

## Intracoronary Ultrasound Assessment of Directional Coronary Atherectomy: Immediate and Follow-Up Findings

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**Objectives.** This study was conducted to assess the relations among intracoronary ultrasound, angiographic and histologic data obtained from patients with coronary artery disease successfully treated by directional coronary atherectomy. In addition, it was designed to elucidate whether some aspects of intravascular ultrasound or pathologic findings could predict a propensity to restenosis.

**Background.** Intracoronary ultrasound is a useful technique in guiding and assessing atherectomy. However, there is little information about the characterization of the different types of coronary plaques and the changes observed in them after resection. Furthermore, the follow-up ultrasound appearance of previously treated lesions remains undepicted.

**Methods.** Fifty-two patients (54 ± 10 years old) were studied. All were successfully treated by atherectomy with the aid of intracoronary ultrasound guidance. Qualitative and quantitative ultrasound and angiographic variables were derived before and after resection. Quantitative histologic morphometric information was also obtained from the specimens. In 22 patients, a follow-up echoangiographic reevaluation was performed 6 ± 4 months later.

Intracoronary ultrasound appears to be a useful technique for guiding and assessing the results of directional coronary atherectomy (1,2). This procedure allows for pathologic analysis of the resected material, which could help to improve our knowledge of the characterization of different lesion types. However, there is little information about the ultrasound appearance of the different types of coronary plaques before treatment and the changes observed after directional coronary atherectomy. Furthermore, the follow-up

**Results.** Echogenic plaques had a higher collagen and calcium content, whereas echolucent plaques had an increased level of fibrin, nuclei and lipids. Ultrasound plaque reduction after atherectomy was greater in echolucent (76 ± 21%) than in echogenic plaques (60 ± 18%;  $p < 0.05$ ). That reduction correlated with the weight of the resected material ( $r = 0.62$ ;  $p < 0.01$ ). At follow-up study, 13 of 22 patients had angiographic and ultrasound evidence of restenosis. Most recurrent lesions had a stenotic three-layer appearance. The incidence of restenosis of primary lesions treated with atherectomy was higher in echolucent (100%) than in echogenic (33%) plaques. Similarly, a higher proportion of nuclear content in the resected material was observed in patients who developed restenosis (2.1 ± 0.7%) than in patients who had late success after atherectomy (1.2 ± 0.4%).

**Conclusions.** Our findings suggest that echolucent plaques are easier to resect than are echogenic plaques but frequently develop restenosis. In contrast, the resection of echogenic plaques, although often incomplete, is associated with better long-term results.

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ultrasound appearance of treated lesions has not been documented.

In the present study we analyze the relations among ultrasound, angiographic and pathologic information obtained in 52 patients with coronary artery disease who were successfully treated with directional coronary atherectomy. In 22 of these patients, echoangiographic reevaluation follow-up was performed.

### Methods

**Study patients.** Of a total of 159 patients with coronary artery disease treated with directional coronary atherectomy, we selected 66 for analysis who had ultrasound guidance during the procedure. Ultrasound guidance during atherectomy was used in the following situations: 1) single-vessel disease with arterial diameter >2.5 mm, 2) single, well defined coronary stenosis located outside of

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angles or tortuosities, and 3) nontortuous proximal or distal arterial segments. Patients were enrolled in the study between September 1990 and January 1992. All gave written, informed consent to enter the study protocol. Eleven of these patients had an echographic study that was considered unsuitable for analysis and were excluded. Another three patients were also excluded because of emerging complications during the procedure that made it inadvisable to continue with the ultrasound protocol. Thus, the study group comprised 52 patients, all having had ultrasound guidance, successful directional coronary atherectomy without the need of adjunctive balloon angioplasty and ultrasound assessment of the result. The mean age was  $54 \pm 10$  years; 45 were male and 7 female. Indication for revascularization was based on the spontaneous or induced evidence of myocardial ischemia. The clinical condition was stable angina in 11 patients and unstable angina in 27. Unstable angina was defined as angina of new onset, worsening effort angina or angina at rest. The remaining 14 patients had residual ischemia after early thrombolytic therapy in an evolving myocardial infarction. After myocardial infarction, the mean time to revascularization was  $22 \pm 25$  days (range 3 to 88). Vessels treated by atherectomy were the left anterior descending artery in 43 patients, the right coronary artery in 6 and the left circumflex coronary artery in 3. The target lesion was primary in 41 cases and restenosis after previous balloon angioplasty ( $n = 5$ ) or directional coronary atherectomy ( $n = 6$ ) in 11. No complications occurred in this group of 52 patients and revascularization was considered angiographically and clinically successful in all.

**Atherectomy protocol.** All patients were premedicated with aspirin and a calcium antagonist and received heparin (2 mg/kg) during the procedure. Directional coronary atherectomy was performed percutaneously through an 11F guiding catheter for the left coronary artery and a 9.5F catheter for the right coronary artery. Once the guiding catheter was engaged within the coronary ostium, a 0.014-in. (0.035 cm) high torque floppy guide wire was introduced through it to cross the target lesion. Baseline ultrasound analysis was then performed under angiographic monitoring. Once finished, the ultrasound catheter was interchanged with a Simpson's atherocatheter and atherectomy was performed according to recommended procedure (3). The size of the catheter was selected according to the angiographic measurements of the arterial diameter. A 7F catheter was used in 20 patients, a 6F catheter in 21 and a 5F catheter in 11. The number of cuts varied from 4 to 28 (mean  $11 \pm 6$  per procedure). The angiographic hand injection monitoring during the procedure enabled identification of an apparently satisfactory result. The catheter was then removed, leaving the wire in place, and the resected material was collected. If the angiographic result was considered satisfactory, the ultrasound catheter was again introduced to evaluate the result and identify the excised and residual plaque, as well as the resultant lumen. In eight patients, the on-line echo-

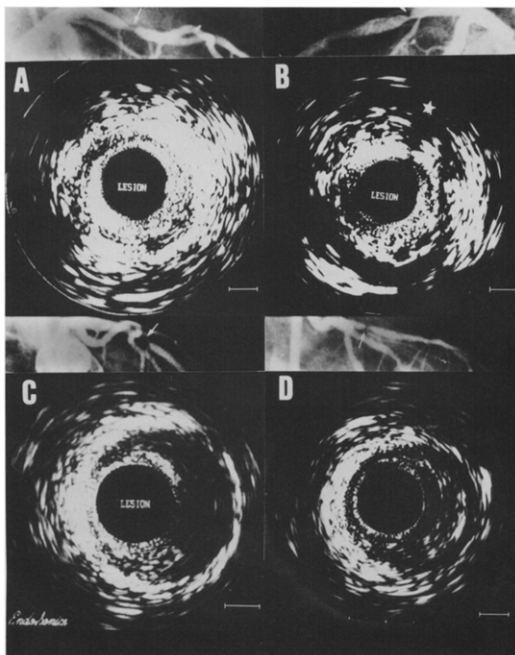
graphic result showed sizable persisting residual plaque, making it advisable to perform additional excision of plaque.

**Angiographic studies.** Angiographic analysis was performed on every patient before and after directional coronary atherectomy. In 22 patients, a follow-up angiographic evaluation was performed after a mean period of  $6 \pm 3$  months (range 2 to 11). Among all viewing angles, the one that better showed the treated segment was selected for analysis. At baseline study, 18 lesions had an irregular contour, suggesting complicated plaque (4,5). According to the American College of Cardiology/American Heart Association morphologic criteria for coronary angioplasty (6,7), 18 lesions were type A, 20 were type B<sub>1</sub> and 14 were type B<sub>2</sub>. The mean length of the lesion was  $5.9 \pm 2.8$  mm (range 1 to 11). Minimal lumen diameter and percent stenosis were measured in each condition. Measurements were taken on projected end-diastolic images by calipers and were corrected for magnification. Restenosis at follow-up study was defined as the loss of  $\geq 50\%$  initial gain. An interobserver variability analysis was undertaken for both angiographic variables obtained from 10 patients. The results for minimal lumen diameter were Observer 2 = 0.827 Observer 1;  $r^2 = 0.946$ , SEE = 0.45. For percent stenosis, they were Observer 2 = 1.056 Observer 1;  $r^2 = 0.96$ , SEE = 12.54.

**Ultrasound studies.** A 64-element, 5.5F, 20-MHz coaxial catheter (Endosonics) was used in every study. The entire study was recorded on video tape. Selected images were frozen and obtained for analysis by a printer during or after the procedure. The catheter was guided by angiographic monitoring and the tip positioned at different sites within the vessel (Fig. 1). Ultrasound gain settings were adjusted for optimal visualization of the arterial wall-lumen interface in normal segments. At the lesion level, the plaque was echographically analyzed, most frequently during conditions of compression because the probe was frequently wedged at the lesion. The probe could pass the lesion in 37 patients; in 15 patients, the ultrasound catheter was unable to cross the stenosis. When the lesion was crossed, a slow pullback was performed from distal to proximal segments to obtain three-dimensional information concerning the architecture of the lesion. Transverse analysis with the probe in wedge conditions revealed a frequent asymmetric distribution of the atheroma. At each site of the study, frequent flushing of angiographic contrast medium was helpful in identifying the lumen and intima, except in wedge conditions where flow was stagnant. Echogenicity of the plaque was always estimated under individual conditions of gain and gray-scale settings: plaques were considered as predominantly echogenic or predominantly echolucent by the agreement of three observers (Fig. 2); in seven patients, a mixed pattern was observed where no clear predominant distinction of echogenicity could be estimated. This mixed pattern was excluded for analysis of echogenicity of the plaque. To assess histologic differences, echogenic and echolucent plaques were compared. Focal calcium was identified as a dense



**Figure 1.** Study methodology. In every condition, ultrasound analysis was performed at different sites of the coronary tree, including the lesion site, under angiographic guidance. The arrows show the sites of ultrasound interrogation.



**Figure 2.** Ultrasound and angiographic appearance of different types of coronary lesion. A, Fully echogenic; B, predominantly echogenic with focal calcium; C, fully echolucent and D, predominantly echolucent. All ultrasound observations were performed in the wedge condition (arrows). Star = shadow effect of focal calcium; bars = 1 mm.

**Table 1.** Angiographic and Ultrasound Measurements Before and After Atherectomy

	Before Atherectomy (n = 52)	After Atherectomy (n = 52)	Follow-Up (n = 22)	
			Restenosis 5 ± 3 Months (n = 13)	Late Success 8 ± 2 Months (n = 9)
<b>Angiography</b>				
MLD (mm)	0.80 ± 0.8	2.98 ± 2.0	0.84 ± 0.4	2.8 ± 0.6
% stenosis	77 ± 8	15 ± 20	73 ± 13	15 ± 16
<b>Ultrasonography</b>				
MLD (mm)	—	3.8 ± 0.7	—	3.5 ± 0.6
Plaque area (mm <sup>2</sup> )	7.3 ± 3.3	—	2.1 ± 1.0	2.2 ± 1.0
Plaque reduction (mm <sup>2</sup> )	—	5.2 ± 3.5	2.7 ± 4.3	4.3 ± 1.7
Plaque reduction (%)	—	62 ± 21	21 ± 37	65 ± 19

MLD = minimal lumen diameter.

echogenic zone producing a characteristic shadow effect (8,9).

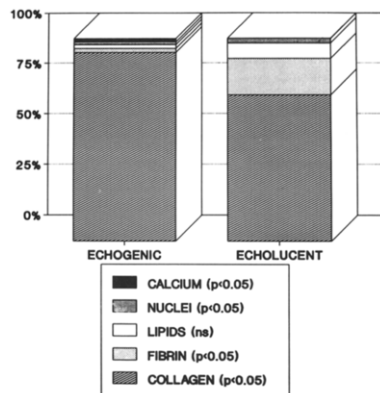
Quantitative echographic studies were performed from static end-diastolic selected images at different sites of analysis. The diameter and area of the lumen were measured in every condition and site. At the level of maximal stenosis, we outlined the plaque cross-sectional surface by identifying the media-intima interface in 18 patients. When this was not possible, the circumferential adventitial echoes were superimposed on those obtained from immediately proximal non-diseased segments where lumen was clearly delineated. The resultant cross-sectional plaque area was also outlined and determined by planimetry. The same method was used to measure residual plaque after treatment and at follow-up. Percent plaque reduction after treatment was calculated in every patient. The variability analysis of the ultrasound variables (plaque area and lumen area and diameter) was performed in 10 patients. Plaque area: Observer 2 = 0.95 Observer 1;  $r^2 = 0.995$ ; SEE = 0.583. Lumen area: Observer 2 = 0.91 Observer 1;  $r^2 = 0.99$ ; SEE = 0.583. Diameter: Observer 2 = 0.98 Observer 1;  $r^2 = 0.996$ ; SEE = 0.236.

**Pathologic studies.** Resected material was weighed and fixed in formalin for standard pathologic analysis. Qualitative inspections were performed to determine the presence or absence of several components of the plaque, as well as to identify the depth of the cuttings. Quantitative studies were performed with the aid of digital morphometric analysis screening entire plaque sections. Previous analysis in our laboratory showed a good reproducibility of the method (n =

10); Observer 2 = 0.9 Observer 1;  $r = 0.86$ ;  $p < 0.01$ ). Five areas of components were distinguished: 1) collagen or fibrous tissue, 2) lipids, 3) nuclei, 4) calcium, and 5) fibrinohematic material.

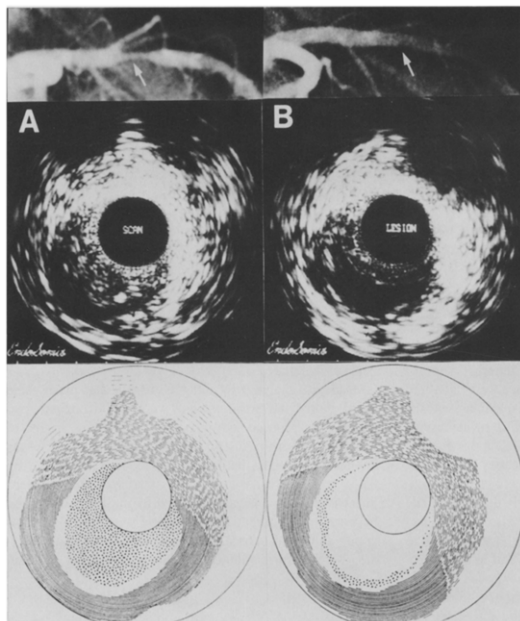
**Statistical analysis.** Results are expressed as mean value ± SD. Paired and unpaired *t* tests were used to compare two mean values proceeding from normal distribution. In case of values not normally distributed, a Mann-Whitney test was applied. Differences between proportions were studied by chi-square and Fisher exact tests as appropriate. Standard linear regression analysis was used to study the variability between two different observers (SAS Institute Inc. program), as well as correlation of plaque reduction and specimen weight. Correlation coefficients (*r*) and linear equation

**Figure 3.** Differences in mean percent of content areas observed in material retrieved from echogenic or echolucent plaques.



**Table 2.** Quantification of Content Areas in Material Removed From the Overall Series

	Primary Lesion (%)	Restenotic Lesion (%)	p Value
Nuclei	2.3 ± 2	1.7 ± 1	NS
Collagen	75.8 ± 25	92.6 ± 5	<0.001
Lipids	8.6 ± 14	2.4 ± 2	<0.001
Fibrin	11.0 ± 19	1.4 ± 4	<0.001
Calcium	2.3 ± 8	1.9 ± 4	NS



**Figure 4.** Angiographic and ultrasound changes after atherectomy. **A.** Before treatment, eccentric echolucent plaque can be observed in the wedge condition. **B.** After atherectomy, a wide lumen and almost complete ablation of the plaque surface can be identified, despite some ring-down effect. Note the resultant three-layered appearance and the irregular contour of the inner ring, where morsel traces could be inferred. Arrows show the level of ultrasound interrogation.

were obtained for each comparison. A  $p$  value  $< 0.05$  was considered significant.

### Results

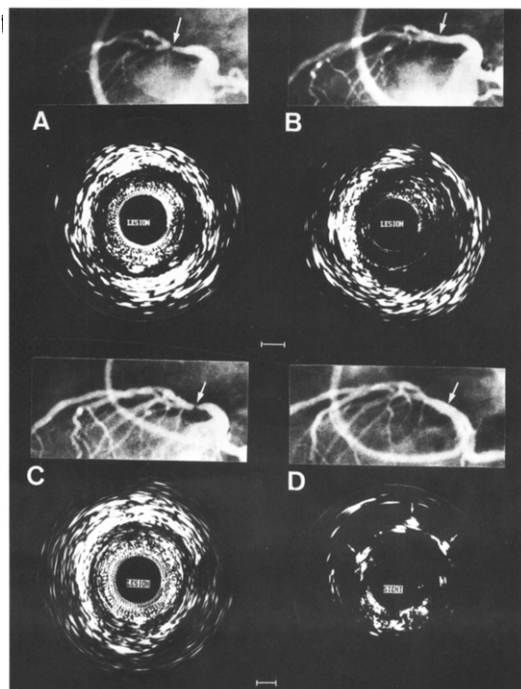
**Atherectomy results.** Table 1 shows the mean changes observed in minimal lumen diameter and percent stenosis after directional coronary atherectomy. All 52 patients became asymptomatic after the procedure and were discharged under medical treatment (aspirin and calcium channel antagonist). Eleven patients became symptomatic again after  $4 \pm 1$  months (range 2 to 6). At angiographic follow-up study performed in 22 patients within 2 to 10 months after directional coronary atherectomy, restenosis was found in 13 patients, whereas 9 continued to demonstrate similar angiographic benefits.

**Pathologic findings.** Resected material had a mean weight of  $15 \pm 11$  mg. Intimal cuts were observed in 43 patients, whereas deeper medial cuts were detected in 7 and adventitial tissue was resected in 2. Focal calcium was observed in

18 patients. Quantitative analysis of the resected material showed a high predominance of collagen or fibrous tissue. Table 2 shows the percent of content areas from the removed material. When considering restenotic versus primary lesions separately, there were significant differences. Plaque composition in restenosis had an even higher fibrous tissue content, whereas primary lesions showed an increased percent of content in fibrinohematic material and lipids.

**Ultrasound findings.** Table 1 shows the evolution of quantitative variables derived from ultrasound studies.

**Baseline plaque characterization.** **Echogenicity.** Twenty-six plaques were full or predominantly echogenic, whereas 19 were full or predominantly echolucent (Fig. 2). In 7 patients a mixed pattern was observed; focal calcium was observed in 17 patients. Compared with pathologic findings, the sensitivity of ultrasound analysis for estimating the presence of focal calcium was 56%, specificity was 76% and predictive value was 60%. Figure 3 shows the differences in the mean composition of the removed material observed in echogenic and echolucent stenosis. As can be seen,



**Figure 5.** Serial ultrasound-angiographic observations in a patient with restenosis. **A**, Baseline conditions of a restenotic lesion after previous balloon angioplasty. **B**, After atherectomy, some residual unresected plaque can be observed by ultrasound. **C**, Three months later, showing restenosis. **D**, After deployment of the Palmaz-Schatz stent where the gain has been attenuated, small arrows show the struts. Ring artifact was previously unmasked by contrast hand injections. Large arrows show the site of observation. Bars = 1 mm.

echogenic plaques had a greater collagen and calcium content, whereas echolucent plaques had a higher percent of fibrinohematic material, nuclei and lipids.

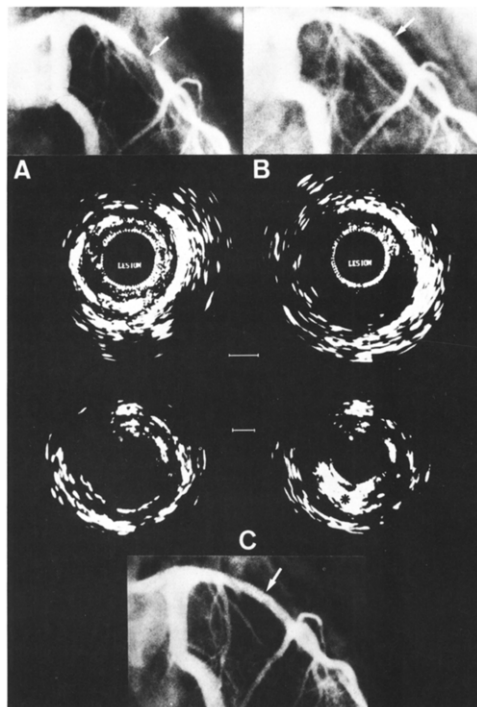
**Stenotic three-layer pattern.** A three-layered pattern of the arterial wall was always observed in nondiseased segments, although the inner echogenic layer tended to fade as the diameter of the vessel increased. However, when evaluating stenotic segments, we found in 18 patients a concentric three-layered ultrasound appearance with a thicker echogenic inner ring; 9 of 11 restenotic lesions had this pattern, whereas only 9 of 41 primary lesions presented a concentric three-layered appearance ( $p < 0.05$ ).

**Assessment of immediate directional coronary atherectomy results.** After completion of the procedure, the ultrasound probe always crossed the lesion and the pull-back scanning frequently demonstrated different degrees of residual unresected plaque in an asymmetric fashion. In other

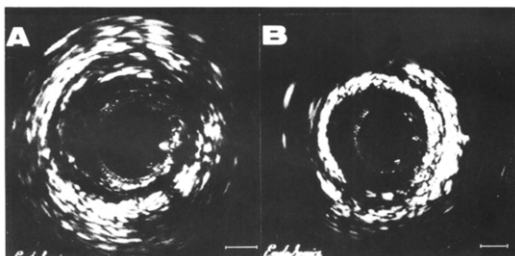
instances, the resection seemed more complete and a dense thin inner layer was identified as the resultant remaining structure interfacing with the neolumen. This layer was frequently depicted in an irregular circumferential contour where morsel traces could be inferred (Fig. 4). The mean cross-sectional plaque reduction at the level of minimal lumen diameter was  $65 \pm 21\%$ . This reduction did not correlate with the angiographic reduction in percent stenosis; however, it correlated significantly with the weight of the resected material ( $r = 0.62$ ;  $p < 0.01$ ;  $y = 5.22 + 2.13x$ ;  $SEE = 9.1$ ). The ultrasound estimation of plaque reduction was higher in echolucent ( $76 \pm 21\%$ ) compared with echogenic plaques ( $60 \pm 18\%$ ;  $p < 0.05$ ).

**Assessment at follow-up.** Analysis at the time of follow-up made a clear distinction between restenosis and late success (Table 1).

**Restenosis.** Thirteen of 22 patients had angiographic and



**Figure 6.** Serial ultrasound-angiographic observations in a patient with late success after atherectomy. **A**, Before treatment; **B**, immediately after atherectomy; **C**, at follow-up study, 8 months later, where no residual plaque can be identified; a three-layered appearance of the arterial wall at the treated site makes no difference to the appearance of nondiseased segments. A wide lumen filled by contrast medium (\*) can be identified. Bars = 1 mm.



**Figure 7.** Two different echographic patterns of successfully repaired arterial segments at follow-up study. Both show a wide lumen and a three-layered appearance of the wall. However, the inner echogenic ring is thin in **A** and thicker in **B**, suggesting different degrees of neointimal proliferation after plaque resection. Bars = 1 mm.

ultrasound evidence of restenosis; 9 of them showed a stenotic three-layered appearance in wedge conditions (Fig. 5); the remaining 4 showed a similar appearance to that observed in baseline conditions. All restenotic lesions were easily crossed by the probe. Factors that could influence restenosis were analyzed. No clinical, procedural or angiographic predictors were identified in this group of patients, as occurred in the overall series. However, the incidence of restenosis on primary lesions ( $n = 19$ ) was influenced by the echogenicity of the plaque. There was a higher significant proportion of echolucent plaques that were restenosed at follow-up (7 of 7 echolucent lesions vs. 4 of 12 echogenic lesions;  $p < 0.05$ ). Another significant predictor of restenosis at follow-up was obtained from the pathologic study; a higher proportion of cellular content (nuclei) obtained at the time of treatment was observed in patients with restenosis at follow-up study ( $2.1 \pm 0.7\%$ ) than in patients who did not develop restenosis ( $1.2 \pm 0.6\%$ ;  $p < 0.05$ ). These findings were also confirmed in 72 patients from the overall series who underwent reevaluation. The restenotic lesions were treated during the same procedure by repeat directional coronary atherectomy in seven patients, balloon angioplasty in three and Palmaz-Schatz intracoronary stent in three.

**Late success.** Angiographic and ultrasound late ( $8 \pm 2$  months) success was detected in nine patients (Table 1). No wedge condition of the probe was observed at the treated segment. A wide lumen filled by echo contrast during hand injections was always detected (Fig. 6). The ultrasound appearance of the arterial wall was characterized by a three-layered pattern, as observed proximally and distally in nondiseased segments (1,8,10). The inner echogenic ring at the treated segment showed various degrees of thickness ( $0.2$  to  $0.7$  mm) and density (Fig. 7). When this thickness was slightly increased (Fig. 7B), it was the only transitional change to be observed at the treated segment when the probe was slowly pulled back from distal to proximal segments.

## Discussion

**Plaque characterization.** As techniques of revascularization diversify, information on lesion subtypes becomes increasingly necessary. Angiography defines the contour of the blood vessel wall but provides only inferential information about abnormalities of the blood-vessel interface and arterial wall. However, studies (4,5,11) of angiographic morphology have characterized different lesion subtypes corresponding to clinical syndromes and lesion morphologic criteria have been closely related to procedural outcome after balloon angioplasty or atherectomy (6,12-16).

Intracoronary ultrasound provides cross-sectional images of the arterial wall and has the potential of characterizing ultrasound properties of the different atheroma components. An excellent correlation between ultrasound and histologic measurements has been observed for lumen area and diameters, as well as for wall thickness (2,8,9,17-20). Meyer et al. (10) described the three-layered appearance of the ultra-

sound images obtained from samples of muscular arteries. The intima and the elastic internal lamina are echogenic, the muscular media hypoechoic and the adventitia hyperechoic. Different *in vitro* studies (8,9,17,19) have confirmed these findings in nondiseased segments of muscular arteries. The ultrasound analysis of diseased coronary segments seems to be more difficult, because the three-layered appearance of the artery may be obscured (21,22). In most cases, ultrasound examination of the plaque has to be performed under circumstances of compression because the actual size of the probe is wider than most stenotic lumens. In addition, the arterial media may become attenuated in advanced atherosclerosis (23). Despite this, *in vitro* experiments (9,17,22,24) have shown that intravascular ultrasound images provide accurate microanatomic information on the histologic characteristics of atherosclerotic plaques. Thus, fibrous lesions produce dense homogeneous echo reflections and calcific deposits, bringing bright echoes that shadow onto deeper zones. The sensitivity, specificity and predictive value of these findings have been recently established in comparison with angiography (24). However, *in vivo* confirmation has not been documented until now.

If we compare the content of the removed plaque material obtained by atherectomy with the main ultrasound features observed before treatment, we could obtain individual information for better characterization of the different types of coronary lesions. Our findings confirm *in vivo* that ultrasound density of the lesion varies, depending on the tissue components of the plaque. The echogenic plaques correspond to more organized structures with higher collagen and calcium content. Macroscopic focal calcium is easily identifiable because of its shadow effect (8,9); however, microscopic aggregates of calcium in the atheroma may be undetectable by ultrasound analysis. Fully dense echogenic plaques most frequently distort or obscure the three-layered appearance of the arterial wall. However, predominantly echogenic areas may preserve visualization of outer layers if echodensity is evenly distributed throughout the plaque surface; this occurs frequently in restenotic lesions. Furthermore, dense zones may alternate with hypoechoic areas over the entire stenotic surface; this mixed pattern is infrequent and may correspond to heterogeneous lesions with different areas of evolution. Conversely, full or predominantly echolucent plaques are lesions that contain a higher percent of fibrinohemorrhagic material, lipids and cells (nuclear surface). Delimitation between atheroma and muscular media is rarely possible in fully echolucent lesions but usually is recognizable in predominantly echolucent lesions. After plaque resection, the arterial wall frequently shows a three-layered appearance (Fig. 4 and 6).

**Guidance and assessment.** The combination of intracoronary ultrasound and angiography provides an additional source of information in guiding and assessing the result of several interventional techniques of coronary revascularization (1,2,25). Its use in directional coronary atherectomy seems to be of particular interest. When compared with



balloon angioplasty, this removal-based procedure is usually performed on patients with larger coronary artery diameters, which allows for better technical conditions for ultrasound analysis of the lumen and wall characteristics. Moreover, the wider lumen of the guiding catheter permits both easier manipulation of the probe into the coronary tree and a better quality of flushing of contrast medium for identification of the lumen-wall interface. All these advantages could help in 1) better characterization of the plaque subtype before resection, and 2) the recognition of resected areas and residual plaque. Our study shows that cross-sectional reduction of plaque burden is a useful variable for assessing results after atherectomy, that could provide an opportunity for optimizing the resection when significant residual plaque persists after initial cuttings. The percent plaque reduction after atherectomy was higher in echolucent than in echogenic plaques. This finding probably means that echolucent plaques are easier to resect because they are softer.

**Follow-up. Restenosis.** Although directional coronary atherectomy is of proved validity in treating ischemic coronary syndromes, restenosis occurs in nearly 50% of patients after initially successful resection (26,27). The response to the injury of the atherectomy procedure leads to neointimal proliferation similar to that which may develop after balloon angioplasty. The extent of fibrous hyperplasia appears to be related in part to the depth of tissue resection (26). However, no other clinical, angiographic or pathologic variables have been identified as potential predictors of restenosis after directional coronary atherectomy. In our study, we identified two factors with a significant influence on the development of restenosis. First, the nuclear content of the resected material from primary lesions was significantly higher in those patients who later developed restenosis, thus, an increased cellular content in the target plaque might also be a determining factor for an increased hyperplastic response after injury. Second, the restenosis rate was significantly higher in patients with echolucent plaque at baseline conditions. This higher rate could also be facilitated by the higher cell content observed in echolucent lesions (Fig. 4). The denudation of a plaque with increased content in fibrin and lipids may induce platelet deposition with subsequent release of growth factors (5,12,28).

The histopathologic characteristics of restenotic lesions differ from those of primary atherosclerotic lesions (26). Our study also shows quantitative differences in the content of components between the tissue obtained from restenotic or primary lesions (Table 2). The greater predominance of collagen observed in stenosis recurrence could represent the extracellular matrix content produced by an increased synthetic process (29). The ultrasound features observed in restenotic lesions most frequently can be differentiated from those observed in primary atheromatous lesions (30). The restenotic pattern is usually characterized by a concentric and thick inner echogenic ring with preservation of the hypochoic medial circumference (Fig. 5). This provides a characteristic three-layered stenotic appearance in which the

predominantly echogenic and thick inner layer probably corresponds to collagen.

**Late success.** Ultrasound patterns of successfully repaired arterial segments have not been evaluated. After initially successful atherectomy, remodeling of the arterial wall and residual atheroma are favored by partial resection of plaque and normalization of coronary flow. Denudation and stretching of the diseased segments and adjacent areas seem to represent a potent stimulus to intimal hyperplasia (29,31), which is thought to develop within 1 to 4 months (29). This may create some degree of thickening, but if the healing process is not exaggerated, completion of full-covering neointimal layer produces a persistent nonstenotic smooth intimal surface, as can be observed in follow-up angiographic studies (Fig. 6). The interrogation by ultrasound of these treated segments might provide new insights into the understanding of the different responses to injury after atherectomy. Our findings show that these segments are characterized by a three-layered appearance very similar to that observed in normal segments (30). A wide lumen was always documented by contrast medium during hand injections (Fig. 6). The resultant inner layer is echogenic, which facilitates its differentiation from the medial interface. Thus, this inner ring seems to represent the modulated neointimal proliferation after injury. Its echodensity suggests that fibrous tissue could be the main histologic component, as occurs in the thick inner ring of restenotic lesions. Its width is variable, which suggests that neointimal proliferation may oscillate between a minimal value, with no ultrasound distinction from normal segments (Fig. 7A), increased (but not stenotic) (Fig. 7B) or exaggerated, resulting in re-narrowing or restenosis of the lumen (Fig. 5).

**Limitations of the study.** Several limitations of the study should be emphasized. 1) Our study group of patients had a predominance of unstable angina. Unstable and postfibrinolytic lesions are considered as complicated plaques in which aggregates of fibrohemostatic material may participate in the stenosis (5,11,14,32). Although some investigators (22) have described the ultrasound appearance of intracoronary thrombotic material as speckled ultrasound signals, they are difficult to differentiate from other predominantly echolucent components of the plaque. 2) Our quantitative pathologic study does not differentiate among the different types of cells present in the resected plaque but only quantifies the nuclear surface of the sample. Effort is underway to understand the range, origins and functions of intimal and lesion cells. Endothelial, smooth muscle, inflammatory cells and macrophages may be present in different amounts and stages (33). The percent of nuclear surface may be an index of cellularity but does not reveal cell family. Similarly, the type of collagen was not differentiated in our study. 3) Several technical problems may hamper the differentiation of plaque subtypes. Echolucent and echodense appearance are potentially subjective observations. However, if one can adjust gain and gray scale settings for the optimal three-layered appearance of the arterial wall in normal proximal

segments, individual standardization can be obtained. Using circumferential measurements from proximal sites may also introduce potential error. Nevertheless, the percent plaque reduction estimated by ultrasound correlated with the weight of the resected material, which could validate the method. Furthermore, we tried to quantitate in a cross-sectional view types of measurements similar to those obtained by angiography.

**Conclusions.** We believe that ultrasound guidance of directional coronary atherectomy is an easy and safe procedure that may provide information regarding plaque composition as well as important, on-line, decision-making information on residual plaque. With increasing knowledge, the ultrasound appearance of plaque might become a subject of interest in the improving selection of the revascularization technique for each patient.

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