

# Quantitative Assessment for Confluent Plaque Area Related to Diagnostic IVUS/VH Images

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## Abstract

*Virtual histology modality uses in-depth analysis of the backscattered RF-signal in order to provide a detailed description of the atheromatous plaque composition. The amount of one type of tissue (Necrotic Core) which is confluent is an important marker in diagnosis of various medical conditions. Confluent plaque that borders the Lumen is medically relevant (TCFA, CaTCFA). Measurements of the plaque area and span are the most important in assessing how dangerous plaque could be.*

*The goal of custom-developed complementary software was to maximize the automation of these measurements, giving the analyst only the relevant information and presenting the final results. Computer software Macro-Plaque has been developed to provide quantitative assessment of confluent plaque area and other parameters related to diagnostic IVUS/IVUS-VH images.*

## 1. Introduction

Macro-plaque is specifically designed to be used within the ImageJ work environment due to its intuitive graphical interface and various built in functions useful in image analysis [1]. The following research has been logically divided into sections corresponding to the diagram in Figure 1. These sections are intended to follow each step of the development process, beginning at the concept stage and documenting the path the software had to take until the final product was ready. The beginning stage of the design process corresponds to a specific requirement for the software and the initial idea of an acceptable solution. Next two stages are highly interconnected since this is when the actual software code is being developed and tested to comply with user specifications.

This is the process where the idea comes into life through coding and beta testing until a satisfactory product has been formed and complies with all initial requirements from the first step. When the final software

is released, validation of its performance is needed, especially for software that is intended to provide specific, quantifiable data for medical research.

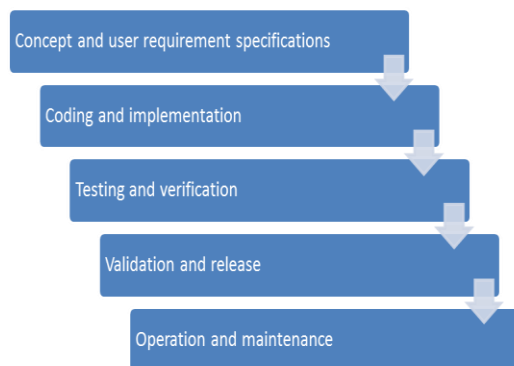


Figure 1. Chart of software design and release process.

## 2. Concept and user requirement specifications

Virtual histology-intravascular ultrasound has the potential to provide detailed qualitative and quantitative information about atherosclerotic plaque components in coronary arteries. In Intravascular Ultrasonography a number of parameters are important in diagnosis of various medical conditions. Software that has been used for image analysis up to date was a commercial package called VIAS (Volcano Corporation - San Diego, California, CA). Often undergoing projects require various area calculations, angle measurements, as well as mathematical data manipulation. If the Necrotic Core is scattered, the commercial software provided a single area measurement, while only the Confluent Necrotic Core that borders the Lumen is relevant (TCFA, CaTCFA) (Figure 2). The goal of this software was to maximize the automation of these measurements, giving the analyst only the information needed and presenting the final results in a way that is easy to read and understand.

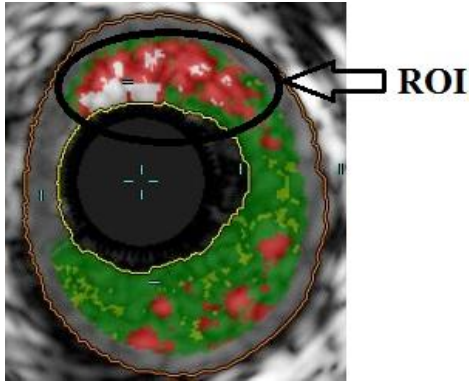


Figure 2. Example of Confluent Necrotic Core that borders the Lumen in IVUS images.

### 3. Coding and implementation

Computer software Macro-Plaque has been created to provide quantitative assessment for confluent plaque area and other parameters related to diagnostic IVUS/IVUS-VH images. Macro-Plaque requires ImageJ 1.43u or later to work properly due to certain functions that are not present in previous releases. The program automatically checks the version of ImageJ and will not execute if it finds an older version. Program is designed to work with images exported from VIAS software. These images have dimensions 648x648 pixels, corresponding to a square field of view with dimensions 1cm x 1cm. Because of this, the first action performed after Macro-Plaque is executed is proper image scaling: 648 pixels is equivalent to 10 mm in real life (individual pixel size is roughly 0.0154321 mm). Variable called “scaling” is also created and later used to relate between positions in pixel and real life dimensions. Apart from the scaling other editable setup parameters are set. Parameter “interval” determines how many points from a wand selection will be available for editing (interval = 1 means every point will be editable; interval = 5 means that every 5<sup>th</sup> point will create the new, editable selection). Parameter “lw” specifies the line width of regions of interest (ROI’s) on the image. In this stage the colors and name templates of ROI’s are initiated and are later used as well as an option to display all ROI’s. Before any actual image analysis and processing takes place, Macro-Plaque checks if an image is opened and deletes any previous entries in ImageJ’s ROI Manager and a popup dialog is shown with a short explanation on how to use the software.

#### 3.1. Stages of image processing: Lumen and vessel selection

The first idea was to select lumen using the border line from VIAS software, but this proved to be unreliable because of border degradation probably caused by jpg

image compression during exporting the images from VIAS software. Similar problems have been encountered when trying to automatically select the vessel wall. In this situation the best way to proceed is to binarize the image and perform other morphological image transformations until the lumen and vessel wall are clearly distinguishable from the background and automatic selection is possible. Once the image is sufficiently transformed, the wand tool is chosen as a selection method, because this is the most convenient selection method available, requiring only a single mouse click. When the lumen is selected the following lines of code are responsible for getting the centroid (center point; this is the average of the x and y coordinates of all of the pixels in the selection) of the selection, which is later used as angle origin. After initial automatic lumen or vessel selection is performed, the user confirms the selection (Figure 3). Software will not proceed into further analysis until there is a valid selection made and confirmed.

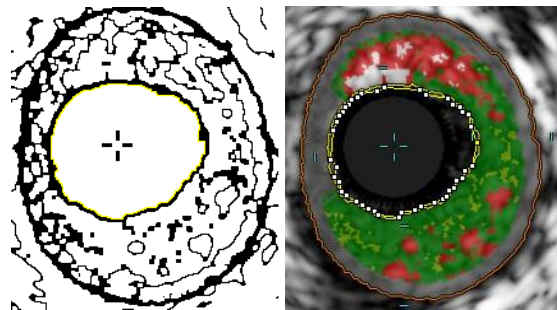


Figure 3. Left: Automatic lumen selection (yellow line); Right: Selection can be modified by dragging white points to desired positions.

#### 3.2. Stages of image processing: Confluent plaque selection

Software enables the user to adapt measurement options according to plaque morphology. User can select (Figure 4):

- number of confluent plaques,
- number of angles,
- arbitrary number of angle measurements for each plaque.

During IVUS images analysis often the number of confluent plaques are different between analyzed images. Therefore, first the user should specify the number of confluent plaques that will be selected on the current image, as well as the preferred selection method (either “polygon” or “freehand”).

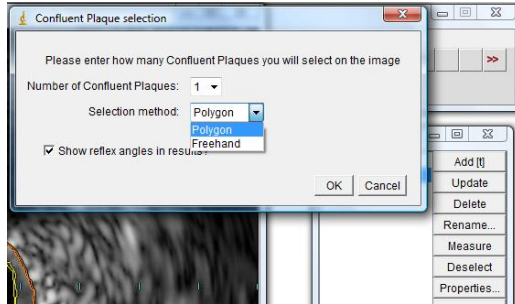


Figure 4. User can specify number of confluent plaques and the selection method of choice.

There is also an option to print or omit reflex angles in the final results files (useful when measured angles are over 180 degrees). After the confluent plaque has been added to the ROI Manager, but still for the same loop iteration over the number of confluent plaques, the user is asked to specify the number of angles (default: 1) that will be measured for the current confluent plaque. When the loop thru the number of plaques that will be selected is over, all selections are complete and Macro-Plaque proceeds to the results stage (Figure 5). Results are shown after the last angle is drawn and confirmed by the user. Finally, an image with selected regions and results will be displayed.

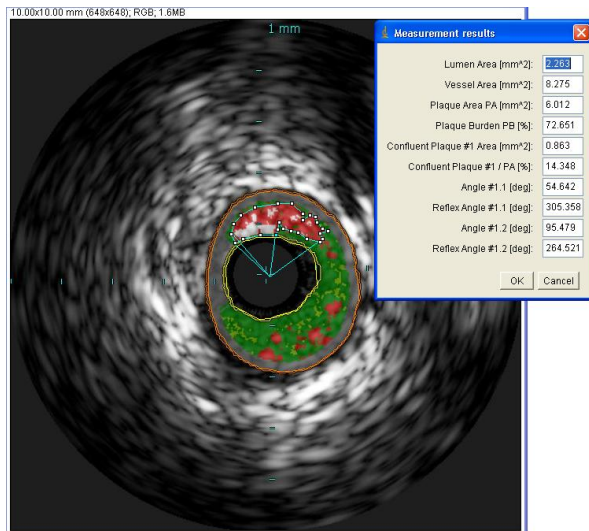


Figure 5. Original IVUS image with selected confluent plaque, angles and results

After measurements are finished and displayed in the popup window, the user has two options on how to proceed. The popup window has two options: OK and Cancel. If Cancel is chosen, then Macro-Plaque aborts and analysis results are not saved to disk, but if OK is chosen then Macro-Plaque takes action and saves the results in text format, as well as saves an image with all the ROI's and measurement results, where on the left side

is the original IVUS VH image with selection and angle ROI's superimposed, while on the right all measurement results are summarized.

#### 4. Testing and validation

This stage of the software design process is closely related to source code development and optimization. Each piece of software code when ready needs to be tested for any bugs that might have been overlooked during code design and any potential loop holes in the user-software interaction layer need to be found and fixed. Constant cooperation with intended users allows for fast feature addition and enhancement, before the final product is prepared. Macro-Plaque has been through several iterations of this process. There have been about ten beta versions of Macro-Plaque, each adding new functionality and/or including various bug fixes, before it became polished enough to be subjected to the validation procedure outlined in the next paragraph. These included added security from user selection mistakes, multiple confluent plaque selection option, user specified number of angles for the current plaque, enhanced result display template and save results to disk option, only to name a few more obvious.

#### 5. Results

For the purpose of Macro-Plaque validation, a phantom image has been used. This phantom has been created in Inkscape 0.48, an open source vector graphics editor with capabilities similar to Adobe Illustrator. The design concept of this image phantom was for it to closely resemble the images Macro-Plaque has been designed to analyze (Figure 6).

The phantom is similar to real images exported from VIAS Volcano software. It has the same pixel dimensions (648x648) as images exported from VIAS for analysis, since only in that case it is possible to estimate any deviation of measurements in analyzed IVUS images. Typical areas of interest in IVUS images are marked on the image phantom with colors: lumen is black, vessel wall is the outer circumference of the green ring, plaque is marked with green and red color marks the confluent plaques. There are also three known angles to be measured in this phantom. Dimensions of these specific areas on the image phantom are known: diameter of lumen is 3mm, diameter of vessel is 6mm, therefore lumen area is 7.07 mm<sup>2</sup> and vessel area is 28.27 mm<sup>2</sup> (calculated on the basis of circle area). In a similar way confluent plaque areas have been calculated: nr 1 is 0.59 mm<sup>2</sup>, nr 2 is 1.18 mm<sup>2</sup> and nr 3 is 1.77 mm<sup>2</sup>. Known angles are also marked on Fig. 1 and they are: angle 1 is 30°, angle 2 is 60° and angle 3 is 90°.

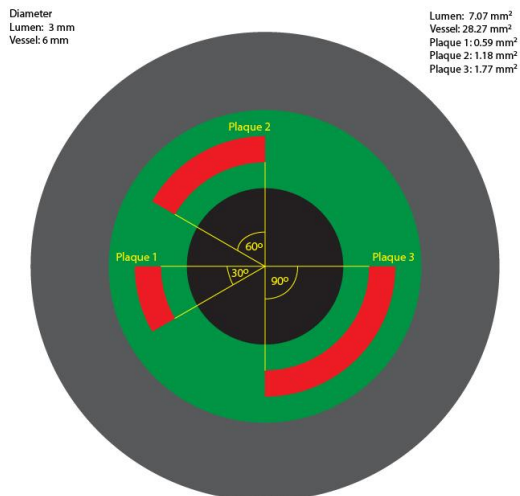


Figure 6. Image phantom used for validation.

Test measurements were carried out and results are shown below. A total of 50 measurements were used to perform statistical analysis. The mean, standard deviation and percentage error have been calculated and results are presented in Table 1.

Table 1. Test measurements.

	Reference	Mean	Error [%]	SD
Lumen Area [mm <sup>2</sup> ]	7.07	7.01	0.81	0.01
Vessel Area [mm <sup>2</sup> ]	28.27	28.21	0.21	0.02
Plaque Area PA [mm <sup>2</sup> ]	21.20	21.20	0.02	0.02
Plaque Burden PB [%]	74.99	75.14	0.20	0.04
<b>Confluent Plaque #1</b>				
Area [mm <sup>2</sup> ]	0.59	0.58	1.72	0.00
Area / PA [%]	2.78	2.75	1.28	0.01
Angle #1.1 [deg]	30.00	30.10	0.34	0.36
<b>Confluent Plaque #2</b>				
Area [mm <sup>2</sup> ]	1.18	1.17	0.85	0.00
Area / PA [%]	5.56	5.53	0.61	0.01
Angle #2.1 [deg]	60.00	59.88	0.20	0.41
<b>Confluent Plaque #3</b>				
Area [mm <sup>2</sup> ]	1.77	1.75	1.11	0.00
Area / PA [%]	8.34	8.27	0.79	0.01
Angle #3.1 [deg]	90.00	89.97	0.03	0.46

Results from Table 1 can lead to a conclusion that for this specific resolution of the images, best measurement results are obtained for regions of interest larger than about 1 mm<sup>2</sup>, yielding a percentage error of less than 1%. The key factor determining the difference between measured values and image phantom dimensions is the image resolution, therefore it is suggested to increase the

resolution of exported VIAS Volcano images that are intended for Macro IVUS analysis in order to provide better precision.

## 6. Clinical implications

Several IVUS-VH studies have demonstrated that type of VH-derived plaque type were the independent predictors of periprocedural complications and long term follow-up results. Investigators reported that the percentage of NC and its ratio to DC in diseased coronary segments are positively associated with a high-risk acute coronary syndrome presentation. Others reported that NC volume clearly predicted some periprocedural complications (i.e. distal embolization) after stent deployment in patients suffering from myocardial infarction [2-4].

## 7. Conclusion

Custom software for IVUS/VH image analysis has been developed to aid specific research applications. Software was written in the open source image analysis environment of ImageJ, allowing cross-platform portability. Every aspect of desired measurement application was validated with a phantom, showing over 99% accuracy compared with reference values. Software is now used in daily IVUS/VH quantitative analysis in clinical trial Core Laboratory.

## References

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