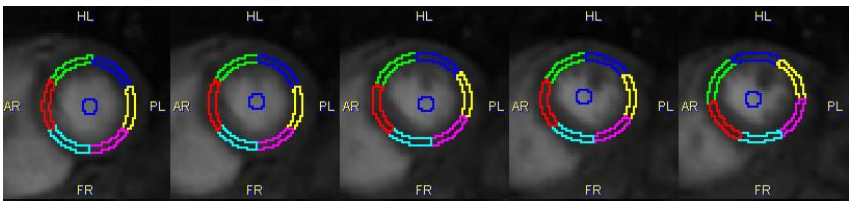
Points By creating circular regions of interest at the location of each marker.



Line By connecting the markers by lines and sampling the pixels in a certain window along the lines.



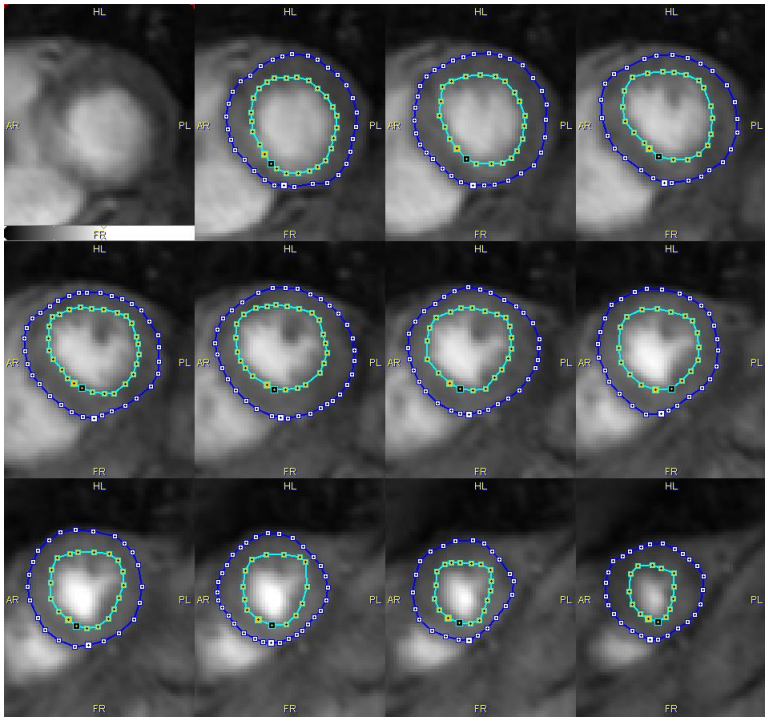
Ellipse By fitting an ellipse to the markers and sampling the pixels in a certain window along the ellipse.



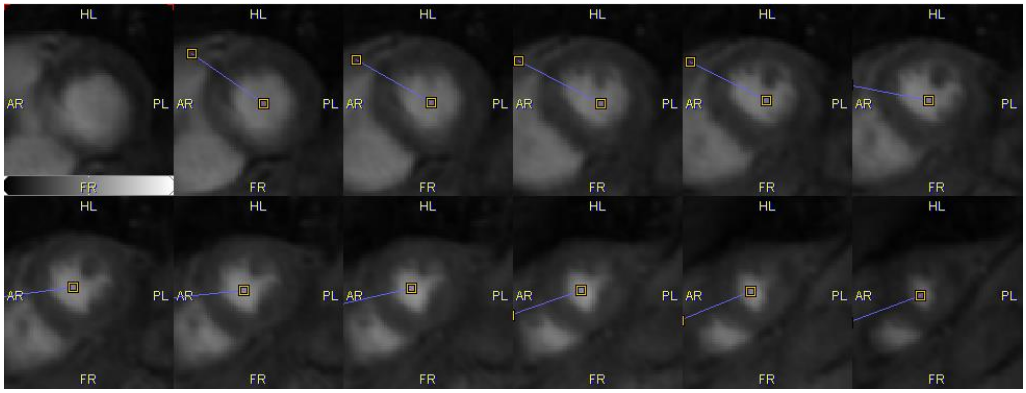
Note that the **Line** and **Ellipse** segmentations result in a well-defined number of segments per slice which can be defined by the user, and for which the user has to manually define a starting point.

Manual Segmentation with Epi/Endo Contours

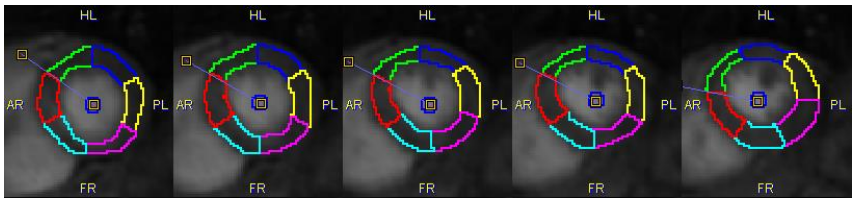
This method requires the user to manually outline the outer boundary (epicardium) and inner boundary (endocardium) of the left ventricular wall.



In addition he has to define a divider line by marking the LV center and the location of the RV edge:



The **Epi/Endo** then divides the area between the two contours into a specified number of segments, resulting in a segment definition as illustrated below.

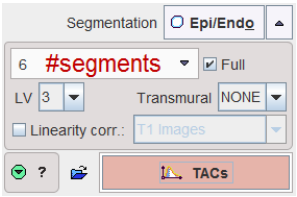


Automatic Segmentation with Active Contours

This method is experimental. It also requires markers along the centerline and tries to automatically detect the epi-and endocardial boundaries. Please refer to the online **?** for some additional hints.

Sectoral Schemes

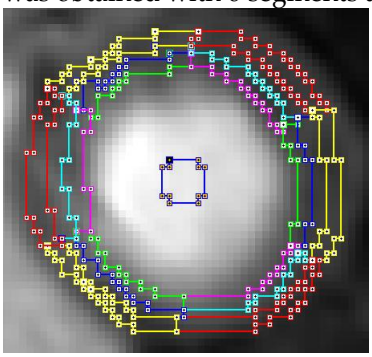
The generation of segments for the different segmentation schemes is driven by additional configurations such as illustrated below for the **Epi/Endo** segmentation.



Configuration items:

- **6** Number of segments (N): The 360° of a full rotation will be divided into (N) equal angles. 6 is the recommended setting.
- **Full** box: If enabled, sectors with an angle (360°/N) will be used, otherwise (360°/N-20°) creating gaps of 20°.
- **LV**: Radius in pixels of the circular LV ROI representing contrast in the cavity.
- **Transmural**: This setting allows subdividing the sectors in the radial direction in an attempt to quantify the transmural perfusion gradient. The example illustrated below

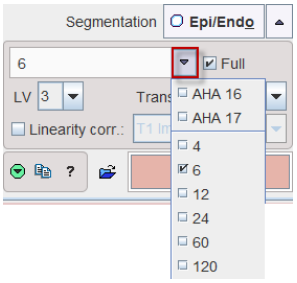
was obtained with 6 segments and 3 transmural sectors.



- **Linearity corr**: If this box is enabled, the program will perform a correction as described *below* (on page 25).

Segments Number

The selection for the segments number is illustrated below. It includes the division into **4**, **6**, **12**, **24**, **60** and **120** angular segments of decreasing size.



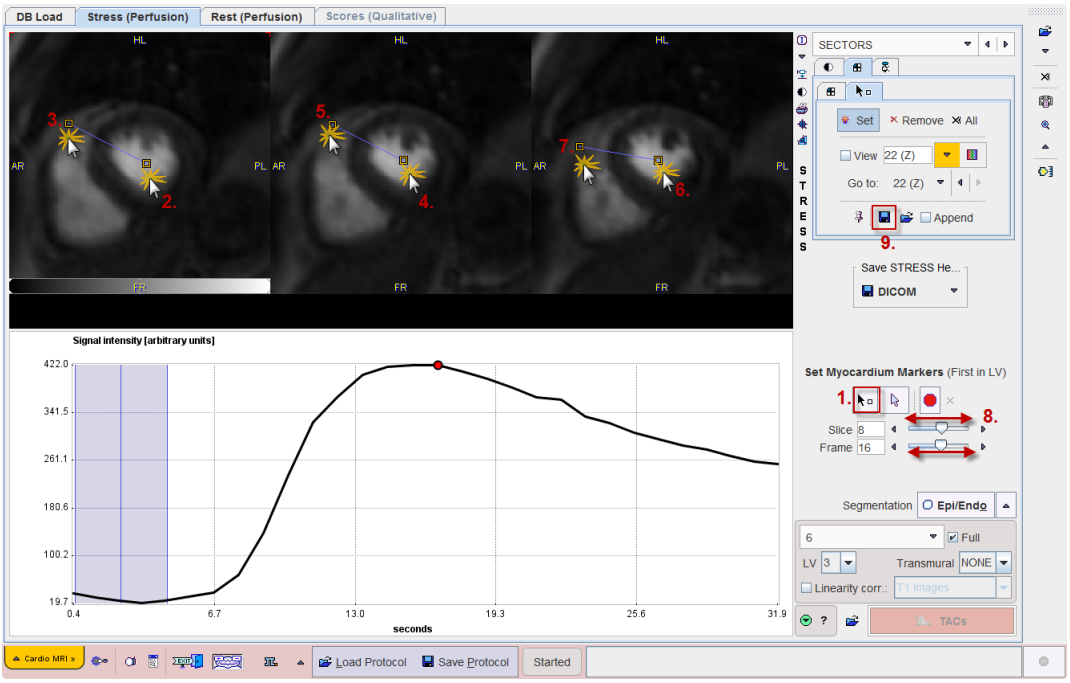
The **AHA 16** and **AHA 17** selections are specific: they will apply 6 sectors in the basal and mid-cavity slices, and 4 sectors in the apical slices. **AHA 17** includes as a 17th segment the apical cap. These definitions can only be applied with at least 4 slices.

Epi/Endo Segmentation

The Epi/Endo segmentation is the recommended analysis methodology. It consists of three steps which are described below.

Septal Angle Definition

The first step consists of defining in each relevant slice the center of the LV cavity and the edge of the right ventricle.



Please proceed as described below and indicated in the illustration above by the numbers.

1) Switch on markers definition by activating the button.

2) In each slice, first click into the LV center, then to the RV edge as illustrated.

3) Use the **Slice** slider to move to the next short-axis slices. Repeat markers placement, until all slices are covered.

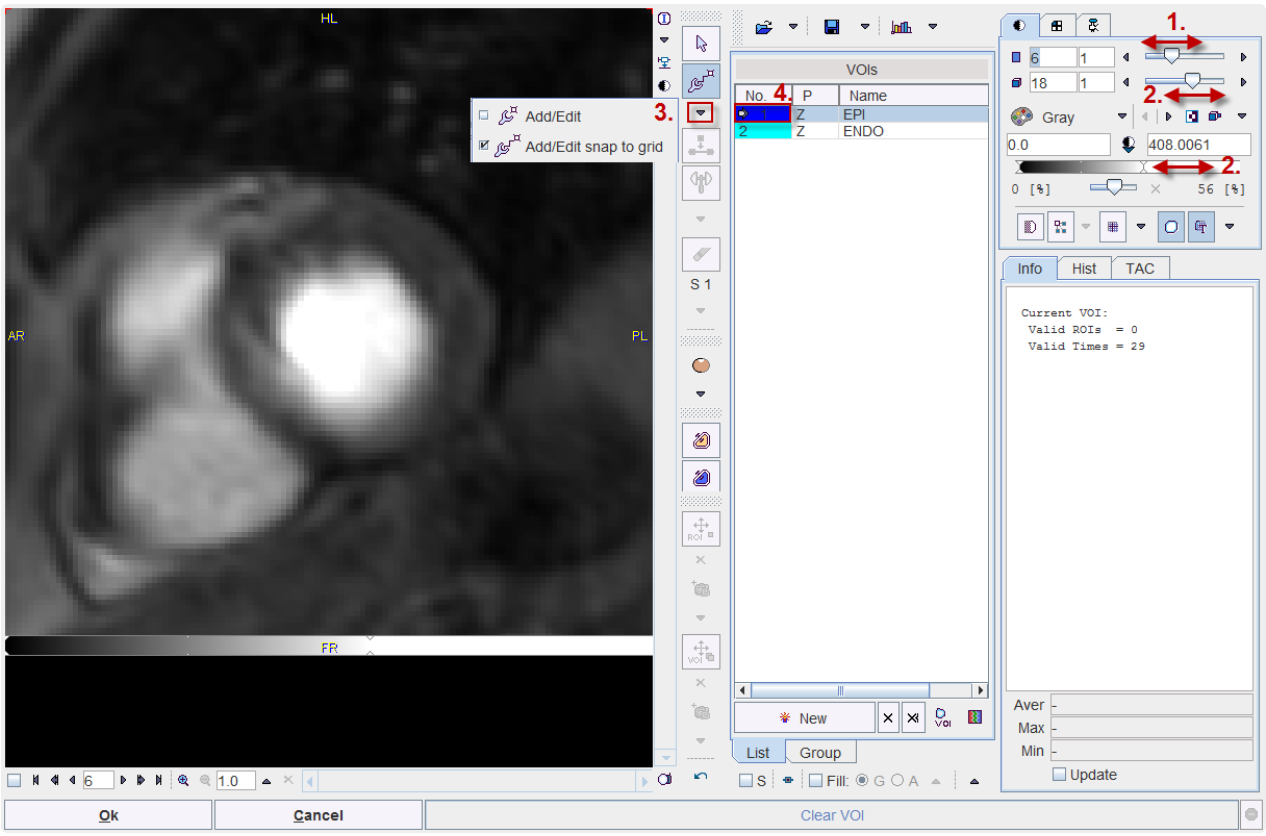
4) Use the **Frame** slider to change the image contrast.

5) Optionally, save the markers definition with the indicated button (9.). Note that the markers are automatically saved if the data resides in a PMOD database.

Contour Definitions

The second step is the definition of the epi- and endocardial contours. It is started with the red (indicating empty definition) button in the lower right.

A dialog window opens which shows one slice together with tools for the contour definition.



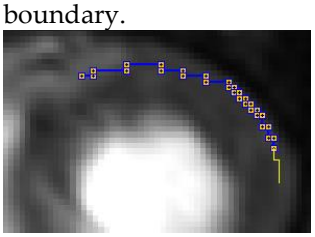
Perform the contouring as follows:

1) Select the most basal slice with the slice slider (1.).

2) Optimize the image contrast for identifying the myocardium by changing the dynamic acquisition (2.) or the upper threshold level (2.).

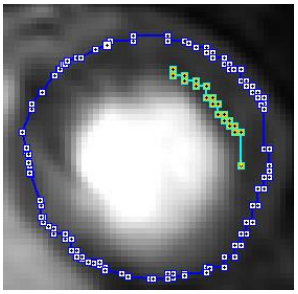
3) Select a contouring tool (3.): **Add/Edit** or **Add/Edit snap to grid**. The task with both tools is to click along the boundaries. **Add/Edit** will generate straight lines between the clicked points, whereas **Add/Edit snap to grid** generates staircase-like lines following the pixel edges. This has the advantage that the pixels to be included are apparent.

4) Select the **EPI** contour by clicking into the **VOIs** list (4.) and click along the outer boundary.



Close the contour by holding down the Ctrl key and clicking.

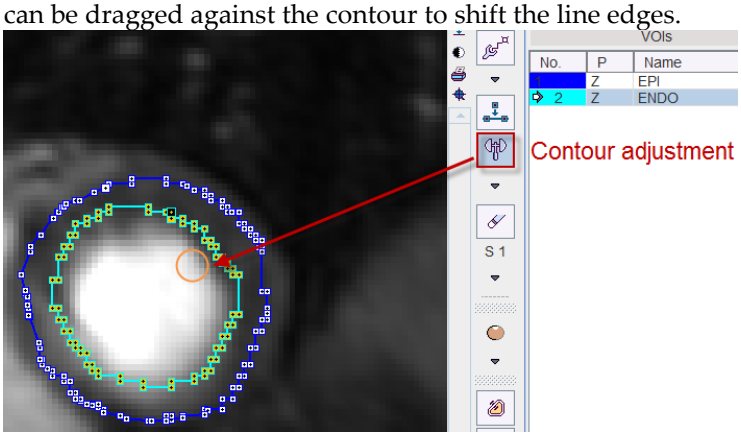
5) Select the **ENDO** contour by clicking into the **VOIs** list and then click along the inner boundary. Here it is very important to stay away for the contrast agent in the cavity, because a small number of contrast pixels can distort the signal dramatically and result in erroneous perfusion values.



Close the contour by holding down the Ctrl key and clicking.

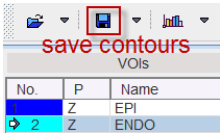
6) Verify that during the definition is appropriate for all dynamic acquisitions by moving the frame slider (2.) and observing the placement of the contours on the myocardium.

7) If necessary adjust the contour shape using the hammer tool illustrated below. If the cursor is moved over the image and the left mouse button pressed, a circle appears. It can be dragged against the contour to shift the line edges.



8) Changes to the contours are delicate and sometimes a user may like to go back to a prior definition. This can easily be achieved by the **Undo/Redo** buttons

After the definition has been completed for the first slice, repeat the definition sequence 1.-8. for the next slice. In the end, when all relevant slices have been processed please save the contour definitions for later use with the button indicated below.

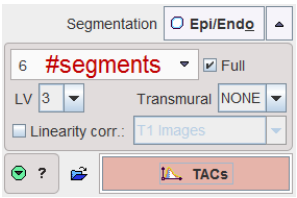


Finally close the VOI editing window with the **Ok** button.

Segmentation Procedure

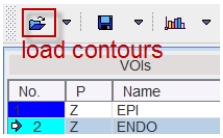
After closing the VOI definition window the segmentation is immediately started. It will use the definition which was applied most recently.

The **Epi/Endo** segmentation configuration elements are illustrated below.



Applying a Changed Configuration

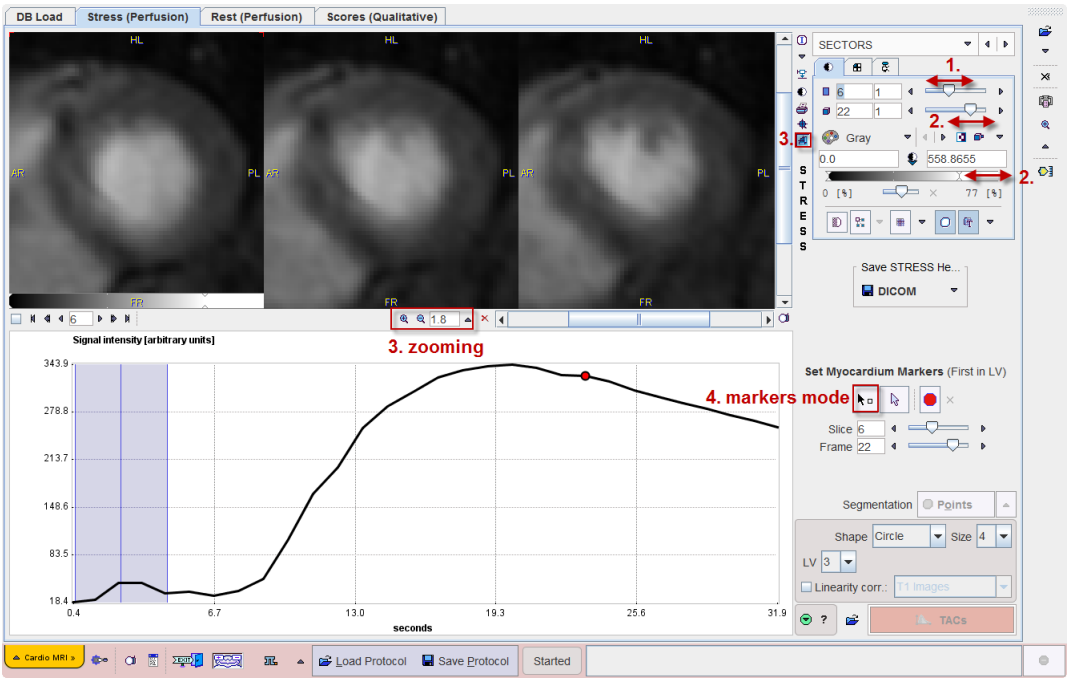
Whenever one of the configurations items has changed, the **Epi/Endo** button has to be activated again to start the new segmentation. It will open the VOI editing window with empty **EPI** and **ENDO**, so that the initial contour definitions need to be loaded again.



Marker-based Segmentations: Points, Line, Ellipse

Marker Definition

For the **Points**, **Line** and **Ellipse** methods the user has to manually place markers into the LV center, and all along the central line of the myocardium. This task is performed in the **SECTORS** page of PCARDM.



Please proceed as follows:

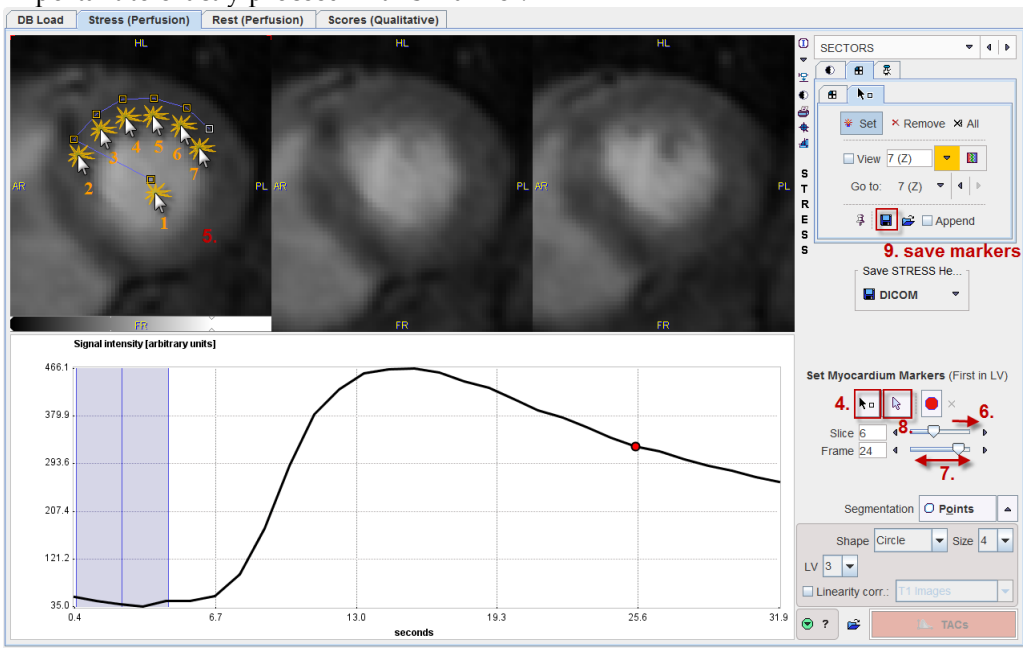
1) Adjust the slices slider (1.) so that the first basal slice to be assessed appears to the left in the image area.

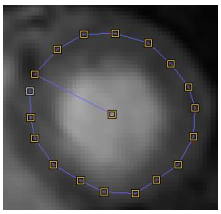
2) Optimize the image contrast for identifying the myocardium by changing the time of the dynamic acquisition (2.) or the upper threshold level (2.).

3) Zoom the images so that the myocardium wall is shown clearly. To this end enable the zoom button to the right of the image (3.). In the appearing boundary area use the zooming functionality to enlarge the image. Then disable zooming mode again with the zoom button (3.)

4) Activate the button for markers definition (4.).

5) With the left mouse button, first click into the center of the LV, next to the point in the myocardial wall where the RV ends, and continue clicking in clockwise direction along the center of the myocardium (5.). Set the last marker close to the first. Note: It is very important to exactly proceed in this manner.





6) Perform the same marker definition in the two other visible slices.

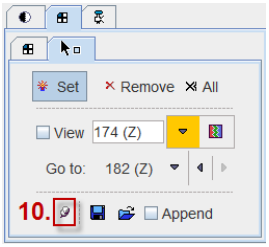
7) Use the **Slice** increment button (6.) to show the following three slice images and define the markers in the same way. Continue until all slices are processed.

8) In order to verify the markers location on different acquisitions use the **Frame** slider to shift times.

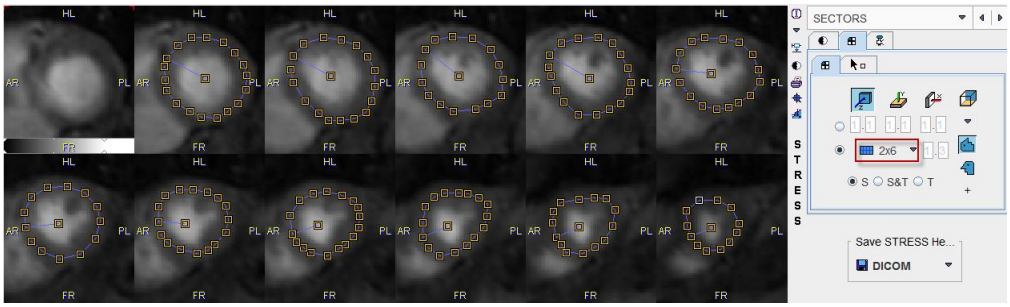
9) If there is a need to avoid markers generation activate the **Neutral mode** button (8.) In order to continue marker placement just activate the markers button (4.) again.

10) After all markers have been set it is highly recommended saving them in a definition file (9.)

At this time the resulting definition can be visualized as follows. First enable the pushpin on the markers panel so that the markers are always shown, even when the panel is hidden.



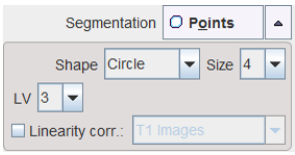
Then switch the layout such that it shows more slices.



The next step consists of configuring and applying the actual segmentation.

Points Segmentation

The **Points** segmentation offers the following configurations.

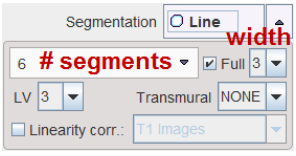


The **Shape** configuration is particular. It has two selections, **Circle** and **Rectangle** with a **Size** in pixel. A ROI corresponding to the shape definition will be created and centered at each marker location.

To perform the segmentation and create all the ROIs please activate the **Points** button.

Line Segmentation

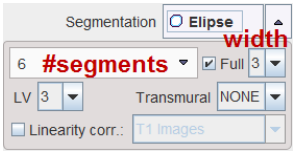
The **Line** segmentation connects all markers by lines and includes pixels along the lines into the ROIs. It offers the standard configurations.



To perform the segmentation and create all the ROIs please activate the **Line** button.

Ellipse Segmentation

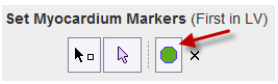
The **Ellipse** segmentation fits an ellipse through the markers and includes pixels along the ellipse into the ROIs. It offers the following configuration:



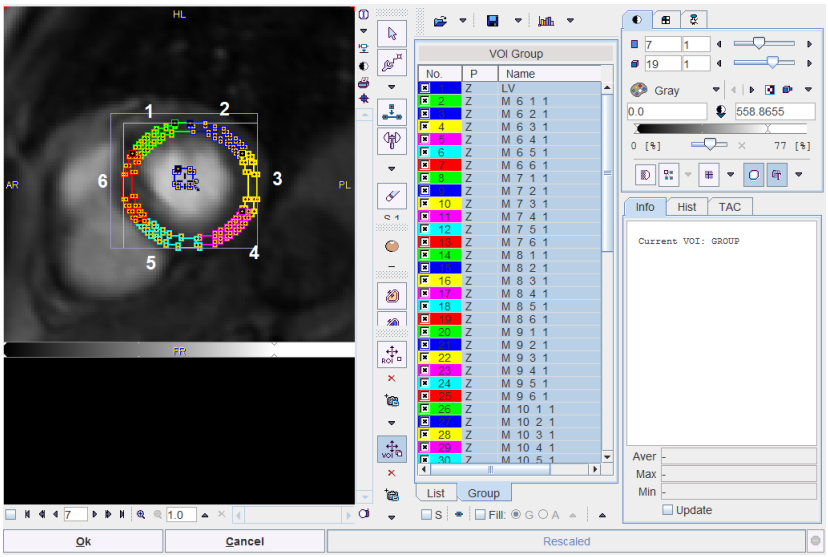
To perform the segmentation and create all the ROIs please activate the **Ellipse** button.

Segments Inspection

All of the segmentation methods result in VOI definitions, indicated by the green bullet (a red bullet indicates empty segmentation).



To inspect and potentially correct the segments please activate the green button. A VOI editor opens in a new window, as illustrated below.



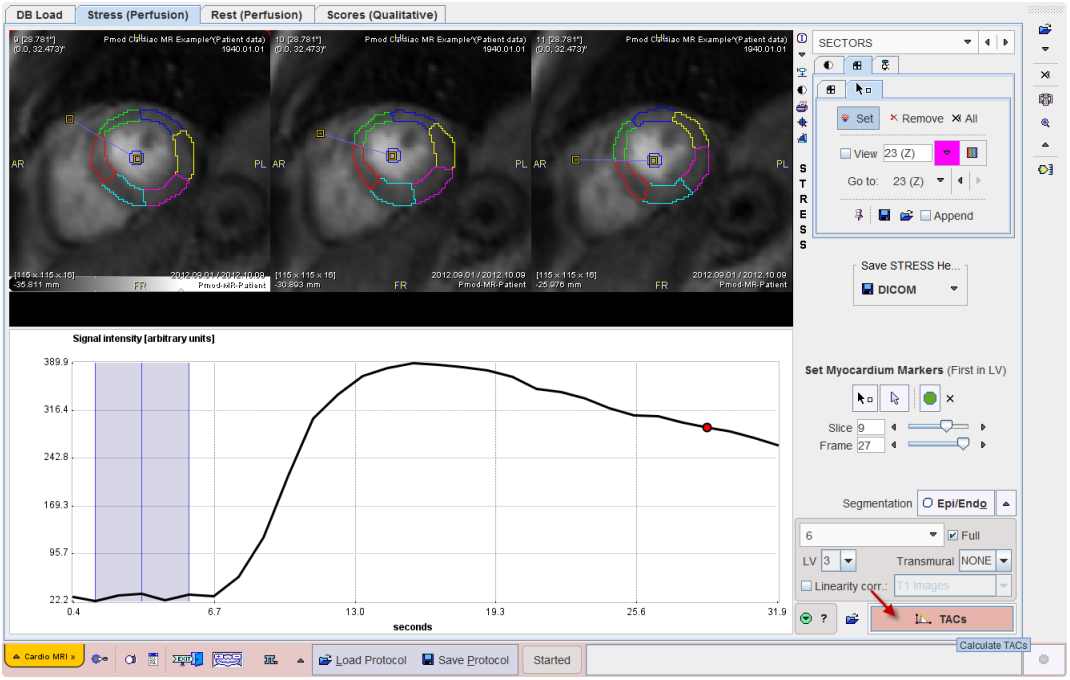
Each segment which will result in a time-contrast curve is represented as an entry in the VOI list. The naming convention is as follows:

- **M** indicates a myocardial curve, **LV** corresponds to the contrast curve in the ventricle center which will be used as the input curve for modeling.
- The first number corresponds to the slice number in the data set.
- The second number corresponds to the sector number. Numbering is clockwise, starting after the RV edge.
- The third number corresponds to the transmural sector. Numbering is from the inner to the outer.

Please refer to the *PMOD Base Functionality Guide* to learn about methods how to edit VOIs.

Contrast Curve Calculation

Once the segmentation has been performed, the VOIs are ready to be applied to the dynamic CMR series.



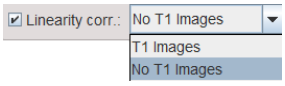
The average MR signal in each segment is calculated. If the **Linearity corr**ection is enabled in the segmentation definition, the signal curves will be corrected so that the relation between the concentration of contrast agent and signal intensity becomes linear. If **Linearity corr**ection is not enabled, it is inherently assumed that due to the low concentration of the agent the relation is already linear.

Note: As of now the linearity-correction is not recommended because of lacking stability. As simplified alternative, baseline subtraction should be applied.

The process is started by activating the red **TACs** button in the lower right corner, and the resulting TACs will be shown on the next page **MODELING**.

Linearity Correction

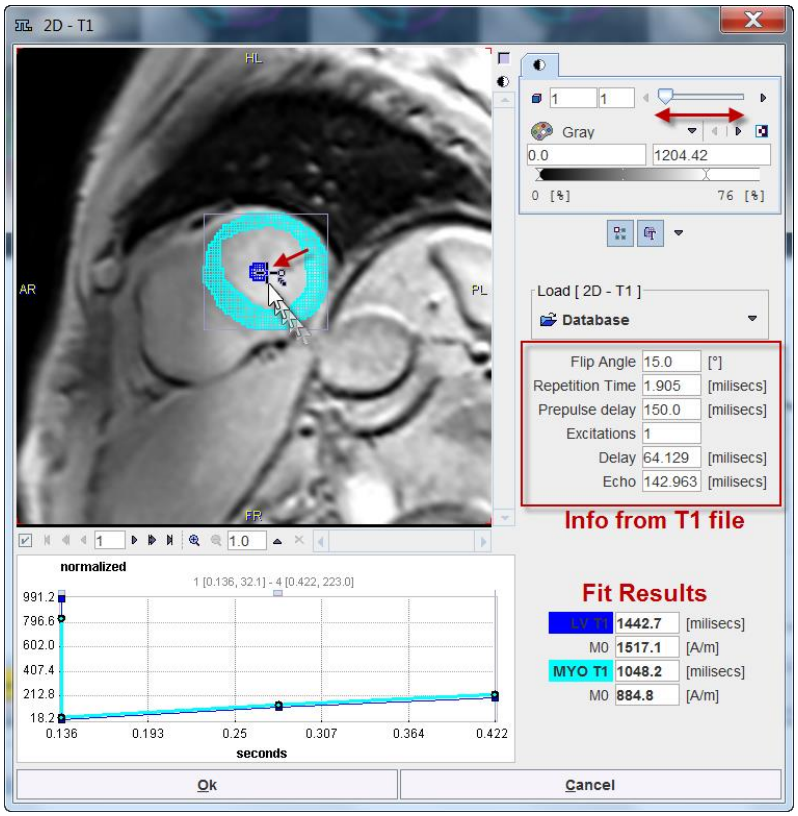
Note that if **Linearity corr** is enabled there are two choices:



During the TAC calculation, a corresponding dialog window will open .

T1 Images

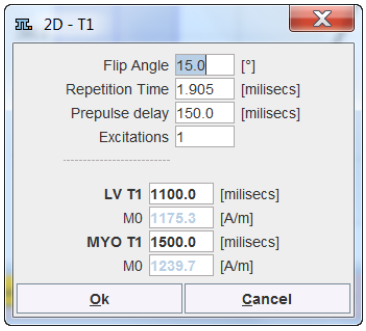
With the first **T1 images** choice an image selection window opens. The user has to select the T1 scan which corresponds to the perfusion data set being analyzed, eg. **T1 STRESS**. PCARDM will load the images, interpolate them to the geometry of the perfusion scan and then show them in a window as illustrated below. A mask of the myocardium and the LV derived from the segmentation are shown in the overlay. It is the task of the user to shift the mask by dragging the handle such that it fits to the anatomy as illustrated below.



The program reads sequence parameters from the T_1 scan file and uses them for fitting an average T_1 time for the left ventricle (**LV T1**) and the myocardium (**MYO T1**) from the recovery of the magnetization. These values are shown in the fit results section. **LV T1** will be used for correcting the LV TAC, and **MYO T1** for correcting all segmental TACs.

No T1 Images

If no T1 images are available the relevant information can be manually entered into a dialog window.



Correction Procedure

In principle the relaxivity R_1 is first calculated [4]:

For the signal intensity *SI* including readout trajectory, we have for each dynamic scan *i*:

$$SI(R_1) = M_0 \sin(\alpha)\left(\left[1-\exp(-T_D R_1)\right]\cdot\left(\cos(\alpha)\exp(-T_R R_1)\right)^{n-1} + \left[1-\exp(-T_R R_1)\right]\cdot\frac{1-\left(\cos(\alpha)\exp(-T_R R_1)\right)^{n-1}}{1-\cos(\alpha)\exp(-T_R R_1)} \right)$$

where

$SI(R_1)$	is the model for the signal intensity for each scan as a function of tissue relaxivity R_1, i.e. the c
M_0	is the equilibrium magnetization (which must be guessed/evaluated from a scan)
α	is the flip angle used (DICOM field: (0018,1314): Flip Angle)
T_D	is the time from saturation prepulse to the centre of acquisition space (=*k*-space center) (Private DICOM field: (2001,101b))
T_R	is the repetition time (DICOM field: (0018,0080): Repetition Time)
n	is the number of excitations (readout lines) processed before *k*-space center is reached, no DI

R_1 is then applied for the conversion from MR signal to contrast agent concentration by [4]:

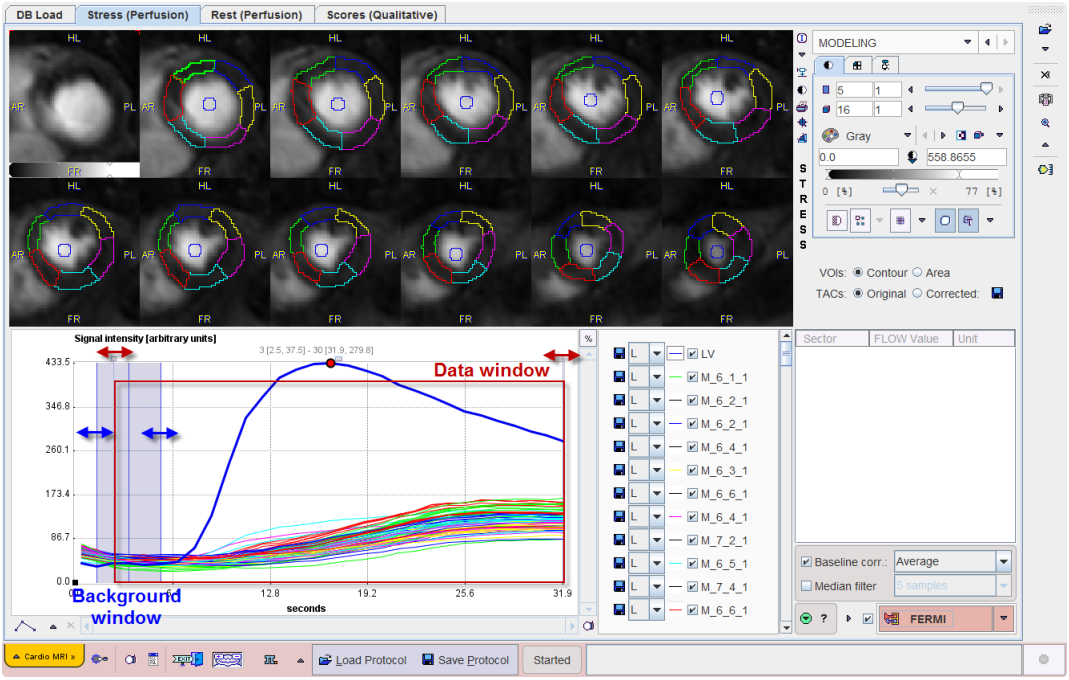
$$R_1(c(t)) = \frac{1}{T_1(c(t))} = \frac{1}{T_{1base}} + c(t)\cdot R$$

where

T_{1base}	is the *T1* value without contrast (which we measure with the T1 scan)
$c(t)$	is the concentration of the contrast medium (here as fcn of time)
$R = 4.5\ \left(s\frac{mmol}{L}\right)^{-1}$	is the relaxivity of the pure contrast medium
$R_1(c(t)) = \frac{1}{T_1(c(t))}$	is the relaxivity of the tissue with contrast medium applied, which changes as contrast concentration changes with time.

Perfusion Calculation

After a segmentation scheme has been applied and the time-contrast curves calculated, they are shown in the lower left on the **MODELING** page.

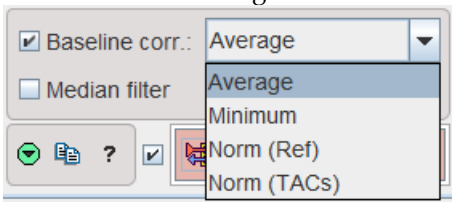


The LV curve represents the concentration of contrast agent in the center of the LV cavity. It should rise earlier than the segmental curves as the contrast arrives first in the ventricle, before being transported to the myocardium via the coronary artery system.

Baseline Correction

The concentration of contrast agent should be zero before arrival of the contrast bolus. The MR signal, however is not zero. Assuming that the relation between contrast concentration and MR signal is similar in blood and myocardium, the baseline signal of each curve can be subtracted to arrive at an approximate contrast curve.

Baseline correction can be enabled with the **Baseline corr** box. Correspondingly, a blue shaded area is shown in the curve area. It should be adjusted such that it covers a sufficient window before the signal rise. There are 4 choices for the curve correction:



With **Average** (recommended), the signal average in the background window will be calculated for each curve, and then subtracted. The **Minimum** setting works similarly with the minimal value in the baseline window.

The **Norm (Ref)** and **Norm (TACs)** choices normalize the curves in a different way. They are aimed at correcting regional coil sensitivity differences [5]. With **Norm(Ref)** a calibration factor is calculated from the relative baselines of the TAC and the LV. With **Norm (TACs)** the calibration factor is calculated from the TAC baseline and the average of all TAC baselines.

Signal Filter

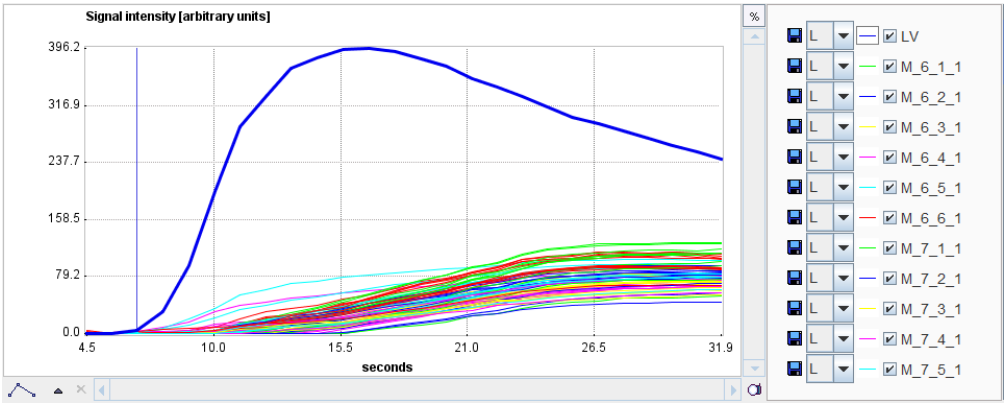
In order to filter noisy signals a **Median filter** can be enabled. It allows filter widths of **5**, **7** and **9 samples** which are applied along the time. An advantage of using the median is that it does not affect the upslope shape.

Data Cropping

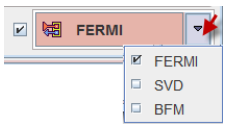
A data window can be placed to crop the signal in the time domain as illustrated above. Default is to use the whole signal. Please drag the handles to reduce the window, for instance to remove most of the baseline signal, and to cut a tail affected by recirculation.

Starting the quantification

The curves which will be used for quantification can be visualized by enabling the **Corrected** radio button in the **TACs** area. For the quantification it is important that the LV curve starts from a value close to zero and the upslope part is not truncated.



The red action button in the lower right starts the quantification. It has three settings which correspond to the quantification model which is applied to the curves. Recommended is the **FERMI** model.

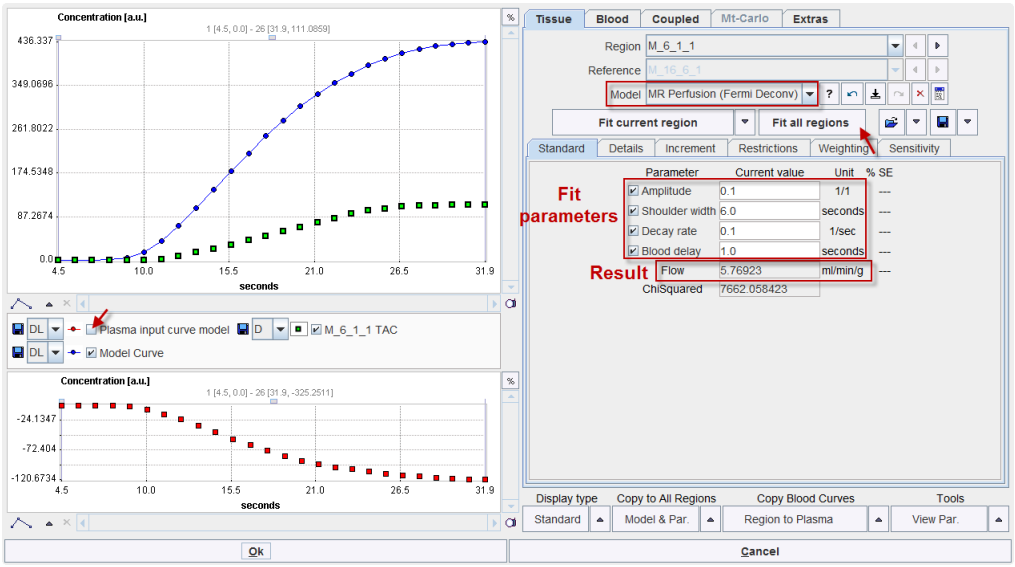


Note the check box next to the action button. If it is enabled, the program module applied for the quantification will open with loaded data, and the user can perform the curve modeling interactively. The advantage is that the outcome can be easily inspected, and any failures most probably fixed as described in the next section.

Otherwise, the quantification is performed in the background and the resulting perfusion values returned for the results display. Quantification failures in the segments are indicated by returning **NaN** values.

Interactive Model Fitting

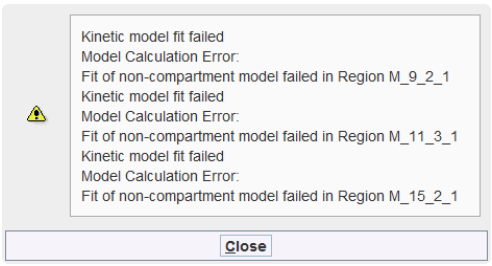
When interactive modeling is enabled, a dialog window of PMOD's PKIN modeling tool appears with the prepared contrast concentration curves loaded.



The upper left curve window shows the signal curve as green squares and the current model curve as connected blue dots. The LV curve is initially hidden. It can be shown by enabling the **Plasma input curve model** box.

The **Model** selection is set according to the action button for starting the tool, but can be switched if needed. The MR Perfusion (Fermi Deconv) model has four parameters for fitting the shape of the signal, and the result parameter **Flow** which is derived from them.

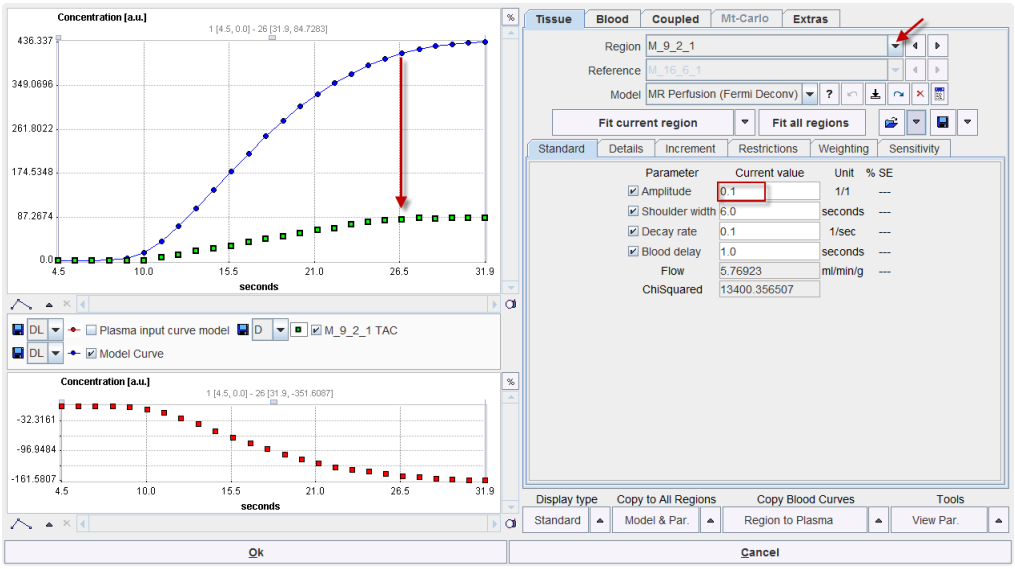
Please use the **Fit all regions** button to adjust the model to each segmental curve. There might be a message indicating that for some TACs the fit failed.



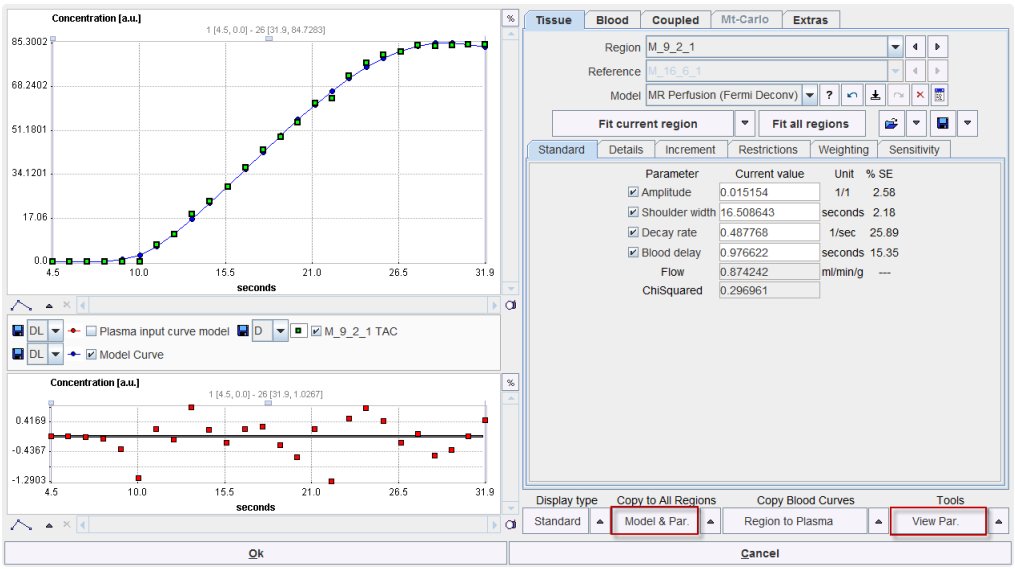
The first thing to try is to activate **Fit all regions** again. This time fitting will start from changed initial parameter values and there is a chance that the indicated problem disappears.

Trouble-Shooting

Switch to the problematic TAC by selecting the corresponding entry in the **Region** list, in the example below M_9_2_1.



It is apparent that the model is too high. So reduce the **Amplitude** parameter to a smaller value, e.g. 0.05. Then try fitting with the **Fit current region** button. If it works, the problem is solved. This is the case in the example where a **Flow** value of 0.874 ml/min/g resulted.

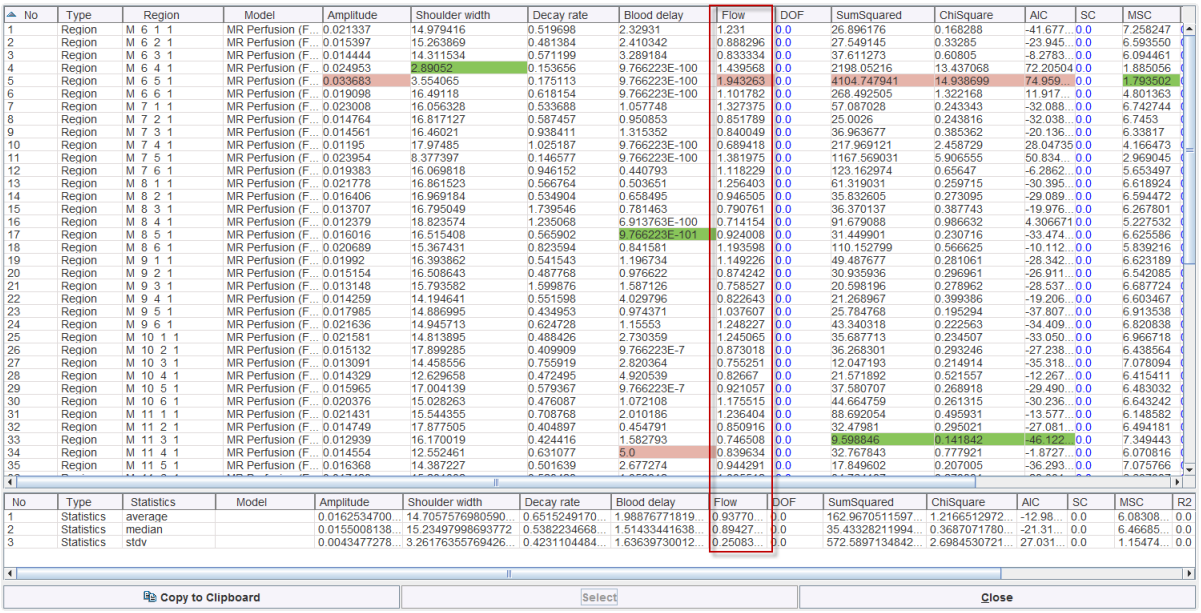


If the fit worked, the next problematic TAC can be addressed in a similar manner. If not, try to change the parameters such that the model shape comes even more close to the measurement, and try again.

Another alternative is to switch the **Region** to a neighboring TAC which was successfully fitted. Then propagate the successful model parameters as initial parameters to all TACs with the **Model & Par** button in the **Copy to All Regions** area. Finally activate **Fit all regions** again. This approach may fix all problems at once.

Parameters Summary

A convenient summary of the resulting parameters can be obtained with the **View Par** button in the **Tools** are. It shows a dialog window with all parameters for all segments, as illustrated below.



No	Type	Region	Model	Amplitude	Shoulder width	Decay rate	Blood delay	Flow	DOF	SumSquared	ChiSquare	AIC	SC	MSC
1	Region	M 6 1 1	MR Perfusion (F...	0.021337	14.979416	0.519698	2.32931	1.231	0.0	26.896176	0.168288	-41.677...	0.0	7.258247
2	Region	M 6 2 1	MR Perfusion (F...	0.015397	15.263869	0.481384	2.410342	0.888296	0.0	27.549145	0.33285	-23.945...	0.0	6.593550
3	Region	M 6 3 1	MR Perfusion (F...	0.014444	14.311534	0.571199	3.289184	0.833334	0.0	37.611273	0.60805	-8.2783...	0.0	6.094461
4	Region	M 6 4 1	MR Perfusion (F...	0.024953	3.89052	0.153656	9.766223E-100	1.439568	0.0	2198.05216	13.437068	72.20504	0.0	1.885056
5	Region	M 6 5 1	MR Perfusion (F...	0.033683	3.554065	0.175113	9.766223E-100	1.943263	0.0	4104.747941	14.938699	74.959...	0.0	1.793502
6	Region	M 6 6 1	MR Perfusion (F...	0.019098	16.49118	0.618154	9.766223E-100	1.101782	0.0	268.492505	1.322168	11.917...	0.0	4.801363
7	Region	M 7 1 1	MR Perfusion (F...	0.023008	16.056328	0.533688	1.057748	1.327375	0.0	57.087028	0.243343	-32.088...	0.0	6.742744
8	Region	M 7 2 1	MR Perfusion (F...	0.014764	16.817127	0.587457	0.950853	0.851789	0.0	25.0026	0.243816	-32.038...	0.0	6.7453
9	Region	M 7 3 1	MR Perfusion (F...	0.014561	16.46021	0.938411	1.315352	0.840049	0.0	36.963677	0.385362	-20.136...	0.0	6.33817
10	Region	M 7 4 1	MR Perfusion (F...	0.01195	17.97485	1.025187	9.766223E-100	0.689418	0.0	217.969121	2.458729	28.04735	0.0	4.166473
11	Region	M 7 5 1	MR Perfusion (F...	0.023954	8.377397	0.146577	9.766223E-100	1.381975	0.0	1167.569031	5.906555	50.834...	0.0	2.969045
12	Region	M 7 6 1	MR Perfusion (F...	0.019383	16.069818	0.946152	0.440793	1.118229	0.0	123.162974	0.65647	-6.2862...	0.0	5.653497
13	Region	M 8 1 1	MR Perfusion (F...	0.021778	16.861523	0.566764	0.503651	1.256403	0.0	61.319031	0.259715	-30.395...	0.0	6.618924
14	Region	M 8 2 1	MR Perfusion (F...	0.016406	16.969184	0.534904	0.658495	0.946505	0.0	35.832605	0.273095	-29.089...	0.0	6.594472
15	Region	M 8 3 1	MR Perfusion (F...	0.013707	16.795049	1.739546	0.781463	0.790761	0.0	36.370137	0.387743	-19.976...	0.0	6.267801
16	Region	M 8 4 1	MR Perfusion (F...	0.012379	18.823574	1.235068	6.913763E-100	0.714154	0.0	91.679088	0.986632	4.306671	0.0	5.227532
17	Region	M 8 5 1	MR Perfusion (F...	0.016016	16.515408	0.565902	9.766223E-101	0.924008	0.0	31.449901	0.230716	-33.474...	0.0	6.625586
18	Region	M 8 6 1	MR Perfusion (F...	0.020689	15.367431	0.823594	0.841581	1.193598	0.0	110.152799	0.566625	-10.112...	0.0	5.839216
19	Region	M 9 1 1	MR Perfusion (F...	0.01992	16.393862	0.541543	1.196734	1.149226	0.0	49.487677	0.281061	-28.342...	0.0	6.623189
20	Region	M 9 2 1	MR Perfusion (F...	0.015154	16.508643	0.487768	0.976622	0.874242	0.0	30.935936	0.296961	-26.911...	0.0	6.542085
21	Region	M 9 3 1	MR Perfusion (F...	0.013148	15.793582	1.599876	1.587126	0.758527	0.0	20.598196	0.278962	-28.537...	0.0	6.687724
22	Region	M 9 4 1	MR Perfusion (F...	0.014259	14.194641	0.551598	4.029796	0.822643	0.0	21.268967	0.399386	-19.206...	0.0	6.603467
23	Region	M 9 5 1	MR Perfusion (F...	0.017985	14.886995	0.434953	0.974371	1.037607	0.0	25.784768	0.195294	-37.807...	0.0	6.913538
24	Region	M 9 6 1	MR Perfusion (F...	0.021636	14.945713	0.624728	1.15553	1.248227	0.0	43.340318	0.222563	-34.409...	0.0	6.820838
25	Region	M 10 1 1	MR Perfusion (F...	0.021581	14.813895	0.488426	2.730359	1.245065	0.0	35.687713	0.234507	-33.050...	0.0	6.966718
26	Region	M 10 2 1	MR Perfusion (F...	0.015132	17.899285	0.409909	9.766223E-7	0.873018	0.0	36.268301	0.293246	-27.238...	0.0	6.438564
27	Region	M 10 3 1	MR Perfusion (F...	0.013091	14.458556	0.755919	2.820364	0.755251	0.0	12.047193	0.214914	-35.318...	0.0	7.078094
28	Region	M 10 4 1	MR Perfusion (F...	0.014329	12.629658	0.472495	4.920539	0.82667	0.0	21.571892	0.521557	-12.267...	0.0	6.415411
29	Region	M 10 5 1	MR Perfusion (F...	0.015965	17.004139	0.579367	9.766223E-7	0.921057	0.0	37.580707	0.268918	-29.490...	0.0	6.483032
30	Region	M 10 6 1	MR Perfusion (F...	0.020376	15.028263	0.476087	1.072108	1.175515	0.0	44.664759	0.261315	-30.236...	0.0	6.643242
31	Region	M 11 1 1	MR Perfusion (F...	0.021431	15.544355	0.708768	2.010186	1.236404	0.0	88.692054	0.495931	-13.577...	0.0	6.148582
32	Region	M 11 2 1	MR Perfusion (F...	0.014749	17.877505	0.404897	0.454791	0.850916	0.0	32.47981	0.295021	-27.081...	0.0	6.494181
33	Region	M 11 3 1	MR Perfusion (F...	0.012939	16.170019	0.424416	1.582793	0.746508	0.0	9.598846	0.141842	-46.122...	0.0	7.349443
34	Region	M 11 4 1	MR Perfusion (F...	0.014554	12.552461	0.631077	5.0	0.839634	0.0	32.767843	0.777921	-1.8727...	0.0	6.070816
35	Region	M 11 5 1	MR Perfusion (F...	0.016368	14.387227	0.501639	2.677274	0.944291	0.0	17.849602	0.207005	-36.293...	0.0	7.075766

No	Type	Statistics	Model	Amplitude	Shoulder width	Decay rate	Blood delay	Flow	DOF	SumSquared	ChiSquare	AIC	SC	MSC	R2
1	Statistics	average		0.0162534700...	14.7057576980590...	0.6515249170...	1.98876771819...	0.93770...	0.0	162.9670511597...	1.2166512972...	-12.98...	0.0	6.08308...	0.0
2	Statistics	median		0.0155008138...	15.2349799869377 2	0.5382234668...	1.51433441638...	0.89427...	0.0	35.4332821199 4...	0.3687071780...	-21.31...	0.0	6.46685...	0.0
3	Statistics	stdv		0.0043477278...	3.26176355769426...	0.4231104484...	1.63639730012...	0.25083...	0.0	572.5897134842...	2.6984530721...	27.031...	0.0	1.15474...	0.0

Copy to Clipboard | Select | Close

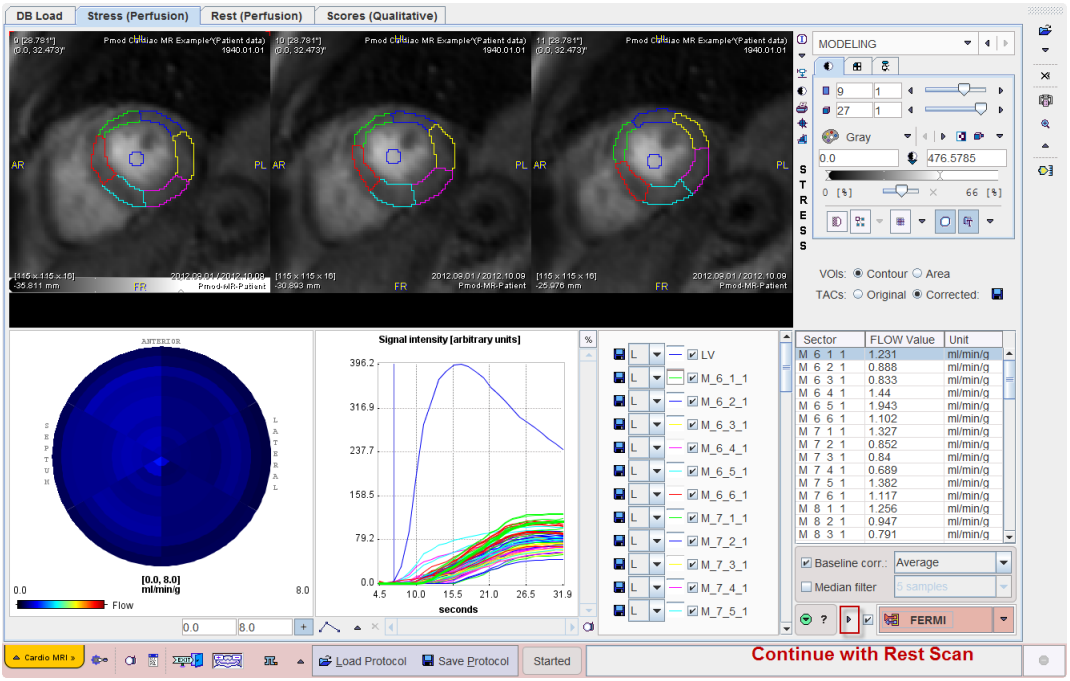
The minimal and maximal values per row are easy to find because they are highlighted in green and red. Please refer to the *Kinetic Modeling Tool (PKIN) Guide* to learn more about the features of the quantification module.

Returning the Quantification Results

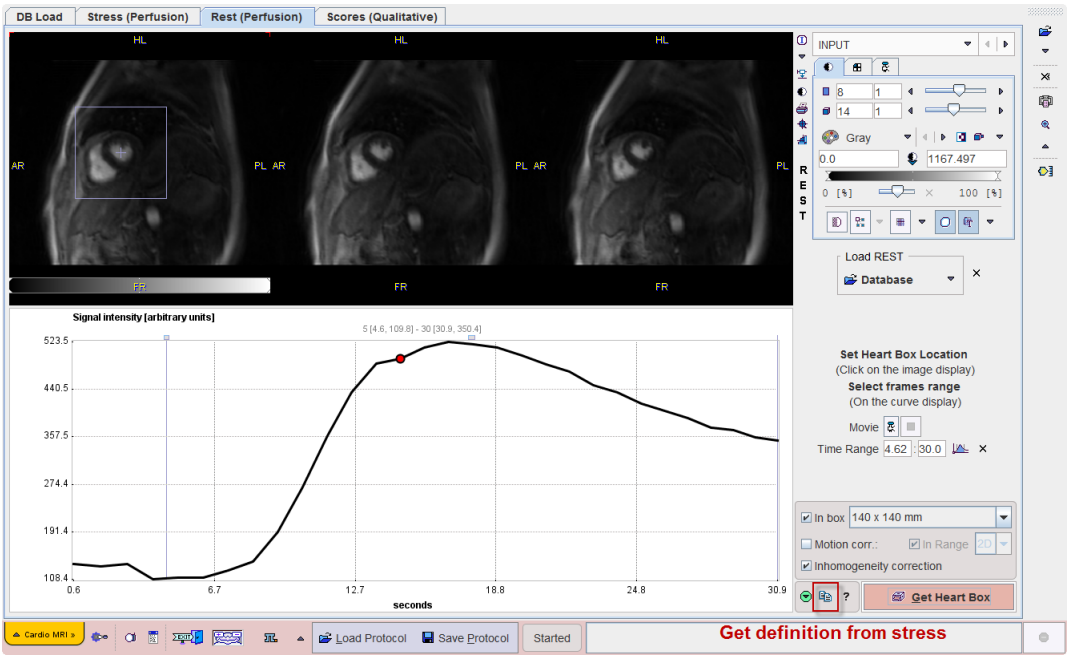
Once the model has successfully been fitted for all TACs, use the **Ok** button to close the quantification module and return the flow values to the PCARDM tool.

Analysis of the Rest Scan

When the analysis of the stress scan has been completed, the results are listed in the table to the lower right, and visualized in a polar plot to the lower left (subject to segmentation method).



Please use the arrow button indicated above to proceed to the analysis of the rest scan, arriving at the **INPUT** page of **Rest (Perfusion)**.



Please perform the same sequence of processing steps which were explained above for the stress scan:

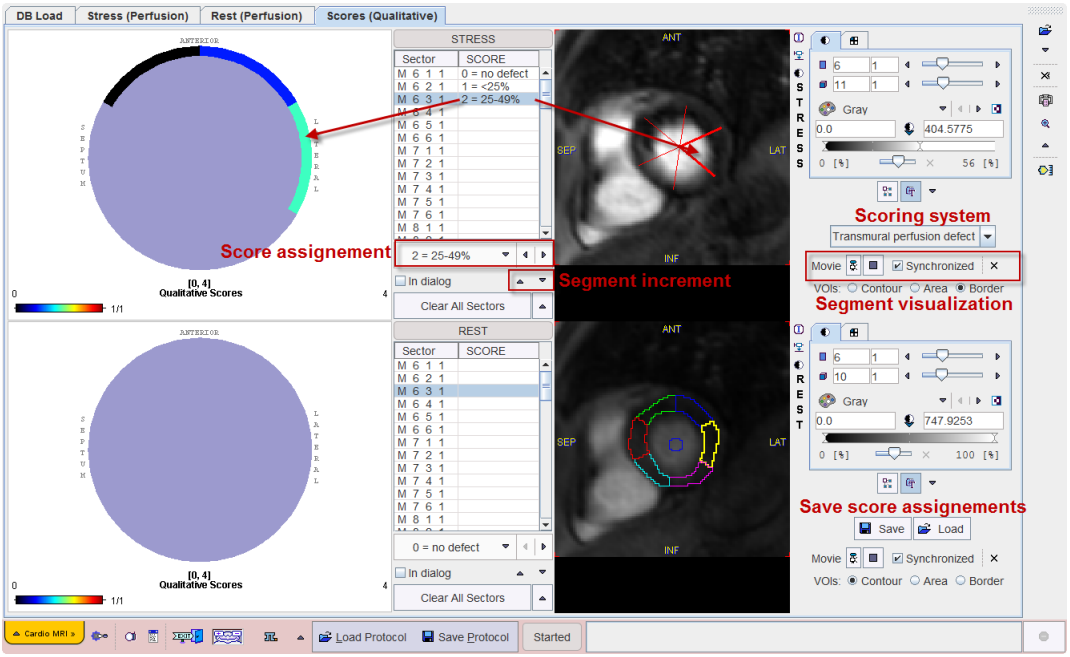
- ***data loading*** (on page 9) (with B_1 inhomogeneity correction),
- ***heart segment definition*** (on page 13),
- calculation of the ***contrast concentration curves*** (on page 25), and
- ***perfusion quantification*** (on page 28).

Note that on the pages in **Rest (Perfusion)** there is a shortcut to conveniently copy the definitions from the corresponding page of **Stress (Perfusion)** as indicated in the illustration above.

Qualitative Scoring of the Heart Segments

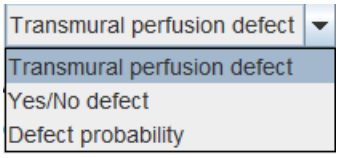
The current standard of CMR image analysis is the visual scoring of defects in cardiac segments. This task is also supported by PCARDM on the **Scores (Qualitative)** page.

Note: The **Scores (Qualitative)** page becomes only active after the cardiac segmentation has been performed and the TACs were calculated.



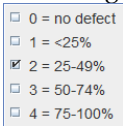
Scoring Systems

The task of qualitative scoring consists of manually assigning to each segment an index corresponding to a certain scoring system. In PCARDM three scoring systems are supported:

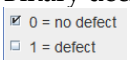


They include the following scores:

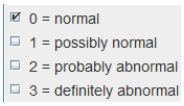
Transmural perfusion defect Percentage of transmural perfusion defect



Yes/No defect Binary decision of defect in segment:



Defect probability Likelihood of defect presence:



Score Assignment

Please proceed as follows for the assignment of scores to the segments:

1) Run the acquisition sequence as a movie to see the dynamics of contrast enhancement.

2) Select a segment in the **STRESS** or **REST** list.

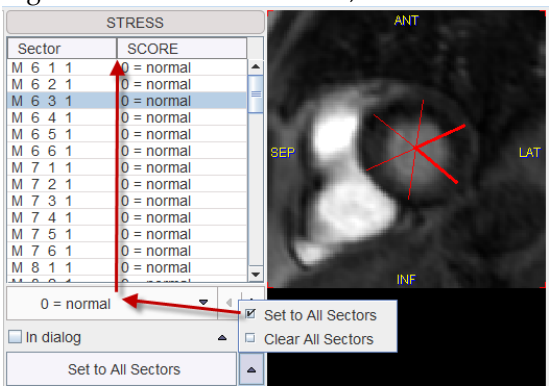
3) The corresponding sector is highlighted as an overlay to the images. There are three ways of visualizing the sectors via the VOIs radio button setting: as outline contours (Contour), as filled areas (Area), or as a star-like set of lines dividing the myocardium (Border). The selected sector appears emphasized.

4) 4) Observe whether the dynamics of contrast enhancement in the sector indicates a perfusion defect.

5) 5) Select the corresponding score value from the score list. The area in the polar plot corresponding to the segment is colored accordingly.

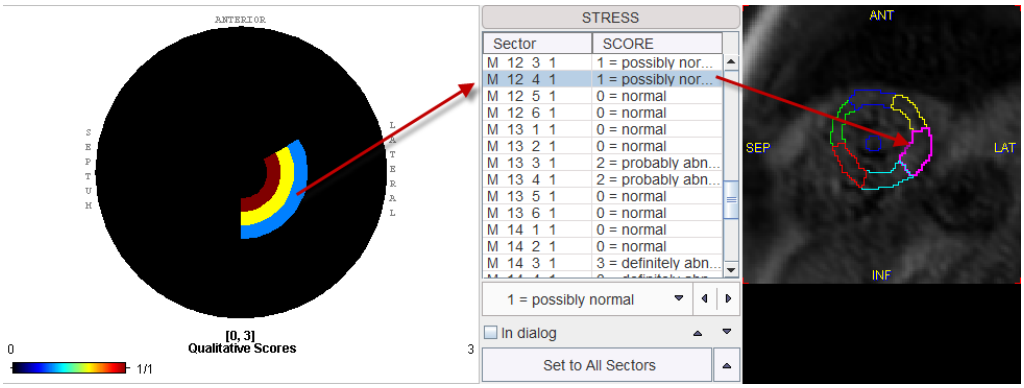
6) 6) Repeat the process for the next segment which can directly be selected in the list, or by incrementing the segment selection with the down arrow.

If only a few segments are defect, the easiest approach is to first set the normal score to all segments as illustrated below, and then selectively score the defect segments.



Polar Score Plot

Given proper order of the loaded images, the polar plot is arranged such that the apical segments are located in the center and the basal segments along the outer border. The polar plot, the list and the images with the sectors are synchronized. When clicking into the polar plot the corresponding entry in the list and the corresponding segment in the image are highlighted. Similarly, the list entry or the image segment can be selected.

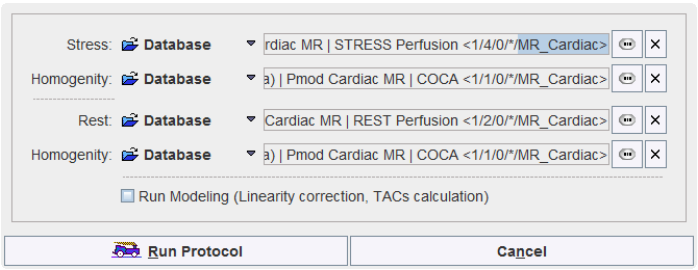


After all assignments of the stress and rest scan have been completed, it is recommended to save the score configuration. The saving format is intended for restoring the assignments in the user interface. Please use the ***results*** (on page 38) table for exporting the numeric scores for an external statistical analysis.

Protocol Saving/Retrieving

It is highly recommended saving the configuration of an analysis in a protocol file with the **Save Protocol** button. The protocol will include all types of definitions such as the heart segments, signal corrections, the applied models and the assigned scores.

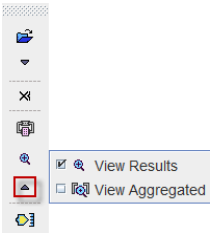
Once a protocol has been saved, processing can be repeated by retrieving the protocol with the **Load Protocol** button. A dialog window will be shown



which allows changing the data paths. The **Run Modeling** box determines, whether the data should just be prepared or also fully quantified.

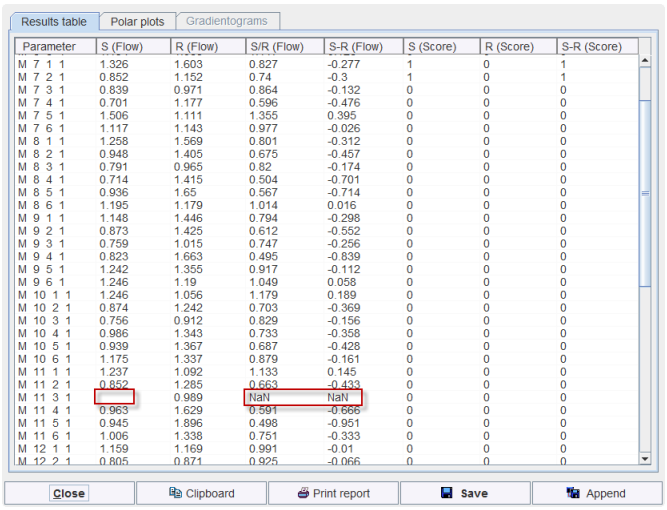
Results and Documentation

The analysis results are available from the lateral task bar



Results Summary

The button opens a window which assembles all the results:

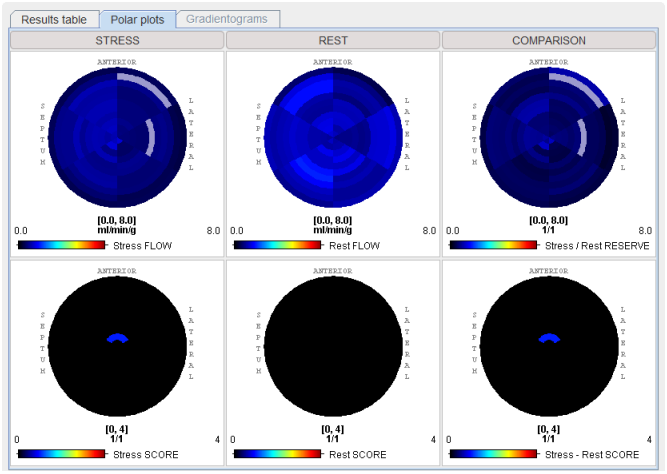


The numeric results are available on the **Results table** page. For each cardiac segment the results are listed in a row:

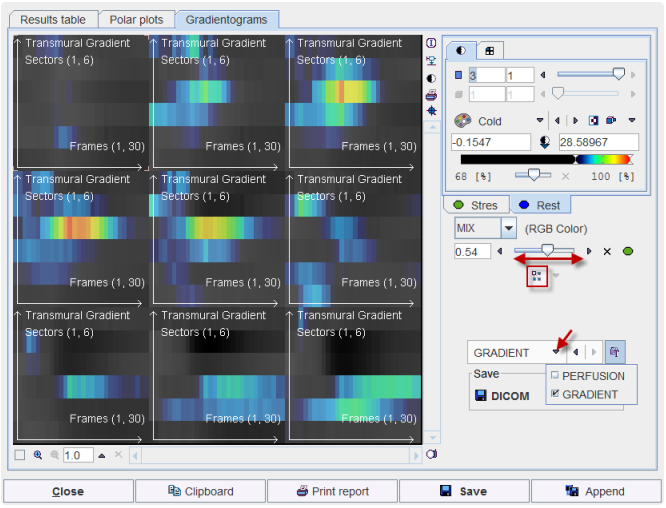
- stress flow **S (Flow)** and the rest flow **R (Flow)** in ml/min/g
- cardiac perfusion reserve measured by the ratio of stress/rest flow **S/R (Flow)** and their difference **S-R (Flow)**
- the assigned score codes at stress **S (Score)** and rest **R (Score)** as well as their difference **S-R (Score)**

The values can be copied to the **Clipboard** for pasting into a different program like MS Excel, **Print**ed, **Save**d into a text file, or **Append**ed to a previously saved result. A saved

The **Polar plots** page visualizes the results as polar plots.



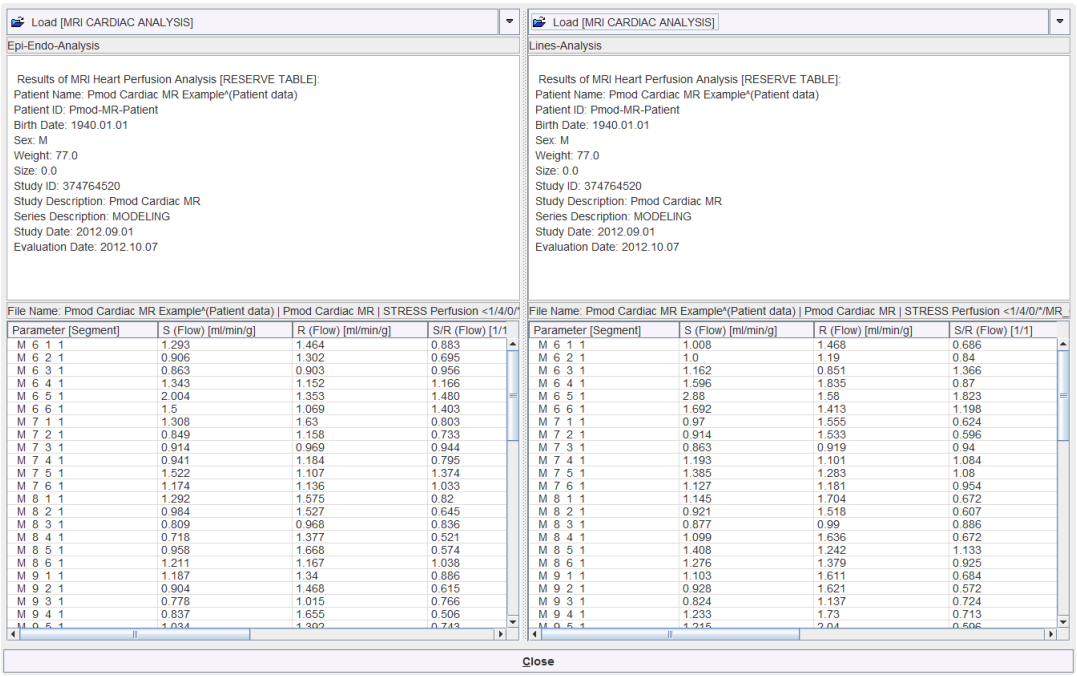
The **Gradientogram** visualizes the change of the perfusion across the myocardial wall. It is calculated as the difference between the inner- and outermost segment. Naturally it is only available if the segmentation distinguishes between several transmural segments. In this case the following arrangement is shown:



A plot is shown for each quantified slice. The illustration above shows the **GRADIENT** plots of 9 slices. Each plot shows the values around 360° along the y-axis, and along the dynamic acquisitions along the x-axis. Note that the gradientograms of the **Stress** and **Rest** studies are fused. Their relative emphasis can be changed with the fusion slider.

Results Viewer

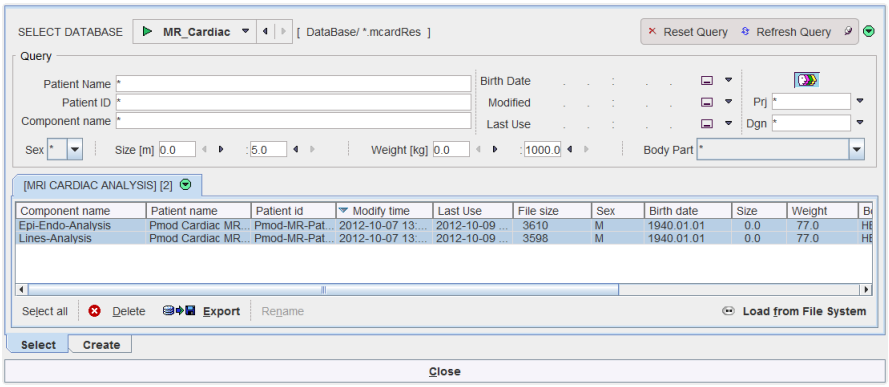
Saved results can be viewed with the **View Results** button. It opens a dialog viewer, showing the selected result to the left. With the **Load** button in the upper right, an additional result can be opened so that they can be compared side by side as illustrated below.



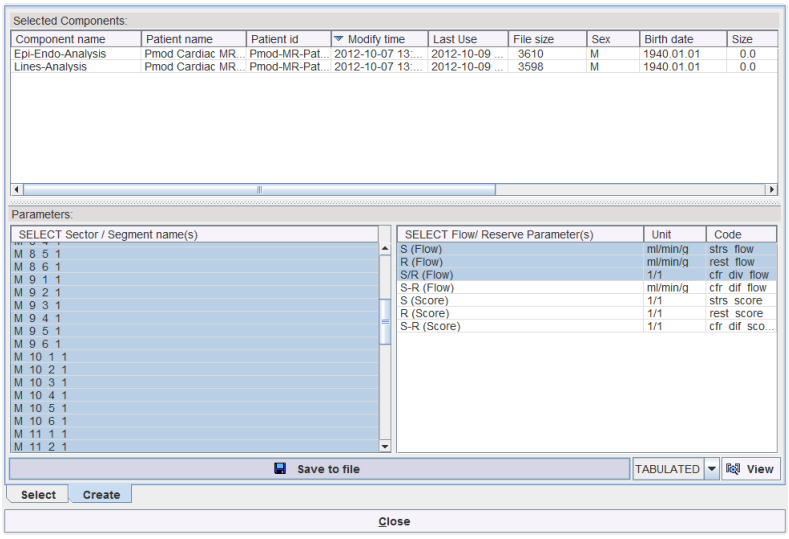
Results Aggregation

Results aggregation can be used for assembling the PCARDM results saved with the **Save** button. For instance, the results when applying different quantification models or heart segmentation schemes can be assembled for statistical analysis.

Aggregation is started with the button. It opens a window which allows selecting previously saved results. In the example below the results of two segmentations are compared. Note that the number of segments resulting from both methods must be the same.



On the **Select** panel select the results to be aggregated, then go to the **Create** tab.



There the common segments of the selected results are shown in the left area, and the common result parameters in the right area. Select the segments to be considered, and the parameters to be listed, and then use **Save to file** for saving the aggregate. The example outcome is illustrated below when opened in MS Excel.

	A	B	C	J	K	L	M	N	O
1	# PMOD_PCARD_MRI_PARAMETERS								
2	# FORMAT[UNI]								
3	# DATE_TIME[2012.10.09 17:40:48]								
4	# VERSION[3.401]								
5	# DATA								
6	// Compone	File [s	PatientN	VoiName	Time [sector]	S (Flow) [{strs	R (Flow) [{rest	S/R (Flow) [{cfr_div_flow}1/1]	
7	Epi-Endo-An	Pmoc	Pmod Ca	1	M_6_1_1	1.293	1.464	0.883	
8	Epi-Endo-An	Pmoc	Pmod Ca	1	M_6_2_1	0.906	1.302	0.695	
9	Epi-Endo-An	Pmoc	Pmod Ca	1	M_6_3_1	0.863	0.903	0.956	
10	Epi-Endo-An	Pmoc	Pmod Ca	1	M_6_4_1	1.343	1.152	1.166	
11	Epi-Endo-An	Pmoc	Pmod Ca	1	M_6_5_1	2.004	1.353	1.48	
12	Epi-Endo-An	Pmoc	Pmod Ca	1	M_6_6_1	1.5	1.069	1.403	
13	Epi-Endo-An	Pmoc	Pmod Ca	1	M_7_1_1	1.308	1.63	0.803	
14	Epi-Endo-An	Pmoc	Pmod Ca	1	M_7_2_1	0.849	1.158	0.733	
15	Epi-Endo-An	Pmoc	Pmod Ca	1	M_7_3_1	0.914	0.969	0.944	
16	Epi-Endo-An	Pmoc	Pmod Ca	1	M_7_4_1	0.941	1.184	0.795	
17	Epi-Endo-An	Pmoc	Pmod Ca	1	M_7_5_1	1.522	1.107	1.374	
18	Epi-Endo-An	Pmoc	Pmod Ca	1	M_7_6_1	1.174	1.136	1.033	
19	Epi-Endo-An	Pmoc	Pmod Ca	1	M_8_1_1	1.292	1.575	0.82	
20	Epi-Endo-An	Pmoc	Pmod Ca	1	M_8_2_1	0.984	1.527	0.645	
21	Epi-Endo-An	Pmoc	Pmod Ca	1	M_8_3_1	0.809	0.968	0.836	
22	Epi-Endo-An	Pmoc	Pmod Ca	1	M_8_4_1	0.718	1.377	0.521	
23	Epi-Endo-An	Pmoc	Pmod Ca	1	M_8_5_1	0.958	1.668	0.574	

Aggregation

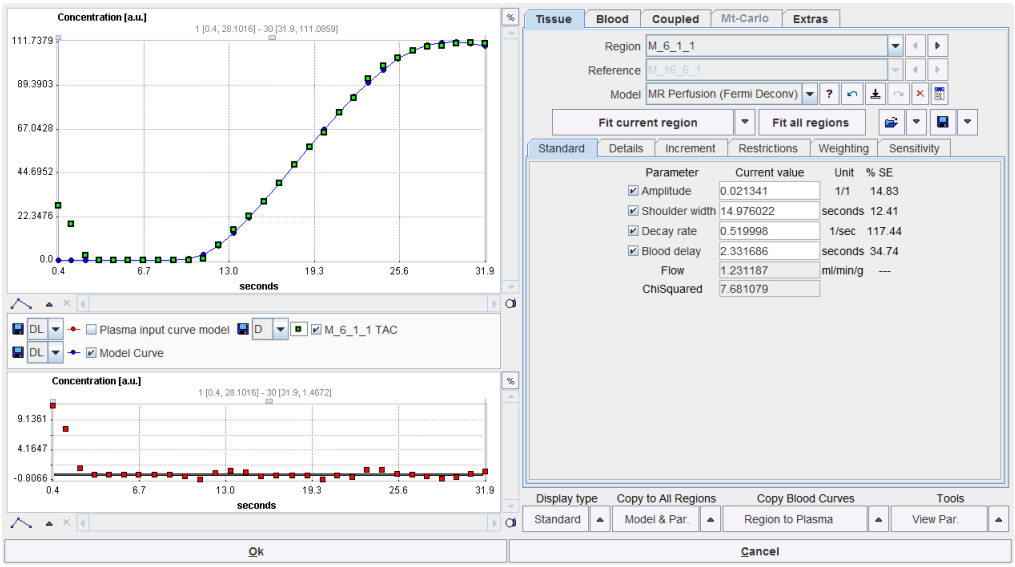
The results of aggregation can be inspected with the button. Please refer to the *PMOD*

MR Perfusion Models

Base Functionality Guide for learning about the statistics with are possible with aggregations.

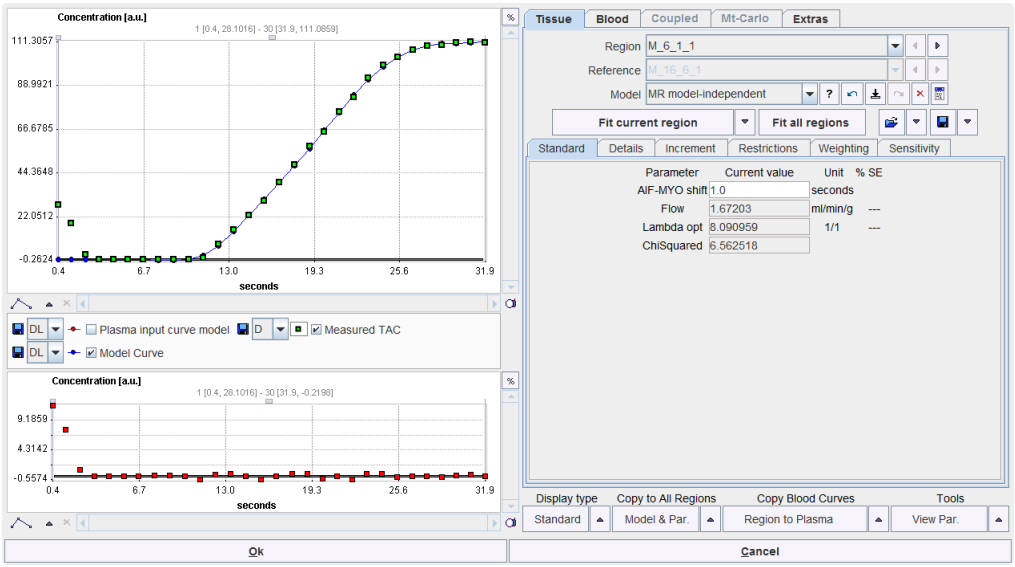
Fermi Function

This model was implemented according to Jerosch-Herold et al. [1]. It includes four fit parameters as illustrated below. They include the 3 shape parameters **Amplitude**, **Shoulder width** and **Decay rate**, and the **Flow** estimate which is obtained from the impulse response function at time t=0.



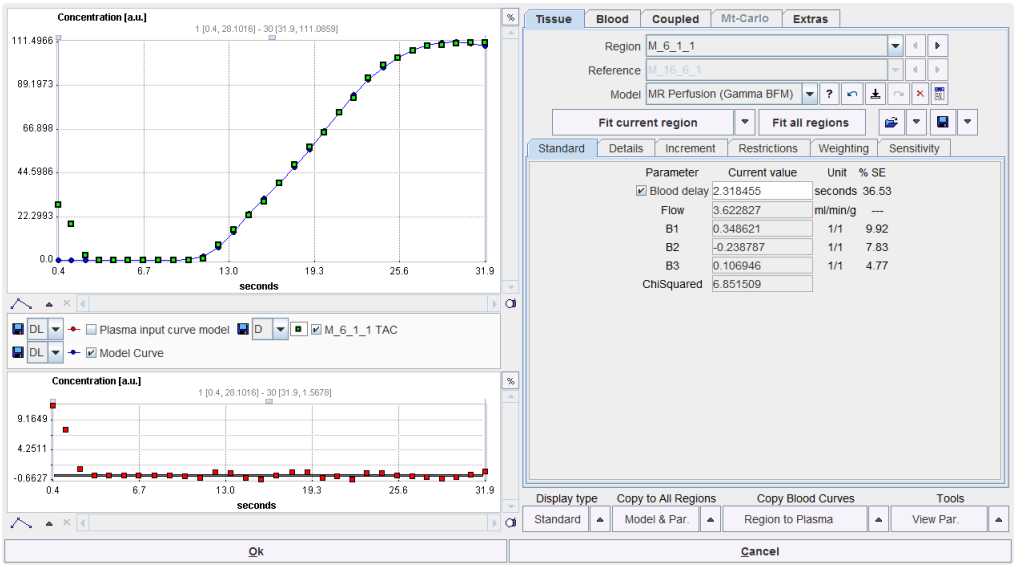
Model-independent Deconvolution

The **MR model-independent** method is highly complex. It includes the modeling of the impulse response function by B-splines and applies Tikhonov-style regularization. For details please refer to Jerosch-Herold et al. [2].



Basis of Gamma-variate Functions

The **MR Perfusion (Gamma BFM)** model describes the impulse response function as a weighted sum of three gamma variates. The weights and the **Blood delay** are the fit parameters of the model. The **Flow** estimate is obtained as the peak value of the impulse response function. For details please refer to Goldstein et al. [3].



References

1) Jerosch-Herold M, Wilke N, Stillman AE. Magnetic resonance quantification of the myocardial perfusion reserve with a Fermi function model for constrained deconvolution. Med Phys. 1998;25(1):73-84.

2) Jerosch-Herold M, Swingen C, Seethamraju RT. Myocardial blood flow quantification with MRI by model-independent deconvolution. Med Phys. 2002;29(5):886-97.

3) Goldstein TA, Jerosch-Herold M, Misselwitz B, Zhang H, Gropler RJ, Zheng J. Fast mapping of myocardial blood flow with MR first-pass perfusion imaging. Magn Reson Med. 2008;59(6):1394-400.

4) Wissman, L. Internal note 2011. Institute for Biomedical Engineering, University and ETH Zurich, Zurich, Switzerland.

5) Pack NA, DiBella EV. Comparison of myocardial perfusion estimates from dynamic contrast-enhanced magnetic resonance imaging with four quantitative analysis methods. Magn Reson Med. 2010;64(1):125-37.

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