

Successful Directional Atherectomy of De Novo Coronary Lesions Assessed With Three-Dimensional Intravascular Ultrasound and Angiographic Follow-Up

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Recent histopathologic and intravascular ultrasound (IVUS) data indicate that inadequate compensatory enlargement of atherosclerotic lesions contributes to the development of significant arterial stenoses. Such lesions may contain less plaque, which may have implications for atheroablative interventions. In this study, we compared lesions with (group A, $n = 16$) and without inadequate compensatory enlargement (group B, $n = 30$) as determined by IVUS. The acute results and the follow-up lumen dimensions of angiographically successful directional coronary atherectomy procedures were compared. Inadequate compensatory enlargement was considered present when the preintervention arterial cross-sectional area at the target lesion site was smaller than that at the (distal) reference site. Three-dimensional IVUS analysis and quantitative angiography were performed in 46 patients before and after intervention. IVUS measurements included the arterial, lumen, and plaque (ar-

terial minus lumen) cross-sectional areas at the target lesion site (i.e., smallest lumen site) and the (distal) reference site. Angiographic follow-up was performed in 42 patients. Preintervention and postintervention angiographic measurements and IVUS lumen cross-sectional area measurements were similar in both groups. However, at follow-up, the angiographic minimum lumen and reference diameters were significantly smaller in group A compared with group B (1.71 ± 0.47 mm vs 2.14 ± 0.73 mm, $p < 0.03$, and 2.97 ± 0.29 mm vs 3.39 ± 0.76 mm, $p < 0.02$; group A vs B). The data of this observational study suggest that lesions with inadequate compensatory enlargement, as determined by IVUS before intervention, may have less favorable long-term lumen dimensions after directional coronary atherectomy procedures. ©1997 by Excerpta Medica, Inc.

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Histopathologic studies in primates and humans have demonstrated that atherosclerotic arteries tend to undergo compensatory enlargement to accommodate an increasing plaque burden to preserve luminal dimensions until the progressive accumulation of plaque exceeds the ability of the vessel to compensate.^{1,2} Subsequently, Clarkson et al³ extended this concept by suggesting that failure of compensatory enlargement may be important in the development of significant arterial stenoses. Intravascular ultrasound (IVUS) provides transmural images of coronary vessels in vivo. The coronary vascular wall, the cross-sectional area of the atherosclerotic plaque, accurate lumen dimensions, and the serial changes that occur with the atherosclerotic disease process can be studied in humans in a manner previously not possible.⁴⁻⁷ The initial studies with IVUS and epicardial ultrasound confirmed the concept of compensatory vascular enlargement.⁴⁻⁸ However, recent histopathologic and IVUS data in atherosclerotic peripheral⁹ and coronary arteries^{10,11} supported the hypothesis of Clarkson et al³ and showed evidence of inadequate compensatory

vascular enlargement. Lesions with inadequate compensatory enlargement have been shown to contain less plaque burden; this may have implications for atheroablative interventions such as directional coronary atherectomy.¹¹⁻²⁰ Therefore, we compared lesions with and without inadequate compensatory enlargement, as determined by preintervention IVUS, with regard to the acute results and follow-up lumen dimensions following successful directional coronary atherectomy procedures.

METHODS

Study population: The study groups consisted of 46 symptomatic patients who were treated by directional coronary atherectomy procedures at the Washington Hospital Center, the Kokura Memorial Hospital, or the Thoraxcenter Rotterdam. Patients were included if they met the following criteria: (1) successful directional atherectomy (with or without adjunctive balloon angioplasty) of a single, primary nonostial lesion with limited calcification throughout its length, (2) high-quality IVUS recordings using motorized transducer pull-back through a stationary imaging sheath both before and after the intervention, and (3) lack of complete occlusion of the stenotic lumen during the initial IVUS imaging run. There were 38 men and 8 women who ranged in age from 37 to 76 years (mean 59 ± 9). Lesion location was the left anterior descend-

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ing coronary artery (n = 29), right coronary artery (n = 12), and left circumflex coronary artery (n = 5); 37 lesions were proximal and 9 were midvessel.

Lesions were divided into 2 groups based on pre-intervention IVUS measurements: (1) lesions with inadequate compensatory enlargement (group A) and (2) lesions with adequate compensatory enlargement (group B). There was no significant difference between group A and B with regard to the characteristics of the patients and lesion location. The study was approved by the Local Councils on Human Research. All patients signed a written informed consent form approved by the Local Medical Ethics Committees.

Interventional procedure: All patients received 250-mg aspirin and 10,000-U heparin intravenously. If the duration of the entire catheterization procedure was >1 hour, the activated clotting time was measured, and intravenous heparin was administered in order to maintain an activated clotting time of >300 seconds. After intracoronary injection of 0.2-mg nitroglycerin, the coronary artery was examined with IVUS. Directional coronary atherectomy (Devices for Vascular Intervention, Redwood City, California) was performed according to standard protocols. If required, predilation before the atherectomy (but after the initial IVUS run) was performed (n = 3). A final IVUS imaging run was then performed at the end of the procedure. In the patients with adjunctive balloon angioplasty, the final IVUS imaging run was performed after the balloon dilation. Follow-up angiography was performed after 6 months in 42 patients (91.4%), using a standard cardiac catheterization and angiography protocol.

Atherectomy was performed using an average of 23 ± 10 cuts and a mean pounds per square inch (lbs/in²) of 26 ± 11 . The maximum cutter size of the atherectomy device was 7Fr in 43 patients and 6Fr in 3 patients. In 31 patients (67.4%), adjunctive balloon angioplasty was performed, using a nominal balloon size of 3.9 ± 0.6 mm at a maximum pressure of 10.0 ± 4.9 atm. There was no significant difference between group A and B with regard to the characteristics of the interventional procedures; adjunctive balloon angioplasty was performed in 68.7% (11 of 16 patients) and 66.7% (20 of 30 patients), respectively.

Intravascular ultrasound imaging: A mechanical IVUS system (CardioVascular Imaging Systems Inc., San Jose, California) and a sheath-based imaging catheter were used. The catheter incorporated a 30-MHz beveled, single-element transducer rotating at 1,800 rpm within a stationary echolucent imaging sheath. Two catheter designs were used: (1) a 3.2Fr short monorail version or (2) a 2.9Fr long monorail version. The common distal lumen of the latter version alternatively houses the guidewire (during catheter introduction) or the transducer (during imaging after the guidewire is pulled back), but not both. These sheath-based catheter designs avoid direct contact of the imaging core with the vessel wall. The ultrasonic transducer was withdrawn through the stationary imaging sheath using a motorized pull-back device at a constant speed of 0.5 mm/s. The IVUS catheter was

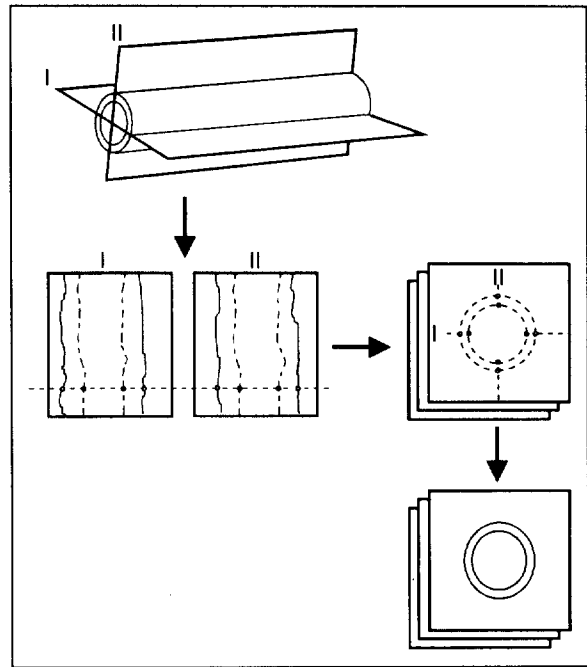


FIGURE 1. Automated contour detection of the luminal and arterial boundaries was first performed on 2 perpendicular longitudinal sections (I, II) that were reconstructed from the image data of a 3-dimensional stack of IVUS images. The 3-dimensional approach permitted interpretation in the longitudinal dimension and facilitated the detection of the contours on the planar images. Edge information from the longitudinal contours was represented as points on the planar images, defining the center and range for the final automated contour detection process. The contours on the planar images were checked and edited if required. Measurements were derived from these contours.

advanced ≥ 10 mm distal to the lesion segment, the motorized transducer pull-back device was then activated, and imaging continued (uninterrupted) until the transducer reached the aorto-ostial junction. All IVUS studies were recorded on high-resolution s-VHS videotape for off-line quantitative analysis.

Intravascular ultrasound contour detection algorithm: All preintervention and postintervention IVUS studies were analyzed with a computerized analysis system operating in either a single-frame mode (to analyze a preselected single reference image) or in 3-dimensional mode (to perform a segmental analysis of the entire lesion segment).²¹⁻²³ In 3-dimensional mode, a "stack" of IVUS images (10 images/mm of arterial length) was digitized from videotape. Two longitudinal sections were automatically reconstructed (Figure 1), and the contours corresponding to the lumen-tissue and media-adventitia interfaces were automatically identified. The automatic contour detection was then visually checked; if necessary, the longitudinal contours were edited.

The longitudinal contours generated 8 individual points on the corresponding planar images (4 for the lumen-tissue interface and 4 for the media-adventitia interface) which defined the range of interest for contour detection on the planar images.²¹⁻²³ Automated detection and computer-assisted editing of the contours assigned to the tissue-lumen and media-adven-

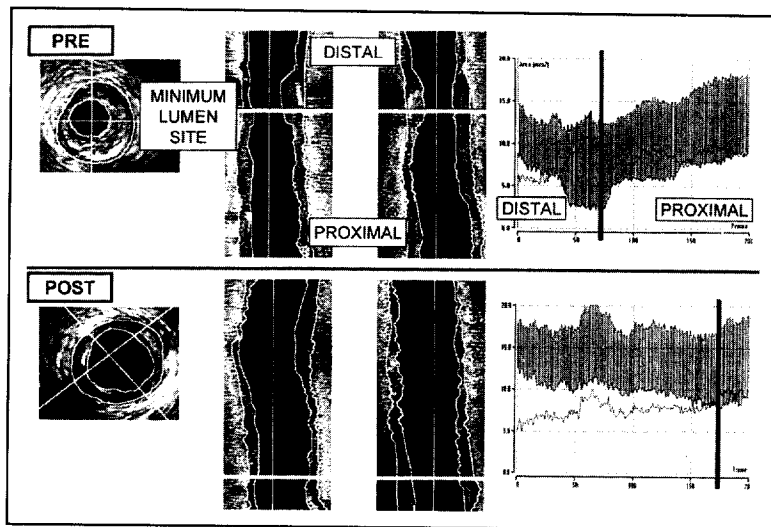


FIGURE 2. Three-dimensional IVUS analysis of an entire lesion segment (i.e., the treated vascular segment) before (*PRE*, upper panels) and after directional coronary atherectomy with adjunctive balloon angioplasty (*POST*, lower panels); lesion location was the mid-segment of a right coronary artery. The cut-planes of the longitudinally reconstructed IVUS sections (middle panels) are indicated on the planar IVUS images (left panels), which represent the target lesion sites (i.e., minimum lumen site). Markers on both, the longitudinal sections (white horizontal markers) and the result displays (black vertical markers, right panels) indicate the site of the image with the smallest lumen cross-sectional area. The results of cross-sectional area measurements (in square millimeters) on 200 planar IVUS frames are displayed in the right panels. Linear functions of the arterial and lumen cross-sectional area form the upper and lower boundaries of the grayish area, which represents the plaque plus media cross-sectional area. Note that before the intervention (right upper panel), the arterial area was smallest at the target lesion site (12.9 mm^2), indicating inadequate compensatory enlargement.

titia interfaces on the planar image slices were based on the application of a minimum-cost algorithm. Each digitized IVUS image was resampled in a radial format (64 radii per image); a cost matrix representing the edge strength was calculated from the image data. For the boundary between lumen and plaque, the cost value was defined by the spatial first derivative. For the media-adventitia boundary a cross-correlation pattern matching process was used for the cost calculations. The path with the smallest accumulated value was determined by dynamic programming techniques. Small side branches or small calcified deposits were generally ignored by the algorithm as a result of its robustness.

The axial location of an individual planar image on the longitudinal presentation was indicated by a cursor; this cursor was used to scroll through the entire set of planar images to visually check the contours. Careful checking and editing of the contours of the planar images was performed. The computer-assisted editing differed considerably from conventional manual contour tracing. The computer mouse was pointed on the correct boundary to give that site a very low value in the cost matrix, which "forced" the contour through that point. Editing the contour of a single slice caused the entire data set to be updated. Finally, the contour data of the planar images were used for the computation of the results (Figure 2).

Previous validation of this algorithm has been per-

formed in tubular phantoms.²² A comparison between automated 3-dimensional IVUS measurements in atherosclerotic coronary specimen *in vitro* and morphometric measurements on the corresponding histologic sections revealed good correlations ($r = 0.80$ to 0.94 for cross-sectional area measurements).²¹ The cross-sectional area measurements agreed well with results obtained by manual tracing of IVUS images (mean differences $\pm 3.7\%$; $r = 0.97$).²¹ *In vivo*, the intraobserver and interobserver comparison of the analysis method revealed a high correlation ($r = 0.95$ to 0.98 for cross-sectional area measurements) and small mean differences ($\pm 1.1\%$), with SD, for lumen, arterial, and plaque plus media cross-sectional areas not exceeding 7.3%, 4.5%, and 10.9%.²²

Intravascular image analysis: The arterial cross-sectional area was measured as the area within the border between the hypoechoic media and the echoreflexive adventitia. As in many previous studies using IVUS,^{17,18,23,24} the plaque plus media cross-sectional area was used as a measure of atherosclerotic plaque, because ultrasound cannot measure media thickness accurately.²⁵

As in previous 3-dimensional IVUS studies,²⁴ the entire lesion segment (i.e., entire region of treatment) was identified by (1) comparing the ultrasound images before and after the intervention, noting lumen increase, topographical landmarks (such as side branches and calcification), and typical postintervention findings of plaque defects and flaps; and (2) the tape-recorded comments of the operator. The lesion segments ($19.3 \pm 4.3 \text{ mm}$) were digitized (193 ± 43 images/segment) and analyzed with the contour detection system. The target lesion site (i.e., the site of the smallest lumen cross-sectional area) was automatically identified from the computerized analysis of the entire lesion segment. The reference site was visually determined from the preintervention IVUS study as the image slice with the smallest plaque burden within 3 mm distal to the lesion segment, but before any major side branch (on average $10.2 \pm 2.9 \text{ mm}$ distal to center of the lesion site). Measurements at the target lesion and reference sites included the arterial, lumen, and plaque plus media (arterial minus lumen) cross-sectional area and the cross-sectional area plaque burden (plaque plus media divided by arterial cross-sectional area).

Inadequate compensatory enlargement was determined from preintervention IVUS imaging, comparing the target lesion with the distally located reference site. Using a definition, initially suggested by Nishio et al¹⁰: "inadequate compensatory enlargement was considered present when the arterial cross-

TABLE I Intravascular Ultrasound Data of Target Lesion Sites			
	Group A	Group B	p Value
Preintervention			
Arterial CSA (mm ²)	13.2 ± 3.0	17.6 ± 5.1	<0.001
Lumen CSA (mm ²)	2.5 ± 1.0	2.7 ± 1.5	NS
Plaque + media CSA (mm ²)	10.8 ± 2.8	14.9 ± 4.4	<0.0005
CSA plaque burden (%)	84.6 ± 6.5	80.9 ± 7.5	NS
Postintervention			
Arterial CSA (mm ²)	15.4 ± 2.3 [†]	18.4 ± 6.3	<0.03
Lumen CSA (mm ²)	6.4 ± 1.5 [‡]	6.9 ± 2.2 [‡]	NS
Plaque + media CSA (mm ²)	9.1 ± 1.5 [*]	11.5 ± 5.1 [‡]	<0.03
CSA plaque burden (%)	58.7 ± 6.5 [‡]	61.2 ± 8.8 [‡]	NS

Data are mean values ± 1 SD.
Pre- versus postintervention data: *p <0.01; †p <0.001; ‡p <0.0001.
CSA = cross-sectional area.
Target lesion sites were determined by the smallest lumen cross-sectional area.

tional area at the target lesion site was smaller than that at the reference site.’’

Quantitative coronary angiography: Quantitative angiographic analysis was performed offline on end-diastolic frames with homogeneous opacification of the coronary lumen acquired after intracoronary application of nitrates, as previously described.¹⁴ We used a computer-based Coronary Angiography Analysis System (CAAS, PieMedical, Maastricht, The Netherlands). The measurements were performed by an experienced analyst in 22 angiograms and obtained from opposite (ideally orthogonal) angiographic views without overlapping side branches or foreshortening. The absolute angiographic diameter of the stenosis was determined using the nontapering part of the contrast-free guiding catheter as a scaling device. The minimal lumen diameter was measured by edge detection; the interpolated reference diameter was based on a computerized estimation of the original lumen dimension at the site of the obstruction. The diameter stenosis was derived from the measured minimal lumen diameter and the reference diameter.

Statistical analysis: Quantitative data were given as mean value ± SD. Dichotomous variables were expressed as frequencies and compared using chi-square statistics. Continuous variables were compared using the 2-tailed Student’s *t* test and linear regression analysis. A *p* value <0.05 was considered statistically significant.

RESULTS

Intravascular ultrasound data (Table I): Inherent with the IVUS-based classification, in group A the preintervention arterial cross-sectional area was smaller at the target lesion than at the reference site (13.2 ± 3.0 mm² vs 14.4 ± 3.5 mm², *p* <0.003; difference: -0.1 to -3.2 mm²). In group B the arterial cross-sectional area was larger at the target lesion site than at the reference site (17.6 ± 5.1 mm² vs 14.0 ± 5.3 mm², *p* <0.0001; difference: 0.1 to 9.6 mm²). Both the arterial cross-sectional area and the plaque plus media cross-sectional area of the target lesion site were smaller in group A than in group B (*p* <0.001).

During intervention, lumen dimensions increased

significantly (*p* <0.0001) with a residual cross-sectional area plaque burden of 58.7 ± 6.5% versus 61.2 ± 8.8% for groups A and B, respectively. Residual arterial and plaque plus media cross-sectional areas were smaller in group A (*p* <0.03 for both).

Quantitative angiographic measurements (Table II): During the intervention, overall the minimal lumen diameter increased significantly from 1.13 ± 0.35 mm to 2.7 ± 0.49 mm (*p* <0.0001); the reference diameter increased from 3.26 ± 0.57 mm to 3.44 ± 0.51 mm (*p* <0.002); and the diameter stenosis decreased from 64 ± 13% to 21 ± 12% (*p* <0.0001). When group A was compared with group B, there was no significant difference in pre- and postintervention reference diameter, minimal lumen diameter, or diameter stenosis.

Angiographic follow-up was available in 42 patients (91.4%) (group A, 15 of 16 or 93.7%, and group B, 27 of 30 or 90%). Overall, the minimal lumen diameter measured 1.99 ± 0.68 mm, the reference diameter 3.24 ± 0.66 mm, and the diameter stenosis 39 ± 14%. Both the reference and minimal lumen diameters measured at follow-up were significantly smaller in group A than in group B (Figure 3). Because the reference diameters at follow-up were significantly smaller in group A, there was no difference in diameter stenosis (42 ± 15% vs 38 ± 14%, *p* = 0.37); a diameter stenosis of 50% was found in 5 patients of each group (group A, 5 of 15 or 33.3%, and group B, 5 of 27 or 18.5%, *p* = 0.28).

DISCUSSION

In the current study inadequate compensatory enlargement was present before intervention in 35% of the de novo coronary lesions treated with directional coronary atherectomy. The main finding of the present study is that despite similar postintervention lumen dimensions of both lesions with and without inadequate compensatory enlargement, the angiographic minimal lumen and reference diameters at follow-up were significantly smaller in lesions with inadequate compensatory enlargement, as determined by IVUS before intervention.

Quantitative coronary angiography²⁶ and planar IVUS studies²⁷ have previously shown that the postintervention lumen dimensions and the residual cross-sectional area plaque burden at the lesion site are predictors of the follow-up lumen dimensions. The findings of this study suggest that the arterial remodeling state before directional atherectomy procedures could be another factor that may influence the follow-up lumen dimensions.

As in previous IVUS studies, both plaque ablation and vessel wall stretch accounted for the procedural lumen gain in the present study. The residual postintervention cross-sectional area plaque burden at the

	Group A	Group B	p Value
Preintervention			
Reference diameter (mm)	3.14 ± 0.50	3.32 ± 0.60	NS
MLD (mm)	1.08 ± 0.38	1.16 ± 0.33	NS
Diameter stenosis (%)	66 ± 10	64 ± 14	NS
Postintervention			
Reference diameter (mm)	3.26 ± 0.45	3.54 ± 0.52	NS
MLD (mm)	2.65 ± 0.45	2.74 ± 0.51	NS
Diameter stenosis (%)	18 ± 12	22 ± 12	NS
Follow-up			
Reference diameter (mm)	2.97 ± 0.29	3.39 ± 0.76	<0.02
MLD (mm)	1.71 ± 0.47	2.14 ± 0.73	<0.03
Diameter stenosis (%)	42 ± 15	38 ± 14	NS

Data are mean values ± 1 SD.
MLD = minimal lumen diameter.

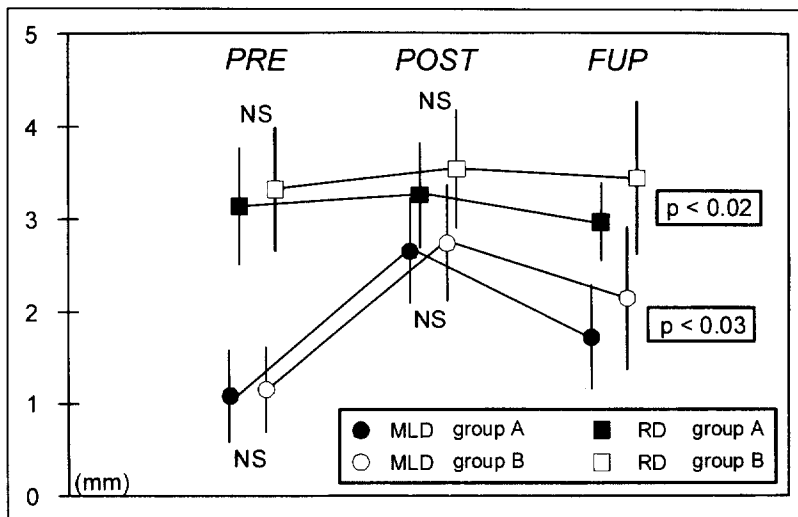


FIGURE 3. Between groups A and B, there was no significant difference in pre-(PRE) and postintervention (POST) reference diameter (RD) and minimal lumen diameter (MLD) as measured by quantitative coronary angiography. However, at 6-month angiographic follow-up (FUP) both minimal lumen and reference diameters were significantly smaller in group A.

smallest lumen site (60%) was comparable to that of most previous studies using planar IVUS analysis.^{15-18,24,28}

Three-dimensional IVUS image analysis: Three-dimensional reconstruction of the ultrasonic images was initially used to visually assess the spatial configuration of the lumen and plaque and to perform elementary measurements.^{29,30} Recently, algorithms for automated quantification of the lumen dimensions have been introduced.^{21-23,31} The automated 3-dimensional IVUS analysis system applied in the present study (Figure 2) can be used to detect the tissue-lumen boundary as well as the media-adventitia (external elastic membrane) boundary on a relatively larger number of IVUS images per millimeter arterial length.²¹⁻²³ In addition, it facilitates the detection of the target lesion site with the smallest lumen size.³¹

Study limitations and potential sources of error: (1) Because our data were derived from a nonconsecutive series of patients (only successful directional atherectomy

procedures), no conclusion regarding the primary success rate of directional coronary atherectomy in lesions with or without inadequate compensatory enlargement can be made. (2) Because the external vascular boundary cannot be seen in the acoustic shadowing behind calcium, we excluded cases with severe calcification. (3) Intracoronary injections of nitrates were used to prevent vasospasm, and no angiographic changes were observed before and after the IVUS imaging procedure; nevertheless, local vasospastic activity cannot completely be excluded. (4) The follow-up examination was performed with angiography only (no IVUS follow-up); however, coronary angiography is not able to distinguish between late unfavorable remodeling and intimal hyperplasia, the principal mechanisms of lesion recurrence at follow-up. (5) Coronary angiography delineates only the vessel lumen as a silhouette and foreshortens vessel segments, depending on the projection used. (6) Electrocardiographic gated image acquisition can facilitate the automated quantitative analysis of 3-dimensional IVUS image sets,^{23,31} but at the time of the present study, the electrocardiographic gated approach was not yet available.

Clinical implications: Coronary lesions with inadequate compensatory enlargement, as defined by IVUS, may have less favorable long-term lumen dimensions, despite initially successful directional atherectomy procedures. Selection of lesions with more favorable remodeling before intervention may help to improve the long-term outcome after directional coronary atherectomy.

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