Assessment of coronary plaque morphology by contrast-enhanced computed tomographic angiography: comparison with intravascular ultrasound
Margaret Leila Rasouli, David M. Shavelle, William J. French, Charles R. McKay and Matthew J. Budoff

Background Computed tomographic (CT) angiography provides accurate noninvasive assessment for coronary artery stenosis. The ability of CT angiography to determine plaque morphology remains unclear.

Methods Twelve patients undergoing intravascular ultrasound for clinical indications underwent CT angiography for the evaluation of plaque morphology. Plaque morphology was classified as (1) soft, (2) fibrous, (3) fibrocalcific or (4) calcific. CT angiography data sets were evaluated for the presence and morphology of plaque in the coronary artery segments. The results were blindly compared with intravascular ultrasound results on a segment by segment basis using angiographic landmarks.

Results Fifty-nine coronary segments were analyzed; 10 segments were normal and 49 contained plaque. Plaque morphology by intravascular ultrasound was soft in 12 segments, fibrous in four, fibrocalcific in 29 and calcific in four. To determine coronary segments with any plaque, CT angiography had a sensitivity of 100% (49 of 49) and specificity of 90% (9 of 10). To determine plaque morphology as calcified (fibrocalcific and calcific) versus noncalcified (soft and fibrous), CT angiography had a sensitivity of 100% (33 of 33) and a specificity of 94% (15 of 16). Overall accuracy for CT angiography to determine plaque morphology was 92% (54 of 59). CT angiography density values (Hounsfield units, mean ± standard deviation) were significantly different for each plaque morphology: soft 23 ± 71, fibrous 108 ± 79, fibrocalcific 299 ± 112 and calcific 404 ± 264 (P<0.0001).

Conclusions CT angiography accurately characterized plaque morphology and may be a useful tool in noninvasive evaluation of plaque morphology during drug therapy trials. Coron Artery Dis 17:359–364 © 2006 Lippincott Williams & Wilkins.

Keywords: computed tomography angiography, coronary plaque, intravascular ultrasound

Introduction Computed tomographic (CT) angiography provides accurate noninvasive assessment of coronary artery stenosis as well as detection and quantification of calcified coronary plaques [1,2]. Coronary artery calcium is a surrogate for total plaque burden and may predict future coronary events [3–5]. The American College of Cardiology/American Heart Association expert consensus document indicates that a positive noncontrast electron beam CT scan confirms the presence of coronary atherosclerosis [6]. The mere presence of coronary artery calcium, however, is unable to identify an unstable plaque [7]. Critics of electron beam CT argue that calcium is associated with stable coronary plaques and that acute coronary syndromes are often the result of unstable, noncalcified lesions [8–11]. A noninvasive imaging tool that allows for accurate determination of plaque morphology would be essential for risk stratification of future cardiac events and in the assessment of the progression of atherosclerosis.

Recent studies have demonstrated the diagnostic accuracy of multidetector spiral CT in the identification of different plaque compositions [12,13]. No data are available, however, on the assessment of coronary plaque composition by using electron beam CT angiography. Our study represents the first prospective intravascular ultrasound (IVUS)-based study to evaluate coronary plaque morphology by using e-Speed CT angiography, the newest iteration of the electron beam CT scanner, that enables higher spatial and temporal resolution than its predecessor.
Methods
Study population
The study group consisted of 12 consecutive stable patients (nine men; three women; mean age, 56 ± 6 years) who were recruited from the outpatient cardiac catheterization clinic at Harbor-UCLA Medical Center. Enrolment criteria included men and women between 18 and 80 years of age referred for elective coronary angiography. Exclusion criteria were unstable cardiovascular disease symptoms, abnormal baseline creatinine (>1.5 mg/dl), known iodine allergy and class III or IV congestive heart failure. At the time of enrolment, medical history – including the presence of diabetes mellitus, hypertension, smoking, cholesterol status – and family history were obtained. The Harbor-UCLA Institutional Review Board approved the research protocol and all patients gave written, informed consent.

Computed tomographic angiography
Within 1 month before scheduled coronary angiography, study patients underwent contrast-enhanced CT angiography (e-Speed, GE Medical Systems, San Francisco, California, USA), in the high-resolution volume mode. Sixty contiguous axial images were acquired to cover the entire cardiac tree with 1.5 mm slice thickness and 1.5 mm table incrementation. The image acquisition time was set at 50 ms per image. Reconstruction of images using 512 incrementation. The image acquisition time was set at 50 ms and triggered to 20% of the R–R interval, with one image acquisition acquired every other heart beat. Contrast flow rate and total levels of the ascending aorta were acquired in multi-slice mode. Acquisition time was set at 50 ms and triggered to 80% of the R–R interval, with one image acquisition acquired every other heart beat. Contrast flow rate and total contrast dose (100–120 ml per study) were determined on an individual basis by the CT investigator on the basis of the weight and heart rate. Reconstruction of the highest and lowest images was automatically performed by the e-Speed host computer to ensure that the required anatomy was covered. A dual injector was used with a new three-phase protocol, including a reduced contrast load followed by a saline flush [14]. In axial images and three-dimensional reconstructions, all coronary arteries and side branches with a diameter of 1.5 mm were assessed.

CT angiography data were interpreted by an experienced investigator (M.J.B.), blinded to clinical history, the results of angiography and IVUS, using AccuView Software (AccuIMage Diagnostics Corporation, South San Francisco, California, USA). All vessels > 1.5 mm were analyzed and no vessel was excluded because of image quality. Sections containing a coronary stent were not evaluated. Plaque was defined as present if tissue thickening was > 1.0 mm within or next to the artery lumen. Segments corresponding to IVUS analysis were defined as fibrous and with less density was regarded as soft. Plaques containing atheroma were areas of greater density/brightness and equal density were considered to represent mixed lesions and were defined as fibrocalcific.

Coronary angiography and intravascular ultrasound
Selective coronary angiography was performed in multiple orthogonal views using standard techniques. Indications for IVUS imaging were to examine a culprit lesion of intermediate angiographic severity (n = 3) and to evaluate stent apposition following deployment (n = 9). IVUS imaging included both the culprit lesion and several coronary segments proximal and distal to the culprit lesion. IVUS images were acquired under fluoroscopic guidance using a 2.9F Volcano Avanar FX 20 MHz single-element ultrasound catheter (Volcano Therapeutics Inc., Rancho Cordova, California, USA). Intravenous heparin at 60 units/kg and 200 μg of intracoronary nitroglycerine were given and the IVUS catheter was advanced distal to the culprit lesion. A manual pullback was performed through the segments of interest. Each imaging segment of interest was documented using a short cineangiographic filming sequence combined with voice annotated video imaging. All data were systematically stored on a videotape system for offline plaque analysis using the Volcano Goldvision software package by a cardiologist (D.M.S.) well versed in IVUS analysis and blinded to CT angiography findings. Segments of interest were identified using characteristic anatomic landmarks such as bifurcation points.

Plaque composition was classified according to the American College of Cardiology report on standards for IVUS acquisition, measurement and reporting [15]. Coronary plaque was defined as present if intimal thickness was > 0.5 mm. Plaque morphology was classified as (1) soft, (2) fibrous, (3) fibrocalcific or (4) calcific. Soft plaque was defined as plaque tissue producing echogenicity less than that of the surrounding adventitia, in the absence of any calcium. Fibrous plaque was defined as atheroma having density equal to that of the adventitia without any detectable calcium. Fibrocalcific plaque was defined as plaque tissue having more echodensity than the adventitia. Calcific plaque was defined as atheroma brighter than the adventitia with acoustic shadowing. Maximum vessel diameter (maximum external elastic membrane) was identified for each segment.

Statistical analyses
The sensitivity and specificity for CT angiography to detect the presence of plaque and calcified (calcific and fibrocalcific) versus noncalcified plaque (soft and fibrous)
were determined using the IVUS findings as the gold standard. Mean maximum vessel diameter was compared between CT angiography and IVUS with Pearson’s correlation coefficient. Statistical analyses were carried out using SAS v8.01 statistical software (SAS Institute Inc., Cary, North Carolina, USA).

**Results**

**Patient characteristics**

Twelve patients, nine men and three women with a mean age of 56 ± 6 years, were studied. Medical history included eight patients (66%) with hypertension, eight patients (66%) with a family history of premature coronary artery disease, six patients (50%) with hypercholesterolemia, four patients (33%) with prior tobacco use and three patients (25%) with diabetes mellitus. IVUS was performed in one vessel (right coronary artery) in four of 12 patients and in two vessels (target vessel and left main) in the remaining eight patients.

Fifty-nine coronary segments of interest were identified on the basis of angiography and IVUS (left main 19 segments, left anterior descending 20 segments, right coronary artery 19 segments and left circumflex one segment). IVUS plaque morphology was normal (intimal thickness < 0.5 mm) in 10 segments, soft in 12 segments, fibrous in four segments, fibrocalcific in 29 segments and calcific in four segments (Table 1).

**Computed tomographic angiography**

CT angiography analysis was performed on all 59 coronary segments and no coronary segment was excluded because of poor image quality. CT angiography defined plaque morphology as normal in nine segments, soft in 12 segments, fibrous in three segments, fibrocalcific in 31 segments and calcific in four segments (Table 1). To determine coronary segments with any plaque, CT angiography had a sensitivity of 100% (49 of 49) and a specificity of 90% (9 of 10). To determine plaque morphology as calcified (fibrocalcific and calcific) versus noncalcified (soft and fibrous), CT angiography had a sensitivity of 100% (33 of 33) and a specificity of 94% (15 of 16). The overall accuracy for CT angiography to determine the various plaque morphologies was 92% (54 of 59). Figure 1 shows the different plaque morphologies by IVUS and CT angiography. Figure 2 shows a complex bifurcation lesion of the mid portion of the left anterior descending involving the origin of the diagonal vessel with the corresponding IVUS and CT angiography assessment of plaque morphology.

CT angiography density values (mean ± standard deviation) for each plaque morphology were as follows: soft 23 ± 71 Hounsfield units (HU), fibrous 108 ± 79 HU, fibrocalcific 299 ± 112 HU and calcific 404 ± 264 HU (P < 0.0001, Fig. 3). CT angiography mean maximal vessel diameter was compared with IVUS using 47 segments (left main 18, left anterior descending 17, left circumflex one and right coronary artery 11). Good correlation was observed between the mean maximum vessel diameter by IVUS and CT angiography, 4.93 ± 0.86 versus 4.94 ± 0.86 mm, respectively (correlation coefficient r = 0.781, P < 0.001, Fig. 4).

**Discussion**

The majority of acute coronary syndromes result from plaque rupture and superimposed thrombosis in the setting of a moderate coronary stenosis [16]. The occurrence of individual plaque rupture is a component of a systemic process that involves the entire coronary tree and may in part be related to individual plaque morphology [17]. In addition to plaque morphology, overall plaque burden and progression of coronary atherosclerosis may be important factors influencing the risk of plaque rupture and future coronary events [8,18]. A noninvasive imaging tool that could reliably determine plaque morphology and overall plaque burden would be important to identify high-risk patients and enable serial assessment during therapeutic interventions. In the present study, we evaluated the diagnostic accuracy of the recently developed e-Speed technology CT, the newest iteration of the electron beam CT, to detect and characterize coronary plaques.

Improved spatial and temporal image acquisition of the newer CT systems has facilitated atherosclerotic plaque detection. Visualization of coronary atherosclerotic plaques is more challenging than visualization of the coronary lumen owing to the smaller size of the plaque. On the basis of tissue-specific X-ray attenuation
characteristics, CT can now accurately distinguish between fatty tissue, fibrous tissue and calcium. Thus, CT angiography may be able to identify coronary plaques that are calcified, fibrous or those that contain a large lipid pool (soft), similar to plaque classifications developed with IVUS [15].

With this background, we performed a detailed segment by segment evaluation using IVUS as the reference. We found a sensitivity of 100% and a specificity of 90% for the detection of plaque by CT angiography. To differentiate between calcified and noncalcified plaques, CT angiography had a sensitivity and specificity of 100% and 94%, respectively. In addition to visual evaluation of plaque morphology by CT angiography, we also applied density measurements using Hounsfield units. We found that the lowest density values correlated well with soft plaque, the intermediate values correlated with fibrous lesions and the highest values correlated with calcified plaques. Vessel diameters measured by CT angiography were accurate when compared with those measured by IVUS.

Several previous studies have documented the ability of multi-slice detector CT to determine coronary plaque morphology with an overall sensitivity of approximately 82% [12,19]. For coronary segments containing noncalcified plaque, however, the sensitivity decreased to 53%. Ours is the first study to evaluate electron beam CT for the assessment of coronary plaque morphology and to specifically evaluate the complete range of plaque morphology, including soft, fibrous, fibrocalcific and calcific plaques. We found an overall accuracy of 92% and were able to accurately differentiate between soft, fibrous, fibrocalcific and calcific plaques. Measurement of plaque density using the Hounsfield units was particularly useful and statistically different among each of the plaque morphologies.

**Limitations**

The soft plaque is more prone to modification with statin therapy, and may prove more accurate in assessing the adequacy of therapy [20,21]. Before using CT angiography to noninvasively track atherosclerosis burden and progression, additional studies are needed. Reproducibility and longitudinal studies, evaluating more than one time point, are required. As the accuracy to evaluate soft plaque improves with technological advancements, we are coming closer to defining the vulnerable plaque in a noninvasive manner [22,23]. The true prognostic value of
soft plaque detection with CT angiography awaits large, prospective cohort studies in asymptomatic populations. These studies have the potential to determine the predictive value for future cardiac events and assess changes over time of plaque morphology under the influence of various therapeutic interventions. CT angiography requires both contrast administration and radiation exposure. Currently, in the asymptomatic person, it is likely that the risks of the procedure outweigh the benefits of detecting soft plaque.

Conclusions
A noninvasive tool that provides sequential imaging of coronary plaque morphology in a safe and reliable manner would be highly desirable. The results of our study suggest that CT angiography can accurately assess coronary plaque morphology. We observed a strong correlation between CT density measurements within the plaque and lesion echogenicity on IVUS. State-of-the-art CT angiography can accurately provide a noninvasive assessment of plaque morphology.
Acknowledgement
Robert M. Shavelle, PhD, assisted with the statistical analysis.

References