Title

Intracoronary ultrasound imaging before and after directional coronary atherectomy: In vitro and clinical observations

Journal

American Heart Journal, 129(5)

ISSN

0002-8703

Authors

Nakamura, Shigeru
Mahon, Donald J
Leung, Cyril Y
et al.

Publication Date

1995-05-01

DOI

10.1016/0002-8703(95)90102-7

American Heart Journal

Founded in 1925

May 1995 Volume 129, Number 5

CLINICAL INVESTIGATIONS

Intracoronary ultrasound imaging before and after directional coronary atherectomy: In vitro and clinical observations

The rate of restenosis after directional coronary atherectomy (DCA) is higher than expected. To elucidate why, the current study used intravascular ultrasound (IVUS) imaging to investigate the mechanism of DCA. An in vitro validation study was performed to determine the accuracy of the measurement of plaque removal by IVUS. DCA was performed in eight human atherosclerotic artery segments. The volume of removed plaque was measured by water displacement and was compared with the volume calculated from IVUS images. A clinical study of DCA was performed in 32 lesions. IVUS was performed in 28 lesions after successful DCA. Measurements of lumen dimensions from digital angiograms before and after DCA were compared with observations of lumen and plaque size from the cross-sectional IVUS images. In the in vitro study, the mean plaque volume removed by DCA was 19.9 ± 8.5 μl. The calculated estimate of removed plaque volume by IVUS was 18.6 ± 7.9 μl and correlated closely with the volume by water displacement ($r = 0.92$). The calculated volume of plaque removed from histologic sections was 14.3 ± 6.0 μl and was linearly correlated with plaque volume by water displacement ($r = 0.81$). In the clinical study, the angiographic mean minimum lumen diameter increased from 1.0 ± 0.4 to 2.7 ± 0.5 mm and the percentage stenosis decreased from 70% to 19% ($p < 0.0001$). The IVUS images before and after DCA showed that the lumen DCA improved from 2.9 ± 1.5 to 7.0 ± 1.5 mm^2 ($p < 0.0001$). In addition the vessel cross-sectional area (CSA) increased from 17.1 ± 5.9 to 18.7 ± 5.5 mm^2. The atheroma CSA was reduced from 14.2 ± 5.0 to 11.7 ± 4.8 mm^2. This combined effect of reduction in atheroma CSA and stretching of the outer vessel diameter resulted in an improvement in percentage plaque area stenosis from 83% ± 7% to 61% ± 9%. It is concluded that despite a successful angiographic appearance, DCA removed an average of 2.5 mm^2 from the atheroma, which corresponds to only 18% of the atheroma CSA. The total lumen CSA increased 4.1 mm^2; 61% of the new lumen was created by cutting and removal of plaque, whereas 39% of the new lumen was made by stretching the external wall of the artery. Despite an excellent angiographic result, IVUS imaging reveals that after DCA a significant amount of residual atheroma remains. As in balloon dilatation, a stretching effect is a significant component of DCA. (Am Heart J 1995;129:841-51.)

Shigeru Nakamura, MD, Donald J. Mahon, MD, Cyril Y. Leung, MD, Bavani Maheswaran, MBBS, Dan E. Gutfinger, PhD, Jenchen Yang, MD, Robert Zelman, MD, and Jonathan M. Tobis, MD *Irvine, Calif.*

From the Division of Cardiology, University of California, Irvine.

Received for publication Sept. 28, 1994; accepted Nov. 1, 1994.

Supported in part by National Institutes of Health grant HL 45077-02.

Reprint requests: Jonathan M. Tobis, MD, Division of Cardiology, University of California, Irvine, Bldg. 53, 101 City Dr. South, Rt. 81, Orange, CA 92668.

0002-8703/95/$3.00 + 0 **4/1/61623**

Directional coronary atherectomy (DCA) was developed to address the high incidence of restenosis after percutaneous transluminal coronary balloon angioplasty (PTCA).[1-5] The underlying hypothesis of this technique is that restenosis may be diminished if a sufficient amount of plaque can be removed. A second hypothesis is that a more successful initial result may

be obtained compared with standard balloon dilatation.[6-9] However, despite angiographic evidence of a satisfactory acute gain, the rates of restenosis are similar to those after PTCA (27% to 46%).[10-18] The results from the Coronary Angioplasty Versus Excisional Atherectomy Trial (CAVEAT) show a modest improvement in restenosis compared with restenosis after PTCA, but the angiographic restenosis rate for DCA is higher than expected, at 50%.[19] This observation challenges the assumption that removing atheroma will reduce restenosis; an alternative explanation is that the atherectomy device does not remove as much plaque as predicted. In addition to cutting the plaque, the device may act in a mechanical fashion to stretch the lumen and outer wall of the artery. Angiography is incapable of distinguishing between the cutting effect and the mechanical stretching effect. Intravascular ultrasound (IVUS) imaging provides a method for obtaining quantitative information about the cross-sectional area (CSA) of the lumen and the atheroma burden.[20-26] By imaging the narrowed segments with IVUS before as well as after atherectomy, it may be possible to obtain a better understanding of the mechanism of action of DCA.

METHODS

In vitro study. To visualize the morphometric effects of DCA and to validate the quantitative findings by IVUS, an in vitro study was performed. Eight human atherosclerotic specimens from the iliac artery were obtained at autopsy. Each artery was cut into 3 cm–long segments. The arteries were stored in normal saline at 4° C and were not fixed in formalin until after the images were obtained. The artery segments were connected to an 8F coronary guiding catheter. Two surgical needles were placed through the adventitia of the artery approximately 15 mm apart to provide acoustic reference points.[27] A 25 MHz IVUS catheter (InterTherapy/CVIS, Sunnyvale, Calif.) was advanced through a Touhy-Borst adaptor on the guiding catheter into the artery segments. The guiding catheter was connected to pressurized normal saline within a closed system to permit imaging under physiologic pressures. The eight arterial segments were imaged before DCA between the two reference needles with use of a motorized pullback device at 0.21 mm/sec. Cross-sectional images were obtained continuously at 30 frames/sec.

After the initial images were obtained, the artery was removed from the guiding catheter platform, and a 7F device (Simpson Atherocath, Devices For Vascular Intervention, Redwood City, Calif.) was placed within the lumen. Multiple passes of the device were made between the two reference needles to acquire material from only one side of the artery. No attempt was made to remove all of the visible atheroma, and one side of the artery was left unaltered to provide a visual comparison of the atherectomy results. The cut pieces of plaque were weighed on an electronic balance. The removed plaque was then dropped into a small graduated cylinder filled with saline with marked gradations of 0.1 ml. The volume of water displaced by the atherectomized plaque was used as the measure of cut plaque volume. After the measurements of weight and volume, the artery was remounted for IVUS imaging after DCA in the same locations relative to the position of the needles in the artery.

At the completion of the study, the arterial segments were pressure perfused for 12 hours in 10% formalin and then placed in decalcification solution for 24 hours. The arteries were imbedded in paraffin after the needle site had been marked with silk suture. Histologic sections were obtained at 1 mm intervals along the length of artery between the reference needle sites. The sections were stained with trichrome. A video image of each histologic section was fed from a microscope (Leica, WILD M3Z, Deerfield, Ill.) through a video camera (Sony, DXC-151A, Tokyo, Japan) into a computer (Macintosh IIci, Apple, Cupertino, Calif.) and digitized (RasterOps 24STV board; Mediagrabber software, Santa Clara, Calif.). Quantitative measurements of the lumen, the plaque, and the atherectomized areas were made with an operator-directed cursor (NIHimage). The IVUS images were digitized from the super-VHS videotape at 0.5 mm intervals along the artery length. The CSAs of the lumen and the plaque before and after atherectomy were measured with the same graphics software as that used for the histologic sections. Each pair of IVUS images (before and after DCA) were placed next to each other to facilitate the identification of the DCA cut. The atherectomized area was measured at each digitized cross-sectional image along the length of the DCA cut. A calculated estimate of plaque volume removed by DCA was obtained by integrating the cut area on each IVUS cross section over the length of the artery segment. A similar calculation of plaque volume was derived from the measurements of the cut areas from the histologic images. The calculated atherectomy plaque volumes from the IVUS images and histologic cross sections were compared by regression analysis with the measured plaque volume by water displacement.

Clinical study

Patient population. Thirty-two lesions in 29 patients were treated with DCA and were studied with IVUS imaging. Of the 32 lesions, 30 (94%) were treated successfully with DCA alone or adjunctive PTCA. Twenty-four (75%) lesions had atherectomy performed alone, without adjunctive PTCA. IVUS imaging was performed in 28 lesions after completion of the procedure and was obtained before and after DCA in 19 of the lesions. Patients were selected for DCA rather than conventional PTCA on the basis of presence of localized stenosis in a nontortuous proximal or mid-portion of a major epicardial vessel the reference diameter of which was $\geq$2.5 mm. Successful DCA was defined as removal of tissue, a residual diameter stenosis <50% on digital quantitative angiographic assessment, and absence of major complications (death, myocardial infarction, or emergency coronary artery bypass graft surgery).

DCA. Before initiation of the atherectomy procedure,

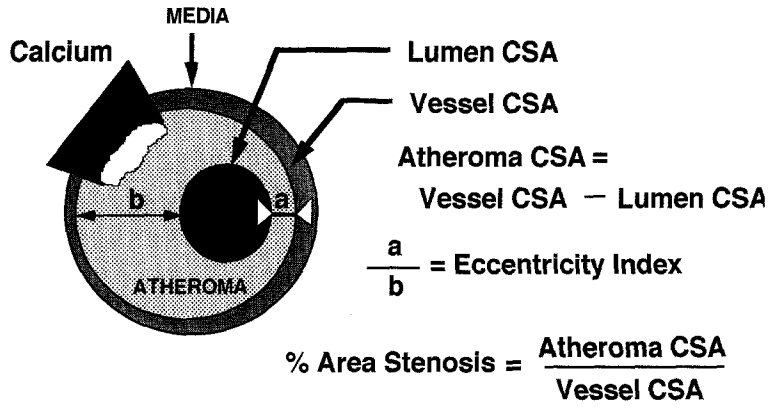

Fig. 1. Schematic cross-section of coronary artery demonstrates how measurements were made from IVUS images. Boundary of vessel was taken as intersection of echogenic atheroma and echolucent band of media. Lumen CSA was measured at intersection of echolucent lumen and echogenic plaque. Atheroma CSA was then calculated by subtracting lumen CSA from total vessel CSA. Percentage plaque area stenosis was defined as atheroma CSA divided by total available vessel CSA within boundary of media. This definition is similar to histologic definition of percentage area stenosis and differs from angiographic definition of percentage stenosis, which uses proximal segment of vessel as normal reference.

the iliac artery size was determined by angiography to ensure that a 10F or 11F sheath would fit adequately in the artery without causing obstruction. The preshaped DCA guiding catheter was positioned at the coronary ostium. Heparin was given to each patient to maintain activated clotting time >300 seconds. Baseline coronary angiograms were obtained in several projections, and then a 0.014-inch-diameter flexible guide wire was manipulated across the stenosis. A 3.9F rapid exchange IVUS imaging catheter (InterTherapy/CVIS) was advanced over the guide wire across the stenosis with fluoroscopic control. The catheter consisted of a mechanically rotating 25 MHz ultrasound transducer 1 mm in diameter and was positioned within a 1.3 mm plastic introducing sheath. A full description of the technique of IVUS imaging has been published previously.[24] IVUS imaging was recorded continuously during manual pull-back from the distal segment of the artery to the ostium of the aortic root. Very severe stenoses that would not initially accept either the IVUS catheter or DCA catheter, were predilated with a 2.0 mm balloon. Patients in whom the IVUS catheter could not be passed before DCA were analyzed separately. The DCA catheter was advanced across the stenosis with manual rotation.[28] A 6F or 7F catheter was chosen depending on the size of the artery. The standard recommended procedure was used.[29] Several cuts were made with various orientations of the cutting window as monitored by fluoroscopy. The atherectomy device was withdrawn from the coronary artery after 6 to 10 cuts to remove the tissue in the nosecone. If subsequent angiography showed incomplete resolution of the stenosis, the device was reintroduced and additional cuts were performed using a higher inflation pressure. After DCA was completed as determined by angiography, a second IVUS examination was performed. If the IVUS images showed a significant amount of residual plaque, the information from the IVUS study was used to guide additional DCA cuts.

Analysis of coronary angiograms. Digital coronary angiograms were recorded in at least two projections before and after DCA. These angiograms were stored on computer disk of a digital-acquisition x-ray system (DCI Philips, Skelton, Conn.) and were archived onto 35 mm cine film. After the atherectomy procedure was completed, the digital angiograms were recalled from the x-ray system memory, and the lumen diameter of the treated area and the proximal angiographically normal segment were measured. The diameter of the guiding catheter was used as a reference for calibration. Measurements were made with an operator-defined digital caliper from end-diastolic frames or the frame that best demonstrated the stenotic area. Percentage diameter stenosis was calculated by comparing the diameter of the stenotic segment with an angiographically normal proximal segment as the reference point. Lumen CSA was calculated from orthogonally projected angiograms; internal cross-sectional geometry was assumed to be an ellipse. Lesion length was measured as the distance from the proximal to the distal shoulder of the lesion in the projection that best elongated the stenosis.[30] An eccentric lesion was defined as a stenosis with asymmetry in any angiographic projection.[7] Calcification was defined as a radiopaque density within the vascular wall of the artery at the site of the stenosis.[30]

Analysis of IVUS images. IVUS measurements were calculated as demonstrated in Fig. 1. The lumen CSA was defined as the area encompassed by the inner boundary of the intimal surface. The major and minor lumen diameters were measured at the long axis and short axis of the lumen. The vessel CSA was defined as the area bounded by the hypoechoic medial ring. If the vessel area could not be traced because of calcium, a proximal adjacent noncalcified site was measured as the vessel area. The major and minor vessel diameters were measured at the long axis and short axis of the vessel at the border between the atheroma and media. The atheroma CSA was calculated as the vessel CSA

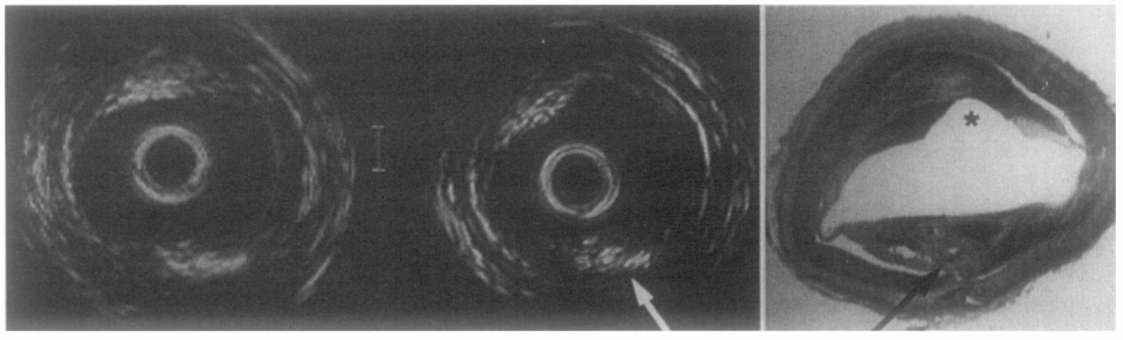

Fig. 2. Atherectomy in vitro. *Left*, IVUS image before DCA shows catheter in center of vessel surrounded by thin echogenic band caused by reflections from catheter sheath. Echolucent lumen is oblong. Speckled echogenic plaque is visible *(top* and *bottom)*. *Middle*, After one passage of DCA device a trough has been cut in upper section of artery between 12- and 1-o'clock positions. *Arrow* indicates calcification. *Right*, Trough observed on the IVUS image corresponds closely with area *(*)* on histologic section. There is small area of calcification *(arrow)* at base of plaque.

Table I. In vitro data

	Water displacement	*Histologic section*	*IVUS*
Plaque volume (μl) (mean ± SD)*	19.9 ± 8.5	14.3 ± 6.0	18.6 ± 7.9

	Linear regression analysis	
	r Value	*p Value*
Water displacement vs histologic section	0.81	0.01
Water displacement vs IVUS	0.92	0.001
IVUS vs histologic section	0.74	0.04

*p = NS.

minus the lumen CSA. The percentage area stenosis was defined as the atheroma CSA divided by the vessel CSA. This approach is similar to a histologic definition of stenosis and does not depend on a proximal reference segment. All measurements were performed during diastole.

To quantitate plaque eccentricity, an eccentricity index was calculated from the IVUS image as the thinnest dimension of the plaque divided by the width of the opposite wall.[25] A stenosis was defined as concentric if the atherosclerotic plaque was distributed circumferentially, corresponding to an eccentricity index ≥0.50. The stenosis was defined as eccentric if the index was <0.50. Calcified tissue was defined as an area of intense echogenicity with acoustic shadowing. The calcium score was quantified as absent (0), mild (1+) when calcification was localized to ≤90 degrees of arc, moderate (2+) when it involved 91 to 180 degrees of arc, severe (3+) when it incorporated 181 to 270 degrees of arc, and (4+) when >270 degrees of arc was calcified.

Statistics. Group data were tabulated as means ± SD. Comparison of the CSA of the lumen, vessel, plaque, and percentage stenosis before and after the atherectomy procedure were performed by the paired Student's t test. Two-by-two comparison tables were assessed by chi square analysis. Differences were considered to be statistically significant at $p < 0.05$. Linear regression analysis was performed to compare different measurements. Comparisons between more than two groups were performed by analysis of variance. The variability of IVUS measurements from our laboratory has been reported previously.[31] Correlation coefficients for intra- and interobserver measurements of minimum lumen diameter (MLD) and lumen CSA ranged from 0.92 to 0.99 after PTCA.

RESULTS

In vitro study. The mean plaque volume removed by the DCA device from the eight artery segments was 19.9 ± 8.5 μl as measured by water displacement. The mean weight was 21.0 ± 7.0 mg. Representative cross-sectional IVUS images before and after DCA compared with the histologic section are presented in Fig. 2. All of the artery segments demonstrated the typical groove cut into the fibrous plaque capsule. The DCA plaque volume calculated from the ultrasound images was 18.6 ± 7.9 μl, and the value calculated from the histologic cross sections was 14.3 ± 6.0 μl. The correlation between the measurements of cut plaque volume between IVUS images and histologic sections was $r = 0.74$. The correlation coefficients between the measured plaque volume by water displacement compared with histologic sections and IVUS images are presented in Table I.

Table II. Patient profile

Patients (no.)	29
Age (yr)	61.5 ± 11.1
Male/female (%)	93/7
Unstable angina (%)	54
Acute myocardial infarction (%)	7
Angina class	
I or II (%)	43
III or IV (%)	57
Previous myocardial infarction (%)	55
Previous coronary artery bypass graft operation	10
Coronary risk factors	
Diabetes (%)	21
Hypertension (%)	54
Family history (%)	65
Hyperlipidemia (%)	58
Smoking (%)	14

Table III. Lesions and procedures

Vessel (n = 32)	
Left anterior descending coronary artery	21
Right coronary artery	9
Left circumflex	1
Saphenous vein graft	0
Left main coronary artery	1
Restenosis lesion	9 (27%)
Predilatation	6 (18%)
Angiographic calcified lesion	4 (12%)
Eccentric lesion	18 (54%)
Lesion length (mm)	10.1 ± 4.8
Reference vessel diameter (mm)	3.3 ± 0.6
Lesion type	
A	1
B1	7
B2	19
C	6
Device size	
7F	27 (84%)
6F	5 (16%)
Maximum balloon pressure (psi)	28 ± 16
Cuts (No.)	25 ± 22
Adjunctive PTCA	7 (21%)
DCA alone (success rate)	75%
DCA and PTCA (success rate)	94%

The comparison of the IVUS images before and after DCA showed significant variability in lumen dimensions caused by stretching of the artery during the manipulation to mechanically cut the plaque from the arterial segments. The mean lumen CSA before atherectomy was 25.4 ± 2.2 mm^2 and was 28.2 ± 1.9 mm^2 after DCA ($p < 0.05$).

Clinical study. Table II summarizes the clinical characteristics of the patients who were treated with DCA during this study. Table III lists the stenosis and procedure characteristics. The average lesion length was 10.1 ± 4.8 mm. Only 4 of the stenoses showed obvious calcification by cineangiographic criteria. Eighteen (54%) of the stenoses were eccentric by angiography. The number of cuts obtained with the atherectomy catheter varied between 7 and 73 (average of 25 ± 22 cuts). The average balloon inflation pressure during atherectomy was 28 ± 16 (range 10 to 60) psi. Twenty-four (75%) lesions were successfully treated with DCA alone. Because of the severity of disease, PTCA before DCA was performed in six patients to facilitate passage of the atherectomy catheter. Six (19%) patients also received adjunctive PTCA after DCA.

In two patients DCA was unsuccessful. In 1 case, the procedure was performed during an acute myocardial infarction in the proximal right coronary artery. It was difficult to deliver the DCA device because of superior angulation in the proximal segment. The other patient had previous bypass surgery with severe disease in the left main coronary artery. There was circumferential dense calcification in the area of stenosis as revealed by IVUS examination before DCA. It was difficult to establish proper positioning of the guiding catheter in this case, and the DCA device could not be delivered appropriately. These two patients underwent successful PTCA alone.

Table IV. Angiographic measurements

	Before DCA	*After DCA alone (n = 24)*	*All patients (n = 30)*
MLD (mm)	1.0 ± 0.4	2.7 ± 0.5*	2.7 ± 0.5†
Angiographic lumen CSA (mm^2)	1.1 ± 0.8	6.4 ± 2.2*	5.8 ± 2.0†
Percentage diameter stenosis	70 ± 12	19 ± 14*	19 ± 14†

Of all patients, 24 received DCA alone, and 6 had DCA and PTCA.
*$p < 0.0001$ (before and after DCA alone).
†$p < 0.0001$ (comparison of all patients before and after DCA).

Quantitative results. The angiographic measurements before and after DCA or DCA plus PTCA are listed in Table IV. The mean MLD increased significantly, from 1.0 ± 0.4 mm to 2.7 ± 0.5 mm, and the percentage stenosis decreased from 70% to 19% ($p < 0.0001$). There was a smooth angiographic appearance in 23 lesions; 5 lesions had a hazy luminal border; and 2 revealed a dissection (1 resulting from adjunctive PTCA).

Table V provides the quantitative measurements from the IVUS studies before and after DCA at the same cross section. Data are presented only for the

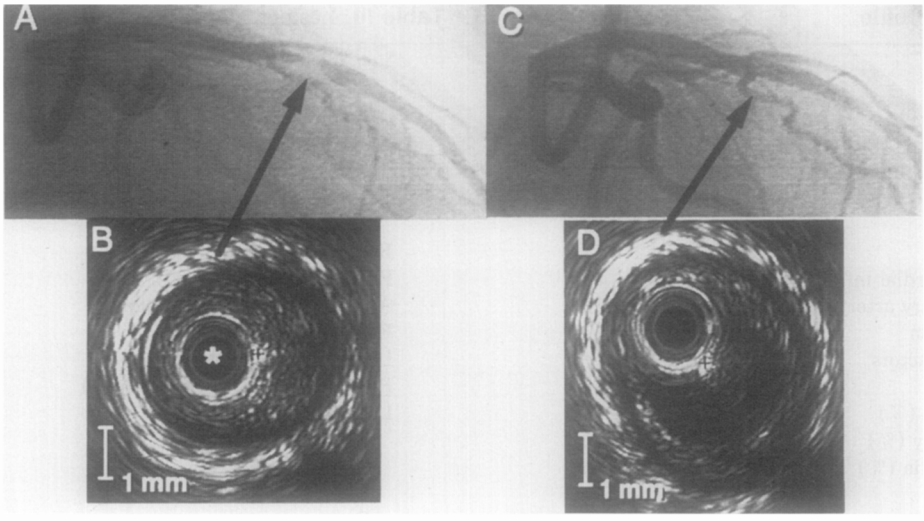

Fig. 3. Angiographic images before **(A)** and after **(C)** DCA performed with a 6F DVI catheter. The angiogram of this 49-year-old woman shows severe eccentric stenosis in mid-left anterior descending coronary artery. IVUS image **(B)** taken at level of stenosis demonstrates eccentric plaque that completely surrounds IVUS imaging catheter. Guide wire is demonstrated as bright echo reflection just external to IVUS sheath at 3-o'clock position *(+)*. The angiographic result after DCA **(C)** demonstrates large lumen without any apparent residual atheroma. IVUS image **(D)** taken at same level shows that significant amount of plaque has been removed and lumen enlarged. However there also is stretching effect as demonstrated by enlargement of major vessel diameter from 3.5 to 4.3 mm. Vessel CSA has increased 28%. Original atheroma CSA of 7.4 mm^2 was reduced to 6.1 mm^2. Excellent angiographic result is attributable to combination of removal of some atheroma and stretching of external arterial wall.

Table V. IVUS measurements (DCA without adjunctive PTCA)

	Before DCA	*After DCA (n = 19)*
Lumen CSA (mm^2)	2.9 ± 1.5	7.0 ± 1.5*
Major lumen diameter (mm)	1.9 ± 0.5	3.2 ± 0.3*
Minor lumen diameter (mm)	1.7 ± 0.4	2.5 ± 0.4*
Vessel CSA (mm^2)	17.1 ± 5.9	18.7 ± 5.5†
Major vessel diameter (mm)	4.7 ± 0.8	5.0 ± 0.8‡
Minor vessel diameter (mm)	4.3 ± 0.7	4.5 ± 0.6§
Atheroma CSA (mm^2)	14.2 ± 5.0	11.7 ± 4.8§
Atheroma CSA/vessel CSA (%)	83 ± 7	61 ± 9‡
Calcium score	1.5 ± 0.7	1.2 ± 0.9
Eccentric lesion	8/18 (44%)	11/18 (61%)
Eccentric index	0.57 ± 0.27	0.35 ± 0.23‡

*$p < 0.0001$.
†$p < 0.001$.
‡$p < 0.01$.
§$p < 0.05$.

patients who received DCA without adjunctive PTCA to prevent mixing the effects of these two procedures ($n = 19$). After DCA, the lumen CSA improved significantly, from 2.9 ± 1.5 mm^2 to 7.0 ± 1.5 mm^2. Major and minor lumen diameters also were improved, by 70% and 47%, respectively. In addition, the vessel CSA increased from 17.1 ± 5.9 mm^2 to 18.7 ± 5.5 mm^2. This increase corresponded to an increase in the diameter of the vessel (measured at the boundary of the media and atheroma) from stretching. The atheroma CSA was reduced from 14.2 ± 5.0 mm^2 to 11.7 ± 4.8 mm^2. This combined effect of reduction in atheroma CSA and stretching of the outer vessel diameter resulted in an improvement in percentage area stenosis from 83% ± 7% to 61% ± 9% (Fig. 3).

The calcium score as measured from the IVUS images was 1.5 ± 0.7 before and 1.2 ± 0.9 after DCA (p not significant). This indicates that the vessels chosen for DCA were not heavily calcified nor was there a significant amount of calcium removed from the plaque (Fig. 4). The majority of these lesions were mildly concentric stenoses as measured by intravascular cross-sectional imaging, with a mean eccentricity index of 0.57 ± 0.27 at baseline. This index was reduced to 0.35 ± 0.23 after DCA. The increase in the eccentricity of the plaques indicates that the atherectomy cuts were not circumferentially uniform but tended to remain in one quadrant despite attempts to rotate the cutter (Fig. 5).

Figs. 6 and 7 demonstrate the correlation between IVUS and angiography for the MLD and lumen CSA after DCA without adjunctive PTCA. The tightest angiographic MLD was selected from at least two

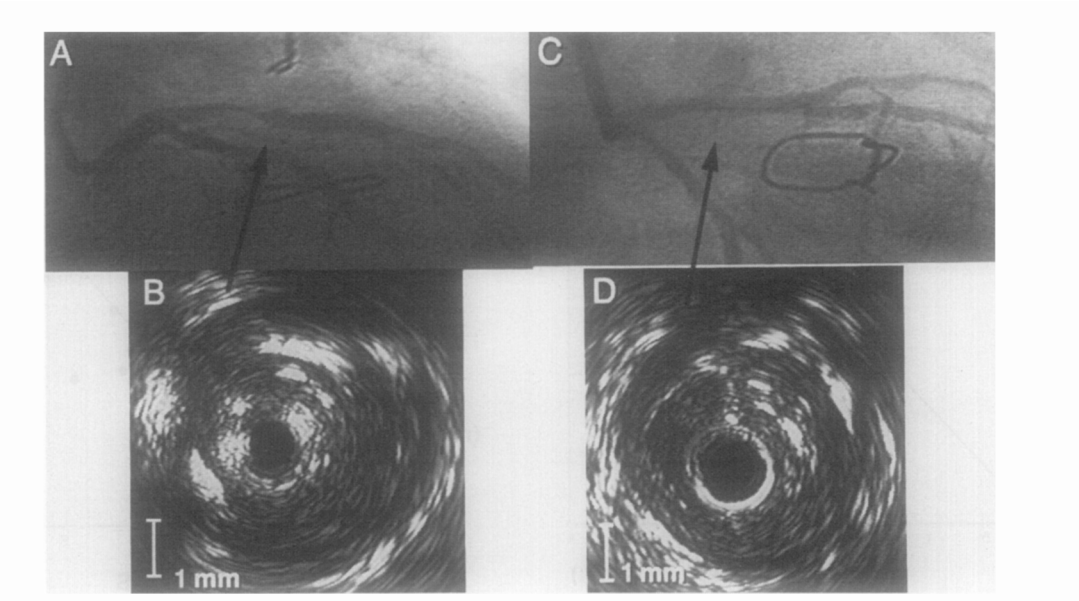

Fig. 4. This patient had diffuse coronary artery disease and had undergone coronary artery bypass operation. PTCA was performed in proximal left anterior descending coronary artery, but patient returned with unstable angina, and angiogram **(A)** demonstrated restenosis of proximal left anterior descending coronary artery with diffusely narrowed vessels. This stenosis was initially dilated with 2.0 mm balloon at 3 atm. IVUS imaging was then performed **(B)** and revealed concentric atheroma with mild calcification as demonstrated by more intense echoes at 12- to 2-o'clock and 8-o'clock positions. After successful DCA with 7F device and 14 cuts, residual lumen **(C)** appears adequate and is as large as other segments of artery. IVUS imaging after DCA **(D)** demonstrates that only small percentage of atheroma CSA was removed. Despite some enlargement of lumen to diameter of 2.7 mm, there is still large residual plaque burden.

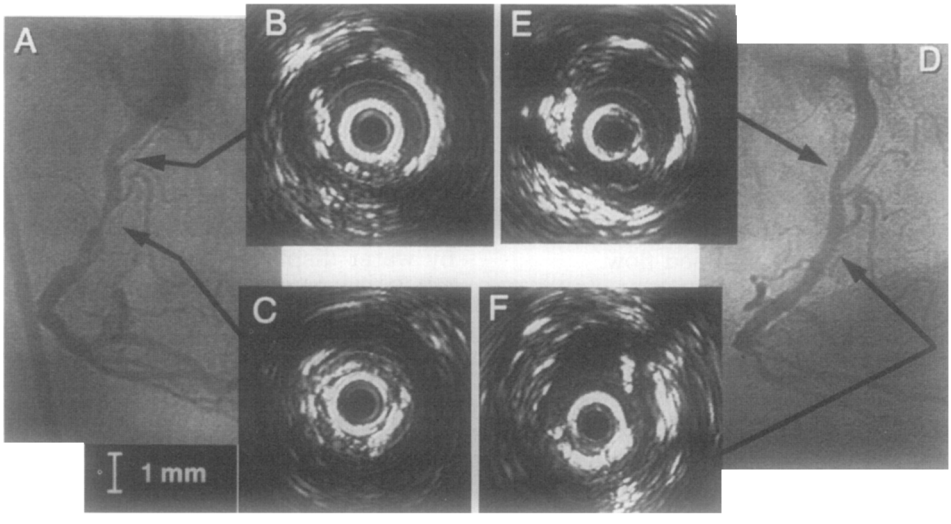

Fig. 5. This 83-year-old man had class I angina with tandem lesions in proximal and mid-right coronary artery **(A).** There was no evidence of calcium by fluoroscopy. IVUS revealed 3+ calcification in proximal lesion **(B)** and 2+ calcification in mid lesion **(C)** in this vessel. After multiple cuts, IVUS was performed but revealed significant residual atheroma in the vessel wall. Additional DCA cuts were performed. In the mid lesion, a small amount of additional plaque was removed (12 o'clock) **(F).** In proximal lesion **(E)**, although atheroma area did not change, lumen was stretched, resulting in satisfactory angiographic result **(D).**

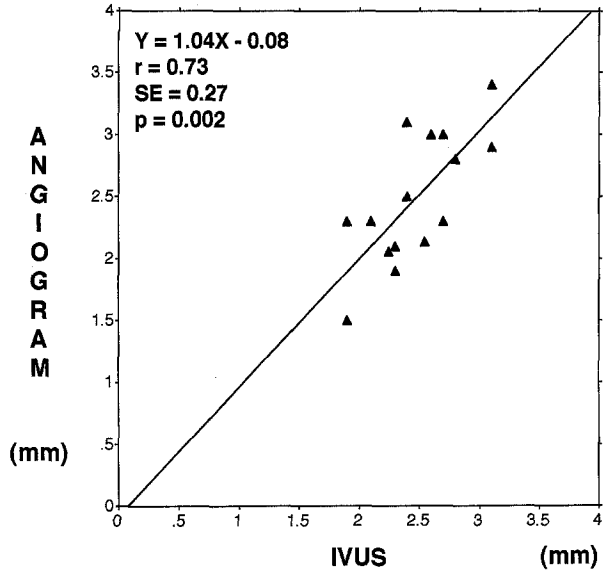

Fig. 6. Correlation for MLD between angiography and IVUS after DCA.

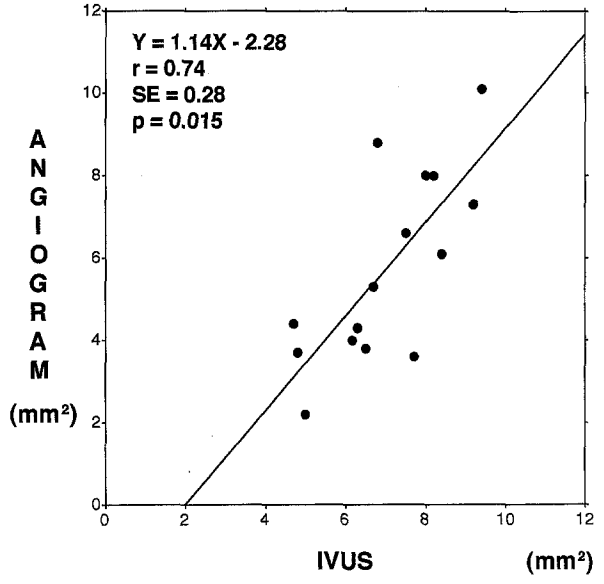

Fig. 7. Correlation of lumen CSA between IVUS and angiography after DCA.

projections. If the lesion was observed in only one projection, the lesion was excluded for analysis. Fifteen lesions were obtained with orthogonal projections. There was a significant correlation of MLD between angiography and IVUS after DCA ($r = 0.73$; $p = 0.002$). There also was a significant correlation of lumen CSA between both measurements after DCA ($r = 0.74$; $p = 0.0015$).

Complications. There were no instances of myocardial infarction, emergency bypass surgery, or death during any of these procedures. One patient had ventricular tachycardia during DCA associated with prolonged ischemia from the guiding catheter and the cutter. The patient recovered after removal of the catheter and electric cardioversion. The procedure was continued and yielded a successful result with significant improvement in blood flow.

DISCUSSION

The IVUS observations obtained in this study help to explain the mechanism of DCA more accurately than does angiography. DCA removed an average of 2.5 mm^2 from the atheroma, which corresponds to 18% of the atheroma CSA. The total lumen CSA increased 4.1 mm^2; thus 61% of the new lumen was created by DCA, and 39% of the new lumen was made by stretching the external wall of the artery (Fig. 8).

It has been assumed that the fundamental mechanism of DCA is the excision of plaque. However, lumen diameter improvement on angiography does not prove that all of the effect is attributable to removal of plaque. Safian et al.[32] concluded that lumen enlargement with DCA is caused in part by mechanical dilatation in addition to tissue removal. Their conclusion was derived from angiographic observations compared with the amount of tissue removed. In another angiographic study Penny et al.[33] concluded that the average cutting effect contributed 28% of the new lumen. Our study corroborates this data by direct observation with IVUS imaging. In contrast to our findings, Tenaglia et al.[34] using IVUS reported that the effect of stretching during DCA was small.

In vitro study. The results from the companion in vitro studies demonstrate that IVUS imaging accurately represents the amount of plaque that is removed by DCA. Compared with direct measurement by water displacement of removed plaque volume, IVUS provided a close estimate of the mean plaque volume (19.9 vs 18.6 μl). In addition the individual IVUS measurements correlated more closely with water displacement ($r = 0.92$) than did histologic measurements ($r = 0.81$). These observations give credibility to the IVUS measurements obtained during the clinical studies. During the clinical cases, measurements were made of the residual lumen and plaque CSAs. Although plaque volume calculations were not performed during the clinical studies, the method of integrating the areas over the length of the treated artery could be applied at the time of the procedure to quantitate the volume of plaque removed.

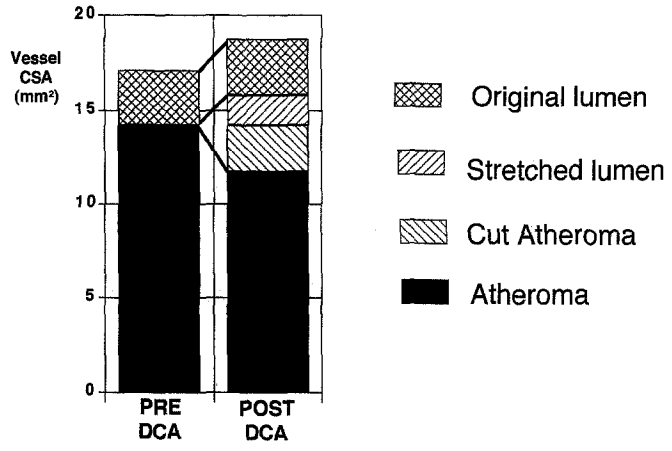

Fig. 8. Mechanism of DCA: total vessel CSA plotted before and after DCA. Total vessel area after DCA is composed of plaque, original lumen, and new lumen. Portion of this new lumen was produced by removal of some atheroma, but 40% of new lumen was produced by external stretching of media.

The in vitro IVUS images showed that a successful DCA demonstrated a smooth groove or "bite" in the atheroma, without separation of plaque from the media. In distinction to a previous study using this imaging technology to understand the mechanism of PTCA no intimal dissections were observed with the DCA device.[27]

Clinical study. The angiographic results in our patients are similar to the results from larger series of patients that were analyzed with angiography only. Popma et al.[35] reported that the lumen CSA increased from 1.2 ± 0.9 mm^2 to 6.4 ± 4.4 mm^2 after DCA in left anterior descending lesions.[35] Ellis et al.[7] demonstrated that the lumen dimensions increased from 1.1 ± 1.0 mm to 2.6 ± 2.3 mm. The diameter stenosis reported by Mueller et al.[36] improved from 69% ± 10% to 22% ± 20%. These studies did not use IVUS imaging to assess the effect of DCA.

Angiography versus IVUS. There was a significant correlation between angiography and IVUS for the measurements of lumen diameter after DCA ($r = 0.73$). This is in distinction to previous studies using IVUS to assess the results of PTCA alone.[24] In those series the correlation coefficient range was $r = 0.12$ to 0.21 after PTCA. It was concluded that the poor correlation was due to the dissections produced by balloon angioplasty. Contrast streaming into these dissection planes produces a wider apparent diameter on projection imaging techniques compared with that produced by cross-sectional imaging methods such as IVUS. Garratt et al.[37] showed no plaque fracturing or medial dissection after DCA in an autopsy study. The current study also demonstrated a low rate of dissection following DCA in vivo or during the in vitro studies. Penny et al.[33] suggested that DCA produces cloverlike bites into the plaque. Although this may be true for larger peripheral arteries, in coronary arteries the cross-sectional IVUS images suggest that an eccentric single trough is the usual morphologic result.

The majority of the stenoses that were studied before DCA had a concentric morphology by IVUS. The IVUS description of eccentricity corresponds to a histologic definition using measurements of the maximum and minimum thickness of the plaque. A plaque wall ratio >0.5 is considered a concentric stenosis with relatively equal distribution of plaque around the circumference of the lumen, whereas a major to minor plaque wall thickness of <0.5 is defined as an eccentric stenosis. The mean eccentricity index was 0.57 ± 0.27 at baseline, consistent with a definition of mildly concentric stenoses. After DCA the lesions were transformed to a predominately eccentric morphology with an index of 0.35 ± 0.23 ($p < 0.01$). This observation indicates that DCA did not cut the atheroma uniformly despite the attempt to rotate the atherectomy canoe radially and the use of IVUS to redirect the cutting assembly. This result may be caused by areas along the circumference of the plaque that are more resistant to the cutting effect of the DCA device (perhaps because of dense fibrosis or calcium). Alternatively, it is possible that once an initial trough is made in the atheroma, the canoe tends to slip back into the same position, resulting in an eccentric morphology. This may help explain the observation that despite an increased number of cutting passes, no more material may be removed.

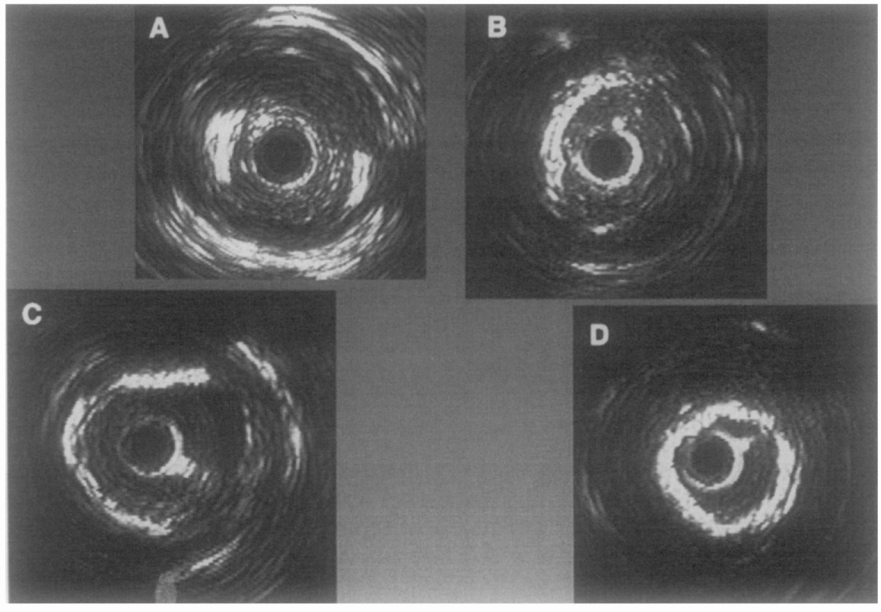

Fig. 9. Varieties of calcification as demonstrated by IVUS imaging. Areas of calcification may be present in various distributions in artery that cannot be appreciated by angiography. **A,** Two areas of calcium at 4- and 9-o'clock positions occur at base of plaque. **B,** Hemicircle of calcium occurs at base of plaque near media. **C,** Three fourths of circumference is involved with thin band of calcified matrix. **D,** Circumferential calcified atherosclerotic plaque has fibrocalcific cap in contact with lumen from 6- to 1-o'clock positions.

Whether a plaque is designated to be concentric or eccentric may have a significant effect on the treatment strategy. This is usually defined angiographically, and the information is used by the operator to direct the cutting blade. However, the results of IVUS imaging demonstrate a poor correlation between angiography and IVUS for the diagnosis of eccentricity.[25] In the present study, 55% of angiographic eccentric lesions were found to be concentric on cross-sectional IVUS imaging. In addition, 70% of angiographic concentric lesions were found by IVUS to be eccentric. This information was used by the operator in an iterative process to alter the approach and direction of the DCA device. In addition, the information provided by the IVUS images was used to perform further DCA cuts despite an adequate angiographic result in 17% of cases.

The low calcium score indicates a bias of patient selection for less calcified lesions. The calcium score did not improve after DCA, consistent with previous observations that DCA is less effective for calcified lesions[38] especially if the calcium is located superficially at the lumen interface.[39, 40] Cross sectional imaging by IVUS is more explicit than angiography in defining the presence and location of calcified plaque (Fig. 9).

Conclusions. Although DCA produces significant improvement in angiographic lumen dimensions, observations from IVUS imaging reveal that 40% of the angiographic effect is due to stretching of the external vessel wall. There is frequently a large residual plaque after DCA which encompasses a mean of 59% of the available vessel CSA. These findings may help to explain the unexpectedly high incidence of restenosis after DCA. Because only 18% of the atheroma CSA is removed by DCA, it would require a relatively minor amount of cellular matrix proliferation and elastic recoil to produce restenosis with a 50% lumen diameter.

We thank Constance Taylor for assistance in preparing this manuscript. Specimens for this study were provided by the Orange County Coroner's Office, James Beisner, Chief Deputy Coroner.

REFERENCES

1. Holmes DR, Veletstra RE, Smith HC, Vetrovec GW, Kent KM, Cowley MJ, Faxon DP, Gruenzig AR, Kelsey SF, Detre KM, Van Raden MJ, Mock MB. Restenosis after percutaneous transluminal coronary angioplasty (PTCA): a report from the PTCA registry of the National Heart, Lung and Blood Institute. Am J Cardiol 1984;53:77C-81C.
2. Serruys PW, Luijten HE, Beatt KJ, Geuskens R, De Feyter PJ, Van den Brand M, Reiber JH, Ten Katen HJ, Van Es GA, Hugenholtz PG. Incidence of restenosis after successful coronary angioplasty: a time-related phenomenon. Circulation 1988;77:361-71.
3. Rubin GS, Douglas JS, King III SB, Lin S, Hutchinson N, Thomas RG, Gruntzig AR. Influence of balloon size on initial success, acute complications, and restenosis after percutaneous transluminal coronary angioplasty. Circulation 1988;78:557-65.
4. Nobuyoshi M, Kimura T, Nosaka H, Mioka S, Veno K, Yokoi H, Hamasaki N, Horiuchi H, Ohishi H. Restenosis after successful percuta-

neous transluminal coronary angioplasty: serial angiographic follow-up of 229 patients. J Am Coll Cardiol 1988;12:616-23.
5. Hirshfield JW, Schwartz JS, Jugo R, MacDonald RG, Goldberg S, Savage MP, Bass TA, Vetrovec G, Cowley M, Taussig AS, Whithworth HB, Margolis JR, Hill JA, Pepine CJ. Restenosis after coronary angioplasty: a multivariate statistical model to relate lesion and procedure variables to restenosis. J Am Coll Cardiol 1991;18:647-56.
6. Rowe MH, Hinohara T, White NW, Robertson GC, Selmon MR, Simpson JB. Comparison of dissection rates and angiographic results following directional coronary atherectomy and coronary angioplasty. Am J Cardiol 1990;66:49-53.
7. Ellis SG, De Cesare NB, Pinkerton CA, Whitlow P, King III SB, Ghazzal ZB, Kereiakes DJ, Popma JJ, Menke KK, Topol EJ, Holmes DR. Relation of stenosis morphology and clinical presentation to the procedural results of directional coronary atherectomy. Circulation 1991; 84:644-53.
8. Hinohara T, Rowe MH, Robertson GC, Selmon MR, Braden L, Leggett JH, Vetter JW, Simpson JB. Effect of lesion characteristics on outcome of directional coronary atherectomy. J Am Coll Cardiol 1991;17:1112-20.
9. Feld H, Schulhoff N, Lichstein E, Greengart A, Frankel R, Hollander G, Shani J. Coronary atherectomy versus angioplasty: the CAVA study. Am Heart J 1993;126:31-8.
10. Umans VA, Beatt KJ, Rensing BJ, Hermans WR, de Feyter PJ, Serruys PW. Comparative quantitative angiographic analysis of directional coronary atherectomy. Am J Cardiol 1991;68:1156-563.
11. Kuntz RE, Safian RD, Levine MJ, Reis GJ, Diver DJ, Baim DS. Novel approach to the analysis of restenosis after the use of three new coronary devices. J Am Coll Cardiol 1992;19:1493-9.
12. Hinohara T, Robertson GC, Selmon MR, Vetter JW, Rowe MH, Braden LJ, MacAuley BJ, Sheehan DJ, Simpson JB. Restenosis after directional coronary atherectomy. J Am Coll Cardiol 1992;20:623-32.
13. Kuntz RE, Hinohara T, Robertson GC, Safian RD, Simpson JB, Baim DS. Influence of vessel selection on the observed restenosis rate after endoluminal stenting or directional atherectomy. Am J Cardiol 1992; 70:1101-8.
14. Fishman RF, Kunz RE, Carrozza JP, Miller MJ, Senerchia CC, Schnitt SJ, Diver DJ, Safian RD, Baim DS. Long-term result of directional coronary atherectomy: predictor of restenosis. J Am Coll Cardiol 1992; 20:1101-10.
15. Kuntz RE, Gibson M, Nobuyoshi M, Baim D. Generalized model of restenosis after conventional balloon angioplasty, stenting and directional atherectomy. J Am Coll Cardiol 1993;21:15-25.
16. Umans VA, Hermans W, Foley DP, Strikwerda S, van den Brand M, de Jaegere P, de Feyter PJ, Serruys PW. Restenosis after directional coronary atherectomy and balloon angioplasty: comparative analysis based on matched lesions. J Am Coll Cardiol 1993;21:1382-90.
17. Medina A, de Lezo JS, Hernandez E, Pan M, Ortega JR, Romero M, Melian F, Pavlovic D, Morales J, Marrero J, Cabrera JA. Serial angiographic observations after successful directional coronary atherectomy. Am Heart J 1993;125:1217-21.
18. Adelman AG, Cohen E, Kimball BP, Bonan R, Ricci DR, Webb JG, Laramer L, Barbean G, Traboulsi M, Corbett BN, Schwartz L, Logan AG. A comparison of directional coronary atherectomy with balloon angioplasty for lesions of the left anterior descending coronary artery. N Engl J Med 1993;329:228-33.
19. Topol EJ, Leya F, Pinkerton CA, Whitlow PL, Hofling B, Simonton CA, Masden RR, Serruys PW, Leon MB, Williams DO, King SB, Mark DB, Isner JM, Holmes DR, Ellis SG, Lee KL, Keeler GP, Berdan LG, Hinohara T, Califf RM. A comparison of directional coronary atherectomy with coronary angioplasty in patients with coronary artery disease. N Engl J Med 1993;329:221-7.
20. Yock PG, Fitzgerald PJ, Linker DT, Angelsen BAJ. Intravascular ultrasound guidance for catheter-based coronary interventions. J Am Coll Cardiol 1991;17:39B-45B.
21. Keren G, Leon MB. Characterization of atherosclerotic lesions by intravascular ultrasound: possible role in unstable coronary syndromes and in interventional therapeutic procedures. Am J Cardiol 1991;68:85B-91B.
22. White NW, Webb JG, Rowe MH, Selmon MR, Hinohara T, Linker DT, Yock PG. Atherectomy guidance using intravascular ultrasound: quantitation of plaque burden [Abstract]. Circulation 1989;80:II-374.
23. Davidson CJ, Sheikh KH, Kisslo KB, Phillips RR, Peter RH, Behar VS, Kong Y, Krucoff M, Ohman M, Tcheng JE, Stack RS. Intravascular ultrasound evaluation of interventional technologies. Am J Cardiol 1991;68:1305-9.
24. Tobis JM, Mallery J, Mahon D, Lehmann K, Zalesky P, Griffith J, Gessert J, Moriuchi M, McRae M, Dwyer M, Greep N, Henry WL. Intravascular ultrasound imaging of human coronary arteries in vivo: analysis of tissue characterizations with comparison to in vitro histological specimens. Circulation 1991;83:913-26.
25. Honye J, Mahon DJ, Jain A, White CJ, Ramee SR, Wallis JB, Al-Zarka A, Tobis JM. Morphological effects of coronary balloon angioplasty in vivo assessed by intravascular ultrasound imaging. Circulation 1992; 85:1012-25.
26. De Lezo JS, Romero M, Medina A, Pan M, Davlovic D, Vaamonde R, Hernandez E, Melian F, Rubio FL, Marrero J, Segura J, Irurita M, Cabrera J. Intravascular ultrasound assessment of directional coronary atherectomy: immediate and follow-up findings. J Am Coll Cardiol 1993;21:298-307.
27. Tobis JM, Mallery JA, Gessert J, Griffith J, Mahon DJ, Bessen M, Moriuchi M, McLeay L, McRae M, Henry WL. Intravascular ultrasound cross sectional arterial imaging before and after balloon angioplasty in vitro. Circulation 1989;80:873-82.
28. Simpson JB, Selmon MR, Robertson GC, Cipriano PR, Hayden WG, Johnson DE, Fogarty TJ. Transluminal atherectomy for occlusive peripheral vascular disease. Am J Cardiol 1998;61:96G-101G.
29. Robertson GC, Hinohara T, Selmon MR, Johnson DE, Simpson JB. Directional coronary atherectomy. In: Topol EJ, ed. Textbook of interventional cardiology. Philadelphia: WB Saunders, 1990:563-79.
30. Ellis GS, Vandormael MG, Cowely MJ, DiSciascio G, Deligonul V, Topol EJ, Bulle TM, and the Multivessel Angioplasty Prognosis Study Group. Coronary morphology and clinical determinants of procedural outcome with angioplasty for multivessel coronary disease: implications for patient selection. Circulation 1990;82:1193-202.
31. Nakamura S, Mahon DJ, Maheswaran B, Gutfinger DE, Colombo A, Tobis JM. An explanation for the discrepancy between angiographic and intravascular ultrasound measurements after percutaneous transluminal coronary angioplasty [Abstract]. Circulation 1994;90:I-551.
32. Safian RD, Gelbfish JS, Erny RE, Schnitt DA, Schmidt DA, Baim DS. Coronary atherectomy, clinical, angiographic and histologic findings and observations regarding potential mechanisms. Circulation 1990; 82:69-79.
33. Penny WF, Schmidt DA, Safian RD, Erny RE, Baim DS. Insights into the mechanism of luminal improvement after directional coronary atherectomy. Am J Cardiol 1991;67:435-7.
34. Tenaglia AN, Buller CE, Kisslo KB, Stack RS, Davidson CJ. Mechanism of balloon angioplasty and directional coronary atherectomy as assessed by intravascular ultrasound. J Am Coll Cardiol 1992;20:685-91.
35. Popma JJ, De Cesare NB, Ellis SG, Holmes DR, Pinkerton CA, Whitlow P, King SB III, Ghazzal ZB, Topol EJ, Garratt KN, Kereiakers DJ. Clinical, angiographic and procedural correlates of quantitative coronary dimensions after directional coronary atherectomy. J Am Coll Cardiol 1991;18:1183-9.
36. Mueller DW, Ellis SG, Debowey DL, Topol EJ. Quantitative angiographic comparison of the immediate success of coronary angioplasty. Am J Cardiol 1990;66:938-42.
37. Garratt KN, Edwards WD, Vlietstra RE, Kaufman VP, Holmes DR. Coronary morphology after percutaneous directional atherectomy in humans: autopsy analysis of three patients. J Am Coll Cardiol 1990; 16:1432-6.
38. Robertson GC, Vetter JW, Selmon MR, Bartzokis TC, Shahan DJ, MacAuley BJ, Braden LJ, Simpson JB. Directional coronary atherectomy is less effective for calcified primary lesions [Abstract]. Circulation 1991;84:II-520.
39. Fitzgerald PJ, Muhlberger VA, Moes NY, Friedrich G, Connolly AJ, Strunk BL, Amidon TM, Robertson GC, Selmon MR, Vetter JW, Yock PG. Calcium location within plaque as a predictor of atherectomy tissue retrieval: an intravascular ultrasound study [Abstract]. Circulation 1992;86:I-516.
40. Suneja R, Nair RN, Reddy KG, Rasheed Q, Sheehan HM, Hodgson JM. Mechanisms of angiographically successful directional coronary atherectomy: evaluation by intracoronary ultrasound and comparison with transluminal coronary angioplasty. Am Heart J 1993;126:507-14.