

## Bruker PET: Workflow and Techniques in Dynamic PET Imaging and Special Focus in Cardiac Kinetic Analysis

B Kundu<sup>1</sup>, C Molinos<sup>2</sup>, T Sasser<sup>2</sup>, M Chordia<sup>1</sup>, J Li<sup>1</sup>, C Correcher<sup>2</sup>, M Heidenreich<sup>2</sup> and S Berr<sup>1</sup>

Author Information: 1 - University of Virginia School of Medicine, 480 Ray C. Hunt Dr., Rm 183, Charlottesville, VA 22908, US; 2 - Bruker NMI (Nuclear Molecular Imaging), Bruker BioSpin Preclinical Imaging Division, Rudolf-Plank-Str. 23, 76275 Ettlingen, Germany

Corresponding author: C Molinos [cesar.molinos@bruker.com](mailto:cesar.molinos@bruker.com)

Dynamic PET imaging is a powerful tool for testing and validating tracer kinetic modeling. Tracer kinetic modeling is a method for extracting transfer rate constants, volumes of distribution or binding potentials from the radiotracer to the target, by describing the mechanism of transport and biochemical reactions of the tracer in tissue. Blood samples are often taken from the animal to obtain the so-called input function. This is compared to the PET image to obtain the dynamics of the radiotracer concentration in local tissue over time.

PET has been shown to outperform SPECT in dynamic imaging like myocardial perfusion imaging due to the true quantification capabilities and superior image quality.<sup>1</sup>

The Bruker PET platform includes PET/CT systems like Albira Si and PET/MRI options for both sequential and simultaneous imaging. The PET platform for MRI sequential imaging is available as a PET/MRI 3T integrated system and also as a PET Inline module compatible with all Bruker High Field MRI portfolio. The PET Insert enables simultaneous PET/MRI for High Field MRI systems with bore sizes of 30 mm. All these systems share the same PET hardware architecture and core software.<sup>2</sup>

This document is an introductory guide to carrying out dynamic experiments with the Bruker PET Imaging portfolio. It covers experiment preparation including animal preparation, injection dose, data acquisition to image analysis. This note uses an PET FDG acquisition from a rat applied to cardiac imaging as an example of dynamic imaging, using the Albira Software Suite. However, most of the procedure will not differ greatly with other types of dynamic experiments when for instance other PET tracers are employed. In imaging systems where Paravision integrates all software interfaces, only the software acquisition and reconstruction will differ.

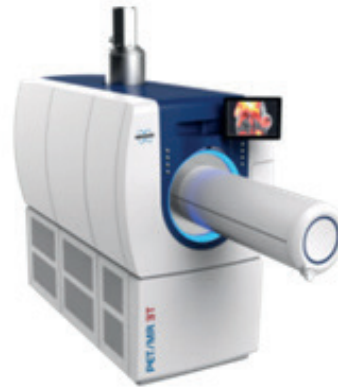
### Requirement for the User

The user of this guide is required to have successfully completed the Bruker training course that normally follows scanner installation. Familiarity is also assumed with small animal lab handling practices, as well as compliance with local rules on animal handling and care, and dealing with ionizing radiation.

Figure 1



Albira Si  
PET/CT/SPECT



PET MRI 3T



PET Inline for  
HF MRI Systems



PET Insert for  
HF MRI Systems

Bruker PET Systems

## Software Template

As part of the experiment planning, it is important to prepare the acquisition settings to be used on the software. There are 2 options for defining a dynamic acquisition. On the first option, the user labels the acquisition as “Dynamic” on the Manager module of the Albira Software Suite. The desired number of frames and their duration can be set, as well as pauses, which are acquisition intervals during which data will not be recorded. On the second approach, a sufficiently long single scan is defined so that the actual rebinding into different time frames is performed over the resulting single List Mode file.

Please refer to the Albira Si Manual for details on how to define the acquisition using the Manager module.<sup>3</sup>

If the acquisition is defined as dynamic beforehand, bear in mind the ‘H Offset’ column on the frame list refers to the bed offset relative to the starting frame.

The option of LM file rebinning at the end of the acquisition provides additional flexibility for trying different framing options, as well as allowing for a higher timing precision. Frames can be as short as 1 second and since the rebinning is performed reading the event time stamps on the LM file, the precision is very high (20 ns).

The details of the LM file rebinning are covered in the section after the data acquisition.

Figure 2

**PET Parameters**

Quality: Standard

Capture Time: 60 s

Delay: 10 s

Capture Mode: Time

Frames: 4

**Frames**

Order	Total	Stop	Delay	Gated	Gated Steps	H Offset
1	70	60	10	False	1	0
2	140	60	10	False	1	0
3	210	60	10	False	1	0
4	280	60	10	False	1	0
5	350	60	10	False	1	0

New

Defining a Dynamic Acquisition in Albira Manager.

## Experiment and Animal Preparation

Dynamic acquisition involves positioning the animal in the field of view and starting the acquisition before the injection has taken place. The injection can be a slow infusion or a bolus dose. The latter is shown in this example.

The technical features and the animal management capabilities of the Bruker PET imaging platform make it suitable for routine dynamic imaging. To maximize operator safety and minimize interference between the different imaging modalities, the Bruker systems present a fully enclosed shell. Dynamic imaging differs from static imaging in that the systems must be operated with the animal access door open. Therefore a short catheter is used to perform the injection from outside the instrument.

What follows is a suggestion for this catheter injection procedure via the tail vein. Experienced users may choose different components and procedures.

### Materials

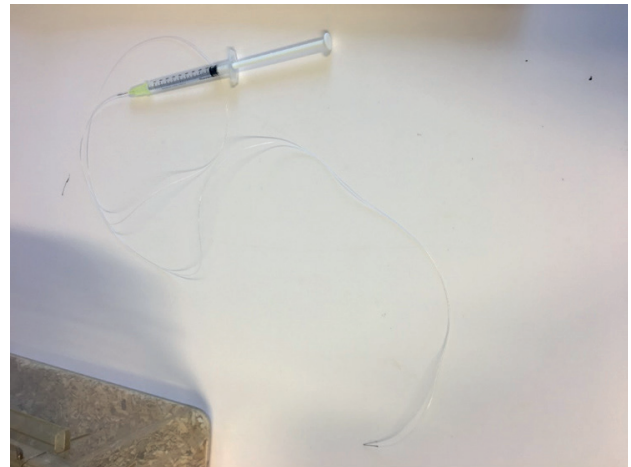
- Polyethylene tubing 0.28 x 0.60 mm (0.011 x 0.024 in). See for instance INSTECH's BTPE-10.
- 2 x Needle 0.4x16 (27Gx5/8").
- 1 ml syringe
- Anticoagulant. For instance, Heparine LEO 5000 U.I/ml

### Procedure

Cut the required length of tubing. In most cases 30 to 50 cm will suffice. Bear in mind that the volume inside this catheter length will be 74 and 123 ul respectively. Add a needle at one end and insert the syringe in the other. Fill the syringe with a solution containing 0.1ml heparine and 0.9ml saline. Connect the tubing with a needle at the end and fill the whole catheter with heptamerized saline. Then let a small air bubble at the end of the catheter and withdraw your activity or contrast agent. After this, repeat the last operation to have a small volume of heparinized saline for when you will cannulate the tail vein.

The two liquids are normally separated by a micro bubble which does not cause a problem for small rodents. New pre-clinical lab users will require further advice for a successful tail vein injection. Further details in this useful reference.<sup>4</sup> As advanced reading, the following reference assesses the impact of the injection quality in small animal PET imaging.<sup>5</sup>

Figure 3



Catheter and syringe.

Place the animal under anesthesia in the animal bed on the animal transport system as shown below. Insert needle into tail vein. Prepare to start acquisition in the software.

Figure 4



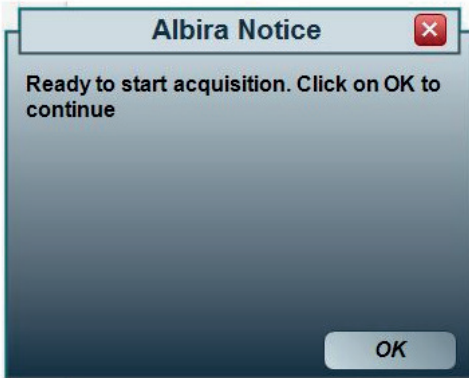
Animal in the Albira Si Animal Handling System.

### Image Acquisition

With the animal placed in the bed, click on the Start button to commence acquisition. The automatic animal transport system will place the bed in the selected location in the FOV. Please note that for attenuation correction a CT will be necessary. It is recommended to carry out the CT prior the PET acquisition.

If the acquisition is defined as "Dynamic" on the Acquisition template, after the bed is positioned, a window will pop up prompting the user to start the acquisition:

Figure 5

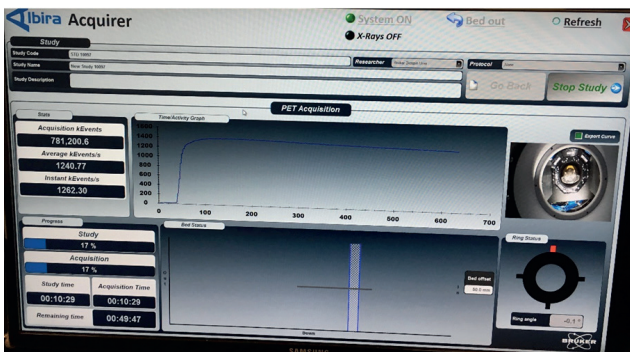


The system will start acquiring when you click OK if the acquisition template is labelled as dynamic.

It is possible for this window to be hidden by the operative system behind other open applications. If this happens, simply press the Windows keyboard shortcut Alt + Tab to show all open windows, select the one shown above and press OK to start the acquisition.

The large FOV of a 3R PET configuration allows simultaneous imaging of the brain and heart. Wait for the first few events to be shown on the Acquirer screen and then inject. If the pressure is abnormally high, this usually indicates that the needle has not been inserted properly in the tail vein. The Acquirer window shows the acquisition event rate. This is particularly useful for monitoring the injection effect, whereby the rate increases very rapidly. Failed injections can also be detected by checking the curve's ramp. If the curve climb is small showing a low detection rate or if the ramp is too slow, the user can realize that the activity did not enter the blood stream.

Figure 6



Acquirer Software Window showing the acquisition event rate when the initial ramp produced by the injection is shown.

The rate trend line shows a low count rate at the beginning, due to noise from the LYSO inherent activity. When the bolus is injected, a sharp rise is observed. The example shows an FDG injection of around 16 MBq, with a rat positioned with the heart approximately in the centre of the FOV. Different tracers, activities and animal positions will result in different peak activities.

As the acquisition advances, the total counts slowly decrease. This will depend on the Half Life of the tracer, as this curve is not corrected for decay.

### Image Reconstruction

If the acquisition was performed as a dynamic study from the beginning, reconstruction can be performed normally. If the LM was acquired as a single LM file, the file must be rebinned into different LM files with the desired duration. Before this can take place, the recently acquired file needs to be prepared. An ordinary reconstruction will prepare the file and will also help in confirming that the acquisition was successful. Once this is complete, the LM is ready for rebinning.

The time bins used can vary depending on the study. Here are two example rebinning schemes:

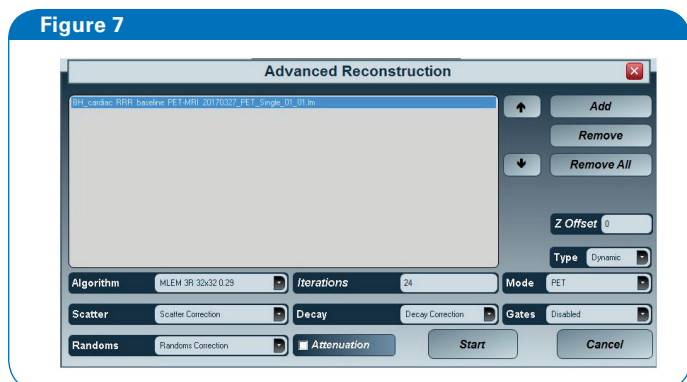
Example 1		Example 2	
Number of bins	Duration(s)	Number of bins	Duration(s)
11	8	10	1
1	12	10	5
2	60	6	10
1	180	6	30
8	400	10	60
		4	600

Table 1. LM rebinning scheme 1. Total duration 60 min.

Example 1: Cardiac imaging, 23 frames, total duration 3600s.

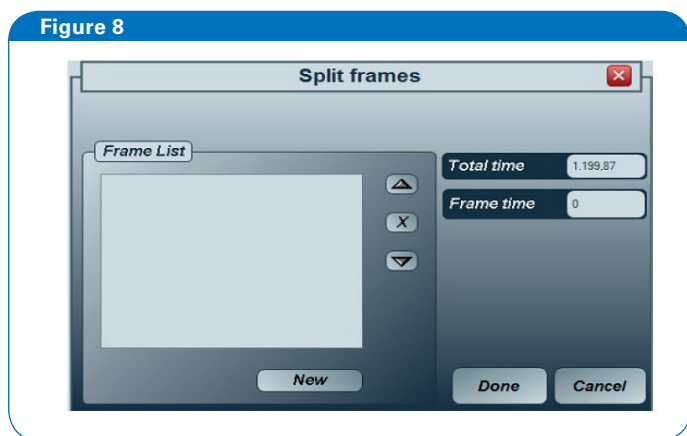
Example 2: Brain imaging, 46 frames, total duration 3300 s.

On the Advanced Reconstruction Menu, the frame rebinning dialogue tool will appear if dynamic type is selected and only one LM file is introduced as input.



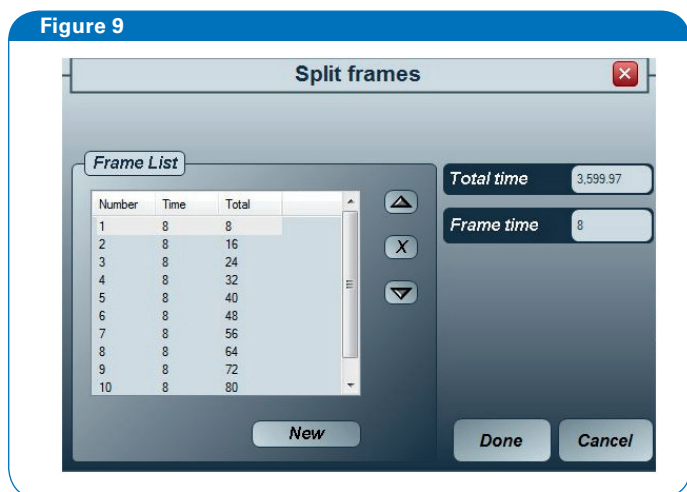
Advanced Reconstruction Menu.

The following figure shows the LM rebinning tool:



LM file rebinning tool of the Advanced Menu.

The total acquisition time is shown. Enter the duration of the first frame and click on Add. If more frames of the same duration are required, simply click New as many times as necessary. When changing the frame duration, ensure the cursor is situated at the bottom of the list.



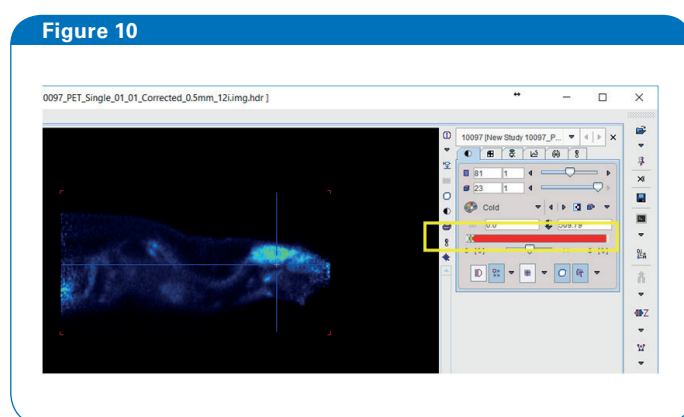
LM file rebinning tool showing defined frames.

The frame list shows the cumulative duration, which is useful for checking consistency before finishing the list. If an input error is detected, simply navigate to the incorrect frame using the up and down arrows and click the cross to delete it.

After the list has been defined, click Done and the file rebinning process will start. The last frame duration will be adjusted to match the actual file length.

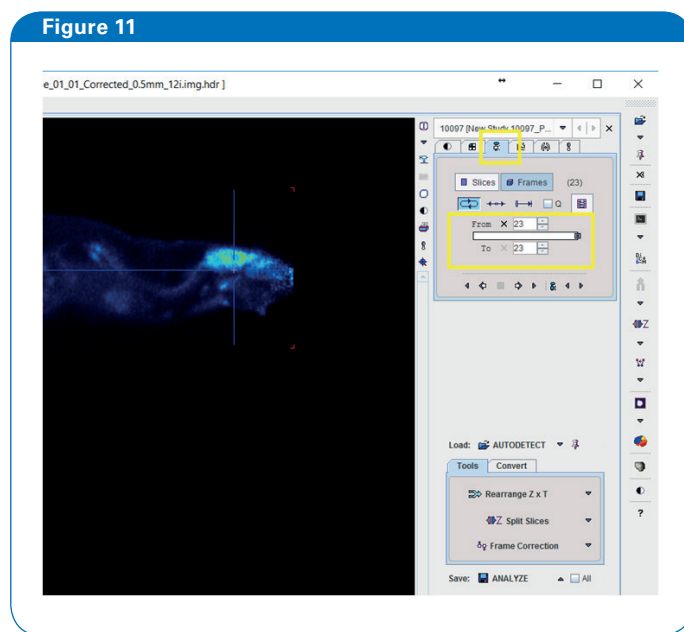
## Image Analysis

The image can be analysed in the View module of PMOD. The first frames will have few events, so it is useful to visualize the whole sequence at once. Simply saturate the color palette:



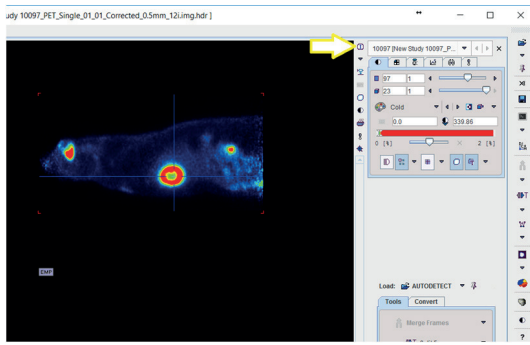
The VIEW module of PMOD

Then merge the different frames into a single image:



Merging a whole dynamic sequence of 23 frames.

Figure 12



PMOD View Module "info and edit" button.

Figure 13

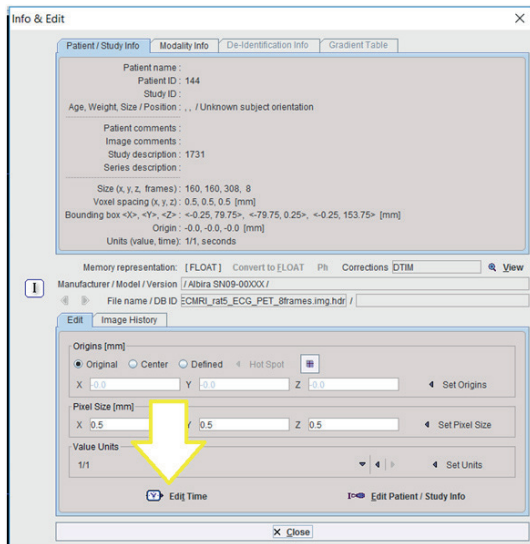
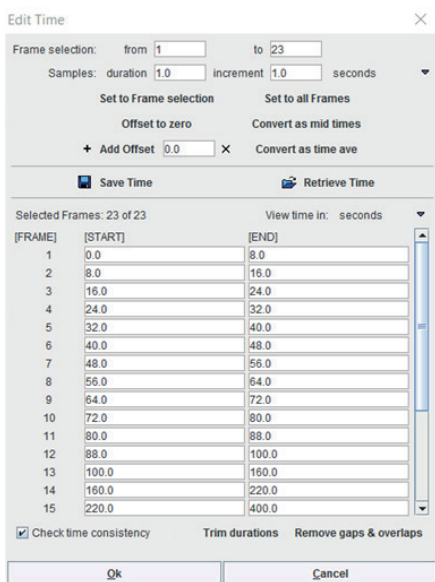


Image Information Menu.

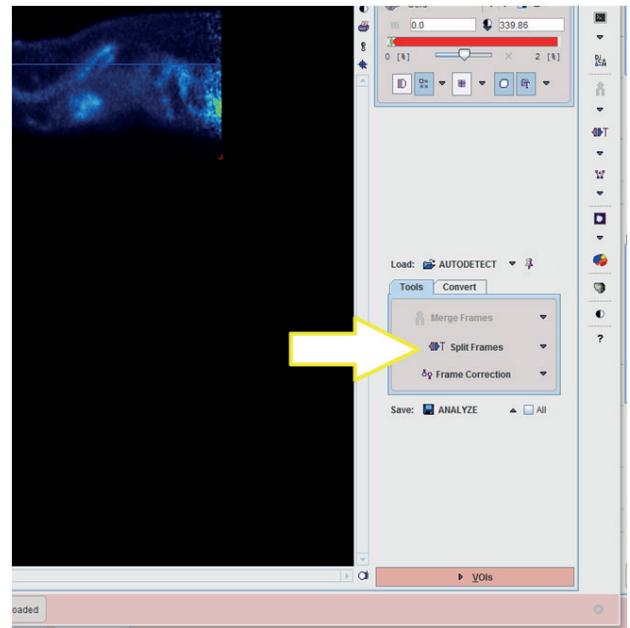
Figure 14



Time Frame Menu.

Frames can be removed, altered or rearranged using the split feature. After splitting and making the desired changes, a new image can be created by saving the changes.

Figure 15



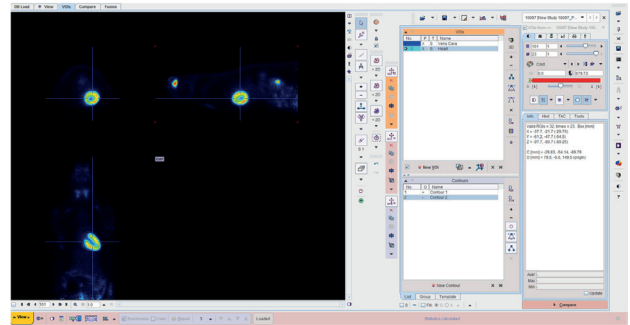
Frame splitting tool.

The next step is generating VOI (Volumes of Interest), for which there are several methods in PMOD. A fast and effective approach is to define a Cube or Sphere object and use the Automatic Isocontour Selection to shape it around the organ to be analyzed.

A typical use of this feature would be to remove frames at the start or at the end.

### PMOD VOI Generation

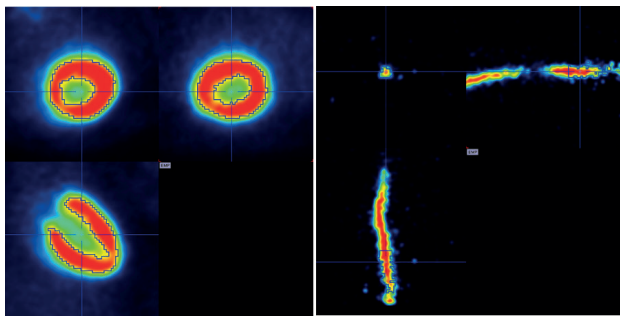
Figure 16



PMOD VOI Menu.

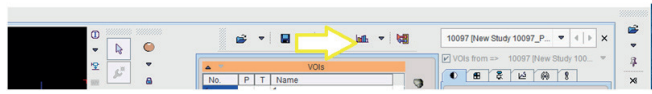
A TAC of the Myocardium and the Blood will be shown. For this procedure, the inferior vena cava will be used.<sup>5</sup>

Figure 17



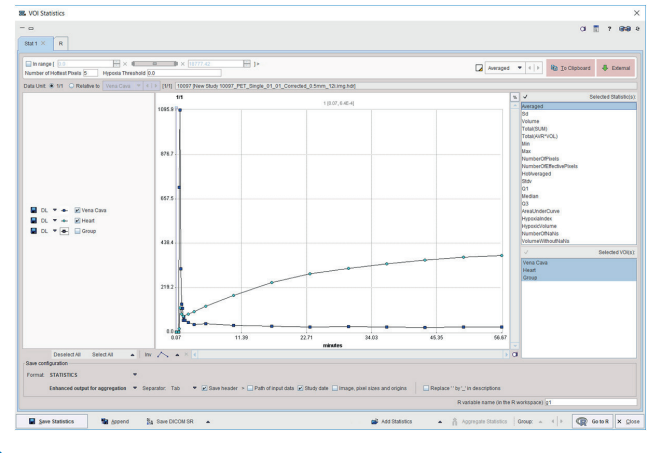
VOIs defined in the heart left ventricle and inferior vena cava.

Figure 18



Statistics calculation button

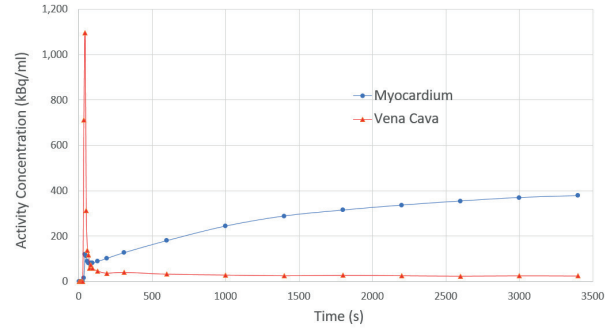
Figure 19



VOI statistics results.

PMOD will automatically plot the statistics of the VOI analysis. Exporting the data to a spreadsheet enables data processing, as well as more formatting options when generating charts.

Figure 20



VOI statistics data exported and plotted in MS Excel.

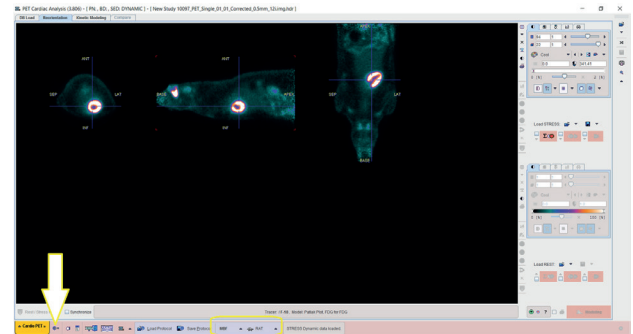
The chart shows the spike in the blood following the moment of the injection and then the subsequent washout of activity. The myocardium nevertheless presents a trend showing the gradual uptake of FDG.

### PCARD

PMOD offers a software package specially designed for analyzing cardiac PET images known as “Cardiac PET Modelling” or simply “PCARD”. PCARD allows short-axis reorientation of the heart. Based on this orientation and the semi-automatic definition of VOIS, PCARD is able to carry out Myocardial Segmentation and TAC Calculation and Quantification of Dynamic as well as Gated Cardiac PET or SPECT. Please refer to the user guide for details.<sup>4</sup>

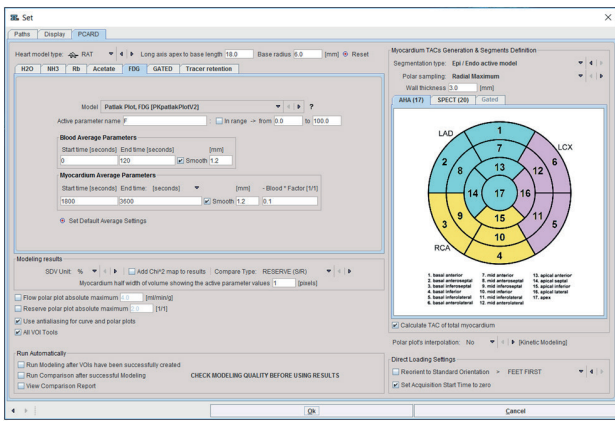
Load the image in PCARD and make sure the settings are consistent with the analysis to be carried out. In this example, it is a dynamic study based on the FDG tracer for studying myocardium blood flow.

Figure 21



PCARD main screen showing settings button and the current configuration.

Figure 22

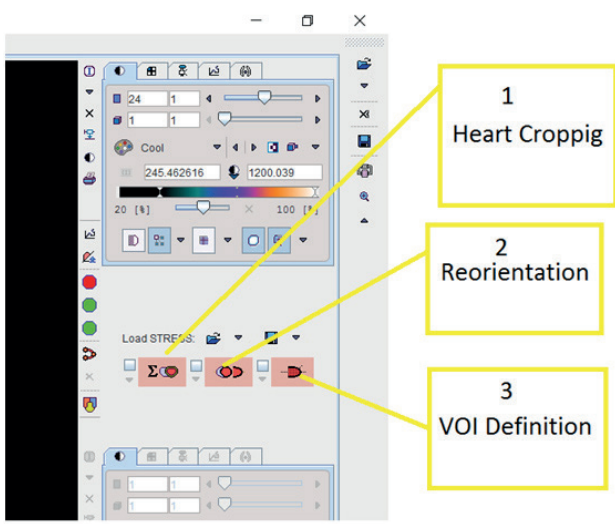


Default settings for a rat configuration.

The preparation of the cardiac VOI involves 3 steps:

1. Heart cropping
2. Reorientation to SA
3. Definition of VOI

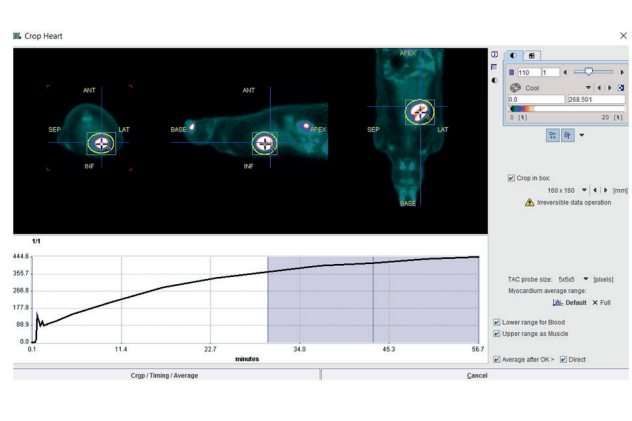
Figure 23



PCARD Caridac VOI creation steps

When the crop button is pressed, a new window appears. The time interval for image averaging must be selected. To save processing time it is important to restrict the region of interest to the boundaries of the heart.

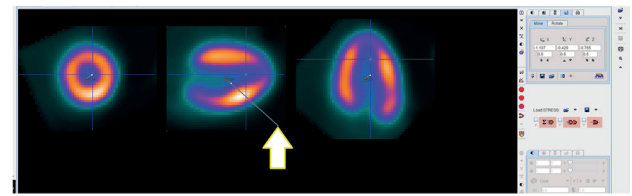
Figure 24



Crop Heart Menu.

The next step adjust the image orientation to show the SA of the heart. This is normally quick but sometimes the algorithm fails to get the right orientation, in which case it is necessary to adjust manually. Rotate each of view so the correct orientation is achieved.

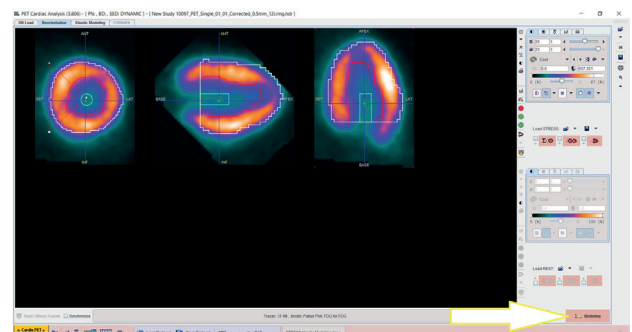
Figure 25



Manual adjustment of SA Orientation

Next press the VOI creation button. This step will normally take a few seconds.

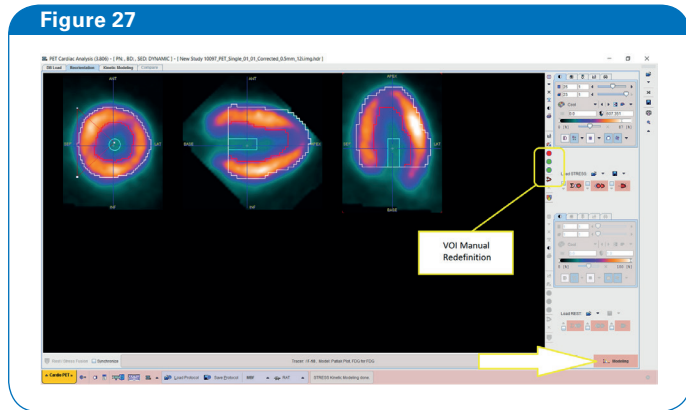
Figure 25



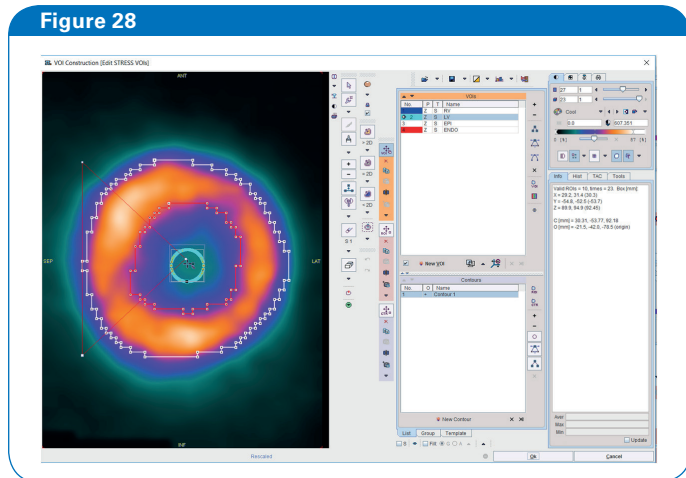
VOI defined just prior modelling.



Once complete, myocardium is shown with the relevant VOIs overlaid: epicardium, endocardium, LV and RV. The latter is not always be visible. The VOIs can be edited manually:



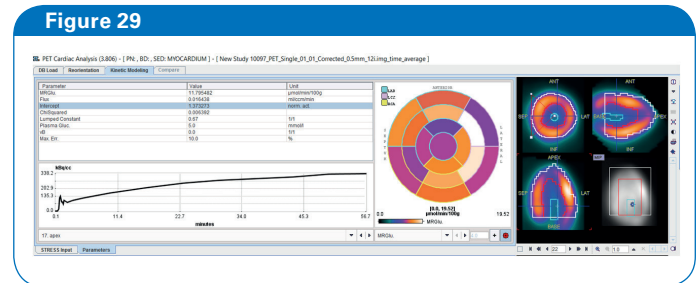
Controls for manual redefinition of the VOIs



Edition of selected VOIs

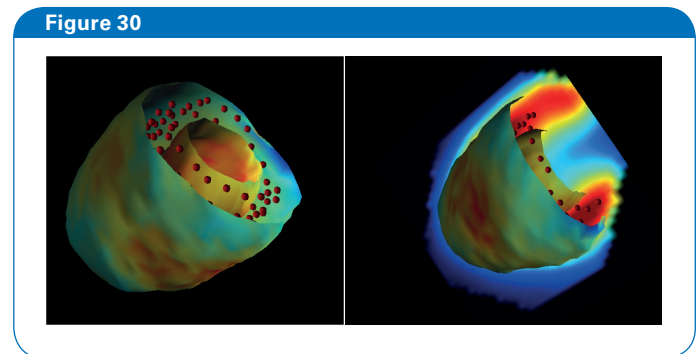
After this step, modelling can be performed by pressing the modelling button.

TACs of the MRGlux, Flux and Intercept can be shown with the different VOIs as well as the total myocardium and each of the 17 segments on the polar plot.



PCARD Results screen.

PCARD is linked to the PMOD 3D rendering tool. If this tool is available, a rendering of the myocardium can be created easily. This will show the LV and algorithm sampling points, and cross planes can be placed.



3D renderings of the cropped heart.

## Acknowledgements

CM would like to thank Dr David Viertl from CHUV (Lausanne, Switzerland) and Dr Willy Gsell from KU Leuven (Leuven, Belgium) for their advice on preclinical laboratory practices.

BK's research is funded by the NIH.

## References

- [1] Quantification of myocardial blood flow and flow reserve: Technical aspects. Ran Klein et al. *Journal of Nuclear Cardiology* 2010; 17:550-70
- [2] Next Generation of the Albira Small Animal PET Based on SiPM Detectors and Continuous Crystals. A Gonzalez et al. *Bruker White Paper* 2015
- [3] Albira Si Instructions for Use User. Bruker 2017.
- [4] Mouse Tail Vein Catheterization/Injection. May 2008. Online note from UC Davis Biomedical Engineering. [https://bme.ucdavis.edu/cmgi/files/2015/01/Mouse\\_Tail\\_Vein\\_Catheter\\_Procedure\\_Rev2.pdf](https://bme.ucdavis.edu/cmgi/files/2015/01/Mouse_Tail_Vein_Catheter_Procedure_Rev2.pdf)
- [5] Evaluation of Mouse Tail-Vein Injections Both Qualitatively and Quantitatively on Small-Animal PET Tail Scans. DC Vines et al. *J. Nucl. Med. Technol.* December 1, 2011 vol. 39 no. 4 264-270
- [6] PMOD Cardiac PET Modeling (PCARDP) User's Guide. Version 3.8. PMOD Technologies October 2016
- [7] Image-Derived Input Function from the Vena Cava for 18F-FDG PET Studies in Rats and Mice. B Lanz et al. *The Journal of Nuclear Medicine* 2014 Vol 55 No 8

## Further Reading

- [1] Quantitative PET imaging detects early metabolic remodeling in a mouse model of pressure-overload left ventricular hypertrophy in vivo. Min Zhong, Clayton E. Alonso, Heinrich Taegtmeyer, and Bijoy K. Kundu. *J Nucl Med* 2013; 54:609–615 DOI: 10.2967/jnumed.112.108092
- [2] Remodeling of Glucose Metabolism Precedes Pressure Overload-Induced Left Ventricular Hypertrophy: Review of a Hypothesis. Bijoy K. Kundu, Min Zhong, Shiraj Sen, Giovanni Davogusto, Susanna R. Keller Heinrich Taegtmeyer. *Cardiology* 2015;130:211–220. DOI: 10.1159/000369782



info@bruker.com  
www.bruker.com