EDITORIAL COMMENT

Can Computed Tomography Angiography of the Coronary Arteries Characterize Atherosclerotic Plaque Composition?

Is the CAT (Scan) Out of the Bag?*

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Several different methodologies are available for the visualization of coronary atherosclerotic plaques, including invasive modalities, such as intravascular ultrasound (IVUS) (1), angioscopy (2), and optical coherence tomography (3), and noninvasive modalities, such as magnetic resonance coronary plaque imaging (4), computed tomography-based coronary artery calcium imaging (CAC) (5), and multislice computed tomography (MSCT) (6). Because angioscopy and optical coherence tomography are not approved by the Food and Drug Administration in the U.S., IVUS remains the predominant invasive modality for coronary arterial plaque characterization. More recently, radiofrequency analysis of the backscatter data from IVUS (7) has been introduced as a novel method for more refined characterization of atherosclerotic plaques. A commercially available software based on this approach (Virtual Histology [VH-IVUS], Volcano Corp., Rancho Cordova, California) identifies 4 different tissue types, dense calcium, fibrous, fibro-fatty, and necrotic core, in atherosclerotic plaques; this algorithm has been validated both in vitro and in vivo (8).

As a noninvasive modality, CAC has been introduced by Agatston et al. (5) to quantify the total burden of coronary atherosclerosis and has been shown to correlate well with long-term clinical outcomes (9). More recently, MSCT has been used to visualize coronary atherosclerotic plaques and has been shown to have reasonably good correlation with grayscale ultrasound evaluation of coronary atherosclerotic plaque composition (10).

The potential for MSCT evaluation of coronary plaques is enormous, given its noninvasive nature, its excellent soft-tissue contrast, and the fact that, in contrast to IVUS, it has the ability to evaluate the entire coronary arterial tree.

In this issue of JACC: Cardiovascular Interventions, Pundziute et al. (11) present an intriguing analysis describing VH-IVUS features of plaques identified and characterized by MSCT. A total of 168 plaques in 50 patients were characterized and classified by MSCT into 1 of 3 categories using a visual, qualitative approach: noncalcified plaques (29%), mixed plaques (42%), and calcified plaques (29%).

Before examining the individual findings of the study in context, it is important to point out some general observations. First, MSCT plaque characterization was based on a qualitative, visual approach using consensus between 2 expert observers, who were interpreting the MSCT datasets together. Although there were no formal, quantitative criteria for the classification of plaques by MSCT, the investigators’ approach is an important step toward the validation of the MSCT technology. Second, the novelty of the study lies in the fact that the investigators used radiofrequency analysis of backscatter data (VH-IVUS) as the reference standard. Although the accuracy of VH-IVUS has been recently challenged on the basis of some experimental studies (12), there is considerable accumulating evidence that VH-IVUS is quite powerful in the characterization of plaque components in human coronary plaques in vivo (8). Furthermore, at least in retrospective studies, VH-IVUS has been able to distinguish lesions that were stable from those that were associated with acute coronary syndromes (13). Therefore, despite some limitations, VH-IVUS remains the most obvious choice as the reference standard for coronary plaque characterization at this time.

Against this background, the study by Pundziute et al. (11) had 4 important findings.

The first important finding was that on a segmental basis, there was a modest but highly significant correlation between the Agatston score and the total volume of dense calcification measured by VH-IVUS (r = 0.69; p < 0.0001). Historically, CAC has been shown to be accurate in detecting calcifications using intravascular ultrasound as a reference standard (14), but the current study takes it 2 steps farther by quantifying calcium on MSCT and by using the novel, radiofrequency analysis method as the reference standard. Although the quantitative correlation was only modest (r = 0.69), it is important to keep in mind that the Agatston score was originally developed to standardize the quantification of total coronary arterial plaque burden; it takes into consideration both the total number of voxels that contain calcium as well as the density of the calcification. Therefore, direct measurements of the volume of calcium by MSCT (volume score) might correlate better with volume...
measurements on IVUS and VH-IVUS. Nevertheless, the correlation between the 2 modalities should further increase our confidence in the value and validity of CAC scoring by MSCT.

The second and third major findings are closely related: noncalcified plaques by MSCT contain more fibrous and fibrofatty tissue by VH-IVUS compared with calcified plaques, and calcified and mixed plaques contain more dense calcium compared with noncalcified plaques. These are very important observations, because they validate a visual, qualitative, and clinically applicable approach to plaque characterization by MSCT. Leber et al. (15,16) have shown that both 16-slice (15) and 64-slice (16) MSCT are accurate in the detection of hypoechoic, hyperechoic, and calcified plaques using grayscale IVUS as the reference standard. Furthermore, they showed that attenuation values on MSCT (in standard computed tomography Hounsfield units) were different among hypoechoic, hyperechoic, and calcified plaques, although there was significant overlap. The present study did not present any quantitative measurements on the MSCT datasets; this remains a major focus of current computed tomography research. Nevertheless, the ability of MSCT in the current study to correctly classify plaques in 3 major categories using a semiqualitative, visual approach should significantly increase our confidence in MSCT technology and justify the current practice and reporting patterns for MSCT datasets.

The fourth and most interesting finding of the study was the fact that VH-derived thin-cap fibroatheromas (VH-TCFAs) were most prevalent in plaques that were classified as mixed plaques by MSCT: 32% of mixed plaques met criteria for TCFAs by VH-IVUS compared with 13% of noncalcified and 8% of calcified plaques. This is a very significant observation. There has been tremendous focus on VH-TCFAs, as these are presumed to be the most potentially vulnerable lesions. A VH-TCFA is typically described as one without evidence of a thick cap (i.e., <200 μm) for at least 33% of the lesion circumference and requires a confluent necrotic core of >10% in ≥3 consecutive frames. Based on preliminary data from the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) trial, 28.4% of patients had VH-TCFAs present in a nonculprit lesion. Although many questions remain, the finding of the present study adds supportive evidence to anecdotal observations that mixed plaques detected by MSCT might be associated with subsequent coronary events. This is supported by observations that noncalcified components and spotty calcification were more prevalent in culprit lesions of patients with acute coronary syndromes (79% and 63%, respectively) compared with stable lesions (9% and 21%, respectively) (17). Furthermore, Pundziute et al. (18) previously reported the first outcomes’ data in 100 patients with MSCT and showed that in multivariate analysis, the number of segments containing mixed plaque was a significant predictor of more adverse events. These data taken together suggest that MSCT is accurate in detecting mixed lesions that might be associated with downstream adverse events and might predict worse prognosis.

Figure 1. Coronary Artery CTA and IVUS-VH

Invasive X-ray angiography reveals an intermediate stenosis in the left anterior descending artery (A). Quantitative coronary angiography showed a 53% stenosis. Computed tomography angiography (CTA) of the same patient reveals more extensive atherosclerosis than appreciated on the invasive X-ray angiogram (B). Quantitative stenosis measurement on CTA shows a 55% stenosis in the same region (C). Different plaque components are identified on the basis of different Hounsfield unit values in the plaque (green = blood pool, yellow = calcium, blue = high-density noncalcified plaque, red = low-density noncalcified plaque) (D). Cross-sections of the reference segment (E) and of the lesion (F) are shown; computed tomography-derived minimal lumen diameter (MLD) and minimal lumen area (MLA) were 1.5 mm and 3.3 mm², respectively. Intravascular ultrasound (IVUS) (G, H) and virtual histology (VH) (I) of the same region confirm similar MLD and MLA (1.7 mm and 3.4 mm², respectively) and similar distribution of the plaque components.
Overall, this study should increase our confidence in the ability of MSCT to characterize coronary artery plaques and justify the use of a semiquantitative approach to plaque characterization for clinical reporting purposes. Furthermore, we should pay particular attention to mixed plaques in designing larger-scale outcomes studies using MSCT technology.

Naturally, several important issues and questions remain. The present study used a semiquantitative approach for MSCT plaque characterization; it remains to be seen whether quantitative approaches will be feasible, reliable, and reproducible (Fig. 1). This is a crucial question, especially as we are seeking novel, noninvasive methods for coronary artery plaque characterization for the purposes of pharmaceutical atherosclerosis regression trials. In addition, it will be important to evaluate the prognostic value of the information gained on plaque composition on MSCT. The incremental value of such compositional information will have to be rigorously evaluated over coronary artery calcium scoring and over geometrical parameters such as the remodeling index. Finally, with the introduction of more advanced MSCT imaging systems that significantly reduce radiation dose, an interesting question is whether MSCT will enter the realm of atherosclerosis screening in asymptomatic individuals.

Overall, this study is an important step in furthering the role of MSCT in clinical cardiology; it seems that with regards to coronary plaque characterization, the CAT (scan) is indeed out of the bag. Pundziute et al. (11) are to be commended on performing this important study.

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REFERENCES