Chapter 8 Myocardial Blood Flow and Reserve

Quantitative Coronary Flow Reserve (CFR)

The **Reserve** screen *(Figure 8.1)* provides the capability to process and review dynamic cardiac PET and SPECT datasets from validated camera systems. Dynamic datasets can be used to estimate absolute myocardial blood flow and coronary flow reserve (CFR). Such measures often provide a more reliable assessment of perfusion abnormalities than conventional quantification of myocardial perfusion.

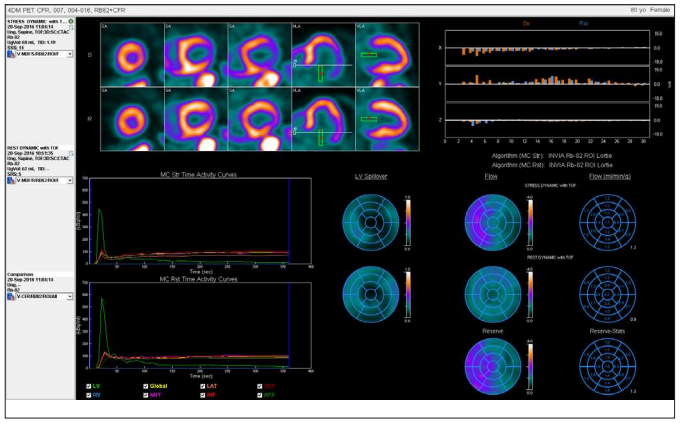


Figure 8.1: *The Corridor4DM Reserve Screen*

CFR processing should be preceded by the QA workflow on the MI Processing screen to verify accurate automated LV contour generation on all datasets. These LV contours are used for ROI/bounds placement within the Reserve screen and also to help do quality checks for patient motion and flow model processing.

Input Data

A dynamic dataset consists of a series of 3D image volumes acquired at different time points (called frames) during the first pass and uptake of the radiotracer in the heart. When a dynamic dataset is loaded into Corridor4DM, static images are automatically generated by summing the frames from a portion of the dynamic series. The portion of the dynamic series to be summed is configurable in **Preferences**, on the **Image Display** page *(Figure 8.2)*. Generally, the Summed Volume Start Time should be set to a time after the tracer has cleared from the RV and LV blood pool, and the Summed Volume Stop Time should be set to the end of the last frame. In addition, options are available to adjust smoothing filters that can be applied to summed datasets. These summed static datasets are displayed on all image review and processing screens, as well as the **Reserve** screen.

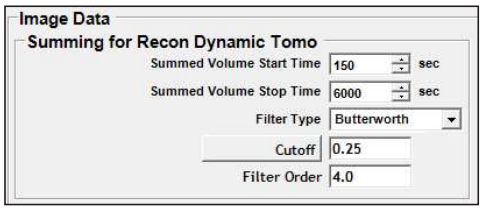


Figure 8.2: *Image Data section of the Image Display Page within Preferences*

CFR QA, Processing, and Results Review

Stress and rest datasets are displayed and processed together on the Reserve screen which has two modes: **QA** and **Results Mode**. The Reserve screen defaults to the **QA Mode** when unprocessed stress and/or rest dynamic data is displayed. Once flow results are processed and saved, the Reserve screen defaults to display the **Results Mode**.

QA Mode Workflow

1. **Evaluate data for motion and correct frames if:** Respiratory motion prevalent in dynamic data and is known to affect flow and reserve results so it is important to evaluate every patient's

dynamic dataset(s) for the presence of motion. To check this, click the Cine tool in the toolbar and view the dynamic frame sequences for motion of the blood pool uptake spilling over into the Corridor4DM-generated LV contours *(Figure 8.3)*, or for the LV tissue frames to show tissue uptake outside of the LV contours.

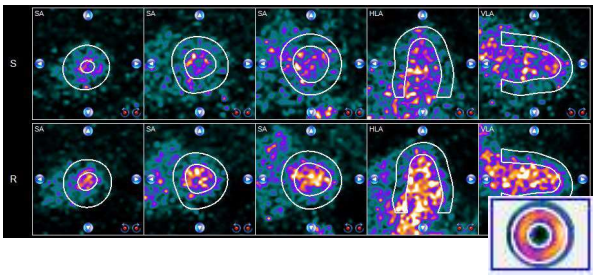


Figure 8.3: *Dynamic frame sequences with contours enabled*

- To evaluate for motion frame-by-frame, pause the Cine, and click the **Cine** tool drop-down arrow *(Figure 8.4)* to access the frame slider. Scroll the slider through all frames in the sequence and review the stress and/or rest slice viewports below.

Figure 8.4: *Cine tool with frame slider*

- If motion is present, manually correct for motion in each frame where the dynamic tracer activity does not align properly to the displayed LV contours, by clicking directly on the image and dragging it to the desired location. Alternatively, apply adjustments in the X (left/right) and/or Y (up/down) directions *(Figure 8.5)* using the Fine Pan arrow tools where each click represents 1 mm of movement. Adjust rotation (Z-direction) using the Fine Rotate tools located in the lower right corner of each viewport.

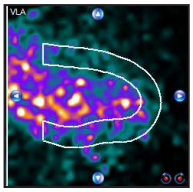


Figure 8.5: *Fine Pan arrow tools and Fine Rotate tools*

- All preliminary motion correction changes to the data appear on the motion correction graph to the right of the viewports, showing X, Y, and Z updates made throughout the frame sequence, in mm of motion. To view preliminary flow results and apply the corrections, click the **Apply** tool *(Figure 8.6)* after corrections are made.

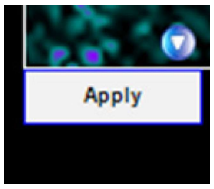


Figure 8.6: *Apply tool*

2. **Verify the bounds/ROI are properly positioned, depending on default method selected**: Turn the Cine tool off to view the bounds/ROI placement. Corridor4DM defaults to the ROI method, with others available.

- When either the Factor Analysis or the Factor Analysis-Hybrid algorithms are applied, the ellipsoid-cylindrical bounding volume can be dragged to change the height or width of the factor analysis bounds in each viewport *(Figure 8.7)*. The user should adjust the size of the bounds to ensure inclusion of the blood pool regions and to exclude non-cardiac regions.

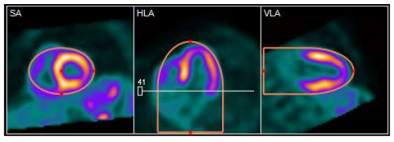


Figure 8.7: *Factor Analysis algorithm*

- When the ROI algorithm is applied, the rectangular ROI can be dragged to change the height or width of the LV blood pool sampling region in the HLA and VLA viewports *(Figure 8.8)*. The user may increase the size of the ROI to improve statistics in the LV blood Time Activity Curve (TAC).

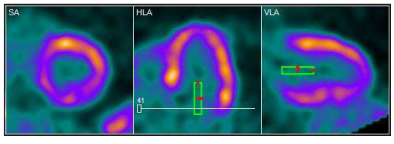


Figure 8.8: *ROI algorithm*

Prior to proceeding to the Results Mode, check to verify the perfusion and flow normals databases are selected for stress, rest and CFR. Selection of these ensures CFR quantification of perfusion defect regions on the Reserve Results page, as well as other derived comparison results to relative perfusion polar maps.

3. **Corridor4DM automatically processes flow results when: any motion correction is applied; changes are made to the ROI/Bounds; or a different flow model is selected for processing.** Both stress and rest datasets are processed at the same time. The processing is fully automated and typically takes 1-2 minutes to complete for Factor Analysis, and a few seconds to complete for ROI analysis.

4. **Review Preliminary Results**: Once processing completes, additional QA results display on the QA Mode of the Reserve screen to permit detailed analysis of the acquisition, motion correction, and kinetic flow model results. **It is important to click Save in the Control Panel once completed with Reserve processing and QA.** Once reviewed, to enter the Results Mode, click the **Next** button *(Figure 8.9)* in the Toolbar.

Figure 8.9: *Next tool*

Preliminary Results Review in QA Mode

It is important to click Save in the Control Panel once completed with Reserve processing and QA. Review the following information prior to continuing to the Results Mode.

Time Activity Curves (TACs)

When using the ROI algorithm, the user can assess the quality of the CFR processing results by also reviewing the blood and tissue TACs *(Figure 8.10)*. The RV curve (blue) is flat with a value of zero. The LV curve (green) should peak and then gradually approach zero toward the end of the dynamic series. The QA Images toggle is not available for the ROI algorithm.

After processing with the Factor Analysis algorithm, the Reserve screen provides two components to assess the quality of the CFR processing results.

- First, the user should review the blood and tissue TACs *(Figure 8.11)*. The RV curve peak (blue) should be somewhat higher than the LV curve peak (green), and should occur earlier than (to the left of) the LV curve peak. Both RV and LV curves should gradually approach zero toward the end of the dynamic series. The myocardial tissue TACs should have peak magnitudes that are lower than RV and LV TACs, and should be relatively flat.

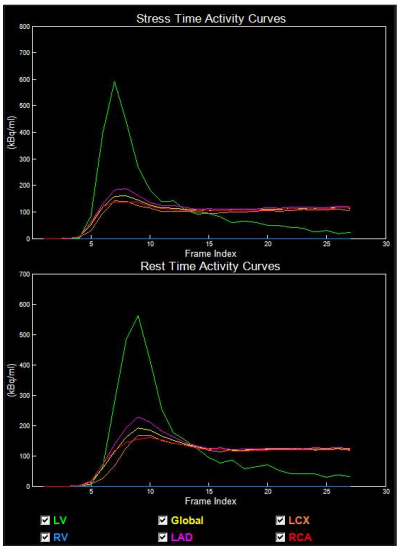


Figure 8.10: *Time Activity Curves*

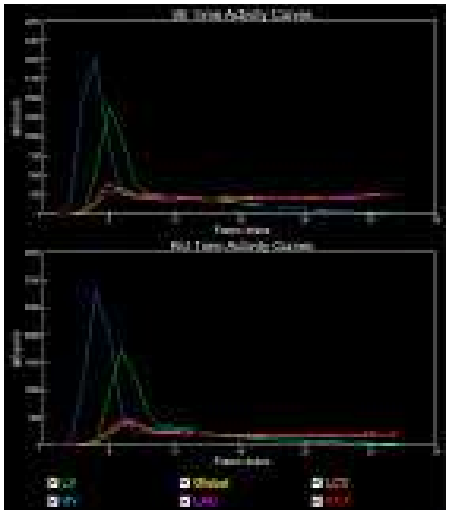
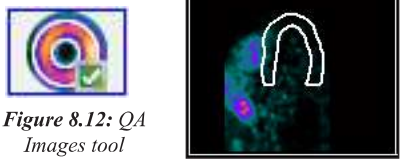
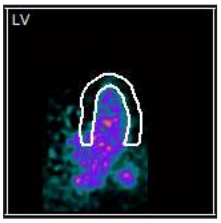


Figure 8.11: *TACs after Factor Analysis algorithm is processed*





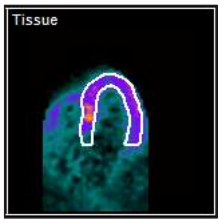


Figure 8.12: *QA Images tool*

Figure 8.13: *Correspondence of the RV factor to the RV blood pool.*

Figure 8.14: *Correspondence of the LV factor to the LV blood pool.*

Figure 8.15: *Correspondence of the tissue factor to the myocardium.*

- Second, the user should examine the factor analysis by clicking the QA Images tool *(Figure 8.12)*. The image viewports display the output of the factor analysis for stress and rest. The user should confirm the factor analysis in the RV *(Figure 8.13)*, LV *(Figure 8.14)*, and tissue factor images *(Figure 8.15)*.
- If this is not the case, the flow results will be incorrect. The user can reassign the factor analysis labels (RV, LV, and Tissue) in the image viewports by clicking the drop-down button and selecting the correct label. The flow and CFR values are then recalculated automatically.

Several tools are provided to modify the appearance of the TAC graphs:

Figure 8.16: *Time Activity Curve check boxes*

- **LV, RV, Global, ANT, LAT, INF, SEP, APX check boxes** *(Figure 8.16)***:** Allow the user to selectively display the color-coded TACs on the graph (unchecking the RV or LV curves automatically rescales the y-axis, and allow more detail to be seen in the relatively low myocardial tissue TACs).
- **Start/Stop blue reference lines** *(Figure 8.17)***:** Allows manual updates to the start and end point of CFR analysis. Click and drag to the desired point on the TAC.

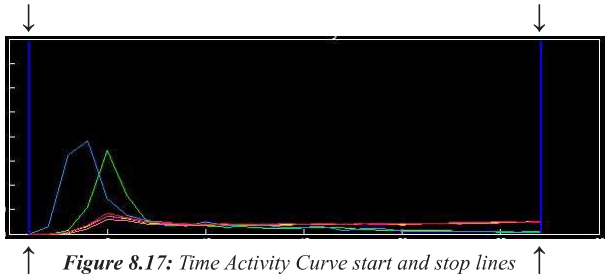


Figure 8.17: *Time Activity Curve start and stop lines*

- Right-click the Time Activity Curves to display the Curves Options window *(Figure 8.18)* and further customize the display by selecting any of the following:
  - **Kinetic Model:** When checked, the kinetic model fitted tissue TACs (solid line), the measured tissue TACs (circular markers), and kinetic model parameters (rate constants K1, K2, K3, spillover values FV and RV, and model fit error ChiSq) are displayed. When unchecked, only the measured tissue TACs are displayed (solid line).

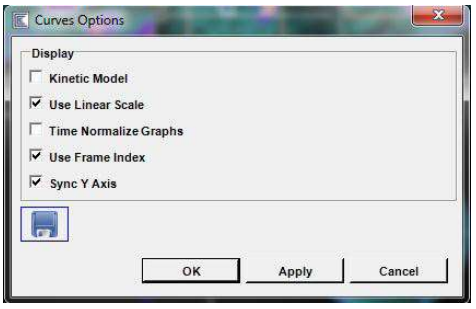


Figure 8.18: *Curve Options window*

- **Use Linear Scale:** When unchecked, the vertical axes are converted to a log-scale.
- **Time Normalize Graphs:** When checked, scales the activity concentration in each frame by the frame duration. When unchecked, no scaling is applied.
- **Use Frame Index:** When checked, graphs the activity concentration versus frame index. When unchecked, graphs the activity concentration versus time.
- **Sync Y Axis:** Synchronizes the y-axis scales for stress and rest to compare curve peaks more accurately.

LV Spillover

Corridor4DM displays stress and rest Spillover maps *(Figure 8.19)* next to the TACs to help aide in the detection of patient motion after results have been processed. The polar maps represent a summed image of the dynamic sequence. These should show little to no activity with homogenous appearance, signifying that blood pool activity is not spilling over into the LV contours displayed above in the slice viewports. If the polar maps show mottled, heterogeneous activity, this signifies a need to make additional motion correction changes in the viewports above.

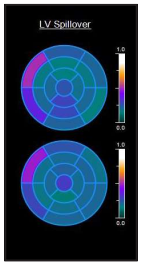


Figure 8.19: *Spillover maps*

Flow Polar Maps

Preliminary stress, rest, and reserve flow calculations *(Figure 8.20)* display in two columns:

- The middle column displays, top-down: the absolute stress, rest, and reserve flow values in units of ml/min/g, sampled over 460 sectors to provide a pixel-level flow polar map for review.
- The right-most column displays the flow values without pixel data included, called Stats maps. These show the absolute flow and reserve value results based on the overlay map selected. The global LV flow value is displayed at the 5 o'clock position just outside of each of these polar maps, for stress, rest, and reserve.

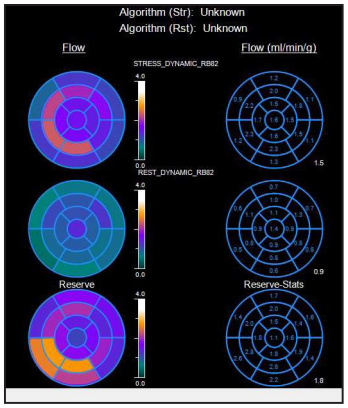


Figure 8.20: *Flow Polar Maps*

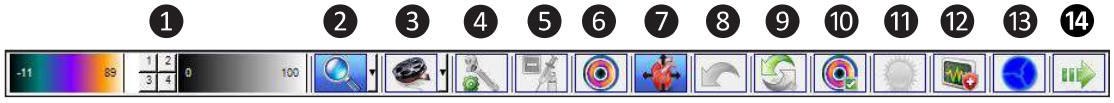


Figure 8.21: *QA Mode Toolbar Options*

QA Mode Toolbar Options *(Figure 8.21)*:

1. **Dual Colorbar Tool:** The color control tool is comprised of the two colorbars separated by a numbered panel. Right-click the colorbar to customize color schemes and adjust intensity mappings. For more information on colorbar management, see the Colorbar Tools section.
2. **Magnification Tool:** Adjust the image display size.
3. **Cine Tool:** Activate/Deactivate cine of dynamic sequences. When active, motion correction tools display on all viewports. When deactivated, using the frame slider from the drop-down also activates the motion correction tools. Cine must be deactivated to view the flow ROI or Bounds.

Prior to processing the flow results, check to verify the perfusion and flow normals databases are selected for stress, rest and CFR. Selection of these ensures CFR quantification of perfusion defect regions on the Reserve Results page, as well as other derived comparison results to relative perfusion polar maps.

4. **Processing Options Tool:** Click to view and select the available flow models defined to fit the dynamic data for estimating myocardial blood flow and reserve. Click the Details icon next to the Flow Model Name to view the characteristics of each flow model *(Figure 8.22)*. Corridor4DM can be defaulted within Preferences to the preferred model for each tracer, to permit skipping this step each time the data is launched.

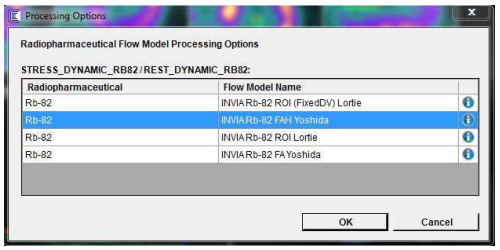


Figure 8.22: *Processing Options Tool*

   - For the **ROI Compartment** model, only the LV blood TAC is sampled from a ROI. The flow and CFR values are then calculated from the blood and tissue TACs using the compartment model.
   - The **FlowQuant (FQ) ROI Lortie** processing option samples the LV and blood TAC from a ROI, but uniquely utilizes a constant distribution volume and frame time weighting in the kinetic modeling.
   - For the **Factor Analysis** (FA) model, the LV and RV blood time activity curves (TAC) are estimated using the factor analysis algorithm. The flow and CFR values are then calculated from the blood and tissue TACs using the compartment model.
     NOTE: With v2018 and later, this model must be manually created.
   - The **Factor Analysis-Hybrid** (FAH) model uses a subset of the pixels from Factor Analysis for the RV and LV blood TACs. This derivative algorithm has shown improvements for studies where there is significant overlap between the blood and tissue factors.
     NOTE: With v2018 and later, this model must be manually created.

5. **Residual Subtraction Toggle Tool:** This tool is necessary in current SPECT dynamic protocols using Tc99m-based tracers, where due to the longer half-life of approximately 6 hours, there is residual activity remaining in the heart from the first to the second acquisition. This tool is enabled/available in cases where the time between the first and second acquisitions is less than the time difference threshold, where the tracer level of the second dataset hasn't decayed to 5% or less from the first dataset acquisition time. Corridor4DM will use the frame prior to the start of the input curve on the TAC of the second acquisition as the baseline activity and subtract this from all subsequent frames in the dynamic sequence.
   - To apply this tool, click to turn on Residual Subtraction in the Toolbar. Once the Residual Subtraction tool is clicked, Corridor4DM automatically computes the second acquisition with residual subtraction applied. To permanently save the CFR processing, click the Save button in the Control Panel.
   - Corridor4DM will disable this tool when the dataset acquisition times between the first and second datasets meet or exceed the time difference threshold. The time difference threshold is calculated taking into account the radiotracer's half-life, decay ratio, and the timestamp of the first and second acquisitions.

6. **Contours Toggle Tool:** Overlay Corridor4DM-generated LV surface contours on the images.

7. **Auto Motion Correction Tool:** This tool turns on and off the ability to automatically correct the image data for motion that may occur during the dynamic acquisition.

8. **Undo Tool:** Once changes are made to correct for motion or ROI placement, this tool becomes active to undo the last move with each click of the tool.

9. **Reset Tool:** Resets the screen to an unprocessed state.

10. **QA Images Tool:** Available for FA and FAH methods only. The image viewports display the output of the factor analysis for stress and rest. The user should visually confirm the factor analysis accurately identified the RV, LV, and tissue factor time points by showing RV blood pool uptake, LV blood pool uptake and Tissue uptake in these viewports. Click the RV, LV or Tissue viewport labels to change assignments if necessary.

11. **Frame Normalization Tool:** Available only when Cine mode is on, this normalizes each frame in the dynamic sequence to the peak intensity in the volume.

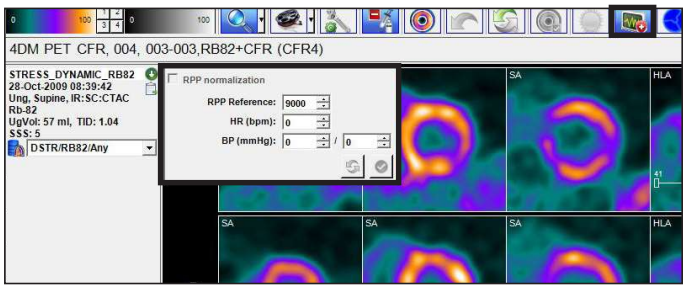


Figure 8.23: *Rate Pressure Product tool*

12. **Rate Pressure Product (RPP)** *(Figure 8.23)*: RPP is defined as the heart rate (HR) in beats-per-minute (bpm) multiplied by the systolic blood pressure (SBP, in mmHg). RPP provides a measure of a patient's cardiac workload and hemodynamic response. Due to patient-to-patient variation in HR and SBP during stress and rest imaging, this can affect the absolute coronary flow and coronary flow reserve values. The RPP tool is available to provide RPP-normalized flow values on a case-by-case need.

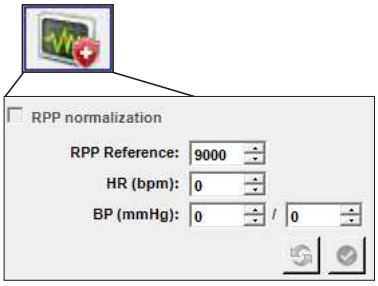


Figure 8.24: *RPP options window*

- Click the RPP toggle to access the RPP options window *(Figure 8.24)*, where stress and/or rest HR and blood pressure are manually input. For the BP, enter the systolic BP in the left field, and the diastolic BP in the right field.
- The RPP Reference value is defined at 9000, the mid-point of the normal range (6000 – 12000) in the normal patient population. The RPP Reference is definable, but likely rarely changed unless a particular RPP reference value is preferred.
- Once the HR and BP are entered, click the RPP corrected checkbox, and then click Apply, to calculate new flow and reserve calculations for the patient.
- To see the dataset's updated flow calculations, without calculating new reserve calculations, after entering HR and BP, click Apply, but do not click the RPP normalization checkbox.
- Click the Reset button to reset the values.
- Click Save in the Corridor4DM Control Panel to save the reserve results and all other Corridor4DM calculations before exiting the program. Once a dataset has been RPP-normalized, the global flow value and tabular flow values for that dataset will display an asterisk (*) next to them. Additionally, a footnote with an asterisk (*) appears below the Flow Table Results.

13. **Segmental Overlay Tool:** Displays blue overlays on the Spillover, Flow, and Reserve polar maps. Options range from the default vascular option to 20 segments.

14. **Next Tool:** Clicking this moves the user from **QA Mode** to **Results Mode**.

Once all data is confirmed in QA Mode, click the Next button in the Toolbar to enter the Results Mode.

Figure 8.25: *Manual Processing tool*

Results Mode Workflow:

1. Once the **Next** button is clicked, the **Results Mode** displays primary information needed to interpret flow and reserve findings. From this screen, if changes to the results are desired, click the **Manual Processing** tool *(Figure 8.25)* in the Toolbar to return to QA Mode.

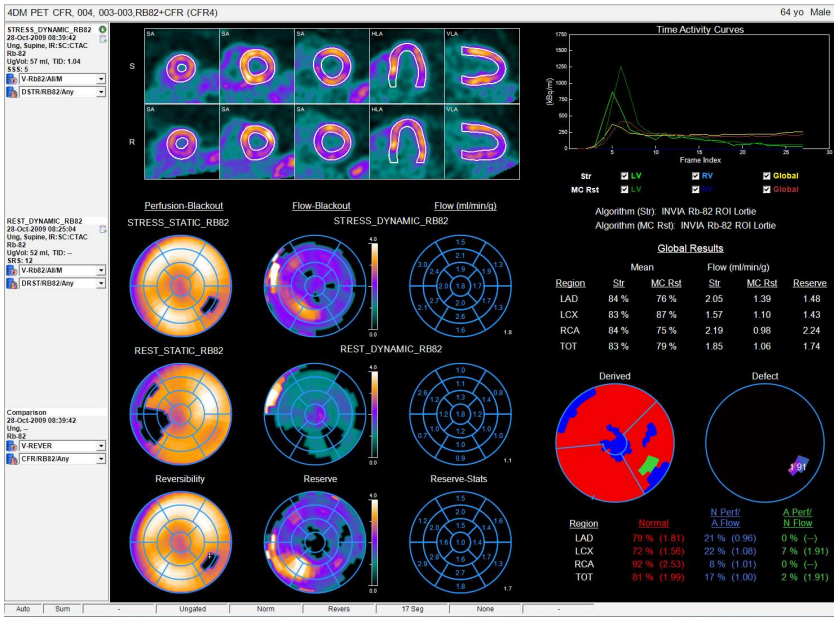


Figure 8.26: *Results Mode*

2. In **Results Mode**, the dynamic input data is available to cine and review LV contours while viewing statistical results of the processing *(Figure 8.26)*.

Global Results					
	Mean		Flow (ml/min/g)		
Region	Str	MC Rst	Str	MC Rst	Reserve
LAD	84 %	76 %	2.05	1.39	1.48
LCX	83 %	87 %	1.57	1.10	1.43
RCA	84 %	75 %	2.19	0.98	2.24
TOT	83 %	79 %	1.85	1.06	1.74

Figure 8.27: *Global Results table*

3. The **Global Results Table** *(Figure 8.27)* shows regional results for perfusion (Stress Mean, Rest Mean) and absolute blood flow (Stress Flow, Rest Flow) for each of the vascular territories (LAD, LCX, and RCA), as well as globally (TOT). Also shown is the regional CFR (Reserve), which is the ratio of Stress to Rest blood flows. The algorithms used for both Stress and Rest are displayed beneath the table for reference.

4. Review the **Polar Maps** and **Tables** *(Figure 8.28)*, left-to-right, to compare relative perfusion findings to absolute flow findings.

   - The left-most column displays, top-down: the stress, rest, and comparison of the two, in standard relative distribution format.

     - The default quant map display is Blackout, where any sector with uptake below the normal threshold is 'blacked-out' to distinguish it from normal uptake

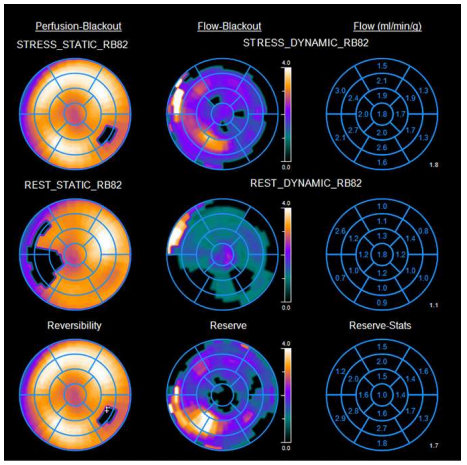


Figure 8.28: *Result Mode Polar Maps and Tables*

sectors. Options for the quant map are available for selection from the Quant Map Tool in the toolbar (e.g., Norm option shows normalized maps to peak intensity within the myocardium).

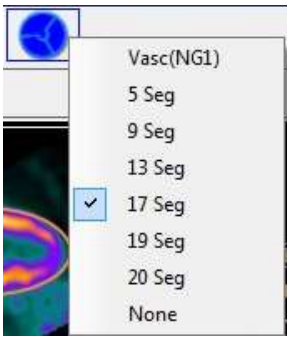


Figure 8.29: *Segmental Overlay Options dropdown*

- The left-middle column displays, top-down: the absolute stress, rest, and reserve flow values in units of ml/min/g, sampled over 460 sectors to provide a pixel-level flow polar map for review.
- The right-middle column displays the flow values without pixel data included, called Stats maps. These show the absolute flow and reserve value results based on the overlay map selected. The global LV flow value is displayed at the 5 o'clock position just outside of each of these polar maps, for stress, rest, and reserve.
  - The vascular overlay displays on the polar maps by default. Click the **Segmental Overlay Options** tool in the toolbar *(Figure 8.29)* to select a different overlay (e.g., select 5 Seg option to review the walls).
- The right-most column displays a **CFR Defect Polar Map** above a **CFR Derived Polar Map** *(Figure 8.30)*.
  - **The CFR Defect Polar Map** shows areas of perfusion defect on the Reversibility map in the selected color scheme. All other sectors are blacked out. Segmental overlays are not allowed on this polar map. Defects are labeled with reserve mean value, with a maximum of 5 non-contiguous defect regions allowed.
  - **The CFR Derived Polar Map** incorporates the CFR Defect Polar Map results and the Reversibility Polar Map results and compares them in vascular territories and globally, to provide the map and the percentage information below in the Derived Results Table. Region color in the polar map corresponds with the text colors in the table, with exception of the black areas which use white text due to the black background of the application.
    - **Red:** Areas quantified as normal perfusion and normal reserve. Table heading shows as "Normal."
    - **Blue:** Areas quantified as normal perfusion with abnormal reserve. Table heading shows as "N Perf/ A Flow."
    - **Green:** Areas quantified as abnormal perfusion with normal reserve. Table heading shows as "A Perf/N Flow."

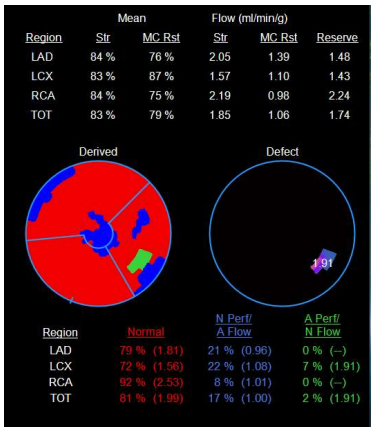


Figure 8.30: *CFR Defect and Derived Polar Maps*

Results Mode Toolbar Options *(Figure 8.31)*:

Figure 8.31: *Results Mode Toolbar*

1. **Dual Colorbar Tool:** The color control tool is comprised of the two colorbars separated by a numbered panel. Right-click the colorbar to customize color schemes and adjust intensity mappings. For more information on colorbar management, see the Colorbar Tools section.
2. **Magnification Tool:** Adjust the image display size.
3. **Cine Tool:** Activate/Deactivate cine of dynamic sequences. When active, motion correction tools display on all viewports. When deactivated, using the frame slider from the drop-down also activates the motion correction tools. Cine must be deactivated to view the flow ROI or Bounds.
4. **Manual Processing Tool:** Click to return to the QA Mode within the Reserve Screen.
5. **Contours Toggle Tool:** Overlay Corridor4DM-generated LV surface contours on the images.
6. **Quant Map Menu:** Controls the type of quantification (Quant) performed on the raw data. See Chapter 3: Corridor4DM Screens and Controls for more information.
7. **Segmental Overlays Menu:** Changes the overlay used to calculate regional statistics for the Quant or Comparison map. Note that the CFR Defect Polar Map is locked to not allow overlays. The Derived Polar Map is locked to showing a vascular overlay to correspond with results calculated in the Derived Results Table. See Chapter 3: Corridor4DM Screens and Controls for more information.
8. **Comparison Map Menu:** Controls the information displayed in a comparison map, representing data generated from a comparison of two datasets. See Chapter 3: Corridor4DM Screens and Controls for more information.

- Prior to exiting Corridor4DM, ensure to click Save in the Control Panel to save all perfusion and flow results information *(Figure 8.32)*.

Figure 8.32: *Save control*