# Quantification of Coronary Artery Stenosis by Area Stenosis from Cardiac CT Angiography

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***Abstract*—Non-invasive cardiac computed tomography angiography (CTA) is widely used to assess coronary artery stenosis and give clinical decision-making support to clinicians. The severity of stenosis lesion is commonly graded by a range of percent Diameter Stenosis (DS), which can introduce false positive diagnoses or over-estimation, triggering unnecessary further procedures. In this paper, a system and the associate methods to quantify stenosis by the percent Area Stenosis (AS) from cardiac CTA is presented. In the process, coronary artery tree is segmented and the centerline is extracted by Hessian filtering and the minimal path method. After a serial of 2D cross-sectional artery images along the artery centerline are obtained, lumen areas are segmented by ellipse-fitting with deformable models, and consequently to compute the lesion's AS. Experimental results on 5 CTA data sets show that compared to DS, AS better correlates to the reference standard for stenosis quantification, suggesting the efficacy of the proposed system.**

## I. INTRODUCTION

Coronary heart disease (CHD), affecting about 6% of general adult population, is a common but life-threatening cardiovascular disorder where a portion of the coronary artery is blocked by plaque, causing the narrowing (stenosis) of artery lumen and the reduced blood supply to the heart.. Timely and accurate evaluation of suspected CHD patients is among the keys to improving patient care, highlighting the importance of accurate detection and quantification of coronary artery stenosis in clinical decision-making. Although invasive catheterized coronary angiography (ICA) with fractional flow reserve measurement is the gold standard to evaluate anatomical and functional stenosis, non-invasive cardiac CT angiography (CTA) is a popular diagnostic alternative to ICA, due to its high sensitivity, excellent spatial resolution, low cost and easy acceptance.

Currently cardiac CTA data are clinically interpreted by well-trained physicians and the severity of a coronary artery stenosis lesion is graded by a range of percent Diameter Stenosis (DS), i.e., <25% (light), 25-40% (mild), 40-70% (moderate), and >70% (severe). More specifically, DS is obtained by 2D quantitative coronary angiography (QCA) where images are projected unto multiple planes and arterial lumen diameter is assessed accordingly [1]. It is rather a kind of estimation, as different rating results may be obtained on the same lesion with different projection angles and different interpreters. Clinical studies have suggested that DS-based CTA assessment for stenosis introduced a significant number of false positive diagnoses or over-estimation, triggering unnecessary further examinations (e.g., costly ICA and FFR measurement) and treatments (e.g., balloon angioplasty and stenting) [2]-[5]. In contrast, the percent Area Stenosis (AS, 1 minus the ratio of actual lumen area to the stenosis-free lumen area) will not vary. AS, together with the length of lesion, would provide more accurate, reproducible and informative indicators to the severity of stenosis for clinical decision making. Several automatic systems with centerline extraction and learning-based regression for cross-sectional lumen area estimation have been developed to detect, grade and classify coronary stenosis in CTA [6][7]. However lumen area calculation is still based on lumen diameter profile, which may introduce considerable errors.

In this paper, we present a system and the associate methods for the quantification of coronary artery stenosis by the percent AS from cardiac CTA data. The whole process includes coronary artery segmentation from CTA data, centerline extraction and tracking, cross-sectional artery lumen segmentation, and stenosis quantification. This system was tested on clinical CTA data and the results were benchmarked with DS obtained from CTA and ICA.

## II. METHOD

### A. System Overview

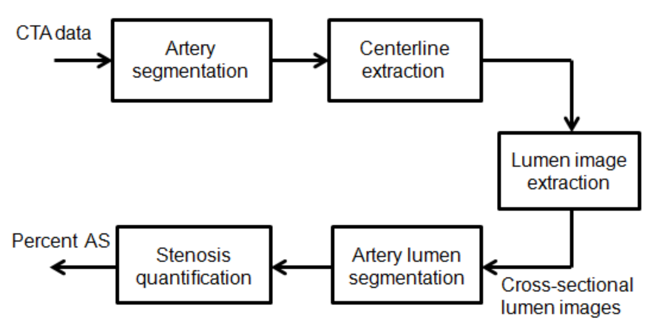


Figure 1. The flowchart of the proposed system for stenosis quantification

Figure 1 shows the flowchart of the proposed system. Given a cardiac CTA data set, coronary arterial tree will be segmented and the corresponding centerlines will be extracted.

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By tracking centerlines of the three major coronary arteries, i.e. left anterior descending (LAD), left circumflex (LCX) and right coronary artery (RCA), three serial of 2D cross-sectional arterial images will be extracted. From the 2D cross-sectional arterial images, arterial lumen areas which are enhanced by contrast agent will be segmented by an ellipse-based fitting step and the deformable model. Then for each artery, the cross-sectional lumen area with the advancing of centerline from root (proximal) to tip (distal) will be plotted and the severity of stenosis will be assess by the segmented artery lumen area and the corresponding restored lumen area from a stenosis-free artery.

## B. *Coronary Artery Segmentation and Centerline Extraction*

In a CTA data set, a multi-scale vessel enhancement filtering proposed by Frangi et al is used [8]. The approach searches for geometrically tubular structures, which are detected by particular eigenvalue pattern analysis of the Hessian matrix (low value for $\lambda_1$ and high value for $\lambda_2$ & $\lambda_3$), to extract the principle direction. This increases the contrast (or difference) between vessel-like structures and other structures. By applying a suitable threshold, coronary arteries can be segmented from the CTA data set.

After the coronary artery was segmented, its centerline was extracted by a minimal path approach [9][10], which is briefly described below: In Hessian matrix, for tubular or vessel-like structures, the eigenvector $e_1$ corresponding to the smallest eigenvalue $\lambda_1$ points in the longitudinal direction of the vessel, which has the smallest curvature and the normal plane to this direction (i.e., eigenvectors corresponding to $\lambda_2$ and $\lambda_3$) forms the cross-sectional plane to the vessel. Hence for each coronary artery branch of interest, given two endpoints specified, a 3D path tracking for the artery centerline between these two endpoints can be modeled into a minimal path problem. By defining a cost function, the centerline can be approximated by the path for which the integral of costs is the minimum. With the extracted artery centerline, a serial of images representing the intersections of 3D CTA volume and the cross-sectional planes which are along and perpendicular to the centerline trajectory can be obtained.

## C. *Segmentation of Artery Lumen*

Given the cross-sectional artery images, it is still challenging to extract the lumen and measure the stenosis in the normal plane of the artery, due to variation of image density, vessel change in radius, calcification, and bifurcation. That may partially explain why cross-sectional lumen area is still estimated by lumen diameter profile in a few recently developed methods [6][7]. In this study, based on the lumen gradient change at the vessel wall, an ellipse-based fitting procedure has been developed to approximate the lumen and the steps are introduced as follows:

For a cross-sectional artery image **I**, a smoothing filter $G$ is applied first to remove the noise and then the local peak point $C$ can be located as the center of the vessel. The possible calcification, which has an extremely high density, is removed based on a naive Bayesian classification using the training data from CTA image. The gradient $L$ on the smoothed image is expressed as

$$L = \left|\nabla(G * \mathbf{I})\right|^2 . \quad (1)$$

By measuring the gradient change of the image profile at discrete directions via $C$, the maximum of the gradient will be taken as the boundary of lumen, as shown in Fig. 2. It is equivalent to computing the first derivative of the image density via the image profile at discrete directions. The maximum of the first derivative along the rays from the center are located as the possible lumen edge.

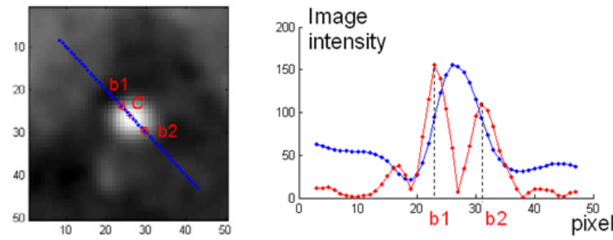


Figure 2. Left, a cross-sectional artery image; Right, the change of intensity (blue) and gradient (red) profile along the blue ray at angle of $3\pi/4$ via lumen center $C$. Points b1 and b2 with the maximum of the gradient will be taken as the lumen boundary points.

This procedure is applied to 16 profiles distributed uniformly from 0 to $2\pi$. More profiles can be used with more computational cost. Figure 3 shows an example of the detected boundary points for one cross section of an artery. Due to the intensity variation around the vessel, the boundary points are not always distributed around a circle. However we can approximate the vessel using a circular or an elliptic fitting. To eliminate the possible impact from vessel bifurcation, an inscribed ellipse or circle fitting is used to fit the vessel as the vessel lumen, as shown in Fig. 3. The vessel can be further refined with deformable models such as snake, balloon, level sets, etc [11]. With the ellipse/circle fitting as initialization, the segmentation is robust for the deformable models which are usually sensitive to the initialization.

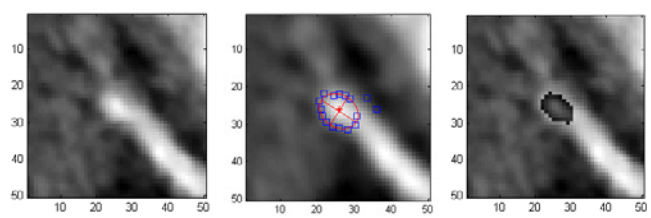

Figure 3: Left, a cross-sectional artery image; middle, the detected boundary points; and right, the corresponding ellipse fitting which indicates the approximate lumen area.

## D. *Identification and Quantification of Stenosis*

For one coronary artery branch, cross-sectional artery images along the extracted centerline with a small internal (1 mm) are generated and the lumen area in each image is extracted using the method described above. The vessel lumen areas with the advancing of centerline can be plotted and the curve is filtered by a median filter to smooth the noise, as shown in Fig. 4. A sharp drop of the lumen area suggests the presence of a stenosis lesion. As it is the nature tendency that a vessel becomes thinner gradually from proximal to distal, a linear fitting is employed to estimate the restored lumen area on a local stenosis lesion-free artery branch, by considering the nature regression of the lumen area along the vessel centerline from proximal to distal. For a particular stenosis lesion, AS is defined as

$$AS = A1/(A1 + A2) \times 100\%, \tag{2}$$

where $A1$ is the actual lumen area obtained by segmentation and ($A1$+$A2$) is the lumen area of the restored stenosis-free artery, as shown in Fig. 4.

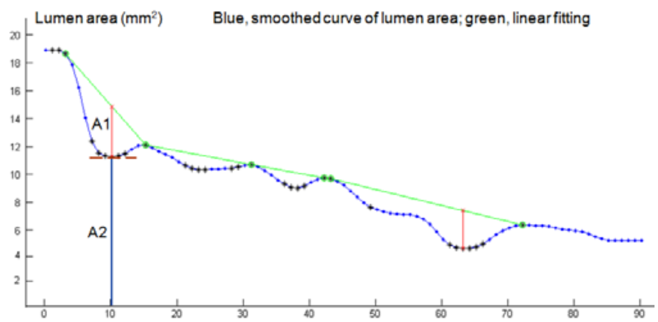


Figure 4: An example of lumen areas from cross-sectional artery images along the artery centerline from proximal to distal. Stenoses are quantified by percent AS. Blue curve is a smoothed curve recording the lumen area, green curve is a linear fitting one to approximate a stenosis-free artery segment.

## III. Experiment

Approved by the Institutional Review Board, five cardiac CTA scans, which were acquired using a multi-detector dynamic volume CT scanner with ECG gating from five CHD patients in the National Heart Centre Singapore, were used in this study. Diastolic reconstructions were applied into the data sets and the voxel resolution is 0.39 mm × 0.39 mm × 0.25 mm. CTA scans were interpreted by a radiographer and the categorized percent DS (CTA-DS) was given for each significant stenosis lesion observed. In addition for each CHD patient, the corresponding ICA data were also collected and the percent DS (ICA-DS) was measured by QCA for each significant stenosis lesion by a cardiologist. With the current C-arm angiography equipment, the imaging of coronary arterial vasculature can be acquired in the formation of a 3D volume, hence an artery branch can be observed and assessed by multiple projection orientations to obtain an overall percent DS. It is clinically concluded that ICA-based percent DS is more accurate than CTA-based percent DS in stenosis assessment [4][5], therefore in this study, ICA-based percent DS was used as the reference standard (RS).

CTA data acquired were processed according to the steps described in Section II, to compute the percent AS (CTA-AS) for each stenosis lesion. Algorithms were implemented by C++ with Insight Toolkit (ITK), Visualization Toolkit (VTK) and Vascular Modeling Toolkit (VMTK). Both CTA-DS and CTA-AS were benchmarked to ICA-AS for correlation analysis, respectively.

## IV. Results

Totally 13 stenosis lesions locate in 10 coronary artery branches from 5 CTA data sets were identified and assessed. Figure 5 shows a CTA data set and the 3D view of the segmented coronary artery tree. Four cross-sectional artery images from LAD of this data set demonstrating the change of lumen areas before, within and after a stenosis lesion are shown in Fig. 6, Row I. The lumen areas along this vessel from proximal to distal is plotted in Fig. 6, Row II. Two significant stenoses can be identified and the AS are 67% and 54%, respectively. The sites of stenoses correspond well to the 2D longitudinal projection of this LAD and its centerline by curved multi-planar reconstruction (Fig.6, Row III). A 3D reconstructed model of this LAD is shown in Fig. 7. Two stenosis lesions are highlighted from the model and corresponding CT images showing the lumen narrowing sites were displayed as well.

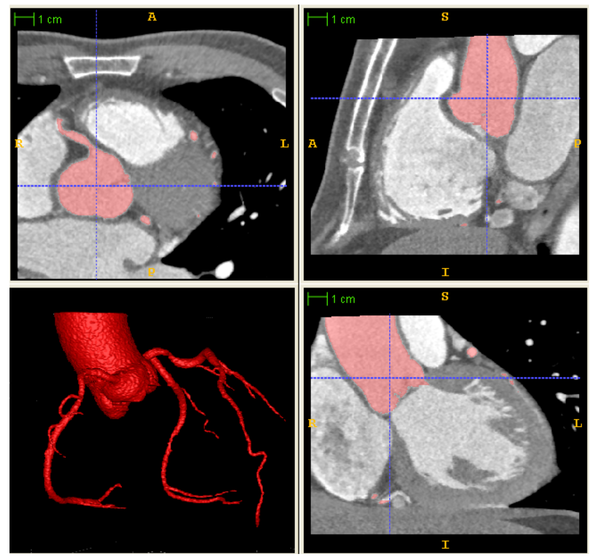


Figure 5: A CTA data set in axial, coronal and saggittal views and the 3D view of the segmented coronary arterial tree.

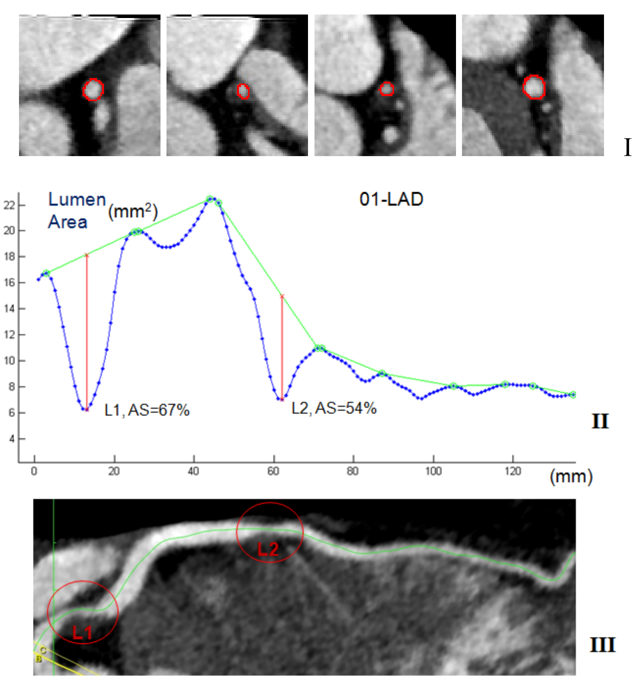


Figure 6: Row I, cross-sectional artery images from a LAD, the contours of lumens are labeled by red; Row II, lumen areas from cross-sectional artery images along the artery centerline from proximal to distal, 2 significant lesions were identified and quantified; Row III, a 2D longitudinal projection of this vessel and its centerline by curved multi-planar reconstruction showing the 2 stenosis lesions.

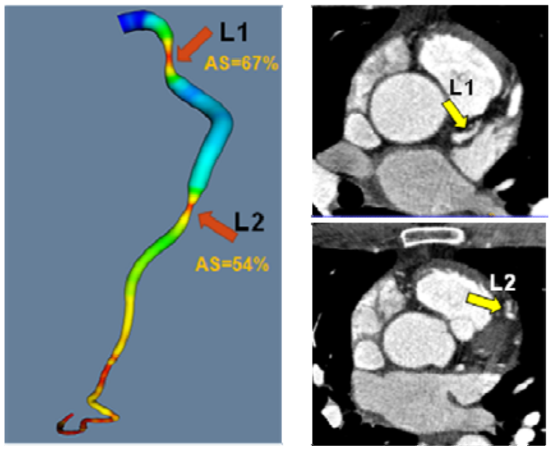


Figure 7. Left, a 3D reconstructed model of this LAD showing 2 lesions; right, the corresponding CTA slices showing the 2 lesions.

The detailed stenosis quantification by CTA-DS, CTA-AS and ICA-AS is shown in Table 1. To better benchmark the correlations between CTA-AS to ICA-DS and CTA-DS to ICA-DS, the distributions of CTA-DS to ICA-DS and CTA-AS to ICA-DS were plotted in Fig. 8, and the correlation analysis was performed. It is suggested that compared with CTA-DS, CTA-AS is a more reliable and quantitative measure for stenosis lesion which better correlates to ICA-DS, the RS (Pearson coefficient of 0.66 vs. Spearman's rank coefficient of 0.50).

TABLE I. STENOSES QUANTIFIED BY CTA-DS, CTA-AS AND ICA-DS

| CTA data | Lesion site | CTA-DS | CTA-AS | ICA-DS |
|---|---|---|---|---|
| #1 | Proximal LAD | >70% (S) | 67% | 70% |
| | Mid LAD | 40-70% (Mo) | 54% | 70% |
| | Proximal RCA | 25-40% (Mi) | 51% | 50% |
| #2 | Proximal LAD | 50-69% (Mo) | 64% | 60% |
| #3 | Proximal LAD | <25% (L) | 37% | 30% |
| | Mid LAD | 25-40% (Mi) | 39% | 60% |
| | Distal LAD | >70% (S) | 26% | 40% |
| | Proximal RCA | <25% (L) | 25% | 30% |
| #4 | Proximal LAD | 50% (Mo) | 66% | 70% |
| | Proximal LCX | 40% (Mo) | 53% | 50% |
| | Proximal RCA | <40% (Mi) | 55% | 30% |
| | Distal RCA | 50-70% (Mo) | 52% | 60% |
| #5 | Proximal LAD | 40-70% (Mo) | 49% | 40% |

L, light; Mi, mild; Mo, moderate; S, severe.

## V. CONCLUSION

A system to quantify the severity of coronary artery stenosis using CTA data and percent AS has been developed. The whole process includes coronary artery segmentation, centerline extraction and tracking, cross-sectional artery lumen extraction, and stenosis quantification. This system was tested in 13 stenosis lesions from 5 CTA data sets. Pilot experimental results suggest that compared with conventional CTA-DS, the derived CTA-AS has a higher correlation to RS. The efficacy of the proposed system in stenosis quantification was preliminarily demonstrated. In future this system can be further extended to quantify the Volume Stenosis, which might be better to reflect the real functional stenosis and the affected hemodynamics.

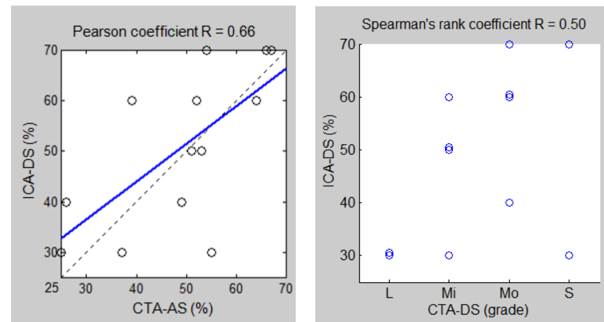


Figure 8. Left, correlation analysis on CTA-AS to ICA-DS, blue line stands for linear regression; right, correlation analysis on CTA-DS to ICA-DS.

## REFERENCES

[1] M.J. Boogers, J.D. Schuijf, P.H. Kitslaar, et al., "Automated quantification of stenosis severity on 64-Slice CT: a comparison with quantitative coronary angiography," *JACC Cardiovasc. Imag.*, vol. 3, no. 7, pp. 699-709, Jul. 2010.

[2] S. Zhang, D.C. Levin, E.J. Halpern, et al., "Accuracy of MDCT in assessing the degree of stenosis caused by calcified coronary artery plaques," *Am. J. Roentgenol.*, vol. 191, no. 6, pp. 1676-1683, Dec. 2008.

[3] G. Mowatt, J.A. Cook, G.S. Hillis, et al., "64-Slice computed tomography angiography in the diagnosis and assessment of coronary artery disease: systematic review and meta-analysis," *Heart*, vol. 96, no. 11, pp. 1386-1393, Nov. 2008.

[4] A. Arbab-Zadeh, and J. Hoe, "Quantification of coronary arterial stenoses by multidetector CT angiography in comparison with conventional angiography methods, caveats, and implications," *JACC Cardiovasc. Imag.*, vol. 4. no. 2, pp. 191-202, Feb. 2011.

[5] J.H. Doh, B.K. Chang, JH. Kim, et al. "Diagnostic value of coronary CT angiography in comparison with invasive coronary angiography and intravascular ultrasound in patients with intermediate coronary artery stenosis: results from the prospective multicentre FIGURE-OUT (Functional Imaging criteria for GUiding REview of invasive coronary angiOgraphy, intravascular Ultrasound, and coronary computed Tomographic angiography) study," *Eur. Heart J. Cardiovasc. Imag.*, vol. 15, vol. 8, pp. 870-877, Aug. 2014.

[6] B.M. Kelm, S. Mittal, Y. Zheng, et al., "Detection, grading and classification of coronary stenoses in computed tomography angiography," in *Proc. Med. Image Comput. Comput. Assist. Interv.*, 2011; pp. 25-32.

[7] R. Shahzad, H. Kirişli, C. Metz, et al., "Automatic segmentation, detection and quantification of coronary artery stenoses on CTA," I*nt. J. Cardiovasc. Imag.*, vol. 29, no. 8, pp. 1847-1859, Dec. 2013.

[8] A.F. Frangi, W.J. Niessen, K.L. Vincken, and M.A. Viergever, "Multiscale vessel enhancement filtering," In *Proc. Med. Image Comput. Comput. Assist. Interv.*, 1998; pp. 130–137.

[9] L. Antiga, "Patient-specific modeling of geometry and blood flow in large arteries," Ph.D. dissertation, Bioeng. Dept., Politecnico di Milano, Milan, Italy, 2003.

[10] H. Li, and Yezzi, "Vessels as 4-D curves: global minimal 4-D paths to extract 3-D tubular surfaces and centerlines," *IEEE Trans. Med. Imag.*, vol. 26, no. 9, pp. 1213-1223, Sept. 2007.

[11] M. Papadogiorgaki, V. Mezaris, Y.S. Chatzizisis, et al., "Image analysis techniques for automated IVUS contour detection," Ultrasound Med. Biol., vol. 34, no. 9, pp. 1482-1498, Sept. 2008.