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# Intravascular imaging of coronary artery: bridging the gap between clinical needs and technical advances

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## Abstract

Coronary artery disease is the leading cause of mortality worldwide. Almost seven million deaths are reported each year due to coronary disease. Coronary artery events in the adult are primarily due to atherosclerosis with seventy-five percent of the related mortality caused by plaque rupture. Despite significant progress made to improve intravascular imaging of coronary arteries, there is still a large gap between clinical needs and technical developments. The goal of this review is to identify the gap elements between clinical knowledge and recent advances in the domain of medical image analysis. Efficient image analysis computational models should be designed with respect to the exact clinical needs, and detailed features of the tissues under review. In this review, we discuss the detailed clinical features of the intracoronary plaques for mathematical and biomedical researchers. We emphasize the importance of integrating this clinical knowledge validated by clinicians to investigate the potentially effective models for proper features efficiency in the scope of leveraging the state-of-the-art of coronary image analyses.

**Keywords:** Coronary artery disease, Atherosclerotic plaque, Optical Coherence Tomography, Medical image analysis, Deep learning

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## 1. Introduction

Atherosclerosis is recognized as the main cause of cardiovascular disease and the leading cause of death worldwide. Plaque development, progression, and rupture caused by atherosclerosis result in myocardial infarction and stroke, which are respectively the first and the fifth causes of death [1, 2]. Advances in interventional cardiology, the catheter-based treatment procedure of heart disease, could improve the treatment strategy and contribute to assist millions of patients, thus avoiding coronary bypass surgery [3, 4]. But before any treatment, cardiologists need to understand the type, location, and the level of progression of the atherosclerotic plaques to personalize their treatment strategy. Understanding the plaque morphology and its sub-components is fundamental to assist clinicians by providing them with the accurate information of plaque progression. This is where advanced cardiovascular imaging systems play the role of providing automatic plaque morphology assessment. Investigating the performance, effectiveness, advantages, and limitations of the cardiovascular imaging systems in plaque morphology accuracy as well as the clinical needs are the first important steps to define the effective scientific research projects. As we take these first steps firmly and correctly, new image analysis computational models and artificial intelligence algorithms come into play to fulfill the needs efficiently.

The main goal of this review article is to strictly underline a very critical fact that technical and clinical needs in development of medical imaging systems are tightly linked to each other. The focus of the survey is not only to assess the existing computational models proposed for analyzing the OCT images, but also to highlight a significant factor to be considered in the field of research and development, which is understanding the clinical aspects of the problem prior to developing any computational model. This is important since most of the time, the proposed models are not useful in clinical applications although they

are all grounded on very strong mathematical concepts. The reason is that the  
30 clinical needs have not been targeted correctly or the clinical features of the  
tissues under review have not been investigated and understood for designing  
an applicable analytical model. This is a repeating cycle which is taking our  
research far from being advanced in terms of clinical use. In this review, we aim  
to provide a reference for clinical aspects of the atherosclerotic coronary artery,  
35 and the features of such atherosclerotic tissues in OCT images.

We review the trending clinical needs, display the difference between various  
coronary artery sequelae and plaques, and we review the emerging technical  
solutions for identifying, characterizing, and predicting the rupture of the vul-  
nerable plaque. We address the issues from the following angles:

- 40 • Explore the existing intravascular imaging systems and their limitations  
(section 2).
- Describe the normal structure of coronary artery and visualization of var-  
ious arterial wall tissues in OCT images (section 3).
- Review the process of atherosclerotic plaque development and clinical fea-  
45 tures of plaques and other atherosclerotic tissues in OCT images (section  
3).
- Discuss the technical innovations, which should be considered to improve  
the imaging systems.
- Review the existing technical studies to investigate the needs and further  
50 technical improvements (section 4).
- The limitations of recent studies, the clinical needs, and possible future  
development of the state-of-the-art intravascular imaging is discussed in  
section 5.
- Section 6 is a summary with conclusion remarks on findings from the body  
55 of the paper.

Sections 2,3, and 5 present specifically the interventional cardiologists' views. For related technical studies, we considered sixteen related works, which were performed in 2019-2021 to improve the plaque indication in intravascular Optical Coherence Tomography imaging. The studies are assessed based on targeted  
60 clinical needs, and the designed computational models based on machine learning and deep learning approaches in various stages of the disease.

## 2. Review of the intravascular imaging systems

Intravascular imaging evolved in response to the limitations of the cardiac imaging systems to indicate intracoronary plaque morphology and their sub-components. For x-ray based imaging systems, the penetration depth is  
65 inversely proportional to tissue density. Intravascular structures cannot be determined by radiography unless they become calcified to attenuate more radiation and are visualized radiopaque. This is the main limitation of invasive coronary angiography (CA), and non-invasive coronary computed tomographic angiography (CCTA), which are both in the category of cardiovascular anatomic imaging systems. Consequently, both systems are limited to indicate intracoronary  
70 plaque sub-components [5, 6, 7, 8]. Compared against x-ray-based imaging systems, Magnetic Resonance Angiography (MRA) should have better soft-tissue characterization as well as lacking harmful radiation. Despite the strength, in coronary circulation, MRA is not recommended to be used. High quality coronary image acquisition using MRA is challenging considering its motion artifacts caused by extended acquisition time, low spatial resolution, and low volumetric coverage [9, 5, 6, 8].

Detailed indication of plaque morphology is possible by imaging the arterial  
80 wall in cross-sectional view. Intravascular Ultrasound (IVUS) is a catheter-based imaging system. The IVUS catheter generates sound wave in the range of 20 to 60 MHz and provides gray-scale cross-sectional images of arterial wall tissues. IVUS is limited to indicate plaque components. Using virtual histology (VH-IVUS), spectral analysis of back-scattered IVUS radio-frequency data,



85 characterization of four plaque types is possible. Although VH-IVUS can in-  
 dicate fibrous, fibrofatty, necrotic core, and dense calcium, but detection of  
 the thin cap fibroatheroma, which is the most important predictor of plaque  
 rupture is not possible using VH-IVUS. The limitation is due to noise enhance-  
 ment, system artifacts, and low spatial resolution of the system (100-150  $\mu\text{m}$ )  
 90 [\[5\]](#), [\[10\]](#). Optical Coherence Tomography (OCT) is an interferometric imaging  
 modality with high resolution that maps the back-scattered near-infrared light  
 to create cross-sectional images of the tissues under review. OCT is a turning  
 point in medical imaging techniques. Intravascular OCT has become an increas-  
 ingly powerful tool in interventional cardiology with the highest resolution of  
 95 10-15  $\mu\text{m}$  to provide detailed intracoronary tissue information, including various  
 elements of vascular wall infiltration, and indication of atherosclerotic plaque  
 morphology. Despite its high resolution, there is no harmful radiation involved,  
 and image acquisition is very fast with minimum risk for patients (excluding  
 the risk inherent to the invasive nature of the image acquisition). Compared  
 100 against other intracoronary imaging systems, this state-of-the-art imaging sys-  
 tem has incredible advantages. But OCT has some important limitations to be  
 addressed [\[11\]](#), [\[5\]](#), [\[12\]](#). Various generations of the OCT system were developed  
 to ease the interpretation of the OCT images such as multi-modality IVOCT  
 imaging and dual-modality catheter endoscope. Although the new generations  
 105 of the OCT system could improve the quality of the acquired images, but inter-  
 pretation of various pathological tissue types remains challenging [\[13\]](#), [\[14\]](#). As  
 the main limitation, interpretation of the acquired images is operator depen-  
 dent, which is not only very time-consuming but also highly error prone from  
 one observer to another. The gap is identified as being the lack of a precise and  
 110 accurate automated technology for analyzing OCT images of coronary artery,  
 which would enable widespread use of this technology for diagnosis and inter-  
 vention purposes. Being innovative to design a technique, which can accurately  
 address this issue of the OCT imaging system, we have to understand the exact  
 mechanism and clinical features of the atherosclerotic plaques. Full understand-  
 115 ing of the plaque formation mechanism depends on comprehensive knowledge

of the structure and functionality of normal arterial wall.

### 3. Intracoronary plaque development & rupture

#### 3.1. Normal coronary artery

Normal arterial wall has three-layered structure. Intima is the first and closest layer to the arterial lumen, which is covered by single layer of endothelial cells. Normal intima is nourished by oxygen diffusion of the lumen. Endothelial cells have significant responsibilities in arterial wall functionality. They are responsible to provide anti-thrombotic molecules to prevent blood clot. In addition, they secrete substances (vasodilators and vasoconstrictors) to adjust contraction of the smooth muscle cells (SMCs) in the media layer. To deal with the local inflammations and adjust the immune responses, endothelial cells resist leukocyte adhesion, which are white blood cells of immune system. It is very important to know that being exposed to different stressors, endothelial cells can produce pro-thrombotic molecules[1]. Intima is visualized as homogeneous signal-rich layer in OCT images. It is difficult to specify the exact thickness of the intima layer by pathology since intima thickness depends on various factors such as age, gender, and bio-mechanical characteristics. But, in OCT, the thinnest intima is defined as intima layer with the thickness of  $4\text{-}5\mu\text{m}$ , which becomes thicker by age. Intima layer with the thickness of  $300\text{-}600\mu\text{m}$  is considered as non-atherosclerotic intimal thickening [15]. Media is the second and thickest layer of normal arterial wall, which is mainly responsible of elastic functions of the artery. It is nurtured by vasa vasorum in the outermost layer of arterial wall, adventitia. Two boundaries of elastin called internal and external elastic lamina separate media from intima, and adventitia respectively. Media composed of SMCs and extracellular matrix (ECM), which they tightly work together. SMCs not only provide vasoactive and inflammatory mediators, but also they synthesize the collagen, elastin, and proteoglycans, which form the bulk of ECM. ECM is responsible for retaining the structural integrity of the arterial wall, which composed of collagen, and elastin. Collagen provides the

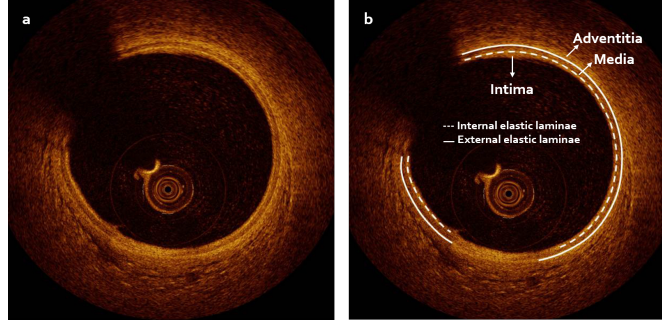


Figure 1: OCT image of normal arterial wall: Intima is visualized as a signal-rich layer, Media is shown as a signal-poor layer by OCT, adventitia is characterized as a signal-rich layer. Internal and external elastic laminae are shown as signal-rich bands with dashed and filled lines respectively [15].

145 bio-mechanical strength of the artery to avoid failure at high pressure, while elastin provides flexibility and control the reversible extensibility of the arterial wall during cardiac cycles[1, 16]. Media layer is characterized as a signal-poor layer in OCT images with the thickness of  $125\text{-}350\mu\text{m}$ . Internal and external elastic lamina are signal-rich bands in OCT images with the thicknesses  $< 3\mu\text{m}$ ,  
 150 and  $3\text{-}6\mu\text{m}$  respectively (figure 1) [15].

### 3.2. Atherosclerosis and plaque development

Atherosclerosis initiates by accumulation of low-density lipoprotein (LDL) in the arterial wall, which results in an active inflammatory process. Various factors contribute to the inflammatory process of atherosclerosis, which can be  
 155 categorized accordingly: Endothelial dysfunction, accumulation of lipids in the intima layer, deployment of leukocytes and SMC to the vessel wall, foam cell formation, and deposition of ECM [1]. Based on the classification of atherosclerotic lesions by the American Heart Association (AHA) [17], development of atherosclerosis includes various stages: 1. Non-atherosclerotic intimal thickening as a result of SMCs accumulation in the intima while lipid or macrophage  
 160 foam cells are not developed in this stage. 2. Fatty streak or intimal xanthoma which appears as a result of accumulation of foam cells in the luminal side of the

arterial wall while no necrotic core and fibrous cap are seen in this stage of the disease. 3. Pathological intimal thickening is defined as accumulation of SMCs  
165 in a proteoglycan-rich matrix with areas of extracellular lipid accumulation while there is no sign of necrotic core. This stage of the disease can be followed by the luminal thrombus 4. Fibroatheroma (fibrous cap atheroma) is developed as a result of the necrotic core formation with an overlying fibrous cap. This stage can be followed by luminal thrombus. 5. Thin cap fibroatheroma (Thin fibrous  
170 cap atheroma) which is characterized by infiltration of macrophages and lymphocytes with SMCs and an underlying necrotic core. This stage can be followed by plaque rupture. 6. Fibrocalcific plaque which is a collagen-rich plaque with large calcification and few inflammatory cells. This results in a severe stenosis with or without necrotic core development. The process of plaque development  
175 is explained in the following sections.

### 3.2.1. *Intimal thickening*

#### *Non-atherosclerotic intimal thickening*

Accumulation of SMCs and proteoglycan-rich ECM results in intimal thickening. In the absence of the inflammatory infiltration, lipid accumulation, and  
180 macrophage foam cells, the intimal thickening is considered as non-atherosclerosis. Although this type of intimal thickening occurs in atherosclerosis-prone arteries including coronary artery, but they do not result in atherosclerosis necessarily. In OCT, non-atherosclerotic intimal thickening is visualized as signal rich region with the thickness of 300-600  $\mu\text{m}$  [1, 15]. Figure 2 shows partial intimal  
185 thickening with partial media disappearance in OCT images.

#### *Pathological intimal thickening*

Pathological intimal thickening (PIT) is the earliest stage of the atherosclerotic lesion formation. In histological point of view, PIT is characterized by intimal thickening  $> 600\mu\text{m}$  with small area of lipid pool ( $< 1$  quadrant of  
190 the OCT cross-sectional image), which may follow by macrophage accumulation in luminal side of the lipid pool (figure 3). Micro-calcification emanated by

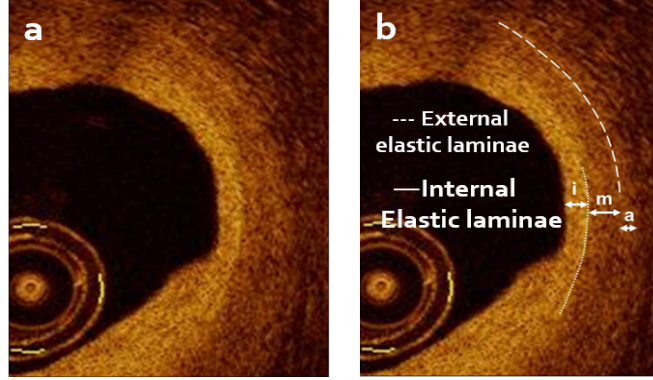


Figure 2: Part of OCT coronary cross-section with partial intimal thickening and media disappearance [15].

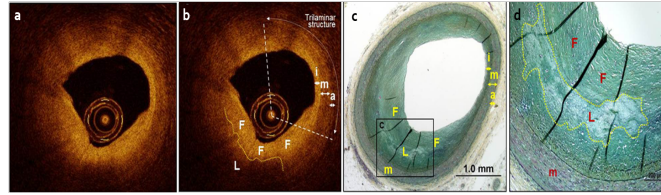


Figure 3: Pathological intimal thickening/fibrous plaque. (a) shows the original OCT image. (b) is annotated OCT image: F: Fibrous tissue, L: Lipid pool, i: Intima, m: Media, and a: Adventitia. Corresponding histological sections are shown in (c) and (d) [15].

SMCs, and free cholesterol crystals can be found in lipid pools as well (figure 4) [18, 19, 1, 15].

### 3.2.2. Fibrocalcific plaque

195 Intimal calcification is the most common type of calcification. The process of calcification formation and progression is not completely known. Apoptosis of SMCs and macrophage may contribute in development of fibrocalcific plaques. Lowest grade of calcification is seen in pathological intimal thickening close to internal elastic lamina and healed plaque rupture followed by fibroatheroma  
200 show the highest grade of calcification. It is important to mention that stable plaques are more calcified than vulnerable plaques. Calcification is visualized in OCT images as sharply delineated signal-poor regions (figure 6) [20, 19, 1, 15].

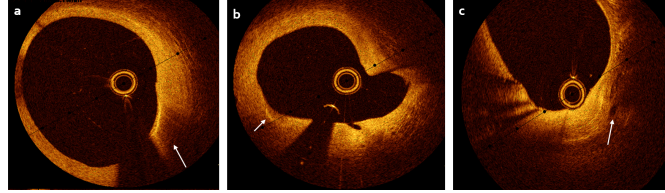


Figure 4: Examples of intimal thickening with macrophage infiltration, cholesterol crystal, and micro-calcification, which are shown with arrows in (a), (b), and (c) respectively.

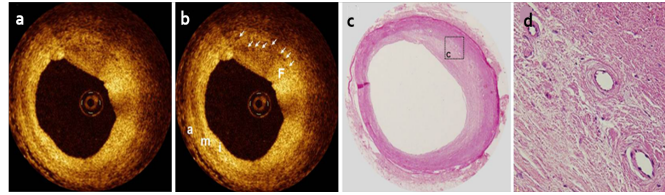


Figure 5: OCT images with micro-vessels: (a) Original image, (b) annotated image. Corresponding histological sections are shown in (c) and (d) [15].

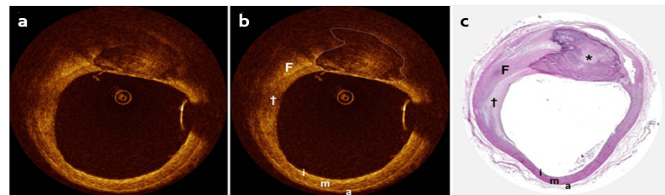


Figure 6: Calcification in OCT imaging: (a) Original OCT image, (b) Annotated image: F: Fibrous tissue, t: Fibrous tissue with low signal intensity, i: Intima, m: Media, a: Adventitia, (c) Corresponding histological image [15].

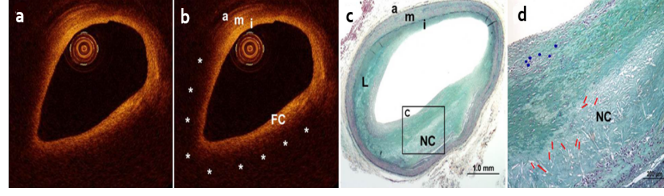


Figure 7: Example of early-stage fibroatheroma with lipid pool/necrotic core. (a) Original OCT image. (b) Annotated OCT image: FC: Fibrous cap, i: Intima, m: Media, a: Adventitia, L: Lipid pool, start shows lipid pool/necrotic core. Corresponding histological images are shown in (c) and (d) [15].

### 3.2.3. Fibroatheroma

In progressive atherosclerosis, secreting proteolytic enzymes particularly matrix metalloproteinases (MMPs) at luminal border of the plaques degrade the collagen and allow infiltration of SMCs. This results in thinning the fibrous cap and remodelling of the arterial wall. Macrophages act as mediators in response to the remodelling of the vessel, which leads to excessive infiltration of macrophages. Death macrophages create necrotic core, which is surrounded by fibrous cap. This is the most important characteristic of fibroatheroma as a sign of progressive stage of the atherosclerosis process. Fibroatheroma progression associates with different stages of the necrotic core formation, which results in either early-stage or late-stage fibroatheroma. Early-stage fibroatheroma is distinguished by presence of the proteoglycans in the lipid pool and macrophage accumulation (figure 7). Late-stage fibroatheroma is characterized by the excessive amount of cellular debris, free cholesterol, calcification, intra-plaque haemorrhage, and fully evacuated ECM (figure 8). Fibroatheroma is distinguished in OCT images with signal-poor regions of lipid pool and necrotic core. Since necrotic core is not distinguishable by OCT, lipid pool/necrotic core is considered as a single signal-poor region in the OCT images and commonly this region takes  $> 1$  quadrant of the arterial cross-section. Fibrous cap thickness is an indicator of plaque vulnerability and is categorized as follows: 1. Fibrous cap thickness  $< 55 \mu m$  is related to ruptured plaques. 2. Fibrous cap thickness



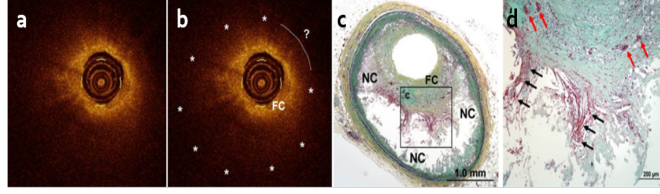


Figure 8: Example of late-stage fibroatheroma with necrotic lipid pool/necrotic core, micro-vessels, and intra-plaque haemorrhage. (a) Original OCT image. (b) Annotated OCT image: FC: Fibrous cap, and star shows lipid pool/necrotic core region. Corresponding histological images are shown in (c), and (d): NC: Necrotic core, red arrows show micro-vessels, and black arrows represent intra-plaque haemorrhage [15].

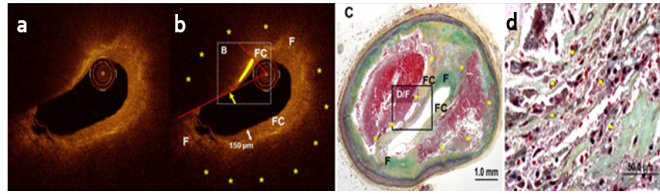


Figure 9: Example of thin-cap fibroatheroma with fibrous cap thickness of  $65 \mu m$ . (a) Original OCT image. (b) Annotated OCT image: FC: Fibrous cap, F: Fibrous tissue, stars show lipid pool/necrotic core region, direction of light beam is shown in red, and signal rich band is shown in yellow. Corresponding histological images are shown in (c), and (d): Yellow dots show macrophages [15].

>  $84 \mu m$  is defined as stable fibroatheroma. 3. Fibrous cap thickness in the  
 225 range of  $55-84 \mu m$  is characterized as thin cap fibroatheroma (TCFA). TCFA  
 usually have necrotic core arcs  $> 120^\circ$  (figure 9) [1, 15, 21, 22, 23].

#### 3.2.4. Determinants of plaque rupture

Atherosclerosis is a complex inflammatory disease of coronary artery. Macrophage  
 accumulation is the most important and the main factor and effector of the  
 230 inflammatory process, which associates with almost all stages of the atheroscle-  
 rotic plaque development and progression. In early stages of the disease, macrophages  
 infiltrate in intima to respond the cholesterol uptake, and LDL phagocytosis,  
 which results in foam cell formation. Macrophages are characterized by OCT  
 as signal-rich bright bands or spots with a dorsal shadow in the direction of



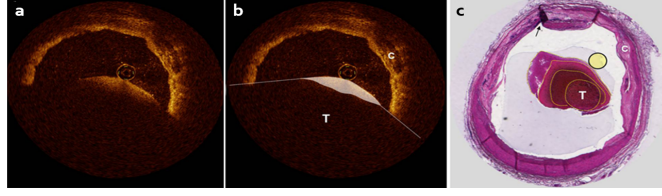


Figure 10: Example of thrombus: (a) Original OCT image. (b) Annotated OCT image: C: Calcification, T: Thrombus. Corresponding histological image is shown in (c) [15].

the light ( one example is shown in figure 4) [24, 1, 15]. By progression of the atherosclerosis, in intimal thickening of about  $500 \mu m$ , hypoxia, lack of optimal oxygen supply in intima, results in progression of micro-vessels. Micro-vessels density depends on chronic inflammatory cell infiltration. Due to their defective endothelial junctions, micro-vessels are characterized by weak and permeable structure, which results in invasion of lipids and inflammatory cells into the intima and intraplaque haemorrhage, which they can highly contribute in plaque vulnerability. Micro-vessels are shown in OCT images as rounded signal-poor structures (figure 5). Extensive macrophage infiltration results in plaque rupture, which causes coronary thrombosis and acute coronary syndrome. Coronary thrombus is categorized in two types: 1. White thrombus is composed of platelets and fibrin, which is visualized as homogeneous signal-rich region in OCT images. 2. Red thrombus is composed of the red blood cells, and characterized by OCT as signal-poor region since blood highly attenuates the light (figure 10) [1, 15, 25].

As it was mentioned previously in this review article, medical imaging systems play significant role in early detection, diagnosis, effective decision-making and treatment of the disease. Interpretation of the medical images by human experts including radiologists, clinicians, and trained technicians is non-accurate and highly challenging considering high variation of pathological features of the disease and possible human errors. We investigated the state-of-the-art imaging system for coronary plaque indication and understood the mechanism of plaque development and clinical features of the coronary plaques. Now it is the time to

integrate machine learning approaches and design proper computational models which can provide clinicians with a real-time fully analytical model of coronary artery with high precision. To this end, we refer to recent related technical studies to realize what needs to be done further considering the limitations of the existing studies in both technical and clinical aspects.

#### 4. Review of algorithms & their applicability in image interpretation

Artificial intelligence, computer-aided models, is rapidly evolving in various medical fields. Due to their high fidelity and efficiency, these machine learning-based, and specifically deep learning-based techniques can improve medical image analysis for fast and accurate interpretation of the medical images [26, 27]. Therefore, deep learning is widely used to provide accurate analysis of the images in various medical fields. The most important characteristic of deep learning models is their strength to extract features, which can accurately provide distinctive descriptions of various tissue types [28, 29, 30, 31]. In this section, we focus on reviewing the most recent studies related to the coronary plaque characterization using OCT imaging.

A CNN-based approach was used by Athanasiou et al, for patch-based classification of coronary plaques including calcium, lipid, fibrous, mixed tissues, and non-pathological tissues. Training and validation was performed on OCT images of 26 patients (the total of 700 cross-sections). Pre-processing was performed using bilateral filtering, and K-means approach to detect the arterial wall prior to applying CNN for tissue classification [32]. Although the work is interesting to classify different plaques, but there are some limitations to be considered. In clinical point of view, definition of non-pathological arterial wall should be clarified. Also, there are other significant factors of plaque development and rupture such as macrophage infiltration, type of fibroatheroma and micro-vessels that are not considered in this study. In technical point of view, pre-processing steps are time-consuming and may result in losing important information. It is difficult to generalize the pre-processing steps to all the cases

considering the artifacts of the system, and disease progression stage, which can completely deform the arterial wall. Also, patch-based CNN has some limitations. Pre-processing steps are required considering the huge computation time, patch size selection is challenging, and redundant feature extraction process because of overlapping patches is another limitation of the patch-based classification using CNNs. Ren et al proposed another patch-based classification approach using CNN to detect lipid and fibrous plaque. As pre-processing steps, intensity based approaches were used to detect catheter. Lumen boundary was detected by applying dilation and erosion. Then, the images were cropped based on the lumen boundary to reduce the image size and make the feature extraction process faster. Proposed CNN model was inspired by the VGG architecture [33].

Miyagawa et al proposed a CNN-based approach to detect vascular bifurcation using OCT imaging. Although this study is not concentrated on the atherosclerotic plaque characterization, but the risk of atherosclerosis is higher in vessel bifurcation. This can be an important complementary study to be considered. In technical point of view, the pre-processing was performed in various steps including binarization, morphological gradient, Hough transform, and cropping. Then, combination of four different CNN architectures were used to detect the region with bifurcation in the images [34]. Normalized-intensity standard deviation (NSD) was used to detect regions of the arterial wall with macrophage accumulation by Rico et al. An intensity-based method was used to detect the punctuated signal rich areas of the arterial wall followed by the signal-poor area with high and low NSD value respectively [35]. Although macrophage infiltration is associated with every stage of the atherosclerotic plaque development, but it is not coronary plaque by itself. Moreover, intensity based characterization of macrophage is not accurate since residual blood, which highly attenuates the light, can create the same visualization as macrophage in the OCT images. The signal-poor area followed by the punctuated signal-rich area can be lipid pool, which is not necessarily followed by the macrophage infiltration, specifically in early stages of the atherosclerosis

development. A deep residual U-net was designed for binary classification to discriminate between the areas in the OCT images with vulnerable plaques versus other tissues. Resnet101-based U-net was modified by adding the residual units to the network architecture. Loss function was replaced by a combination of weighted cross-entropy loss and dice coefficient to improve the segmentation performance. The results were compared against the results of the Resnet50-based U-net, Resnet101-based U-net, and VGG-based U-net [36]. Although the work is very interesting, specifically to detect vulnerable plaques, but plaque types and vulnerable plaque components should be considered in future studies to assist clinicians in decision-making and personalized treatment strategies. U-net is robust for binary classification. Although it is used for multi-class classification problems, but the performance is not as accurate as binary classification. The other work was focused on discriminating between OCT images with and without fibroatheroma. Pre-processing steps and cropping the images were performed to reduce the feature extraction computational burden. Then, three types of features including Local Binary Patterns, Haar-like, and Histogram of Oriented Gradients were extracted from the region of interest (arterial wall). Support Vector Machine was used for binary classification to distinguish between images with and without fibroatheroma [37]. Although hand-crafted features can provide a fair description of the tissues, but considering the challenges of the OCT images, detailed tissue information is required for better representation and evaluation of the intracoronary plaques. Lipid, fibrous, and calcified plaques were detected by Ren et al. An intensity-based approach was used for pre-processing to detect the catheter. Lumen border was detected by considering local maximum of standard deviation. Multi-layer model was proposed for classification task. Training and validation was performed using OCT images obtained from seven patients [38]. The other study focused on detection of lipid and calcified plaque from OCT images. Pre-processing was performed in five different steps to detect the lumen border, denoising, and extraction of the region of interest. Then, ResNet was trained to segment lipid and calcified tissues. Training and validation were performed on 57 OCT pullbacks obtained

from different patients [39]. Using fully convolutional networks, pre-processing  
 is not required. Accurate choice of parameters at each layer of the network and  
 right choice of loss function, which is sensitive enough for the segmentation task  
 create a fast and precise network configuration to avoid pre-processing steps.  
 Secondly, the clinical need is not clear in this study. Pre-trained SegNet was  
 used to detect calcification and lumen area in OCT images. Conditional Ran-  
 dom Fields (CRFs) was applied to refine the classification results. The model  
 was trained and validated on 34 OCT pullbacks [40]. The clinical need is not  
 clear in this study since calcification can be detected using coronary angiog-  
 raphy as well. Dong et al proposed a finite element method to evaluate stent  
 placement in calcified coronary arteries. Cross-sectional area, angle, and maxi-  
 mum thickness of the intracoronary calcified regions were quantified to analyze  
 stent implementation [41]. This work is interesting since such information is  
 useful in accurate stent placement. Lack of information regarding the dimen-  
 sion, type, and location of the plaque in the process of stent placement can  
 result in plaque rupture. In the other study, combination of deep features and  
 hand-crafted features were used to detect lipid and fibrocalcific plaques versus  
 other coronary tissues. Different pre-processing steps were performed to extract  
 the region of interest (arterial wall). Then, a CNN with three convolutional and  
 three fully connected layers was applied to extract deep features from the OCT  
 images. Combination of deep features and lumen morphology features were  
 used for classification task using Random Forest. At the end CRF method was  
 used to refine the classification result [42]. Combination of deep features and  
 texture features were used to detect coronary plaques including lipid and calci-  
 fication. Random forest was used as the classifier [43]. Since detailed texture  
 information was included in deep features, this question should be investigated  
 that how much it is efficient to combine texture or lumen morphology features  
 with deep features to improve classification accuracy. Combination of U-Net-  
 and residual learning-based model was used for segmentation of intima, media,  
 lumen, guidewire shadow and plaques by [44]. The model does not characterize  
 the plaque types. A clustering method to discriminate between calcified versus

380 other tissues using auto-encoders were proposed by [45]. Although creating the  
 ground-truth for supervised learning is time-consuming but this method is not  
 validated on characterizing all types of atherosclerotic plaques. Attenuation  
 coefficients are estimated for OCT images by [46]. These measurements and  
 investigations are important for better understanding of the optical properties  
 385 of various tissues, which is crucial in quantitative analysis of the OCT images.  
 A complete model to analyze coronary artery in OCT imaging was proposed by  
 our team. Combination of CNN and FCN was used to design the model not  
 only to avoid pre-processing steps, but also to apply the end to end networks  
 for segmentation instead of using patch-based CNN. The model starts by eval-  
 390 uating the arterial wall to distinguish between normal three-layered structure  
 and intimal thickening with media disappearance. If the arterial wall is recog-  
 nized as normal in the first step, various arterial wall layers (intima and media)  
 will be detected for accurate evaluation of each layer thickness in early stages  
 of the disease, which three-layered structure is maintained. If the arterial wall  
 395 is recognized as pathological in the first step, a FCN model is used to detect  
 all possible plaques and pathological formations to be characterized by type in  
 the final step. Figure 11 demonstrates all the steps of our model, which will  
 be extended to characterize all types of the atherosclerotic plaques [47]. Recent  
 studies to indicate coronary plaque morphology is summarized in table 1.

## 400 5. Discussion

Deep learning and machine learning methods are evolving to meet many  
 clinical needs. Before proposing mathematical solutions using physical concepts  
 and deep learning models, technical researchers need to understand the prob-  
 lem in detail. Teamwork between mathematicians, physicists, machine learning  
 405 and deep learning experts is required to converge with clinical needs. Con-  
 ducting a successful and effective research project, which can be applicable to  
 improve patient's outcome has significant requirements. Without understanding  
 the process of plaque development and having adequate knowledge of clinical

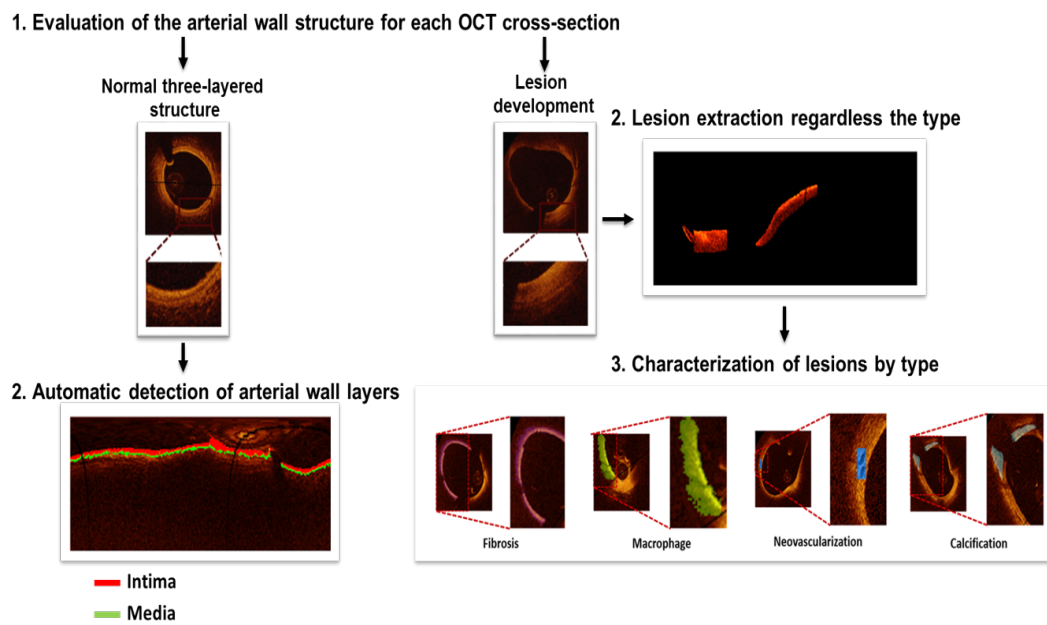


Figure 11: Deep learning based model for fully analysis of coronary arteries in OCT imaging

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Table 1: Recent studies concentrated on indication of plaque morphology in OCT images.

Reference	Proposed method	Contribution	Model validation
[32]	Patch-based CNN for plaque classification.	Detection of calcium, lipid, fibrous, mixed and non-pathological tissues.	Accuracy varies from 73% to 93% based on the tissue type.
[33]	Patch-based CNN for plaque classification	Detection of healthy tissues, lipid and fibrous plaque.	Accuracy, precision, specificity, and sensitivity vary as follows respectively: 87% to 88%, 75% to 94%, 90% to 94%, and 61% to 90%
[34]	CNN-based classification	Detection of vascular bifurcation	Depends on the network architecture and in Cartesian coordinate, accuracy, specificity, and precision respectively vary as follows: 97% to 98%, 97% to 99%, and 96% to 98%
[35]	Normalized-intensity standard deviation (NSD)	Detection of macrophage accumulation	Using NSD, accuracy, specificity, and sensitivity vary as follows respectively: 53% to 88%, 54% to 89%, and 51% to 84%



Reference	Proposed method	Contribution	Model validation
[36]	Deep residual U-net for binary classification	Detection of vulnerable plaques versus other tissues	Using U-Net+ResNet101, mean accuracy, mean precision, mean IOU, and mean recall vary as follows respectively: 90%, 94%, 85%, and 91%
[37]	Combination of LBP, Haar-like, and HOG features for classification using SVM	Detection of fibroatheroma	Using all three types of features, accuracy, specificity, and sensitivity vary as follows respectively: 88%, 91%, and 89%
[38]	Multi-layer model for tissue classification	Detection of lipid, fibrous, and calcified plaques	Accuracy varies from 90% to 94% based on the plaque type
[39]	Pre-trained ResNet	Detection of lipid and calcification	Compared to other methods, sensitivity, specificity, and dice of the proposed method vary based on the plaque type, which are respectively reported as: 85% to 98%, 70% to 90%, and 82% to 90%

Reference	Proposed method	Contribution	Model validation
<a href="#">[40]</a>	Pre-trained SegNet	Detection of calcification and lumen area	Sensitivity, specificity, and F1score respectively: Lumen: 97% to 100%, 97% to 99%, 89% to 91%, Calcification: 76% to 88%, 96% to 98%, 39% to 45%
<a href="#">[41]</a>	Finite element method	Evaluation of stent placement in calcified coronary artery	Material coefficients were reported for this study.
<a href="#">[42]</a>	Combination of deep CNN features and hand-crafted features to train Random Forest	Detection of lipid and fibrocalcified plaques	Different features and methods were compared against each other in this study.
<a href="#">[43]</a>	Combination of deep features and texture features for classification using Random Forest	Detection of lipid and calcification	Sensitivity, specificity, and dice after applying CRF vary based on the tissue type as follows: 67% to 97% for sensitivity, 84% to 97% for specificity, 63% to 89% for dice.
<a href="#">[44]</a>	Combination of U-Net and Residual learning-based models was used in this study.	Detection of intima, media, lumen, guidewire, and plaques.	Metrics are not reported for all the tissue types.

Reference	Proposed method	Contribution	Model validation
[45]	A clustering method using auto-encoders.	Discrimination between calcified versus other tissues.	The best average precision of the model obtained for one-half clustered as 76%.
[46]	Estimation of attenuation coefficients for intracoronary OCT images.	Various optical parameters were estimated.	Only measured parameters were reported.
[47]	Combination of CNN and FCN models	Complete analysis of coronary arteries in OCT images	Accuracy, specificity, and sensitivity respectively vary as follows based on the plaque type: 90% to 95%, 95% to 97%, and 84% to 90%.

features of the plaque formation, it is hardly possible to propose a model, which  
410 can efficiently address this problem. The clinical needs in the opinion of the  
interventional cardiologists lay the ground for future works based on the com-  
putational models will help describing the exact features of the tissues under  
review with the means of deep learning algorithms. Although interventional  
cardiology created a new platform to help millions of patients avoid bypass  
415 surgery, the current upper edge need is as follows: 1. Understanding the clin-  
ical features of the various coronary plaques in OCT images can improve the  
inter-observer agreement in various degrees depending on the type of pathology  
[48]. This improved interpretation comes following extensive focused training,  
and yet remains sub-optimal to general practice. 2. Considering recent stud-  
420 ies and discussing with different interventional cardiologists to understand the  
unmet needs, we realized that lack of an integrated automatic tissue character-  
ization software system in OCT imaging for real-time high precision analysis of  
intracoronary tissues remains a major problem.

Applying artificial intelligence paradigms will overcome the following limitations inherent to subjective operator-dependent interpretation:

- Understanding the features of various plaques in OCT images requires intensive training and visual interpretation of the OCT images is still highly error prone.
- complete interpretation and manual detection of the various lesions may take weeks and even months for clinicians given the diffuse nature of the coronary artery disease sequelae, which postpones the diagnostic process, decision making, and possibility of the accurate personalized treatment strategy for better patient's outcome.
- The current cardiac imaging systems have many limitations when it comes to detecting vulnerable plaques, those types of plaques prone to rupture. Considering the advantages and incredible functionality of the intravascular OCT imaging, evaluation and automatic indication of the vulnerable plaques in OCT images is another important clinical need.

Considering the clinical features of the coronary plaques and various stages of disease progression. We should divide our technical solution into three different steps. Classification, segmentation, and prediction (figure 12). Since we need to have an automatic analytical model of coronary artery, which can be applied in real-time for immediate and accurate analysis of the images during intervention, the models with pre-processing steps are not desirable for the following reasons: 1. Pre-processing steps are additional computational burden. 2. We may lose some important information regarding tissue features during pre-processing. 3. Pre-processing steps are not certainly generalized to all the cases since we have vessel remodelling caused by the disease, which can result in complete deformation of the arterial wall. There are various types of deep learning architectures, which should be chosen wisely to design an appropriate model. Considering the related studies, CNNs are used in different studies for segmentation purpose. CNNs are very strong feature extractors and can be

trained and used efficiently for classification purposes. Although patch-based CNN can be used for segmentation task, but it has some important limitations:

455 1. Path-based segmentation using CNN is computationally very expensive because patches are overlapped, which results in redundant feature extraction. 2. Pre-processing steps are inevitable since we need to extract the region of interest (arterial wall tissues) to reduce the computational time. 3. Choosing the right patch size, which is not too small or too large considering the max-pooling  
460 steps, is another challenge of using CNNs for segmentation task. Therefore, CNN models can be used mainly for feature extraction and classification, while we are characterizing various types of plaques or tissues. On the other hand, fully convolutional networks, which are trained end-to-end can be used for segmentation tasks. The advantage of using them is that the arbitrary size of the  
465 images can be used as the network input since there is no fully connected layer involved in the network architecture. Without involving the fully connected layers, the number of parameters will be reduced considerably. This can highly accelerate the process of network training. Therefore, the original images can be fed to the network for segmentation. For any other type of deep learning  
470 architectures, we need to investigate if they can properly be used to address the problems related to different stages of the disease (figure 12). It is also important to note that the quantitative evaluations that we report in research papers are important in research point of view but such measurements do not demonstrate the readiness of the proposed model for clinical applications. Research usually  
475 performs using limited data. The quantitative evaluations become important if the method will be applicable and it can be generalized to the challenging cases. These evaluations are useful not only by testing a method on large datasets, but also by evaluating its performance on various challenging cases.

## 6. Conclusion

480 In this review article, we investigate different aspects of the coronary artery disease from both clinical and technical perspectives. We aim to underline the

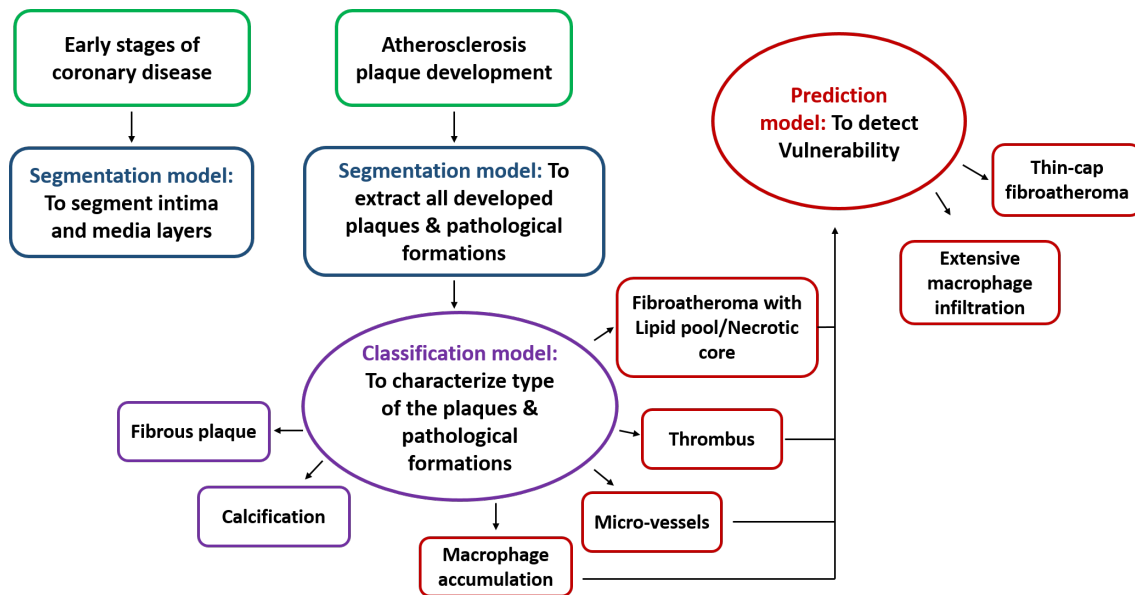


Figure 12: Complete model to analyze coronary artery in OCT imaging. Deep learning models should be chosen by considering the step of problem solving to select appropriate networks for classification, segmentation, and prediction purposes.

importance of having thorough and detailed knowledge of the clinical features of the disease as well as the clinical needs to find the mathematical solution, which can address the problem accurately. Since OCT is a turning point and powerful  
485 tool in cardiovascular imaging for coronary plaque detection, we investigated its limitations to be addressed. Based on the discussions with different interventional cardiologists, we realized that there is a clear need for an automatic fully analytical model to accurately evaluate coronary artery in real-time using OCT  
490 imaging. By reviewing the existing technical studies, we divide different steps of the model into three categories of segmentation, classification, and prediction not only to detect coronary plaque morphology, but also to predict the plaques prone to rupture using various machine learning approaches. Future studies can be concentrated on the physics of the system during image acquisition and the limitations such as low penetration depth of the OCT imaging, and the need  
495 of blood clearance during image acquisition. We may also consider the optical properties of the various plaque sub-components for detailed analysis of the tissues.

### **Conflicts of interest**

The authors declare no conflicts of interest.

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### **Ethical approval**

The ethical approval is not required for this study.

### **505 References**

- [1] L. S. Lilly, Pathophysiology of heart disease: a collaborative project of medical students and faculty, Lippincott Williams & Wilkins, 2012.

- [2] R. Pahwa, I. Jialal, Atherosclerosis. statpearls. treasure island (fl) (2018).
- [3] M. J. Cowley, Tribute to a legend in invasive/interventional cardiology  
510 melvin p. judkins, md (1922–85), Catheterization and Cardiovascular In-  
terventions 64 (2) (2005) 259–261.
- [4] E. T. Carreras, D. O. Williams, Interventional cardiology: The in and the  
out, Circulation: Cardiovascular Interventions 11 (4) (2018) e006709.
- [5] J. M. Tarkin, M. R. Dweck, N. R. Evans, R. A. Takx, A. J. Brown,  
515 A. Tawakol, Z. A. Fayad, J. H. Rudd, Imaging atherosclerosis, Circula-  
tion research 118 (4) (2016) 750–769.
- [6] M. Daghem, R. Bing, Z. A. Fayad, M. R. Dweck, Noninvasive imaging to as-  
sess atherosclerotic plaque composition and disease activity: Coronary and  
carotid applications, JACC: Cardiovascular Imaging 13 (4) (2020) 1055–  
520 1068.
- [7] V. Sandfort, J. A. Lima, D. A. Bluemke, Noninvasive imaging of atheroscle-  
rotic plaque progression: status of coronary computed tomography angiog-  
raphy, Circulation: Cardiovascular Imaging 8 (7) (2015) e003316.
- [8] T. Noguchi, K. Nakao, Y. Asaumi, Y. Morita, F. Otsuka, Y. Kataoka,  
525 H. Hosoda, H. Miura, T. Fukuda, S. Yasuda, Noninvasive coronary plaque  
imaging, Journal of atherosclerosis and thrombosis (2017) RV17019.
- [9] C. H. Jansen, D. Perera, A. J. Wiethoff, A. Phinikaridou, R. M. Razavi,  
A. Rinaldi, M. S. Marber, G. F. Greil, E. Nagel, D. Maintz, et al., Contrast-  
enhanced magnetic resonance imaging for the detection of ruptured coro-  
530 nary plaques in patients with acute myocardial infarction, PloS one 12 (11).
- [10] A. Erglis, S. Jegere, I. Narbutė, Intravascular ultrasound-based imaging  
modalities for tissue characterisation, Interventional Cardiology Review  
9 (3) (2014) 151.



- [11] M. W. Lee, J. W. Song, W. J. Kang, H. S. Nam, T. S. Kim, S. Kim, W.-Y. Oh, J. W. Kim, H. Yoo, Comprehensive intravascular imaging of atherosclerotic plaque in vivo using optical coherence tomography and fluorescence lifetime imaging, *Scientific reports* 8 (1) (2018) 1–12.
- [12] B. E. Bouma, M. Villiger, K. Otsuka, W.-Y. Oh, Intravascular optical coherence tomography, *Biomedical optics express* 8 (5) (2017) 2660–2686.
- [13] X. Chen, W. Kim, M. J. Serafino, Z. Tan, J. A. Jo, B. E. Applegate, Dual-modality optical coherence tomography and frequency-domain fluorescence lifetime imaging microscope system for intravascular imaging, *Journal of Biomedical Optics* 25 (9) (2020) 096010.
- [14] K. Nishimiya, G. Tearney, Multimodality intravascular oct imaging, *Cardiovascular OCT Imaging* (2020) 163–174.
- [15] M. D. Radu, The clinical atlas of intravascular optical coherence tomography for ipad., *European heart journal* 33 (10) (2012) 1174.
- [16] J. E. Wagenseil, R. P. Mecham, Elastin in large artery stiffness and hypertension, *Journal of cardiovascular translational research* 5 (3) (2012) 264–273.
- [17] R. Virmani, F. D. Kolodgie, A. P. Burke, A. Farb, S. M. Schwartz, Lessons from sudden coronary death: a comprehensive morphological classification scheme for atherosclerotic lesions, *Arteriosclerosis, thrombosis, and vascular biology* 20 (5) (2000) 1262–1275.
- [18] F. Otsuka, M. Joner, F. Prati, R. Virmani, J. Narula, Clinical classification of plaque morphology in coronary disease, *Nature Reviews Cardiology* 11 (7) (2014) 379.
- [19] F. Otsuka, K. Sakakura, K. Yahagi, M. Joner, R. Virmani, Has our understanding of calcification in human coronary atherosclerosis progressed?, *Arteriosclerosis, thrombosis, and vascular biology* 34 (4) (2014) 724–736.

- [20] T. Saita, K. Fujii, H. Hao, T. Imanaka, M. Shibuya, M. Fukunaga, K. Miki, H. Tamaru, T. Horimatsu, M. Nishimura, et al., Histopathological validation of optical frequency domain imaging to quantify various types of coronary calcifications, *European Heart Journal-Cardiovascular Imaging* 18 (3) (2017) 342–349.
- [21] F. Otsuka, M. C. Kramer, P. Woudstra, K. Yahagi, E. Ladich, A. V. Finn, R. J. de Winter, F. D. Kolodgie, T. N. Wight, H. R. Davis, et al., Natural progression of atherosclerosis from pathologic intimal thickening to late fibroatheroma in human coronary arteries: a pathology study, *Atherosclerosis* 241 (2) (2015) 772–782.
- [22] P. K. Cheruvu, A. V. Finn, C. Gardner, J. Caplan, J. Goldstein, G. W. Stone, R. Virmani, J. E. Muller, Frequency and distribution of thin-cap fibroatheroma and ruptured plaques in human coronary arteries: a pathologic study, *Journal of the American College of Cardiology* 50 (10) (2007) 940–949.
- [23] K. Yahagi, F. D. Kolodgie, F. Otsuka, A. V. Finn, H. R. Davis, M. Joner, R. Virmani, Pathophysiology of native coronary, vein graft, and in-stent atherosclerosis, *Nature Reviews Cardiology* 13 (2) (2016) 79.
- [24] R. Ganesan, K. M. Henkels, L. E. Wrenshall, Y. Kanaho, G. Di Paolo, M. A. Frohman, J. Gomez-Cambronero, Oxidized ldl phagocytosis during foam cell formation in atherosclerotic plaques relies on a pld2-cd36 functional interdependence, *Journal of leukocyte biology* 103 (5) (2018) 867–883.
- [25] K. Yahagi, H. R. Davis, E. Arbustini, R. Virmani, Sex differences in coronary artery disease: pathological observations, *Atherosclerosis* 239 (1) (2015) 260–267.
- [26] A. Fourcade, R. Khonsari, Deep learning in medical image analysis: A third eye for doctors, *Journal of stomatology, oral and maxillofacial surgery* 120 (4) (2019) 279–288.

- [27] D. Shen, G. Wu, H.-I. Suk, Deep learning in medical image analysis, Annual review of biomedical engineering 19 (2017) 221–248.
- [28] M. Biswas, V. Kuppili, D. R. Edla, H. S. Suri, L. Saba, R. T. Marinho, J. M. Sanches, J. S. Suri, Symtosis: A liver ultrasound tissue characterization and risk stratification in optimized deep learning paradigm., Computer methods and programs in biomedicine 155 (2018) 165–177.
- [29] Y. Dong, Y. Pan, X. Zhao, R. Li, C. Yuan, W. Xu, Identifying carotid plaque composition in mri with convolutional neural networks, in: Smart Computing (SMARTCOMP), 2017 IEEE International Conference on, IEEE, 2017, pp. 1–8.
- [30] K. Lekadir, A. Galimzianova, À. Betriu, M. del Mar Vila, L. Igual, D. L. Rubin, E. Fernández, P. Radeva, S. Napel, A convolutional neural network for automatic characterization of plaque composition in carotid ultrasound., IEEE J. Biomedical and Health Informatics 21 (1) (2017) 48–55.
- [31] R.-M. Menchón-Lara, J.-L. Sancho-Gómez, A. Bueno-Crespo, Early-stage atherosclerosis detection using deep learning over carotid ultrasound images, Applied Soft Computing 49 (2016) 616–628.
- [32] L. S. Athanasiou, M. L. Olender, M. José, E. Ben-Assa, E. R. Edelman, A deep learning approach to classify atherosclerosis using intracoronary optical coherence tomography, in: Medical Imaging 2019: Computer-Aided Diagnosis, Vol. 10950, International Society for Optics and Photonics, 2019, p. 109500N.
- [33] X. Ren, H. Wu, Q. Chen, T. Kubo, T. Akasaka, A tissue classification method of ivoct images using rectangle region cropped along the circumferential direction based on deep learning, in: International Forum on Medical Imaging in Asia 2019, Vol. 11050, International Society for Optics and Photonics, 2019, p. 1105015.

- [34] M. Miyagawa, M. G. F. Costa, M. A. Gutierrez, J. P. G. F. Costa, C. F. F. Costa Filho, Detecting vascular bifurcation in ivoct images using convolutional neural networks with transfer learning, *Ieee Access* 7 (2019) 66167–66175.
- 620 [35] J. J. Rico-Jimenez, D. U. Campos-Delgado, L. M. Buja, D. Vela, J. A. Jo, Intravascular optical coherence tomography method for automated detection of macrophage infiltration within atherosclerotic coronary plaques, *Atherosclerosis* 290 (2019) 94–102.
- [36] L. Li, T. Jia, Optical coherence tomography vulnerable plaque segmentation based on deep residual u-net, *Reviews in cardiovascular medicine* 20 (3) (2019) 171–177.
- 625 [37] Q. Yan, M. Xu, D. W. K. Wong, A. Taruya, A. Tanaka, J. Liu, P. Wong, J. Cheng, Automatic fibroatheroma identification in intravascular optical coherence tomography volumes, *Journal of Ambient Intelligence and Humanized Computing* (2019) 1–7.
- 630 [38] X. Ren, H. Wu, Q. Chen, T. Imai, T. Kubo, T. Akasaka, A local multi-layer model for tissue classification of in-vivo atherosclerotic plaques in intravascular optical coherence tomography, *IEICE Transactions on Information and Systems* 102 (11) (2019) 2238–2248.
- [39] J. Lee, D. Prabhu, C. Kolluru, Y. Gharaibeh, V. N. Zimin, H. G. Bezerra, D. L. Wilson, Automated plaque characterization using deep learning on coronary intravascular optical coherence tomographic images, *Biomedical Optics Express* 10 (12) (2019) 6497–6515.
- 635 [40] Y. Gharaibeh, D. Prabhu, C. Kolluru, J. Lee, V. Zimin, H. Bezerra, D. Wilson, Coronary calcification segmentation in intravascular oct images using deep learning: application to calcification scoring, *Journal of Medical Imaging* 6 (4) (2019) 045002.
- 640

- [41] P. Dong, H. Mozafari, D. Prabhu, H. G. Bezerra, D. L. Wilson, L. Gu, Optical coherence tomography-based modeling of stent deployment in heavily calcified coronary lesion, *Journal of Biomechanical Engineering* 142 (5).  
645
- [42] J. Lee, D. Prabhu, C. Kolluru, Y. Gharaibeh, V. N. Zimin, L. A. Dally, H. G. Bezerra, D. L. Wilson, Fully automated plaque characterization in intravascular oct images using hybrid convolutional and lumen morphology features, *Scientific reports* 10 (1) (2020) 1–13.
- [43] J. Lee, C. Kolluru, Y. Gharaibeh, D. Prabhu, V. N. Zimin, H. Bezerra, D. Wilson, Automatic a-line coronary plaque classification using combined deep learning and textural features in intravascular oct images, in: *Medical Imaging 2020: Image-Guided Procedures, Robotic Interventions, and Modeling*, Vol. 11315, International Society for Optics and Photonics, 2020, p. 1131513.  
650  
655
- [44] M. Haft-Javaherian, M. Villiger, K. Otsuka, J. Daemen, P. Libby, P. Golland, B. E. Bouma, Segmentation of anatomical layers and artifacts in intravascular polarization sensitive optical coherence tomography using attending physician and boundary cardinality loss terms, *arXiv preprint arXiv:2105.05137*.  
660
- [45] C. Kolluru, J. Lee, Y. Gharaibeh, H. G. Bezerra, D. L. Wilson, Learning with fewer images via image clustering: Application to intravascular oct image segmentation, *IEEE Access* 9 (2021) 37273–37280.
- [46] B. Ghafaryasl, K. A. Vermeer, J. Kalkman, T. Callewaert, J. F. de Boer, L. J. Van Vliet, Analysis of attenuation coefficient estimation in fourier-domain oct of semi-infinite media, *Biomedical Optics Express* 11 (11) (2020) 6093–6107.  
665
- [47] A. Abdolmanafi, F. Cheriet, L. Duong, R. Ibrahim, N. Dahdah, An automatic diagnostic system of coronary artery lesions in kawasaki disease using intravascular optical coherence tomography imaging, *Journal of biophotonics* 13 (1) (2020) e201900112.  
670

- [48] A. S. Kini, Y. Vengrenyuk, T. Yoshimura, M. Matsumura, J. Pena, U. Baber, P. Moreno, R. Mehran, A. Maehara, S. Sharma, et al., Fibrous cap thickness by optical coherence tomography in vivo, *Journal of the American College of Cardiology* 69 (6) (2017) 644–657.