

# iVIEW

EDITOR'S PAGE



## Ruptures and Thickening

### Optical Coherence Tomography as the Arbiter of the Fibrous Cap



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Coronary artery disease remains a leading cause of mortality worldwide, primarily through acute events mediated by progression and disruption of thrombosis-provoking atheroma. The necrotic core of advanced atheroma harbors highly prothrombotic material, including components of tissue factor, von Willebrand factor, and plasminogen activator inhibitor-1. Exposure of these contents to flowing blood can spur thrombosis and is a critical feature of many acute coronary syndromes (ACS). It is therefore vital that the fibrous cap, a collagen-rich structure overlying advanced atheroma, resist disruption and maintain separation of blood from thrombogenic necrotic cores.

Intravascular imaging using intravascular ultrasound (IVUS) and optical coherence tomography (OCT) is becoming increasingly important for improving outcomes of percutaneous coronary intervention (PCI) and helps reduce “geographic miss” or inadequately covering residual diseased segments when deploying stents (1). OCT, a high-resolution imaging modality based on the backscatter of light, also provides valuable insights into the architecture of the fibrous cap. In this issue of *JACC*, 2 studies using OCT provide new understanding of the importance of the fibrous cap. In the

first study, Hougaard et al. (2) investigated plaque ruptures that remained uncovered, as seen with OCT, in patients with ST-segment elevation myocardial infarction undergoing primary PCI with coronary stenting. The key insight motivating this study was the recognition that the most stenotic zone of the angiographic culprit lesion might not always match the site of the culprit plaque (3). The investigators recognized therefore that a subset of stented lesions might not actually cover the actual culprit plaque rupture site driving the ACS.

What might be the frequency of such uncovered plaque ruptures following PCI with stenting? To address this query, the investigators imaged 77 patients with ACS using intravascular OCT as well as IVUS with plaque composition assessment. Patients underwent OCT and IVUS within 48 h of PCI, but not prior to PCI, a potential weakness of the study. In 10 of 77 patients with suitable image quality, the investigators found evidence on OCT of 11 uncovered or partially covered plaque rupture sites in 10 patients. These sites demonstrated a cavity appearance on OCT. All such sites were located proximal to the stent, with the majority located very near to the proximal stent edge (average distance 0.15 mm). Overall, uncovered plaque ruptures were uncommonly found. Intriguingly, uncovered lesions had greater positive remodeling, necrotic cores, and plaque burden and tended to be of shorter length compared with covered lesions. However, as astutely noted by the editorialists Mori et al. (4), cavities have not been observed in patients with coronary artery disease with sudden cardiac death, raising the possibility that the residual cavity may have been caused by PCI itself. Without baseline imaging prior to PCI, it

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is not possible to know if a coronary artery cavity can occur naturally.

What is the natural history of such uncovered plaque ruptures (cavities)? To answer this next important question, the investigators performed follow-up intravascular OCT and IVUS with plaque composition assessment at the 12-month mark in the same patients, a strength of this study. They found that 3 of 8 upstream uncovered culprit plaque ruptures did not sufficiently heal and remained with residual cavities. Notably, uncovered plaque rupture sites experienced a reduction of about 50% in luminal area, and 2 of 3 patients with persistent cavities developed recurrent symptoms. Perhaps persistent ruptures could provide a highly accessible route for inflammatory leukocytes to enter the uncovered plaque site and drive plaque progression. Overall, this intriguing paper reinforces that OCT could help avoid harmful geographic miss (5) by identifying accurately the culprit rupture site. However, optical coherence tomographic studies prior to primary PCI are needed to test this hypothesis.

At the other end of the spectrum, Nishiguchi et al. (6) harnessed OCT to study the thickness rather than the rupture or absence of the fibrous cap. It is well recognized that the high-resolution capabilities of OCT allow reliable measurement of the fibrous cap thickness, especially when enhanced imaged analysis is performed (7). In an intriguing randomized study of 3-week delayed versus immediate moderate-dose statin therapy in 53 patients with ACS, the investigators performed OCT imaging of nonculprit plaques at 3 time points: baseline, 3 weeks, and 36 weeks. Remarkably, immediate prescription of statins

(even just moderate, not high intensity) conferred a benefit on fibrous cap thickening beyond delayed statin prescription. As eloquently articulated by the editorialists Min et al. (8), this observation could provide a new mechanism as to why immediate statin therapy in patients with ACS might acutely stabilize plaques and reduce event rates, far before a reduction in plaque burden might occur.

OCT continues to shed valuable light on mechanisms of ACS and plaque stabilizing pharmacotherapy, and even though there are challenges for precise diagnosis of thin-capped fibroatheroma (9), OCT remains the current gold-standard method to assay the fibrous cap in patients, provided its limitations, artifacts, and mimics are carefully recognized (7). What of the future of fibrous cap assessment? Novel imaging technologies such as micro-OCT (10) and optical coherence tomographic near-infrared fluorescence molecular imaging (11) could provide even greater insights into fibrous cap structure and its proruption milieu, such as penetrating cholesterol crystals and heightened inflammatory proteolytic activity. More recent advances such as polarization sensitive OCT (12) will possibly reveal even more about the fibrous cap dynamics. The fibrous cap surface-lumen interface is where substantial risk resides for patients with ACS, and OCT is illuminating the path forward.

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