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Limitations of Coronary Angiography Compared With Intravascular Ultrasound: Implications for Coronary Interventions

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The use of intravascular ultrasound catheters to produce images of lumen and plaque cross-sectional areas has had a profound effect on the practice of interventional cardiology. This imaging modality provides, for the first time, a low-power microscopic view of vascular anatomy within a living patient. This article will review some of the advantages of intravascular ultrasound imaging compared with angiography when used for diagnostic or interventional therapeutic procedures.

Coronary angiography is the primary mode of imaging coronary artery disease and guiding interventional procedures. Although coronary angiography was essential for the development of catheter-based coronary interventions, as the complexity of interventional cases increased, several limitations of angiography surfaced. Problems associated with coronary intervention, such as acute closure and restenosis, are related in part to properties of the lesion. Angiographic studies have reported inconsistent predictors of such adverse events.[1,2] One of the main reasons for this inconsistency is the limited power of angiography to delineate the complex anatomy of coronary atherosclerotic lesions. Intravascular ultrasound (IVUS) is a technique that provides two-dimensional, tomographic views of the coronary lumen and wall morphology in vivo, which has several advantages compared with angiography.[3]

This article reviews the limitations of angiography and describes the information that IVUS imaging provides to complement angiography during diagnostic and interventional procedures. The ability of IVUS to evaluate lesion characteristics and dimensions alters therapeutic decisions and permits the operator to optimize each intervention.

Lesion Evaluation

Evaluation of coronary atherosclerotic lesions by angiography has been described by the joint American College of Cardiology/American Heart Association (ACC/AHA) committee.[4] This system delineates lesions by the degree of eccentricity and complexity. However, this analysis is limited by the ability of angiography to visualize only the lumen and not the atherosclerotic plaque itself.

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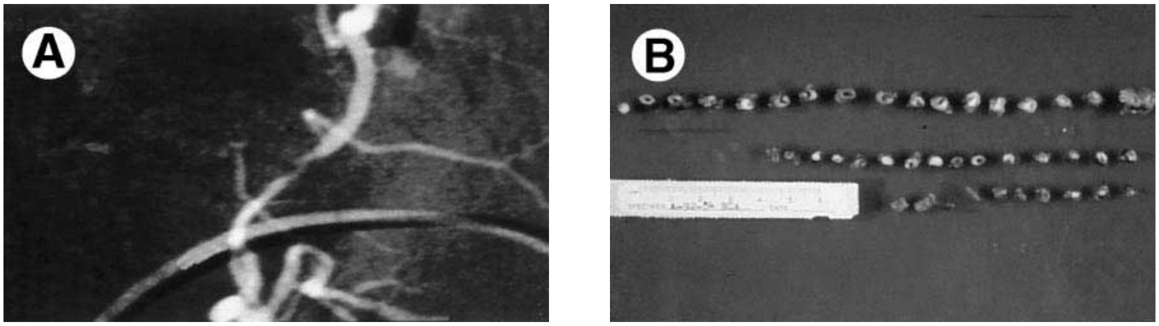


Fig 1. (A) A case example of a right coronary artery disease. (B) Pathologic cross sections of the right coronary artery.

IVUS provides new insights for lesion evaluation because it produces a tomographic view of the artery and it is the only technique that permits visualization of the diseased artery wall in vivo. This capability is especially useful for diagnosing disease when vessels overlap or if there is a short stenosis. In addition, IVUS images are at a higher magnification than angiography, and its internal scale has been shown to be more accurate than angiographic assessment of plaque dimensions. Moreover, the ability of angiography to provide information on tissue characterization is limited. The following discussion will attempt to describe these differences between angiography and IVUS.

Tomographic Imaging

An angiogram shows a longitudinal, two-dimensional view of the lumen of the vessel and does not directly show us the pathology, that is, the atherosclerotic plaque. If the plaque impinges on the lumen, then the indentation is used as a measure of the severity of the atherosclerosis. This method may lead to a false sense of security for several reasons. Because the lumen edges of an angiogram may have a smooth border, we assume that there is not a lot of disease in the vessel.[5] Pathologic studies show that the amount of atherosclerosis is underrepresented by angiography.[6-12] In Fig 1A, the angiogram of a right coronary artery (RCA) shows severe stenosis in the mid portion, but it was felt that the rest of the artery did not have significant disease. Unfortunately, this patient did not survive an intervention of balloon angioplasty for the mid RCA stenosis (this study was performed before stents became available). The corresponding pathologic cross sections (Fig 1B) were taken every 5 mm along the length of the RCA, posterior descending, and posterior lateral branches. The diffuse nature of atherosclerosis is shown in every cross section. Although this phenomenon was counterintuitive to most angiographers, it became more readily accepted throughout the 1980s with the concept of vascular remodeling and compensatory dilatation proposed by Glagov et al.[13] In their pathologic study of 125 left main coronary arteries, it was shown that as the amount of atherosclerosis increased, the outer diameter of the vessel increased but the lumen remained constant until approximately 40% of the cross-sectional area was filled with plaque. At that point, the outer dimension could not enlarge adequately to compensate for the increase in plaque area; the lumen became narrow and only then would it be recognized as diseased on angiography. As shown in Fig 2, the lumens from artery sections 1 through 4 would all appear to be the same on angiography, and all four would be erroneously considered normal. In distinction to angiography, IVUS looks beyond the lumen and reflects information directly about the pathology within the arterial wall. Thus, IVUS can distinguish normal from progressive stages of atherosclerosis in vivo.[14] IVUS studies confirm that arteries frequently expand radially as the

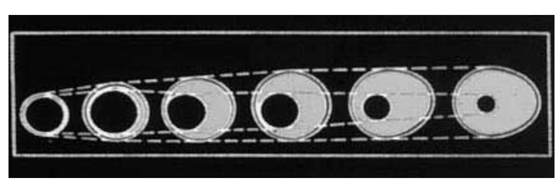


Fig 2. Compensatory enlargement of a coronary artery.

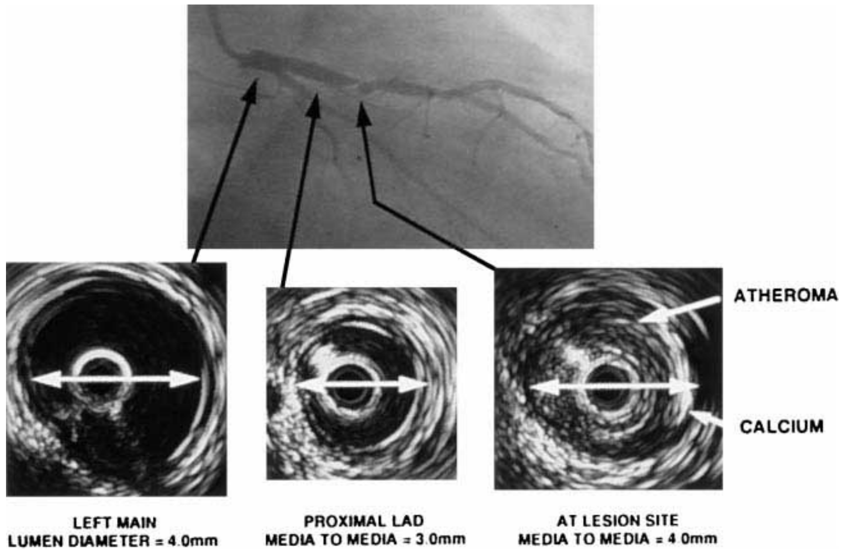


Fig 3. A case example of compensatory enlargement.

plaque enlarges while maintaining the lumen cross-sectional area so that adequate blood flow is provided (Fig 3).

Vessel Overlap or Short Stenoses

Several in vitro and clinical studies have shown that IVUS and angiographic measurements of lumen diameter correlate well when there is minimal disease or if the lumen is circular.[15] However, angiography can be misleading, especially when there is an overlap of vessels or if a short stenosis is present. Figure 4 provides evidence for what has been called a "napkin ring" stenosis.[16] This is a very short stenosis, only 1 to 2 mm in length, such that even in multiple angiographic projections, contrast is in front of or behind the stenosis, which makes the stenosis appear less significant than it is. The angiogram of this symptomatic patient suggests that a mild stenosis is present in the proximal left anterior descending coronary artery (LAD), but on IVUS imaging, the real stenosis is in the mid LAD, where the ultrasound catheter is wedged into the speckled reverberations of plaque. The mid LAD was treated with balloon angioplasty with relief of the patient's symptoms.

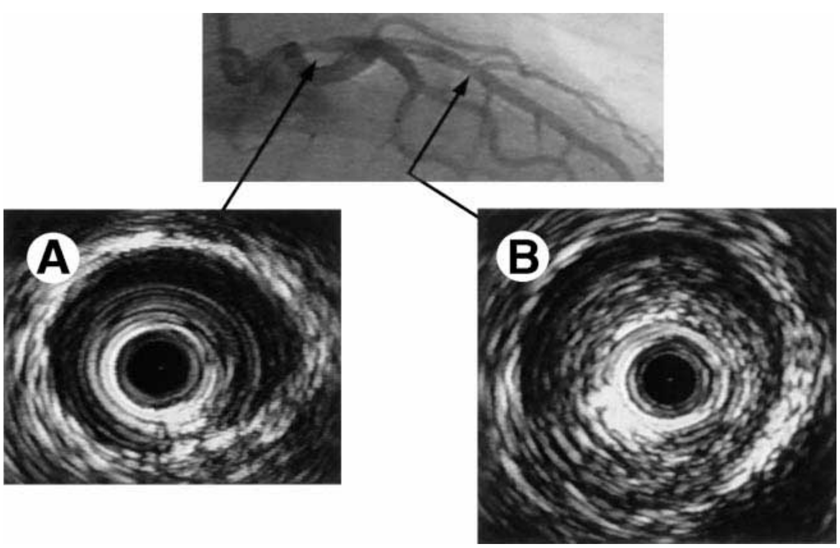


Fig 4. A case example of a napkin ring stenosis.

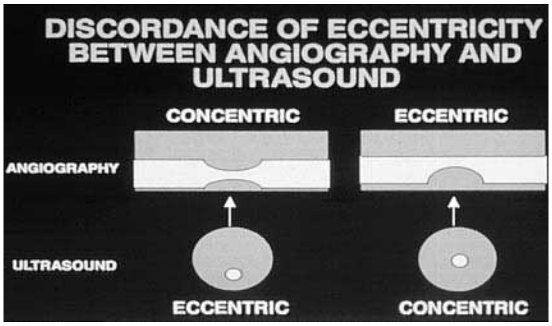


Fig 5. Misdiagnosis of eccentric lesions.

Accurate Measurements—Magnification and Scale

Magnification and scaling errors reveal another major difference between angiography and IVUS for quantitative analysis.[17,18] With angiography, there are significant magnification assumptions when using the guiding catheter as the ruler. A 2.7-mm guide catheter represents only 11 pixels in a 640 × 480 pixel matrix. When measuring an artery edge, one could easily be off by 1 or 2 pixels, which for an artery between 1 and 4 mm is nearly 10% of the ruler. With IVUS imaging, the "ruler" is inherent in the image and is based on the speed of sound in tissue at 37°C. These observations suggest that quantitative coronary angiography has been given too much credence in our literature and design of studies. We should not confuse the reproducibility that computerized measurements provide with accuracy in representing complex luminal topography. It is similar to squeezing a 3–decimal place accuracy from a technique whose scale may be incorrect by several tenths of a millimeter.

Misdiagnosis of Eccentric Lesions

Another area where there is disagreement between ultrasound and angiography is in the description of plaque eccentricity.[14,19-21] As schematically shown in Fig 5, an angiogram that is described as showing a concentric lesion may, in fact, appear to be eccentric on cross-sectional imaging with ultrasound because the plaque itself is not visualized on the angiogram. Conversely, an eccentric plaque by angiography may appear to be concentric on cross-sectional imaging with ultrasound, as shown in the right-hand panel. This discordance between angiography and ultrasound for the description of plaque eccentricity occurs in approximately 20% of lesions. This observation undermines the validity of this angiographic descriptor as a predictor of responses to coronary interventions.

Tissue Characterization

Because angiography describes only the lumen of the vessel, this method cannot identify characteristics of the plaque beyond gross thrombus or calcification. Ultrasound patterns of tissue reflection can be used to characterize more subtle plaque composition.[22-25]

Although calcification can be visualized with fluoroscopy, IVUS provides information about plaque morphology and composition such as fibrous tissue and lipid components or intralumi-

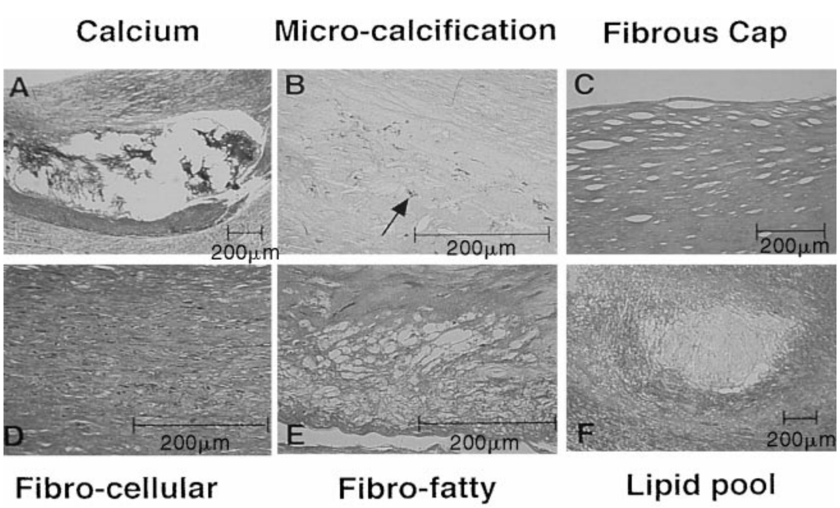


Fig 6. Histologic tissue types.

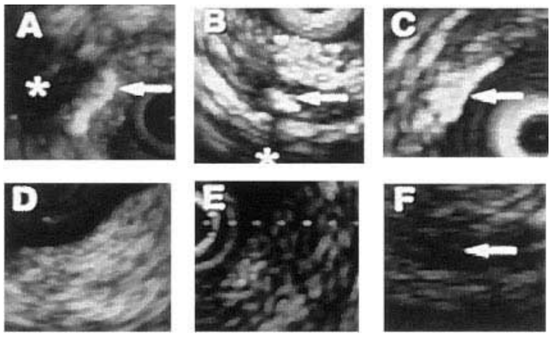


Fig 7. Tissue characterization by intravascular ultrasound imaging.

nal thrombus. As shown in Fig 6, when histologic tissues are segregated into 6 general types, such as calcification, microcalcification, fibroacellular, fibrocellular, fibrofatty, and fatty tissue, the corresponding ultrasound pictures show the following characteristics (Figure 7): (1) calcium has the unique characteristic of being intensely echo reflective at the initial interface with dropout of echoes peripherally, which is termed *shadowing* (Fig 7A); (2) using the same description, microcalcification can be identified as a very small area, 0.1 to 0.2 mm in diameter with intense echo reflections and a small radiating arc of shadowing behind it (Fig 7B); (3) a fibrous acellular capsule (Fig 7C) appears on ultrasound as an intense echo reflection that may be equal or greater than the adventitia echogenicity, but it is distinguished from calcification because there is no shadowing behind it; (the next three categories show a more mixed pattern) (4) mixed cellularity interspersed within fibrous tissue is depicted on ultrasound images as a homogenous black and white speckled pattern with moderate echogenicity (Fig 7D); (5) as fatty elements increase within the plaque, the echogenicity decreases as reflected in the fibrofatty plaque of Fig 7E, which has more black or echolucent areas within the echogenic fibrous tissue; and (6) a large deposition of lipid or necrotic tissue within the body of the plaque is more likely to be represented by a homogenous echolucent zone as shown in Fig 7F.

Angiography may also be misleading in the diagnosis of thrombus formation. This can have significant implications in terms of the type of

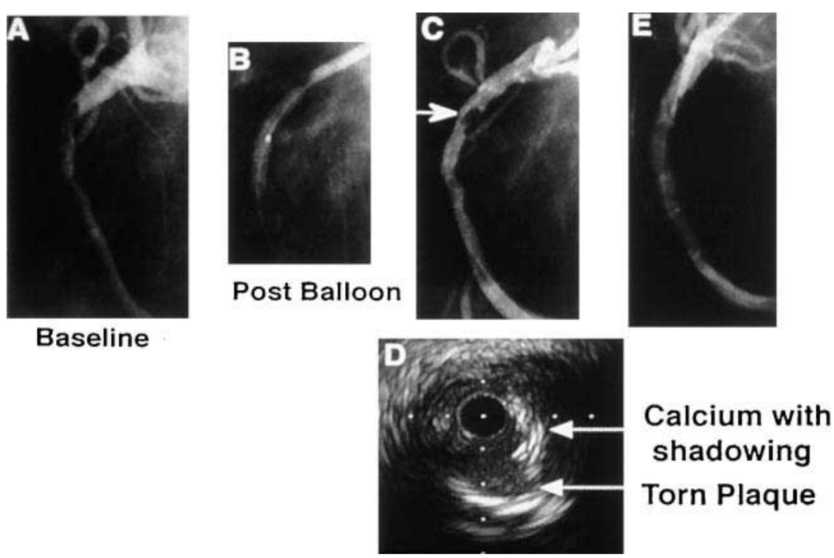


Fig 8. Acute inferior wall myocardial infarction. The baseline angiogram revealed a filling defect in the proximal right coronary artery consistent with thrombus (A). Following several balloon dilatations, flow was improved, but there was still a significant residual filling defect that had the appearance of thrombus (C). Rather than proceeding with thrombolytic therapy, TEC, or Angiojet thrombectomy, an IVUS catheter was passed, with the results shown (D). The IVUS image revealed the presence of intense calcification between the 1- and 7-o'clock positions, with evidence for torn plaque, which has also shifted its position. Based on the IVUS information, an AVE-GFX stent was deployed without the persistent recoil that was seen following balloon dilatation alone (E).

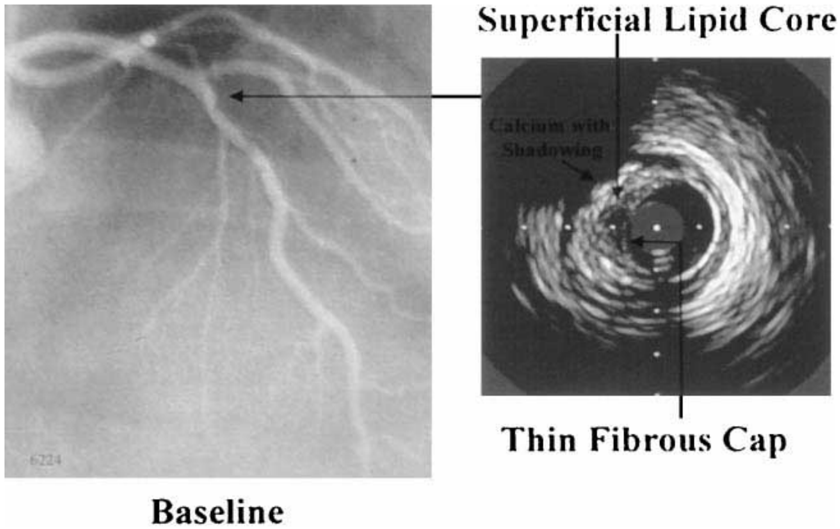


Fig 9. The angiogram reveals a linear stenosis in the proximal LAD before the first septal perforator. Just proximal to the stenosis is an eccentric plaque that appears to have a mixed composition based on tissue characterization. Between the 9- and 12-o'clock positions, there are some intense echo reflections with shadowing peripherally consistent with calcified tissue. In the central portion of the plaque between the 8- and 10-o'clock positions, the plaque is more echolucent with a thin band of echogenic reflection at the lumen surface. This image indicates that under the thin fibrous capsule, there is a central core of lipid laden cells with denser fibrocalcific disease at the base of the plaque.

treatment that is attempted. An example of an apparent thrombus diagnosed by angiography is depicted in Fig 8.

Most investigators report a high sensitivity of identifying calcium as a hyperechogenic area with shadowing.[26-28] Unfortunately, the ability of IVUS to distinguish fibrous from fatty tissue becomes less exact with sensitivity on the order of 50%.[29] It would be beneficial if IVUS images could consistently and accurately identify those plaques with a thin fibrous capsule and a lipid-rich core that are ripe for rupture (Fig 9).[30,31] This type of histologic pattern has been described as a likely precursor to acute plaque rupture and thrombus formation that may precipitate unstable syndromes or acute myocardial infarction.[32,33] Unfortunately at the present time, the sensitivity for identifying these plaques is limited, and we have not used this information to preemptively treat a plaque based solely on its tissue components of a lipid core. It has been reported that analysis of unprocessed radiofrequency (RF) signals may work better for tissue characterization than conventional video IVUS images.[34] Moore et al performed RF analysis in an in vitro setting and showed that parameters of power and spectral slope could discriminate between various tissue types. Clinical studies are needed to test if the RF analysis is more reliable than the image interpretation computer in our brain.

Representation of Calcium Amount and Position

One of the important observations of IVUS is the recognition of a higher incidence of plaque calcifi-

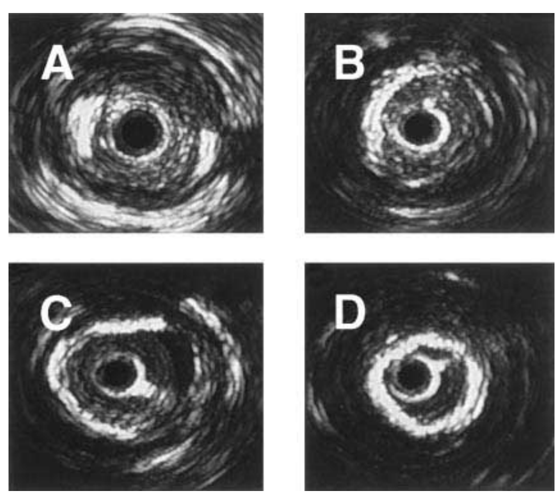


Fig 10. Varieties of calcification.

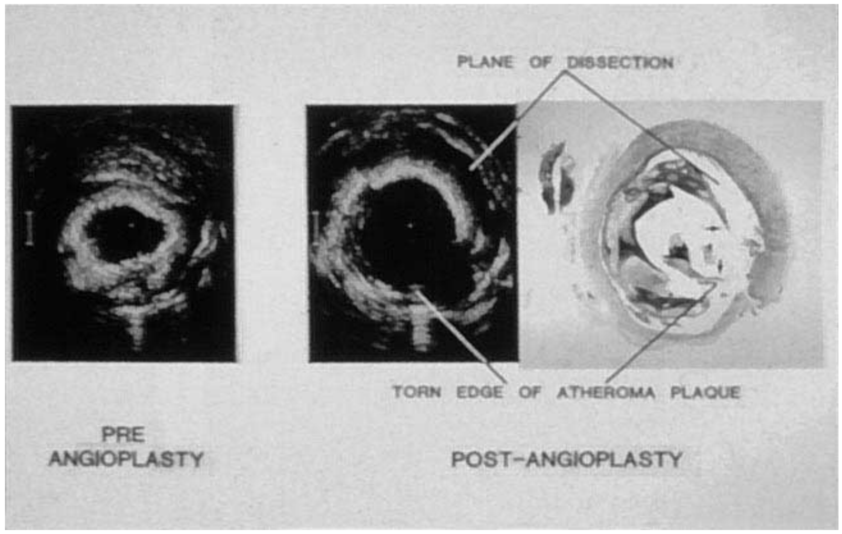


Fig 11. Mechanism of lumen enlargement by balloon angioplasty.

cation than is appreciated by angiography.[35-37] Angiography identifies calcium at the site of a stenosis in only 15% of cases, whereas some degree of calcium is seen by ultrasound in up to 85% of these stenoses. The high sensitivity for depicting calcified areas of plaque has been useful in showing the distribution of calcium throughout the length and circumference of an artery on a micro-anatomic scale.[38,39] As shown in Fig 10, calcified areas frequently occur at the base of the plaque but may subtend a variable circumference. Figure 10 shows calcified plaque at the lumen-plaque interface. These types of plaque are very resistant to balloon dilatation alone and impede stent expansion. When calcification is seen at the lumen-plaque interface, rotational atherectomy is usually necessary. Understanding the composition and biomechanical hardness of the plaque may be very useful when deciding what type of interventional device should be used.

Balloon Angioplasty

Overestimation of Percutaneous Transluminal Coronary Angioplasty (PTCA) Effect

In vitro studies using IVUS before and after balloon dilatation of atherosclerotic segments help to explain the mechanism of action of balloon angioplasty. Histologic studies show that the plaque is frequently torn at its thinnest segment or, if the plaque is calcified, the tear usually occurs at the junction of fibrous tissue and the calcified portion.[40-49] Compared with histologic assessment, IVUS has the benefit of

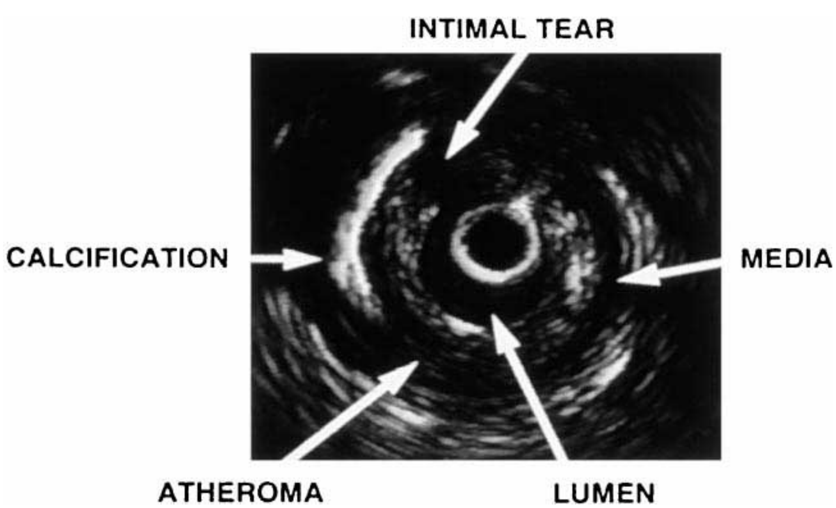


Fig 12. Intravascular ultrasound imaging after successful balloon angioplasty.

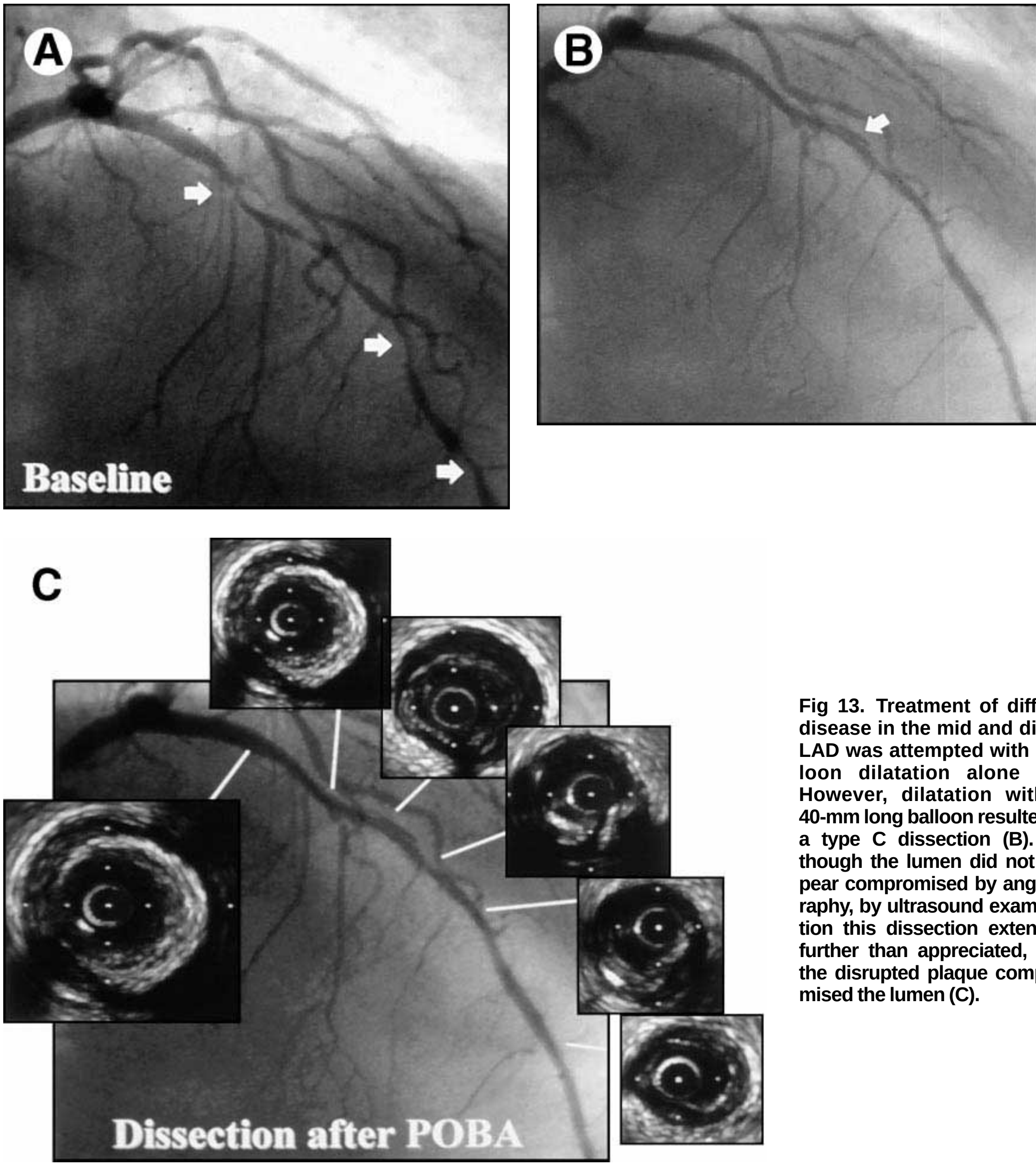


Fig 13. Treatment of diffuse disease in the mid and distal LAD was attempted with balloon dilatation alone (A). However, dilatation with a 40-mm long balloon resulted in a type C dissection (B). Although the lumen did not appear compromised by angiography, by ultrasound examination this dissection extended further than appreciated, and the disrupted plaque compromised the lumen (C).

being able to image the artery before, as well as after, balloon dilatation.[50] As shown in Fig 11, IVUS images before and after balloon dilatation show that the lumen enlarges because of plaque fracture and separation of the torn ends. In addition, a new echolucent zone behind the plaque corresponds to dissection of the artery where the plaque is separated from the media. Occasionally, when larger balloons are used, the entire plaque may be rotated free from the media due to torsional forces that leave an entire ring of dissection around the circumference of the plaque. These dissections do not necessarily result in collapse of the plaque into the artery because it may be supported at its proximal and distal ends to the vessel wall.

When IVUS imaging was initially applied to patients who had balloon angioplasty, some of the observations were quite unexpected.[51,52] As opposed to the angiographic results that suggested that a large lumen had been obtained, the usual

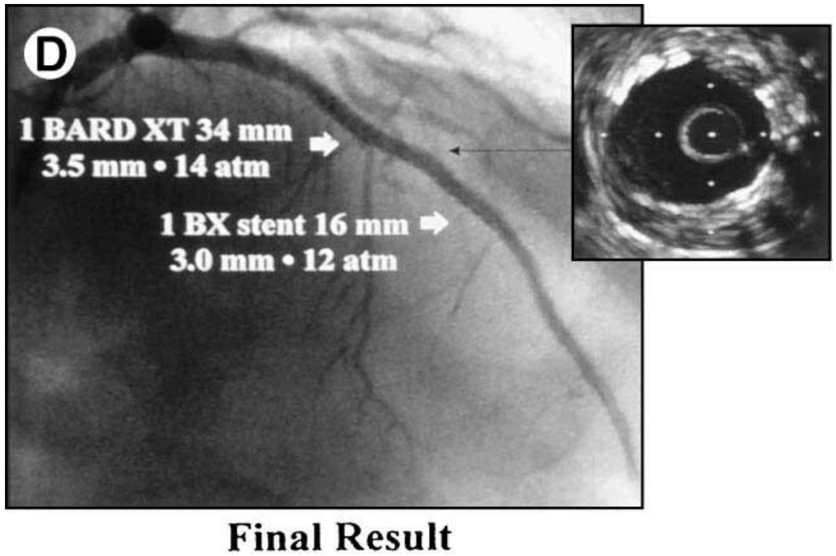


Fig 13. (Cont'd) This dissection was treated with a 34-mm long Bard XT stent and a 16-mm long BX stent (D). Although the risk of restenosis may be over 40% due to the length of these stents, it is imperative that arterial patency is maintained.

finding with IVUS was that only a relatively small tear had occurred in the plaque with separation of the torn ends (Fig 12). One was immediately impressed with the large amount of residual plaque that remained after balloon dilatation.[53] After seeing IVUS images, one could understand how easily restenosis occurs by elastic recoil and mild intimal proliferation; the wonder was how balloon dilatation yielded as high a degree of long-term success as it did.

The second major observation on the mechanism of balloon dilatation was the change in the lumen area from systole to diastole once the plaque had been fractured by the balloon. Although the volume of plaque had not been altered by balloon dilatation, the lumen cross-sectional area was dramatically increased by pulsatile blood flow in diastole. Conceptually, the plaque acts as a scar that immobilizes the wall of the artery. By cutting the plaque, balloon dilatation permits freer mobility of the arterial wall in response to the change in lumen pressure, thus increasing blood flow.[54]

Assessment of Dissections

A dissection after balloon angioplasty was originally thought to be a predictive marker of acute closure; however, abrupt closure occurs in only 5% of PTCAs with angiographic signs of dissection.[55] Inducing dissections has been considered an integral part of lumen enlargement with balloon angioplasty, but not all dissections are equivalent. A dissection represents an adverse event when it compromises the lumen. If a dissection is associated with less than Thrombolysis in Myocardial Infarction (TIMI) 3 flow, it should be treated. However, when dissections are associated with TIMI 3 flow, further evaluation beyond angiographic assessment should be considered, such as IVUS interrogation[56] or coronary flow measurements. IVUS can detect circumferential and longitudinal extension of plaque fracture or dissection after balloon angioplasty.[51,57] In a study comparing quantitative coronary angiography and IVUS,[58] a large discrepancy between these two modalities was reported, particularly when dissections were present after balloon angioplasty. These results indicate that angiography is not an optimal means to evaluate the vessel lumen after trauma from balloon dilatation. A case example of how IVUS helps in the decision to place a stent for the treatment of a coronary dissection is shown in Fig 13.

Other Stenoses Within the Target Vessel

IVUS may be helpful during percutaneous coronary interventions to discover other lesions in the vessel that require treatment to obtain an optimal result. An example of this is shown in Fig 14.

Underestimation of Vessel Size

Many studies have shown that a major determinant of restenosis is the percent diameter stenosis

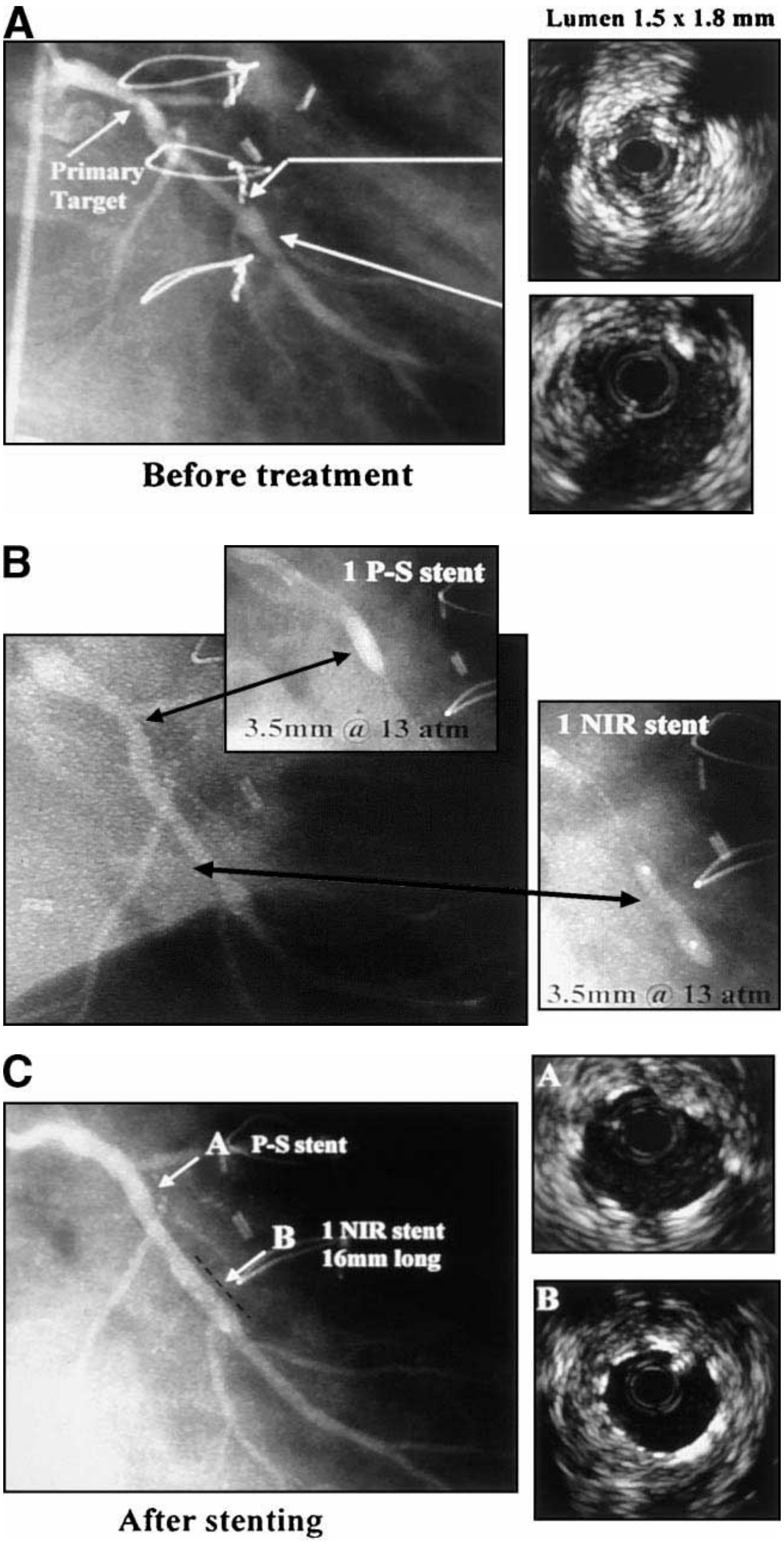


Fig 14. (A) A significant stenosis in the distal left main and proximal circumflex artery, which was the target lesion to be treated. IVUS was performed before the intervention. In addition to recognition of the disease in the proximal artery, IVUS showed a tight stenosis in the mid portion of the obtuse marginal artery that was underestimated by angiography. A 16-mm long NIR stent was placed at 13 atm using a 3.5-mm diameter balloon in the mid portion of the obtuse marginal artery (B). The proximal lesion was then treated with a Palmaz-Schatz stent deployed on a 3.5-mm balloon at 13 atm. The final angiographic result (C) reveals a satisfactory lumen in the proximal and mid portion of the obtuse marginal artery. By IVUS, the lumen measured 3 mm in diameter.

or minimal luminal diameter achieved after intervention.[59-65] Based on these findings, Don Baim introduced the so-called "the bigger, the better" doctrine. Although this rule of thumb may be appropriate for stents and directional atherectomy, indiscriminate use of balloons larger than the angiographic reference segment lumen may result in unacceptably high rates of ischemic complications after PTCA.[66,67] Since its initial description by Andreas Gruntzig in 1978,[68,69] PTCA has been performed by selection of a balloon with a nominal diameter approximating that of the normal-appearing reference segment adjacent to the lesion. A distinction needs to be made between the angiographic definition of artery size and the vessel size observed on IVUS. Whereas angiography uses the proximal reference lumen diameter to denote the artery size, IVUS defines the vessel size as the media-to-media diameter. Because arterial remodeling with compensatory vessel enlargement develops to preserve the lumen,[7,13,70] the vessel size by IVUS may be significantly greater than the lumen size by angiography. The extent of atherosclerosis in both the lesion and reference segments can be accurately measured on-line with IVUS imaging.[71-73] It was hypothesized that IVUS guidance could be used safely to accommodate oversized balloons in selected patients undergoing PTCA. Stone et al[74] showed that despite the presence of atheromatous remodeling, IVUS permits the safe use of balloons traditionally considered oversized, resulting in significantly improved luminal dimensions without increased rates of dissection or ischemic complications (Clinical Outcomes With Ultrasound Trial [CLOUT] Pilot Trial). Because the degree of plaque burden and the true vessel size can be determined only with IVUS, the use of ultrasound is thought to be essential for the accurate selection of properly sized balloons if an aggressive balloon strategy is to be safely performed.[74] Figure 15 shows an example how quantitative coronary angiography (QCA) may be misleading compared with IVUS imaging for assessing the artery size.

Understanding the Mechanisms of Restenosis

Restenosis remains a major limitation to percutaneous coronary revascularization. It occurs in 30% to 50% of transcatheter procedures within the first 6 months.[75-78] Animal models,[79-82] human necropsy studies,[43,83-92] and analyses of retrieved atherectomy specimens[93-99] originally suggested that an exaggeration of the normal reparative processes after angioplasty-induced local vessel trauma leads to uncontrolled smooth muscle cell proliferation and restenosis.[100-102] However, these early studies that showed restenosis was due primarily to intimal hyperplasia may have been misleading. Animal and clinical studies suggest that arterial remodeling with constriction of the adventitia might be a major contributing factor to the development of restenosis.[103-111] Using serial IVUS, Mintz et al observed that two thirds of restenosis was due to adventitial contraction, or "negative remodeling," and only one third of restenosis was explained by intimal proliferation.[112] Kimura et al reported that the time course of arterial remodeling after coronary angioplasty or atherectomy was characterized by early enlargement of the vessel (1 day to 1 month) and late constriction of the vessel (1 to 6 months).[113] They called the early and late vessel changes adaptive and constrictive remodeling, respectively. Recently, this postintervention arterial remodeling process was confirmed by a serial volumetric (three-dimensional) IVUS analysis.[114]

Patients with diabetes appear to respond differently to coronary interventions.[115] Although both diabetics and nondiabetics develop adventitial constriction to produce late lumen loss in nonstented lesions, diabetics show exaggerated tissue proliferation, which may explain their increased rate of restenosis.

Future strategies to reduce restenosis should target prevention of late constrictive remodeling and enhancement of adaptive remodeling as well as suppression of intimal hyperplasia.

Directional Atherectomy

Directional Atherectomy (DCA) was introduced to reduce the restenosis rate compared with balloon angioplasty; however, two initial randomized trials reported no significant benefit with this technique.[60,116]

Overestimation of Cutting Versus Stretching Effect of DCA

IVUS has provided significant insights into the mechanism of action of DCA and helps us to understand why the restenosis rate of early trials, such as the Coronary Angioplasty versus Excisional Atherectomy Trial (CAVEAT) or the Cana-

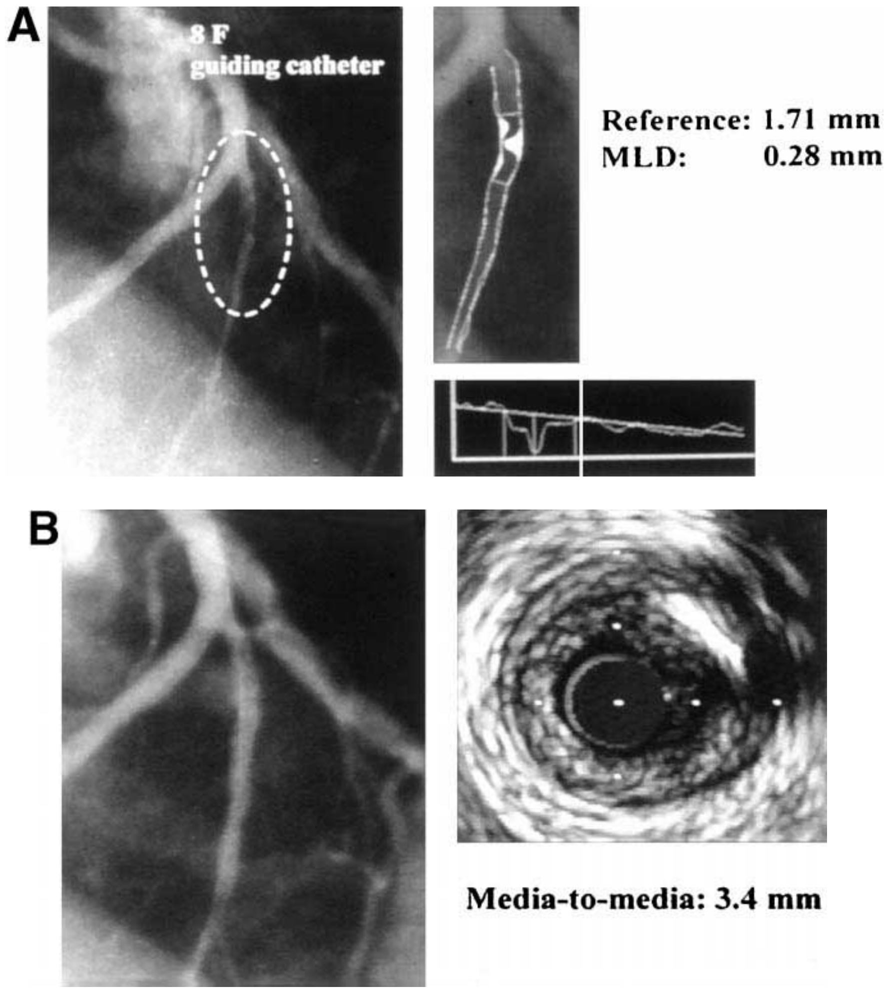


Fig 15. The tight stenosis shown (A) measured 0.3 mm by QCA with a reference diameter measurement of 1.7 mm. Based on this measurement, an aggressive balloon size was chosen at 2.5 mm diameter, which was expanded to 16 atm. The angiogram following the initial angioplasty (left) is shown (B) along with the IVUS image (right). The angiogram shows a successful angioplasty result, and although there is some haziness around the lumen, the boundary shows complete effacement of the stenosis. The corresponding ultrasound image reveals that the lumen size has enlarged to 1.5 mm in diameter; however, the vessel diameter from media to media is much larger than expected at 3.4 mm. The large amount of plaque distributed uniformly throughout the length of the vessel forces QCA to underestimate the true size of this large diagonal branch. Based on the IVUS assessment of vessel diameter, a 3.5-mm balloon was chosen and expanded to 10 atm.

dian Coronary Atherectomy Trial (CCAT), were so high.[60,93,103,116-127] In vitro studies have shown that IVUS is very accurate in identifying the amount of material that is removed by DCA compared with histology.[128] When the angiographic results of DCA are compared with IVUS, an important lesson of this technology is revealed[129]: angiography tends to overestimate the debulking or atherectomy component of DCA. Examples that emphasize this observation are shown in Figs 16, 17,[130] and Fig 18.

It should be noted that when DCA is performed with IVUS guidance, the procedure is performed in an iterative fashion.[131] That is, after an adequate number of cuts with the DCA device, IVUS imaging is performed. The DCA device is then reinserted and directed to the quadrants that reveal residual plaque by IVUS. In addition, if IVUS reveals that a section of plaque has been removed from the artery wall and only the media and adventitia remain, then the DCA device is directed away from those quadrants.[132] Figure 19

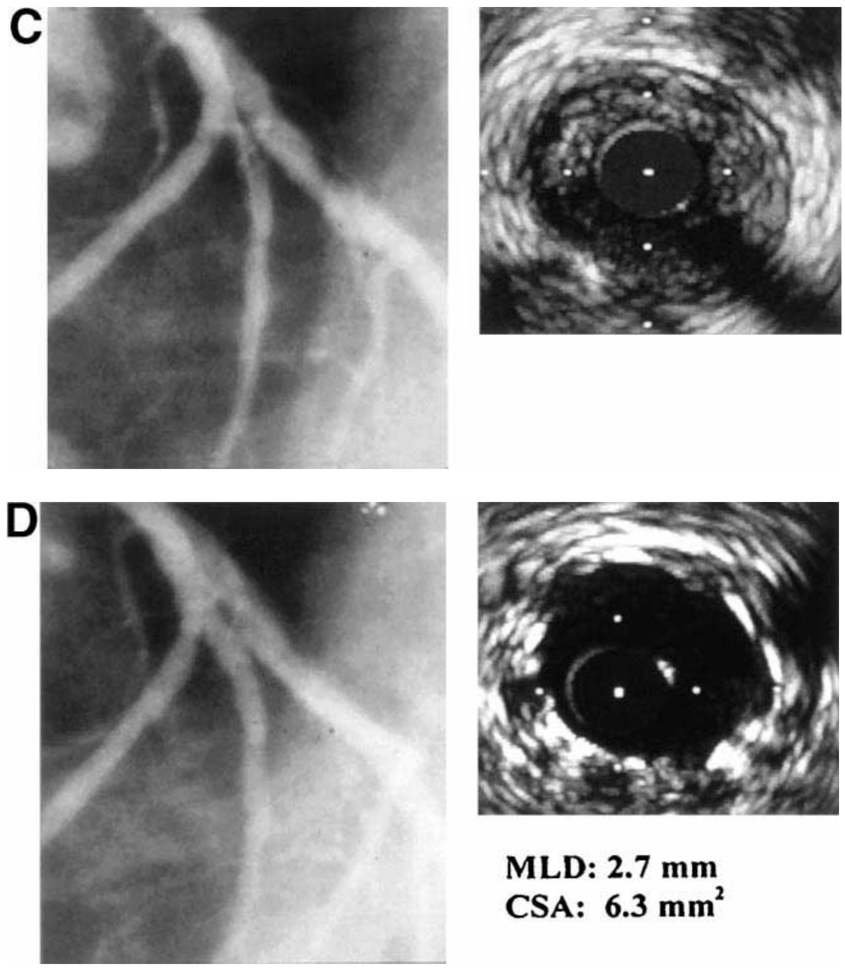


Fig 15. (Cont'd) Despite the use of a much larger balloon, there is significant recoil and the residual lumen is not much better than that obtained with the 2.5-mm balloon (C). The angiogram (left) appears to have a wider diameter because there are dissections behind the plaque into which contrast passes, thus making it seem that the diameter of the lumen is larger than it really is. Based on these IVUS observations (right) that this artery was not a "small vessel," a decision was made to proceed with coronary artery stenting. A Palmaz 104 stent was placed in the diagonal branch and expanded with the 3.5-mm diameter balloon at 14 atm (D). Not only does the angiogram (left) show a more satisfactory result, but the IVUS cross section (right) is now 2.7 × 3.0 mm and shows a circumferential patent lumen without dissections.

shows that IVUS can identify if the media or adventitia has been removed by DCA and this may not be evident by angiography. This method of IVUS-guided DCA therefore improves the safety of the procedure and maximizes the amount of material that is removed. In the CAVEAT Trial, IVUS imaging was not used, and it is likely that a greater amount of plaque was left behind than was appreciated by angiography.[60] Because the stretching effect was probably significant in that study, it may help explain why the restenosis rate was similar to the group treated with angioplasty alone (50% *v* 57%). With this new awareness, other DCA trials were designed to be more aggressive. In the Optimal Atherectomy Restenosis Study (OARS) Trial, directional atherectomy was optimized and the restenosis rate was reduced significantly to 29%.[133] In the Adjunctive Balloon Angioplasty following Coronary Atherectomy Study (ABACAS) Trial, IVUS imaging was used to guide the atherectomy so that a residual plaque cross-sectional area (CSA) of 47% was left.[134] This resulted in a restenosis rate of 21%.

These observations have led to a renewed interest in debulking lesions under IVUS guidance before stenting.

Stents and IVUS

The Influence of Stent Deployment on Subacute Thrombosis

When stents were initially used, the primary concern was the high rate of subacute stent thrombosis that inhibited the widespread use of coronary stents.[135-149] Initial observations of coronary stents with IVUS led us to an alternative explanation of why sub–acute stent thrombosis occurred. The first observation by IVUS was that

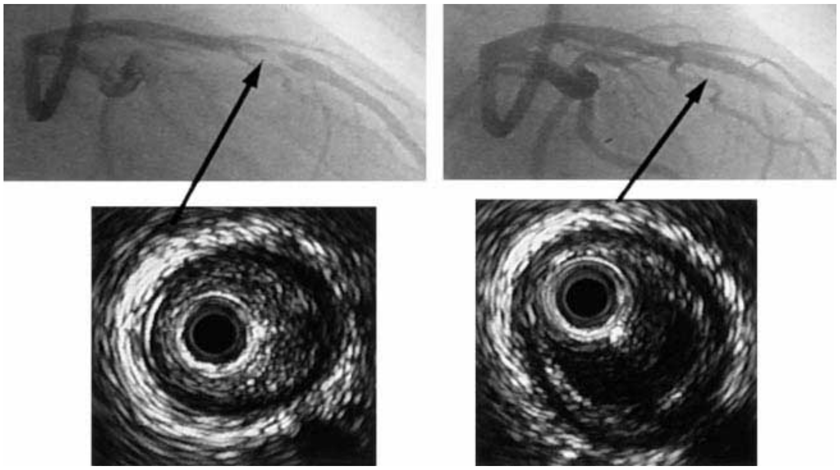


Fig 16. A severe stenosis in the mid LAD was successfully treated with DCA. The ultrasound image shows that before DCA (left) the catheter has been wedged into the plaque. Following atherectomy (right), the lumen is significantly enlarged, but measuring the diameter of the vessel from media to media, the vessel has also been significantly enlarged by stretching, similar to the effect of balloon dilatation.

there often was incomplete apposition of the metal struts against the arterial wall.[150] As shown in Fig 20, despite the use of a large balloon and a successful angiographic result, IVUS showed that the stent struts were not fully apposed to the arterial wall and were stranded in the middle of the lumen. By using a larger balloon, the stent struts were appropriately positioned against the arterial plaque. The second observation was that a number of stents were asymmetrically deployed, as shown in Fig 21. At the time this was thought to create turbulent flow and to be another initiating factor for subacute thrombosis. Based on these ultrasound observations, stents were redilated with either a larger balloon or at higher pressures to attempt to get a more symmetrical distribution of lumen shape.[151] The third observation provided by IVUS imaging was that many stents were inadequately expanded despite what appeared to be an appropriate angiographic result, as seen in Fig 22.

The Predictors and Outcomes of Stent Thrombosis (POST) registry[152] showed that 90% of patients with subacute thrombosis had IVUS-defined abnormalities, whereas only 25% of angiograms showed an abnormality that could explain why thrombosis occurred. These types of observations with IVUS led us to believe that the high incidence of subacute stent thrombosis was perhaps not as much due to any inherent thrombogenicity of the metal and the presence of a foreign body in the artery, as much as it was due to inadequate deployment with an insufficient lumen cross-sectional area resulting in diminished flow or turbulence that would promote thrombosis.

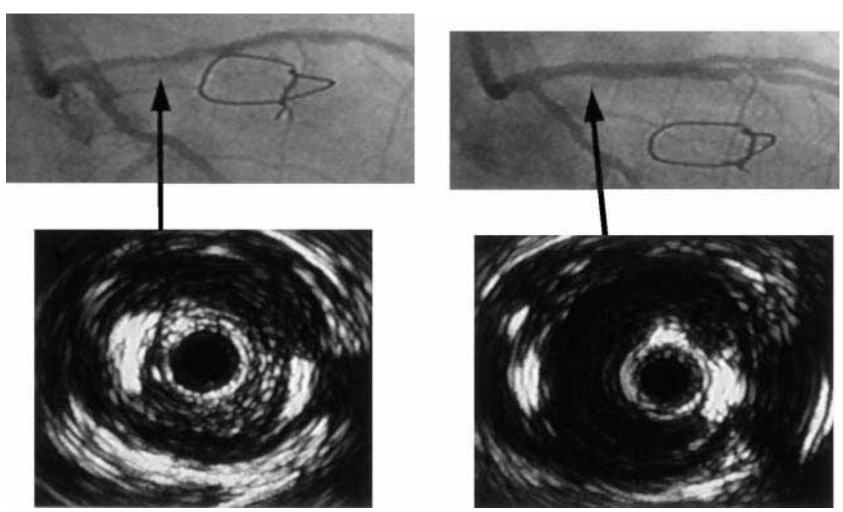


Fig 17. A successful DCA by angiography is shown. IVUS reveals that a significant amount of the plaque has been removed, but not the two calcified segments of plaque at the 9- and 3-o'clock positions.[130]

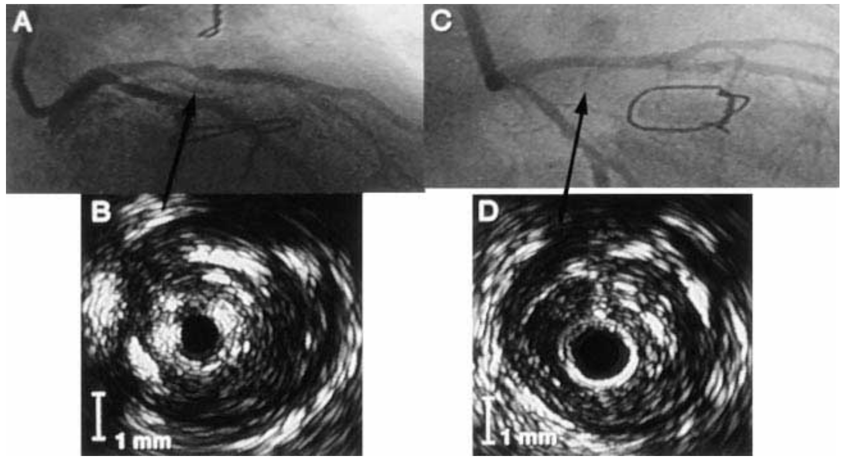


Fig 18. An example of a successful angiographic result with DCA is shown. In this case, the ultrasound study shows that only a very small amount of plaque has been removed despite multiple passes.

Coronary Artery Stenting with IVUS Guidance but Without Coumadin

When the Palmaz-Schatz and Gianturco-Roubin stents were first released, an attempt was made to diminish the catastrophic sequelae of subacute stent thrombosis by using an aggressive anticoagulation regimen.[61,143,153,154] This included heparinization following the procedure until an adequate elevation of the protime could be obtained with coumadin. This prolonged the hospital stay and produced major bleeding complications at the site of the arterial puncture.[155] Given the results of the ultrasound observations of the large lumen area that could be achieved with IVUS guidance, we withheld coumadin from the stented patients and slowly began to diminish the time of heparin treatment following the procedure. In addition, the antiplatelet regimen of aspirin was augmented with ticlopidine. The results of this study were published in 1995 and had a significant impact on the way that coronary artery stenting has since been performed.[156] By deploying stents with IVUS guidance, subacute thrombosis occurred in only 1.4% despite the absence of coumadin therapy or heparin following the procedure. Without the use of an aggressive anticoagulation regime, the vascular complication rate was significantly reduced to 0.6%. The hospital stay was decreased from an average of 5 days with coumadin therapy to 1 day. Moreover, the final minimum lumen diameter was markedly improved to 3.39 mm as compared with the results that were obtained without ultrasound guidance, such as the Stent Restenosis Study (STRESS) or Belgium Netherland Stent Investigators (BENESTENT) Trial, where the mean final Minimum Lumen Diameter (MLD) in the stent group was 2.45 mm and 2.48 mm, respectively.[61,62,157]

Using our approach, the overall angiographic restenosis rate at 6 months was 20%, and was 14% for single stents, which was significantly lower than 29% reported in the STRESS Trial.

The technique of larger balloons and higher pressure inflations to deploy coronary artery stents without subsequent anticoagulation was

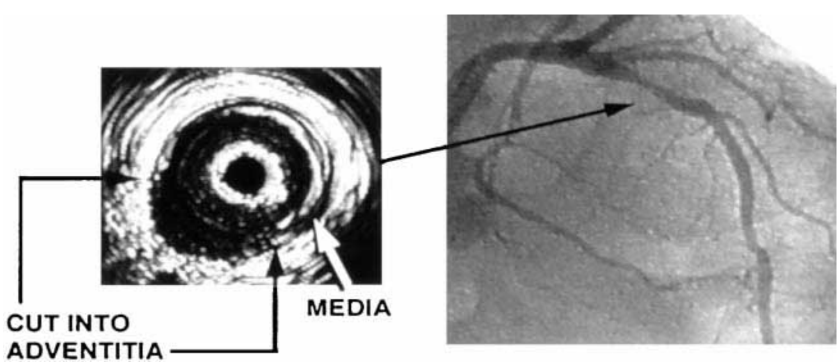


Fig 19. Removal of media and adventitia by directional atherectomy.

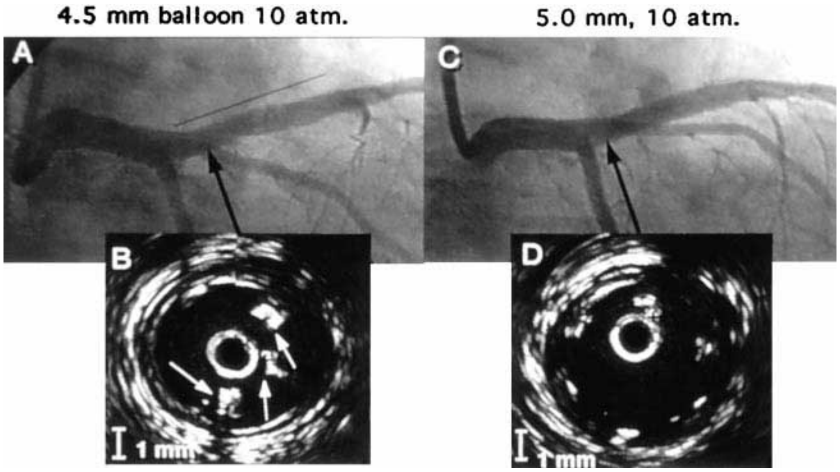


Fig 20. Incomplete stent apposition.

rapidly adopted by most interventional cardiologists. Subsequent papers showed a marked reduction in subacute stent thrombosis, vascular complications, and patient stay.[158-161] Several authors also reported excellent results using this balloon dilatation strategy without IVUS guidance to assess their results.[162-164] It now appears that IVUS imaging is not necessary to obtain a low incidence of subacute stent thrombosis.[165-167] There still are other potential advantages of using IVUS during stent deployment, the most significant of which is the influence of ultrasound guidance on restenosis, which is discussed next.

Can IVUS Improve Late Outcomes?

From a retrospective analysis of 2,343 stented lesions comparing IVUS and no-IVUS guidance,[168] the group with IVUS guidance had a larger final minimal luminal diameter and a smaller final percent diameter stenosis as well as a significantly lower restenosis rate (24% *v* 29%, $P = .03$). The recent Can Routine Ultrasound Improve Stent Expansion (CRUISE) Trial[169] also showed such an effect. The preliminary results of this trial showed a significant reduction in the need for lesion revascularization in the patients treated with IVUS guidance as compared with angiographic guidance (8.9% *v* 14.8%, $P = .004$). The preliminary results of the Angiography Versus IVUS-Directed Stent Placement (AVID) Trial[170] showed a 1-mm^2 increase in minimum stent area with IVUS guidance compared with angiographic guidance alone. These studies indicate that IVUS imaging can improve late outcomes by permitting a larger lumen to be obtained during stent implantation.

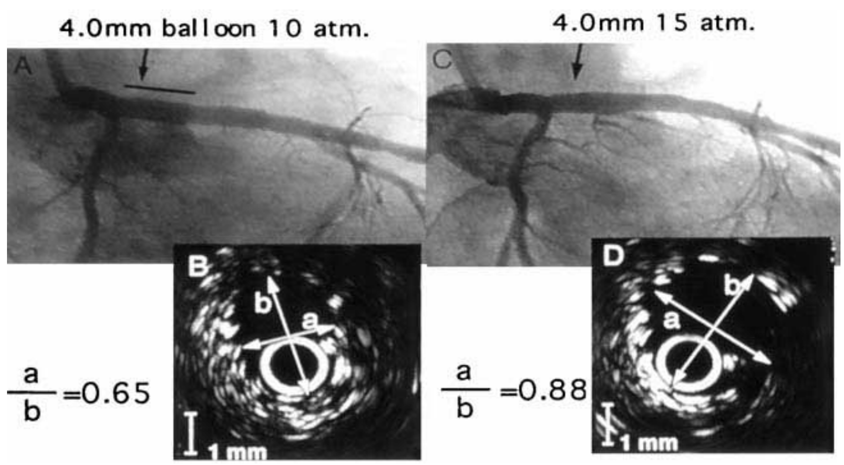


Fig 21. Asymmetric stent expansion.

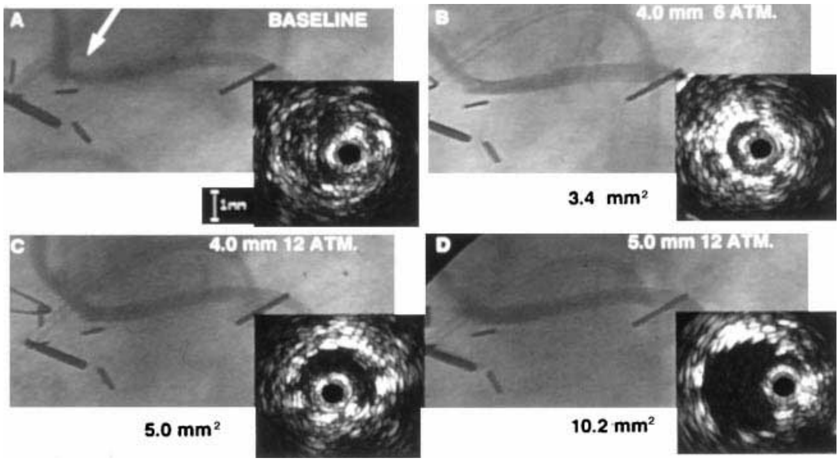


Fig 22. The baseline study reveals an ostial stenosis of a saphenous vein graft that is significant both by angiography as well as by ultrasound. Following inflation of the stent with a 4-mm balloon at 6 atm (which at the time was the recommended pressure) the angiographic result is significantly improved; however, the ultrasound cross-sectional lumen area was only 3.4 mm^2. By using higher pressures (12 atm) with the same balloon we were able to increase the dimensions to 5 mm^2. By using a larger balloon and higher pressure the final result was 10.2 mm^2. This use of IVUS-guided stent deployment increased the residual lumen cross sectional area 300% from 3.4 to 10.2 mm^2.

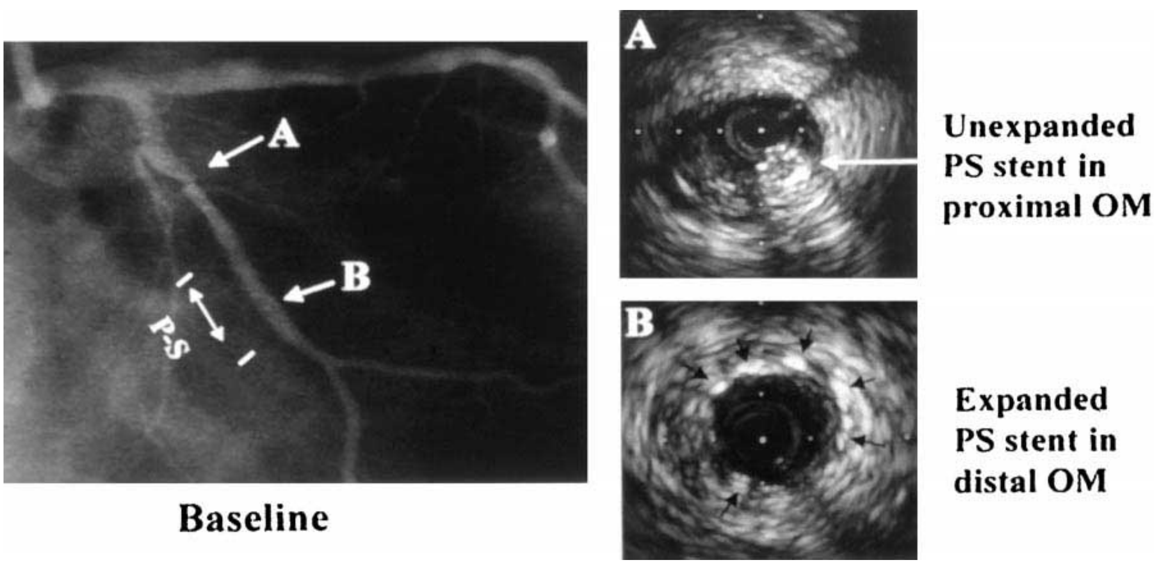


Fig 23. A Palmaz-Schatz stent was placed with great difficulty in the distal portion of the obtuse marginal artery. During the struggle to place a second Palmaz-Schatz stent in the proximal segment, the guiding catheter and guide wire suddenly flipped out of the artery. When the balloon was examined, the stent was not present. It was not known if the stent had been stripped off in the coronary artery or embolized in the aorta. After rewiring the artery, the ultrasound image (A) showed an unusual pattern where the echogenic stent struts were seen at the 4-o'clock position in a collapsed state to the side of the ultrasound catheter. For comparison, the IVUS image shown (B) reveals the circumferential struts of the adequately placed first Palmaz-Schatz stent in the distal section of the artery.

Undeployed Stents

One of the most dramatic examples of a case in which IVUS imaging has been essential for understanding complications that occur with coronary artery stenting is the discovery of a stent that has slipped off the delivery balloon and is sitting in the artery in an undeployed state. An example of this is provided in Figs 23 and 24.

Tissue Prolapse Through Stent Struts

IVUS can identify the presence of tissue prolapse through stent struts. Prolapse of atherosclerotic plaque into the lumen through stent struts may be a precipitating cause of subacute stent thrombosis or restenosis. This problem is rarely identified by angiography alone.

An example of this is shown in Fig 25.

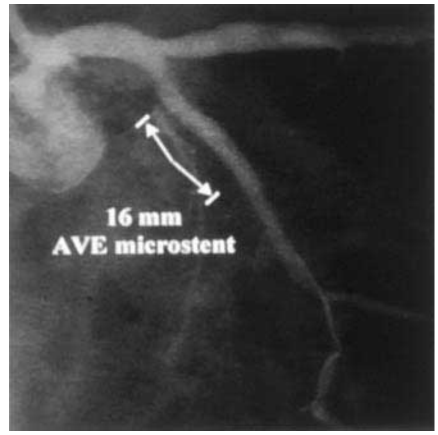


Fig 24. To treat the complication in Fig 23, a new 16-mm AVE stent was placed in the main lumen of the artery, external to the undeployed stent and was expanded with a 3.5-mm balloon at 10 atm. This compressed the Palmaz-Schatz stent to the side and provided adequate expansion.

Complex Anatomy During Stent Implantation

Coronary stenting reduces restenosis and clinical events in focal de novo lesions compared with balloon angioplasty.[61,62,157] However, when stents are implanted in complex lesion subsets, such as ostial lesions, lesions at bifurcations, or in the left main artery, bypass grafts, and small vessels, the process of stenting is technically challenging and restenosis remains a problem. IVUS provides important information in such situations and may facilitate the procedure or reduce the risk of complications.

Ostial Lesions

Aorto-ostial stenosis is a rare manifestation of multivessel coronary artery disease. The incidence varies between 0.13% and 2.7% of patients with angiographic coronary disease.[171-173] On the other hand, non–aorto-ostial stenosis is not an uncommon finding in patients with atherosclerosis.

Although the efficacy of surgical revascularization in patients with ostial stenosis is well recognized,[174] catheter-based coronary revascularization also has been applied successfully to this lesion subset. With improvements in operator experience, angioplasty technique, and evolution of equipment, the successful treatment of ostial lesions has evolved.

Aorto-ostial stenosis. The treatment of aorto-ostial lesions by conventional balloon angioplasty[175,176] and other devices, such as laser[177] or directional atherectomy,[178] has been limited by a low success rate and high incidence of restenosis. Coronary stenting is an attractive alternative for this subset of lesions because it provides the necessary scaffolding to support the artery.[179] However, preparing the lesion for a stent with balloon dilatation may be a significant challenge because these lesions tend to have a high incidence of calcification[180] or are very resistant because the balloon has to stretch against the longitudinal direction of the aortic wall. To address these issues, rotational atherectomy or directional atherectomy is frequently performed before stenting to debulk the plaque and prepare the entrance for the stent.

Stent implantation in the aorto-ostial location is technically challenging because of difficulties in seating the guiding catheter, obtaining adequate images to enhance stent placement, ensuring proper stent position to adequately cover the entire lesion, and preventing stent migration or embolization. Precise stent placement can be facilitated by using a stent that is clearly visible, such as the Palmaz biliary or MultiLink Duet stent. Moreover, the use of IVUS guidance is critical for optimum deployment and correct positioning during ostial lesion stenting. The ultrasound images are used to determine the media-to-media diameter of the vessel, which in

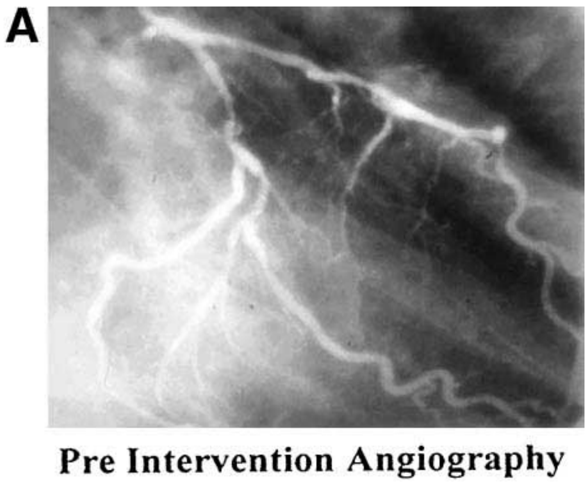
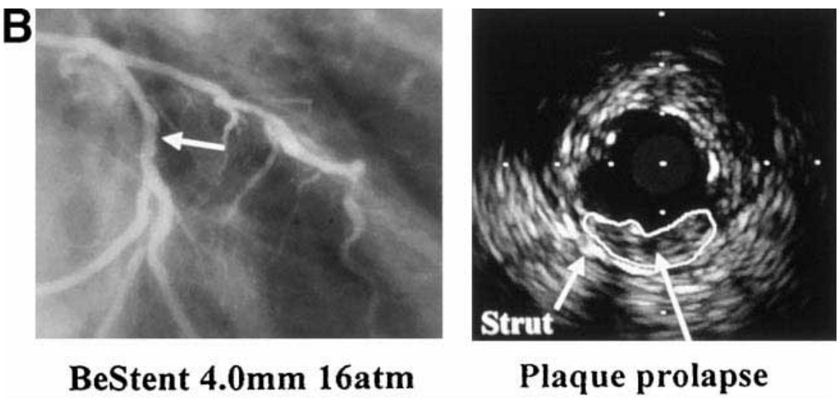


Fig 25. Diffuse disease in the LAD and circumflex systems (A). A BeStent stent was placed in the proximal circumflex artery and expanded with a 4.0-mm balloon at 16 atm. Despite a satisfactory angiographic result, the ultrasound image shown (B) shows that there was prolapse of tissue through the stent struts that diminished the effective lumen cross-sectional area. A PURA stent was placed in the proximal circumflex artery to treat the tissue prolapse through the BeStent.



turn allows us to choose the correct stent and balloon size. In addition, contrast can be injected under fluoroscopy during ultrasound imaging to correlate the exact ostium of the artery with the angiographic appearance in the view that we are going to place the stent. The ultrasound distinction between the aorta and the ostium of the artery is very obvious and is not obscured by the superimposed projection of the sinus of valsalva and the ostium of the artery as occurs with x-ray imaging. After the stent is placed and expanded to high pressure, the artery and stent are again interrogated with IVUS to confirm that the stent struts extend right up to the ostium or perhaps 1 mm beyond into the aorta. If the ostium appears compromised or the stent is not within 1 mm of the true ostium, then a second stent should be placed.

Another concern when stenting ostial lesions is the higher restenosis rate. The best approach for decreasing restenosis in ostial lesions should be to maximize the lumen cross-sectional area. This can be obtained by: (1) debulking the lesion with rotational atherectomy or directional atherectomy, (2) using a stent that has very high radial strength such as the Palmaz biliary stent, and (3) expanding the stent with an optimally sized balloon as determined by IVUS measurements of the media-to-media diameter.

An example of treating an aorto-ostial lesion is presented in Figs 26 and 27.

Non–aorto-ostial stenosis. Although stenoses of the initial portion of the LAD or circumflex arteries are referred to as ostial lesions, these differ somewhat from the true aorto-ostial lesions described above. The obvious difference is that the takeoff of these vessels is not from the aorta itself so that the ostial LAD or circumflex lesion usually does not have the same resistance as a true aorto-ostial lesion. The other major difference between these two sets of lesions is that the LAD or circumflex ostial lesion frequently involves the bifurcation either because the disease extends into the bifurcation, although it may not be apparent by angiography, or placement of the

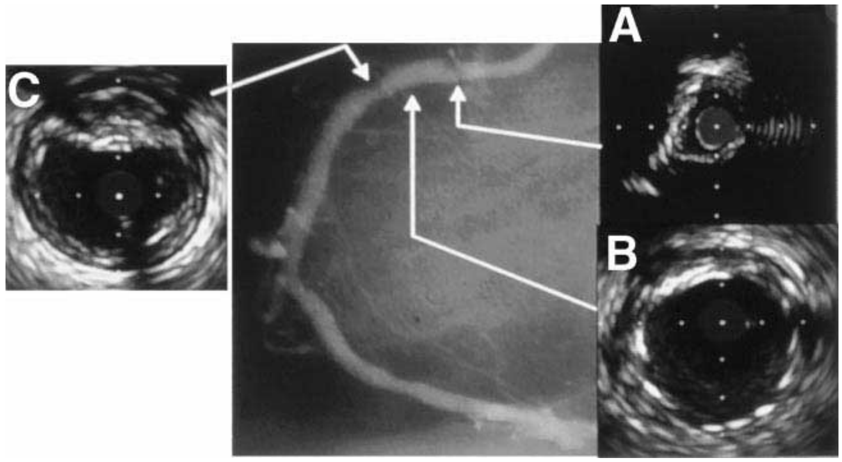


Fig 26. This case shows a right coronary artery in which a stent was deployed for a proximal stenosis. After placement of a 15-mm long ACS MultiLink stent expanded to 14 atm with a 4.0-mm balloon, there is an irregular linear density at the interface of the guiding catheter and coronary artery. The linear density is not very long, which makes it difficult to assess. The IVUS image (A) at the ostium shows that the lumen is oblong in shape with intense superficial calcification. The lumen at the aorto-ostial inlet measures only 1.5 × 2.0 mm. The proximal RCA portion covered by the stent was adequately expanded with a lumen of 4.0 × 3.5 mm by IVUS (B). Distal to the stent, there is some lumen narrowing, but the eccentric lumen is adequate at 3.5 × 2.3 mm (D). Five millimeters distal to the stent, the artery is quite large and measures 5 × 4 mm in diameter (media to media).

stent too proximal may entrap the other vessel. In addition, retrograde dissection may cause complications at the bifurcation and involve the branch vessel. The similarities in treating the ostial LAD or circumflex lesions compared with aorto-ostial lesions are that precise placement of the stent may be difficult, and that both sets of lesions respond better to debulking with directional atherectomy, or rotational atherectomy if the arteries are calcified. Figures 28, 29, and 30 provide dramatic examples of how IVUS may be critical in the treatment of ostial lesions.

Bifurcations

The treatment of stenoses at a bifurcation remains one of the most challenging lesion subsets in coronary angioplasty. Bifurcation lesions carry a risk of side branch occlusion because of plaque redistribution or so-called "plaque shift" across the carina of the bifurcation. The risk is increased if there is an eccentric lesion at the bifurcation site and a stenosis in the ostium of the side branch.[181,182] To diminish this plaque shifting, the "kissing" balloon technique was developed.[183]

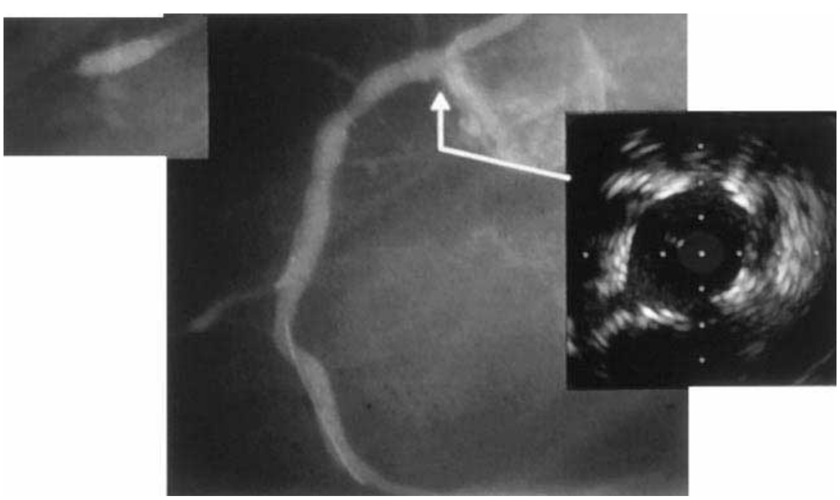


Fig 27. Based on this ultrasound evaluation, a Palmaz 104 biliary stent was placed on a 4.5-mm Chubby balloon and deployed at 14 atm at the ostium of the right coronary artery. The final angiogram shows an expanded ostium, and the ultrasound study shows that the lumen at the ostium is 3.5 × 3.0 mm.

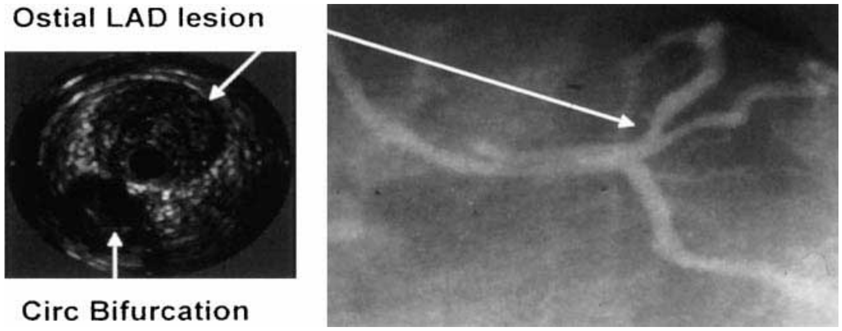


Fig 28. The angiogram at baseline revealed an eccentric stenosis at the ostium of the LAD that was not dramatic by angiography. However, the IVUS exam showed that there was extensive eccentric plaque that surrounded the ultrasound catheter and extended up to the bifurcation with the circumflex artery. In addition, the takeoff of the LAD was tortuous, which could make placement of a stent more difficult. A Palmaz-Schatz stent was hand crimped onto a balloon and was placed in the ostium of the LAD under fluoroscopic guidance.

However, the results with balloon dilatation of bifurcation lesions still had a high incidence of complications, suboptimal results, and restenosis.[181,184-186] Treatment of bifurcations with directional atherectomy (without stenting) has been shown to improve the immediate procedural outcome compared with balloon dilatation alone, but the incidence of restenosis remains high.[187] The use of coronary stents has improved the treatment of bifurcation lesions, but it is technically challenging and there is still a high incidence of compromising the branch vessel.[188-190] Stent implantation on both the main vessel and the side branch, which is called "kissing stents," is a useful technique for maintaining maximum expansion of both vessels. The use of two stents minimizes lumen loss of one side during expansion of the other branch.[191] The four main techniques used for bifurcation stenting (the coil stent, the "T" stent, the "Y" stent, and the "V" stent technique) have been described step by step with their advantages and disadvantages.[192]

Whatever technique is selected, IVUS guidance is of critical importance for optimizing the result. Bifurcation lesions are very difficult to examine completely despite multiple angiographic projections because of vessel overlap. IVUS imaging can facilitate placement of the stents and confirm

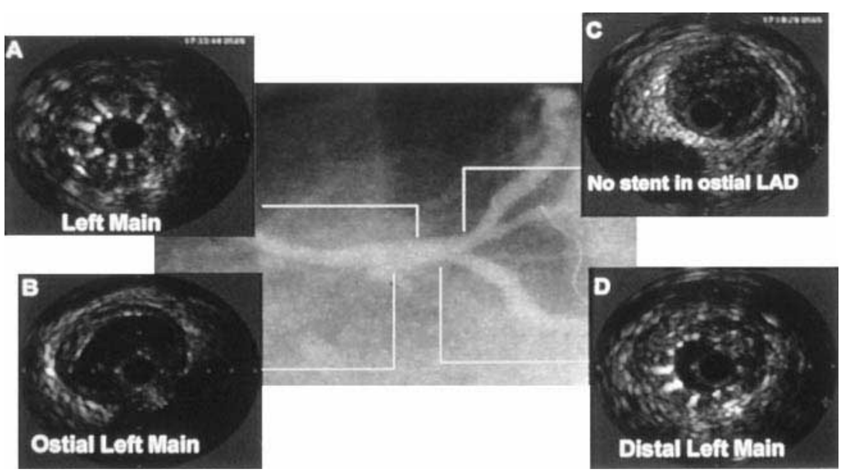


Fig 29. An acceptable angiographic result was obtained. IVUS was then performed to confirm that the stent had been placed precisely at the ostium without obstructing the circumflex artery. The ultrasound images provided a surprise. The reflections from the metallic stent struts were seen in the mid (A) and distal left main artery (D) and no stent struts were seen at the ostium of the LAD (C). In addition, the stent struts were only mildly expanded in the distal left main and were not expanded at all in the mid left main. This indicates that the stent had slipped off of the balloon and migrated to the more proximal left main artery.

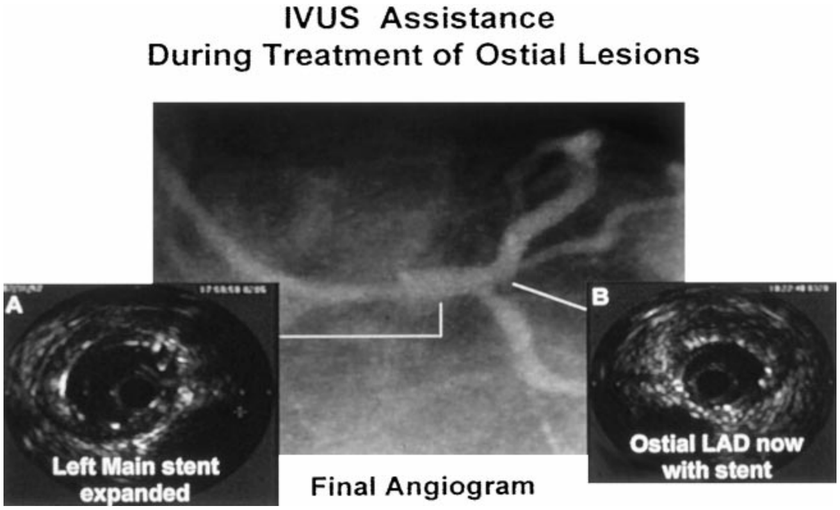


Fig 30. To correct the problem in fig 29, a 4.0-mm balloon was positioned across the stent and was expanded in the left main coronary artery to secure the migrated stent. In addition, a second Palmaz-Schatz stent was cut in half, and this half stent was placed into the ostium of the LAD and expanded with a 3.0-mm balloon shown as documented by IVUS.

optimal lesion coverage, stent expansion, and strut apposition.[192] In addition, if feasible, bifurcation lesions should be pretreated with rotational atherectomy, or directional atherectomy, to diminish plaque shifting. The choice of device is aided by the use of preintervention IVUS imaging according to the composition and distribution of plaque and the size of the vessel. Compression of the adjacent branch is enhanced after stenting because of the absence of mural support at the carina. In addition, the larger balloon size and high pressure applied to achieve large luminal gain and optimal stent expansion may compromise the ostium of side branches in bifurcation lesions.[192] On occasion, a three-dimensional reconstruction of the IVUS images obtained on pullback may be helpful for understanding the anatomy immediately surrounding a bifurcation. An example of this is provided in Fig 31.

Left Main Artery Stenting

In contrast to "protected" left main (LM) stenosis, that is, at least one patent coronary artery bypass graft supplying the left coronary artery system, "unprotected" LM stenosis has been considered a contraindication for percutaneous catheter-based revascularization. During balloon angioplasty there may be severe hemodynamic compromise, or disastrous consequences following abrupt vessel closure. Recent advances in stent implantation techniques[156] and poststent antithrombotic regimens[193,194] have caused some centers to reconsider the role of percutaneous treatment of patients with unprotected LM stenoses. Several groups have reported acceptable short- and long-term results in treating LM stenosis.[195-202] IVUS is an important adjunctive imaging modality for LM intervention. Despite its clinical significance, LM disease may not be accurately evaluated by coronary angiography alone.[203,204] In addition, stenting the LM lesion has several unique characteristics. By IVUS, the LM is frequently 5 mm in diameter (media to media) despite the narrowed appearance by angiography. Compared with the rest of the artery, there is a much larger amount of plaque per cross-sectional area. Because the risk of restenosis is critical when stenting the LM, debulking the lesion before stenting is preferred, which not only facilitates deployment of the stent but should lower the restenosis rate by half. IVUS provides accurate sizing of the LM and visualizes the amount of plaque that may need to be removed. Operators must pay attention to the differences between placing a stent at the aorto-ostial junction, in the body of the LM, or if the lesion encompasses the bifurcation of the LAD and circumflex arteries. Even though an angiogram shows a stenosis isolated to the body of the LM, there may be involvement of the bifurcation that is not appreciated until IVUS is performed. The information that IVUS provides is important in planning the approach to this high-risk lesion subset. Figure 32 is an example in which IVUS enabled optimal stent implantation for a LM trunk stenosis.

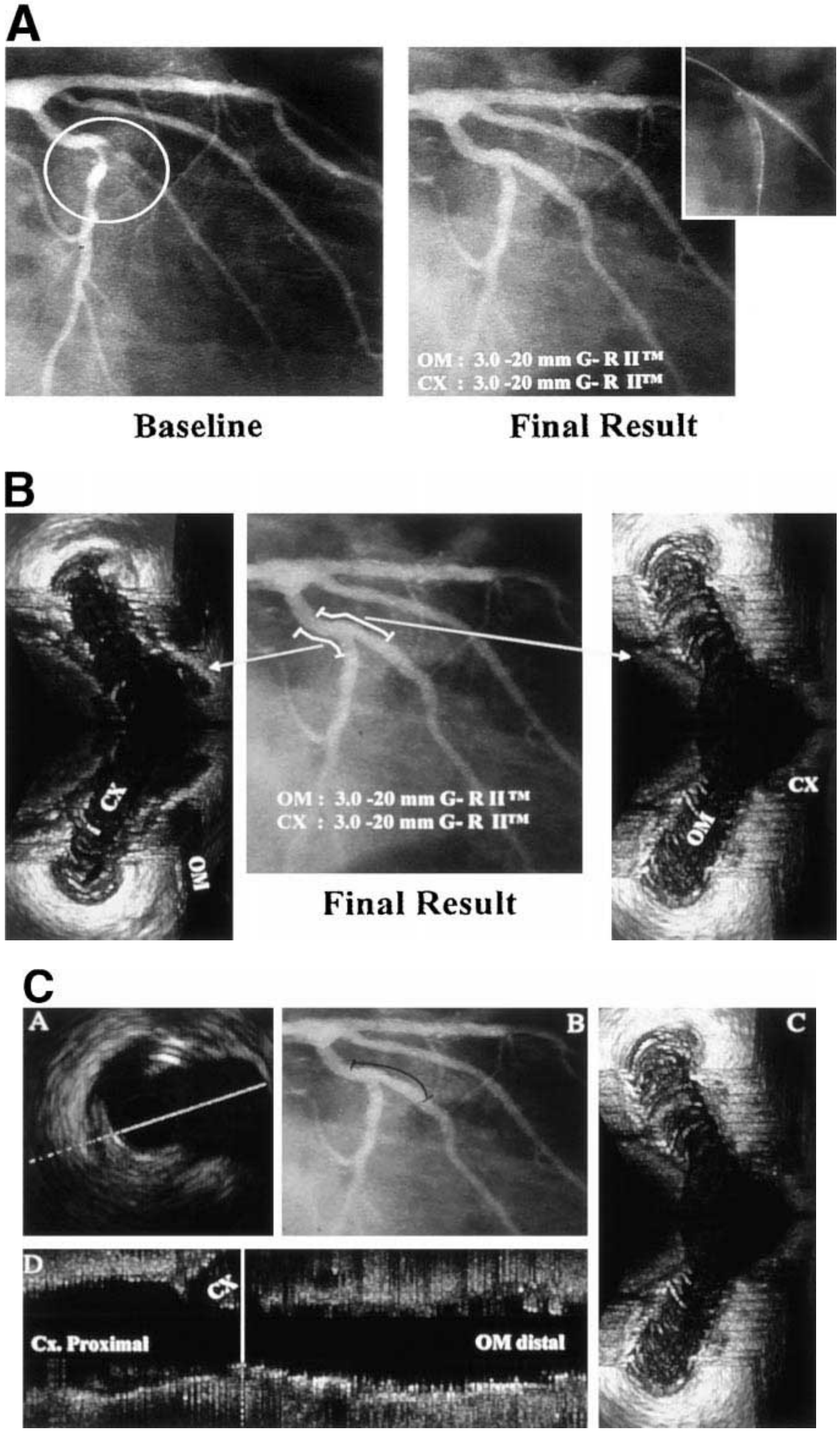


Fig 31. The bifurcation of this circumflex and obtuse marginal branch was treated with two Gianturco-Roubin II stents, each 20 mm long (A). IVUS imaging was obtained in each branch and three-dimensional reconstructions of the pullback from the circumflex artery and obtuse marginal artery are shown on the left and right hand panel (B), respectively. IVUS images can be presented in a variety of ways (C), to more clearly define the anatomy at a bifurcation.

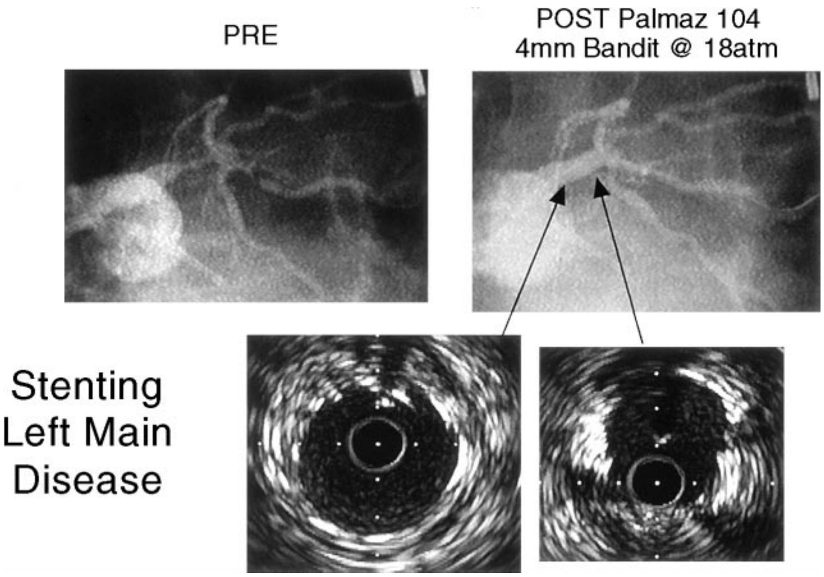


Fig 32. The left main artery is severely narrowed in the mid to distal segment, which then enters into a confluence from which 4 vessels emanate like spokes in a wheel. Because each of these vessels was comparatively small and had a sharp angle relative to the left main, it was elected not to debulk the left main trunk. After placing an intraaortic balloon pump, the left main was predilated with a 4.0-mm balloon. A Palmaz 104 stent was deployed in the left main at 18 atm. Despite a satisfactory angiographic result, the IVUS images show that the distal section was asymmetric and underexpanded. Repeat dilatation increased the lumen diameter to 3.5 × 3.8 mm.

Bypass Grafts

The treatment of patients with obstructive disease in coronary artery bypass grafts poses a challenge of increasing magnitude as the population of patients who have undergone bypass surgery continues to grow.

Saphenous vein graft. Within a decade after surgery, half of all saphenous vein bypass grafts have severe atherosclerotic disease.[205-209] Management of graft disease is problematic, because repeat surgery entails substantial risk, and the results of conventional angioplasty have been disappointing.[176,210-216] However, recent studies have suggested more favorable results in diseased vein grafts.[217-221] As compared with repeat coronary artery bypass grafts, it was reported that catheter-based revascularization procedures have similar efficacy for the patient with vein graft disease in the new device era and that the choice of therapy should consider patient preference as well as clinical and angiographic suitability.[222]

Although some authors indicate that revascularization strategies in saphenous vein grafts are less often influenced by IVUS than in native arteries,[223] other authors have shown that IVUS provides useful information when applied to this lesion subset.[224] Vein grafts may have variations in their external width that lead to an underestimation, compared with angiography, of the diffuseness of the disease.[225] IVUS enables accurate device sizing by measuring the true diameter of the graft at the lesion site. This is particularly useful for appropriate sizing of stents in these large conduits. One report showed that with angiographic guidance, only 9% of stents were optimally expanded to match the reference cross-sectional area.[226] IVUS examination may identify lesions at high risk of rapid progression or may induce referral of patients to surgery who have diffuse vein degeneration with friable plaque (low echoreflectivity with irregular borders).[223] The distinction between degenerated and fibrotic vein grafts is important. Even if distinct thrombi are not seen, degenerated lesions may have embolic potential. Lytic therapy and atheroablative techniques (transcutaneous extraction catheter [TEC], DCA, or laser atherectomy) are important adjuncts in the transcatheter approach to degenerated lesions. If degenerated lesions have intraluminal thrombus, new thrombectomy catheters such as the Angiojet (Possis, Minneapolis, MN)[227,228] or Hydrolyser (Cordis Europa NV, Roden, The Netherlands)[229] might help remove nonorganized thrombus.

Of the various stents currently available, the Wallstent has been found to be a useful device for treating saphenous vein graft stenosis.[230] Because the disease process in vein grafts tends to be diffuse and the conduits are long, the self-expanding Wallstent is ideal for this application. In addition, the Wallstent comes in variable lengths and diameters. Covered stents such as an autologous saphenous vein-covered stent[231] or polytetrafluoroethylene (PTFE)-covered stent[232] may have additional advantages in treating degenerated lesions. Covered stents may prevent prolapse of friable tissue through the stent struts and thereby decrease embolization. Preintervention IVUS examination can assist in making these critical decisions.

Small Vessels

One of the important anatomic factors of restenosis after balloon angioplasty, DCA, or stenting is vessel size because the restenosis rate is inversely related to the reference vessel diameter.[62,233,234]

The advantage of stenting instead of using balloon angioplasty in small vessels is still controversial. A retrospective study suggested that balloon angioplasty was equivalent to stents in patients with small vessels.[235] On the other hand, two studies indicated that stenting was more efficacious than balloon angioplasty for small vessels between 2.6 and 3.0 mm in diameter.[236,237] Although the immediate success rate and complications in stenting small vessels may be equivalent to those found in larger vessels, the 6-month restenosis rate is higher in smaller vessels (19.9% *v* 32.6%).[238,239] The fact that intimal hyperplasia at follow-up was independent of stent size might explain the high restenosis rate in small vessels after stenting.[240-242]

IVUS may potentially improve the outcome of stenting small vessels. Akiyama[238] analyzed patients who received coronary stents in a small (less than 3.0 mm) artery with or without IVUS guidance. The restenosis rate was significantly lower when IVUS guidance was used (29% with IVUS guidance *v* 38% without, $P = .04$). The use of IVUS guidance was thought to facilitate decision making in terms of balloon sizing, especially in angiographically small vessels that might in fact be large vessels with diffuse atherosclerosis. It was hypothesized that a greater balloon-to-vessel ratio used in the small-vessel group might have led to greater wall injury and more reactive neointimal proliferation followed by a higher restenosis rate.[243] However, this was recently denied by several studies.[238,242] The discrepancy between angiography and IVUS of accurately determining reference diameter is shown in Fig 33.

Debulking Before Stenting

Restenosis remains a problem when stents are implanted in complex lesion subsets, such as long lesions,[244,245] ostial lesions,[179,246,247] chronic total occlusions,[248-252] and bifurcation lesions.[253] Restenosis after implantation of slotted tube stents is

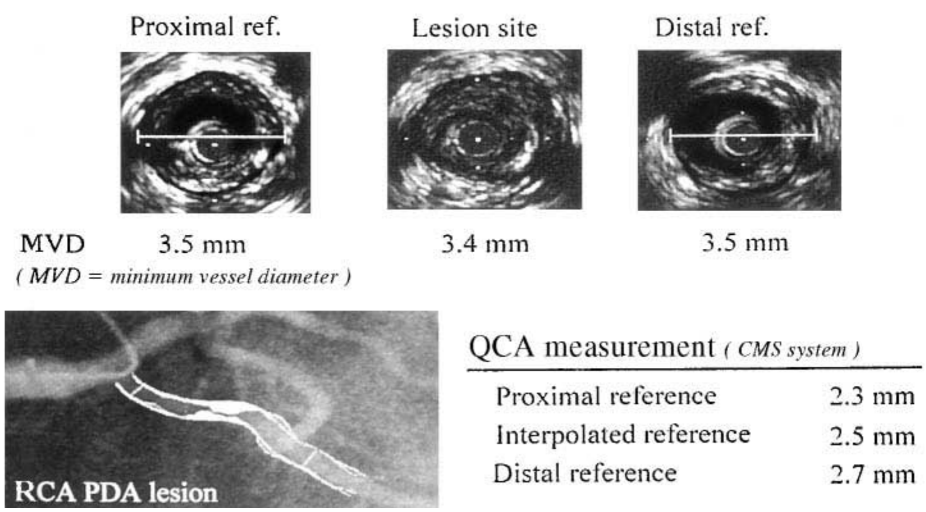


Fig 33. The angiogram shows the results of QCA measurement of a posterior descending artery with a severe stenosis. The proximal reference was measured as 2.3 mm and the distal reference was 2.7 mm, giving an average reference of 2.5 mm. However, by IVUS, the media-to-media diameter was 3.5 mm, both proximally and distally. Based on this observation, the decision was made to debulk the lesion with rotational atherectomy. A larger burr (2.0 mm) and a larger balloon (3.25 mm) were used than would have been chosen if the decision were based on angiographic guidance. In addition, a stent was placed with greater expansion than would be deemed appropriate based on the angiographic measurement alone.

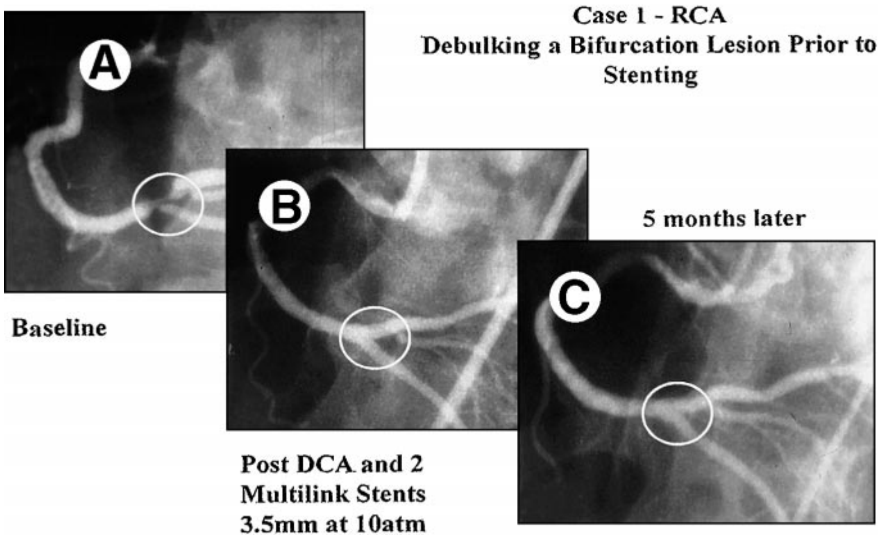


Fig 34. The distal RCA lesion is located at the bifurcation of the PDA and posterolateral (PL) branch (A). The interpolated QCA reference diameter was 2.87 mm (toward the PDA) and 2.88 mm (toward the PL). Two high-support guide wires were used to cannulate both the posterior descending artery (PDA) and PL branches. Directional atherectomy was then performed using a 7 French GTO cutter toward the PDA and PL. Two MultiLink stents were implanted at the bifurcation, and both stents were expanded simultaneously using the kissing balloon technique (balloon diameter 3.5 mm inflated at 10 atm in both branches). The final result is shown (B). There was no significant restenosis at the 5-month follow-up angiogram as shown (C).

mainly due to neointimal proliferation.[254] Observational IVUS data indicate that a larger plaque burden, either before[241,255] or after stenting,[256] leads to a higher rate of late lumen loss after stenting. In addition, angiographic data[257] indicate that after stent implantation, restenosis tends to occur at the original lesion site (where the plaque burden is largest). Based on these observations, it was proposed that removal of atherosclerotic plaque before stenting would lead to a reduction in neointimal hyperplasia, thereby reducing the incidence of restenosis. Recently, several studies have supported this hypothesis. Two different debulking devices were applied before stenting according to the lesion characteristics: directional atherectomy for noncalcified large vessels[258-261] and rotational atherectomy for calcified and/or small vessels.[262-264]

DCA Plus Stenting

Currently, DCA is the most effective device to remove noncalcified plaque,[133] thus transforming the atherosclerotic arterial wall to a thinner structure that is more compliant to dilatation.[265] Even with optimal atherectomy, compared with PTCA, restenosis remains about 30% with no difference in the need for repeat revascularization at 1-year

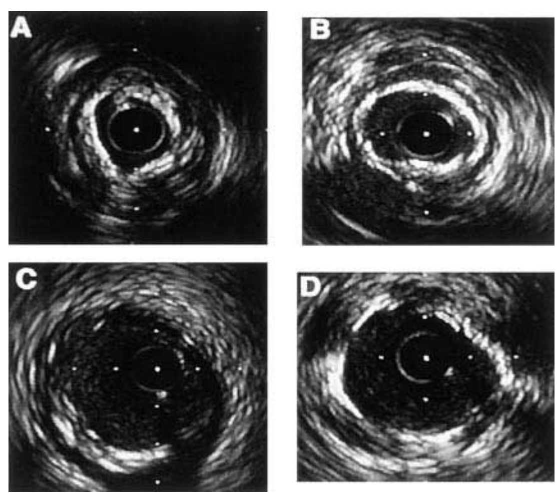


Fig 35. Using IVUS imaging before the intervention, tissue characterization reveals significant calcification at the lumen plaque interface (A). Therefore, progressive rotational atherectomy burrs were used from 1.5 mm to 2.5 mm (B). Although the lumen was now slightly larger than 2 mm in diameter, the vessel size measured at the media was greater than 4 mm. Based on this IVUS observation, directional atherectomy was performed with a 7 French cutter, which removed a significant amount of plaque (C). At this cross section, the lumen measured 7.3 mm^2 and the area bounded by the media measured 15 mm^2, giving a lumen-to-vessel ratio of 49%. After removing the bulk of this plaque, a Crown stent was deployed on a 4-mm balloon at 16 atm. The final dimensions of the lumen were 3.0 × 3.5 mm or 8.1 mm^2 (D).

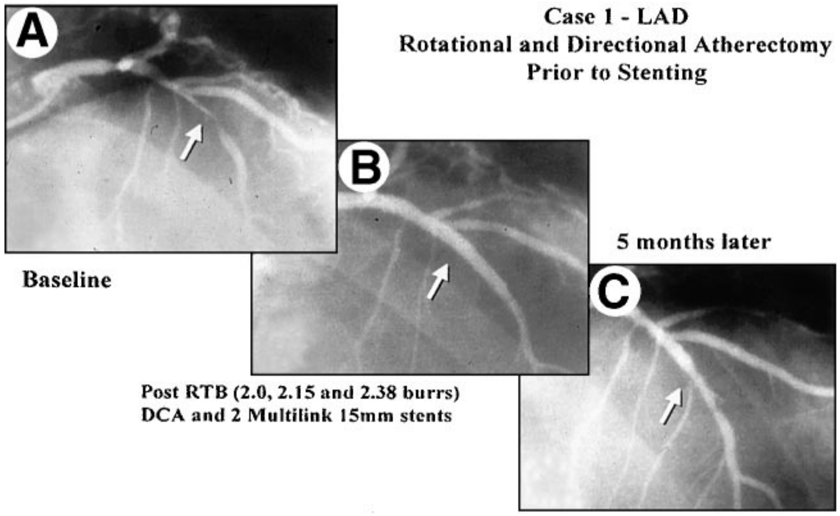


Fig 36. The lesion in the proximal LAD was calcified on angiography and measured 30 mm in length with a reference diameter of 2.98 mm (A). Preintervention IVUS was attempted; however, the IVUS catheter could not cross the lesion. Rotational atherectomy was then performed using a stepped burr approach (2.0, 2.25, and 2.38 mm). IVUS imaging postrotablation showed a large residual plaque burden. Therefore, DCA was then performed using a 7 French GTO cutter. Two MultiLink stents were implanted and expanded using a 3.5-mm balloon inflated at 11 atm (B). Follow-up angiography was performed at 5 months. There was no evidence for restenosis (C).

follow-up.[266] Late lumen loss after DCA has been shown by IVUS to be the result primarily of late arterial constriction in addition to neointimal hyperplasia.[112,113]

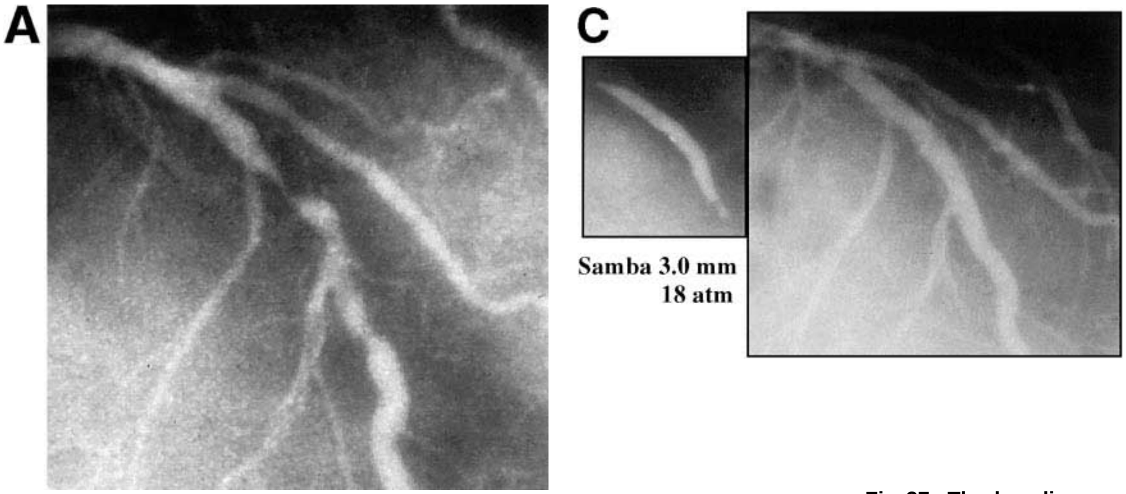
Therefore, the failure of stand-alone stenting or stand-alone DCA to reduce restenosis in complex lesion subsets suggested the need to explore the synergistic role of combining both techniques to reduce restenosis. The hypothesis is that plaque removal with DCA before stenting may lower the intensity of late neointimal hyperplasia, reducing the incidence of in-stent restenosis. This hypothesis has been supported by several recent studies that report a better early and late outcome for the DCA-plus-stenting group than the stenting-alone group.[258-261]

This DCA-plus-stenting approach may be optimized by using IVUS to guide the atherectomy cuts, similar to the procedure outlined in the OARS Trial.[133] The data of the Stenting after Optimal Lesion Debulking (SOLD) Registry[258] showed that the lower the residual plaque after DCA, the lower the loss index will be, with an amazing restenosis rate below 5% in the group that achieves an optimal removal of plaque burden using ultrasound guidance.

Figure 34 shows the use of directional atherectomy at a bifurcation to optimize the placement of two stents using IVUS guidance.

Rotational Atherectomy Plus Stenting

Rotational atherectomy is the preferred strategy to ablate calcified plaque.[267] Despite the high procedural success rate, significant restenosis rates of 37% to 57% were observed after stand-alone rotational atherectomy.[268,269] A recent histopathologic study showed that the presence of calcium is a powerful predictor of the amount of plaque burden in atherosclerotic arteries.[270] In addition, in vivo IVUS ultrasound studies have shown that coronary calcium is an important determinant of decreased wall compliance,[271] and it leads to a high incidence of dissections when these lesions are dilated[27] and a high rate of suboptimal expansion when stents are used.[272] It was hypothesized that pretreating the lesion with atheroablative techniques to reduce the calcified plaque burden would improve vessel wall compliance. This in turn would optimize stent expansion and consequently lower the restenosis rate. This hypothesis was supported by recent studies.[262-264] These authors showed that adjunctive rotational atherectomy before stenting (rotastenting) for calcified or undilatable lesions improved not only the procedural result but also the late outcome. It was also shown that lesion morphology evaluated by IVUS before stent placement identified lesions with a greater likelihood of



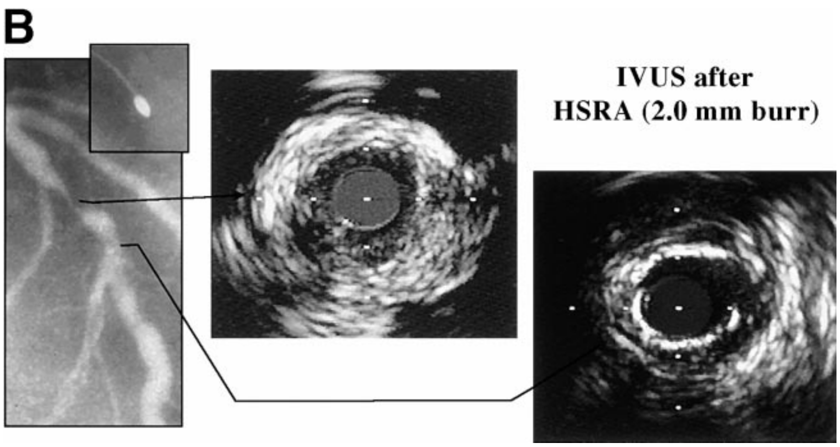


Fig 37. The baseline angiogram shows a diffusely involved mid section of the LAD (A). The lesion was 30 mm long and involved both the first and second septal perforating branches. This was initially treated with a 1.5-mm and then a 2.0-mm rotational atherectomy burr. The IVUS images, after rotational atherectomy, are shown (B). The lumen measured less than 2 mm in the proximal portion and exactly 2.0 mm in the calcified distal half. This was then dilated with a 3.0-mm balloon at 18 atm, with the final angiogram (C).

eccentric stent expansion and a smaller poststent MLD.[264] Therefore, preintervention IVUS can identify which lesions should be rotablated before stenting.

It remains unclear how aggressively rotational atherectomy should be performed before stenting. Using rotational atherectomy alone, a higher target lesion revascularization rate was reported (25%) when a burr/vessel ratio greater than 0.85 was used.[273] This effect was presumably due to the increased vessel trauma produced by the oversized burr. The use of a coronary stent might eliminate the chronic shrinkage triggered by rotablation with an oversized burr. Aggressive rotablation before stent placement would reduce the plaque burden and improve vessel compliance, and thus possibly reduce the late lumen loss associated with calcified lesions, similar to those reported for noncalcified lesions treated with DCA plus stenting.[258] IVUS provides more precise information than angiography about the amount and position of calcification, residual plaque burden, and vessel size of the target lesion. The use of IVUS in a repetitive process to image the artery before the intervention, after sequential atherectomies, and following stent insertion facilitates the procedure and improves the final lumen cross-sectional area within the stent zone.

A case example of the iterative use of IVUS to guide the atherectomy process is shown in Fig 35.

An example where IVUS guidance of rotational atherectomy plus directional atherectomy was used to optimize stent placement in the LAD is shown in Fig 36.

PTCA Provisional Stenting

Although intracoronary stenting represents the only currently available strategy shown to limit both clinical and angiographic restenosis,[61,62,274]

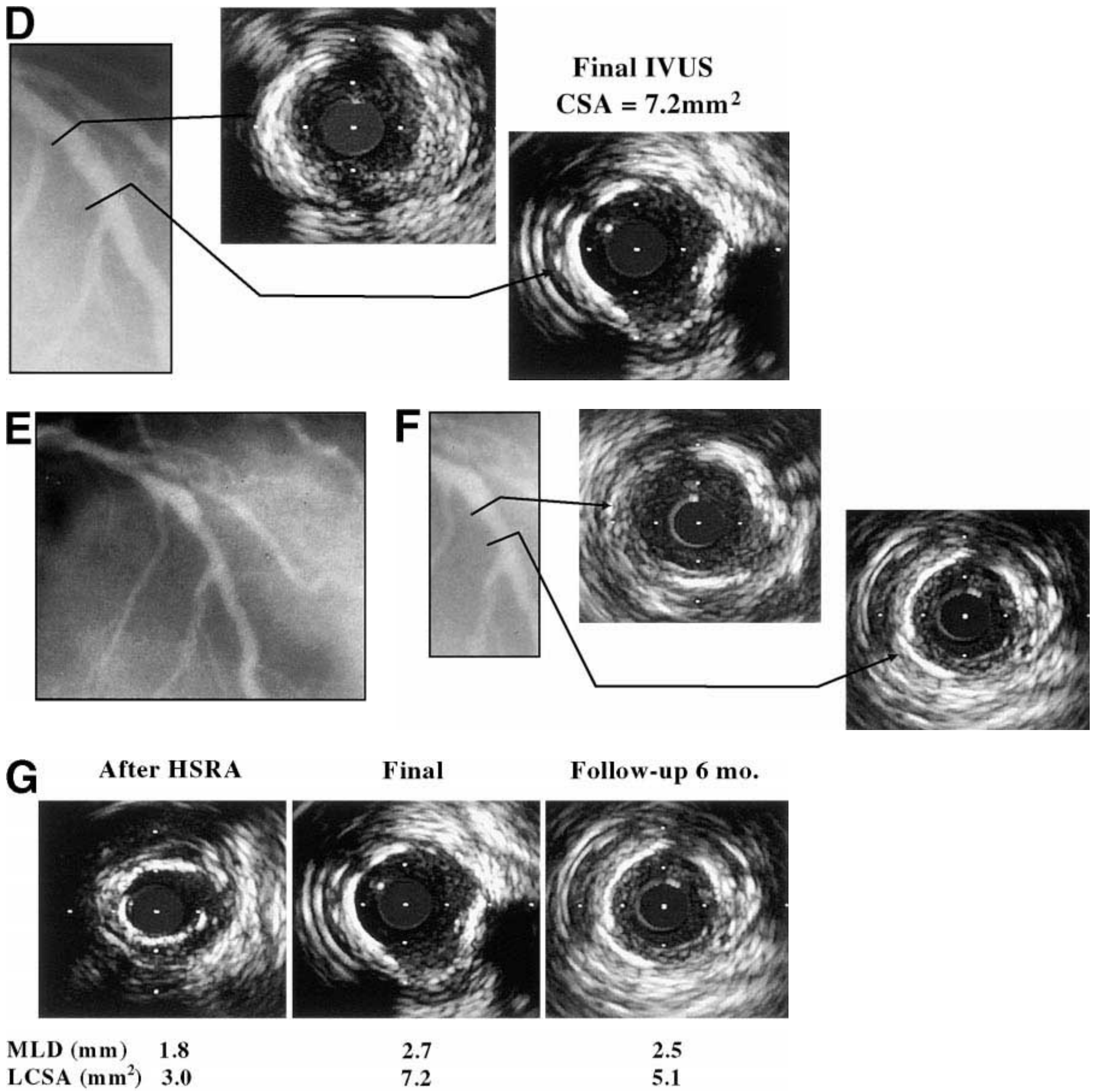


Fig 37. (Cont'd) Following rotational atherectomy and balloon dilatation, the final examination shows an adequate lumen cross-sectional area of 7.2 mm^2 (D). Based on these ultrasound measurements, a decision was made not to place a stent in this artery. The follow-up angiogram obtained 6 months after the procedure shows patency of the vessel with minimal restenosis (E). The angiographic results are confirmed by the follow-up IVUS study (F). These sequential changes in the IVUS images after initial rotational atherectomy, final balloon dilatation, and the follow-up are summarized (G).

it continues to be accompanied by several limitations. Stents are costly[155,275] and difficult to use with some complex lesion subsets such as bifurcation lesions,[188-190,192] lesions in small vessel,[235,238,239] and diffuse long lesions.[168,276] Most importantly, stents have engendered a new and difficult-to-treat entity of in-stent restenosis. In addition, there are many times when balloon dilatation alone provides an adequate long-term result. To address these issues, the strategy of "provisional stenting" has been developed.[277] In this method, an attempt is made to use balloon dilatation alone. IVUS guidance is used to choose the balloon size to obtain the best possible angioplasty result in terms of lumen cross-sectional area. However, if ultrasound imaging reveals an inadequate lumen or the presence of a dissection that compromises the lumen, then a stent is placed electively.

Several studies have shown that IVUS can provide essential information during the provisional stenting procedure. In the CLOUT Pilot Trial,[74] Stone reported that the early angiographic and clinical results of IVUS-guided PTCA without stenting were promising. On the basis of the vessel size and extent of plaque burden in the reference segment evaluated by IVUS, 73% of the lesions required larger balloons even after achieving an optimal angiographic result (final balloon/artery ratio = 1.30 ± 0.17). The success rate of IVUS-guided PTCA was 99%. Only one patient who developed acute closure received a stent. This angiographic oversized balloon angioplasty with IVUS guidance resulted in a larger final MLD without increased rates of significant dissections or ischemic complications. In the Strategy of Intracoronary Ultrasound Guided PTCA and Stenting (SIPS) trial,[278] 269 patients (358 lesions) were randomized to IVUS-guided intervention or angiography-guided intervention. Stenting was performed in about 50% of lesions in both groups. Major adverse cardiac events (MACE) during hospitalization were less with the IVUS-guided group. The reduction of MACE by IVUS guidance was 79%. They concluded that IVUS-guided intervention could reduce acute MACE. The Washington Hospital Center reported acute and late benefits of IVUS-guided balloon angioplasty using balloons sized according to the media-to-media diameter as determined by IVUS.[279] The end point used in this study was achieving a minimum lumen cross sectional area (MLCSA) greater than 70% of the average reference vessel area with no lumen compromising dissections. Crossover to stenting was needed in 61% of lesions. They showed that IVUS-guided PTCA achieved a "stent-like" lumen in 39% of patients with no abrupt closure episodes. An acceptable target lesion revascularization rate of 17% was reported. Recently, from a similar analysis for LAD lesions, they reported that 43% of lesions did not need stent implantation, and the target lesion revascularization was only 8.0% at 9 months.[280]

Clinical examples of "provisional stenting" are shown in Figs 37 and 38. Figure 37 shows how IVUS guidance revealed that placement of a stent was not necessary. Figure 38 shows how IVUS helped determine which of several lesions needed a stent despite the angiographic result.

Recently, a strategy of provisional stenting with a delayed angiogram at 30 minutes was suggested as an alternative to IVUS guidance.[281] It remains to be clarified if this strategy provides comparative results to those with IVUS guidance.

These preliminary results support the utility of IVUS-guided provisional stenting and have provided the impetus to extend this approach to the treatment of long lesions. This technique is called *spot stenting* and is described in the following paragraph.

IVUS-Guided Spot Stenting

To address the high restenosis rate associated with stenting long lesions or lesions in small vessels, the concept of spot stenting has evolved. The treatment of long lesions and lesions in small vessels has historically yielded poor immediate and long-term results when approached with traditional balloon angioplasty.[236,282-285] Angiographic restenosis rates for these lesions have ranged from 41% to 55%. In the STRESS subanalysis, smaller vessels treated with PTCA had a restenosis rate of 53%. Treatment of focal lesions with coronary stenting in vessels greater than 3.0 mm reduces restenosis when compared with balloon angioplasty.[61,62,274] However, stenosis length, length of the stent deployed, and small reference diameter were reported to be independent predictors of restenosis within stents.[168,276] Spot stenting is an attempt to use IVUS guidance to treat long lesions by taking advantage of the benefits of balloon angioplasty and reserving the use of stents to treat residual focal stenoses.

Based on the provisional stenting data, it was hypothesized that the restenosis rate for long lesions and diffuse disease could be reduced if IVUS-guided PTCA would be used as the primary modality while reserving coronary stents to those segments of a lesion where lumen dimensions did not meet prespecified IVUS criteria. Instead of traditional stenting where a lesion is covered from a proximal normal segment to a distal normal segment, the concept behind the spot stenting approach is to avoid stenting long segments even if small dissections are left behind, provided that the dilated sections have an adequate lumen CSA by IVUS. Preliminary data to support the use of this approach have been provided.[286] In that

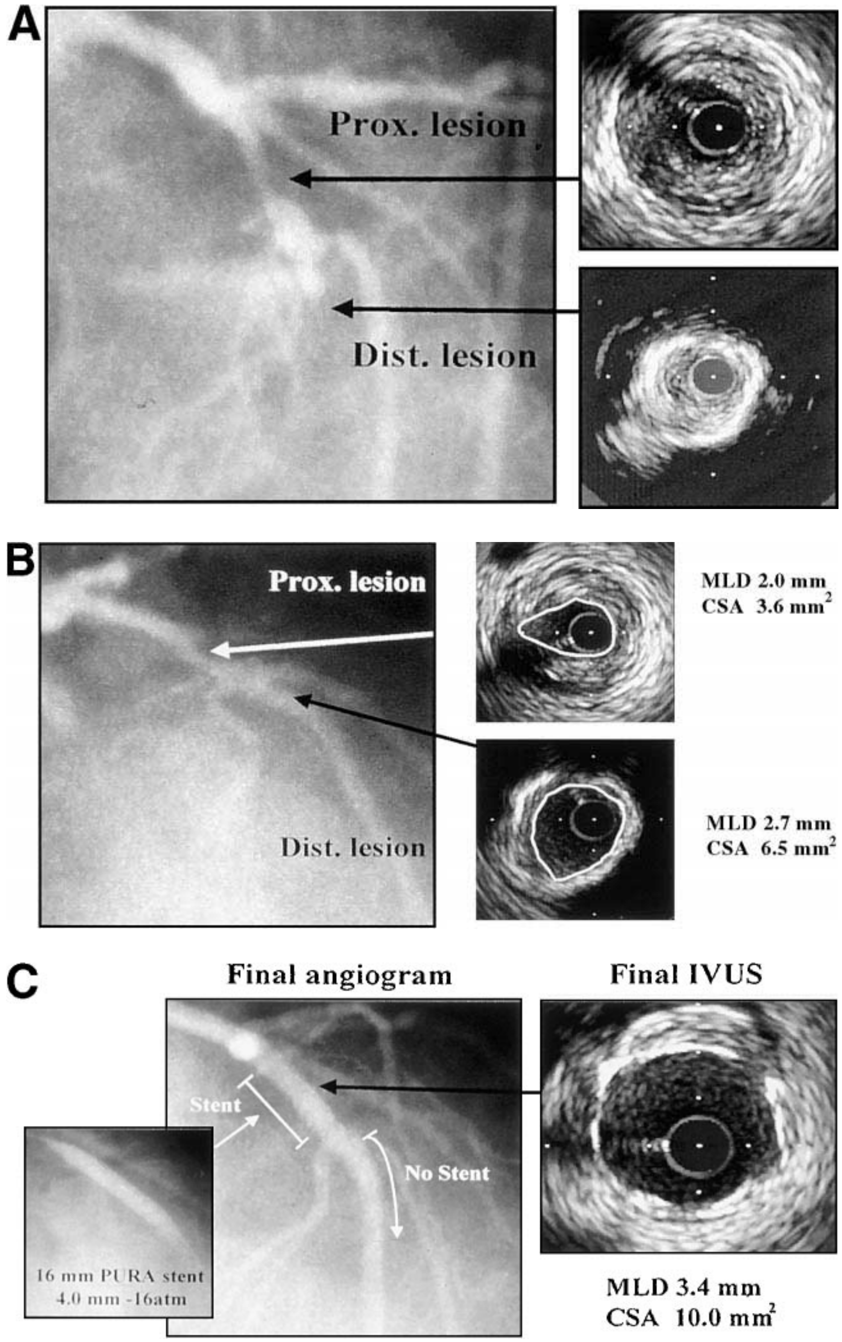


Fig 38. This proximal LAD has a significant stenosis followed by complete occlusion after the bifurcation of the diagonal and first septal perforator. The lesion was dilated with a 30-mm long, 3.0-mm diameter balloon at 14 atm. The corresponding IVUS images following recanalization and balloon dilatation at the proximal and distal lesions are shown to the right of the preintervention angiogram (A). Proximally the vessel was about 4 mm in diameter media to media. The lumen size was still inadequate at a 2-mm diameter following the 3-mm balloon dilatation. The distal lesion was intensely calcified, although the majority of the calcium was positioned toward the base or mid portion of the plaque. Instead of using rotational atherectomy, a larger balloon was chosen. A 20-mm long by 4-mm diameter balloon was expanded at 14 atm. The subsequent angiogram (B) showed an adequate angioplasty result in both the proximal and distal segments. However, the IVUS exam revealed an unexpected disparity. The distal lesion, despite being heavily calcified, was expanded adequately by the balloon dilatation, whereas the fibrotic proximal lesion showed more elastic recoil with a minimum lumen diameter of only 2 mm. Based on these observations, a 16-mm long PURA stent was placed in the proximal, but not the distal lesion, and inflated with a 4-mm balloon at 16 atm. The final angiogram is provided (C). The final IVUS study showed that the proximal lesion was now 3.4 mm in diameter with a CSA of 10.0 mm^2.

report, long lesions (greater than 15 mm) or lesions located in small vessels (less than 3.0 mm) were approached with primary PTCA using a balloon-to-vessel ratio of 1:1. The vessel size was defined as the reference media-to-media diameter measured by a preintervention IVUS study. IVUS criteria for success were defined as achievement of a lumen CSA greater than 50% of the vessel CSA at the lesion site or a minimum lumen CSA greater than 5.5 mm^2. If the IVUS criteria were met in all segments of the lesion after initial balloon dilatation, the procedure was considered complete. If the IVUS criteria were not met, the operator would consider using a larger balloon or higher pressure if deemed possible. If this were not possible, a stent was implanted focally only in

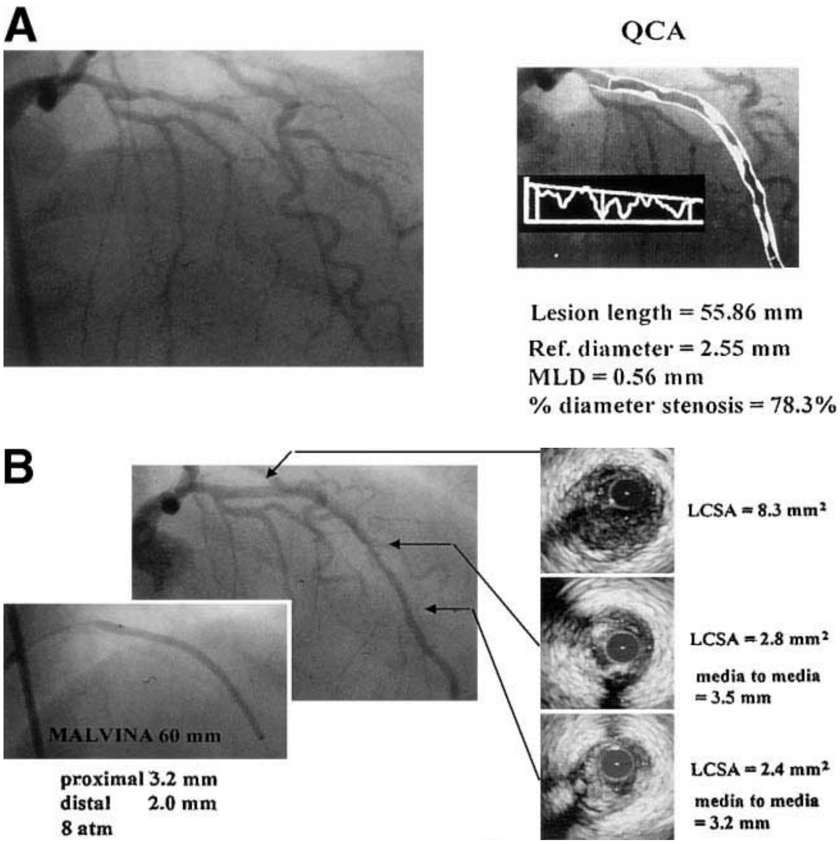


Fig 39. This case represents another diffusely diseased LAD where not many treatment options are available, which would benefit from the spot stenting approach (A). This lesion was 56 mm in length, and the reference lumen diameter measured 2.55 mm by QCA. QCA measurements in sizing vessels has been shown to be less accurate than IVUS measurements, especially in small vessels and vessels with diffuse disease. A long tapering balloon was used for predilatation that was 60 mm in length and tapered from 3.2 mm in diameter in the proximal portion to 2.0 mm in the distal portion. After the first inflation to 8 atm, IVUS was performed and showed that the lesion in the mid to distal segment of the artery was fibrocalcific in nature and that the media-to-media diameter in the distal lesion was 3.2 mm (B). Based on these observations, a 3.0-mm cutting balloon was applied only in the mid to distal segment of the lesion where the lumen CSA did not meet our minimal criteria.

the segment or segments of the lesion where the IVUS criteria had not been achieved, taking care to use the shortest stent length necessary to obtain an optimal result. Fifty percent of all treated lesions achieved the IVUS criteria with PTCA alone, whereas the other 50% required the placement of a focal stent. The average stent length used in the lesions that did not meet IVUS criteria by PTCA alone was 19.0 ± 12 mm. This was actually shorter than the average lesion length (20.7 ± 12 mm). In contrast, in previous studies it was common that stent length significantly exceeded lesion length, such as in the STRESS, BENESTENT I, and BENESTENT II Trials.[61,62,165] This is an important concept because evidence shows that the length of deployed stent is a major contributing factor to restenosis.[168,276] Overall results for this approach in 109 lesions in 71 patients were reported as follows: a MACE occurred in 25%, the angiographic restenosis rate was 18%, and the target lesion revascularization rate was 15%. This approach of IVUS-guided PTCA with spot stenting allowed safe treatment of long lesions and lesions in small vessels and achieved 6-month MACE and restenosis rates that appear to be lower compared with historic controls in these difficult lesion subsets. In addition to maximizing the acute gain, IVUS plays an essential role for this approach in terms of procedural safety. Historically, balloon angioplasty performed with angiographically oversized balloons without IVUS guidance was reported to be associated with a poor outcome.[66,67] Furthermore, placing a stent without fully covering the lesion has been viewed as dangerous because of the theoretical risk of acute or subacute stent thrombosis due to the potential flow disturbance and lesion reactivity. However, when IVUS is used to guide the intervention, any flow limiting segments or dissections can be more accurately assessed and a more educated decision made as to whether this segment can be left untreated.[287] The incidence of acute and subacute thrombosis in the spot stenting trial was as low as any of the major stent trials where less complex lesions were treated.

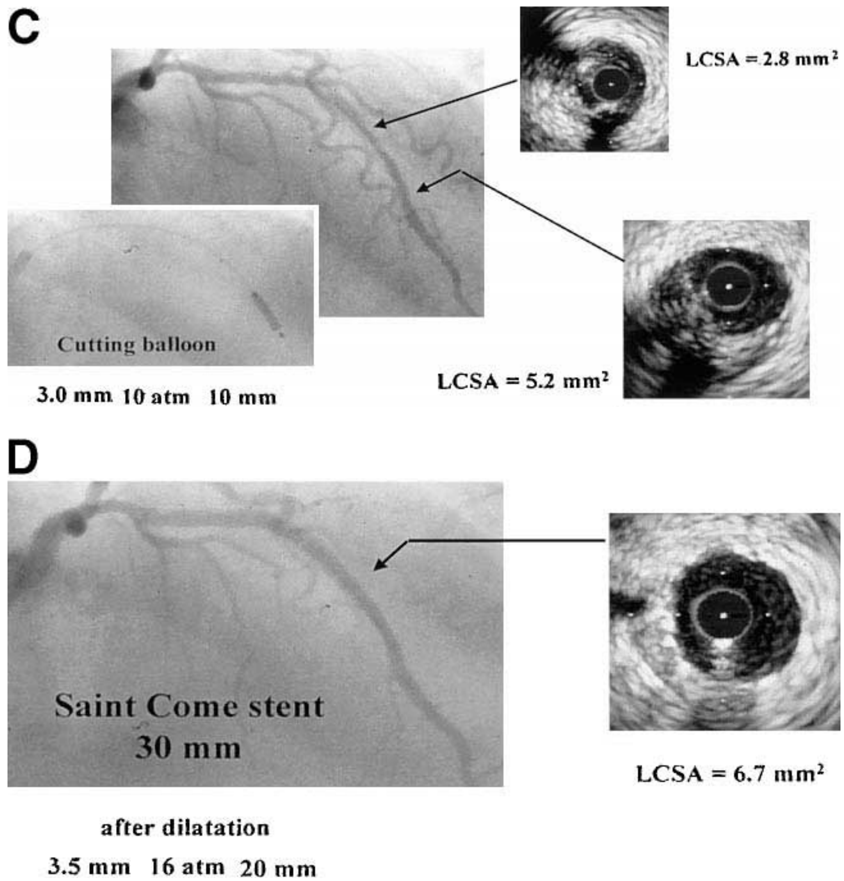


Fig 39. (Cont'd) The cutting balloon was effective in achieving the minimal criteria in the more distal segment where the lumen by IVUS now measured greater than 50% of the reference vessel area (C). In the mid portion, the luminal result was still unsatisfactory, with a CSA of 2.8 mm^2, so a stent was deployed only in the mid segment. This stent was 30 mm in length and was postdilated with a 3.5-mm balloon to 16 atm. The final angiogram shows an excellent result, and the IVUS measurement shows the new CSA in the mid portion to be 6.7 mm^2 (D).

An example of the spot stenting strategy is shown in Fig 39. An example of spot stenting with a 6-month follow-up study is shown in Fig 40.

Treatment of In-Stent Restenosis

With the explosion in the use of intracoronary stents in recent years, the problem of in-stent restenosis has been receiving increased attention. Ideally, to minimize further recurrences, the management of in-stent restenosis should not only address the new tissue growth but also the predilection for the exuberant proliferative response present in such lesions. Balloon angioplasty is safe, relatively inexpensive, and appears to be reasonably effective for focal in-stent restenosis.[288,289] Debulking devices such as DCA,[95] rotational atherectomy,[290,291] laser atherectomy,[292,293] and other tools such as the cutting balloon,[294,295] also appear to be safe and possibly somewhat more effective than balloon angioplasty. However, they have limited power to reduce rerestenosis so that optimal strategies need to be defined. Additional stents might be effective,[296-301] especially in combination with the use of antiproliferative strategies such as radiation therapy.[302] Additional stents should be used to cover important dissections occurring in the therapy of in-stent restenosis[303] and also may be effective in reducing the problem of "instant" restenosis,[304] ie, recoil of fibrous tissue through the stent struts back into the lumen.

How does IVUS help during treatment of this lesion subset? IVUS may be helpful by detecting "pseudo–in-stent restenosis"[305] and "instant" restenosis[304] better than angiography.

Pseudo–In-Stent Restenosis

After the implantation of a rigid slotted tube stent, neointimal proliferation occurs in response to the barotrauma applied to the vessel wall as

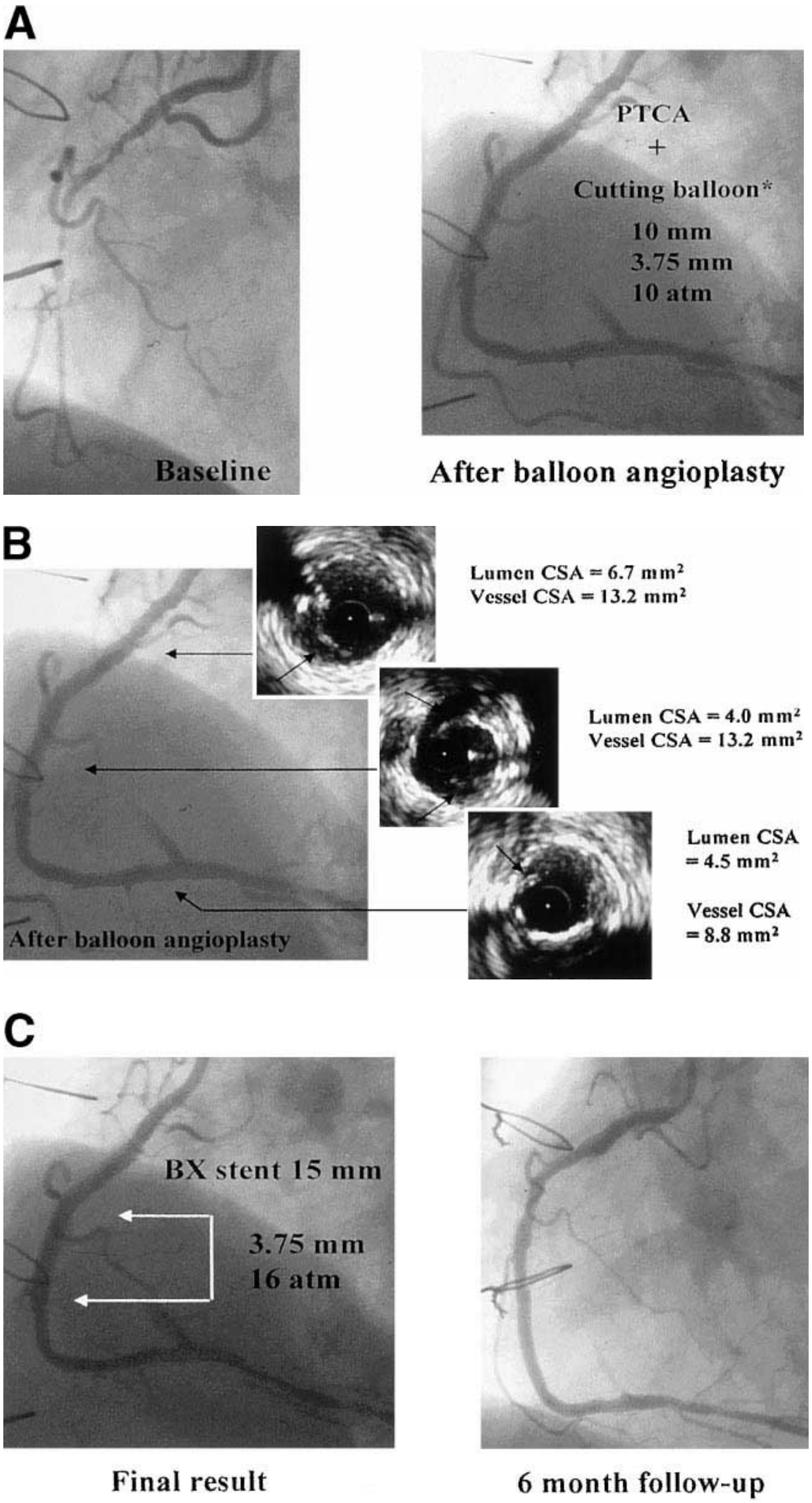


Fig 40. The initial approach to this subtotal occlusion in the right coronary artery was to use balloon angioplasty followed by a cutting balloon (A). This produced a good angiographic result. IVUS interrogation showed that there was an inadequate CSA in the mid portion (CSA less than 5.5 mm^2 and less than 50% of the reference vessel area at the lesion site) even though there was an optimal angiographic result (B). The lumen in the distal portion met minimal criteria of being greater than 50% of the vessel area. The final step was to place a 15-mm BX stent only in the specific site with the inadequate result in the mid portion. The 6-month angiographic follow-up showed an excellent long-term result with minimal recoil and little intimal hyperplasia (C).

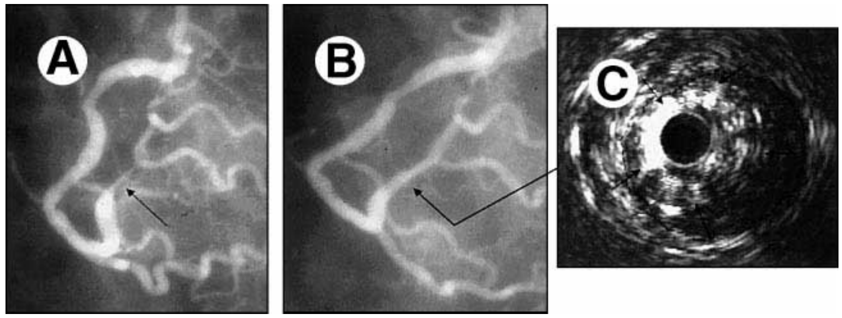
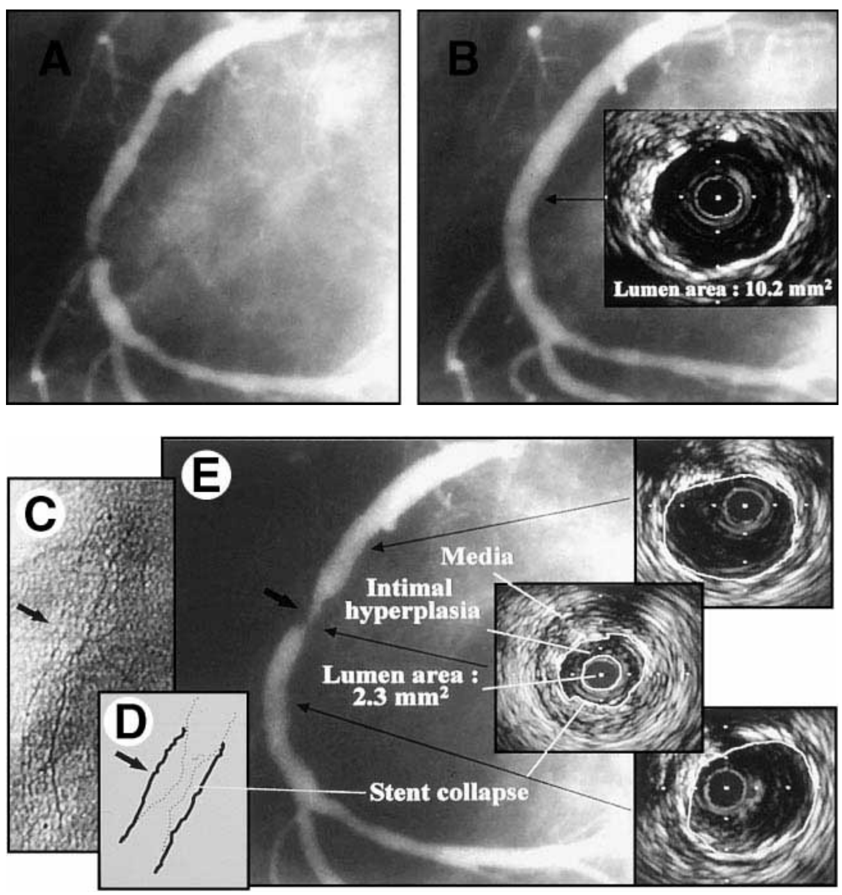


Fig 41. Angiogram and IVUS image of inadequate stent expansion, not seen angiographically. (A) Baseline stenosis in the posterolateral branch of a RCA. (B) Angiogram after a Palmaz-Schatz stent is implanted. An acceptable result is seen. (C) IVUS image showing unsuccessful stent expansion at this site. The arrows point out the struts of the stent. Because the stent is porous, the contrast streams outside the stent struts giving the illusion by angiography of a well-expanded stent. If this is not recognized and recoil of the artery on the stent occurs, the angiographic appearance would be indistinguishable from in-stent intimal hyperplasia, but this would actually be an example of stent pseudo-restenosis.

well as the persistent irritation of the foreign body.[254,306] Pseudo–in-stent restenosis is defined as a stenotic lesion within the stent at follow-up that is caused by inadequate stent expansion during the initial use rather than intimal hyperplasia (Fig 41). Alternatively, a stent may be compressed by external vessel recoil[305] (Fig 42). If the stent is not radio-opaque, the cause of the angio-

Fig 42. A stenosis in the RCA treated with a long stent. (A) Baseline. (B) After stenting with an acceptable angiographic and IVUS image. (C) At 6-month follow-up. Fluoroscopic outline of the stent showing partial stent collapse (arrow). (D) A cartoon outlining the stent as seen in (C). (E) Angiogram showing stent restenosis at the site of the partial stent collapse (short arrow). IVUS images are seen at the site of stent restenosis showing a smaller intrastent area than seen at the time of stent implantation, as well as some intimal proliferation. IVUS images of the stent (long arrows) proximal and distal to the site of restenosis reveals no evidence of stent collapse or intimal proliferation.



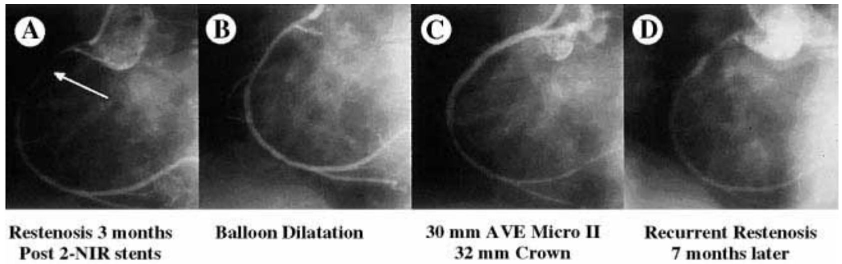


Fig 43. Treatment of in-stent restenosis with additional stent placement. (A) In-stent restenosis in an ostial/ proximal RCA. Two 16-mm NIR stents had been placed 3 months previously. Arrow points to lesion. (B) After treatment with balloon angioplasty of the in-stent restenotic lesion. (C) After placement of a 30-mm long Microstent II and a 32-mm Crown stent, an improved angiographic appearance compared with after balloon angioplasty alone. (D) Recurrent in-stent restenosis 7 months later. Despite improving the initial angiographic appearance with the placement of additional stents, aggressive recurrent restenosis has occurred.

graphic restenosis may not be appreciated unless IVUS is performed.

The "Instant" In-Stent Restenosis

The concept of "instant" in-stent restenosis, termed by the Washington Hospital Center group, was derived from the observation that, although the neo-intimal tissue decreased immediately after balloon angioplasty (or ablative therapy) for in-stent restenosis, it might recur after only a few minutes by prolapse of the extruded tissue.[304] Placement of an additional stent prevents this tissue from reentering the lumen.[299] IVUS should

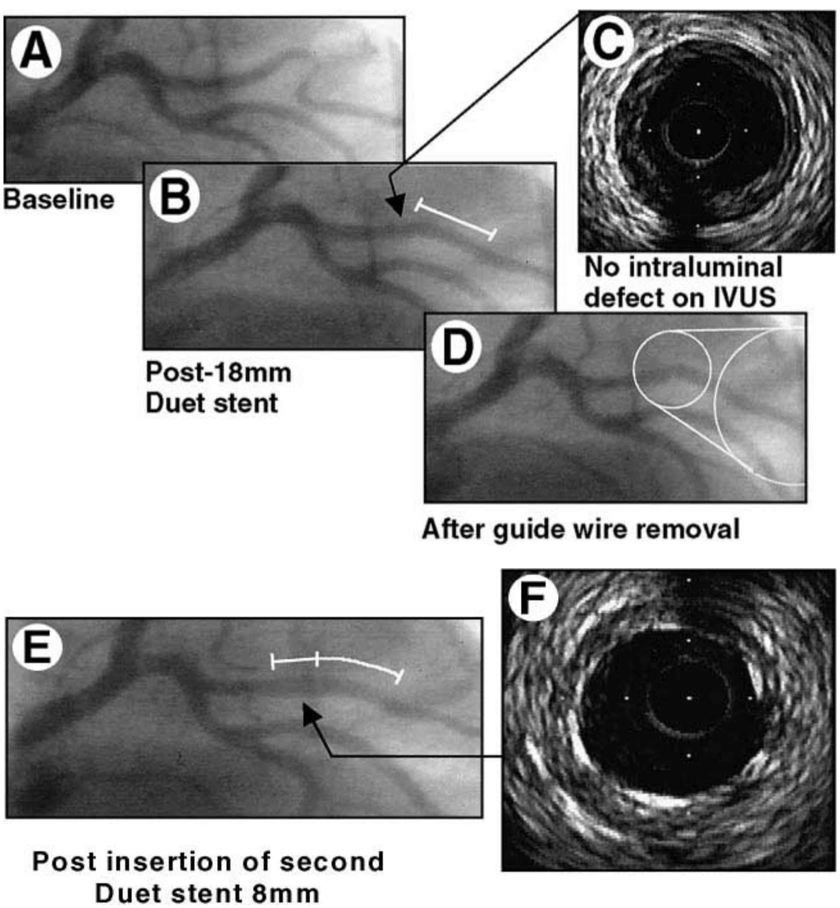


Fig 44. After implanting an 18-mm MultiLink Duet stent to treat a tortuous obtuse marginal artery, examination with angiography (B) and IVUS imaging (C) showed no intraluminal problem. However, after removing the catheter and guide wire, a linear lucency was noticed at the proximal stent edge (D). It was speculated that IVUS catheter and guide wire straightened the sharp bend created by the intersection of the tortuous artery and the edge of the stent, and thus temporarily effaced the lumen encroachment by a fold in the artery. Based solely on the angiographic appearance, an 8-mm long Duet stent was implanted to buttress the proximal entrance to the first stent (E, F).

detect this phenomenon with greater sensitivity than angiography and help determine whether additional stenting is necessary. Despite these favorable results on acute luminal results, the subsequent event rate has been high after repeat stent implantation to treat in-stent restenosis (Fig 43).

Limitations of IVUS

Despite the many benefits to using IVUS as an adjunct to coronary angiography, there clearly are several limitations of this method. First, with a simple injection of contrast, angiography can delineate a coronary artery with its branches, whereas IVUS imaging can examine only one artery at a time. Additional passes are needed to assess branch vessels. Second, IVUS can examine only the portion of the artery that accommodates the diameter of the IVUS catheter, which is more than 2.5 F at the present time. Third, IVUS images may be blemished by artifacts that interfere with the correct interpretation of the image. This includes ringdown artifact, guide wire artifact, acoustic shadowing, position-related artifacts, movement artifacts, and nonuniform rotational distortion.[307] Fourth, some IVUS systems have an acoustic dead zone around the catheter on the image, which may limit the evaluation of lesions with very tight stenosis.[308] Fifth, IVUS cannot evaluate angulation of the arterial segment because the device provides an instantaneous cross-sectional view along the length of the artery. Three-dimensional reconstructions stack up these slices into a straight line. In addition, the IVUS catheter may mechanically straighten a bend in the artery. This occasionally produces a false negative ultrasound result. An interesting case example of this is shown in Fig 44.

Summary

This review has attempted to show the areas where IVUS may provide additional information that is not available by angiography alone. Not only does the use of IVUS facilitate the performance of interventional procedures, especially in complex lesion subsets, the use of IVUS may lead to lower complication rates as well as improved restenosis data and target lesion revascularization. These advantages of IVUS have led to a cost-benefit analysis that suggests that the use of IVUS guidance is cost-effective.[169,278,309-311]

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