

# Bruker PET: Workflow and Techniques in Gated Imaging with Special Focus in Cardiac Analysis

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## Requirement for the user

The user of this guide is required to have successfully completed the Bruker training course that normally follows the scanner installation. It is also assumed for the user to be familiar with small animal handling practices, comply with the local rules on animal care as well as ionizing radiation work.

## Introduction

Bruker offers a whole range of high performing instruments for preclinical PET cardiac imaging both as PET/CT and PET/MR hybrid systems. A technical description on the new Bruker PET design and performance can be found in ref. 1. The impact of Bruker's new PET technology in cardiac imaging has been discussed in the following ref 2. For a good general overview on cardiac radionuclide imaging in rodents, the reader is suggested to see ref. 3.

ECG-gated PET acquisitions are often required to investigate myocardial viability, left ventricular (LV) function and myocardial metabolic rate but also to extract accurate arterial input function from left cardiac ventricles while minimizing the corruption by myocardial uptake due to cardiac motion, see ref. 4.

For a guide on Dynamic imaging with special focus on cardiac kinetic analysis see Bruker's note ref. 5.

Bruker PET systems offer retrospective gating. The gating trigger is embedded on the list mode file and the data sorted into time bins right before reconstruction. In PET, this implementation is considered the most accurate and has the advantage of allowing different gate number definitions (currently 4, 8 or 16 cardiac frames) post acquisition.

## Experiment preparation

### Software Settings

The Bruker software interface can be the Albira Software Suite 6.1 or higher (ref. 6) or Paravision 7. This guide uses

the former to illustrate software operation but the gated acquisition concepts and possibilities are the same under Paravision 7.

Albira and Biopac gating kit users are recommended to refer to the following reference for a dedicated discussion on the use of these combined systems, see ref. 7.

In order to perform a gated acquisition, the user has to load a template acquisition on the Albira Acquirer module, making sure the gated box is checked (Figure 1)

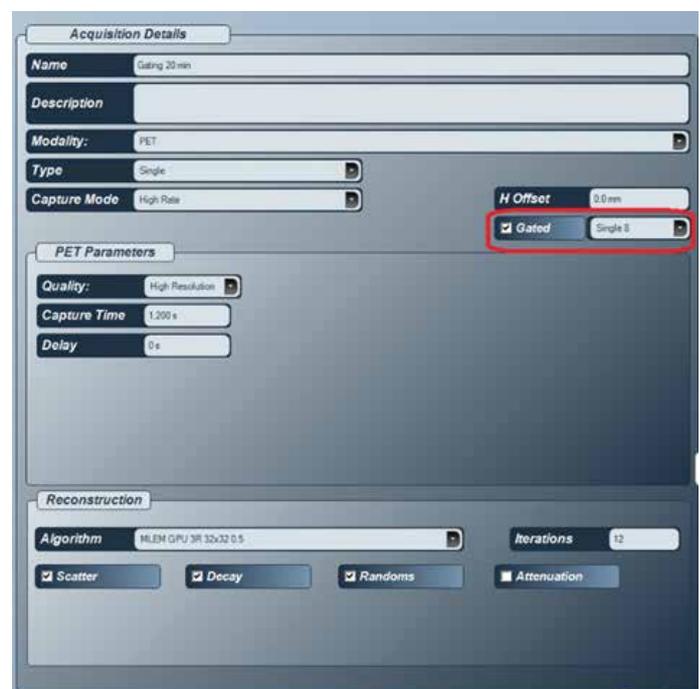


Figure 1. Manager Acquisition Definition. Checkbox for gating. Options are 4, 8 and 16 gates

A dropdown menu allows the user to choose among 4, 8 and 16 gates. Normally 8 gates achieve the best compromise between sufficiently high cardiac cycle time sampling and good counts statistics. Regarding acquisition time, it is recommended to acquire for a minimum of 10 min but 20 min or up to 60 min are more common.

FDG(F-18) doses for mice will typically range between 3.5 MBq to 10 MBq and for rats between 7 and 15 MBq. Exact values will depend on the system sensitivity, scan times, gated frame number, type of anesthesia and dose uptake by the animal.

## ECG monitoring

Bruker recommends using the small animal monitoring system by SA Instruments but the same procedure can also be used with other monitoring systems like Biopac. For rats, good results have been obtained using 3M neonatal patch electrodes and for mice using needle electrodes (figure 2).

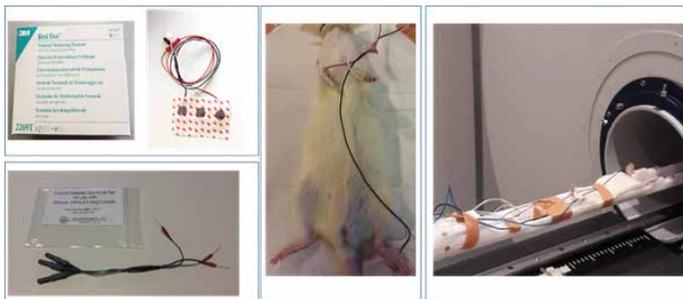


Figure 2. Mouse and rat cardiac imaging setup showing the ECG electrodes. The picture in the middle illustrates the positioning of the ECG patch electrodes and the picture on the right the positioning of the animal in the animal bed provided by Bruker with the MRI scanner.

After placement of the electrodes, the ECG signal should look like the one displayed in figure 3. Physiological heart

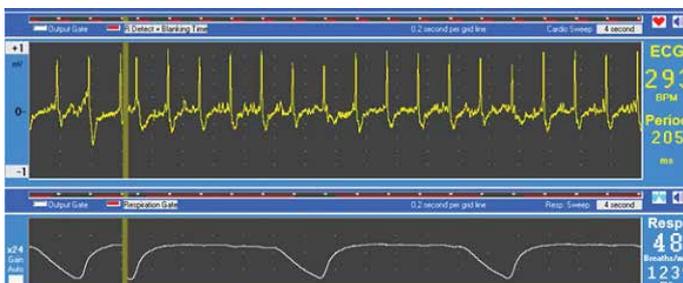


Figure 3. Rat ECG and respiration traces obtained from SA instruments

rate values are in the order of 300 bpm for rats and 500 bpm for mice (Note: The automatic detection of R waves or in some situations with noisy ECG signal may lead to erroneous values). For SA instrument systems, some user settings may need to be verified to ensure proper gating. In the gating tab (from the bottom of the ECG trace screen), you will have access to the control of the gating. From the main gating window (gating setup form), one can select the channels to

be used for gating (ECG will need to be selected for cardiac gating) and basic parameters can be controlled, such as the delay from the detection of the R wave and the duration for which the gate will be open (Max width). The white bar from the monitoring trace window (fig 3) correspond to the gate detection and gate length. The red bars correspond to the duration of the blanking period. For further control of the R wave detection, you can click on the ECG button or right click on the ECG waveform.

One of the key setting is to use a blanking period that covers most of the cardiac period but with some margin to enable detection of the next R-wave in the vent of decrease cardiac period during the duration of the PET scan. Then select positive peak for positive R-wave or negative peak for negative R-wave. In these settings, the gate is going to be generated just after the detection of the R-wave (after crossing the rising and falling voltage threshold). (Note: The default is 200  $\mu$ V but it can be adjusted depending the amplitude of the ECG signal). If you wish to generate the gate at the beginning of the R-wave then select rising edge or falling edge depending on the sign of the ECG waveform.

When the acquisition and data preparation (some systems prepare the data for reconstruction only before clicking the Start on the Reconstructor) finishes, the following files appear on the study folder:

- Large binary file with the extension .dat. This is a backup of the List Mode file in raw format.
- Large binary LM file with extension .lm
- Small text file with extension .csv with the rate trendline shown during the acquisition on the Acquirer main screen
- A medium size text file (few KB) with extension .gatelist. This file contains the time stamps of the moment when a gated trigger has been detected by the PET electronics. This file can be understood as a summary extracted from the LM data file and is read by the Reconstructor to generate the gated image.
- A very small text file with the extension .gatelist.stats. This file contains a very basic statistical analysis of the gated trigger signal:

- Total Gates
- Mean Period
- Max Period
- Min Period

It is recommended that the user always checks the latter two files to make sure values are consistent with the expected biological signals.

Healthy rats will typically have a heart rate around 300 bpm, in terms of period this is 200 ms. Mice will have a heart rate around 500 which corresponds to a period of 120 ms.

The direct subtraction of the two columns in the gatelist file is the time interval between the detected gating trigger in seconds. This chart shows an example for a cardiac acquisition with a rat:

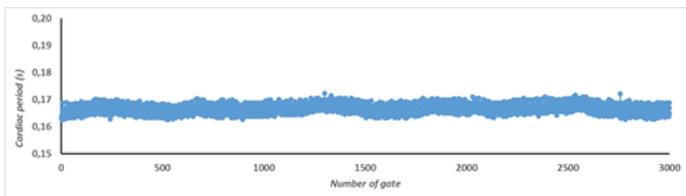


Figure 4. Gatelist generated for PET acquisition of a rat with an average cardiac period of 165 ms.

A flat trend of 0.05 s indicates that there has been a problem and the gating trigger signal has not been read correctly. Also, a flat trend of a different value, too large fluctuations or repetitive patterns also indicate potential problems, in the latter case noise induction.

The most common problem is a wrong or missing connection between the imaging equipment and the small animal physiological monitoring and gating kit.

## Reconstruction

On the automatic Reconstructor workflow, click on 'Add' to the reconstruction list and then 'Start'. The image generated will have as many frames or gates as selected on the Acquisition template. Now, it is also possible to vary the number of gates through the Advanced Menu of the Reconstructor module. The LM file can also be reconstructed, ignoring the gating trigger so that a non-gated static scan can be achieved.



Figure 5. Gate number selection

## Image Analysis

The software module PCARD will be used in this section, see the manual on ref. 8 for details on its use. PCARD is software module available from PMOD.

Open the image file with PCARD. The image can have different formats. Typically, the image will be in microPET format or DICOM. The following screen capture shows PCARD's main window.

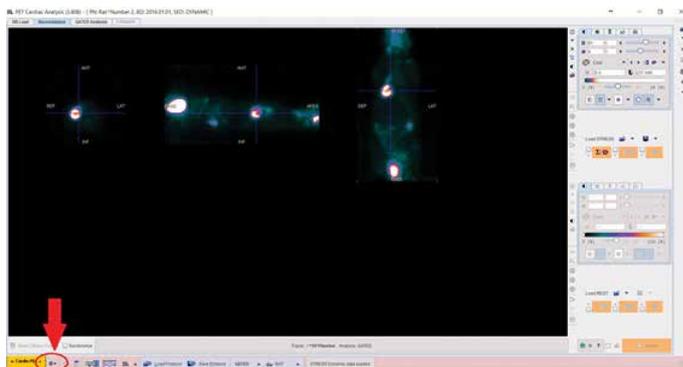


Figure 6. PCARD's main window. The color palette has been adjusted so that the heart is clearly visible. The red arrow shows the configuration button.

Click on the configuration icon, indicated by the red arrow (fig. 6). Next, make sure to select the type of subject. See red arrow in fig.7. Possible choices are 'human', 'rat' and 'mouse'. For animal models in which for instance myocardial hypertrophy is expected, this value might be set manually by the user. An immediate effect of this selection is the (default) setting of the cardiac wall thickness (for rats 3 mm and for mice 1 mm).

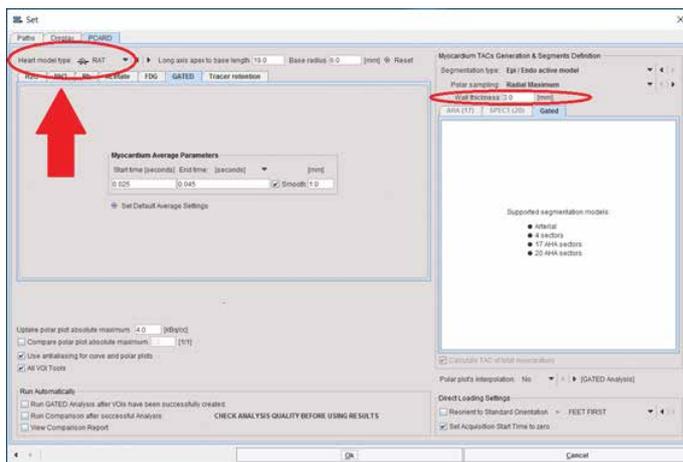


Figure 7. PCARD configuration

After clicking OK and back on the main menu, select the crop heart button marked below with a red arrow (fig. 8).

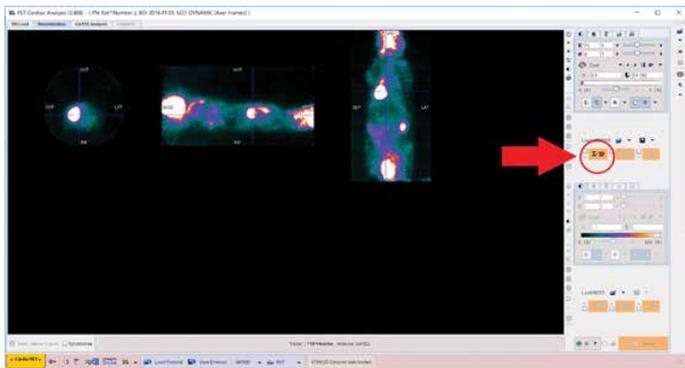


Figure 8. Heart cropping icon

This opens a new window:

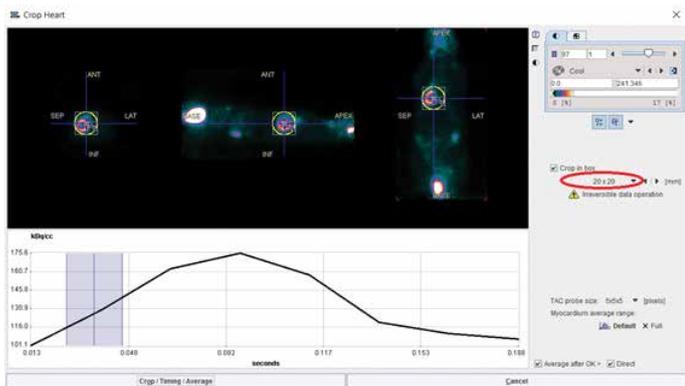


Figure 9. Heart Cropping Window

The objective is to generate a ROI around the heart. To achieve this easily, choose 20x20 as shown on the screen capture (fig. 9). You might need to reposition the circular ROI so that the whole heart lies within the ROI's boundaries. Then click on Crop/Timing/Average button. This takes you back to the main screen with only the cropped heart. This operation is not reversible and if your selection needs revision you have to load the image again.

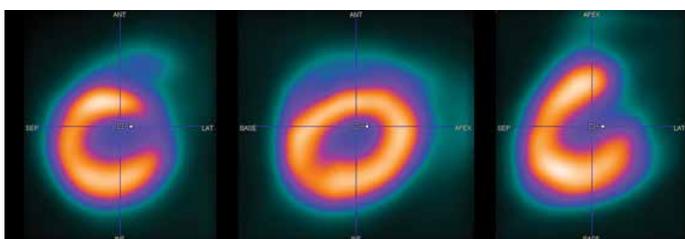


Figure 10. Heart original orientation. This may vary.

Next, you need to rotate the heart so that it complies with the standard short axis orientation. PMOD offers an automatic function to perform this action quickly but it can happen this feature does not work correctly so the user has to orient the image manually with the different tools provided. There are different ways of accomplishing this. We will start by clicking on the Reslicing button: This shows a marker in the centre of each projection (fig. 11).

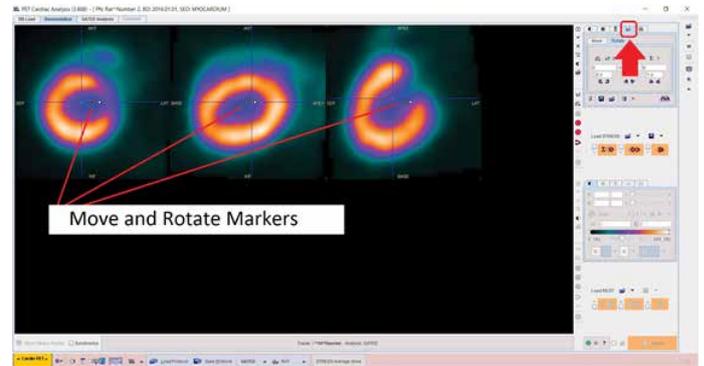


Figure 11. Changing the image orientation manually.

To bring the heart to the short axis orientation, we will carry out 3 rotations by clicking on the solid small square, then dragging the mouse out towards the myocardial wall, we draw a line, which is the radius of the circumference.

First rotate the sagittal view so that the heart apex is at the top resembling an inverted U (fig. 12).

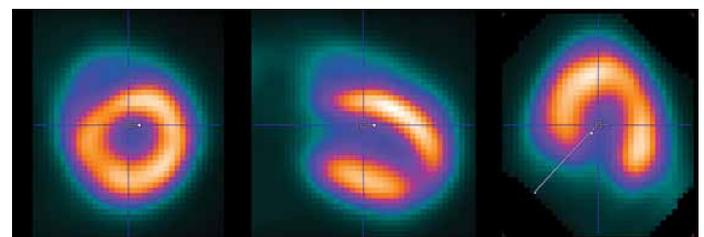


Figure 12. Rotation of sagittal view.

Then rotate the transverse view so that the right ventricle lies on the left-hand side (fig. 13).

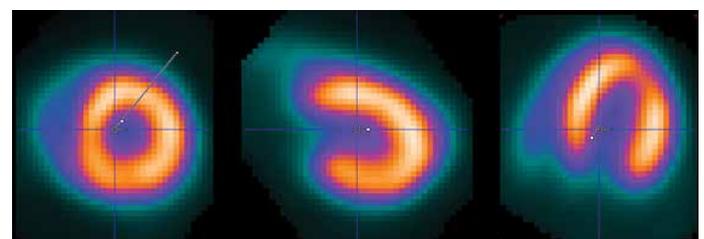


Figure 13. Rotation of transverse view.

Finally, rotate the coronal view so the longer myocardial wall is on top:

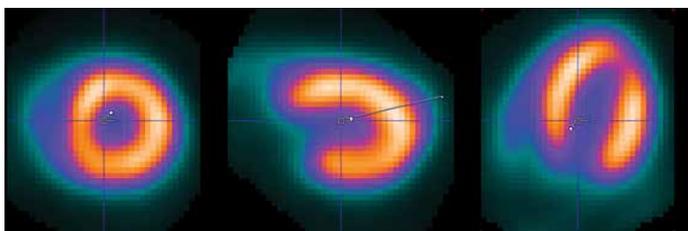


Figure 14. Rotation of coronal view

After this we should end up with the following final orientation:

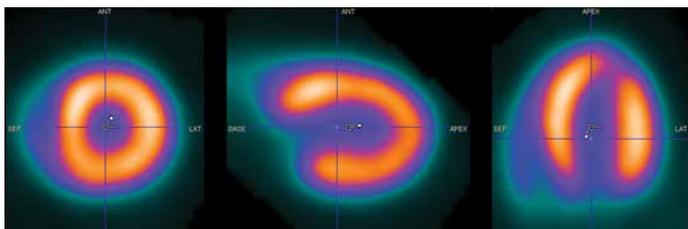


Figure 15. Heart in short axis orientation

Note: Make sure that the left ventricle lies at the centre of the image. For achieving this translation in all 3 axes, click on the large empty square (as opposed to the solid little square for rotations, see fig. 15) and shift the position so the cursor is position on the centre of the left ventricle.

If many images are to be processed and the subjects were scanned all in the same position, the user might find it useful to set the short axis orientation by using the Move and Rotate controls (fig. 16).

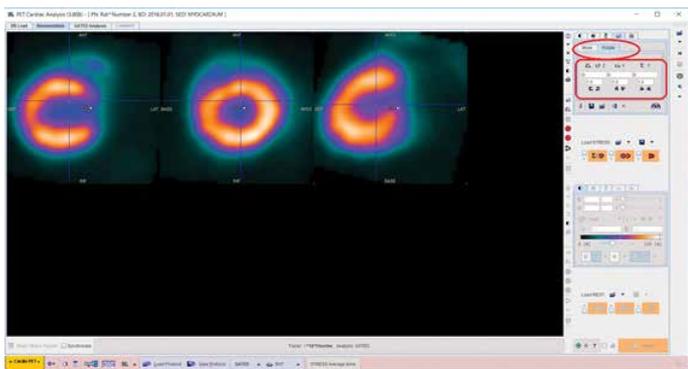


Figure 16. Move and Rotate menus.

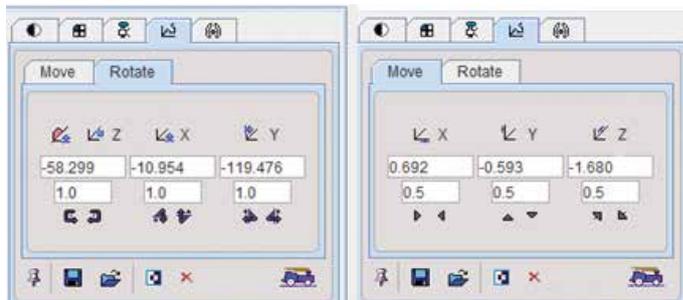


Figure 17. Rotate and Move menus to achieve by entering angle and shift or just incrementally by clicking on the arrows.

Next we generate the required volume of interest (VOI) by clicking on the 'Create VOIs' button:

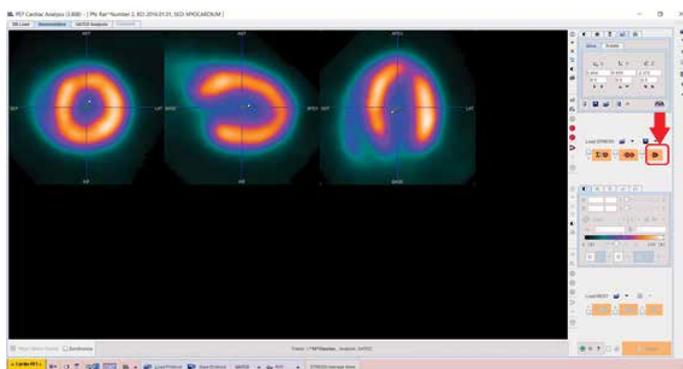


Figure 18. VOI Generation Button

After a few seconds, the VOIs are defined and shown:

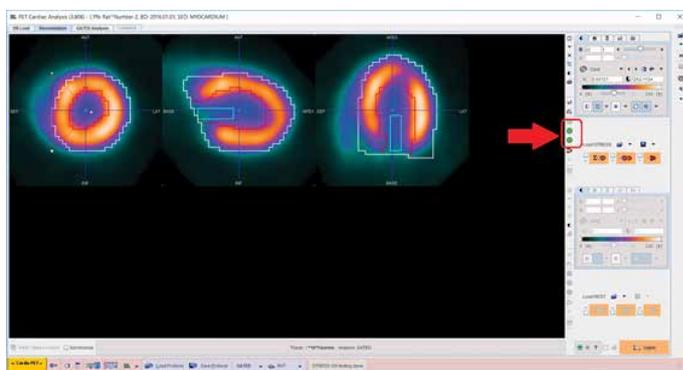


Figure 19. VOIs defined on heart and buttons for manual editing if needed.

In instances where the myocardium contrast is less optimal, it may be helpful to change the base radius value from 6.0 mm to 4.0 mm



Figure 20. If the VOIs returned do not align well with the observed target margins it may be useful to adjust the Base Radius Approximate Value and reanalyze

The white region shows the epicardium, the red region the endocardium and the pale blue shows a region of interest within the left ventricle.

Now, you are ready to execute the gated analysis on the image by simply clicking on the right most button on the lowest part of the window:

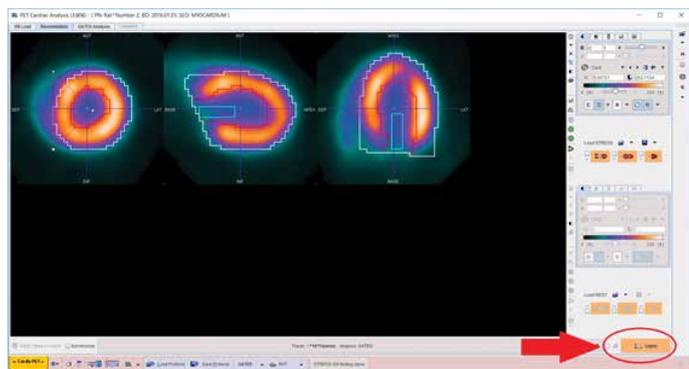


Figure 21. Button to run the analysis after the preparatory work.

Click on the third tab titled 'GATED Analysis' to see the results.

First of all, it is useful to check that the different gates have been well defined. Click on the 'Frames' button and check each of them:

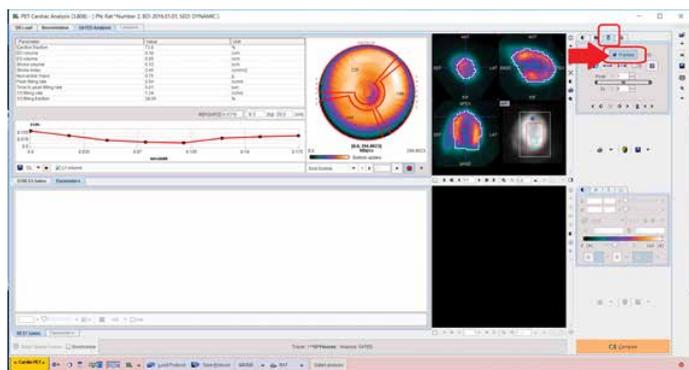


Figure 22. Gated results window and Frames button.

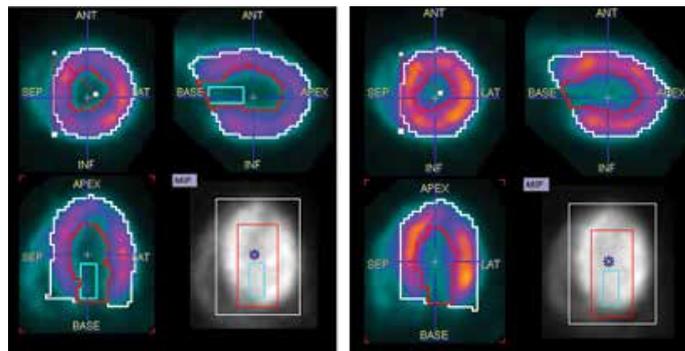


Figure 23. Frame 1 and 2

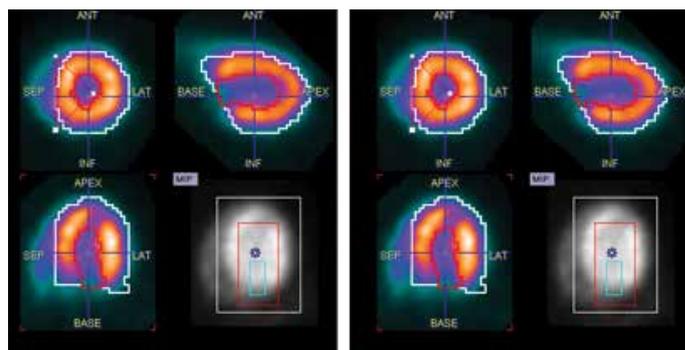


Figure 24. Frame 3 and 4 (End Systole)

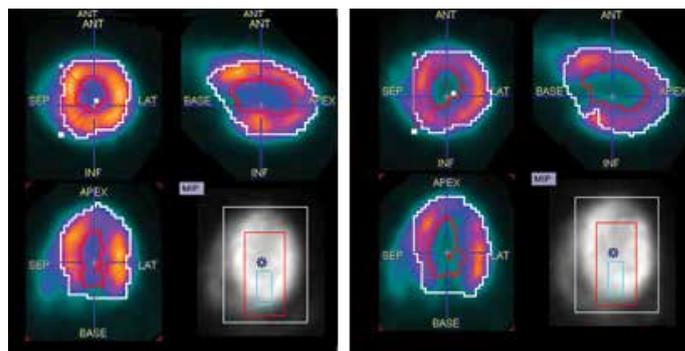


Figure 25. Frame 5 and 6

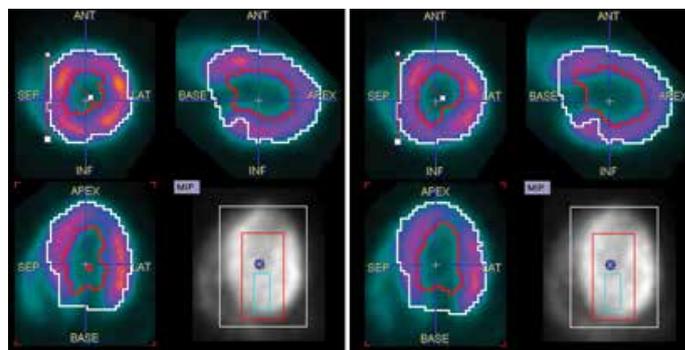


Figure 26. Frame 7 and 8 (End Diastole)

A table is shown with the following numerical results (fig.27). Some old PMOD versions contain a bug such that despite the image is gated correctly, the Ejection Fraction is unrealistically low. For correct values, you should have Versions 3.808 or later.

Parameter	Value	Unit
Ejection fraction	70.3	%
ED volume	0.17	ccm
ES volume	0.05	ccm
Stroke volume	0.12	ccm
Stroke index	3.22	ccm/m <sup>2</sup>
Myocardial mass	0.74	g
Peak filling rate	1.47	ccm/s
Time to peak filling rate	0.04	sec
1/3 filling rate	0.87	ccm/s
1/3 filling fraction	35.46	%

BSA [cm<sup>2</sup>] 0.0378    0.3 [kg] 20.0 [cm]

Figure 27. PCARD results table with summary of analysis

A time chart of the Left Ventricle volume is shown for 1 cardiac cycle in fig. 21 and 27.

By clicking on the drop-down menu marked in red below, a polar plot is shown for different myocardium segments with the following options 'End Systole', 'End Diastole' and 'Wall'.

It is also useful to check that by clicking 'End Systole' and 'End Diastole' that the respective gates or frames are shown, which is an indication that the processing has been successful.

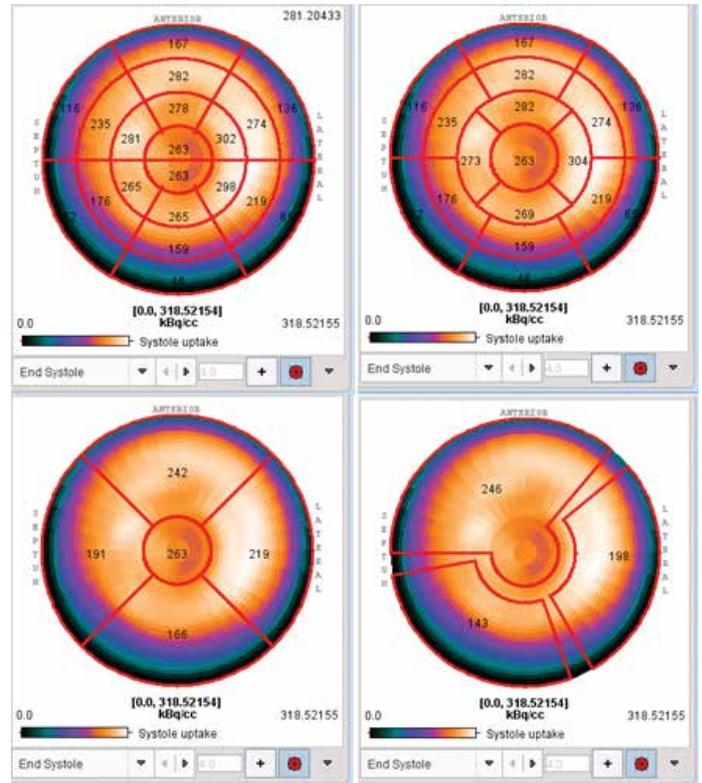


Figure 30. Top left: 20 AHA sectors. Top Right: 17 AHA sectors, Bottom left: 4 sectors. Bottom right: arterial

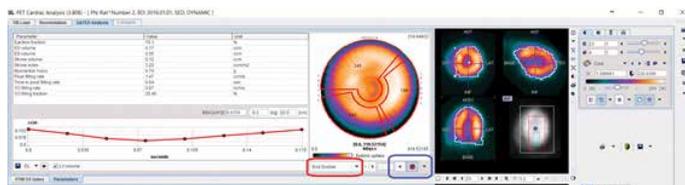


Figure 28. Choosing between End Systole or End Diastole. Also, button to change the number of sectors in polar map.

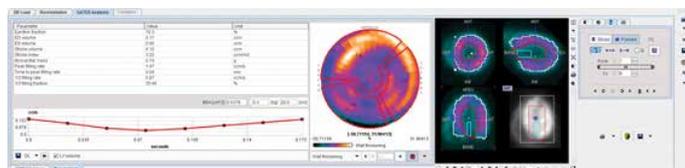


Figure 29. Wall thickening polar chart.

By clicking on the blue square above (fig. 28), one can select the number of sector into which the polar plot is to be divided:

## References

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