3D Analysis of Thin-Cap Fibroatheromas by an Automatic Graph-Based Approach in Intravascular Optical Coherence Tomography

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Abstract

Background: Thin-cap fibroatheromas (TCFAs) are the most well-known reason for plaque rupture leading to the acute coronary syndrome. Although optical coherence tomography (OCT) has the potential for use in the identification of TCFAs, the conventional analysis of this modality alone in the 2D domain is not sufficient for detecting TCFAs.

Objectives: The present study proposes a fully-automated method for the 3D analysis of vulnerable plaques, especially TCFAs, in OCT sequence frames.

Methods: A new 2-step graph-based method was used to extract the 3D morphology of the fibrous cap in an intravascular OCT image sequence. A linear cost function was applied by adding novel hard constraints. Then, an undirected graph was performed with specified edge weighting. The min-cut problem was solved for segmentation. It was divided into 2 phases: The former extracted a media region from the lumen region, and the latter extracted the fibrous cap from the media. Finally, the TCFA was extracted by the quantification of the fibrous cap thickness.

Results: The method was validated using 3 sets of OCT raw image sequences. The proposed method was evaluated on an OCT dataset. It was composed of 3 groups of 264 consecutive intravascular OCT frames acquired from the left coronary artery. On the real data, the lumen diameter and 3D TCFA thickness achieved 88.28% and 85.5% accuracy, respectively, in comparison with manual segmentation.

Conclusions: An appropriate correlation was obtained between the TCFA detected by the proposed method and the one selected manually. The proposed method was able to speed up atherosclerosis assessment; therefore, it can be used to improve the management of the acute coronary syndrome.

Keywords: Optical Coherence Tomography, Graph, 3D Reconstruction, Thin-Cap Fibroatheroma

1. Background

The acute coronary syndrome (ACS) is the primary cause of death in high-income countries (1, 2). Early and accurate ACS detection can greatly reduce the mortality rate. Plaque rupture plays a major role in the ACS, and it occurs in plaques covered with a fibrous cap (3). Thin-cap fibroatheromas (TCFAs) constitute the most frequent fibrous caps leading to plaque rupture (2). TCFAs are defined as plaques containing a large lipid necrotic core covered by a thin fibrous cap (3). Ex vivo morphometric assessments show that the thickness threshold of fibrous caps is a stable parameter for determining plaques prone to rupture (vulnerable plaques) (2). The identification of vulnerable plaques can allow clinicians to prevent sudden death, and the improvement of imaging techniques through better characterization of TCFAs in vivo can achieve this goal.

Because of the thickness of a TCFA (< 64 µm), intravascular optical coherence tomography (IVOCT) at a resolution of 10 to 20 µm is currently the only in vivo imaging modality to measure the thickness of fibrous caps (4, 5). Clinical research has evaluated the similarity between the manual detection of TCFAs using cross-sectional IVOCT images and that using experimental observations (ex vivo and in vivo) (6). Katouzian et al. (7) concluded that IVOCT was more appropriate than other imaging modalities to depict and measure TCFAs. Manual methods encounter instability caused by visual uncertainty. For this reason, several semi-automated and fully-automated approaches have been proposed.

A semi-automated method was presented by Zahnd et al. (8) to quantify the coronary thickness of fibrous caps in IVOCT. This method extracts the contours of a fibrous cap using a robust dynamic programming framework based on a priori geometry; however, this approach must initialize some parameters. Roy et al. (9) proposed a lumen-segmentation method using OCT imaging physics-based graph representation of signals and random walks image segmentation approaches. Automatic lumen segmentation is the 1st step in plaque analysis. Ughi et al. (10) developed an automated algorithm for the automated represen-
tation of IVOCT vulnerable plaques for the supervised classification of image pixels based on textural features combined with the estimation of the optical attenuation coefficient.

Single-frame evaluations cannot describe the actual characteristics of a fibrous cap because it has a 3D structure naturally (11). Wang et al. (11) proposed a semi-automated algorithm to quantify volumetric fibrous caps using IVOCT. They proposed a novel computer-aided algorithm combined with human analysis for the quantification of fibrous caps; however, this method is limited by inter-observer variability.

2. Objectives

The present study proposes a fully-automated method for the 3D analysis of vulnerable plaques. A new self-determining graph-based method was used for the extraction of the 3D morphology of fibrous caps in IVOCT image sequencing. The TCFA was extracted by the quantification of the thickness of the fibrous cap. The 3D morphology of the fibrous cap was evaluated using a 3D structure created by manual segmentation.

3. Methods

An IVOCT image can be divided into the regions of the lumen, media, and plaque in the media close to the luminal border. The lumen is a complete signal-poor region. A signal-poor region with bright borders contains all types of plaques (11), especially lipid/necrotic plaques, which are depicted with brightly-diffused borders. The primary step for the 3D analysis of a TCFA is the segmentation of the fibrous cap into sequential frames. The differences between the main regions in IVOCT are the basis of the proposed segmentation algorithm. For this purpose, 2-phase segmentation based on an undirected graph is proposed. The flowchart of the proposed method is illustrated in Figure 1. Each step is detailed in the following section.

In the 1st step, an undirected graph is defined as a set of nodes and the set of undirected edges that connects these nodes. A non-negative weight is assigned to each edge (cost). The graph nodes denote pixels and the edge denotes the neighborhood relationship between the pixels. In this manner, sequential frames of IVOCT are put together. The set is then transformed into a 3D undirected graph. The 3 nodes corresponding to the lumen, media, and plaque of the IVOCT image are added to the graph and called “terminals”. The terminal locations and their relation with the other pixels are defined by means of a novel cost function.

A hybrid constraint-based cost function is proposed in this manner. The 1st phase of segmentation is to extract the luminal border by means of the cost function based on the graph-cut approach. For this purpose, the global minimum cut should be computed for the graph with 2 terminals. The max-flow algorithm is the most straight-forward method to produce the global minimum cut of the graph. The max-flow algorithm is computed from the lumen node (as the source) and media node (as the sink) terminals in the 1st phase. The 2nd phase of segmentation is to extract the fibrous cap from the media region. This phase is carried out on a segmented graph as the media. Although the max-flow algorithm is again carried out for this phase, the terminals are different (plaque as the source and media as the sink). Each step is detailed in the following section.

3.1. New Cost Function Definition

Assume that PI = [P1, P2, … P|PI|] specifies a pixel set of 1 frame; therefore, the 3D pixel vector is:

$$P_{vec} = \left( \bigcup_{k=1}^{N_f} P_{IK} \right)$$  \hspace{1cm} (1)$$

Where Nf is the number sequential frames. A pixel can be a lumen, media, or plaque. A lumen region and a media region are selected as the background and object, respectively, in the 1st phase of segmentation. A cost function should be defined to segment the Pvec vector to define the regions. For this purpose, a combined soft constraint and hard constraint approach is proposed. The soft constraint cost function is linear as follows:

$$Cf = E (P_{vec}) + \alpha A (P_{vec})$$  \hspace{1cm} (2)$$

Where E (Pvec) specifies the edge term of the pixels, A (Pvec) is the area term of the pixels, and \( \alpha \) is the relative importance factor of each edge or area term. Segmentation is summarized to minimize the defined cost function.

Several algorithms can be employed to access the minimum of cost function in Equation 2, but the aim here is the computation of the global minimum of the cost function in the equation so the novel automated hard constraint is satisfied. The hard constraints are defined as sets with pixels marked as the lumen region and pixels marked as the media. The segmentation result should cover the 2 sets of pixels. The hard constraints are obtained as described below.

In the 1st step, the IVOCT frames are converted from Cartesian coordinates to polar coordinates. The catheter should then be removed from the image; this is easily possible because of the actual diameter of the polar coordinate catheter. Next, the average of each radius is computed for all \( \theta \) (0 to 2\( \pi \) radian) in the polar IVOCT frames. Then, a 2D longitude image of the defined average is created as a function of frame number and radius. The bright pixels are positioned in the media region. The proposed name
New 2D longitudinal image creation (average of pixels in each radii and all angles)

Define two Hard Constraint: (LHC & MHC-1)

Convert IV OCT sequence to a graph With two nodes: Lumen & Media

Define two Hard Constraint: (MHC-2 & PHC)

Separate Media area of IV OCT Sequence

Segment the Graph By Max-Flow Algorithm

Convert Media area to a graph With two nodes: Plaque & Media

Segment the Graph By Max-Flow Algorithm

Separate Plaque area of Media area

Measure the Volumetric Plaque thickness

Tag plaques with thickness less than 65um as TCFA

The first segmentation phase

The second segmentation phase

TCFA extraction Part

Figure 1. Flowchart of the Proposed Approach, Consisting of a Preprocessing, 2 Main Segmentation Phases, and a Classification Part

for the radii with the lowest intensity selected as the hard constraint of the lumen region is LHC. The proposed name for radii with the highest intensity selected as hard constraints of the media region is MHC-1st.

After the 1st phase of segmentation, 2 hard constraints (plaque and media) are selected from the extracted 2D longitudinal media region. The radii with the lowest intensity selected for the hard constraint of the media region are called “MHC-2nd”. The radii with the highest intensity that are proposed for the hard constraint of plaque region are called “PHC”.

3.2. Cost Function Generalization Using a Graph

This section shows how to generalize a cost function for the soft constraint (Equation 1) with the defined hard constraints. The graph of sequential IV OCT frames is defined as:

$$ G_{3D-IV OCT} = (N, E) $$

Where $N$ is the graph node set and $E$ is the edge set. The graph nodes are associated with the pixels of all frames and the lumen, media, and plaque nodes as:

$$ N = P_{vec} \cup (L, M, P) $$

Where $P_{vec}$ is the 3D pixel vector, $L$ is the lumen terminal, $M$ is the media terminal, and $P$ is the plaque terminal. The edge set consists of undirected edges for the intra-edge and inter-edge. The former denotes the relation of the 3D neighbor pixels. The latter denotes the relation of each pixel with the terminals. The weight of the intra-edge should be distinctly different from the neighbor pixels and is defined as:

$$ W_{ij} = LIG (i, j) $$

Where LIG (i,j) is an energy term that specifies the variation in intensity between the pixels (i,j). For this purpose, local intensity gradient function is used. The inter-edge should specify the similarity between each pixel and each terminal. The area properties of the pixels are computed using the log-likelihood of the intensity distribution LogL (obtained from the intensity histogram). It identifies the regional penalties as negative log-likelihoods. Finally, the edge weights of all the nodes are obtained using Equation 6 as:
Where $S$ and $T$ are the source and sink of the graph and $O$ and $B$ are sets of hard constraints. Source and sink correspond to the lumen region and media region in the 1st segmentation phase, respectively. The $O$ and $B$ sets are $LHC$ and $M_{HC-1st}$, respectively. The source and sink correspond to the media region and plaque region in the 2nd phase of segmentation, respectively, and the $O$ and $B$ sets are $M_{HC-2nd}$ and $P_{HC}$.

The graph is now fully defined. A segmented boundary is obtained by finding the maximum flow of the graph between the defined source and the sink nodes. The rapid max-flow algorithm proposed by Boykov et al. (12) is used to achieve this goal. In the next step, 3D analysis of the fibrous cap is carried out using the thickness of the cap. In this study, the thicknesses of the fibrous caps were greater than 65 $\mu$m, between 65 $\mu$m and 150 $\mu$m, and greater than 150 $\mu$m (4, 10). The 3D rendering of the segmentation phases are shown in Figure 2A to 2B. A plaque in contact with the lumen and belonging in the category with a maximum range of 65 $\mu$m is selected as a TCFA plaque.

4. Results

4.1. Dataset

The proposed method was evaluated on an OCT dataset. The dataset was composed of 3 groups of 264 consecutive IVOCT frames acquired from the left coronary artery. The scan characteristics of the system were 15-$\mu$m axial resolutions, 100 frames per second, and a 200-$\mu$m frame interval. All the frames were provided in TIFF/DICOM format.

4.2. The Used Hardware/Software

The proposed algorithm was implemented in MATLAB on a desktop computer with Intel (R) Xeon(R) CPU E5-2620, 2.10 GHz, and 8GB memory.

4.3. Preprocessing

As was mentioned in the Methods, the polar IVOCT conversion and catheter removing are the 1st preprocessing steps. They are shown for an IVOCT sequence in Figure 3A to 3C. Next, the 2D longitude image of the defined average is created (Figure 3D). LHC and $M_{HC-1st}$ are depicted in Figure 2A. Furthermore, 2 other hard constraints, $M_{HC-2nd}$ and $P_{HC}$, are shown in Figure 2C.

4.4. Manual 3D Structure Segmentation

The 3D lumen extraction and TCFA extraction with the aim of understanding 3D coronary analysis were determined by 2 analysts, who worked independently. For this purpose, each analyst extracted the lumen border for all the IVOCT frames in the 1st phase. In the 2nd phase, the analysts extracted the fibrous cap at the media region. The 3D reconstructions of the lumen border and the fibrous cap were carried out using 3D renderings. The thickness of the fibrous cap was then classified into 1 of the 3 categories. The manual 3D result is depicted in Figure 4C. Samples of the lumen boundary extraction using the proposed algorithm, fibrous cap extraction using the algorithm, manual lumen extraction, and manual fibrous cap extraction are shown in Figure 5.

A 2-step validation was proposed to evaluate the proposed algorithm using the 2-phase segmentation method. In the 1st phase, the segmented lumen for each frame was compared with the experts’ manual segmentations of the corresponding frame. Two statistical parameters were used to evaluate the similarity: the mean absolute error (MAE) and the Jaccard index measurement (JM). The MAE is given by:

$$\text{MAE}_j = \frac{1}{n} \times \sum_{i=1}^{n} \left| R_{ij}^{\text{Auto}} - R_{ij}^{\text{Manual}} \right|$$

Where $R_{ij}^{\text{Auto}}$ and $R_{ij}^{\text{Manual}}$ are the $j$-th radius of the obtained lumen by the proposed method and the manual segmentation in the $i$-th angle, respectively. In this manner, lumen borders were selected in 1-degree intervals. Therefore, ‘$n$’ value was 360.

The JM is used to compare the similarity and diversity of the sample sets (13). The JM is defined as:

$$\text{JM} = \frac{1}{n} \times \sum_{i=1}^{n} \frac{|C_{3DIVOCT} \cap C_{3DManual}|}{|C_{3DIVOCT} \cup C_{3DManual}|}$$

Where $C_{3DIVOCT}$ is the 3D lumen region set from IVOCT and $C_{3DManual}$ is the manual lumen region 3D segmented set.
These 2 statistical parameters were calculated for all the frames existing in a sequence. The mean and standard deviation of each parameter were considered as evaluator values. The JM and the MAE of the 1st segmentation phase are depicted in Table 1. It provides the 3D lumen segmentation of the IVOCT sequential frames proportional to the manual ones with 88.28% accuracy for the diameter and 91% similarity for the 3D structure (lumen mean size obtained = 1.53 mm).

The results of the 2nd segmentation phase were evaluated by the quantification of the fibrous cap volume and the fibrous cap thickness in the TCFA. In this way, the MAE was used to evaluate the results. The evaluation of the 2nd segmentation phase is presented in Table 2. The TCFA thick-
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Figure 4. A, 3D rendering of lumen border of intravascular optical coherence tomography (IVOCT) from the 1st segmentation phase; B, 3D rendering of the lumen border with the fibrous cap region from the 2nd segmentation phase (green object is the extracted fibrous cap); and C, 3D rendering of the manual analysis.

Figure 5. A, Intravascular optical coherence tomography (IVOCT) frame; B, manual lumen border (green curve) and fibrous cap (red area); and C, lumen border (green curve) and the fibrous cap (red area) from the proposed algorithm.

ness of the IVOCT showed 85.5% accuracy in the worst case (TCFA mean size obtained = 10.24 µm).

5. Discussion

5.1. Lumen Boundary Detection

Lumen border extraction is the basic step of coronary artery disease assessment. Unfortunately, manual border extraction endures several critical limitations such as intraobserver and interobserver variability. Computer-aided methods can overcome these limitations. In the latest studies, several automated approaches were proposed to extract the lumen border (9, 14). Ju et al. (14) proposed an automated approach with 90% accuracy in comparison with manual lumen segmentation. However, these methods are independent of assessment methods. In other words, these border detection methods do not have any correlation with other assessment algorithms. Therefore, double implementations are needed in computer-aided designs: 1) a border detection algorithm and 2) an assessment algorithm. In contrast, a 2-phase method was proposed to quantify a TCFA as high-risk atherosclerosis in the current study. Both phases have the same algorithm. They only differ in primary hard constraints. As a result, a single-algorithm implementation is needed. Moreover, the obtained accuracy (88.28 ± 4%) is comparable with recent investigations (Ju et al.’s (14) approach with 90% accuracy).

5.2. Volumetric Fibrous Cap Thickness Measurement

TCFA quantification was applied using fibrous cap thickness by a pathologist for IVOCT images in clinical use (4). It can vary because of visual uncertainty. Moreover, a fibrous cap has a volumetric structure. Therefore, neither manual nor semi-automated fibrous cap quantification is sufficient in the 2D domain. Furthermore, 2D domain fibrous cap thickness measurement has more variance in comparison with volumetric quantification. Interobserver variability is another limitation of manual thick-
ness measurement. As a result, computer-aided methods are very important in the volumetric analysis of IVOC T frames. In the recent decades, some researchers have proposed semi-automated approaches to quantify volumetric fibrous caps in IVOC T frames (8, 11). These methods overcome the uncertainty associated with manual analysis by more accurately determining the true thickness of fibrous caps. Nonetheless, semi-automated methods have intrinsic limitations and suffer uncertainty of initialization. In contrast, the proposed full-automated approach is successful in this context and can be used for vulnerable plaque detection because it shows appropriate similarity with the 3D manual result (85.5%). In addition, TCFA s with a higher volume can be more dangerous than TCFA s with a medium volume. Consequently, the volume measured by the TCFA can be used to set a risk value for vulnerable plaques. The proposed method has a volume accuracy of 82% and is applicable for setting the plaque risk factor.

Nevertheless, the proposed method has a high computation load because of its graph structure. Moreover, it works more effectively in a coronary that consists of a fibrous cap. Therefore, it is not efficient for the media with other kinds of plaques. For example, the negative error of the result may be increased in the presence of calcific plaques.

Super-pixel approaches can be a solution by decreasing the computation load in future works. Moreover, a combination of intravascular ultrasound images and IVOC T should overcome the limitation of fibrous cap quantification in the presence of other plaques.

5.3. Conclusions

We herein presented a full-automated computer-aided method that can extract the lumen border and quantify the volume of fibrous caps. The method has comparable accuracy to the manual method. It may be used to characterize fibrous caps more efficiently. Moreover, it can be drawn up- along with other clinical approaches- to understand the treatment of plaque rupture precisely.

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