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Image-Based Modeling for Atherosclerotic Coronary Plaque Progression and Vulnerability Research

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Abstract: Medical imaging and image-based computational modeling have been used by many researchers in recent years to quantify atherosclerotic plaque morphological and biomechanical characteristics and predict the coronary plaque growth and rupture processes. However, it has been hard to validate model predictions due to imaging resolution limitation, lack of clinical events and plaque rupture data. This article reviews recent advances in coronary plaque research over the past decade, including medical imaging techniques represented by intravascular ultrasound (IVUS) and optical coherence tomography (OCT), computational modeling and their applications in plaque progression and vulnerability analyses and predictions. The clinical application and future development direction are also briefly described.

Cardiovascular disease is a dangerous killer with high mortality rate in human society. *China Cardiovascular Disease Report 2017 (Summary)* [2] pointed out that at present, cardiovascular diseases (CVD) account for the highest number of deaths among urban and rural residents, with 45.01 percent in rural areas and 42.61 percent in urban areas. Coronary heart disease is closely related to coronary atherosclerosis. In the later stages of atherosclerosis, the lesions (also called plaques) become increasingly unstable with high chance to rupture. The sudden rupture of plaque, followed by complete or incomplete occlusive thrombus clinical syndrome is called acute coronary syndrome (ACS). ACS is one of the main forms of acute death from coronary heart diseases. Vulnerable plaques are atherosclerotic plaques which are more likely to rupture causing severe cardiovascular events. Analyzing the vulnerability of plaques effectively could lead to better patient screening strategies and enable physicians to adopt timely and necessary intervention or conservative treatment, and better guide patient's treatment.

Earlier investigations of vulnerable plaques were mostly based on histopathological data. With the accumulation of experience in pathology and the gradual enrichment of autopsy materials, the criteria for the diagnosis of vulnerable plaques appeared in 2001, mainly manifested as the necrotic lipid nuclei, fibrous caps that are infiltrated by a large number of macrophages, and fibrous cap thickness less than 65μm [1,7]. Pathological characteristics such as inflammation, plaque internal bleeding, cholesterol crystals, calcified nodules, and thrombosis are also important aspects of vulnerable plaque investigations [4,9-11]. During the initiation and development of a plaque, macrophages have a high degree of participation. On the one hand, they may increase the area of plaque and the appearance and development of necrotic lipid nuclei. On the other hand, they stimulate inflammatory reactions and promote the formation and lesions of thin fibrous caps. Gene expression, biological and biochemical marker studies, and animal models are some entry points for studying coronary atherosclerosis [3,6,8,14]. Because of the obvious importance of the thin fibrous cap in plaque rupture process, it has been a focus of attention by many investigations. Watson, M.G. et al. (2018) are concerned about the formation of early fibrous caps in recent years [13]. The presentation of local maximum stress on plaque further confirmed the importance of thin fibrous cap [12].

The development of medical images has greatly promoted the study of coronary atherosclerosis. Compared with autopsy *ex vivo*, medical image could provide plaque data under *in vivo* conditions. In coronary studies, Huang XY (2014) used *ex vivo* magnetic resonance imaging (MRI) to study the relationship between plaque wall stress (PWS) and death caused by coronary artery disease [5]. Due to technical limitations and the accessibility of the coronary artery in the body, MRI is not widely used for *in vivo* coronary studies. Interventional intravascular ultrasound (IVUS), with an image resolution of 150-200μm, has been used in research and clinical practice to identify plaques, quantify plaque morphology, and characterize plaque components. More recently, optical coherence tomography (OCT), with its resolution of 5-10μm, has emerged as an imaging modality which can be used to detect thin fibrous caps and improve diagnostic accuracy. The emergence of molecular imaging technology has also opened up new ideas for the study of fragile plaques.

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It is commonly believed that mechanical forces play an important role in plaque progression and rupture. Image-based biomechanical plaque models have been developed and used to quantify plaque mechanical conditions and seek their linkage to plaque progression and vulnerability development activities. Based on recent advances in imaging and modeling, this paper attempts to provide a brief review on plaque research, including histological classification, image preparation, biomechanical modeling and analysis methods. We focus more on human coronary plaque modeling and mainly included results from our group for illustration purpose. We apologize in advance for our limitations.

Keywords: IVUS; OCT; coronary plaque; vulnerable plaque.

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