Appendix 1 Standard operating procedure for AccuFFRangio computation

Loading Images

AccuFFRangio supports image files with compressed or uncompressed DICOM format.
   Proper angiographic projections are required:
    (I)   Image acquisition speed at least 15 frames per second;
    (II)   The 2 angiographic images at least 25° apart;
    (III)   Target vessel without severe overlap/foreshortening in the selected images;
    (IV)   Projection is in optimal perspective viewing angle;
    (V)   Sufficient injected contrast for image analysis;
    (VI)   Sufficient injected contrast for frame count evaluation.

Viewports

The Video Viewports can display 2 matching images of the same patient. The projection angle of these 2 images must be at least 25° and the frame rate should be at least 15 frames per second.

ECG Diagram

If available, the ECG diagrams of images will be shown at the bottom of the viewports (*Figure S1*).
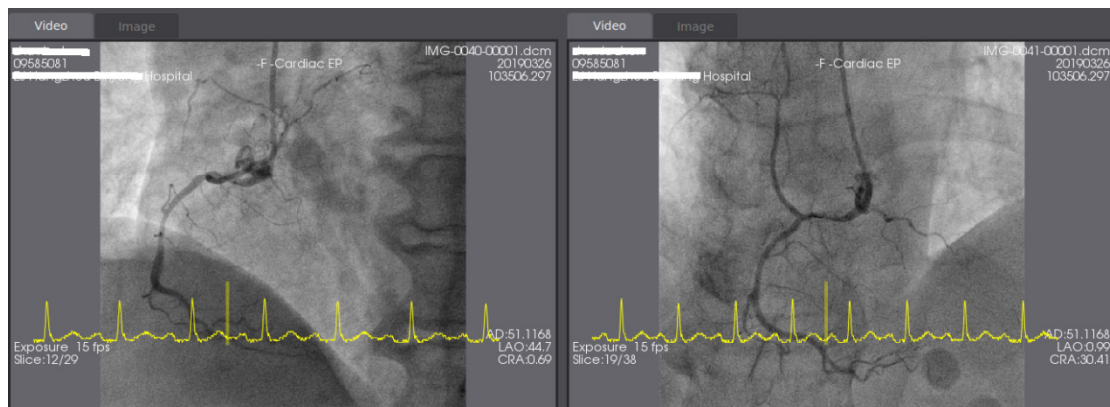
Figure S1 ECG diagrams of images of the same patient.

AccuFFRangio Analysis

Frame Selection

The appropriate frames for analysis should be determined (*Figure S2*):
    (I)   The target vessel without severe overlap;
    (II)   The entire vessel segment is injected with sufficient contrast;
    (III)   Frames are selected at the end-diastolic phase;

Figure S2 Frame selection of the entire vessel segment at the end-diastolic phase with sufficient contrast.

Vessel Reconstruction

Offset Correction

The first step of AccuFFRangio calculation is isocenter offset correction, which aims to correct the angiographic system distortions. Then, the corresponding relationship is created for these 2 images. In other words, for any point in the left viewport, we can find the corresponding point in the right viewport.

To apply offset correction:

(I)   In the upper left-hand viewport, left-click to place 3 reference mark points.

(II) In the upper right-hand viewport, left-click to place reference mark points at the corresponding location.

Besides, make sure to:

(I)   Identify the mark point that is easily identified in both of the 2 projections (i.e., a bifurcation, localized stenosis, or the offspring of a side branch);

(II) If using a side branch:

    a)   Select a side branch that departs perpendicularly from the main branch if possible;

   b)   Place the reference mark points on the main vessel;

If the generated epipolar lines go through the reference mark points in both the left-hand and right-hand viewports, offset correction is successful (*Figure S3*). Otherwise, it fails to correct the offset. Then, users should revise the position of the chosen reference mark points or select different locations for the reference mark points.

Target Vessel Indication

This step aims to define the pathline and contours of the vessel of interest in the upper left-hand and upper right-hand viewports.

You should indicate the proximal and distal points for the target vessel to generate the pathline:

(I)   Users should left-click on the upper left-hand viewport to define the proximal and distal points of the vessel of interest.

(II) Users should left-click on the upper right-hand viewport to define the proximal point and distal point of the vessel of interest.

(III) If the pathline is not located in the region of the vessel, the user can left-click and drag the pathline to be correctly
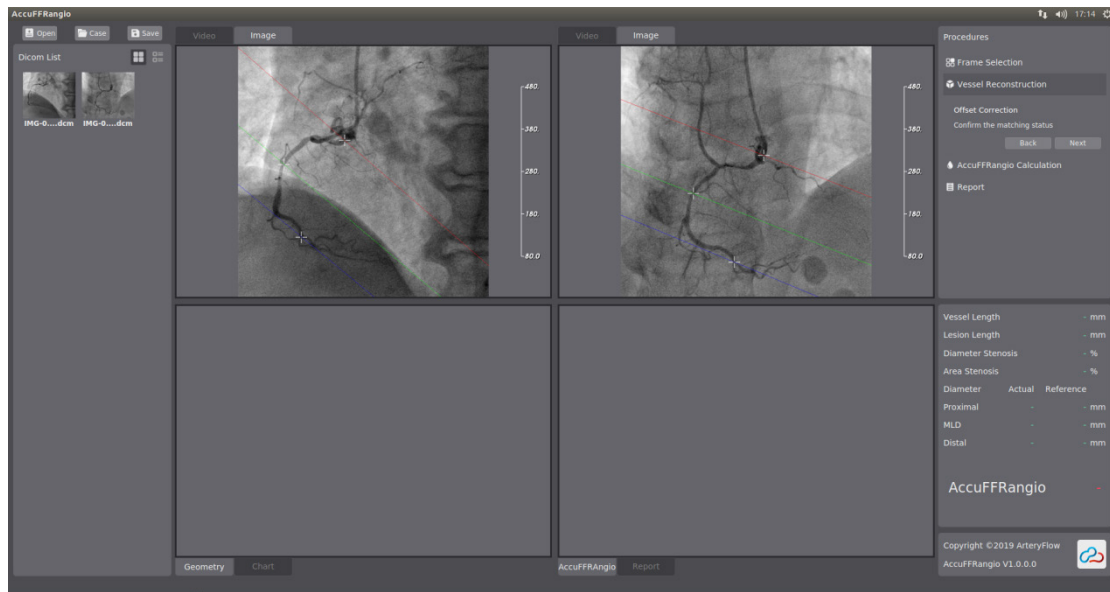
Figure S3 Offset correction.

**Figure S4** The pathline of the target vessel.

placed.

If successful, the pathline is shown correctly in the left and right Viewports (in *Figure S4*).

Lumen Contouring

To generate contours:

(I)   Click in the Procedures toolbar (*Figure S5*). The contours of the target vessel needing to be segmented will be generated automatically and shown in the upper left-hand and upper right-hand viewport.
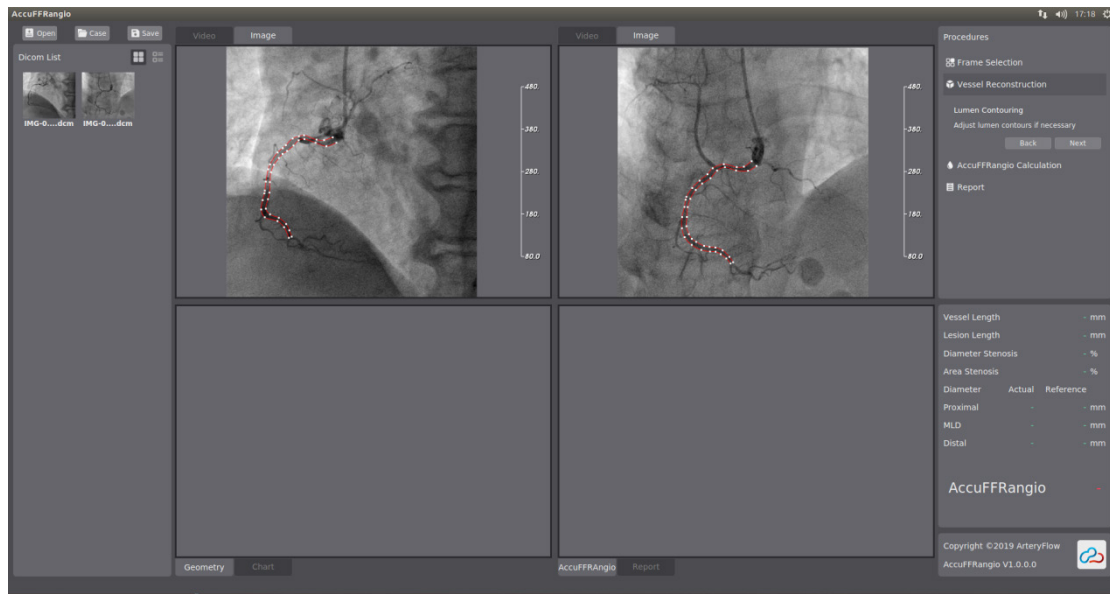
Figure S5 Contours of the vessel.

(II) If needed, the user can left-click and drag the boundary points on the contours to fit the boundary of the vessel.

Users can add boundary points to define the boundary of the target vessel by left-clicking on the contours. Users can also delete points on the contours by pressing the 'Delete' key.

When fitting the red contour lines to the border of the lumen, pay special attention to:

(I) Ensure non-existing narrowing in the proximal and distal ends

(II) Correct contouring of the target vessels

(III) Side branches and overlap

(IV) Ensure that contours are correct in all segments and also non-target segments as it influences AccuFFRangio calculation

Figure S5 shows the final contours of the vessel in the upper left-hand and upper right-hand viewports.

Forced Correspondence

In this step, the lesion of the vessel segment will correspond forcedly and be displayed as a green region. Clicking in the Procedures pane (*Figure S6*), the lesion will be generated and correspond automatically, and will be shown in the upper left-hand and right-hand viewports.

Then, click in the Procedures pane, and the 3D geometry of the vessel will be generated and displayed in the Geometry Viewport (*Figure S7*).

Reference Vessel

The reference vessel is generated based on the three-dimensional reconstruction of the real vessel segment automatically. Any part of the contoured lumen narrowing than the reference vessel is marked the green region as plaque. The reference function can be seen in the lower left-hand pane, in which a red chart means vessel diameter distribution along the pathline of the vessel and the green dashed line represents the reference function (*Figure S11*).

The 3D reference vessel will be displayed in the Geometry Viewport. Besides, QCA results will be calculated and shown in the Properties pane.
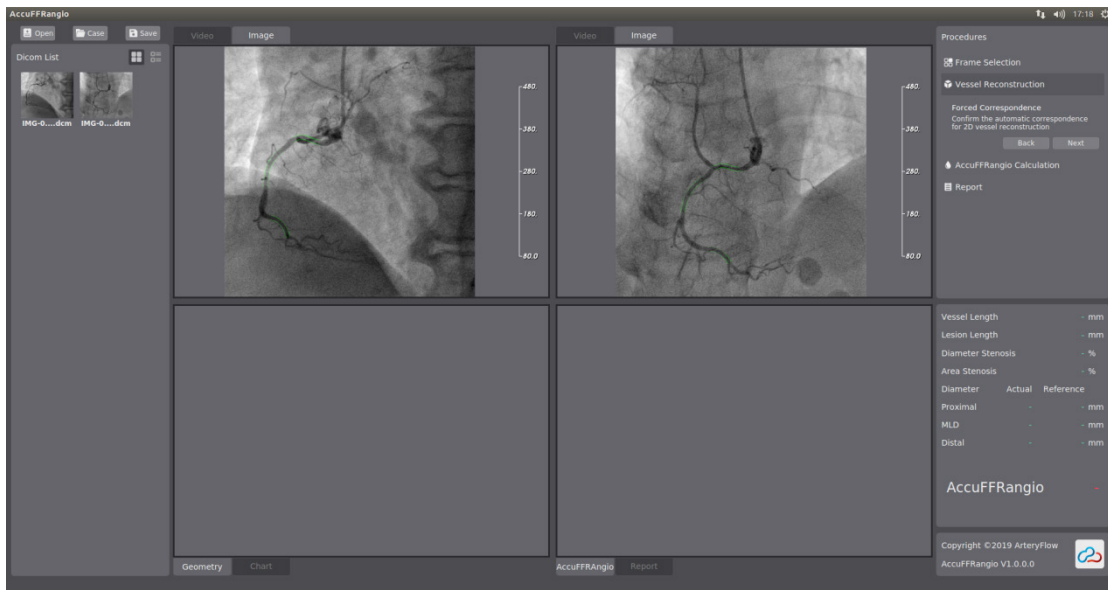
Figure S6 Stenosis of the vessel.

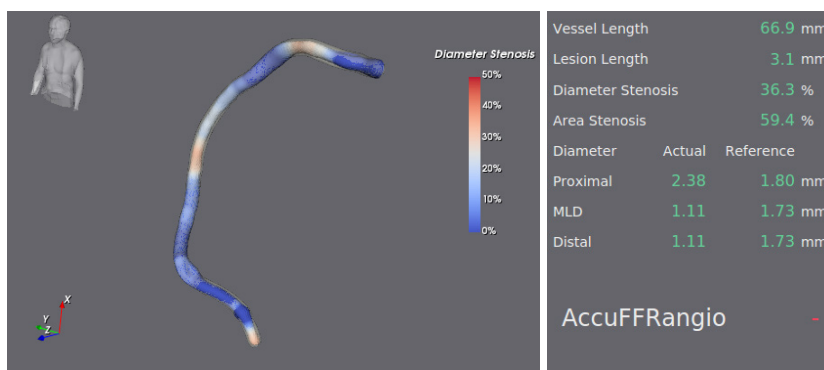**Figure S7** Geometry Viewport.

Figure S8 Geometry Viewport and Properties pane.

Figure S9 Aortic Pressure input.

Figure S10 Frame Count.

AccuFFRangio Calculation

This step details the calculation of AccuFFRangio.

Frame Count

To derive the flow velocity throughout the segmented vessel and to obtain a more accurate AccuFFRangio value, the frame counting method is applied (*Figure S9*).

To perform the frame count:

(I)   Rotate the mouse scroll wheel to navigate through the frames until the start frames in both the upper left-hand and upper right-hand viewports are found. Press the button to record the index of the start frame. The start frame is defined as the frame in which the contrast arrives at the proximal pathline point.

(II)   Rotate the mouse scroll wheel to navigate further through the frames until the end frames in the upper left-hand and upper right-hand video views are found. Press the button to record the index of the end frame. The end frame is defined as the frame in which the contrast arrives at the distal pathline point. Users can also enter the index of the start frame and end frame manually in the input box, as seen in the above figure.

According to whether the patient was injected with vasodilators, you should select the radio button to specify the patient state: Hyperemia or Baseline.

Aortic Pressure

You should specify the aortic pressure to calculate the AccuFFRangio value obtained from the catheter lab's monitoring panel (*Figure S10*).

AccuFFRangio Results

The last step is to determine AccuFFRangio values based on the above operations.

To determine the AccuFFRangio results (*Figure S11*):

(I)   Click on the button, the AccuFFRangio value at the distal end of the segmented vessel is shown at the lower right corner of the Properties pane.

The vessel geometry with different colors representing different AccuFFRangio values is demonstrated in the lower right-hand viewport.

(II)   Users can choose a position at the vessel geometry in the lower right-hand viewport by left-clicking and obtain the AccuFFRangio value.

After the AccuFFRangio calculation, you can edit detailed information in the report.

Then, click on the Report module to generate a report. 2D stenosis of the vessel in 2 projections, the vessel with
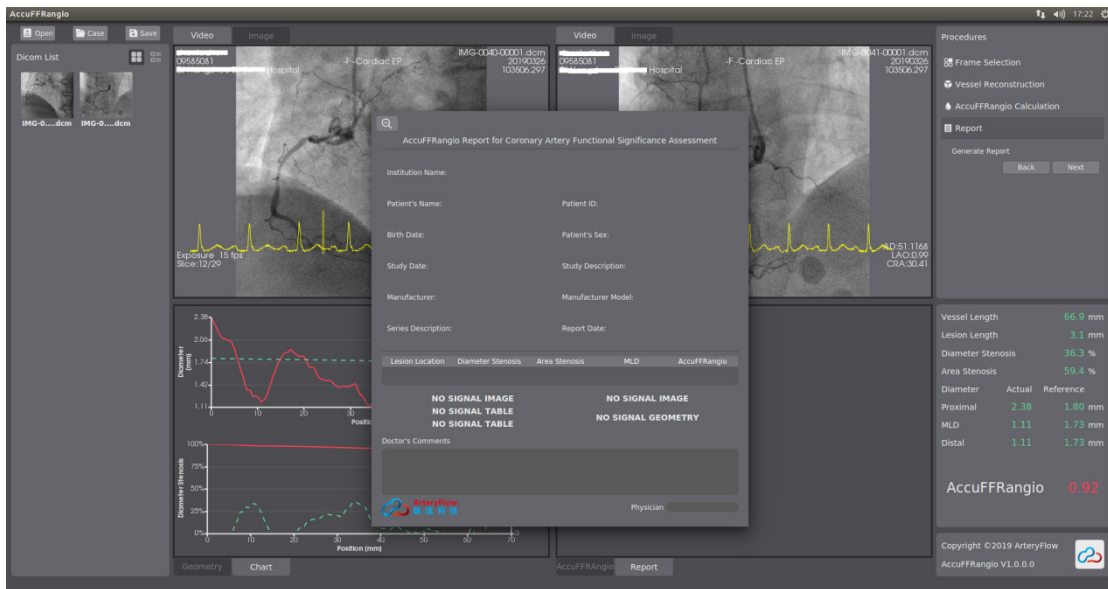
Figure S11 AccuFFRangio results.

Figure S12 Edit the report.

AccuFFRangio contour distribution, 2 charts representing vessel diameter *vs*. position and reference vessel diameter *vs*. position, and AccuFFRangio value *vs*. position and diameter stenosis *vs*. position will be presented in the report. The report can also be exported to PDF files. *Figure S12* is the final report with detailed information.