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Atheroma Morphology and Distribution in Proximal Left Anterior Descending Coronary Artery: In Vivo Observations

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Objectives. **This study sought to examine, in vivo, the shape and position of atheroma in the proximal left anterior descending coronary artery.**

Background. **The prevalence, shape and location of atheromas involving the proximal left anterior descending artery have implications regarding the role of disturbed shear forces in the genesis of atherosclerosis. However, no data are available regarding in vivo findings or advanced disease.**

Methods. **Forty-two consecutive high quality intravascular ultrasound images were examined from patients with atherosclerotic disease in the proximal left anterior descending artery just distal to the left main bifurcation. Lesion percent area stenosis and maximal, minimal and flow divider intimal–medial thickness were measured at the region immediately after the circumflex takeoff. The angle formed by the midpoint of the flow divider, the lumen center of gravity and the maximal plaque thickness were determined.**

Results. **Eccentricity of vessel wall atheroma was observed such that the maximal wall thickness (1.42 ± 0.50 mm [mean ± SD]) differed significantly from minimal wall thickness (0.17 ± 0.098 mm). Further, the region of vessel wall manifesting maximal thickness was greater than the flow divider thickness (0.26 ± 0.17 mm). Maximal plaque thickness spared the region of the flow divider in 100% of cases and was positioned at a mean angle of 193 ± 49° from the center of the flow divider. Eccentric morphology was maintained across the 24% to 80% range of area stenosis.**

Conclusions. **Atheromas in the very proximal left anterior descending artery are located opposite the circumflex takeoff, spare the flow divider and maintain eccentricity across a wide range of vessel stenoses. These in vivo morphologic data support the potential role of fluid dynamic mechanical factors in atherogenesis and have implications regarding the success of catheter-based interventional procedures at the site.**

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Disease involving the proximal left anterior descending coronary artery has both pathophysiologic and clinical significance. Atherosclerosis has a predilection for the proximal portion of the left anterior descending coronary artery (1), possibly related to the fluid dynamics associated with bifurcation of the left main coronary artery. Pathologic studies (2–6) of this region, using reconstructive techniques to approximate the in vivo bifurcation geometry, suggest that early atherosclerotic lesions are localized to the wall opposite the flow divider (i.e., across from the circumflex artery takeoff). Flow theory confirms that this outer "hip" region of a branching bifurcation is characterized by abnormally low or oscillatory shear forces that may contribute to atherogenesis, in part through abnormal lipid transport mechanisms (7–10). From a clinical standpoint, significant stenosis at the proximal left anterior descending artery jeopardizes the anterior left ventricular wall, worsens prognosis in coronary artery disease (11,12) and often prompts evaluation for revascularization. Unfortunately, angioplasty of such lesions appears to be less successful than that for plaques at other sites because of a higher angiographic restenosis rate (13–15).

Despite necropsy data on the presence of early, eccentric disease in the proximal left anterior descending coronary artery in young adults, few in vivo data exist regarding the location and morphologic appearance of the more clinically relevant, advanced stages of disease at this site. Such data could provide important insights into both the mechanisms of formation and clinical behavior of these lesions. Therefore, the present study used in vivo intravascular ultrasound imaging to examine the site and eccentricity of lesions of varying stenotic severity within the proximal left anterior descending coronary artery just distal to the left main bifurcation in patients with known coronary artery disease.

Methods

Subjects. Intravascular ultrasound images were examined from 57 consecutive patients with known or suspected disease

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of the left anterior descending coronary, who underwent both diagnostic angiography and intracoronary ultrasound imaging. To maintain an analysis of only primary lesions, patients who had undergone angioplasty or atherectomy of a proximal left anterior descending lesion at any time before the study were excluded.

Instrumentation and image acquisition. Intravascular ultrasound imaging was performed after diagnostic coronary angiography, as previously described (16). Commercially available, mechanically based intravascular ultrasound catheter systems used in the study included 1) 30-MHz, 3.5F Sonicath catheters (Boston Scientific Corp.) and an HP Sonos system (Hewlett-Packard); 2) a 30-MHz, 3.2F and 2.9F CVIS catheter system (Cardiovascular Imaging Systems); and 3) a 25-MHz, 3.9F Intertherapy catheter system (Cardiovascular Imaging Systems). In each case, system availability and operator preference determined the use of the specific system. The intravascular ultrasound catheter was inserted into an angioplasty guiding catheter and advanced along a guide wire into the coronary lumen to image the specific region of the left anterior descending coronary artery of interest to the operator. In addition to this clinical use, an uninterrupted recording on 0.5-in. SVHS videotape was obtained during manual pullback of the intravascular ultrasound catheter through the left anterior descending coronary artery and left main bifurcation and into the guiding catheter in every case and was the basis for this study.

All patient studies of sufficient quality for analysis, and which demonstrated evidence of vessel wall thickening or atherosclerotic plaque in the proximal left anterior descending coronary artery just distal to the left main bifurcation by intravascular ultrasound, were then collected for analysis. Evidence of vessel wall thickening or atherosclerotic plaque included a minimal intimal–medial thickness of 0.5 mm or the presence of acoustic shadowing due to calcification (17).

Image analysis. Off-line review of the high quality, 0.5-in. videotape images obtained during catheter pullback was then performed for all qualifying lesions. The typical cross-sectional intravascular ultrasound appearance of the bifurcation region was one of two separate circular vessels coalescing to form a larger circular left main coronary artery before entry into the guiding catheter. The proximal left anterior descending coronary artery was defined as the arterial region encountered immediately before the circumflex takeoff (at the left main bifurcation) during pullback of the ultrasound catheter. The left main bifurcation was identified on pullback imaging as the last branch point before entry of the probe into the guiding catheter. Simultaneous fluoroscopic images, when recorded, were also used to further confirm the position of the ultrasound probe. For each study patient, 120 to 150 frames (4 to 5 s) of the proximal left anterior descending artery up to and including the circumflex takeoff were selected from the pullback images, digitized into a 512 × 480-pixel matrix with 256 shades of gray and stored on a computer disk. During replay of these digitized images, a single frame of the proximal left anterior descending artery was selected for analysis on the basis of good image quality and close proximity to the bifurcation.

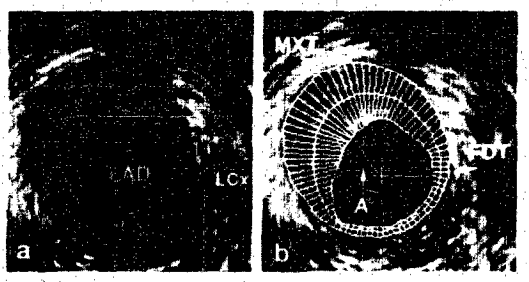

Figure 1. Representative intravascular ultrasound image of (**a**) the left anterior descending (LAD)–circumflex (LCx) bifurcation with (**b**) superimposed measurements. Vessel area, lumen area, centerline, chords (every fourth pixel for illustration), center of gravity and identification of maximal thickness (MXT), flow divider thickness (FDT) and angle (A°) are shown. Note the clockwise measurement of angle from flow divider thickness to maximal thickness.

From the frame selected, the vessel wall dividing the left anterior descending and circumflex arteries was identified and taken as the flow divider, and the midpoint of the length of this structure was marked on the image as its center. Two specific borders were then outlined and the areas within measured using a cursor-controlled planimeter (Fig. 1). The lumen–intimal border defined the lumen area and was identified as the first definite signals recorded outside the transducer artifact. Recognition of the intimal border was often facilitated by visualization of blood backscatter scintillations within the lumen. The medial–adventitial border, representing total vessel area, was identified as the junction of the bright reflectance of the adventitia with the hypoechoic media. Once calibrated to the 0.5- or 1.0-mm reference markers on the video image, an automated program was used to measure the lumen and vessel area from the tracings. Wall area was calculated as the difference between total vessel area and lumen area. An index of stenosis (% stenosis) then was derived as the ratio of the wall area to total vessel area (normal values would approach 0%) in an attempt to normalize the amount of disease for vessel size.

A custom computer program whose measurements were validated by comparison to phantoms (18) was used to construct a centerline midway between the lumen–intimal and medial–adventitial borders. For every pixel of the centerline, orthogonal chords were drawn connecting these borders to provide a measurement of intimal–medial thickness around the circumference of the vessel. For each vessel, maximal thickness was taken as the greatest length measured for any chord. Minimal thickness was determined as the mean value of the smallest chord and the two surrounding chords on each side to enhance the measurement accuracy of short distances. Flow divider thickness was measured and noted on each image as the intimal–medial thickness of the vessel wall at the center of the flow divider. Using the image analysis software, the

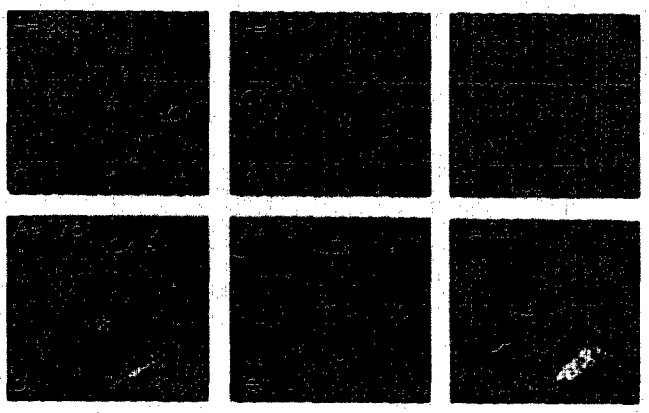

Figure 2. Examples of proximal left anterior descending coronary artery images. Advanced (**a**) and early (**d**) disease stages are shown. Acoustic shadowing can be seen in **a**, **b**, **c** and **e**. In all images, the lumen center of gravity (•) and angle (A) are shown, and the circumflex artery (LCx) can be seen.

center of mass of the lumen was determined, and an angle was constructed by joining the center of mass with the midpoint of the flow divider and the intimal surface of the chord manifesting maximal wall thickness. Using these calculations, maximal lesion thickness located in the flow divider would yield an angle approaching 0°, whereas maximal thickness in the opposite wall of the left anterior descending coronary artery would yield angles approaching 180°. Figure 1 shows these measurements on a representative bifurcation image from this study. Superimposed measurements demonstrate the left anterior descending vessel area, lumen area, centerline, chords, lumen center of gravity and identification of maximal thickness, flow divider thickness and angle.

Lesion eccentricity was defined as asymmetric plaque thickness within the vessel cross section. An index of eccentricity was derived as (Maximal thickness − Minimal thickness)/Maximal thickness, where a value of 0 represents perfect concentricity and a value of 1 represents infinite eccentricity. A lesion was considered *eccentric* when its maximal thickness exceeded three times its minimal thickness on the same cross-sectional image, as represented by an eccentricity index value ≥0.67.

Lumen diameter was measured on the ultrasound image as the length of the line connecting opposing lumen–intimal borders and passing through the center of gravity of the lumen. Minimal lumen diameter was obtained on each image as the smallest diameter constructed radially from the center of gravity of the lumen.

Calcification, as observed on intravascular ultrasound, was defined as an initial high intensity (bright) echo with distal shadowing and was measured as the percentage of acoustic dropout of the total vessel wall circumference. *Superficial calcification* was defined as an initial bright echo at the lumen–intima border, whereas *deep calcification* was defined as an initial bright echo deep within the plaque. A mixed pattern of calcification described high intensity targets with shadowing in both regions. If the vessel was affected by significant calcification and shadowing, the vessel wall position in the region of ultrasound dropout was inferred from proximal and neighboring noncalcified regions.

Statistical methods. Results are expressed as mean value ± SD for each measurement. Comparison of intimal thickness values between groups was performed using the paired, one-tailed Student *t* test. Analysis of interobserver and intraobserver variability in maximal thickness, minimal thickness, flow divider thickness, angle and eccentricity was performed in a subset of 11 patients. The paired *t* test and regression analysis were used to assess differences in maximal, minimal and flow divider thickness and angle. Statistical significance in all comparisons was considered for $p < 0.05$.

Results

Forty-two patients were identified in whom clear evidence of disease in the proximal left anterior descending coronary artery was present by intravascular ultrasound (mean [±SD] age 60 ± 13 years, range 30 to 80; 35 men, 7 women). Of the 15 patients who had intravascular ultrasound examinations but were not entered into the study, 6 had technically inadequate images, 5 had inadequate views of the bifurcation resulting from deep guiding catheter engagement, and 4 showed no evidence of disease at the bifurcation. 2 patients (5%) had suspected or confirmed angiographic disease in the left main coronary artery, 19 in the proximal one-third of the left anterior descending coronary artery (45%) and 21 in the mid or distal vessel (50%). The proximal left anterior descending coronary artery region and the origin of the circumflex artery were identified on intravascular ultrasound imaging in all study patients. The circumflex artery could still be visualized as a separate vessel at the edge of the image in 76% of the frames of the proximal left anterior descending coronary artery selected for analysis. In the remaining 24%, the circumference of the circumflex artery could not be clearly discerned, most likely due to a wide branching angle, and the flow divider was taken as the wall between vessels.

Figure 2 shows representative images from six study pa-

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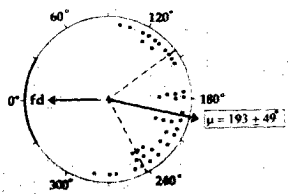


Figure 3. Plot of the number of observations versus angle. Individual **squares** represent lesion maximal thickness and are placed at their corresponding angles from the flow divider (fd). The flow divider region is seen as a **thickened arc** of the vessel circumference. Mean angle is displayed as a **solid arrow**, flanked by **dashed lines** representing standard deviation.

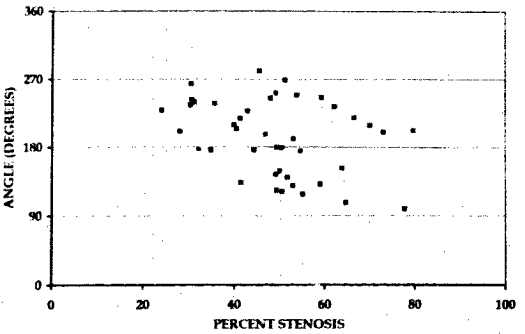


Figure 4. No relation is seen between angle and percent stenosis. **Squares** = individual lesions (n = 42).

tients. Lesions of varying stenosis, eccentricity, calcification and angle to the flow divider are present. In all images, the lumen center of gravity and the circumflex vessel are designated.

Morphology of proximal left anterior descending coronary artery plaque. A wide range of atherosclerotic plaque sizes was identified. Percent area stenosis varied from 24% to 80% (mean ± SD 49 ± 13%); minimal lumen diameter ranged from 1.7 to 3.9 mm (mean 2.8 ± 0.51); mean maximal thickness was 1.42 ± 0.50 mm; mean minimal thickness was 0.17 ± 0.10 mm; and mean flow divider thickness was 0.26 ± 0.17 mm. Although the difference between minimal thickness and flow divider thickness was statistically significant ($p < 0.05$), it was minimal, suggesting that the flow divider is a relatively spared region of the vessel circumference in the atherosclerotic process. This was confirmed subjectively by analysis of the two-dimensional images, which showed lack of abnormal structure in this region. All plaques were eccentric, with a mean eccentricity index of 0.86 ± 0.072 (range 0.68 to 0.98).

Twenty-one lesions (50%) showed evidence of calcification, of which 14 were considered superficial, 4 deep and 3 mixed in pattern. Marked superficial calcification resulting in dropout >25% of the deep vessel wall circumference was seen in 9 patients (21%). No vessel had a concentric ring of calcification or showed evidence of calcification of the flow divider region.

Location of maximal plaque. In 98% of study patients, maximal thickness was located in the hemisphere of the vessel opposite the flow divider region, and the mean angle of maximal involvement was 193 ± 49° (range 99° to 281°) away from the center of the flow divider. Figure 3 illustrates the mean value, SD and distribution of maximal involvement by its angular relation to the flow divider. No patient showed maximal involvement or presence of calcification in the flow divider region. The angle of involvement was unrelated to the amount of plaque, represented as percent stenosis (Fig. 4).

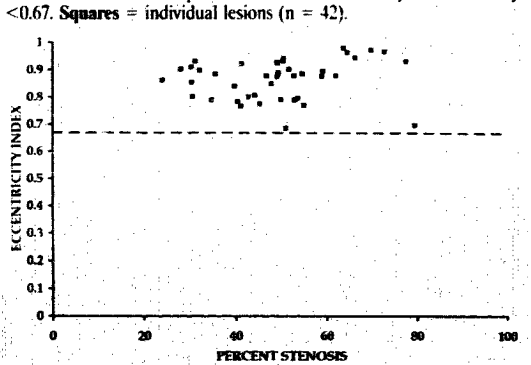
Plaque burden and morphology. With larger stenoses, lesions appeared to remain relatively eccentric, showing little tendency for concentricity with increasing plaque burden. The scatterplot of the values for the index of eccentricity and percent stenosis is shown in Figure 5. The region below the dashed line on this graph represents relative concentricity (i.e., when eccentricity index <0.67). The lack of concentricity, especially with greater stenosis, is indicated by the absence of data points in this region.

Interobserver and intraobserver variabilities in the measurement of maximal thickness, minimal thickness, flow divider thickness and angle were not significant. Regression analysis of repeated measurements of one observer, as well as measurement comparisons between observers, resulted in slopes not statistically different from 1, with r values ranging from 0.63 to 0.97. Morphologies of all 11 lesions were not significantly altered and remained eccentric during repeated observations.

Discussion

The site and spatial distribution of atherosclerotic plaque have been carefully analyzed in an attempt to elucidate mechanisms for the genesis of coronary artery disease. Earlier studies in postmortem specimens, consisting primarily of mild, fatty lesions in nondistended vessels, have suggested that atherosclerosis involving the origin of the left anterior descending coronary artery is common and usually eccentric. We

Figure 5. Index of eccentricity versus percent stenosis. The region below the **dashed line** represents relative concentricity, or eccentricity <0.67. **Squares** = individual lesions (n = 42).



examined atherosclerotic lesions in the proximal left anterior descending coronary artery in patients with coronary artery disease in this in vivo intravascular ultrasound study. Eccentric involvement was universal throughout the spectrum of stenosis severity. Specifically, maximal accumulation of plaque was found in the left anterior descending arterial wall opposite the circumflex, a site believed to be exposed to low or oscillatory shear stresses. We observed relative sparing of the flow divider region separating the left anterior descending and circumflex arteries. These data represent the first systematic analysis of the in vivo morphologic appearance of stenoses of varying severity at this site, and may have implications regarding the genesis of atherosclerosis, the natural history of eccentric lesions and the response of these lesions to interventional techniques.

Fluid dynamics: theory and atherogenesis. Atherosclerosis has a predilection for the proximal 2 cm of the left anterior descending coronary artery (1). The genesis of atherosclerotic lesions in this location may be related to variable shear forces produced by bifurcation of the left main coronary artery. According to fluid dynamics theory, the outer hip of an arterial bifurcation is an atherosclerotic-prone region characterized by low or oscillatory shear, as exemplified by carotid and abdominal aorta bifurcation sites. Regions characterized by abnormally low or oscillatory shear forces have been found to manifest abnormal endothelial permeability to lipids (10) and often show marked intimal hyperplasia (6,9), factors that may be associated with early atherogenesis. Although the shear stresses at the left main bifurcation have not been measured directly, the previous considerations should apply equally as well to the coronary artery circulation. Therefore, the propensity for disease opposite the flow divider observed in our study supports the role of mechanical factors in the genesis of atherosclerosis.

Relation of prior postmortem and in vivo studies. In necropsy studies of young human hearts a high prevalence of abnormalities in the proximal left anterior descending coronary artery, particularly localized to the arterial wall opposite the flow divider, have been reported. These pathologic studies were based primarily on early lesions, such as adaptive intimal thickening and sudanophilic "fatty streaks," in a young population without clinical evidence of coronary artery disease (2–6). In addition, the results may have been partially influenced by attempts to reconstruct the in vivo arterial geometry of longitudinally opened vessels, or by the computer techniques used to "reexpand" the non–pressure-fixed, collapsed cross-sectional specimens. However, these data do validate the susceptibility of the proximal left anterior descending coronary artery to disease and suggest localization of the early atherosclerotic process to the outer wall of the bifurcation. In our older patients with documented atherosclerotic disease, we show, in vivo, the localization of both early and more advanced disease to this region of the proximal left anterior descending coronary artery.

To our knowledge, no prior in vivo study has attempted to relate lesion morphology to its position in the coronary artery tree, partly because of the limitations of angiographic and echocardiographic techniques used prior to intravascular ultrasound. Earlier angiographic study (19,20) of in vivo lesion morphology has been primarily limited to the larger stenotic lesion and may be inadequate to accurately depict the degree of lesion eccentricity (21). Furthermore, initial lesion growth may not be detected by angiography owing to compensatory enlargement of the vessel, which may be capable of accommodating plaque without concomitant lumen encroachment of up to 40% area stenosis (22). Depicting lesion morphology by high frequency (12 MHz) epicardial echocardiography has been demonstrated to be feasible, but only in the limited setting of cardiac surgery (23). With the advent of intravascular ultrasound, accurate measures of lumen and plaque size in cross-sectional images can now be obtained during cardiac catheterization (17,24). A recent study (25) of lesion morphology using intravascular ultrasound demonstrated that 69% of all imaging sites had eccentric involvement, and that the prevalence of eccentricity decreased with increasing stenosis. However, no separate analysis regarding lesion morphology and site within the coronary artery circulation (i.e., proximal or bifurcational) was reported.

The feasibility of intravascular ultrasound in relating lesion morphology to its relative position in the coronary artery tree is seen in the present study. Although an absolute coordinate reference system is inherently lacking, orientation of intravascular ultrasound images can be ascertained by the identification of branching vessels and other landmarks. The identification of the takeoff of the circumflex artery on intravascular ultrasound images was easily performed in all patients, and provided the necessary orientation to evaluate relative position and morphology of proximal left anterior descending coronary atheroma (Fig. 6).

Clinical implications. Studies of angioplasty of the proximal left anterior descending coronary artery lesion have reported high angiographic restenosis rates of 40 to 60% (13–15). Our data indicate that concentric disease in the proximal left anterior descending coronary artery appears to be a rarity. Eccentric lesions may respond to angioplasty, primarily with initial stretching of the nondiseased arterial wall, and subsequent elastic recoil (26,27). Elastic recoil may contribute to the restenotic process by decreasing initial luminal gain (28), inducing late recoil to a proportional degree (29) or stimulating cell proliferation in the overstretched segment (30). Thus, our findings suggest that the relatively higher restenosis rate reported in proximal left anterior descending coronary artery lesions may be due to the inherent eccentricity of lesions at this location and the subsequent recoil or hyperplasia of the noncalcified flow divider region.

Study limitations. The lumen obstruction produced by most lesions included in the present study was of mild to moderate severity. Only 2 of 42 lesions had a minimal lumen diameter <2 mm by ultrasound. In addition, none of the patients in the present study were judged to have proximal left anterior descending coronary artery lesions of sufficient severity to warrant revascularization. However, several patients had

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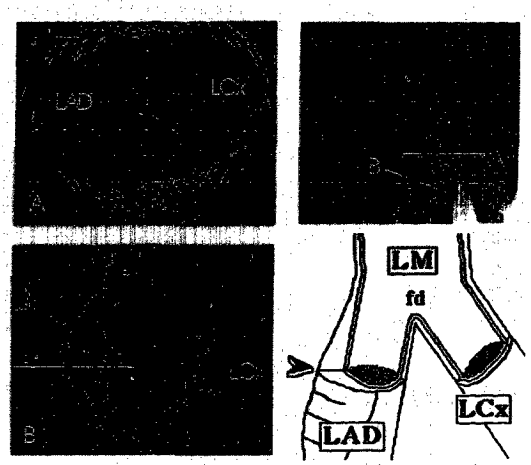

Figure 6. Composite illustration demonstrating orientation of the proximal left anterior descending coronary artery (LAD) lesion. Intravascular ultrasound images from the left main (LM) bifurcation (**A**) and proximal left anterior descending coronary artery (**B**) are shown with accompanying left anterior oblique cranial angiogram (**top right**). Note the lack of angiographic stenosis, despite disease presence by ultrasound, due to compensatory enlargement of the vessel (see text). The accompanying schematic (**bottom right**) demonstrates the location of plaque (**arrow**) opposite the flow divider (fd). LCx = circumflex artery.

advanced lesions (<2.5 mm); therefore, we believe that it is unlikely that our results would differ with lesions of even greater severity.

Because pullback imaging was performed manually at varying rates, the precise distance from the actual left main bifurcation can only be estimated. Because of the presence of the circumflex artery in the far field of many of the frames, we suspect that our images are from within the first 1 cm of the left anterior descending coronary artery and represent a very proximal, or in some instances, even ostial location. We avoided the more distal images of the proximal left anterior descending coronary artery (i.e., nearer to the takeoff of the first septal perforator or diagonal branches) because the orientation and flow patterns at this distance from the left main bifurcation are less certain. Intravascular ultrasound images indicated that atheroma in this region appear to be a continuation of the initial bifurcation lesion with similar orientation.

Other potential factors that may have influenced the results of our study are related to the technical aspects of intravascular ultrasound imaging. Nonuniform rotation of the ultrasound catheter may distort intravascular ultrasound images (31,32), and could have potentially caused errors in the angular measurements performed. Images grossly affected by this distortion were not included in the study. More important, nonuniform rotational distortion would have been expected to produce random changes in the intravascular ultrasound images, yet none of our patients exhibited maximal thickness of the flow divider. Therefore, the conclusions regarding atherosclerotic sparing of the flow divider and eccentricity ratios remain unaffected. Catheter tilt and "blooming" could have caused some artifactual wall thickening. Analysis of image shape and catheter position within the lumen showed no trend to support such an error. We suspect that if such an effect exists, its impact is small and sporadic. Electrocardiographic gated acquisition of intravascular ultrasound images was not used, and may have had a minor, random, occult effect on measurement of vessel morphology. However, changes in vessel anatomy during the cardiac cycle are minimal, and there is no reason to believe that they would have affected the conclusions of this study.

Conclusions. The present study demonstrates the inherent eccentricity of the atherosclerotic lesion in the proximal left anterior descending coronary artery in patients with coronary artery disease. The lesion appears to be universally located on the lateral wall, opposite the circumflex takeoff, regardless of severity of stenosis. This observation supports the role of mechanical fluid dynamic factors in the initiation and growth of atherosclerotic lesions in the proximal left anterior descending coronary artery and provides a potential explanation for the response to catheter-based interventions at this site.

References

1. Montenegro MR, Eggen DA. Topography of atherosclerosis in the coronary arteries. Lab Invest 1968;18:125–33.
2. Fox B, James K, Morgan B, Seed A. Distribution of fatty and fibrous plaques in young human coronary arteries. Atherosclerosis 1982;41:337–47.
3. Svindland A. The localization of sudanophilic and fibrous plaques in the main left coronary bifurcation. Atherosclerosis 1983;48:139–45.
4. Grottum P, Svindland A, Walloe L. Localization of atherosclerotic lesions in the bifurcation of the main left coronary artery. Atherosclerosis 1983;47:55–62.
5. Fox B, Seed WA. Location of early atheroma in the human coronary arteries. J Biomech Eng 1981;103:208–12.
6. Stary HC. Evolution and progression of atherosclerotic lesions in coronary arteries of children and young adults. Arteriosclerosis 1989;9 Suppl I:I19–I32.
7. Nerem RM. Vascular fluid mechanics, the arterial wall, and atherosclerosis. J Biomech Eng 1992;114:274–82.
8. Glagov S, Zarins C, Giddens DP, Ku DN. Hemodynamics and atherosclerosis. Arch Pathol Lab Med 1988;112:1018–31.
9. Friedman MH, Peters OJ, Bargeron CB, Hutchins GM, Mark FF. Shear-dependent thickening of the human arterial intima. Atherosclerosis 1986;60:161–71.
10. Berceli SA, Warty VS, Sheppeck RA, Mandarino WA, Tanksale SK, Borovetz HS. Hemodynamics and low density lipoprotein metabolism: rates of low density lipoprotein incorporation and degradation along medial and lateral walls of the rabbit aorto-iliac bifurcation. Arteriosclerosis 1990;10:688–94.
11. Rahimtoola SH. Left main equivalence is still an unproved hypothesis but proximal left anterior descending coronary artery disease is a "high-risk" lesion. Am J Cardiol 1984;53:1719–21.
12. Klein LW, Weintraub WS, Agarwall JB, et al. Prognostic significance of severe narrowing of the proximal portion of the left anterior descending coronary artery. Am J Cardiol 1986;58:42–6.
13. Frierson JH, Dimas AP, Whitlow PL, et al. Angioplasty of the proximal left anterior descending coronary artery: initial success and long-term follow-up. J Am Coll Cardiol 1992;19:745–51.
14. Whitworth HB, Pilcher GS, Roubin GS, Gruentzig AR. Do proximal lesions

involving the origin of the left anterior descending artery have a higher restenosis rate after coronary angioplasty? [abstract] Circulation 1985;72 Suppl III:III-398.

15. Vandormael MG, Deligonul U, Kern MJ, et al. Multilesion coronary angioplasty: clinical and angiographic follow-up. J Am Coll Cardiol 1987;10: 246–52.
16. Alfonso F, Macaya C, Goicolea J, et al. Intravascular ultrasound imaging of angiographically normal coronary segments in patients with coronary artery disease. Am Heart J 1994;127:536–44.
17. Nissen SE, Gurley JC, Grines CL, et al. Intravascular ultrasound assessment of lumen size and wall morphology in normal subjects and patients with coronary artery disease. Circulation 1991;84:1087–99.
18. Penny WS, Rockman H, Long J, et al. Heterogeneity of vasomotor response to acetylcholine along the human coronary artery. J Am Coll Cardiol 1995;25:1046–55.
19. Ambrose JA, Winters SL, Stern A, et al. Angiographic morphology and the pathogenesis of unstable angina pectoris. J Am Coll Cardiol 1985;5:609–16.
20. Ellis SG, Vandormael MG, Crowley MJ, Deligonul U, Topol EJ, Bulle TM. Coronary morphologic and clinical determinants of procedural outcome with angioplasty for multivessel coronary disease: implications for patient selection. Circulation 1990;82:1193–202.
21. Honye J, Mahon DJ, Jain A, et al. Morphological effects of coronary balloon angioplasty in vivo assessed by intravascular ultrasound imaging. Circulation 1992;85:1012–25.
22. Glagov S, Weisenberg E, Zarins CK, Stankunavicius R, Kolettis GJ. Compensatory enlargement of human atherosclerotic coronary arteries. N Engl J Med 1987;316:1371–5.
23. McPherson DD, Johnson MR, Alvarez NM, et al. Variable morphology of coronary atherosclerosis: characterization of atherosclerotic plaque and residual arterial lumen size and shape by epicardial echocardiography. J Am Coll Cardiol 1992;19:593–9.
24. Liebson PR, Klein LW. Intravascular ultrasound in coronary atherosclerosis: a new approach to clinical assessment. Am Heart J 1992;123:1643–60.
25. Hausmann D, Lundkvist AJS, Friedrich G, Sudhir K, Fitzgerald PJ, Yock PG. Lumen and plaque shape in atherosclerotic coronary arteries assessed by in vivo intracoronary ultrasound. Am J Cardiol 1994;74:857–63.
26. Waller BF. Coronary luminal shape and the arc of disease-free wall: morphologic observations and clinical relevance. J Am Coll Cardiol 1985;6: 1100–1.
27. Rensing BJ, Hermans WR, Strauss BH, Serruys PW. Regional differences in elastic recoil after percutaneous transluminal coronary angioplasty: a quantitative angiographic study. J Am Coll Cardiol 1991;17 Suppl B:34B–8B.
28. Rozenman Y, Gilon D, Welber S, Sapoznikov D, Gotsman MS. Clinical and angiographic predictors of immediate recoil after successful coronary angioplasty and relation to late restenosis. Am J Cardiol 1993;72:1020–25.
29. Waller BF, Pinkerton CA, Orr CM, Slack JD, VanTassel JW, Peters T. Morphological observations late (>30 days) after clinically successful coronary balloon angioplasty. Circulation 1991;83 Suppl I:I-28–41.
30. Liu WM, Roubin GS, King SB III. Restenosis after coronary angioplasty: potential determinants and role of intimal hyperplasia. Circulation 1989;79: 1374–87.
31. ten Hoff H, Korbijn A, Smit TH, Klinkhamer JFF, Bom N. Imaging artifacts in mechanically driven ultrasound catheters. Int J Card Imaging 1989;4: 195–9.
32. Kimura BJ, Bhargava V, Palinski W, Peterson KL, DeMaria AN. Can intravascular ultrasound yield accurate measures of vascular anatomy? Documentation of the critical importance of uniform rotational velocity [abstract]. J Am Coll Cardiol 1994;23:173A.