Estimation of Coronary Atherosclerotic Plaque Composition Based Only on Grey Scale Intravascular Ultrasound Images

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Abstract

In-vivo atherosclerotic plaque composition has been currently assessed by means of techniques based on spectral analysis of backscattered intravascular ultrasonic signals. Conversely, conventional IVUS images are based only on amplitude envelope of ultrasonic signals, discarding some frequency information and, consequently, disabling tissue characterization from spectral features as described previously. In this work, a computational tool has been developed for evaluation of coronary atherosclerotic plaque composition, without using of backscattered radiofrequency attributes. Textural analysis from atheromatous lesions has been combined with pattern recognition techniques in order to solve this problem. A preliminary test sample with 08 coronary arteries from 5 different patients, totalizing regions of interest, resulted into an average error-rate of 5,2%.

1. Introduction

Histopathological studies have shown an association between sudden death from acute coronary syndromes and the presence of ruptured plaques [1-3]. A comprehensive morphologic classification scheme has been developed in order to standardize studies about atherosclerotic disease [1, 4]. Thin-Cap Fibroatheroma (TCFA) has been described as the most frequent coronary ruptured lesions [1, 3, 5, 6]. The definition of TCFA assumes a necrotic-core component, located close to arterial lumen, separated by a thin fibrotic cap (thickness lower than 60mm) [4]. The rupture of this separating interface exposes the necrotic content to blood flow, initiating the formation of intraluminal thrombus, which may occlude the artery – totally or partially –, causing an acute coronary syndrome [2].

Intravascular Ultrasound (IVUS) has been the current gold standard method for in-vivo arterial wall assessment [7-9]. Several studies has been using IVUS to assess the progression of coronary atherosclerosis [8] and therapeutic strategies targeting the coronary disease [7]. Virtual Histology (IVUS-VH) is a new image modality, based on spectral analysis of backscattered acoustical signals before IVUS images formation, which allows in-vivo plaque composition evaluation [10-12]. VH tissue components are divided into four different classes: Fibrotic (FT), Fibro-Fatty (FF), Necrotic-Core (NC) and Dense Calcium (DC), every one of those represented by a different color into VH images, as represented in [10].

Conversely, plaque characterization based only on IVUS image features according to VH-classification scheme has not been developed yet. IVUS has been used in several clinical studies in the last decade. If an IVUS image-based plaque classifier achieves robust and reliable results, innumerable analyses will be performed using current available data and images from those related studies. One possible application with future clinical potential is to assess the evolution of coronary atherosclerotic disease from changes on plaque composition in serial IVUS examinations.

In this work, a computational tool has been developed for evaluation of coronary atherosclerotic plaque composition, without using of backscattered radiofrequency attributes. More details of our methods and results are described in the following sections.

2. Methods

The main objective of the present study was to evaluate, in conventional IVUS images, whether plaque classification should be performed only by means of image features. Our gold standard method for composition assessment was IVUS-VH plaque classification.

2.1. Study population

The present study prospectively included a group of 5 patients (8 arteries) 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

As our main goal is to perform plaque components inference based only on intravascular ultrasound image features, a computational tool have been developed. For this, algorithms have been developed in Java® using the ImageJ platform, an open-source image processing software which contains a set of classes implementing the major image processing techniques [13].

The first step was the feature extraction from gray-scale IVUS images. For training step, we selected regions of interest (ROI) to extract textural information and build a training group. The ROI's determination has been performed according to correspondent IVUS-VH image, splitting it in four different binary masks, each one for one plaque component. In these masks, black pixels correspond to the background and the white pixels correspond to plaque pixels. This way, squared windows of white pixels was selected for textural features calculation. Three different sizes were tested for those centered ROIs: 5x5, 7x7 and 9x9 pixels.

The second step was the selection of textural attributes to compose the feature vector for classification step. Two major sets of descriptors have been selected: invariants based on Hu moments [14] and Haralick's co-occurrence matrix features [15, 16]. More details about chosen features are available on the following section.

2.3. Feature extraction

In order to provide rotational invariance to Haralick's approach, we calculated the co-occurrence matrix for four proposed directions in [15, 16], and we have performed the addition of these four matrixes. Matrix-based parameter estimation was calculated over the summation matrix, which is, in thesis, rotation invariant.

To avoid sparse co-occurrence matrixes, we have evaluated different re-quantizations levels for Haralick's parameter estimation. Three additional gray-scale levels were tested: 32, 62 and 128.

Conventional Hu moments, available in Table 1, have been set as rotational, translational, and scale invariant, however, some experiments performed showed relative sensitivity to those aspects, as described in [17]. In addition to that, Hu moments have not been invariant to affine transforms, for example, multiplication of whole image pixels for a numeric constant. These affine transforms are associated to images with different acquisition gains. To reduce the sensitivity of our method related to the previously related effects, we tested two different sets of invariants used in handwritten characters recognition based in the Unified Moment Invariants (UMI), an approach described in [18] . Those sets are built using UMI and the following formulations for normalized central moments: the Aspect Invariant Moments (AIM) and the Higher-Order Scale Invariant (HOSI), both defined in [18].

Table 1: Hu Moments mathematical expressions

$$\phi_1 = \eta_{20} + \eta_{02} \qquad \phi_2 = (\eta_{20} - \eta_{02})^2 + 4\eta_{11}^2$$

$$\phi_3 = (\eta_{30} - 3\eta_{12})^2 + (3\eta_{21} - \eta_{03})^2 \qquad \phi_4 = (\eta_{30} + \eta_{12})^2 + (\eta_{21} + \eta_{03})^2$$

$$\phi_5 = (\eta_{30} - 3\eta_{12})(\eta_{30} + \eta_{12})\left[(\eta_{30} + \eta_{12})^2 - 3(\eta_{21} + \eta_{03})^2\right] + (3\eta_{21} - \eta_{03})(\eta_{21} + \eta_{03})\left[3(\eta_{21} + \eta_{03})^2 - (\eta_{21} + \eta_{03})^2\right]$$

$$\phi_6 = (\eta_{20} - \eta_{02})\left[(\eta_{30} + \eta_{12})^2 - (\eta_{21} + \eta_{03})^2\right] + 4\eta_{21}(\eta_{30} + \eta_{12})(\eta_{21} + \eta_{03})$$

$$\phi_7 = (3\eta_{21} - \eta_{03})(\eta_{30} + \eta_{12})\left[(\eta_{30} + \eta_{12})^2 - 3(\eta_{21} + \eta_{03})^2\right] + (3\eta_{12} - \eta_{30})(\eta_{21} + \eta_{03})\left[3(\eta_{30} + \eta_{12})^2 - (\eta_{21} + \eta_{03})^2\right]$$

$$where\ \eta_{pq} = \frac{\mu_{pq}}{\mu_{00}^{\gamma}},\quad \gamma = \frac{p+q}{2} + 1,\ for: p + q = 2, 3, \ldots$$

Table 2: UMI moments mathematical expressions

$$\Theta_1 = \frac{\sqrt{\phi_2}}{\phi_1} \qquad \Theta_2 = \frac{\phi_6}{\phi_1.\phi_4}$$

$$\Theta_3 = \frac{\sqrt{\phi_5}}{\phi_4} \qquad \Theta_4 = \frac{\phi_5}{\phi_3.\phi_4}$$

$$\Theta_5 = \frac{\phi_1.\phi_6}{\phi_2.\phi_3} \qquad \Theta_6 = \frac{\left(\phi_1 + \sqrt{\phi_2}\right)\phi_3}{\phi_6}$$

$$\Theta_7 = \frac{\phi_1.\phi_5}{\phi_3.\phi_6} \qquad \Theta_8 = \frac{\phi_3 + \phi_4}{\sqrt{\phi_5}}$$

Legend: $\phi_i, i = 1,\ldots 7 - Hu\ Moments$

In AMI mathematical definition, the normalized central moments are defined according eq. (1), in the other hand, in the HOSI mathematical definition; the normalized moments are defined as described in eq. (2).

$$\eta_{pq} = \left[\frac{(\mu_{00})^{\frac{p+q+2}{2}}}{(\mu_{20})^{\frac{p+1}{2}}.(\mu_{02})^{\frac{q+1}{2}}}\right]\mu_{pq} \qquad (1)$$

$$\eta_{pq} = \left[\frac{(\mu_{20})^{\frac{p+1}{2}}(\mu_{02})^{\frac{q+1}{2}}}{(\mu_{40})^{\frac{p+1}{2}}(\mu_{04})^{\frac{q+1}{2}}}\right]\mu_{pq} \qquad (2)$$

Legend: $\mu_{pq} - Central\ Moments$

In our test, both approaches – AMI and HOSI – have shown a potential problem for proposed problem. When the ROI pixels had the same value, some moments presented were equals to zero, and some mathematical inconsistence appeared, leading to not a number (NaN) values and infinity values (Inf), which was not desirable for our approach.

In order to solve this problem, a new set of invariants were proposed for our group and is described in eq.(3) and eq.(4).

$$R_p(u) = sign(u).|u|^{\frac{1}{p}},\ P \in \square \wedge u \in \square \quad (3)$$

$$FS = \left[\frac{R_2(\phi_2)}{\phi_1}, \frac{R_3(\phi_3)}{\phi_1}, \frac{R_3(\phi_4)}{\phi_1}, \frac{R_6(\phi_5)}{\phi_1}, \frac{R_4(\phi_6)}{\phi_1}, \frac{R_6(\phi_7)}{\phi_1} \right] \quad (4)$$

Legend: $\phi_1, i = 1,...7 - Conventional\ Hu\ Moments$

Our proposed set has shown lower sensitivity to translation, rotation, scale and affine transforms than AMI, HOSI and conventional Hu moments and the mathematical inconsistence problem disappeared with this approach. This way, the feature vector was composed by 22 features: six (06) invariants previously proposed, thirteen (13) features based on Haralick's co-occurrence matrix, two (02) coordinates of ROI's center of mass and one (01) feature representing the summation of whole ROI's intensities.

In order to assess the influence of different acquisition conditions for every patient, intensity normalization was tested. In few words, with this procedure, the median luminal and adventitia intensities are adjusted to be close to reference values. For this, eq. (5) describes the intensity transformation.

$$I(i,j) = \left(\frac{I_{ADV} - I_{LUM}}{\hat{I}_{ADV} - \hat{I}_{LUM}} \right) \left(\hat{I}(i,j) - \hat{I}_{LUM} \right) + I_{LUM} \quad (5)$$

Where: $I_{ADV} = 190$; $I_{LUM} = 5$; $\hat{I}(i,j)$ is the measured intensity in position (x,y); $\hat{I}_{LUM}$: median luminal intensity before normalization and $\hat{I}_{ADV}$: median adventitia intensity before normalization.

2.4. Pattern classification techniques

After the feature extraction step, the classification step was started. K-nearest neighbors rule (k-nn) [19, 20] have been used to assess the classification for every region of interest. We defined that seven nearest neighbors have been used for the decision step. In addition to this, Euclidian Distance and Mahalanobis metric have been tested. Matlab® has been chosen as development framework for pattern recognition routines.

To provide more robustness and reliability to our results, leave-one-out method was applied for cross-validation of proposed approach. Once eight arteries were available, eight different combinations of training and test sets have been built by means of leave-one-artery-out procedure.

3. Results

Firstly, we have shown the distribution of the number of ROIs according to plaque composition for every window size. In table 3, the quantity of fibrotic ROIs was extremely higher than the other components. As ROI dimensions were raised, the number of ROIs matching the selection criteria has decreased significantly.

Table 3: Regions of interest distribution according to plaque composition for every window size

ROI Size	Number of ROIs per component				Total
	DC	NC	FF	FT	
5x5	7643	6962	8794	73093	96492
7x7	3351	1821	2517	31376	39065
9x9	1063	312	723	13252	15350

Legend: DC – Dense-Calcium; NC –Necrotic-Core; FF – Fibro-Fatty; FT – Fibrotic Tissue.

For limited space reasons, the tables containing the performance analysis for every scheme – window size, gray-levels re-quantization, intensity normalization and k-nn metric – were suppressed in this paper.

In the four classes scheme, the best configuration has provided the following average cross-validation error rates per component: (DC) 2.35%; (NC) 20.51%; (FF) 92.22%; (FT) 0.04%, which led to an average error rate of 5.2%, considering the plaque components' distribution. This configuration was achieved using Mahalanobis distance, 9x9 ROI length and normalized images with 256 gray-scale levels.

Those results have demonstrated the inability of our approach to discriminate fibrotic from fibro-fatty tissues. However, if the three classes' scheme was possible – DC, NC and FF+FT – maybe TCFA plaques identification should be feasible in the future.

In face of that, we assessed the performance of our classification process considering the described three classes' scheme. Our findings were: (DC) 2.35%; (NC) 20.51% e (FF+FT) 0.04% and a total average cross-validation error of 0.59%.

4. Discussion and conclusions

According to our findings, plaque characterization into IVUS-VH four classes scheme is not possible using the related methodology. Our method was not able to differentiate fibrotic from fibro-fatty tissue. There are

some possible reasons for these results, however, depth investigation become necessary to achieve feasible and reliable conclusions about the possibility or not to classify plaque based only on IVUS images' features.

In the three classes' scheme, without discrimination between fibro-fatty and fibrotic tissues, some encouraging results have been found. Despite NC average error rate has been around 20%, we believe that those results should be improved with the addition of new textural features. In the first moment, our choice was extremely severe about invariance properties. Our next step is to utilize multiresolution analysis with wavelet transform and assess the effectiveness of our normalization procedure to infer which parameters are leading to the confusion between FT and FF components.

To finalize, this work has shown that plaque composition estimation based only in image features should be possible. However, some improvements have been made necessary, especially for reducing NC error rate and for discriminating FF and FT tissue components. Further efforts will be realized in order to accomplish the promising objective of image-based atherosclerotic plaque characterization. Advances in this area should lead the knowledge about atherosclerotic disease to a new paradigm, once IVUS has become an indispensible tool for atherosclerosis investigation context.

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