The pursuit to identify vulnerable plaque has been relentless, as it is responsible for major healthcare problems, such as sudden cardiac death and acute coronary syndromes, including acute myocardial infarction (AMI). Per definition, vulnerable plaque is plaque that is prone to rupture but has not yet ruptured. The features associated with vulnerable plaque include a large lipid core, thin fibrous cap overlying the lipid core, increased macrophage activity, positive remodeling, and increased vasa vasorum. Among these 5 components, the 2 most important ones are probably the large lipid core and thin fibrous cap.

Since 95% of ruptured fibrous caps are thinner than 65 μm, noninvasive diagnostic tests such as computed tomography and magnetic resonance do not have sufficient resolution to accurately measure this thin structure. Therefore, a number of intravascular diagnostic modalities have been extensively tested over the last decade (Table). Among those most widely tested are radiofrequency intravascular ultrasound, angioscopy, and optical coherence tomography. Recently, near infrared spectroscopy (NIRS) received US Food and Drug Administration approval. It is now being actively investigated.

Radiofrequency intravascular ultrasound was used in the PROSPECT trial and showed that plaque burden >70%, virtual histology-thin–cap fibroatheroma, and minimal luminal area ≤4.0 mm² are factors for composite major adverse cardiac events during the 3-year follow-up period. Although the factors for future cardiac events were identified, all 3 predictors are related to plaque burden, and, therefore, it is not surprising that these factors predict progressive or unstable angina rather than sudden cardiac death or acute myocardial infarction (AMI). Unfortunately, because of the low event rate and a small sample size, the predictors for sudden cardiac death or AMI were not identified. Angioscopy is mainly used in Japan. The main problem with this technology is that interpretation is subjective, and only the information from the luminal surface of the vessel wall can be acquired. Although surface color may reflect underlying pathology inside the vessel wall, accurate information on plaque characteristics is impossible to obtain with this technology.

Optical coherence tomography has become popular over the last several years. With its high-resolution, detailed structural information is easily obtained, and a lot of vascular complications following percutaneous coronary intervention are visualized. The main problem is that the clinical significance of these vascular changes is unknown, and interventional cardiologists are tempted to react to the changes that they see on optical coherence tomography following percutaneous coronary intervention. The current NIRS system, using a wavelength of 800 to 2500 nm, converts diffuse reflectance signals from an object to produce a spectrum. Spectra are used to produce an algorithm to display on a chemogram, on which yellow represents lipid. The original chemogram is then used to create a block chemogram.

In this issue of Circulation: Cardiovascular Interventions, Madder and colleagues showed that lipid core plaque (LCP) was detected in 84.4% of the culprit lesion in acute coronary syndrome (ACS) and in 52.8% of patients with stable angina pectoris. The prevalence of LCP by NIRS in this report is consistent with previous optical coherence tomography studies. In 2005, our group reported that lipid-rich plaque was found in 90% of patients with AMI, in 75% of patients with ACS, and in 58% of patients with stable angina pectoris. Kubo and colleagues also reported very similar data in 2007 and 2008: lipid-rich plaque in 93% of patients with AMI, in 71% of patients with ACS, and in 42% of patients with stable angina pectoris. The novel information from the current study is that, in the remote lesion, LCP was found in 73.3% of patients with ACS and in 17.6% of the stable angina pectoris group. This is an important finding, indicating that there is panvascular inflammation in patients with ACS. Therefore, anti-inflammatory therapy, in addition to cholesterol-lowering treatment, may have additional value in this subset of patients.

Although NIRS may be one of the most sensitive modalities to detect lipid core plaque, the first major problem with this technology is that it does not provide information on the depth of lipid core. As long as the reflectance signal is strong enough, it will produce spectra indicating lipid, regardless of its depth. Second, the accurate measurement of lipid volume/burden with NIRS has not been validated. The definition of LCP by NIRS is fibroatheroma with lipid core >60° in circumferential extent, >200 μm thick, with a fibrous cap having a mean thickness <450 μm. In this report, LCP was defined as a 2-mm segment, and the accurate length was not measured. Instead, LCP was divided, using a cut-off length of 4 mm. These parameters are rather arbitrary, and objective measurements are lacking. Block chemogrom was used in this

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The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

From Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts.

Correspondence to Ik-Kyung Jang, MD, PhD, Cardiology Division, Bigelow 8, Massachusetts General Hospital, 55 Fruit St, Boston, MA 02114. E-mail ijang@partners.org

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study. A block is a summary of 300 NIR measurements in a 2-mm arterial segment. Each reading is ranked from zero to 1 for likelihood of LCP. The 90th percentile reading is considered to represent the summary of the block. For example, chemogram with >0.60 reading would be displayed as lipid, whereas chemogram with ≤0.60 reading would be displayed as nonlipid. With these problems, the detection of lipid with NIRS would have limited clinical value. To overcome these pitfalls, a new combined NIRS and intravascular ultrasound catheter was developed; however, since intravascular ultrasound is known to be insensitive to visualize lipid inside a plaque, the additional value of this new system remains to be evaluated.

The fundamental question relevant to all intravascular diagnostics for detection of vulnerable plaque is whether the information provided has clinical significance. Atherosclerosis is a process of continuous plaque disruption and healing, as evidenced by multiple layers inside plaque in autopsy studies. The majority of plaque disruptions are clinically silent and contribute to progression of plaques. Which plaque disruption would result in the formation of occlusive thrombus is not known. The degree of preexisting plaque size, morphology of plaque rupture, vasospasm, and thrombogenic/inflammatory factors in circulation may all contribute to the ultimate outcome of a plaque disruption. Since no biomarker has been shown to be associated with immediate acute cardiac event, the only information we can obtain with the current technology is plaque morphology; however, in light of the known pathophysiology, it is unlikely that morphology alone will be the answer.

What is the future of NIRS? Is it another tool for research, or is it going to help us improve patient care? As described above, the data from this study is consistent with the previously reported data using another modality and, therefore, confirms the previous findings rather than generating new data. In contemporary practice, patients with acute coronary syndrome will be treated with aggressive lipid-lowering and anti-inflammatory therapy, regardless of the findings from intravascular diagnostics. The future of NIRS and other diagnostic technologies will depend on whether the information obtained from the technology will have additional value in improving the outcomes of our patients.

### Disclosures

Dr Jang has received research grants (>$10K) from the following industry: LightLab Imaging/St Jude Medical, Cordis, Abbott Vascular, Medtronic, GSK, and Helena Laboratory during the last 2 years. He expects a grant (> $10K) from InfraReDx this year. Dr Jang has also received a consulting fee (<$10K) from LightLab Imaging/St Jude Medical in 2011.

### References


### Table.

**Comparison of Invasive Diagnostic Modalities for Detection of Vulnerable Plaque**

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Resolution</th>
<th>Fibrous Cap</th>
<th>Lipid Core</th>
<th>Inflammation</th>
<th>Calcium</th>
<th>Thrombus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greyscale-IVUS</td>
<td>150–250 μm</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>+ + +</td>
<td>+</td>
</tr>
<tr>
<td>RF-IVUS</td>
<td>200–250 μm</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>+ + +</td>
<td>+</td>
</tr>
<tr>
<td>IB-IVUS</td>
<td>150 μm</td>
<td>+</td>
<td>++</td>
<td>–</td>
<td>+ + +</td>
<td>+ +</td>
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<tr>
<td>Angioscopy</td>
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<td>–</td>
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<td>+ +</td>
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<tr>
<td>OCT</td>
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<td>+</td>
<td>–</td>
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<tr>
<td>Raman spectroscopy</td>
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<td>–</td>
<td>++</td>
<td>–</td>
<td>–</td>
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</tr>
<tr>
<td>NIRS</td>
<td>NA</td>
<td>–</td>
<td>+ +</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Thermography</td>
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<td>–</td>
<td>+ +</td>
<td>–</td>
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</tr>
<tr>
<td>IV-MRI</td>
<td>160 μm</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+ +</td>
<td>+ +</td>
</tr>
</tbody>
</table>

 IVUS indicates intravascular ultrasound; RF, radiofrequency; IB, integrated backscatter; OCT, optical coherence tomography; NIRS, near infrared spectroscopy; IV-MRI, intravascular magnetic resonance imaging; UK, unknown; NA, not applicable.

Near Infrared Spectroscopy: Another Toy or Indispensible Diagnostic Tool?
Ik-Kyung Jang

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