Imaging Methods Unveil Rupture-Prone Plaque

BY BRUCE JANCIN
Denver Bureau

CHICAGO — A furiously competitive race is on to develop new imaging methods capable of identifying vulnerable coronary plaques.

The first of these technologies to undergo evaluation in prospective clinical trials are virtual histology, palpography, thermography, and multislice CT. They are being assessed in the pioneering Providing Regional Observations to Study Predictors of Events in the Coronary Tree (PROSPECT) study, a 700-patient international trial whose initial enrollees have completed their first year of follow-up, Dr. Gregg W. Stone said in his Hildner Lecture at the annual meeting of the Society for Cardiovascular Angiography and Interventions.

But PROSPECT is only the beginning. At least 14 different noninvasive and 28 catheter-based invasive diagnostic techniques aimed at detecting vulnerable plaques are in development, according to Dr. Stone, professor of medicine at Columbia University and vice chairman of the Cardiovascular Research Foundation, New York.

The goal of this massive research and development effort is to identify asymptomatic coronary lesions that are active, inflamed, and prone to rupture so that in theory they can be preemptively treated before they cause an acute MI.

At this point, progress in vulnerable plaque imaging is well ahead of actual treatment. It is clear, however, that statins and lifestyle modification are not going to be sufficient. This was amply demonstrated in the Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE-IT) trial, in which patients with a history of acute coronary syndrome had a 22% coronary event rate over 2.5 years despite being on 80 mg/day of atorvastatin, Dr. Stone said.

Once it's established that vulnerable plaques can reliably be identified, more aggressive interventions might include drug-eluting stents for high-risk lesions, or perhaps catheter-delivered cryoplasty or photodynamic therapy for regional treatment, although all of this will require demonstration of clinical benefit in prospective trials, the cardiologist continued.

Noninvasive imaging methods are most attractive as tools for population screening, since they in general pose less risk than invasive methods. That's not always true, though. Multislice CT, the noninvasive method that has garnered by far the greatest interest, entails significant exposure to radiation and nephrotoxic contrast media, Dr. Stone noted.

Invasive imaging techniques are more time consuming. But placing a catheter next to an atheroma yields a wealth of data on structure and function.

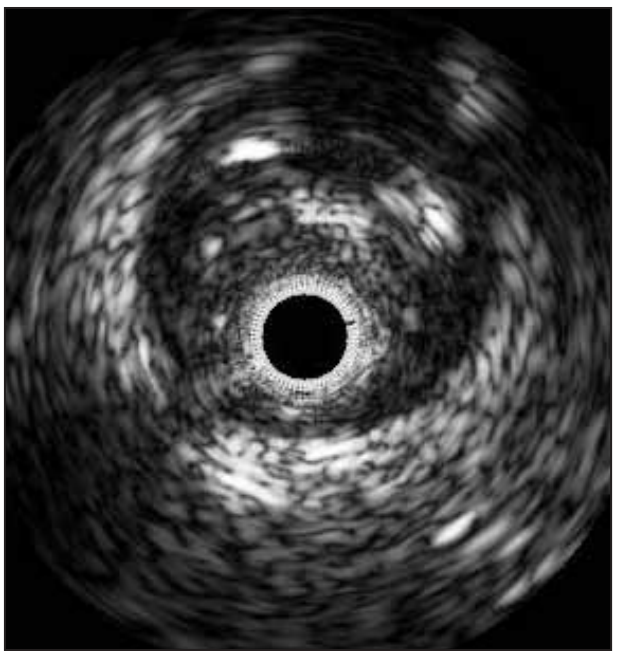
Invasive imaging methods fall into three broad categories: those that assess plaque morphology, such as virtual histology, optical coherence tomography, and vaso vasorum imaging; tools for evaluating plaque activity or composition, including thermography, spectroscopy, and intravascular MRI; and methods of studying a plaque's physical properties, such as palpography, which measures endothelial sheer stress at the plaque's cap.

Thermography relies on the observation that inflamed, unstable coronary plaques have a consistently slightly higher temperature than indolent ones.

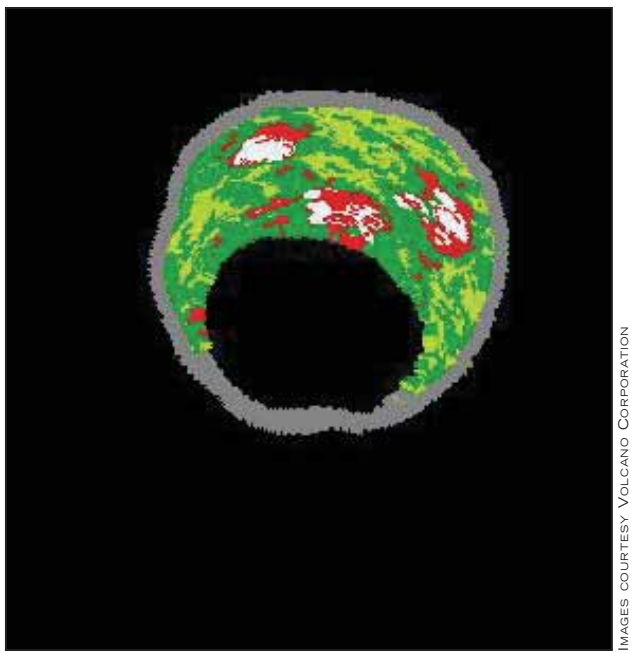
Virtual histology uses intravascular ultrasound (IVUS) spectral analysis to assess plaque composition in four colors rather than the standard IVUS gray scale. This imaging tool, which has been validated in an ex vivo histology study using autopsy specimens, is commercially available from Volcano Corp. Virtual histology permits classification of coronary lesions into four types: fibrous, fibro-fatty, densely calcified, or—what is believed to be most worrisome—plaque having a necrotic core, explained Dr. Stone, who is principal investigator of the PROSPECT study.

PROSPECT, funded by Guidant Corp., is a natural history study in which plaque-imaging findings in patients with acute coronary syndrome will be prospectively correlated with future coronary events during 2-5 years of follow-up.

Dr. Stone is a consultant to Guidant, Volcano, and numerous other medical device manufacturers. ■



A conventional gray scale IVUS image of a coronary atheroma doesn't show the plaque composition details depicted in the adjacent color tissue map image.



A virtual histology image using IVUS spectral analysis: Green is fibrous tissue; red, a necrotic core within the plaque; and white, a calcified area.

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Nontraditional Plasma Markers Fill in LDL's Predictive Gaps

BY ELAINE ZABLOCKI
Contributing Writer

SPARKS, NEV. — Many patients with "normal" levels of LDL cholesterol go on to develop heart disease. "LDL cholesterol is an okay, but not great, predictor of coronary risk," Dr. James A. Underberg said at the annual meeting of the American College of Preventive Medicine.

He urged physicians to look at nontraditional biomarkers that offer new insight into coronary risk and the disease process.

With LDL cholesterol, particle size is not a predictor of risk, said Dr. Underberg, president of the New York Preventive Cardiovascular Society. Instead, "particle number is a predictor and is driving the risk in these patients," he said.

The problem is that LDL cholesterol concentrations often fail to reflect the number of LDL particles and the coronary disease risk associated with them; the number of LDL particles varies widely among patients with similar LDL cholesterol levels.

Several treatments are available for lowering the number of LDL particles, including statins, bile acid sequestrants, niacin, fibrates, and cholesterol absorption inhibitors.

"Counseling about dietary and lifestyle changes tends to get lost in the rush of daily practice because it takes time, but I think it's important," added Dr. Underberg, also of New York University.

"Please note that recommended dietary changes should emphasize fiber and plant phytosterols, not just a low-fat, low-cholesterol diet."

LDL cholesterol concentrations often fail to reflect the number of LDL particles and the coronary disease risk associated with them.

Dr. Underberg also reviewed the importance of lipoprotein (a) as a nontraditional biomarker in cardiovascular risk assessment. It has limited utility as a screening test, but can be a useful measure in patients with a family history of premature coronary disease.

When other risk factors are at an intermediate level, lipoprotein (a) can be useful in deciding how aggressively to treat. Once it has been tested, there is no need to repeat the measurement because it doesn't vary greatly over time.

The high-sensitivity C-reactive protein (CRP) test is another nontraditional but valuable method for assessing cardiovascular risk. CRP is involved in a variety of processes, and probably plays a role in the development of atherosclerosis.

It also helps in predicting coronary risk, and can be used as a prognostic indicator in acute MI. CRP levels do fluctuate, so it is reasonable to repeat this test after 2-3 weeks.

For example, CRP levels can increase in a variety of inflammatory conditions, including acute illness and viral infection, and after dental work.

Physicians should be more aggressive when considering statin use in younger women whose risk justifies use of these drugs.

The Food and Drug Administration requires a "do not use if you are pregnant or breastfeeding" label on prescription statins because of concerns about teratogenic effects. "Many younger women at high risk for cardiac problems are undertreated," Dr. Underberg said.

"Many older women are not counseled about pregnancy risk when using statins, and they should be because they may still be considering childbearing," he added.

Dr. Underberg encouraged physicians to discuss this issue with their patients. In order to treat a younger, high-risk, sexually active woman with statins, consider informed consent and an agreement about use of birth control. If her plans change, then the woman should stop using statins 2-3 months before stopping birth control. Consider hydrophilic statins (pravastatin and rosuvastatin) for use in women of childbearing age, since these drugs are less likely to pass the blood-placenta barrier.

Dr. Underberg is on the speakers' bureau and/or receives research funding or consulting fees from the following companies: Pfizer Inc., AstraZeneca, Sankyo Co., LipoScience Inc., DiaDexus Inc., and Forest Laboratories Inc. ■