Probabilistic Model Based Evaluation of Coronary Artery Stenosis on Computed Tomography Angiography

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Abstract. For evaluating the severity of luminal stenosis of coronary artery, we propose a fully automated probabilistic approach in detecting and quantifying coronary artery plaque which serves as evidence of luminal narrowing of assessed degree in three processing steps. First, a Gaussian distribution is utilized to adaptively allocate the center of cross-sectional plaque with the variance of posterior density as the plausible size. A concentric model fixed to the vessel centerline is applied to roughly segment the vessel lumen in the same fashion as plaque detection. Second, the quantitative evaluation of diameter stenosis is determined using the Kalman filtering formulation. Third, the stenosis degree is given using Bayes classifier based on the posterior probability of severity conditioned on stenosis percentage and plaque type of the training data. The method was evaluated on the 42 challenging dataset of Rotterdam Coronary Artery Algorithm Evaluation Framework. For the detection, a sensitivity of 0.54 and a PPV of 0.13 is obtained as compared to QCA, while a sensitivity of 0.29 and a PPV of 0.03 is achieved as compared to CTA. The stenosis degree is estimated with an absolute average difference of 38.5% as compared to QCA, and a weighted kappa value of -0.04 is obtained as compared to CTA.

1 Introduction

The diagnosis of coronary artery disease (CAD) utilizing computed tomography angiography (CTA) imaging relies on precise phenotype evaluation, which is related to detection and quantification of luminal narrowing and atherosclerotic plaque. While the invasive imaging technique, conventional coronary angiography (CCA) remains as a diagnostic criterion standard to surgical planning and treatment guidance, the non-invasive imaging technique of CTA although not adequately defined at present is anticipated to take place in the future role of understanding CAD progressive pattern via the cross-sectional and tomographic quantification techniques during the routine examination for early detection. However, the discrepancy in evaluations between quantitative coronary angiography (QCA) and CTA is attributed to direct visualization of the coronary vessel wall and thus the presence of coronary atherosclerosis [1].

To provide the comprehensive assessment of symptomatic stages of CAD corresponding to QCA, classification of coronary plaque as calcified and/or non-calcified burden is crucial. Histopathology studies suggest that heavy calcified plaque tend to be non-stenotic because of vessel remodeling, whereas large lipid core with thin fi-
brous cap are at risk to significant narrowing or even occlusion. Limitation of CTA in inferior spatial and temporal resolution may cause the severity of stenosis with calcified plaque being overestimated even though providing the near-perfect negative predictive value. On top of the variation due to partial volume effect, the respective attenuations differentiating the lipid-rich plaque from lumen currently prevents accurate classification into lipid and fibrous subcategories and even results in underestimated non-calcified stenosis percentage [2].

To address the limitation of morphological approach in the context of estimating the minimal diameter of coronary artery segment, we propose a framework which is both segment and lesion based on the prior density distribution of plaque and luminal attenuation. After interpolating the centerline extracted by state-of-art method on vascular segmentation developed by Young et. al. [3, 4], the proposed algorithm measures the attenuation distribution along the centerline. The probabilistic model based evaluation allows both the cross-sectional and longitudinal studies of plaque composition as well as the percent stenosis, since the Gaussian intensity distribution preserves the distribution ratio of vessel and plaque without user-defined attenuation or accurate segmentation. Afterward, the measured diameter is compared to the estimated reference diameter predicted along the arterial branch by Kalman filtering, and the final severity score is determined by Bayes classifier. This paper is organized as follows. After briefly introducing the probability density distribution and the proposed refinement procedures, the overview of the framework is presented and each individual component is described in section 2 with detailed flowcharts. In section 3, the performance of our method on the 24 testing datasets is evaluated and compared with the reference standard given by Rotterdam Coronary Artery Algorithm Evaluation Framework [5].

2 Method

The probability density analysis of coronary artery attenuation is derived from the mean shift of Gaussian distribution as the solution to the model estimation and maximization of density mean and covariance. A similar approach was introduced in the work of Okada et. al. for pulmonary nodules detection [6, 7]. Although their method also utilized the mean-shift as the iterative solution to the local maximum, they did not take into account the covariance during the mean-shift step, which may prevent the method from reaching the desired “outlier”, where the calcified plaque is. Moreover, estimation of the anisotropic covariance based on the mean shift vectors collected during the process of gradient ascent also requires further statistical verification with Gaussian intensity distribution. Here, we propose an EM-based iterative algorithm using principal component analysis (PCA) incorporated with stratified random sampling for solution to local likelihood maximization of both coronary artery and plaque. To the best of our knowledge, Philips CT Plaque Analysis [8] is the only commercial application utilizing the similar Gaussian intensity fitting approach in the assessment of plaque composition. However, instead of applying Gaussian mixture model to the
cross sectional histogram, our approach is based on two local maximums estimated for each point on the centerline; one for the calcified plaque and one for the arterial diameter. Detection and quantification are essentially based on the distribution of both calcified and non-calcified plaque (NCP) and the comparison between cross-sectional “expected” and “measured” diameters along the arterial centerline.

Maximum Likelihood Estimation (MLE) of Gaussian Distribution

\[ I(x,y,z): \text{input intensity image}; \sigma: \text{standard deviation of Gaussian distribution}; W: \text{size weighting} \]
\[ \mu_{\text{curr}}(x,y,z): \text{current mean position}; \mu_{\text{mat}}(x,y,z): \text{mean position of covariance matrix} \]

FWHM: full width at half maximum is used to approximate the size of distribution

\[ N_{\text{rand}}: \text{volume of sampling unit sphere}; \{S[0..N_{\text{rand}}-1]\}: \text{list of all elements within the unit sphere} \]

\[ M[3x3]: \text{converged covariance matrix}; \lambda[3]: \text{eigen values of 3x3 covariance matrix} \]

**procedure** MLE_EM(I[], \( \sigma \), \( \mu_{\text{curr}} \), W) {
  \[ G[] = \text{Gaussian3D}(I[], \sigma); \text{// Gaussian smoothed image}; \]
  while \( |\mu_{\text{curr}} - \mu_{\text{mat}}| > 0 \) {
    \[ \mu_{\text{mat}} = \mu_{\text{curr}}; \]
    \[ FWHM = (2/2ln2)\sigma; \]
    \[ \text{Stratification}(G[], \text{FWHM}); \]
    \[ \text{Sampling}(S[\cdot], N_{\text{rand}}); \]
    \[ \mu_{\text{curr}}, \sigma^2 = \text{Cov}[]; \text{//covariance matrix} \]
  }
  \[ \lambda[] = \text{PCA}(M[]); \text{// eigen decomposition} \]
}

**procedure** Stratification(G[], FWHM) {
  \[ N_{\text{rand}}, \text{total} = 0; \]
  for \( x,y,z = \mu_{\text{curr}}[] - \text{FWHM}/2 \text{ to } \mu_{\text{curr}}[] + \text{FWHM}/2; \text{ continue if } (x,y,z) \text{ is outside the sphere} \]
  \[ S[N_{\text{rand}}].xyz = (x,y,z); \text{// position} \]
  \[ S[N_{\text{rand}}].\text{index} = \text{total} + G[x,y,z]; \text{// incremental population size} \]
  \[ N_{\text{rand}} = N_{\text{rand}} + 1; \]
  \[ \text{total} = \text{total} + G[x,y,z]; \]
  \[ N_{\text{rand}} = 4/3(\text{FWHM}/2)^3\pi; \]
}

**procedure** Sampling(S[], N_{\text{rand}}) {
  for \( \text{itr} = 0 \text{ to } W(N_{\text{rand}}); \text{ } \}
  \[ \text{id} = \text{rand}\%\text{total}; \text{// draw an index from total population} \]
  for \( \text{itr} = 0 \text{ to } N_{\text{rand}}-1; \text{ } \}
  \[ \text{if } \text{id} = S[\text{itr}].\text{index} \]
  \[ \text{then } \text{Cov}[\text{itrR}] = S[\text{itr}].xyz; \text{//adding element to covariance matrix} \]
}

**Algorithm 1.** Stratified random sampling using Monte Carlo method to compute mean and covariance matrix of PCA.
2.1 Gaussian Intensity Fitting Model

Given an initial position on the manually corrected centerline [4] with standard deviation covering the region of interest, the estimation of the centroid on the grayscale image can be thought of as the process of computing the mean centering the population matrix. Before applying Monte Carlo method to randomly approximate an input domain of unit sphere with size of initial standard deviation, stratification is applied to partition all members of the population homogeneously. Assigning each voxel of unit sphere, the proportion of distribution to the sum of entire population according to intensity, a large random sampling selection is drawn independently. A stratified random sampling using Monte Carlo method is given in Algorithm 1. Figure 1 illustrates examples of resulting center and spread estimates on the cross-sectional area of coronary artery with different plaque compositions. Algorithm for plaque categorization is developed in the next subsection based on the result of Gaussian Intensity fitting model.

![Fig. 1. Examples of cross-sectional view of coronary artery: Blue circle is fixed to the center for approximating the size of artery and red circle is for searching the local maxima. As illustrate from left to right, (a) the mean shift of Gaussian distribution converges to where plausible calcified plaque is located disregarding the branches. Comparing the cross-sectional contributions of PID and VID, we can compute that (a) has smaller overlapping due to vessel wall calcification and hence less severe comparing with (b). For the NCP, (c) reveals the likeliness of two distributions giving the normal artery, whereas (d) has the mixed type of plaques causing severe stenosis.](image-url)

2.2 Plaque Detection and Categorization

In this subsection, we adapt the previously introduced Gaussian fitting model algorithm as the basis for detecting heterogeneous distribution and homogeneous distribution, which we will refer to as the “plaque intensity distribution” (PID) and the “vessel intensity distribution” (VID), on cross-sectional area perpendicular to the centerline. Although the detection of CP may seem trivial given higher attenuation than surroundings, due to the blooming and beam-hardening artifacts of CP in CTA [9] as well as the vessel remodeling, for the lesions with vessel wall calcifications, QCA only revealed comparably insignificant stenosis [10]. Hence, there is a tendency to overestimate the degree of luminal narrowing by CT when compared with QCA. The presence of visually evident atherosclerosis on CTA is considered as plaque burden with greater than 45% of cross-sectional area on at least three consecutive frames as suggested in the study of Becker’s work [2]. The detection and characterization is de-
scribed in Algorithm 2. The percent stenosis of lesion identified with CP is then evaluated differently from lesion with NCP. Calcified plaque is identified when exhibiting significant (> 45%) overlapped area between PID and VID where PID also exhibits higher attenuation profile than VID. Otherwise, for the composition of NCP, the cross sectional VID shows higher attenuation than PID’s. Plaque categorization serves two purposes in stenosis quantification, one of which is to act as prior knowledge for severity prediction. Another is to alleviate the stenosis severity caused by calcified plaques. Nevertheless, the lesions from both categories revealing percent stenosis greater than 20% are included in the quantification evaluation. For example, the calcified plaque detected in Figure 1(a) can be exempted from further investigation because of overlap area is not significant enough to cause stenosis.


2.3 Stenosis Percentage Approximation

In this section, we extend the cross sectional study of VID along the centerline toward the longitudinal study of arterial stenosis. Multiplanar reconstruction (MPR) as illustrated in Figure 2 stacks the axial slices to assess the stenosis degree by measuring the ratio of minimal to expected diameter of detected lesion in the presence of calcified
and or non-calcified plaques. One of the challenges in stenosis quantification is to derive the relatively expected diameter within the lesion comparing to those of its adjacent. We integrate Kalman filtering, a linear dynamic algorithm taking the sequentially observed diameter to estimate the current state variable in order to acquire the expected diameter along with their uncertainties within the lesion. Although several related approaches have been proposed in the field of vessel tracking, the result of expected diameter also shows promising result in terms of noise resistant. On top of comparison between the expected diameter and observed diameter for stenosis percentage, we also tackle the problem separately according to the plaque composition (Algorithm 3). As indicated in Figure 2 showing indifference in diameter, the arterial blockage caused by NCP may have same standard deviation of Gaussian intensity distribution as the normal segments have, except with significantly lower attenuation comparing to the average. As mentioned at the beginning, CTA may underestimate those stenosis percentages with NCP; our algorithm for computing non-calcified stenosis by taking intensity into account is in better agreement with QCA reference standard comparing with results of diameter ratio.

![Multiplanar reconstruction (MPR) and its corresponding diameter profile.](image.png)

**Algorithm 3.** Quantification process for stenosis percentage.
2.4 Severity Evaluation

Each stenosis detected can be assigned to the corresponding stenosis degree (mild, moderate, severe, and occluded) by applying QCA stenosis thresholds of greater than 20%, greater than 50%, greater than 70%, and greater than 95% respectively. However, without the prior knowledge of plaque type, the correlations between the CTA and QCA consensus grading of calcified stenosis might be inconsistent comparing with those with non-calcified or mixed plaque. As illustrated in Figure 3, the plaque composition taking place in vascular lesion has complex association with its stenosis degree. As the result, we derive a weighting scheme for severity prediction by employing the Bayes classifier to access the conditional dependent likelihoods of stenosis to take account of its plaque compositions. The generated probabilities is a table all combinations of stenosis percentage (0=0-20%, 1=20-50%, 2=50-70%, 3=70-95%, 4>95%) of QCA and plaque compositions of CTA and each of them has five values indicating the probability of being assigned to each stenosis degree (s0=health, s1=mild, s2=moderate, s3=severe, s4=occluded). The minimal narrowing per lesion is the maximum stenosis percentage of consecutive cross sections with stenosis greater than 20%. The plaque type for the entire lesion is determined by their compositions as whole. The corresponding stenosis degree has the maximum summation of probabilities among the cross sections.

Fig. 3. Statistical comparison of the severity assessment of CTA and stenosis percentage of QCA for each plaque type: s1 = mild, s2 = moderate, s3 = severe, s4 = occluded. NCP = non-calcified plaque, CP = calcified plaque. The ordinate axis is the number of lesions from the reference standard and the abscise axis is the combination of severity from QCA and plaque type from CTA.

3 Results and Discussion

In QCA, only one percent stenosis is given per 17-AHA segment, whereas without partitioning the segment, we assign estimated percent stenosis to each detected lesion. Hence, only the minimal narrowing among lesions of the same segment is compared with the QCA reference. However, the results of stenosis degree are compared per detected lesion according to CTA reference data. Figure 4 illustrates the capability of partitioning the lesions according to vessel intensity profiling, which is not only used to determine the NCP percent stenosis, but also used to separate the regional lesion from its plaque compositions.
Table 1. Results obtained for stenoses detection on the 24 testing datasets

<table>
<thead>
<tr>
<th>Method</th>
<th>QCA Sens. %</th>
<th>QCA P.P.V. %</th>
<th>CTA Sens. %</th>
<th>CTA P.P.V. %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proposed method</td>
<td>0.54</td>
<td>0.13</td>
<td>0.29</td>
<td>0.03</td>
</tr>
<tr>
<td>Observer1</td>
<td>0.88</td>
<td>0.4</td>
<td>0.79</td>
<td>0.58</td>
</tr>
<tr>
<td>Observer2</td>
<td>0.7</td>
<td>0.49</td>
<td>0.64</td>
<td>0.72</td>
</tr>
<tr>
<td>Observer3</td>
<td>0.68</td>
<td>0.45</td>
<td>0.68</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Table 2. Results obtained for stenoses quantification on the 24 testing datasets

<table>
<thead>
<tr>
<th>Method</th>
<th>QCA Avg. Abs. diff. %</th>
<th>QCA R.M.S. diff. %</th>
<th>CTA Weighted Kappa K</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proposed method</td>
<td>38.5</td>
<td>42.5</td>
<td>-0.04</td>
</tr>
<tr>
<td>Observer1</td>
<td>30.6</td>
<td>35.7</td>
<td>0.36</td>
</tr>
<tr>
<td>Observer2</td>
<td>32.6</td>
<td>37.5</td>
<td>0.34</td>
</tr>
<tr>
<td>Observer3</td>
<td>31</td>
<td>37.1</td>
<td>0.28</td>
</tr>
</tbody>
</table>

The performance is shown in Table 1 and 2. The performance in lesion detection also depends on the concentric accuracy and completeness of the centerline. Average execution speed of our method was around 6 minute per case on 1.67GHz Intel Core i7 64 bit system with 8 GB RAM.

Fig. 4. Statistical comparison of the severity assessment of normal artery (left) and abnormal artery (right). Top: blue, red, green lines are Kalman filtered size, estimated vessel size and estimated vessel intensity respectively. Bottom: red blue lines are plaque and vessel Gaussian intensity distribution.

4 Conclusion

This paper presented a method for detection and quantification of coronary CT angiography. The method is based on the combination of probabilistic models, including Gaussian density distribution, Kalman Filtering and Bayes classifier. The proposed method has proved to be sensitive and powerful in plaque characterization, stenosis detection and quantification which play the key role in determining the stenosis severity.
References


