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ANALYSIS OF SOFT PLAQUE DETECTION METHODS IN CTA IMAGES

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ABSTRACT

Cardiovascular diseases are considered primary cause for increasing rate of mortality. Automatic stenosis detection in CTA data is highly demanded by clinicians to analyze the coronary related abnormalities timely. The detection of vulnerable plaques in CTA is challenging because these plaques may exhibit similar appearance to nearby blood and muscle tissues. Moreover, accuracy of stenosis detection heavily depends upon the accuracy of delineation process of coronary arteries. In this paper, we present a comparative study of four different soft plaque detection methods along with their specific strengths and limitations. We have created a table summarizing the comparison of four selected methods against such criteria as imaging modality, segmentation method, level of pre and post processing, user interaction, validation of results, usage of prior knowledge, and effectiveness of segmentation and stenosis detection. The study provides assistance in selecting an appropriate method for detecting vulnerable coronary plaques, suitable for a given segmentation of coronary arteries.

Keywords: *Coronary Artery Segmentation, Stenosis, Soft Plaque, Computed Tomography Angiography, Cardiovascular Disease.*

1. INTRODUCTION

In the last decade, coronary artery disease (CAD) is one of the major causes of death worldwide [1]. The formation of plaque inside the coronary arteries blocks the blood flow and hence leads to cardiovascular disease. Narrowing of blood vessel due to plaque build-up is called as stenosis. Computed Tomographic Angiography (CTA) is considered as the state-of-the-art imaging modality which is proficient in obtaining 3D vascular information [2]. Therefore, CTA has become commonly recommended imaging modality for visualization of coronary arteries. Figure 1 shows the anatomy of coronary arteries, where left (LCA) and right (RCA) coronary arteries are shown to be connected with the aorta and are further branched into left anterior descending (LAD) and left circumflex (LCX) .

Accurate delineation of coronary arteries is the necessary part for planning and diagnosing the proper treatment of cardiac related abnormalities [3]. Modern technology such as CTA produces a large no. of detailed images that need to be interpreted by clinical experts [4].

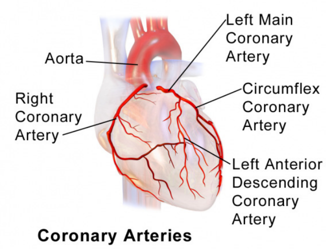

Figure 1: Anatomy of Coronary Arteries

Hence, to lessen the burden of clinical experts automatic and semi-automatic methods are highly required. Despite lots of research, the detection of stenosis still remains a challenging task. The term stenosis describes the abnormal narrowing of the blood flow passage within the arteries. According to the consensus [5], the stenosis is categorized into three classes; calcified, non-calcified and the mixed plaques as shown in Figure 2.

The plaque residing within the lumen is usually calcified plaques which show high density and corresponding bright appearance.

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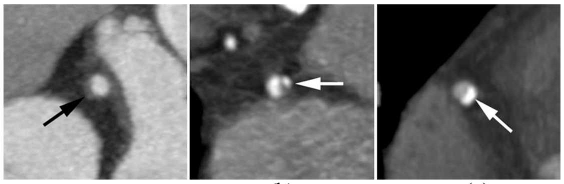


(a) (b) (c)

Figure 2: Types of Plaques (a) Non-calcified, b) Mixed, c) Calcified

The term non-calcified is also pronounced as soft plaque, vulnerable plaque, unstable coronary culprit and rupture prone plaque. These plaques have CT attenuation similar to blood and myocardial tissues making them difficult to detect. The plaque with calcified and non-calcified component is known as mixed plaque. To the authors' knowledge, not many resources are present in the existing literature that addresses the problem of soft plaque detection in coronary arteries. However, various studies can be found where experimentation is being carried out within a controlled environment and which are designed for specific medical centers rather than generalized computerized framework for non-calcified plaque detection and quantification. Furthermore, no such study exists in the literature which has provided the comparative analysis of generalized coronary soft plaque detection methods. Therefore, in this article, we present a comparative analysis of existing soft plaque detection techniques that can be used to locate the stenosis present in the coronary arteries in CTA images with particular interest in their advantages and limitations as well as their clinical implications of the derived findings. The selection of four methods is done on the basis of segmentation criterion used by each method for plaque detection. All of the selected methods obtained their respective segmentation by employing the neighborhood information of the selected voxels. Moreover, the satisfactory performance of these plaque detection methods in a generalized environment has enforced us for their selection in this study.

2. LITERATURE OVERVIEW

Detection of vulnerable plaque mainly depends upon the quality of segmentation. Several publications have addressed segmentation of coronary arteries in the literature [6][7][8]. The method in [9] has combined the intensity and shape information, and gave the improved segmentation result by preventing the contour leak into the neighboring regions. Yang et al. [10] proposed incorporating active contour segmentation into a Bayesian probabilistic framework, where the image-driven energy is redefined by posterior probabilities. Lankton and Tannenbaum [11] proposed the use of different metrics to measure the similar intensity distributions derived from image regions. In another approach, Lankton and his coworkers [12] have utilized localized active contour approach for detecting the coronary vessels by considering only the voxels representing the heart zone and ignoring very dark voxels representing air present in the lungs. However, their method requires a single-point initialization within the vessel by a user which may lead to erroneous segmentation and may also increase the processing time. The use of simple active contour model often produces leakages while segmenting coronary arteries due to the leaning of contour into the nearby voxels exhibiting similar intensities which eventually affects the subsequent step of stenosis detection.

Different methods have been proposed in the literature for grading of stenosis via CT angiographic images. Manual plaque labeling using multi-planar formatting is popularly used in clinical studies to detect and quantify coronary stenosis. A 3D level set segmentation has been employed by Antiga et al. [13] to compute maximal sphere inscribed inside a binary vascular region. A modified 3D approach using manual vessel isolation and different window as well as level setting is also proposed in [14] for evaluation of stenosis higher than 50%. For automatic quantification, Chen and Molloi [15] analyzed length, diameter and angle of bifurcation. Yang et al. [8] used harmonic function for centerline extraction and measured the cross-sectional area of vessel for stenosis quantification. An automatic method is proposed by Blackmon et al. [16] for volumetric plaque analysis in CTA images using centerline computation, thresholding and manual identification of lesions along with adjustment of vessel diameter above and below the lesion. They reported a high reproducibility of plaque measurements among experienced and inexperienced observers. A composite approach has been presented by Oksuz et al. [17] where the vessel segmentation is obtained through Hessian-based vesselness filter and three-dimensional region growing. Further, they analyzed and estimated the expected diameters at the cross-section of each artery point for quantification and detection of stenosis percentage. Xu et al. [18] presented another approach for stenosis detection by employing fuzzy distance transform technique.

The partial volume artifacts and the noise involvement in CTA images make the segmentation of coronaries and stenosis detection task a challenging task. The goal of our contribution is to present a comparative study by discussing the usefulness and limitations of the available plaque detection methods. To this end, we have selected four methods used for locating the stenosis. We focus specially on the techniques which take CTA images as input.

3. MATERIALS AND METHODS

The objective of this study is to provide a platform where different techniques for detection and quantification of coronary stenosis can be analyzed. CTA is mainly an anatomic test with excellent visualization of coronary anatomical structures and detection of coronary lumen stenosis. Therefore, in this study, we will focus on the methods which make use of CTA technology in order to locate the stenosis. Generally, the conventional way of tracking stenosis is to find out the effective cross-sectional areas at each point of coronary arteries which are further analyzed by employing the concept of planar geometry for the detection of stenosis followed by various pre-processing and post-processing steps. In subsequent sections we put light on four stenosis detection methods in detail each of which utilizes a different concept for locating the stenosis.

3.1 Method by Felix Renard

The method proposed by Felix Renard [19] comprises of three steps. Firstly, the method extracts the skeleton of the arterial tree by utilizing Yang's vessel tracking technique [20]. To obtain artifacts free centerline, the disturbances including myocardial cavities and the calcified plaques are isolated during preprocessing stage. After the accurate centerline is obtained lumen and arterial wall segmentation is performed by using statistical modeling. The vessel and its surrounding tissues are represented by Gaussian Mixture Model and then an optimized probability map is constructed by employing Expectation Maximization algorithm. Because of the intensity variations along the vessel, a cylindrical model based on the local neighborhood information at each centerline point is used. This model is used for extracting the segment between two consecutive points of the vessel. The extracted cylinder is then modeled by three class Gaussian mixture model in order to get the distribution parameters for three different classes namely; lumen, wall and myocardium. The probability map is examined to identify the lumen and vessel voxels. Further geometrical analysis of the vessel is performed to locate the plaque locations. Vessel narrowing is computed by measuring the area of lumen and wall cross sections. Then the two area measures are compared to know the presence of either calcified or non-calcified plaque.

This application identifies the plaque location correctly in the coronary arteries and visual results are validated with statistical measures/graph data. Although, the method is computationally efficient for detection of soft plaque in CTA but no clinical validation of the results has been presented. Moreover, the method aims to detect the soft plaques but no detailed quantitative analysis of the detected plaques has been shown. Moreover, the soft plaque detection criterion is based only on area difference which makes the method prone to errors.

3.2 Method by P. Mirunalini

The segmentation and detection method proposed by P. Mirunalini et al. [21] is a simple approach where segmentation of coronaries from

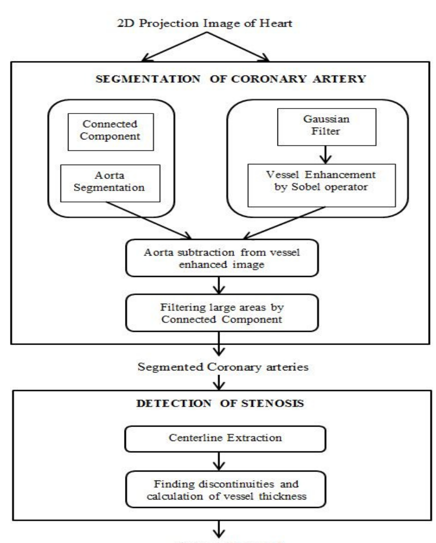


Figure 3: Flow Diagram of Mirunalini's Method [21]

2D projected images is carried out by employing the basic concept of connected component labeling and morphological operations. Before segmentation process starts, the method makes use of sobel operator for the enhancement of the vessels as depicted by the flowchart given in Figure 3. After obtaining the delineated coronary arteries skeletonization is performed to extract the centerline of the coronary arteries by using morphological operations such as erosion.

Further, they analyzed the obtained centerline to check for the discontinuities which may occur due to the contracting of blood vessel. The width of the contour at particular part of the vessel may increase because of the accumulation of the fatty components. Therefore, by analyzing the intensity at that particular contour of the vessel gives the confirmation of the corresponding centerline discontinuities and the calcification as stenosis.

The method detects the stenosis on the basis of gaps in the obtained centerline. However, the soft plaque resides in the lumen wall which remains quite until it ruptures. Therefore, only centerline based analysis is not enough to detect the presence of soft plaque.

3.3 Method by Shawn Lankton

Lankton's method [12] addressed the problem of automatically detecting soft or non-calcified plaque in CTA images. His method commences with the isolation of the coronary arterial tree from the volumetric datasets by using the localized energy model based on the most famous active contour Chan-Vese energy. In the successive step, two surfaces are constructed explicitly inside and outside the original segmentation using morphological operations (erosion and dilation) such that they lie just inside and outside the segmented vessel wall in a respective manner. Both the surfaces are evolved simultaneously using mean separation energy proposed by Yezzi et al. [22] that pulls the contour towards each other so that the non-calcified plaques that reside within the wall can be located between two surfaces. For an ideal case, these two segmentations must match with each other at all the points. The regions where these two curves do not match are identified as the regions with soft plaque.

Initially the local interior region of inside surface contains only the bright voxels, as the contour deforms it expands to capture more voxels containing blood but does not expand into a bit darker soft plaque voxels. Similarly External contour contains initially the myocardium voxels, and it does not contract to accommodate the soft plaque voxels from the boundary. This way soft plaques can be isolated between two contours as neither will move into plaque voxels when driven by localized Means separation energy. Concluding, in case of no soft plaque (no inhomogeneity in intensity values) these two evolving contours meet on the vessel wall, however deposition of the plaque inside wall will stop contours at the boundary of vessel and they will remain separate from each other.

This algorithm is based on a localized active contour framework that employs a scale parameter to restrict the statistical characteristics of the vessel into local regions. Simple probabilistic models based on local means are used to extract the vessel and find areas where soft plaques exist. The beauty of their approach is that, it does not require any pre and post processing of CTA data. This technique has cast the problem of detecting soft plaque in a variational active contour framework that operates directly on the raw CTA volume. Hence, it naturally handles the arterial branches by taking the benefits from the geometric properties of active contour model. The method is effective but requires the initialization of the seed point for each artery by the users which of course requires user expertise without which it may lead to erroneous segmentation. The main focus of their study is to segment the vulnerable lesions present in the coronary arteries. They have used 8 CTA datasets for evaluation of their method which is able to detect 88% of the soft plaque. Detected plaque locations are further verified by the clinical experts.

3.4 Method by Aboulfazal Khedmati

Another semi-automatic computer-aided framework has been presented in the literature [23] for the detection of stenosis from three dimensional CTA data with the goal of reduced processing time and less user involvement. To increase the speed of the whole process, down-sampling is performed using cubic interpolation method. Further, morphological operations and thresholding are performed to get rid of unwanted data including pulmonary regions. After obtaining only the heart region, vessel enhancement procedure is carried out by employing the most famous Frangi vesselness filter [24] that assigns the highest vesselness to the voxels which belong to coronary arteries. To isolate the coronary arteries only starting and ending seed points are provided manually for each coronary artery which is further adjusted to fall into wrong artery extraction by using the concept of mean of voxel intensities. Then the region growing process starts by utilizing the adjusted correct seed information to segment out the coronary arteries. The unwanted regions are further removed from the obtained segmentation before applying skeletonization process to increase the speed. Then skeletonizing of the obtained arteries is performed by applying multistencils fast marching method (MSFM) to get the artefacts free centerline.

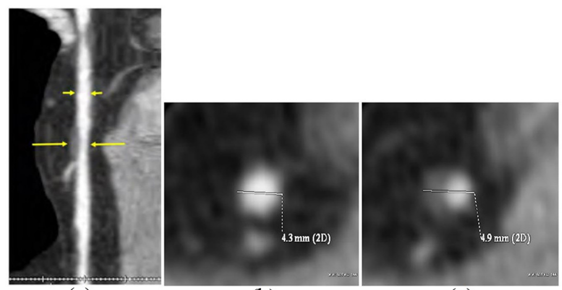
For the detection of stenosis, plane fitting process is carried out to find the cross-sections and then the diameters of these cross-sections are computed for each centerline point of the artery. Linear regression method is used to find out the expected diameters on the basis of centerline points. The percentage of the coronary stenosis is calculated by estimating the difference between the obtained and the expected diameters. The estimation is done on the basis of some threshold which is decided by the radiologists. The method has detected the stenosis which is more than 50% because usually greater than 50% stenosis is of importance.

Although this method has been validated on publically available testing CTA datasets, but it heavily relies on pre and post processing operations. Moreover, the use of fixed threshold value in their method may not work well in all situations as medical images suffer from intensity variation problem hence may lose the potential coronary data due to the use of hard threshold.

4. RESULTS AND DISCUSSIONS

Although all of the methods discussed here have their capacity to detect the plaques but because of certain plaque characteristics they often fail in locating plaques. A summarized analytical comparison has been reported in Table 1, where four different methods are compared with respect to different parameters including input image type, no. of datasets used, pre/post processing, analysis of lumen wall, method used for segmentation and detection of plaque, execution time and their respective limitations.

Each of the four methods discussed here makes use of CT technology for imaging the coronary arterial tree but they differ in various other aspects. As can be seen in Table1, P. Mirunalini's method is completely automatic for finding the stenosis by exploiting the information of centerline, thickness and intensity of the obtained segmented coronary arteries. However, their method identifies the stenosis on the basis of discontinuities in centerline due to narrowing of blood vessel, which is not always the case for soft plaque because, soft plaques often show expansive or positive remodeling shown in Figure 4 , not causing significant narrowing of the coronary lumen [25]. Positive remodeling is an outward compensatory remodeling in which the arterial wall grows outward in an attempt to maintain a constant lumen diameter [26]. In Figure 4(a), the non-calcified plaque shown by the yellow long arrows is positively remodeled as compared to the normal coronary segment indicated by the short arrows. Consequently, Figure 4(b) and (c) represents the diameter computation for normal and lesion segment.



(a) (b) (c)

Figure 4: Positive Remodeling [26]

As far as pre and post processing are concerned, the methods by Felix et al., P. Mirunalini et al., and Khedmati et al. require lots of pre/post processing whereas Lankton's approach does not dependent upon these cosmetics operations. However, Lankton's active contour based evolution takes time and may produce erroneous segmentation due to the leaning of contour into the region of similar intensities which will eventually affect the plaque detection procedure. As compared to Felix and Mirunalini's approach, Lankton and Khedmati's approach requires initial seed points in order to start their segmentation procedure which may not be reproducible due to the manual provision of user's seed point and hence may affect the plaque detection procedure.

Most importantly, with respect to validation, only Khedmati's approach has provided validation of their results by evaluating their method on eighteen testing CTA datasets which are made available publically by Rotterdam framework. Moreover, the rest of other methods need to be run on a large no. of dataset. The percentage of plaque detection by Lankton's method has been reported as 87.5% which is lesser than Mirunalini's and Khedmati's method. However, Felix's method has not mentioned the percentage for their detection method. One good point of Felix approach is the separate analysis of the lumen wall which is necessary because usually soft plaque stays within the wall of the arteries. Hence, it may help the user in detecting the stenosis locating within the wall of the lumen.

Besides, Lankton's approach requires a prior anatomical knowledge for placing the initial seeds in coronary arteries which may require the user expertise. The wrong placement of seed may lead to inaccurate segmentation and hence may affect the detection procedure. However this prior information is not mandatory in other approaches proposed by Felix et al., P. Mirunalini et al., and Khedmati et al. Moreover, as compared to other methods analyzed here only Khedmati's approach has reported the execution time for their framework.

Generally, the high risk plaques are marked by the degree of luminal narrowing but the composition of plaque is much more clinically significant than the luminal narrowing because the arterial lumen is often preserved by positive arterial remodeling. Therefore, the direct evaluation of the arterial wall is important in identifying the soft plaques. Since soft plaques are rupture prone plaque, so a risk of an acute coronary syndrome exists due to the rupture. Therefore, the methods must analyze the CT values so that these plaques may be stabilized by the treatment even when they do not cause a significant stenosis.

The limitation of our study lies in the fact that it focuses only on those plaque detection methods which use CTA imaging modality for their experimentations. Besides, we have not included those stenosis detection methods which address the soft plaque detection problem in a controlled environment for specific medical centers.

In future, we will extend this study to include more detailed analysis of soft plaque detection methods in both controlled as well as generalized environment.

5. CONCLUSION

The study is based on the analysis of stenosis detection methods. Four stenosis detection methods are analyzed and compared. Although, a significant progress has been made by each of the methods discussed in this study, but still there is a room for much improvements in detecting plaques. Since the attenuation values between vessel lumen and the boundary layer of vessel wall have different characteristics, detailed analysis of vessel wall is required for the localization of soft plaques. Moreover, in order to implement these methods in daily clinical practices, their diagnostic and predictive accuracy need to be evaluated in large groups of patients, in multicenter, randomized, controlled trials.

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Table 1: Comparison of Four Stenosis Detection Methods

#	Properties	Felix Renard	Lankton	P.Mirunalini	Khedmati
1	Imaging modality/Input type	MDCT	CTA	CTA	CTA
2	No. of datasets used	2	8	15	18
3	Pre-processing	Yes	No	Yes	Yes
4	Post-processing	Yes	No	No	Yes
5	Fully/Semi-automatic	Semi-automatic	Semi-automatic	Fully automatic	Semi-automatic
6	Separate Lumen and Wall Analysis	Yes	No	No	No
7	Approach for segmentation	Adaptive Region Growing.	Localized Active contour based	Morphological operations	3D Region Growing
8	Approach for detection	Analysis of effective cross-sectional areas of lumen and arterial wall	Localized Active Contour framework	Heuristic based analysis of extracted centerline of vessel.	Plane Fitting and diameter analysis
9	A prior knowledge	No	Yes	No	No
10	User interaction	No	Yes	No	Yes
11	Validation of results	No	No	No	Yes
12	Percentage of detection	-	87.5%	Recall=0.97 Precision=0.266	Sensitivity=88.89% PPV=88.89% Sensitivity=44.2% PPV=34.37%
13	Average execution time	-	-	-	8.5 min
14	Limitations	Require bulk of pre/post processing	Produce leakages during segmentation	Cannot detect stenosis on the interior parts of arteries.	Segmentation produces many irrelevant components.