Quantification of Coronary Arterial Stenosis by Inflating Tubes in CT Angiographic images

Abouzar Eslami[1,2*], Amin Aboee[1], Zardosht Hodaei[1], Mandana Javanshir Moghaddam[3], Stephane Carlier[4], Amin Katouzian[1,5], and Nassir Navab[1]

[1]Chair for Computer Aided Medical Procedures, Technical University of Munich, Germany
[2]Institute for Biomathematics and Biometry, Helmholtz Zentrum Munich, Germany
[3]Royal Institute of Technology KTH ,Stockholm,Sweden
[4]Cardilogy Department, Universitair Ziekenhuis Brussel, Belgium
[5]Biomedical Engineering Department, Columbia University, NY USA

{eslami}@cs.tum.edu

Abstract. Computed tomographic angiography (CTA) is a non-invasive and relatively low cost imaging modality that is employed for stenosis quantification prior to percutaneous coronary intervention (PCI). In this paper we propose a new coronary segmentation method by estimating the likelihood of transversal circles around the manually refined vessel LKEB centerline. A cost function is defined from the similarity of adjacent circles and their likelihoods. The optimal likelihoods are attained from minimization of a functional constrained by predefined likelihoods driven from centerline points (internal seeds) and manually selected external seeds outside the vessel. Following segmentation, stenoses are detected and graded based on the observed and expected cross-sectional area of the vessel as well as the intensity profile. We applied the developed algorithm on 36 datasets and in case of quantitative coronary angiography (QCA) achieved sensitivity of 63% and positive predictive value (PPV) of 13% for detection of stenosis. The same values for CTA images were 43% and 4%, respectively. The stenosis degree was estimated with an absolute average difference of 46.4% and kappa value of -0.15 as compared to QCA.

Keywords: Coronary Artery, Stenosis, Computed Tomographic Angiography.

1 Introduction

Recent advancements in medical imaging technologies have facilitated non-invasive imaging of coronary arteries for diagnosis, monitoring and treatment strategy of atherosclerosis [1]. Computed tomographic angiography (CTA) has become commonly recommended imaging modality for visualization of coronary arteries [2]. Several publications have addressed segmentation of coronary arteries [3][4][5] and quantification of stenosis employing CTA images [1][6]. For example, topology adaptive surface model is proposed by Riedel et al. [7] for vessel segmentation in micro-CT images using *a priori* of the vessel geometry and local adaptive grayscale profile. Another topological approach was proposed by Szymczak et al [8] through extracting a connected forest of persistent maxima and geometric filtering. Particle filtering approach with Monte-Carlo sampling with parallel propagation of multiple hypotheses is proposed by Florin et al. [9] to deal with bifurcation and branches. A hybrid multi-scale filtering strategy and Baysian probabilistic approach through level set segmentation has been also proposed by Yang et al. [10]. The method of Wang et al. [11] includes optimizing a virtual contrast injection using fuzzy connectivity for segmentation of the vessel tree. Fuzzy segmentation is employed by Xu et al. [1] followed by computing the fuzzy distance transform and estimation of observed and expected vessel diameters for stenosis quantification. A review on existing segmentations, models, and feature extraction methods has been provided in [12].

Different methods are 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 stenoses. 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. [5] 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. For a review on different methods of detection and stenosis grading in CTA images refer to **Error! Reference source not found.**.

Nevertheless, segmentation of coronaries and quantification of stenosis in CTA images is still challenging due to low signal to noise ratio, low resolution and partial volume effect. Even with a perfect segmentation, detection and grading of stenosis is still challenging due to lack of appropriate referenced vessel. In this paper we propose a semi-automatic approach for segmentation of coronary arteries based on estimating the likelihood of transversal circles around the centerline, which could be within or outside the lumen, Fig 1(b). Once the vessel is segmented, we use the cross-sectional area as well as averaged intensity value for detection and quantification of stenosis.

2 Methodology

In this section we provide theory and algorithms of proposed method for quantification of coronary arterial stenosis. The proposed method consist of two steps: segmentation of coronary arteries based on inflating tubes followed by quantification of stenosis based on radius and local intensity profile of the segmented vessel.

2.1 Expandable tubes

Our proposed method exploits predefined centerline and a number of manually selected seeds outside the vessel. We make a graph representation of the tubular region of interest around the centerline (manually refined from LKEB [17][18]) of the vessel and then formulate vessel segmentation problem as likelihood estimation of every transversal circle.

One of the key points of the proposed method is the discrete tubular region of interest around the vessel centerline. The tubular region of interest consists of two discretized axes: position and radius. Suppose $\mathcal{P}$ is the centerline of underlying vessel represented by a set of discrete points p. The region of interest is defined by a set of transversal circles $C(p,r) \in \mathcal{C}$ at each point of the centerline. Each transversal circle can be represented by its center $p \in \mathcal{P}$ i.e. one of the centerline points and its radius $r \in \mathcal{R}$. The discrete set of radiuses $\mathcal{R}$ is defined by the region of interest i.e. the maximum radius of the undergoing vessel plus a predefined margin and the resolution of segmentation process for sub-pixel accuracy.

In our graph representation for vessel segmentation, the nodes denote the transversal circles and their relation are represented by the graph edges. Each node n_i refers to one transversal circle $C(p,r)$ with known radius $r \in \mathcal{R}$ and center point $p \in \mathcal{P}$ from the set of centerline points. The number of nodes is equivalent to the number of centerline points multiplied by the cardinality of $\mathcal{R}$. Therefore, for each transversal circle in the tubular region of interest there is one node in the graph.

The graph is assumed to be connected and the connectivity is defined based on vicinity of the circles that the graph nodes represent. Two nodes n_i and n_j are connected if the transversal circles they represent have minimal difference. Fig. 1 shows schematic of the adjacent circles, which are assumed to be connected. Each circle $C(p,r)$ is supposed to be connected to four other circles: two intra- and two inter-plane neighbors. The intra-plane neighbors are the adjacent circles, one bigger and one smaller, in the same transversal plane as the original circle. The two inter-plane neighbors are the two circles in adjacent cross-sectional planes, one before and one after the original circles but with equal size as shown in Fig 1.

The connections between the nodes of the graph are weighted by edge weights. We define the edge weight w_{ij} between graph nodes n_i and n_j based on the averaged intensity difference of corresponding circles. Assume there is a node n_i representing $C(p_i, r_i)$ i.e. the transversal circle with radius r_i and center of p_i. Similarly n_j represents $C(p_j, r_j)$. The edge weight w_{ij} between pair of nodes n_i and n_j is defined as:

$$w_{ij} = \begin{cases} \exp\left(-\beta\left(\mu_i - \mu_j\right)\right) & n_i \text{ and } n_j \text{ connected} \\ 0 & \text{o.w.} \end{cases} \tag{1}$$

where μ_i and μ_j are the average intensities of the circles $C(p_i, r_i)$ and $C(p_j, r_j)$. Based on the defined graph representation and edge weights, we formulate vessel segmentation as minimization of the following cost function:

$$E = \frac{1}{2} \sum_{n_i, n_j \in \mathcal{G}} w_{ij} \left(x_i - x_j \right)^2 \qquad (2)$$

where x_i and x_j denote the likelihood of the transversal circles represented by nodes n_i and n_j of the graph $\mathcal{G}$. For two adjacent circles $C(p_i, r_i)$ and $C(p_j, r_j)$ with similar average intensities, μ_i and μ_j are close and therefore the edge weight w_{ij} from Eq. (1) reaches to its maximum. Then minimization of eq. (2) leads to close likelihoods for the two circles. The rationale behind the proposed method is that if two adjacent circles have similar intensities then they both probably belong to either inside or outside the vessel and therefore should have similar likelihoods. By expanding Eq. (2) and writing it in matrix form, we obtain:

$$E = \frac{1}{2} \sum_{c_{ij} \in \mathcal{C}_{I:I}} w_{ij} \left(x_i^2 - 2x_i x_j + x_j^2 \right) \qquad (3)$$

$$E = \frac{1}{2} \boldsymbol{x}^T L \boldsymbol{x}^T \qquad (4)$$

where $\boldsymbol{x}$ is the vector of the likelihoods and the matrix L is defined as:

$$L_{ij} = \begin{cases} 2 \sum_{n_j \in N_i} w_{ij} & i = j \\ -w_{ij} & \mathrm{O.W.} \end{cases} \qquad (5)$$

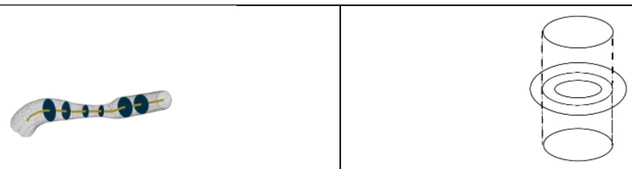
$n_j \in N_i$ denotes all n_j nodes connected to the node n_i. Boundary conditions are required to optimize Eq. (2) with respect to the likelihood values x. These boundary conditions include the internal seeds on the vessel centerline and a number of external seeds outside the vessel where the likelihoods are known. Without loss of generality, we reorder the $\boldsymbol{x}^T = [\boldsymbol{x}_M^T \quad \boldsymbol{x}_U^T\,]$ so that marked nodes are first followed by unmarked nodes. Therefore, we may decompose Eq. (4) into:

$$E(\boldsymbol{x}_U) = \frac{1}{2} [\boldsymbol{x}_M^T \quad \boldsymbol{x}_U^T] \begin{bmatrix} L_M & L_B \\ L_B^T & L_U \end{bmatrix} \begin{bmatrix} \boldsymbol{x}_M \\ \boldsymbol{x}_U \end{bmatrix} \qquad (6)$$

that can be minimized by solving the set of sparse linear equations:

$$L_U \boldsymbol{x}_U = -L_B^T x_M \qquad (7)$$

The solution is unique as L_U is positive definite so the only critical point is the minimum. Finally, the vessel can be segmented by $x > 0.5$.



(a) (b)

Fig. 1. (a) Schematic of tubular representation of vessel, (b) schematic of adjacent intra-and inter-plane connected circles. The

2.2 Stenosis quantification

The main goal in segmentation of coronaries is to detect and quantify stenosis that is clinically imperative. In this study, we propose using cross-sectional area and intensity profile of segmented lumen for quantification of stenosis with sub-pixel accuracy.

The conventional approach of estimating stenosis percentage in coronary angiogram is dividing the minimum lumen diameter by a nearby or reference diameter. However, this approach is inaccurate as finding nearby normal lumen is difficult and susceptible. Alternatively, we grade stenosis once the vessel segmented as follows:

$$S_A(p) = 1 - \frac{A(p)}{A_{ref}(p)} \qquad (8)$$

where $A(p)$ is the cross-sectional area of the segmented lumen at centerline point p and $A_{ref}(p)$ is the reference area of the lumen at that point. Although the definition of stenosis grade is simple, computing the stenosis grade is still challenging. Since the media adventitial border of vessel is not distinguishable in CTA images, determining the reference area of lumen is difficult. Hence, we compute the expected cross-sectional area by fitting a descending quadratic polynomial to the cross-sectional area of the segmented lumen. The expected cross-sectional area, approximated by the quadratic polynomial, is then used as the reference lumen area in Eq. (8) to grade the stenosis at each point of the vessel centerline.

In addition to the cross-sectional area, we consider intensity profile of lumen for quantification of stenosis to deal with partial volume effect. Because of low resolution of vessel diameter depicted in CTA images the partial volume effect is a substantial source of error. Fig. 2 shows a cross section of a vessel and associated grids that discretize the space. The pixels inside the vessel are filled with die and therefore have maximum intensities. However, the peripheral pixels are partially filled with blood and therefore have some interval intensity values. This is more substantial when the vessel is thinner in distal parts of the vessel or because of stenosis. Therefore, in this paper, we estimated the average intensity of the lumen at each cross section and compared it with the maximum (Mx) and minimum (Mn) expected intensities. The maximum intensity is estimated from the aortic arc where it is certainly filled with blood so maximum intensity value is expected. The minimum intensity is estimated from the myocardium where no blood is expected. The stenosis grade is then computed from

$$S_I(p) = \frac{Mx - I(p)}{Mx - Mn} \qquad (9)$$

where $I(p)$ is the average intensity of the vessel over the cross-sectional plane at the centerline point (p). Finally the stenosis grade is computed as the maximum of intensity based (S_I) and area based (S_A) grades.

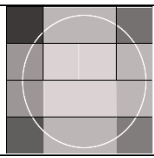


Fig. 2 Cross-sectional drawing of a vessel and the effect of partial volume effect. The lumen border is sketched with white and each square represents one pixel.

3 Experimental Results and Quantification

The proposed method was validated with training and testing database of CTA images provided through Coronary Stenoses Detection/Quantification and Lumen Segmentation challenge within MICCAI 2012. The achieved results for detection and quantification of stenosis are reported in Tables 1 and 2, respectively. Due to unsupervised nature of our developed algorithm, we performed it on all provided datasets (total of 36).

Performance of the proposed method in estimating QCA is better than CTA because of partial volume effects. However, comparing Table 1 and 2 it can be inferred that the proposed method was more successful in detection of stenosis rather than quantification. The main source of error would be inaccurate extracted centerlines that is propagated throughout segmentation. The reason is that the proposed method performs segmentation on the tubular region of interest, which is determined by the vessel centerline. Performance of the method can be further improved by optimizing the centerline before segmentation. As an alternative solution, we will extend our semi-automated algorithm to fully automated by incorporating learning of intensity profiles which are often used for quantification of stenosis. Table 3 and 4 demonstrate the inter-observer variability.

Table 1. Achieved results of the proposed method in detection of stenosis.

	QCA Sens. (%)	QCA P.P.V. (%)	CTA Sens. (%)	CTA P.P.V. (%)
Training and Testing (42)	0.63	0.13	0.43	0.04
Testing (24)	0.75	0.10	0.48	0.04

Table 2. Achieved results of the proposed method in quantification of stenosis.

	QCA Avg. Abs. diff. (%)	QCA R.M.S. diff. (%)	CTA Weighted Kappa (K)
Training and Testing (42)	46.4	51.0	-0.15
Testing (24)	49.2	53.1	-0.14

Table 3. Comparing the experimental results in detection of stenosis from the proposed method and three observers (24 test data).

	Observer 1	Observer 2	Observer 3	Proposed method
QCA Sens. (%)	0.88	0.70	0.68	0.75
QCA P.P.V. (%)	0.40	0.49	0.45	0.10
CTA Sens. (%)	0.79	0.64	0.68	0.48
CTA P.P.V. (%)	0.58	0.72	0.62	0.04

-**Table 4.** Comparing the experimental results in quantification of stenosis from the proposed method and three observers (24 test data).

	Observer 1	Observer 2	Observer 3	Proposed method
QCA Avg. Abs. diff. (%)	30.6	32.6	31.0	49.2
QCA R.M.S. diff. (%)	35.7	37.5	37.1	53.1
CTA Weighted Kappa (K)	0.36	0.34	0.28	-0.14

4 Conclusion

In this paper, we proposed a new approach for segmentation of coronary arteries in CT angiographic images. The proposed method is based on graph representation of a tubular region of interest around the centerline of underlying vessel. Based on the known likelihood of the centerline points and a number of manually selected seeds outside the vessel, the proposed method estimates optimal likelihood of each transversal circle. In order to quantify stenosis, not only the cross-sectional area of the segmented vessel was compared with the expected area but also the intensity profile of the vessel was considered to deal with partial volume effect.

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