EDITORIAL COMMENT

How to Detect and Treat Coronary Fibroatheromas

The Synergy Between IVUS and NIRS*

Emmanouil S. Brilakis, MD, PhD, Subhash Banerjee, MD

As you set out for Ithaka
hope the voyage is a long one,
full of adventure, full of discovery.
—Constantine P. Cavafy, *Ithaka* (1)

Coronary fibroatheromas can cause a wide spectrum of adverse events, such as sudden death, acute coronary syndromes, and procedural complications during percutaneous coronary interventions (PCI) (2). Accurate fibroatheroma detection could significantly enhance our ability to treat these lesions and prevent complications.

FIBROATHEROMA DETECTION DURING CARDIAC CATHETERIZATION

Fibroatheromas can be detected noninvasively with coronary computed tomography angiography. Three imaging modalities are currently available for fibroatheroma detection during cardiac catheterization: intravascular ultrasonography (IVUS), optical coherence tomography (OCT), and near-infrared spectroscopy (NIRS) (3) (**Figure 1**).

Grayscale IVUS, which is the oldest and most widely available intravascular imaging modality, was not developed specifically for the detection of fibroatheroma. However, IVUS-attenuated plaque (attenuation of the ultrasound beam in the absence of calcification), especially when superficial (closer to the lumen than the media), is a specific (but not sensitive) fibroatheroma "signature" (4,5).

Analysis of the backscattered radiofrequency IVUS signals (virtual histology IVUS and integrated back-scatter IVUS) also allows plaque characterization, but it is challenging to perform in real time during the procedure because it requires accurate segmentation of the IVUS images, which is a time-consuming and labor-intensive process (3).

OCT identifies fibroatheromas as signal-poor regions with ill-defined borders (6), but OCT image interpretation is subjective and highly dependent on operator experience (3). Moreover, deep fibroatheromas may be harder to detect due to poor penetration of the near-infrared light beam.
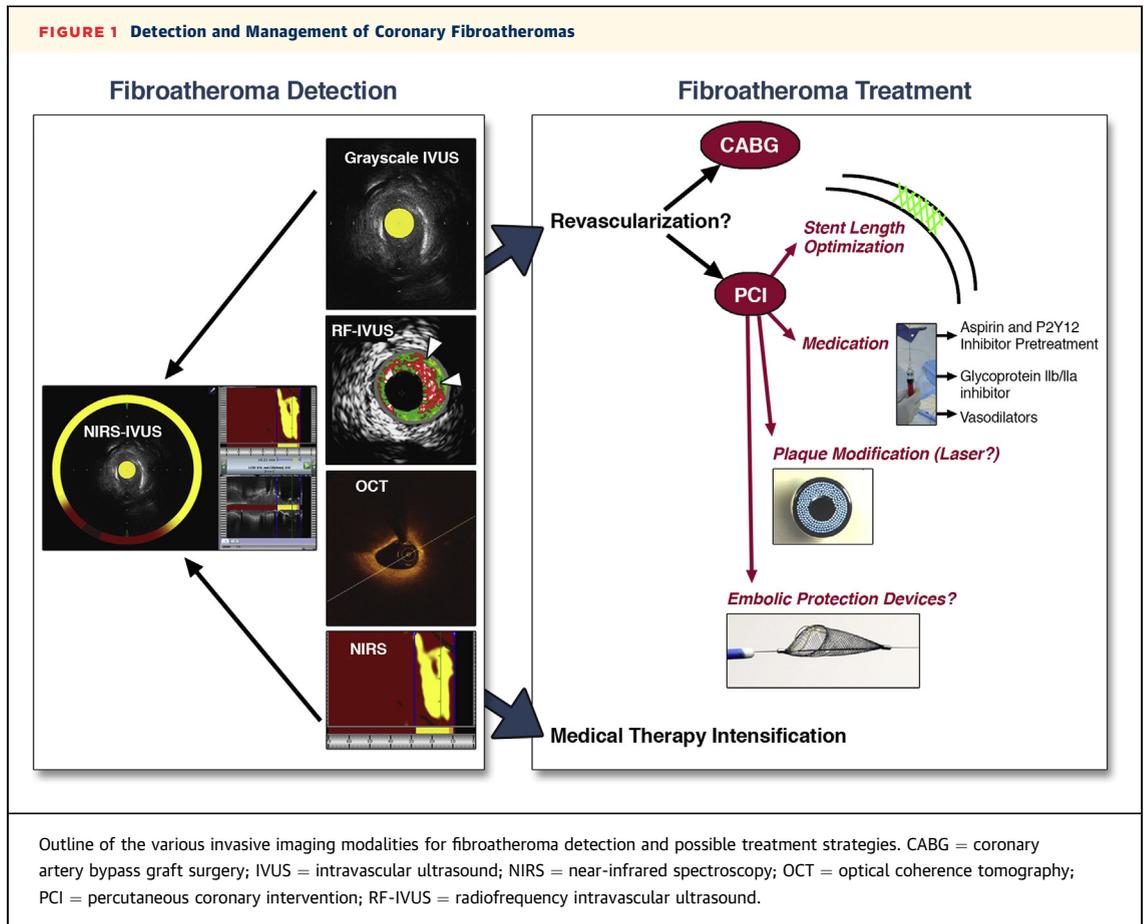
NIRS was developed to specifically detect lipid core plaque in coronary arteries, on the basis of the specific chemical signature of the fibroatheroma (7). Near-infrared light is directed to the coronary artery wall, and the reflected light is collected and analyzed using algorithms developed based on histological analyses (7). NIRS is currently available as a combination catheter with IVUS (TVC, Infraredx, Burlington, Massachusetts)—the only such catheter currently in clinical use.

In this issue of *iJACC*, Kang et al. (8) advance our understanding of fibroatheroma detection with IVUS and NIRS, compared with the gold standard, histology. In an autopsy study of 103 coronary arteries from 56 autopsied hearts, they compared superficial IVUS attenuation (for IVUS) and a yellow or tan block chemogram (for NIRS) with the histopathology obtained from 1,943 sections. Superficial IVUS attenuation had excellent specificity, yet low sensitivity for fibroatheroma detection, which was significantly improved by NIRS. The addition of NIRS significantly increased

FIGURE 1   Detection and Management of Coronary Fibroatheromas

Outline of the various invasive imaging modalities for fibroatheroma detection and possible treatment strategies. CABG = coronary artery bypass graft surgery; IVUS = intravascular ultrasound; NIRS = near-infrared spectroscopy; OCT = optical coherence tomography; PCI = percutaneous coronary intervention; RF-IVUS = radiofrequency intravascular ultrasound.

the accuracy of fibroatheroma detection at the minimum lumen area from 75% to 89% among all of the cross sections ($p < 0.05$) and from 48% to 88% ($p < 0.05$) in cross sections with IVUS-detected calcium $\geq 35.5°$. When either superficial IVUS attenuation or lipid-rich plaque were present, detection of fibroatheroma significantly improved compared with IVUS alone in the overall lesion group, although NIRS alone performed very well at the tightest stenosis cross section.

What do these findings mean for everyday clinical practice? First, they confirm that superficial IVUS attenuation is a highly specific finding for fibroatheroma, which is especially important for centers that do not have the combined NIRS/IVUS system.

Second, they demonstrate that the combined NIRS/IVUS system has good performance characteristics for fibroatheroma detection, by allowing evaluation of both structure and composition.

FIBROATHEROMA DETECTED: NOW WHAT?

What to do after a fibroatheroma is detected during cardiac catheterization is a work in progress (Figure 1).

To date, there are no randomized, controlled clinical trials demonstrating that procedure modification on the basis of fibroatheroma detection improves clinical outcomes. Nevertheless, the following courses of action can be considered.

First, fibroatheroma detection could help identify the culprit lesion (or lack thereof) for an acute coronary syndrome, in cases in which angiographic findings are inconclusive.

Second, fibroatheroma detection within a lesion for which PCI is planned suggests a high risk for periprocedural myocardial infarction (9,10) due to distal embolization and/or aggressive in situ thrombus formation (11). Potential clinical strategies to mitigate this risk include vasodilator administration (nicardipine is the authors' preferred medication due to longer half-life and modest hypotensive effect), aggressive anticoagulation (with addition of a glycoprotein IIb/IIIa inhibitor, which is usually given as bolus only without post-PCI infusion), attempts for plaque "vaporization" (e.g., by using laser), and deployment of an embolic protection device (usually a filter that can capture both embolized plaque and/or thrombus) (12). Although these steps are logical, their

use remains empiric and pre-supposes significant local expertise in complex coronary interventions and use of embolic protection devices. Moreover, use of embolic protection devices in native coronary arteries is off-label (they are only approved for use in saphenous vein grafts).

Third, fibroatheroma detection within a lesion treated with PCI may allow for optimal stent selection (13). Using a long-enough stent to completely cover the fibroatheroma may reduce the rate of acute stent thrombosis (14), and possibly restenosis.

Fourth, fibroatheroma detection within non-PCI target lesions identifies the artery and the patient as potentially being at high risk for coronary events that could potentially be lowered by intensive medical therapy. In patients with multiple obstructive lesions and fibroatheromas, revascularization with coronary artery bypass graft surgery may allow protection of multiple myocardial areas "at risk," although this hypothesis remains to be proven. In the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study, the highest risk plaques (thin cap fibroatheromas with $\geq$70% plaque burden and $\leq$4 mm^2 minimum lumen area) had an 18.2% 3-year risk for causing a major adverse cardiac event (15). Whether fibroatheroma detection using NIRS/IVUS will provide better discrimination for future events is currently being examined in several studies, such as the (LRP) Lipid-Rich Plaque study (NCT02033694) and the PROSPECT II (A Multicentre Prospective Natural History Study Using Multimodality Imaging in Patients With Acute Coronary Syndromes) trial (NCT02171065).

The study has important limitations. Whether additional imaging information (e.g., measurement of cap thickness using OCT) will enhance the predictive capacity of NIRS/IVUS findings and the optimal choice of lesion treatments (either local, e.g., bioabsorbable scaffold implantation, or systemic, e.g., a high-dose statin or in the future administration of a proprotein convertase subtilisin/kexin type 9 inhibitor) will require additional studies. Additional studies are also needed to determine that the performance of NIRS/IVUS in vivo matches the performance observed in this autopsy study. Unraveling the secrets of fibroatheromas and their optimal management promises to be a long voyage, full of adventure and discovery, yet with important critical implications for our patients and our practices.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Emmanouil S. Brilakis, VA North Texas Health Care System, The University of Texas Southwestern Medical Center at Dallas, Division of Cardiology (111A), 4500 South Lancaster Road, Dallas, Texas 75216. E-mail: esbrilakis@gmail.com.

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