A Computational Tool for Coronary Atherosclerotic Plaque Analysis of Virtual Histology Images

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Abstract

Virtual Histology (IVUS-VH) is an image modality, derived from intravascular ultrasound (IVUS), which allows the identification of atheromatous components, providing a frame-by-frame tissue classification into four classes: Fibrotic Tissue, Fibro-Fatty Tissue, Necrotic-Core and Dense Calcium. According to current pathology consensus, intra-plaque spatial distribution of tissue elements has become an important issue for lesion classification. However, there is not an available environment to realize previously described analysis. To attend this demand, a computational tool has been implemented in this work. ImageJ has been used as development framework. Morphological operations and labeling algorithms of binary images were used to determine neighborhood relations between confluent sets of pixels, such as to measure distance to the arterial lumen. In the next months, we intend to distribute this tool for download under request.

1.   Introduction

Histopathological studies have shown an association between sudden death from acute coronary syndromes and the presence of ruptured plaques [1]. This way, several efforts have been made for identifying profiles of rupture-prone atherosclerotic lesions [2]. Diagnosis tools for in-vivo assessment of arterial wall composition have been playing a major role in this context [3]. As known, one of the great challenges of our days is to understand the vulnerable plaque [2]. In addition to that, the most important and difficult challenge is the attempt to avoid sudden events, like acute myocardial infarction, caused by plaque rupture [3]. According to several studies about the vulnerable plaque, lesions containing lipid pools close to the luminal wall and separated by a thin fibrotic cap has been associated with a higher rupture risk. This kind of plaque has been denominated as Thin-cap Fibroatheroma (TCFA) and has been widely studied in the last years [1-3]. In other words, spatial relation among plaque components and the luminal wall has been believed to contain functional behavior related to the vulnerability of atherosclerotic plaque.

Virtual Histology (IVUS-VH) is an image modality, derived from intravascular ultrasound (IVUS), which allows the identification of atheromatous components, providing a frame-by-frame tissue classification into four classes: Fibrotic (FT), Fibro-Fatty (FF), Necrotic-Core (NC) and Dense Calcium (DC) [4]. According to current pathology consensus, intra-plaque spatial distribution of tissue elements has become an important issue for lesion classification [5]. However, several informations available into IVUS-VH images have not been totally used because of the lack of specific tools for processing these data sets. Currently, in most part of the studies, there are basically two different ways for processing information from IVUS-VH examinations: using sectional area of every plaque component or classifying plaque according to the current consensus.

The first option has been the easiest way because does not requires any sort of image processing. Frame-by-frame plaque quantification is available by means of spreadsheets provided jointly with IVUS-VH images. This way, plaque components' analysis, performed slice by slice, has been the most frequent analysis method used in the last years [6,7].

The second option is to classify the atherosclerotic plaque according to the current consensus described into [2,5]. In this case, lesion classification has been performed by means of morphological and topological features of tissue components and luminal wall [8]. Consequently, some image processing is required for these features' extraction. Although, this approach should present better association with clinical parameters than the first one because of its "functional" nature [9].

Currently there is not an available environment to

realize previously described analysis. To attend this demand, a computational tool has been developed for our team, which still implementing new features to our software.

In the following sections, the main features of our IVUS-VH analysis tool will be briefly described, in order to provide necessary information to anyone reproduce our steps. In the next months, we intend to distribute this tool for download under request.

2. Material and methods

2.1. Study population

The present study prospectively included a group of 15 patients who underwent to IVUS-VH examination. IVUS-VH analyses have been performed by a specialist according to current international standards for IVUS analysis.

The study protocol was approved by the local ethics committee and written informed consent was obtained from every patient.

2.2. Image processing tools

Algorithms have been implemented in Java® language using the ImageJ platform (IJ), an open-source image processing software which contains a set of classes implementing the major image processing techniques [10]. This way, our computational tool is compatible with mostly operational systems like Windows, Linux and Mac OS X. In addition to these features, IJ allows the implementation of customized plugins and macros, which has been useful for simple and fast development of image processing tools.

IJ has emerged as a project of the National Institutes of Health some years ago. Today, IJ community has grown and there are several developers worldwide, which have been daily updating and providing new features and functionalities to IJ. In face of that, we have decided to use IJ as our development platform.

Our computational tool has been composed by a set of IJ plugins for IVUS and IVUS-VH images produced by Volcano Therapeutics® devices. We intended to extend our plugins to others IVUS equipments but, in these past years, we have been working basically with Volcano's images.

We have developed plugins for several applications evolving IVUS and IVUS-VH examinations since loading image sequences until grayscale texture descriptors for plaque classification, as described in [11]. In this work, we briefly describe our methodology for information extraction from IVUS-VH series and how to perform morphological plaque classification.

The first step for our analysis is to perform a frame-by-

frame composition analysis. A brief description of our methodology is present in Figure 1.

Frame-by-frame Analysis

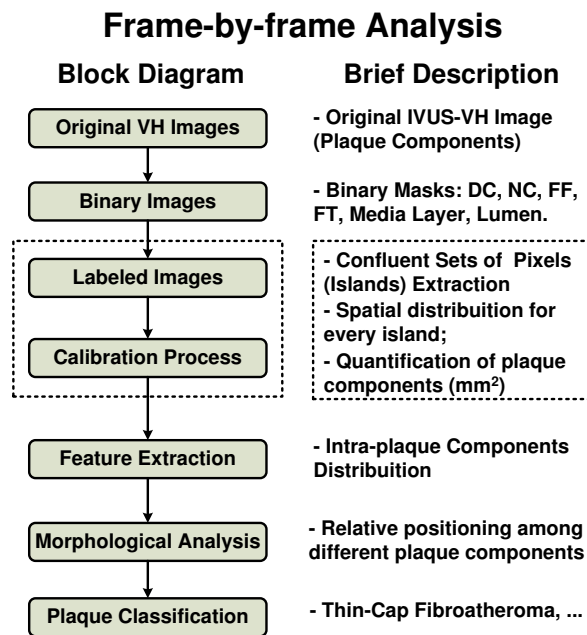**Block Diagram**   **Brief Description**

Figure 1. Block diagram describing the frame-by-frame analysis in order to identify, to quantify and to determine the spatial relation among every sets of confluent plaque components.

From Figure 1, some steps are self-explanatory and some not. In a few words, we create six binary images for every IVUS-VH frame as described in [12]. After that, we perform for every binary mask of interest the labeling process to extract all sets of connected pixels of a same composition of that frame. The labeling process has also been described in [12,13] and is based on Suzuki's algorithm [14]. For example, in [12,13], we were interested in determination of the relation between necrotic-core and dense calcium. For this, we have performed labeling in NC mask and, after this, DC mask have been dilated according to binary dilatation operation, which is exemplified in Figure 2 of this work.

In order to explain how to determine and to quantify the relation between two different sets of components, we prepared the Figure 3.
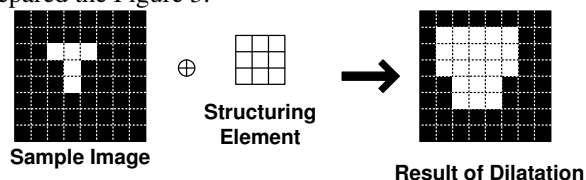

Figure 2. Example of binary dilatation operation of a sample image by a squared structuring element. The result of this operation is a dilated region compared with the original sample image.

The procedure described in figure 3 has been widely used into our tool. For example, to identify a possible TCFA frame, we perform the following steps:

1. Determine the relation between NC component and luminal region;

2. Quantify the necrotic content neighbor to luminal region. If the greater island has more than pre-defined number of pixels, we consider this a lipid pool connected to the lumen;

3. Check the next two frames and the previous two frames to certify that it happens in these frames. In affirmative case, this lesion is a TCFA based on IVUS-VH criteria. Some works have been questioning the ability of IVUS-VH images for determination of TCFA lesions [15]. However, our objective is to infer possible candidates to TCFA lesions which have been named as VH-TCFA lesions in current literature [15].

3.   Results

In this paper, we described our platform for IVUS-VH images processing. Some previous works of our group have used these tools to perform some inferences. In [12], we have used these techniques for estimation of NC component connected to DC components. After this, we compared the variation of those components related to stent implantation. We concluded that an artifactual relation between these components is present in IVUS-VH images. A similar analysis with a greater number of patients and lesions confirmed our hypothesis in [13].

Another application of our methods was described in [11]. The plugins developed there for texture extraction were implemented in Java and will be included in our tool when we distribute it for download under request.

4.   Discussion and conclusions

We have not performed yet experiments using our plaque classification method because we detected one major limitation of our methodology. There are some cases, like side branches, where the luminal contour is not closed. In these cases, our dilatation process has failed. In order to avoid those cases, a manual pre-processing has been required. However, this solution is not desirable because is considerably time consuming. We are still looking for a simple, fast and smart solution for this problem. There is some hypothesis to be tested as soon as possibly. After solving this problem, we decided to release our tool for download under request.

We expect to improve periodically this platform, implementing new features and optimizing the functionalities already implemented. In addition to this, we intend to add other tools for grayscale IVUS images, like segmentation tools, feature extraction and pattern classification methods. Some plugins are already implemented but does not have a friendly user interface. In the next months, we have plans to concentrate efforts in order to achieve these objectives.

In other hand, we have begun to assess the possibility of using part of our methods to study plaque classification with Boston Scientific® devices. We have performed some examinations with Boston Scientific ILab® but we still need a better understanding of their technique.

Acknowledgements

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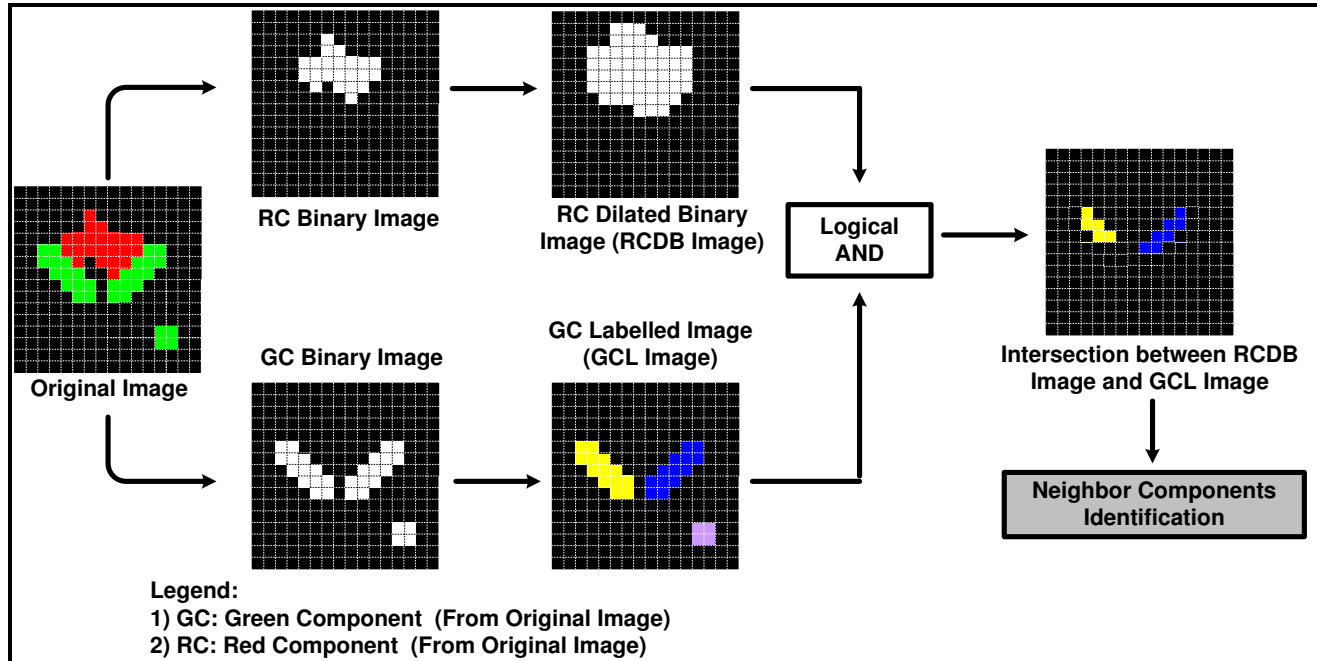E-mail address (optional): fernando.sales@ufabc.edu.br

Figure 3. A visual example of the determination of spatial relation between two different components. The original image (left) has two different components: green and red types, considering the black region as the background. In addition to this, there are three sets of green pixels; however, just two are connected to the red component. The first step consists in obtaining one binary mask for every component, i.e. two binary masks – RC and GC binary images. The challenge is to determine which islands are neighbors and, at the same time, quantify the amount of pixels in every island. In order to achieve these objectives, we perform the dilation of RC image and the labeling of GC image. In labeling process, we quantify, for every island, the number of connected pixels and their position relative to the original image. In addition to this, these informations are stored for further processing and associated with a label, which is represented by a color into GCL image. After those steps, a logical AND is performed between those images, resulting into the intersection image (right). In this image, the remaining pixels are colored according to the labels of GCL image. This way, the labels of interest islands are easily visualized, which allows the identification of neighbor islands. These steps could be repeated in order to determine the spatial relation between components, media layer and luminal region.