Thermography to Detect Inflamed Macrophage-Rich Plaques

To the Editor:

We read with great interest the paper titled “Quantification of Macrophage Content in Atherosclerotic Plaques by Optical Coherence Tomography” by Tearney et al in Circulation.1

It strikes us that the authors state that so far, no approach under investigation for plaque characterization has provided direct evidence of macrophage presence; nevertheless, they feel that their technique is capable of visualizing macrophages. However, we feel that the described technique, although having a good resolution, is just another way of obtaining indirect evidence of macrophage presence.

Furthermore, the authors state that both thermography and near-infrared spectroscopy, although promising techniques, are not specific for macrophages. We do agree that these physiological techniques, in combination with morphological techniques, would optimize the information about the plaque. However, we would like to point out that recent reports have shown that temperature heterogeneity is determined by plaque composition and more specifically by the presence of macrophages.2,3 In atherosclerotic rabbits, we were able to show temperature heterogeneity by using intravascular thermography and to correlate this heterogeneity to the presence of an abundance of macrophages; moreover, lipid-lowering diet, resulting in change of plaque composition by disappearance of macrophages, was associated with disappearance of temperature heterogeneity.2 Recently, Madjid et al4 have shown that temperatures correlated well with cell density and proximity of macrophages and poorly with smooth muscle cells. Moreover, temperature heterogeneity was diminished by incubating living human carotid plaques with indomethacin ex vivo. Finally, Stefanadis et al5 found that temperature correlated with C-reactive protein. These findings suggest that macrophages play a crucial role in temperature heterogeneity. Therefore, we feel that intravascular thermography is a valid technique to identify inflamed “macrophage-rich” plaques.

Stefan Verheye, MD
Mark M. Kockx, MD, PhD
Cardiovascular Translational Research Institute
Middelheim Hospital
Antwerp, Belgium
stefan.verhey@pandora.be

Sish Ward Casscells, MD
University of Texas-Houston Medical School and Texas Heart Institute
Houston, Texas


Response

We agree with Dr Verhey and colleagues, who assert that thermography is a valid means for detecting “inflamed macro-phage-rich plaques.” This statement is well substantiated by studies demonstrating a correlation between (1) temperature changes and plaque macrophage density in both animals in vivo and human plaques ex vivo, and (2) between temperature, clinical syndromes, and C-reactive protein levels in patients. Possibly an even more significant attribute of thermography is its ability to allow assessment of the functional status of plaques in the catheterization laboratory, information that is valuable not only for detecting vulnerable plaques but also for improving our understanding of the pathophysiology of coronary atherosclerosis and acute coronary thrombosis.

We do wish to point out some key differences between optical coherence tomography (OCT) and thermography. In contrast to thermography, which measures the integrated effect of inflammatory cell activation at the luminal surface, OCT provides micron-scale cross-sectional images of pathological structure, including lipid pools and thin fibrous caps.1 In addition, our recent paper2 demonstrates that OCT is capable of detecting a scattering signature unique to atherosclerotic plaque macrophages. The ability of OCT to allow direct, simultaneous visualization of structural characteristics of fibroatheroma (lipid pools, thin fibrous caps, and macrophages) makes this high-resolution imaging modality very promising for identifying the plaque type implicated in the majority of acute coronary events. Because OCT is also capable of localizing macrophages in a cross-sectional image, it may be further utilized to study the relationship between the spatial distribution of these cells, plaque progression, and rupture.

The proliferation of techniques that attempt to identify high-risk plaques using different physical mechanisms is a welcome development. By attacking the complex problem of identifying intrinsic vulnerable plaque features from different angles, these efforts will most certainly lead to an improved understanding of this disease and more effective patient management. Our hope is that these distinct technologies be seen as complementary, with each method adding important data that bring us closer to the goal of eradicating sudden cardiac death.

Guillermo J. Tearney, MD, PhD
Wellman Laboratories of Photomedicine and Department of Pathology
Massachusetts General Hospital and Harvard Medical School
Boston, Mass

Hiroshi Yabushita, MD
Cardiology Division
Massachusetts General Hospital and Harvard Medical School
Boston, Mass

Ik-Kyung Jang, MD
Braimuc MacNeill, MD
Cardiology Division
Massachusetts General Hospital and Harvard Medical School
Boston, Mass

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Stefan Verheye, Mark M. Kockx and S. Ward Casscells

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