Atherosclerosis is the main cause of coronary artery disease (CAD), which is today the leading cause of death worldwide and will continue to be the first in the world in 2030. Vulnerable coronary plaques are usually characterized by a high content of necrotic core, a thin inflamed fibrous cap (intense accumulation of macrophages) and scarce presence of smooth muscle cells. None of these characteristics can be estimated by coronary angiography, which on the contrary underestimates the magnitude of atherosclerotic burden, particularly in earlier stage disease when positive vascular remodeling may allow “normal” lumen caliber despite substantial vascular wall plaque. The recognition of the ubiquity of substantial but non-flow limiting lesions that may be at high risk for subsequent plaque rupture has resulted in a paradigm shift in thinking about the pathophysiology of CAD, with the focus no longer solely on the degree of arterial luminal narrowing. This growing need for more information about coronary atherosclerosis in order to identify patients and lesions at risk for complications during PCI and for future adverse cardiac events has been the primary impetus for the development of novel intracoronary imaging methods able to detect plaque composition, in particular presence of a necrotic core/lipid pool, such as intravascular ultrasound virtual histology and near-infrared spectroscopy. These imaging technologies and their clinical and clinical/research applications are discussed in detail. (Circ J 2014; 78: 1531 – 1539)

Key Words: Atherosclerosis; Imaging; Intravascular ultrasound; Near-infrared spectroscopy

Coronary angiography depicts arteries as a planar silhouette of the contrast-filled lumen; of note, it does not provide visualization of the vessel wall and is unsuitable for complete assessment of atherosclerosis. Angiographic disease assessment is based on comparison of the stenotic segment with the adjacent, “normal-appearing” coronary, which is often an incorrect assumption because of the diffuse nature of atherosclerosis, as shown by pathological and intravascular ultrasound (IVUS) studies.1

Grayscale IVUS is the modality that has been established as the gold standard for in vivo imaging of the wall of coronary arteries.2,3 However, the grayscale representation of the coronary vessel wall and plaque morphology in combination with the limited resolution of the current IVUS catheters makes it difficult, if not impossible, to qualitatively (eg, visually) identify the plaque morphology similarly to histopathology, the gold standard for characterizing and quantifying coronary plaque tissue components.4

This limitation has been partially overcome by new IVUS-based tissue characterization techniques, such as virtual histology IVUS (VH-IVUS; Volcano Therapeutics, Rancho Cordova, CA, USA), which are able to identify the necrotic core of the coronary plaque that has been variously related to clinical risk factors, and to risk of adverse events in the recent PROSPECT study.5-7 However, a lot of concern has been raised about the reliability of this necrotic core detection ability.8,9 For this reason, new tissue characterization imaging techniques have been developed, such as near-infrared spectroscopy (NIRS; Lipiscan, InfraReDx Inc, Burlington, MA, USA), which is based on chemical signals and has been tested in various studies and will be applied in the upcoming PROSPECT II study.10,11

The aim of this review is to discuss the value of these different techniques in identifying vulnerable plaque in interventional cardiology, in the light of past, present and future studies.

Natural History of Atherosclerosis

Although a detailed description of atherosclerosis development and composition is beyond the scope of this review, some concepts are important to support the use of tissue characterization imaging modalities for plaque characterization. In brief, acute coronary syndromes (ACSs) are often the first manifestation of coronary atherosclerosis, making the identification of plaques at high risk of complication an important component of strategies to reduce casualties associated with ath-
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kocyte recruitment, intracellular lipid accumulation (foam cells), smooth muscle cell migration and proliferation, expansion of the extracellular matrix, neo-angiogenesis, tissue necrosis and mineralization in the later stages. The ultimate characteristic of an atherosclerotic plaque at any given time depends on the relative contribution of each of these features. Thus, in histological cross-sections, the pathologic intimal thickening is rich in proteoglycans and lipid pools, without a trace of necrotic core. Conversely, the necrotic core appears in the fibroatheroma (FA), which is the precursor lesion of symptomatic heart disease. Thin-capped FA (TCFA) is a lesion characterized by a large necrotic core containing numerous cholesterol clefts, cellular debris and microcalcifications. The overlying fibrous cap is thin and rich in inflammatory cells, macrophages.

erosclerosis.

Pathological studies have demonstrated that ruptured plaques are mainly located in the proximal portions of the left anterior descending and circumflex arteries, and are more dispersed in the right coronary artery. This tendency of advanced plaques to develop preferentially in these locations has been explained by the low shear stress conditions generated in areas with tortuosity or many branches. Low shear stress may induce the migration of lipid and monocytes into the vessel wall, leading to the progression of the lesion towards a plaque with high risk of rupture.

An atheroma is formed by an intricate sequence of events, not necessarily in a linear chronologic order, that involves extracellular lipid accumulation, endothelial dysfunction, leucocyte recruitment, intracellular lipid accumulation (foam cells), smooth muscle cell migration and proliferation, expansion of the extracellular matrix, neo-angiogenesis, tissue necrosis and mineralization in the later stages. The ultimate characteristic of an atherosclerotic plaque at any given time depends on the relative contribution of each of these features. Thus, in histological cross-sections, the pathologic intimal thickening is rich in proteoglycans and lipid pools, without a trace of necrotic core. Conversely, the necrotic core appears in the fibroatheroma (FA), which is the precursor lesion of symptomatic heart disease. Thin-capped FA (TCFA) is a lesion characterized by a large necrotic core containing numerous cholesterol clefts, cellular debris and microcalcifications. The overlying fibrous cap is thin and rich in inflammatory cells, macrophages.

Figure 1. Intravascular ultrasound (IVUS) signal is obtained from the vessel wall (A). Grayscale IVUS imaging is formed by the envelope (amplitude) (B) of the radiofrequency signal (C). By grayscale, atherosclerotic plaque can be classified into 4 compositional categories: soft, fibrotic, calcified, and mixed plaques. (D) Cross-sectional view of a grayscale image. The blue lines limit the actual atheroma. The frequency and power of the signal commonly differ between tissues, regardless of similarities in amplitude. From the backscatter radiofrequency, virtual histology is obtained (E) and is able to detect 4 tissue types: necrotic core, fibrous, fibrofatty, and dense calcium.
and T lymphocytes with a few smooth muscle cells. Our current understanding of plaque biology suggests that ~60% of clinically evident plaque rupture originates within an inflamed TCFA.16,17

### Tissue Characterization Using VH-IVUS

The first commercial available radiofrequency (RF) signal-based tissue composition analysis tool was the so-called VH-IVUS (Volcano Therapeutics) software. It uses in-depth analysis of the backscattered RF signal to provide a more detailed description of the atheromatous plaque’s composition and is performed with either a 20MHz, 2.9F phased-array transducer catheter (Eagle Eye™ Gold, Volcano Therapeutics) or 45MHz 3.2F rotational catheter (Revolution, Volcano Therapeutics) that acquires ECG-gated IVUS data.7 The main principle of this technique is that it uses not only the envelope amplitude of the reflected RF signals (as grayscale IVUS does), but also the underlying frequency content to analyze the tissue components present in the coronary plaque (Figure 1). This combined information is processed using autoregressive models and thereafter in a classification tree that determines 4 basic plaque tissue components:5 (1) fibrous tissue (dark green), (2) fibrofatty tissue (light green), (3) necrotic core (red), and (4) dense calcium (white). The current software version assumes the presence of a media layer, which is artificially added, positioned just inside the outer vessel contour. This technique has been compared in several studies against histology in humans and other species (Table 1).5,6,9,18-21

### Plaque Characterization by VH-IVUS

Using VH-IVUS (Figure 2), it is possible to define the various stages of atherosclerosis.22 The definition of an IVUS-derived TCFA, for example, is a lesion fulfilling the following criteria in at least 3 consecutive frames: (1) plaque burden ≥40%, and (2) confluent necrotic core ≥10% in direct contact with the lumen (ie, no visible overlying tissue).22

Hong et al23 reported the frequency and distribution of TCFA identified in a 3-vessel VH-IVUS study of patients with ACS (n=105) or stable angina (SAP; n=107). There were 2.5±1.5 TCFAs per patient in the ACS group and 1.7±1.1 in the SAP group (P<0.001). Presentation of ACS was the only independent predictor for multiple VH-derived TCFA (VH-TCFAs) (P=0.011), and 83% of VH-TCFAs were located within the first 40mm of the coronary. By use of VH-IVUS, the serial changes in VH plaque type have been also investigated. In particular, Kubo et al showed that most VH-TCFAs healed during a 12-month follow-up. However, during this time new VH-TCFA developed in general, pathologic intimal thickening and necrotic core plaques had a significant progression compared with fibrotic and fibrocalcific plaques in terms of increase in plaque area and decrease in lumen.24

The potential value of VH-TCFA in the prediction of adverse coronary events was evaluated in an international multicenter prospective study, the Providing Regional Observations to Study Predictors of Events in the Coronary Tree study (PROSPECT study).8 The PROSPECT trial was a natural history study of ACS patients, all of whom underwent PCI for their culprit lesion at baseline, followed by angiography and VH-IVUS of the 3 major coronary arteries. A TCFA with a minimum luminal area ≤4mm² and a large plaque burden

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**Table 1. Comparison of VH-IVUS With Histology in Humans and Other Species**

<table>
<thead>
<tr>
<th>VH-IVUS</th>
<th>Description</th>
<th>Date</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nair et al16</td>
<td>Coronary plaque classification with IVUS radiofrequency data analysis</td>
<td>Ex vivo 2002</td>
<td>95%</td>
<td>98%</td>
<td>94%</td>
</tr>
<tr>
<td>Nasu et al17</td>
<td>Accuracy of in vivo coronary plaque morphology assessment: a validation study of in vivo VH compared with in vitro histopathology</td>
<td>In vivo 2006</td>
<td>92%</td>
<td>94%</td>
<td>91%</td>
</tr>
<tr>
<td>Nair et al18</td>
<td>Automated coronary plaque characterization with IVUS backscatter: ex vivo validation</td>
<td>Ex vivo 2007</td>
<td>92%</td>
<td>96%</td>
<td>98%</td>
</tr>
<tr>
<td>Granada et al19</td>
<td>In vivo plaque characterization using VH-IVUS in a porcine model of complex coronary lesions</td>
<td>In vivo 2007</td>
<td>84%</td>
<td>88%</td>
<td>90%</td>
</tr>
<tr>
<td>Van Herk et al20</td>
<td>Validation of in vivo plaque characterization by VH in a rabbit model of atherosclerosis</td>
<td>In vivo 2009</td>
<td>95%</td>
<td>99%</td>
<td>93%</td>
</tr>
<tr>
<td>Thim et al21</td>
<td>Unreliable assessment of NC by VHTM IVUS in porcine coronary artery disease</td>
<td>Ex vivo 2010</td>
<td>82%</td>
<td>88%</td>
<td>90%</td>
</tr>
<tr>
<td>Brugaletta et al22</td>
<td>Qualitative and quantitative accuracy of VH-IVUS for detection of NC in human coronary arteries</td>
<td>In vivo 2014</td>
<td>95%</td>
<td>99%</td>
<td>96%</td>
</tr>
</tbody>
</table>

DC, dense calcium; FF, fibrofatty; FT, fibrous tissue; IVUS, intravascular ultrasound; NC, necrotic core; VH, virtual histology.
(≥70%) had a 17.2% likelihood of causing an event within 3 years. Interestingly, the anticipated high frequency of acute thrombotic cardiovascular events did not occur, with only a 1% rate of myocardial infarction (MI) and no deaths directly attributable to nonculprit vessels over the 3 years of follow-up. These results suggest that nonculprit, yet obstructive coronary plaques were most likely to be associated with increasing symptoms rather than thrombotic acute events, with 8.5% of patients presenting with worsening angina and 3.3% with unstable angina. The PROSPECT findings were recently confirmed by the VIVA study. Of note, the findings of the PROSPECT trial did not translate in clinical practice into a percutaneous preventive treatment of VH-TCFA.

Assessment of Drug Effect on Atherosclerosis by VH-IVUS

VH-IVUS has so far been used in various studies to show serial changes of plaque composition in patients treated with various drugs (Table 2).

In one of the studies, patients with SAP (n=80) treated with fluvastatin for 1 year had significant regression of the plaque volume, and changes in the atherosclerotic plaque composition with a significant reduction of the fibrofatty volume (P<0.0001). This change in the fibrofatty volume had a significant correlation with changes in the low-density lipoprotein-cholesterol (LDL-C) level (r=0.703, P<0.0001) and in the high-sensitivity C-reactive protein level (r=0.357, P=0.006). Of note, the necrotic core did not change significantly. The same data were found with the use of pitavastatin.

In another study, Hong et al randomized 100 patients with SAP and ACS to either rosvastatin 10 mg or simvastatin 20 mg for 1 year. The overall necrotic core volume significantly decreased (P=0.010) and the fibrofatty plaque volume increased (P=0.006) after statin treatment. In particular, there was a significant decrease in the necrotic core volume (P=0.015) in the rosvastatin-treated subgroup. By multiple stepwise logistic regression analysis, they showed that the only independent clinical predictor of decrease in the necrotic core volume was the baseline high-density lipoprotein-cholesterol level (P=0.040, odds ratio 1.044, 95% confidence interval (CI) 1.002–1.089).

The IBIS-2 study compared the effects of 12 months of treatment with darapladib (oral Lp-PLA2 inhibitor, 160 mg daily) or placebo in 330 patients. Endpoints included changes in necrotic core size (VH-IVUS), and atheroma size (grayscale IVUS). Background therapy was comparable between groups, with no difference in LDL-C at 12 months (placebo: 88±34 and darapladib: 84±31 mg/dl, P=0.37). In the placebo-treated group, however, necrotic core volume increased significantly, whereas darapladib halted this increase, resulting in a significant treatment difference of −5.2 mm³ (P=0.012). These intraplaque compositional changes occurred without a significant treatment difference in total atheroma volume.

Despite all these studies, there is not a single report describing a clear direct association of a reduction in plaque size and/or plaques with a reduction in clinical events. The best attempt was a pooled analysis of 4,137 patients from 6 clinical trials that used serial IVUS: the relationship between baseline and the change in percent atheroma volume (PAV) with incident major adverse cardiovascular events (MACE) was investigated. Each standard deviation increase in PAV was associated with a 1.32-fold (95% CI 1.22–1.42; P<0.001) greater likelihood of experiencing MACE.

### Table 2. Serial Changes of Plaque Composition by VH-IVUS in Patients Treated With Various Statins

<table>
<thead>
<tr>
<th>VH-IVUS studies</th>
<th>Serruys et al</th>
<th>RCT 2008</th>
<th>Darapladib</th>
<th>NC volume by VH-IVUS</th>
<th>Darapladid significantly reduced NC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasu et al</td>
<td>Observational</td>
<td>2009</td>
<td>Fluvastatin</td>
<td>40</td>
<td>Overall tissue characterization by VH-IVUS</td>
</tr>
<tr>
<td>Hong et al</td>
<td>RCT 2009</td>
<td>Simvastatin</td>
<td>50</td>
<td>Overall tissue characterization by VH-IVUS</td>
<td>Both reduced NC and increased FF volume</td>
</tr>
<tr>
<td>Toi et al</td>
<td>RCT 2009</td>
<td>Atorvastatin</td>
<td>80</td>
<td>Overall tissue characterization by VH-IVUS</td>
<td>Pitavastatin reduced plaque and FF volumes</td>
</tr>
</tbody>
</table>

RCT, randomized controlled trial.

### Tissue Characterization Using Intracoronary NIRS

A NIRS catheter system (Lipiscan; InfraReDx Inc) has been recently developed for invasive detection of the lipid core in plaque composition. The development of NIRS for use in human coronary arteries has been a complex process requiring more than 15 years. The initial studies from numerous groups thoroughly demonstrated NIRS as a valid methodology for measuring the chemical components of atherosclerotic plaque. In the next step, a catheter-based system that could access the coronary arteries in vivo and rapidly perform the thousands of longitudinal and rotational measurements necessary to image the coronaries through flowing blood was developed; the system acquires approximately 1,000 NIRS measurements/12.5 mm of artery scanned and each measurement interrogates an approximate volume of 1–2 mm³ of arterial wall perpendicular to the long axis of the catheter and centered on the catheter’s optical tip. This NIRS catheter is well-suited for analysis of lipid core in vivo because it can penetrate the blood and rapidly perform the thousands of longitudinal and rotational measurements necessary to image the coronaries through flowing blood was developed; the system acquires approximately 1,000 NIRS measurements/12.5 mm of artery scanned and each measurement interrogates an approximate volume of 1–2 mm³ of arterial wall perpendicular to the long axis of the catheter and centered on the catheter’s optical tip. This NIRS catheter is well-suited for analysis of lipid core in vivo because it can penetrate the blood and several millimeters into the tissue; it overcomes the problem of cardiac motion because it uses an ultrafast scanning laser, and provides a chemical measure of the LCP target of interest. This catheter was used in an extensive ex vivo study using human coronary autopsy specimens to develop an algorithm for the detection of LCP. The LCP of interest was defined as a FA containing a necrotic core at least 0.2 mm thick with a circumferential span of at least 60 degrees on cross-section. In a prospective validation of the system for detection...
From VH to NIRS

Successfully demonstrated that high-quality NIRS signals, similar to those validated in human coronary autopsy specimens, were obtained from the coronary arteries of living patients, supporting the feasibility of invasive detection of coronary LCP with this novel system. Excellent reproducibility of the NIRS findings during repeat pullbacks has been recently demonstrated.

The NIRS system consists of a 3.2F rapid exchange catheter, a pullback and rotation device, and a console. The probability of the LCP for each scanned arterial segment is dis-

![Figure 2. Examples of various atherosclerotic plaques in different stages, classified by virtual histology (VH). Lumen contour (yellow line) and vessel contour (red line) are shown. In the VH images, necrotic core is coded as red, dense calcium as white, fibrous tissue as dark green and fibrofatty tissue as light green. PIT, pathological intimal thickening; FC, fibrocalcific plaque; FA, fibroatheroma; TCFA, thin-cap fibroatheroma; CaFA, calcified fibroatheroma; CaTCFA, calcified thin-cap fibroatheroma.](image1)

![Figure 3. Image obtained by near-infrared spectroscopy displayed as a chemogram and block chemogram. The chemogram shows the scanned arterial segment as a map, with the x-axis indicating the pullback position in millimeters and the y-axis as the circumferential position of the measurement, as if the coronary vessel was split open along its longitudinal axis. The block chemogram shows the presence of lipid core as a 2-mm segment using the top 90th percentile information within each 2-mm segment. The probability of lipid is displayed in a color scale from red (low probability) to yellow (high probability), through orange and tan. In the example shown, please note the presence of lipid core as yellow from the 20 mm to the 40 mm of the pullback.](image2)
NIRS-IVUS Clinical Applications

Identification of LCP with NIRS has hypothetically the potential to improve the safety of stenting, including optimization of the length of vessel to stent, assurance of adequate stent implantation, and identification of lipid-core lesions at higher risk of distal embolization, possibly leading to effective utilization of distal embolic protection devices (EPDs) in the native coronaries. The NIRS-IVUS device also shows promise in the identification of vulnerable plaque, which may lead to strategies to prevent future coronary events.

Prevention of Periprocedural MI

Periprocedural MI is associated with short- and long-term adverse outcomes. In particular, embolization of the lipid core of stenotic plaques following PCI has been demonstrated as an important cause of periprocedural no-reflow and MI, even in the absence of angiographic intracoronary thrombus. Because periprocedural MI can prolong hospital stay and is an impediment to more frequent performance of stenting in the less costly outpatient setting, pre-PCI identification of such plaques at high risk of embolization could lead to the use of preventive strategies (eg, distal EPD), thereby enhancing the safety, efficacy, and cost-effectiveness of stenting. 

Recent evidence suggested that the large area of LCP identified by NIRS might be associated with distal embolization and periprocedural MI. The COLOR Registry, an ongoing prospective observational study of patients undergoing NIRS prior to PCI, provided additional evidence of this capability of NIRS. In that study, the extent of the LCP in the treated region was calculated as the maximal lipid-core burden index (LCBI) for each 4-mm longitudinal segment (maxLCBI$_{4\text{mm}}$) within the treated region. Results showed that periprocedural MI occurred in 50% of cases of LCP with maxLCBI$_{4\text{mm}}$≥500 (22.6% of the lesions) and in only 4.2% of cases of LCP with a low maxLCBI$_{4\text{mm}}$ (P=0.0002). Periprocedural MI can also develop in association with post-stent disappearance of yellow LCP, presumably because of rupture and release of LCP contents with distal embolization.

The knowledge that dilation of a stenosis containing a large LCP, identified by NIRS, carries a 50% risk of causing a periprocedural MI indicates the need for preventive therapy. The use of an EPD to prevent distal embolization of plaque contents, already used in PCI of vein grafts and carotid arteries, is a particularly promising approach. Although prior studies of rich plaques by NIRS and VH, respectively; however, the correlation between NIRS and VH was poor. There is an important consideration to make regarding the validation of NIRS and VH-IVUS in order to understand the difference in the cardinal features between VH necrotic core and NIRS lipid core, which may be the source of this disagreement. For the validation of NIRS, LCP was defined as a FA with lipid core >60 degrees in circumferential extent, >200 μm thick, with a fibrous cap having a mean thickness <450 μm and correlated with each chemogram block. For the validation of VH-IVUS, necrotic core was defined as the region comprising cholesterol clefts and foam cells. Some lipid components in the presence of collagen are also coded as fibrofatty tissue. The fundamental differences in the principles of each technique—VH is based on pattern classification of backscattering ultrasound signal, whereas NIRS is based on near-infrared spectral signals—and their respective limitations should be therefore taken into account in the interpretation of this disagreement between NIRS and VH-IVUS.
the use of EPDs during stenting of lesions in the native coronary arteries failed to show clinical benefit, those studies did not characterize, by intracoronary imaging, the types of plaques most likely to embolize and therefore to benefit from the use of an EPD. The potential ability of NIRS-guided use of an EPD to prevent periprocedural MI has been tested in a prospective randomized trial, named CANARY (Coronary Assessment by Near-infrared of Atherosclerotic Rupture-prone Plaques), the results of which will be available at the end of 2014 (NCT01268319).

Optimization of PCI
The current standard of care consists of selection and placement of a coronary stent on the basis of angiographic information alone. Although use of angiography alone generally produces good outcomes, it has been suggested that stent complications (dissection, early or late stent thrombosis, or restenosis) might result from a geographical miss in stent placement (stent ends up in an area with high plaque burden) or from incomplete stent expansion or malapposition. There is evidence from prior randomized trials that IVUS guidance reduces complications. Another application of the NIRS-IVUS device in clinical practice would be to assist in decisions regarding the location and length of artery to be stented. Recent clinical cases revealed that placement of the ends of a stent over a LCP could result in high frequency of stent thrombosis. NIRS can therefore help avoid placement of the ends of a stent on a LCP by accurately and precisely revealing the plaque’s location. Longer stents can be chosen to extend into vessel free of LCP or conversely the choice of a shorter stent would be supported by the absence of LCP in a given landing zone. Long-term studies are required to determine whether NIRS-informed stent length decisions result in better clinical outcomes.

Identification of Vulnerable Plaque
Given the validated capabilities of NIRS for detection of LCP, NIRS-IVUS also has the potential to identify vulnerable plaques and in particular to guide the treatment of lesions causing an intermediate degree of coronary stenosis. As early evidence mounts for the greater propensity for rupture and more rapid progression when LCPs are present, the presence of LCPs in an angiographically intermediate stenosis may support a tailored stenting.

The ability of NIRS to identify vulnerable plaque has been confirmed by the fact that a particular longitudinal distribution of LCP can be demonstrated in the 3 coronary vessels similar to that of histology. A recent study has also compared the presence of LCP between ACS and SAP patients: target lesions responsible for ACS were frequently composed of LCP. In addition, LCP were often found in remote, non-target areas, more commonly in patients with ACS than in those with SAP. A threshold of 400 in the maximum LCBI has been demonstrated as signature of plaques causing ST-elevation MI.

InfraReDx Inc has initiated an observational study of cholesterol in coronary arteries to determine the relationship between NIRS findings and subsequent events over a 2-year period (COLOR registry, NCT00831116). The study aims to enroll 1,000 patients in 14 centers across the USA and its results will be available in 2015.

Much interest is already focused on the PROSPECT II trial, announced by the Cardiovascular Research Foundation and the Uppsala Clinical Research Center a few months ago. PROSPECT II is an investigator initiated multicenter, prospective registry study that will assess in 900 ACS patients the ability of NIRS to identify non-flow obstruction vulnerable plaques that subsequently lead to coronary events at 3-year follow-up. All 3 coronary arteries in each patient will be examined by IVUS and NIRS. In the PROSPECT ABSORB substudy, the investigators will evaluate the ability of a biodegradable scaffold to safely increase the luminal dimensions of vulnerable plaque. In this substudy, 300 patients with a plaque at high risk of causing future events, identified according to the original PROSPECT study, will be randomized to treatment with ABSORB BVS plus guideline-directed medical therapy or medical therapy alone, with each patient undergoing angiography and IVUS/NIRS at 2-year follow-up. The findings from these 2 interesting studies, which will be available in 2015, will be determinant for understanding the ability of NIRS to identify high-risk lesions and whether preventive treatment of such lesions is feasible.

Additional Clinical Uses of NIRS
NIRS is likely to be helpful in the choice of more intensive lipid modification or antithrombotic therapies in some patient subgroups. The presence of extensive LCP might, indeed, indicate the need for more intensive or different types of LDL-lowering therapies. NIRS can be used also in the development of antiatherosclerotic medications by providing a surrogate endpoint in plaque regression/stabilization studies. In particular, the ability of NIRS to assess the lipid content of plaques may be a more effective means of identifying the beneficial effect of an agent than IVUS. Given these hypotheses, the IBIS-3 (Integrated Biomarker and Imaging Study) trial has started in order to determine the effect of 12-month intensive rosuvastatin therapy on the content of necrotic core (VH-IVUS) and lipid-containing region (NIRS) at 12 months in a non-intervened coronary artery of ACS patients.

Another potential future use could be to more fully inform the decision to perform PCI vs. coronary artery bypass grafting (CABG), based on the presence, patterns and extent of LCP. Most notably, changes could be envisioned in the determination of the presence of “3-vessel disease” or patients who are “not candidates for PCI”. For example, it is reasonable to hypothesize that LCP-free, fibrotic stenoses in all 3 coronary vessels may be better treated with stents. In contrast, diffuse lipids in all 3 vessels, either stenotic or non-stenotic, may turn out to be better treated by CABG. The usefulness of a combination of Syntax score with NIRS data in the so-called “plaque compositional Syntax score” needs to be tested in future trials.

Conclusions
VH-IVUS and NIRS are useful tools for the evaluation of coronary atherosclerosis. It is, however, noteworthy that despite much data supporting the ability of both techniques to identify vulnerable plaque, neither is currently used for deciding whether a vulnerable plaque should be treated or not in order to prevent a coronary event. The findings of the PROSPECT trial were not sufficient to support it. The data coming in the next years from the PROSPECT II trial will probably answer this question.

References


