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Lessons from Intravascular Ultrasonography: Observations During Interventional Angioplasty Procedures

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Abstract: This article reviews many of the applications of intravascular ultrasonic imaging for coronary and peripheral arterial disease. In vitro studies demonstrate an excellent correlation between ultrasound measurements of lumen and plaque cross-sectional area compared with histologic sections. In vivo clinical studies reveal the enhanced diagnostic capabilities of this technology compared with angiography. Ultrasonic imaging also permits visualization of the atherosclerotic plaque itself for the first time in vivo. In addition to accurately describing the plaque morphology, ultrasonography can identify some of the tissue characteristics of the plaque. During interventional procedures, ultrasonic imaging has been shown to be beneficial for enhanced diagnosis as well as improvement of our understanding of the mechanism of newer interventional devices such as directed atherectomy, rotational or TEC atherectomy, or excimer laser. Initial studies suggest that ultrasound guidance of intravascular stent deployment may be critical for optimizing stent placement. Randomized studies are currently in progress to determine whether the guidance provided by intravascular ultrasonic imaging will alter the results of interventional procedures so that the restenosis rate can be improved. © 1993 John Wiley & Sons, Inc. **Indexing Words:** Intravascular ultrasonic imaging · Coronary artery disease · Angioplasty

THE PROBLEM

Coronary angiography provides a two-dimensional representation of the contour of the vessel lumen but does not give a true picture of the complex three-dimensional morphology of an atherosclerotic coronary artery, nor does it directly visualize the fundamental pathology, the atherosclerotic plaque. In addition, interventions such as balloon angioplasty distort the morphology producing even more complex shapes, which make it difficult to reconstruct the precise effects of invasive devices. Even when using multiple projections, angiograms underestimate the extent of atherosclerosis when compared with histology.[1] Histologic specimens of coronary atherosclerosis demonstrate extensive vessel wall thickening, which cannot be fully appreciated with a technique such as angiography that only evaluates the lumen of the vessel.[2] The angiogram shown in Figure 1A is from a patient with moderately severe disease; however, the lumen seen in the angiogram underrepresents the extent of atherosclerosis demonstrated on the gross pathologic specimen shown in Figure 1B.

Ultrasonography has been used for years to evaluate vascular morphology. Initially, it was used in the study of peripheral vessels that are readily accessible such as the carotid artery circulation. Cross-sectional images of coronary arteries have been obtained using a 12-MHz probe placed externally on the artery, but this technique is limited to the intraoperative setting.[3–5] Catheter-based intravascular ultrasonography has been developing rapidly during the last few years after showing initial promise in vitro in providing high resolution images of the artery lumen and walls.[6–8]

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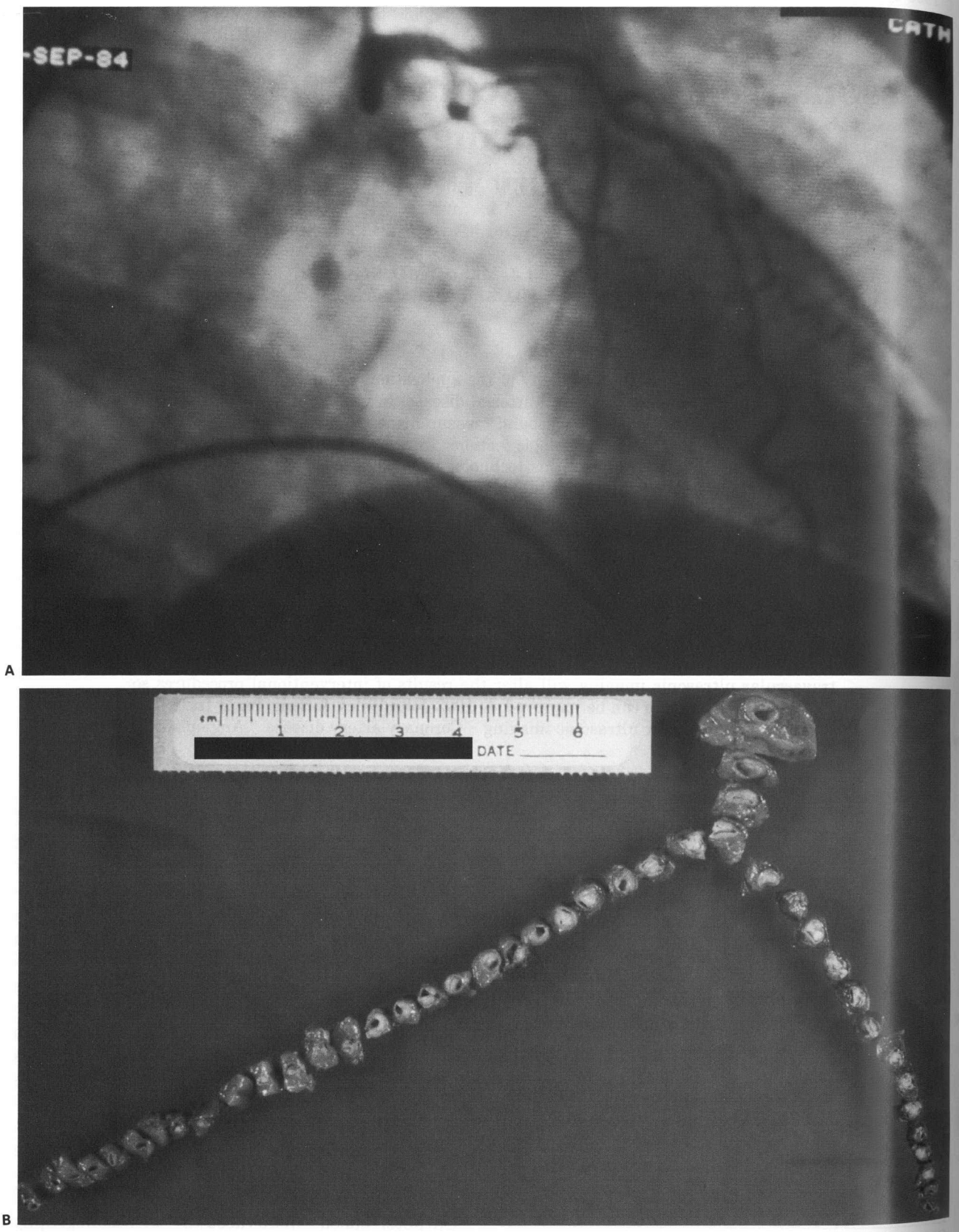
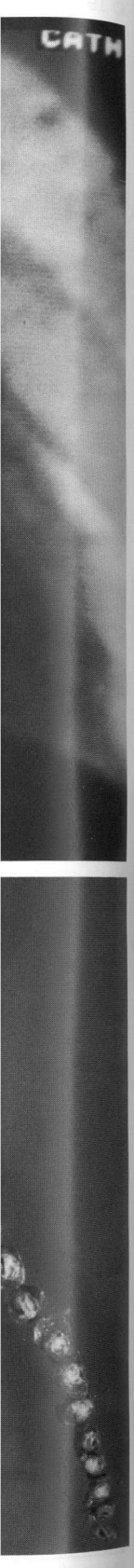


FIGURE 1. (A) Angiogram in the right anterior oblique projection of the left main, left anterior descending and left circumflex artery systems. There is a moderate degree of luminal narrowing. **(B)** The corresponding pathologic specimen of the left main, left anterior descending, and left circumflex arteries are presented in cross section as 5-mm cuts along the length of the arteries. The extent of disease is much greater in the pathologic specimen than is appreciated in the luminogram shown in Figure 1A.



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INTRAVASCULAR ULTRASOUND IMAGING: TECHNICAL CONSIDERATIONS

Currently available catheters image coronary arteries using a frequency range of 20 MHz to 40 MHz, in comparison to the more familiar 3 MHz to 7 MHz transducers used in transthoracic echocardiography. The higher frequency of the smaller intravascular devices allows greater lateral and axial resolution than the larger transducers at the expense of less tissue penetration due to energy dissipation at the higher frequencies. The need for miniaturization of these transducers for application in coronary arteries also affects the frequency of operation.

There are currently two approaches to catheter development that have reached the stage of clinical utility. The first is the mechanically rotating transducer and the second is the development of an electronic array catheter. The mechanically rotating catheter is the simplest approach to obtaining intravascular images. There are three basic configurations of mechanical rotating catheters. In one design, the transducer is offset 10° from being perpendicular to the long axis and is mechanically rotated allowing side viewing of the vessel wall.[9] In the second configuration, the transducer remains stationary but an acoustic reflector mounted at 45° rotates around the long axis.[10] This provides an image perpendicular to the long axis of the catheter. In the third configuration, the transducer and reflecting mirror relationships are fixed and the entire drive shaft assembly rotates mechanically around the long axis.[11] The advantage of the reflecting mirror is to permit ring down artifact to occur within the catheter, therefore allowing image information to be obtained up to the surface of the catheter without any dead space. The electronic array device, on the other hand, has ring down artifact in the region closest to the transducer, and it becomes necessary to eliminate this by computer image enhancement.

Because the mechanical devices all require rotation of some portion of their catheter tip, they are placed within a thin plastic sheath to protect the vessel from trauma. This sheath is advanced into the coronary artery over a guide wire, and various design modifications allow either the catheter to be moved within the sheath or the entire sheath and transducer assembly to be moved to allow longitudinal imaging of the vessel. The catheters rotate at speeds from 1200 rpm to 1800 rpm providing real-time imaging equivalent to 20 to 30 frames per second.

The second major design variation is the electronic array catheter.[12] Currently available catheters consist of a polymeric, 64-element transducer with four integrated circuits incorporated at the tip that serve to digitize, amplify, and multiplex the signal for transmission to the external computer. A complex algorithm termed "synthetic aperture array" is used for image reconstruction. The ultrasound signals are transmitted from single or multiple elements, and the reflected signals are received by all available elements. For points further from the catheter, data from multiple elements are available (wide aperture), whereas for near points, data from one or two elements may be available (narrow aperture). This theoretically allows the beam to be focused along all points. The image currently is updated at 10 frames per second, which is slower than the mechanically rotating devices.

Advantages of the electronic array device are the absence of rotating parts, simplifying the catheter itself, and allowing free movement of the entire catheter over a central guide wire. This design facilitates adaptation of this catheter to a combined imaging and dilatation balloon device. The disadvantage of the electronic array device is that the region closest to the transducer is filled with ring down artifact, and it becomes necessary to eliminate this by computer image enhancement. At the present time, the image quality of the electronic array catheter is not as clear as the mechanically rotating transducer catheters.

Another important factor influencing intravascular ultrasonic image quality is angle dependence, if the ultrasound beam strikes an arterial wall at an angle of more than 15°, much of the reflected information is lost. This effect is greatest when imaging larger coronary vessels or vessels outside the heart where stable catheter positioning is more difficult. Due to the small size of the coronary vessels, the catheter is more inclined to be centered, except in the left main coronary artery or at sharp segmental bends. Cardiac motion is a potential problem that has been overcome with current catheter designs that provide rapid image acquisition up to 30 frames per second.

HISTOLOGIC AND ULTRASOUND CORRELATES OF NORMAL AND ABNORMAL VASCULAR ANATOMY

Arteries consist of three layers distinguished by the differential staining properties of the vessel wall in histologic preparations. The innermost layer, the tunica intima, is composed of a layer

of endothelial cells.[13] This layer is surrounded by the internal elastic lamina and then the more muscular tunica media, containing smooth muscle cells as well as varying amounts of connective tissue and elastin. The external elastic lamina then separates the media from the adventitia, which itself is composed of elastin and connective tissue. For identification of these structures, ultrasound depends on the differential reflection from the interface between layers of varying density and compressibility and on the acoustic reflection of the tissue components within the atherosclerotic plaque.

The tissue interfaces of the arterial wall layers usually are imaged by ultrasound as a three-layered structure (Figure 2). The innermost layer detected by ultrasonography is an echodense structure of varying thickness depending on the extent of intimal proliferation. The internal elastic membrane generates a highly echogenic signal which overestimates the true thickness of this structure. This is referred to as blooming or broadening of the beam from highly reflective structures and limits our ability to distinguish between truly normal tissue and mild intimal proliferation. The muscular media is relatively echolucent and is seen as a dark zone between the intima and the surrounding echogenic adventitia. Accurate measurements in comparison with histology of normal intima, media, or proliferative atheroma have been obtained in several ultrasound studies.[8,10,14–16] Some authors believe that the typical three-layered appearance is a function of intimal thickening due to aging and often is not seen in younger individuals with normal coronary arteries.[17]

Several independent investigators have confirmed that there is a close correlation between the plaque area as determined by ultrasonic imaging and similar measurements made on histologic sections. Due to the effect of blooming of ultrasound reflection, intravascular imaging tends to overestimate the degree of intimal hyperplasia at the low end of the scale where there is only minimal wall thickness and may underestimate plaque thickness with larger plaques due to diminished penetration of the ultrasound energy and block-out of the ultrasound due to intense reflections from calcified portions of the plaque.

TISSUE CHARACTERIZATION

In addition to the quantitative analysis of intimal hyperplasia, the reflected intensity of the ultrasound signal provides a method of characterizing the tissue components of normal and atherosclerotic arteries.[18] When frequencies higher than 30 MHz are used, blood moving within the lumen can be visualized. For catheters that use transducer frequencies of 20 MHz to 25 MHz, blood is not usually seen unless there is significant stasis or the clotting mechanism is initiated locally. Smooth muscle provides poor echo reflections; therefore, the arterial media is seen as a black or echolucent circle. Lipid is also very echolucent, and small lipid collections within an atheroma have been identified. Fibrous tissue and collagen are strong echo reflectors and are visualized as echogenic speckled to homogeneous white structures. Calcium is the strongest echo reflector and can be distinguished by its "echo signature" of intense white areas within the plaque associated with drop out of echoes peripherally due to the intense reflection of the sound waves.

In distinction to the normal artery shown in Figure 2 with the typical three-layered appearance, Figure 3 provides an example of an ultrasound image of an atherosclerotic plaque. The corresponding pathologic specimen reveals an eccentric fibrous plaque which is identified by ultrasound as an inhomogeneous echogenic structure. In addition to the eccentric intimal plaque, there is a small focus of calcification that produces intense echoes with peripheral shadowing or drop out of echo information.

In general, calcium can be located in various areas of the plaque, from the fibrous cap to buried deeply within the atheroma adjacent to the media (Figure 4). This observation has particular relevance to procedures such as directional atherectomy or laser angioplasty. Intravascular ultrasound imaging is more sensitive than angiography for identifying calcium. Calcified plaque is observed in about 80% of stenotic sections by intravascular ultrasound but is recognized by angiography in only 15% of cases. Occasionally, echolucent areas surrounded by plaque are observed and are distinguished from calcium with shadowing because there is no peripheral drop out of echoes; this appearance is most consistent with necrotic liquid or a lipid pool as demonstrated in Figure 5.

Thrombus is differentiated from other structures as an area of speckled echo reflectance present within the vessel lumen. The intensity of reflection is brighter for a more recent thrombus than for organized older clots. Although best appreciated in real time, a finely speckled density

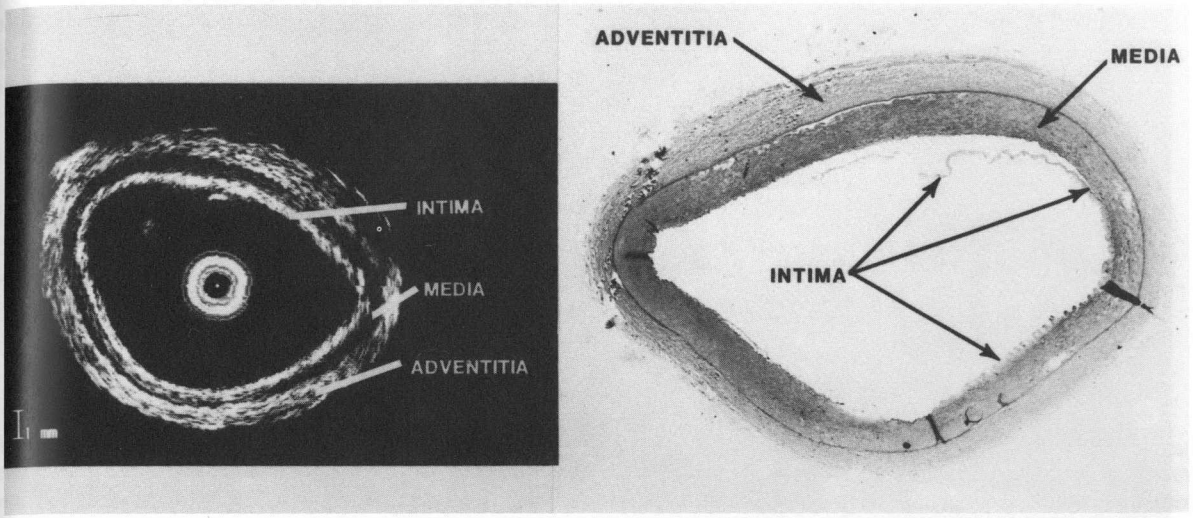

FIGURE 2. Right: A low-power histologic section of a normal human carotid artery shows the thin intimal layer, the thicker muscular media, and the adventitia with dark staining internal and external elastic lamina. The corresponding ultrasonic image is seen on the left. The intima, media, and adventitia are well-defined zones although the intima appears somewhat thicker than in the histologic specimen. (Reprinted from ref. 18 with permission of the American Heart Association.)

can be seen in Figure 6 within the lumen by intravascular ultrasound. During real time imaging, the echo density from a thrombus occasionally may be seen to move with the blood flow or with flushes of saline to help identify it. Although it may be difficult to distinguish thrombus from atheroma by its visual appearance in the ultrasonic image, quantitative information from backscatter frequencies have been used to help identify thrombus.[19] A study by Alibelli-

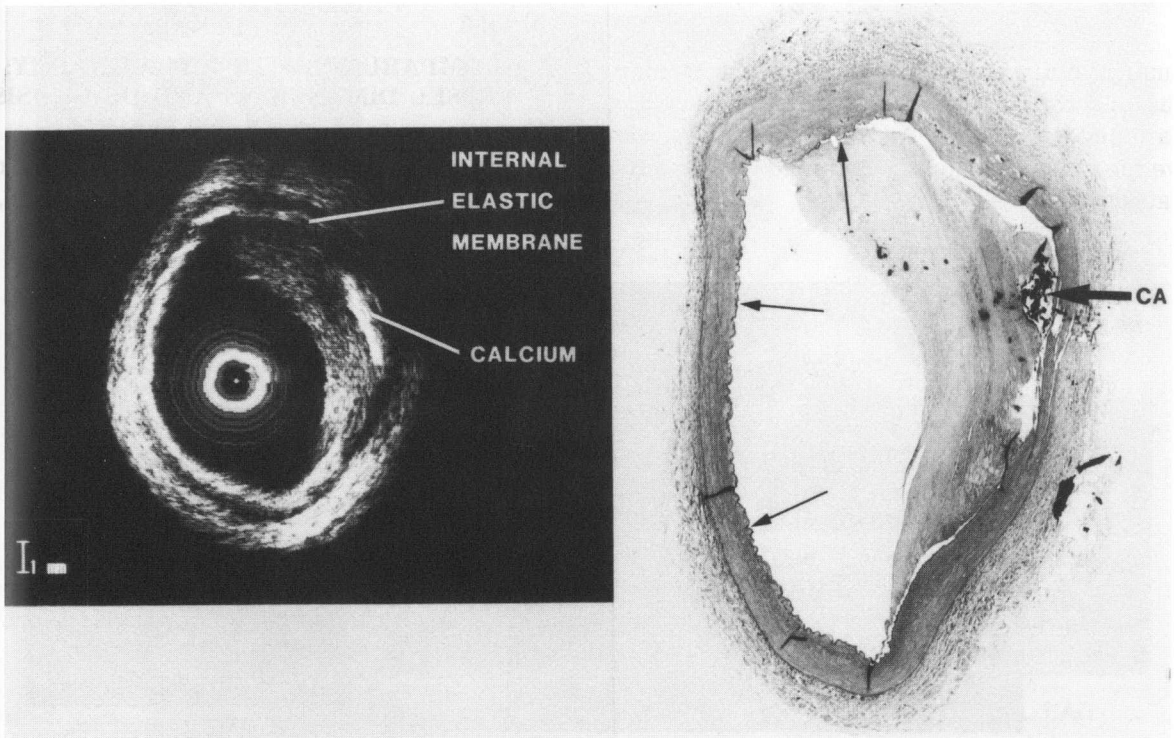

FIGURE 3. This human carotid artery has intimal thickening due to atherosclerotic plaque. The corresponding ultrasonic image has echo reflections from the plaque with intense white reflections and peripheral shadowing that corresponds to the calcification at the base of the plaque. The central bright echo ring is caused by reflections from the intravascular ultrasound sheath, and the dark circle in the middle is due to the intravascular ultrasound drive shaft. The intima and internal elastic lamina appear thicker in the IVUS image than by histology due to the "blooming" effect from the highly echogenic internal elastic lamina. (Reprinted from ref. 18 with permission of the American Heart Association.)

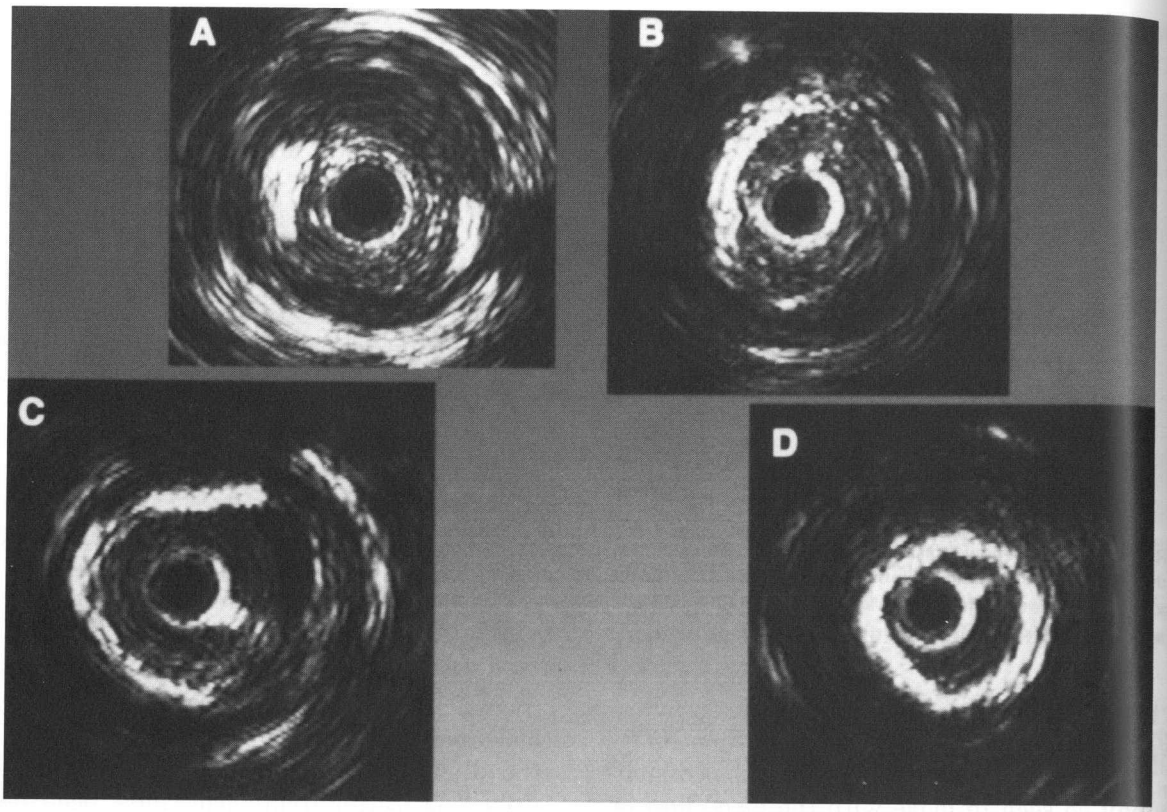

FIGURE 4. Varieties of calcification as seen with intravascular ultrasonic imaging. Calcified plaques have various morphologic patterns ranging from small patches of calcium to concentric bands that may take up the entire circumference of a portion of the plaque. These bands may be at the interface between the lumen and the plaque (D) or may be buried deep within the substance of the plaque closer to the media (A).

Chemarin et al. demonstrated that intravascular ultrasound correctly identifies thrombus in 63% of patients with recent infarction where it was proven to exist by histology obtained in vivo during atherectomy.[20]

COMPARISON WITH ANGIOGRAPHY: VESSEL DIMENSIONS AND DIAGNOSIS

Although there is a close correlation between ultrasonography and histologic measurements, the

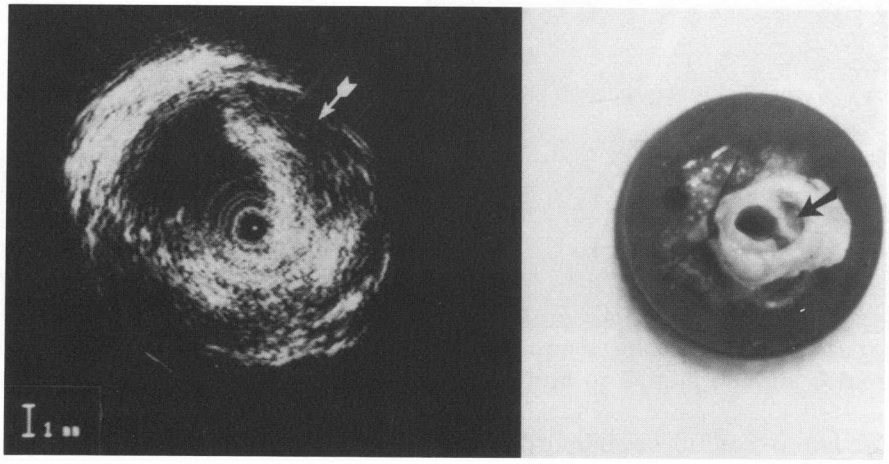

FIGURE 5. On the right is a gross specimen of a human iliac artery. There was necrotic liquid within the plaque (arrow). On the left is the ultrasonic image of the same segment. The white arrow points to the area of necrotic liquid that is hypoechoic, but, unlike shadowing from calcification within a plaque, there are echo reflections around the circumference of this liquid pool. (Reprinted from ref. 18 with permission of the American Heart Association.)

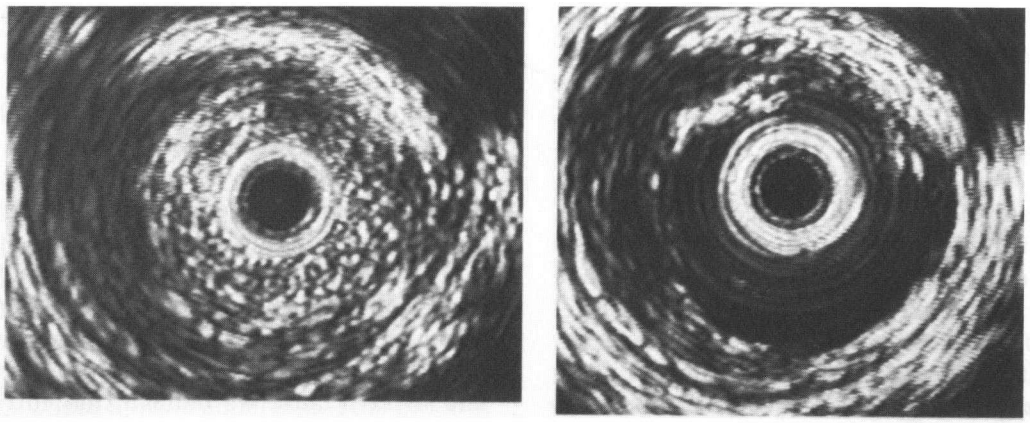

FIGURE 6. This is an example of an acute thrombus in a human peripheral vessel. This patient underwent balloon angioplasty of a totally occluded, superficial femoral artery. Initial imaging (left) showed a fine speckled density within the lumen of the vessel. In real time, this could be seen to move somewhat with pulsatile blood flow. This patient was treated with intravascular urokinase with resolution of the thrombus as seen in the image on the right. There is a residual eccentric fibrous plaque from 6 to 12 o'clock.

results have been less consistent compared with angiography in vivo. In a study of nondilated vessels by Nissen et al,[21] there was a close correlation (r = .88) between angiographic diameters and diameters determined with intravascular ultrasonography. In a study by Honye, et al.,[22] 22 patients were studied following balloon angioplasty by ultrasonography and angiography. In the dilated segment, the lumen cross-sectional area was 5.0 ± 2.0 mm^2 by ultrasonography

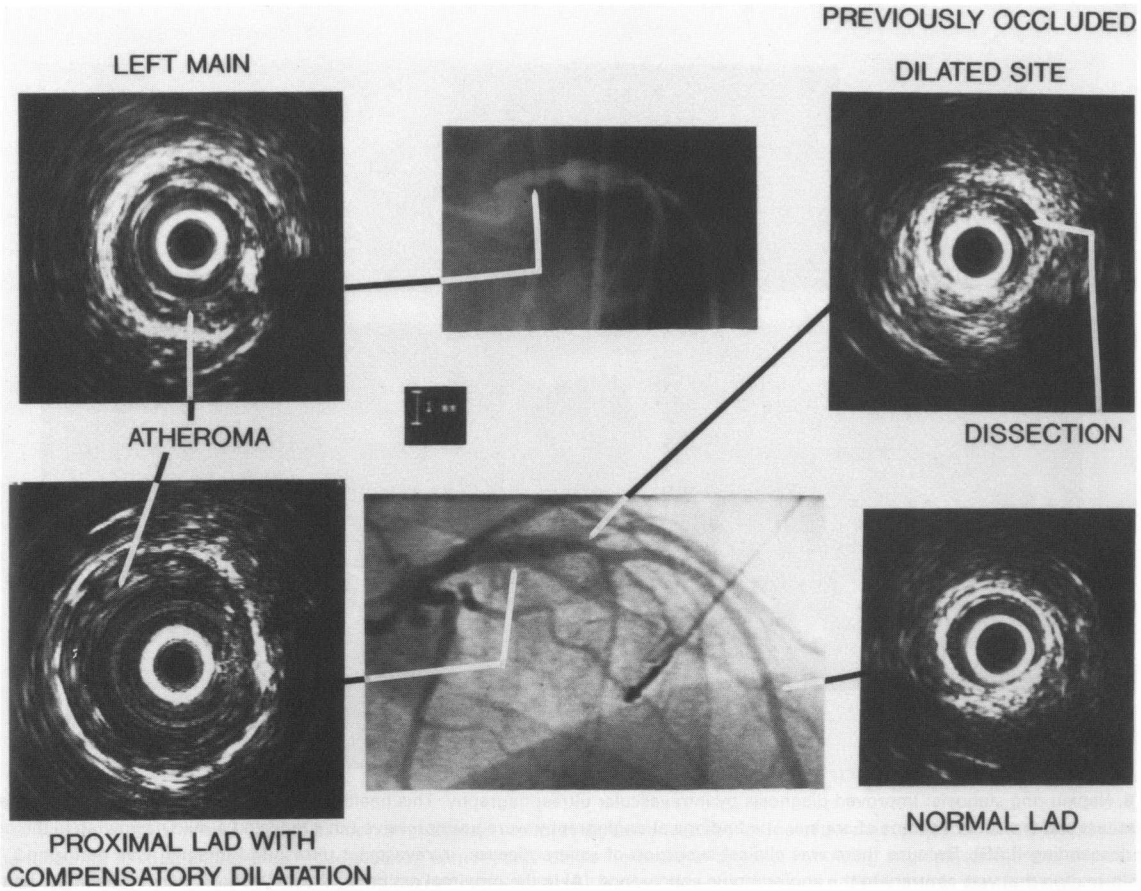

FIGURE 7. Compensatory dilatation: Upper left: An IVUS image of a left main coronary artery with a moderate amount of atheroma. Lower left: A cross-section of the proximal left anterior descending artery with an external diameter, which is larger than the left main artery. This appearance is consistent with compensatory dilatation. A normal segment of distal left anterior descending that is significantly smaller, is seen in the lower right corner. The image in the upper right shows the balloon angioplasty site with a small dissection (white arrow).

and 3.3 ± 1.3 mm^2 by angiography. Similarly, in angiographically normal segments, the lumen area by ultrasonography was 9.2 ± 4.6 mm^2 and was 7.1 ± 2.5 mm^2 by angiography. Both of these differences were statistically significant.

The reasons for these differences are multiple, including the fact that the angiographic assessment of cross-sectional area is derived from a geometric formula using diameter measurements but does not "planimeter" the vessel lumen as ultrasonic and histologic measurements do. The magnification scale is not as great with angiography, and the calibration accuracy is more difficult with angiography than with imaging from within the lumen. Although the presence of the ultrasound catheter may diminish flow or cause spasm, the ultrasound measurements were larger than measurements by angiography in this study. The differences are still significant even in the angiographically normal segments and certainly more abnormal in the previously dilated site, which is consistent with the marked lumen irregularities one finds after balloon angioplasty.

In an in vitro study using an acrylamide cast of a phantom model where x-ray magnification is known exactly, Moriuchi demonstrated that contrast angiography overestimates the true lumen cross-sectional area compared with ultrasonography when the lumen is not elliptical but irregular.[23] This can, therefore, result in an underestimation of the lesion stenosis in diagnostic studies or an overestimation of the beneficial results after balloon angioplasty. Based on the in vitro and in vivo data, we believe that intravascular ultrasonography provides the more accurate assessment of lumen cross-sectional area both before and after interventional procedures such as angioplasty.[24–26]

In addition to the more accurate assessment of the vessel lumen, intravascular ultrasonography reveals information about the atherosclerotic plaque that is unobtainable from angiography.[27] In areas that were felt to be relatively normal by angiography, ultrasonic images demonstrated

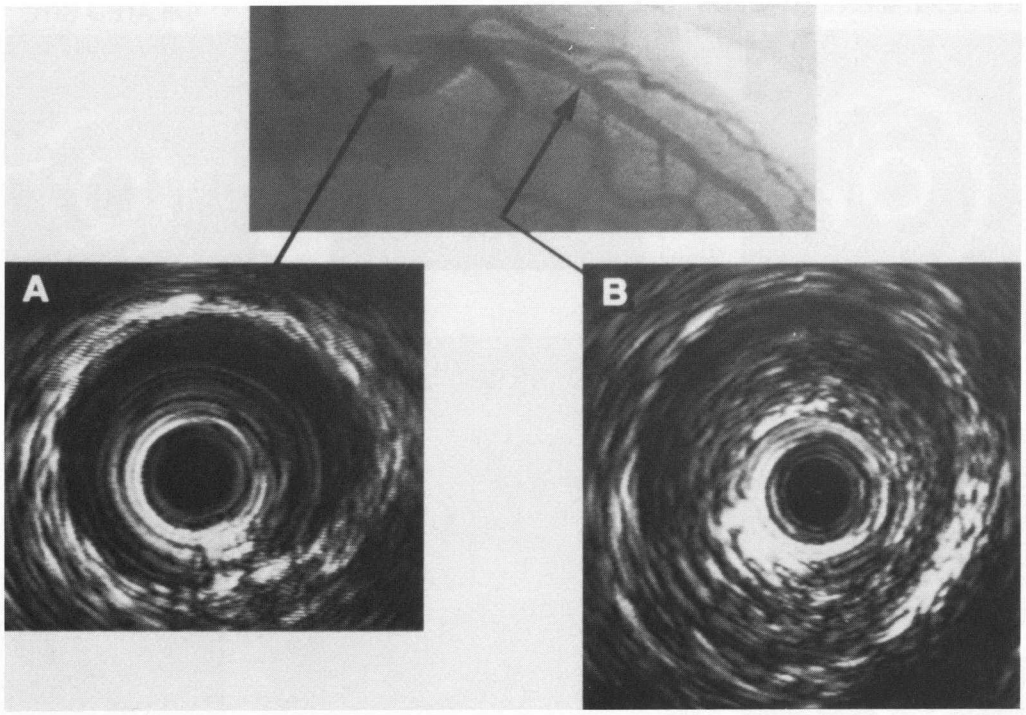

FIGURE 8. Napkin ring stenosis: Improved diagnosis by intravascular ultrasonography. This healthy 47-year-old woman had an abnormal treadmill stress test and typical symptoms of angina. The findings at angiography were unimpressive but suggested a mild narrowing in the ostial left anterior descending (LAD). Because there was clinical suspicion of severe disease, intravascular ultrasound imaging was performed. This revealed information that was contrary to the angiographic appearance. **(A)** In the proximal ostium of the LAD where there appeared to be tapering in the angiographic image, but there was no evidence of atherosclerotic disease was seen with IVUS. Beyond this area, there was a small amount of atheroma and compensatory dilatation. **(B)** An area that showed a less than 50% stenosis by angiography, but where intravascular imaging shows a nearly occlusive, short, napkin ring stenosis.

the presence of atherosclerotic plaque that encompassed an average of 35% of the cross-sectional area of the artery. This is in agreement with pathologic studies that suggest that angiography underestimates the amount of atherosclerosis present.[28] Glagov demonstrated histologically that arteries enlarge centrifugally as atheroma is deposited but retain a normal lumen area until 40% of the available cross-sectional area is filled.[29] At that point, the artery apparently can no longer expand, and new atheroma encroaches into the lumen. It is only at this point that an angiogram would appear abnormal. This process, termed compensatory dilation, has been confirmed in vivo by intravascular ultrasonic imaging, but it is unclear whether all arterial segments react this way (Figure 7). On occasion, angiography is incapable of adequately assessing the severity of an atherosclerotic stenosis either due to excessive vessel overlap or due to a very short "napkin ring" narrowing (Figure 8). In addition, intravascular ultrasonography has been helpful diagnostically in assessing ostial stenoses that might not be interpreted as severe with angiography.

CLINICAL TRIALS

Plaque Morphology Following Percutaneous Transluminal Coronary Angioplasty (PTCA)

The procedure of PTCA traumatizes the vessel and disrupts the plaque, leading to intimal tears and dissection of varying degrees. Although this trauma seems to be an important part of the therapeutic effect of PTCA,[30] it is also likely to be a component of the restenosis problem. Whether extension of the dissection to the media leads to a better angioplasty result or a higher restenosis rate is uncertain.[31–33] In addition, vessel recoil may well be an important component of restenosis. Intravascular ultrasonography is an ideal method to assess devices that claim to ablate or remove plaque because it is the only method that can determine in vivo

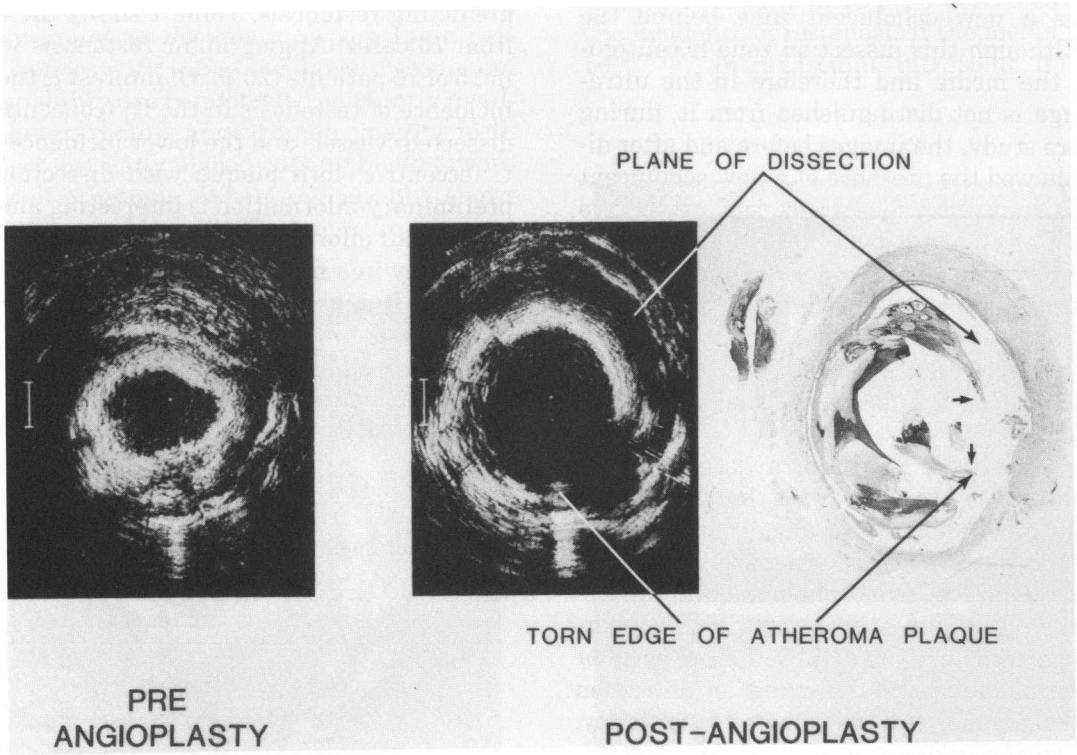

FIGURE 9. In vitro study of mechanism of balloon angioplasty. An intravascular ultrasonic image of an atherosclerotic artery before angioplasty (left) and following balloon angioplasty (middle panel) demonstrate dense fibrocalcific disease. Following angioplasty there is a fracture of the plaque with separation of the torn ends between 3 o'clock and 6 o'clock. This corresponds to the torn fragments in the histologic section (small arrows). In addition, a dissection is identified in the middle ultrasonic image as an echolucent zone behind the plaque from 12 o'clock to 3 o'clock, which corresponds to the separation of the atheroma from the media in the histologic section. (Reprinted with permission of the American Heart Association, *Circulation* 1989;80:873–882.)

whether plaque has actually been removed or whether the vessel wall has simply been stretched outward. Angiographically, either of these mechanisms would result in a larger lumen diameter. Intravascular ultrasonic imaging has provided important insights into the mechanism of action of these new technologies and has demonstrated that less plaque is removed than is assumed by looking at the angiograms.

Following balloon angioplasty, intravascular ultrasonic imaging has proven useful in defining the presence and type of dissection. An in vitro study was performed that compared intravascular ultrasonic images before and after balloon dilatation in human atherosclerotic arteries.[34] An acoustic reflecting needle was passed through the wall of the artery so that the same section of artery was imaged and compared to the histologic cross-section at the same level. As demonstrated in Figure 9, the results of this study showed that the mechanism of balloon angioplasty was to tear the plaque, usually at its thinnest section, which then permitted the lumen and artery outer diameter to expand. In addition, the presence of the dissection as documented histologically could be identified in the ultrasonic images as a new echolucent zone behind the plaque. Although this dissection zone is contiguous with the media and therefore in the ultrasonic image is not distinguished from it, during the in vitro study, the images before and after dilatation showed the presence of a new echolucent layer consistent with dissection. During in vivo imaging, if an image is not obtained prior to balloon dilatation, the criterion for diagnosing a dissection is that the echolucent zone behind the plaque should be greater than 200 μ in width. In most atherosclerotic arteries, the echolucent zone representing the media is usually only 100 μ in width.

In our experience with intravascular ultrasonic imaging in vivo following balloon angioplasty, we have identified a variety of different morphologic patterns that are most commonly observed.[22] Our PTCA morphologic grading system is shown in Figures 10 through 15. The morphologic patterns are defined by the presence or absence of plaque tears, the extent of dissection behind the plaque, and the plaque eccentricity. The first pattern, Type A, reveals a partial thickness intimal tear (Figure 10). In the Type B pattern, the plaque tear extends to the internal elastic lamina and leads to separation of the plaque ends but without a dissection, ie, there is no separation of the plaque from the media surface (Figure 11).

A Type C tear is more extensive with separation of the plaque from the internal elastic lamina with an arc of up to 180° (Figure 12). A Type D morphology is defined as an arc of dissection >180° but has no apparent tear in the plaque (Figure 13). In the Type D dissection, it appears (from in vitro studies) that the plaque is rotated and torn from its base with the media as if the balloon applied a torsional force on the plaque. Contrast injections into the guiding catheter during ultrasonic imaging will frequently show fine echo reflections entering the dissection plane and lumen to help define them. The Type E pattern shows no evidence of dissection, and is divided into Type E_1 with concentric atheroma (Figure 14) and Type E_2, if an eccentric atheroma is present (Figure 15). These last two patterns depend on vessel stretching for their angiographic success but may be more susceptible to recoil, as the plaque has not been significantly remodeled.

We hypothesized that the morphologic patterns observed with intravascular ultrasonography may correlate with restenosis. Patients were prospectively evaluated to obtain information that might support the utility of this grading system in predicting restenosis. Table 1 shows the findings from 76 cases. Angiographic restenosis was seen in 15 of 76 patients (20%). Of interest is the higher incidence of restenosis in the E_1 (concentric, nondissected) vessels and the lower incidence in Type C (eccentric, torn plaque with dissection). This preliminary information is interesting and should support an effort to apply this grading scale prospectively in a multicenter trial to assess its true validity. It might be hypothesized that the E_1 concentric lesion, with no dissection, is susceptible to recoil, as well as the usual process of intimal hyperplasia, leading to a higher restenosis rate. This information, if validated, could aid in the choice of

TABLE 1
Incidence of Angiographic Restenosis in Each Morphologic Type

	Lesions	
	n	%
	14/66	21
Type A	1/7	14
Type B	1/12	8
Type C	2/18	11
Type D	0/4	0
Type E_1	7/14	50[a]
Type E_2	2/11	18

[a] $p = .053$

Reprinted with permission from Honye J et al: Morphologic effects of coronary balloon angioplasty in vivo assessed by intravascular ultrasound imaging. *Circulation* 85:1012-1025, 1992.

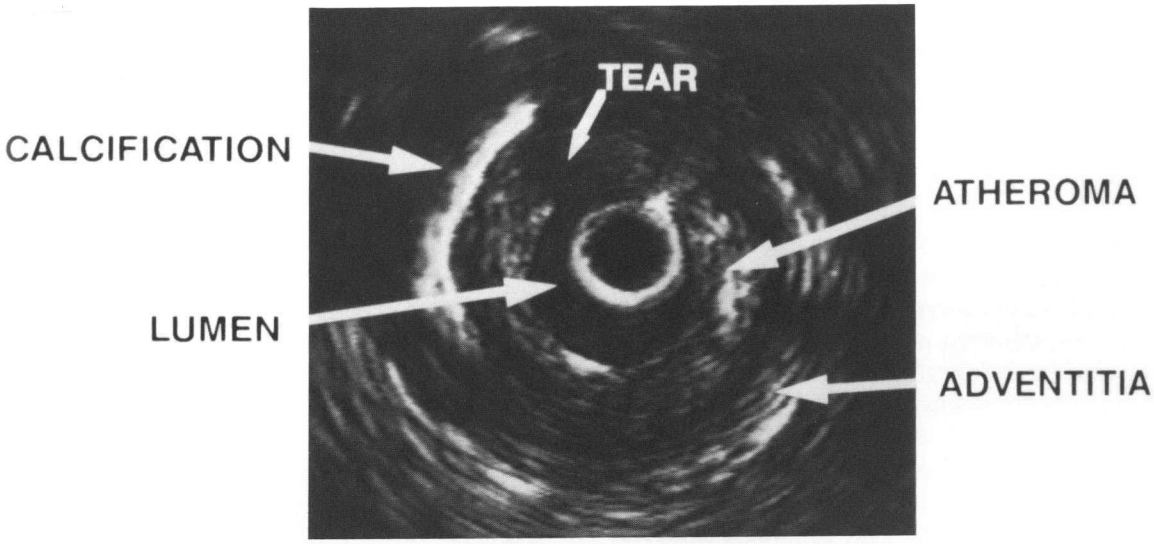

FIGURE 10. Type A tear: A small tear that extends into the atheroma but does not penetrate to the media. Calcification within the plaque is also identified. (Reprinted from ref. 22 with permission of the American Heart Association.)

an alternate technology, such as atherectomy or stents, in those lesions most susceptible to restenosis.

Directional Atherectomy

Although prototype designs incorporating atherectomy devices with intravascular ultrasonic imaging capability are being tested, currently available catheters require angiographic imaging to direct an eccentrically placed cutting blade toward the bulk of atheroma. When angiography shows an eccentric or "one-sided" plaque, in approximately 20% of cases the angiographic appearance of eccentricity or concentricity is contradicted by intravascular ultrasonography. Media and adventitia are obtained inadvertently in 26% to 61% of directional atherectomy specimens,[35,36] and contradictory results have been described regarding the incidence of restenosis if the media is extracted.[35,37,38] Intravascular ultrasonic imaging be-

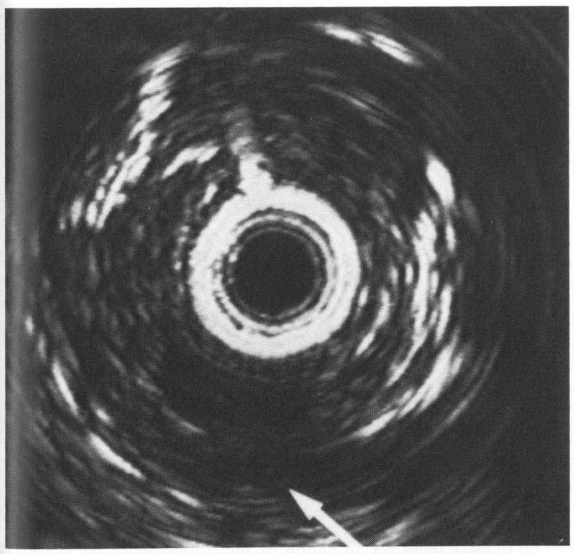

FIGURE 11. Type B tear: The tear (arrow) penetrates the full thickness of the atheroma to the level of the internal elastic lamina but does not extend circumferentially. (Reprinted from ref. 22 with permission of the American Heart Association.)

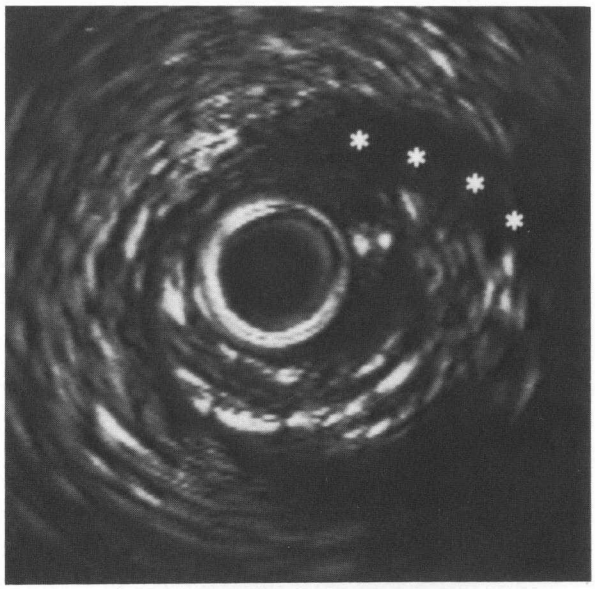

FIGURE 12. Type C tear and dissection: The plaque is fractured through to the media and is dissected from the media circumferentially up to a level of 180 degrees of arc. Injection of contrast at this level would show dense echos created by bubbles within the lumen extending into the dissection plane. Plaque dissections frequently begin at an area of calcification. (Reprinted from ref. 22 with permission of the American Heart Association.)

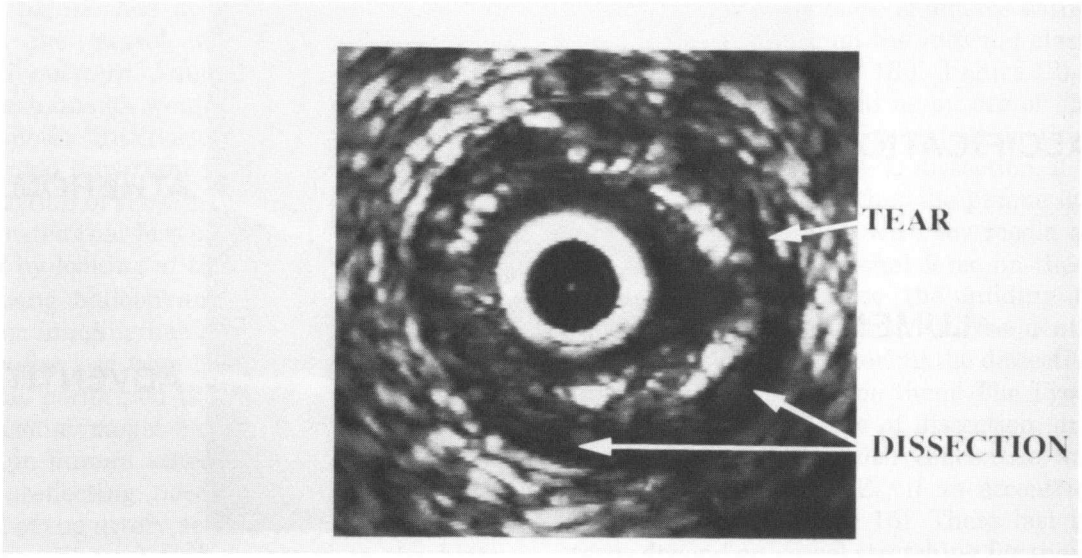

FIGURE 13. Type D dissection: This is a more extensive tear extending behind the atheroma in an arc up to 360 degrees. The plaque appears to be wrenched from its base with the media. (Reprinted from ref. 22 with permission of the American Heart Association.)

fore, if possible, and after initial passes with the atherectomy cutter can help confirm successful reduction in plaque size and proper direction of the cutting blade. Not infrequently, a narrow trough is produced within the atheroma. Instead of obtaining a wider excision of plaque, further cuts, if not properly directed, may only deepen the trough and risk the removal of media and adventitia.

Intravascular ultrasonography is also quite useful in determining the location of calcification within the plaque during atherectomy procedures. Plaques that are severely calcified at the

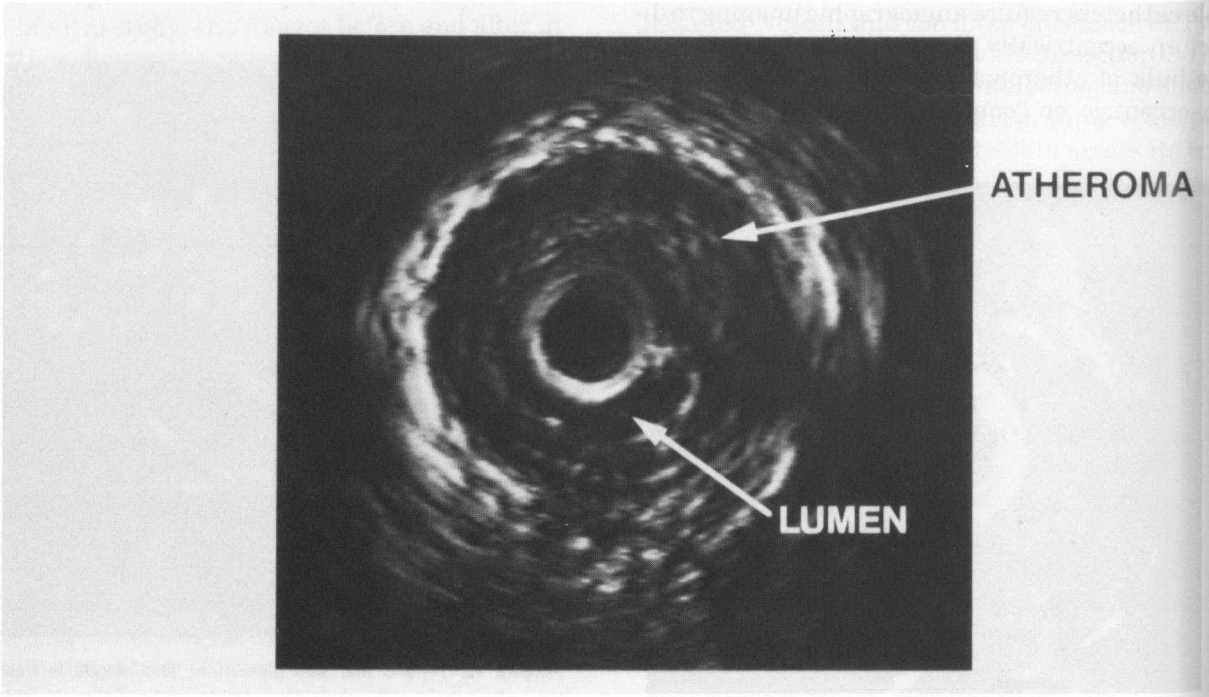

FIGURE 14. Type E1 morphology: A concentric atherosclerotic plaque with no evidence of dissection or plaque fracture by ultrasonic imaging. The mechanism of a successful angioplasty in these cases must be vessel stretching and perhaps a small degree of plaque compression. These lesions are at significant risk for vessel recoil and may have a higher restenosis rate. (Reprinted from ref. 22 with permission of the American Heart Association.)

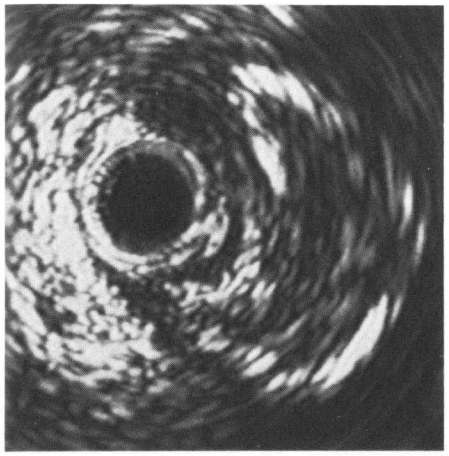

FIGURE 15. Type E2 lesions: These are similar to E1 morphology in that there is no evidence of a plaque tear; however, the plaque is eccentric in E2 lesions. The mechanism of angioplasty in these cases is most likely stretching of the normal segment of the vessel wall. (Reprinted from ref. 22 with permission of the American Heart Association.)

surface of the cap are unlikely to be responsive to directed atherectomy but may respond better to the grinding action of the Rotablator. In contrast, stenoses with calcification deeper within the plaque or at the border with the media can be successfully treated by directional atherectomy (Figure 16). The relationship of side branches to the plaque in ultrasonic imaging can also be used to guide the placement of the atherectomy catheter when angiographic localization is difficult due to multiple side branches or a complex-appearing plaque. Although angiographic results are frequently excellent following directional atherectomy, the intravascular ultrasonic finding of a narrow channel cut within a larger bulk of atheroma provides sobering evidence that current angiographic techniques are inadequate to fully appreciate the effects of this technology.

The improvement in understanding the mechanism of atherectomy may provide information about lesions that may be more inclined to restenosis. Preliminary data from our laboratory in cases imaged before and after directional atherectomy demonstrate that a small amputative effect is obtained with a mean reduction from 13.3 mm^2 to 10.5 mm^2 in atheroma cross-sectional area. Of interest, however, is the finding that the vessel diameter as measured from the internal elastic lamina increased from 4 mm to 4.7 mm, indicating a moderate (18%) dilata-

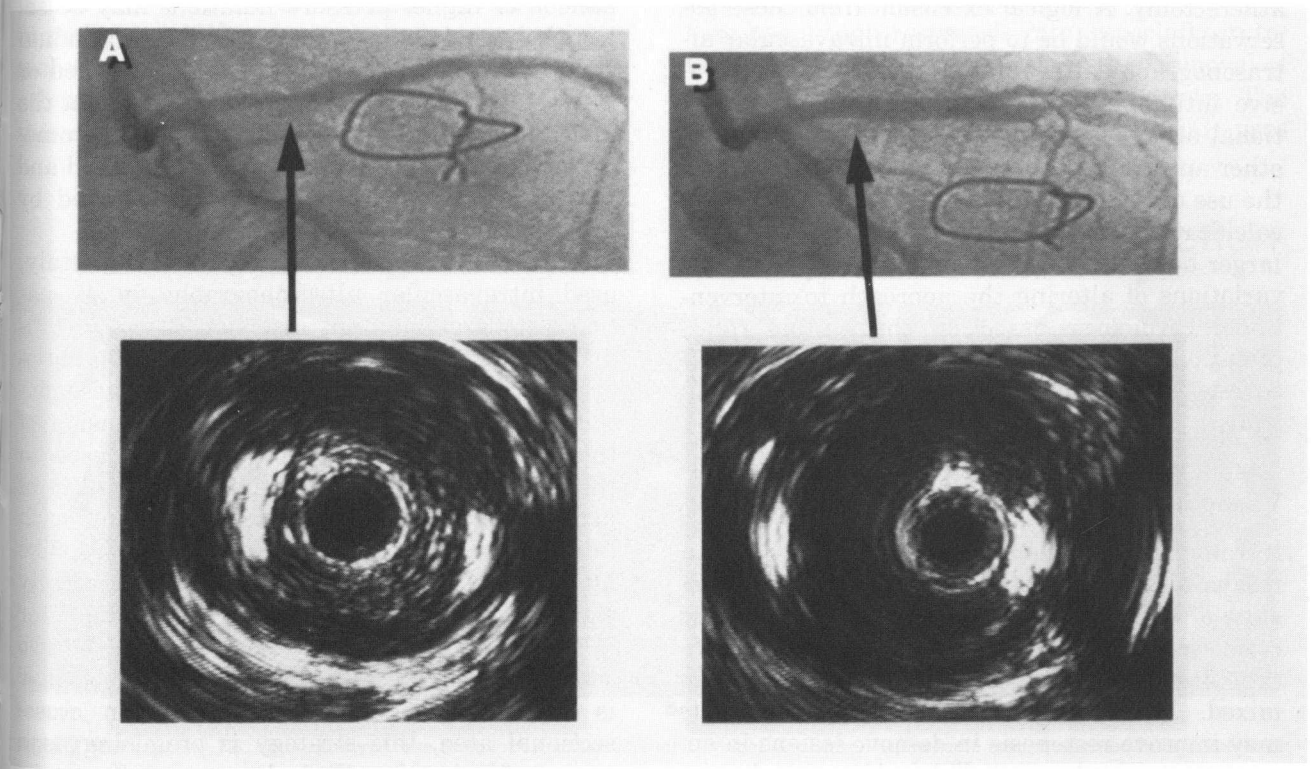

FIGURE 16. Directional atherectomy was performed in this patient who had previous balloon angioplasty with restenosis. **(A)** The proximal left anterior descending stenosis is shown before treatment. There is a near occlusive atherosclerotic plaque with two areas of calcification at 3 o'clock and 10 o'clock. **(B)** Following the atherectomy, the angiographic result was excellent. By intravascular ultrasonography, significant plaque removal was confirmed. There is removal of plaque up to the point of the calcification but not beyond. Attempts at further atherectomy would most likely lead to deflection of the cutter toward the normal vessel wall with removal of media and adventitia.

tion effect. Thus, similar to balloon angioplasty, restenosis after directional atherectomy may be a combination of vessel recoil as well as intimal hyperplasia (see article by Fitzgerald and Yock, p. 579 of this symposium).

Rotational Atherectomy

The effect of rotational atherectomy on plaque and vessel morphology as assessed by intravascular ultrasonography was studied by Mintz, et al.[39] Twenty-eight patients had intravascular imaging after successful rotational ablation. Seventy-one percent of these patients also had adjunctive balloon angioplasty. The residual plaque measured 54% of the arterial cross-sectional area. A considerable amount of calcified plaque remained despite the intervention, which may reflect patient selection. They identified calcified plaque in 78% of lesions after the procedure, with an average arc of calcification of 160° ± 126°. In four patients, they performed intravascular ultrasonic imaging before as well as after the interventions and noted a trend toward a decrease arc of calcium, from 211° ± 126° to 120° ± 83°. There was a distinct, sharp interface between calcified plaque and the lumen, which was felt to be characteristic of rotational atherectomy. A logical extension from these observations would be to perform intravascular ultrasonography after rotational ablation. If extensive intimal calcification is not present, directional atherectomy may be considered, provided other anatomic features are present that support the use of this device. If persistent and extensive calcification bordering the lumen is present, a larger burr size may be more appropriate. These variations of altering the approach to interventional cardiology based on the on-line interpretation of intravascular ultrasonic images is currently being assessed in randomized clinical trials.

Vascular Stents

Intra-arterial stents have been proposed as a means to improve both short- and long-term results of balloon angioplasty. Stents improve the cosmetic results of PTCA complicated by significant dissections, but data on restenosis remain mixed. Preliminary evidence suggests stents may improve restenosis in de-novo lesions in appropriately sized vessels.[40] In addition, subacute thrombosis, a problem unique to stents, remains a factor in 3% to 25% of cases. Full stent expansion with minimal exposure of metal into the lumen may diminish the risk of subacute thrombosis. Stent deployment has been studied by experienced operators using intravascular ultrasonography.[41]

Intracoronary ultrasonography may be useful to assess vessel size more accurately by allowing for a more precise final balloon selection in the deployment of the stent. Because the angiogram depicts the lumen but not the vessel size (defined as media to media diameter), it is not possible to gauge the vessel size at the site of the lesion with angiography alone. Evidence suggests that the amount of acute gain of an intervention is a strong predictor of the rate of restenosis,[42] therefore the use of a larger balloon to expand the stent may increase the lumen area and decrease the restenosis rate.[43]

After deployment of most stents, an improved angiographic lumen is usually seen but the stent itself may not be radiopaque. The metallic stent struts are easily seen by intravascular ultrasonic imaging (Figure 17). An assessment of adequate stent expansion may be made by identifying the position of the stent struts in relation to the vessel wall circumference. If the stent is not fully expanded, a larger balloon size may be considered. Compression of the stent by fibrous or calcific plaque may be seen. Utilization of a larger balloon or higher pressure inflations may be selected in an attempt to expand a short residual stenotic segment. A stenosis in an unstented or "minimally" stented segment of vessel, eg, at the articulation of a Palmaz–Schatz stent, or immediately adjacent to a stent, may be identified and more precisely measured and characterized by ultrasonography than by angiography.

Dr. Antonio Colombo, et al, in Milan, Italy, used intravascular ultrasonography in 40 patients undergoing stent insertion with the Palmaz–Schatz stent.[44] Despite an adequate angiographic appearance, only 5 (13%) of these patients were felt to have adequate expansion of the stent on initial ultrasonic imaging. Based on the initial ultrasound information, 29 (73%) of patients had further balloon dilatations with larger balloons or higher pressure inflations. The final ultrasonic images revealed a statistically significant increase in minimal lumen diameter (19%) and intrastent area (34%) between the two sets of images. Because resistance to blood flow is dependent on the minimum lumen cross-sectional area, this strategy is promising as a means of improving clinical outcome after stent insertion. A randomized clinical trial will be necessary to determine whether this strategy will lead to clinical benefits.

Development in software has allowed intra-

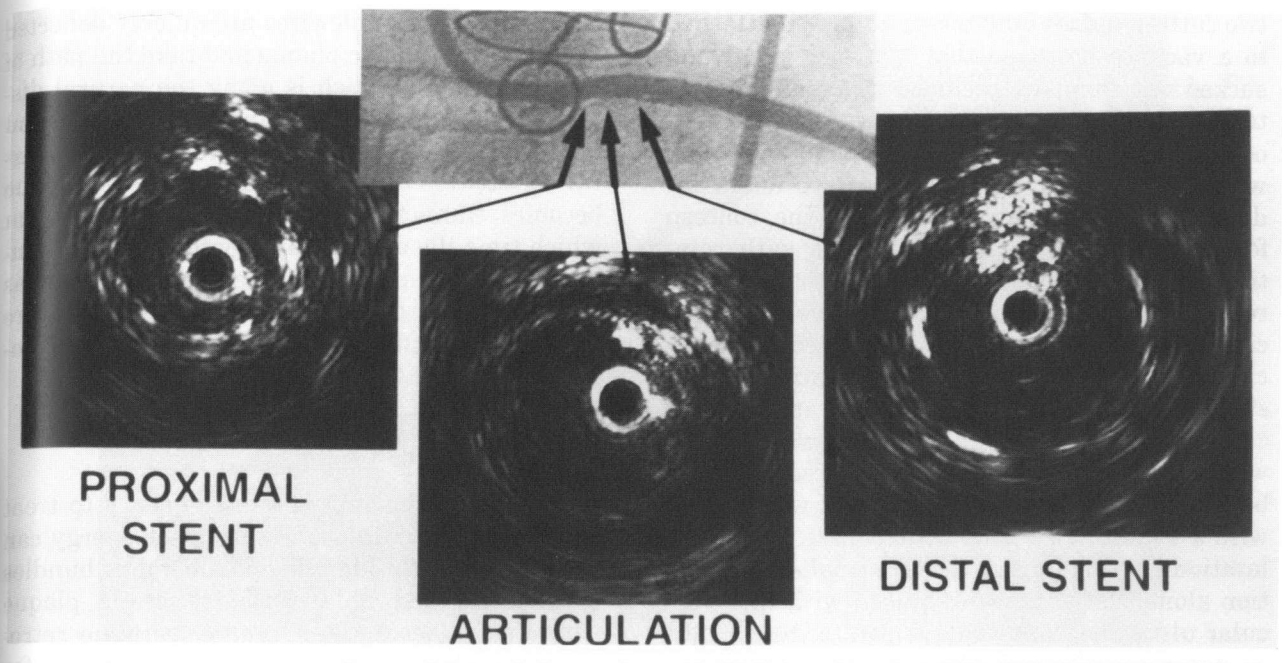

FIGURE 17. Post balloon angioplasty. A successful stent deployment imaged by IVUS. The echogenic metallic struts of the stent are fully apposed to the atherosclerotic plaque. However, the lumen area is still small, and a larger balloon size could be used based on the ultrasonic image guidance.

vascular ultrasonic images to be converted to three-dimensional representations of the vessel lumen and wall.[45] This may improve our ability to guide stent placement or to interpret newer techniques that are proposed to ablate or remove atheroma (see article by Mintz et al, p. 609 of this symposium).

TEC Atherectomy

Balloon angioplasty for peripheral vascular disease has a high restenosis rate, especially in total occlusions. One hypothesis is that removal of plaque may decrease the restenosis rate. The transcutaneous extraction catheter (TEC) uses

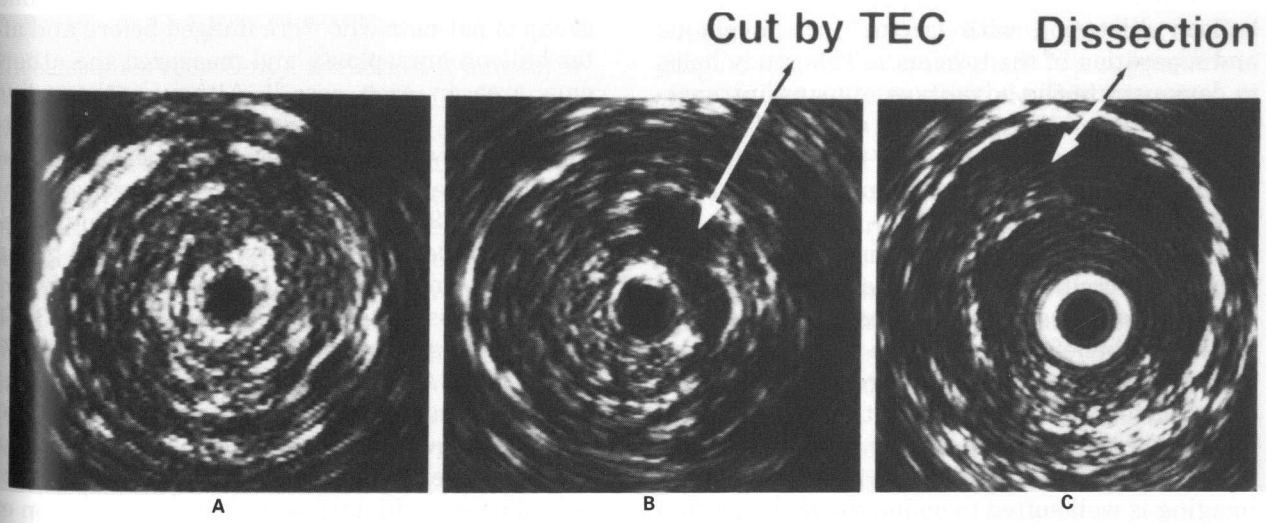

FIGURE 18. Peripheral TEC atherectomy: These three intravascular ultrasonic images were taken at the same section of an occluded superficial femoral artery that was reopened with a standard guidewire and catheter. **(A)** Following recanalization, a huge amount of fibrous plaque surrounds the catheter. At this place in the artery, the pathway of canalization was in the central portion of the plaque. **(B)** Following an atherectomy that was performed with a 2.7-mm TEC device. There has been some enlargement of the lumen and some excision of plaque shaped like a trough (arrow) from 11 o'clock to 1 o'clock. **(C)** Following balloon dilatation with a 7.0-mm balloon, there is fracture of the plaque through to the media with separation of the torn ends and dissection of the ends of the plaque away from the media (arrow). This produces a large increase in lumenal cross-sectional area in this segment.

two cutting blades with a central lumen attached to a vacuum bottle so that material is cut and sucked out from the occluded segment. The potential benefit of using this device is that a long occlusion could be treated relatively quickly without the repeated passes that are necessary during directional atherectomy or the concern for distal embolization of debris as with rotational atherectomy. To test the hypothesis that removal of a larger amount of plaque might decrease restenosis rate, patients with complete occlusion of the superficial femoral artery were studied with two different size TEC atherectomy catheters. One group of patients was treated with a 2.7-mm diameter TEC atherectomy plus balloon dilatation; the second group was treated with a 4.0-mm TEC atherectomy plus balloon dilatation. A third group received balloon dilatation alone. Patients were imaged with intravascular ultrasonography to quantitate the amount of material and residual lumen after each form of therapy. Although this randomized trial has not been completed yet, the observations obtained by intravascular ultrasonic imaging have been enlightening. Even when the angiographic results showed significant improvement in lumen diameter, intravascular ultrasonography revealed significant areas of residual stenosis with a large plaque burden. As demonstrated in Figure 18, the increase in lumen with the 2.7-mm TEC catheter is relatively small. The mean decrease in plaque cross-sectional area due to TEC atherectomy was only 11%. The major effect in increasing lumen cross-sectional area was due to balloon dilatation with fracture of the plaque and separation of the torn ends. This study helps to demonstrate the advantage of using intravascular ultrasonic imaging as a way of clarifying the mechanism of action of the various interventional devices and distinguishing an excision effect from a stretching effect.[46]

Previous work with intravascular ultrasonic imaging in occluded arteries that are recanalized either mechanically or by laser therapy has shown the benefit of using this technique to understand the mechanism of reopening an occluded artery.[47] Because the ultrasound catheter follows the pathway created by the guidewire in reopening the artery, this form of cross-sectional imaging is well suited to define the pathway that any of these devices take in reopening the artery.

The interesting observation from these studies is the recognition that the arteries are usually not reopened by the device going through the center of an occluded plaque. On the contrary, these devices or guidewires are quickly deflected from the fibrocalcific plaque and take the path of least resistance, which is along the natural dissection plane between the internal elastic membrane and the plaque itself. These devices burrow along this dissection plane until the plaque becomes thinner at a more distal segment, at which time the device may reenter the patent lumen. However, if the device is traumatic, such as a 200°C laser heated metal probe, it is more likely to perforate through the media and adventia once it is in this dissection plane.[48]

Excimer Laser

The rationale for applying laser energy to treat coronary artery disease is that laser energy can be transferred through flexible fiberoptic bundles to vaporize and ablate atherosclerotic plaque without the necessity of removing tissue retrograde via the catheter. The case selection for excimer laser angioplasty frequently involves lesions that are unsuitable for other techniques, such as directional atherectomy or balloon angioplasty. This is due to the length of the lesion, the location (such as the ostium), or diffuse disease. Based on the angiographic appearance, it has been assumed that the laser catheter vaporizes and ablates a significant amount of plaque.[49,50] Intravascular ultrasound technology provides a unique opportunity to assess this hypothesis in vivo.

We compared a group of patients who had excimer laser coronary angioplasty to a second group of patients who were imaged before and after balloon angioplasty and measured the atheroma area in each case.[51] Although these two groups were not randomly assigned, an interesting finding was that the mean atheroma cross-sectional area after excimer laser coronary angioplasty (8.9 mm^2) was similar to that found before any balloon angioplasty in the control group (8.7 mm^2). In addition, the mean ultrasonic percentage cross-sectional area stenosis was 73.7% following laser angioplasty compared to 68.8% for the PTCA group. This finding is consistent with our clinical experience that the majority of patients require balloon angioplasty following excimer laser radiation. Both groups then received balloon dilatation, and after completion of the procedure, the amount of residual plaque in the patients treated with excimer laser was no different than in the patients treated with balloon dilatation alone (Figure 18). With these observations from intravascular ultrasonography, it is not surprising to us that the restenosis rate

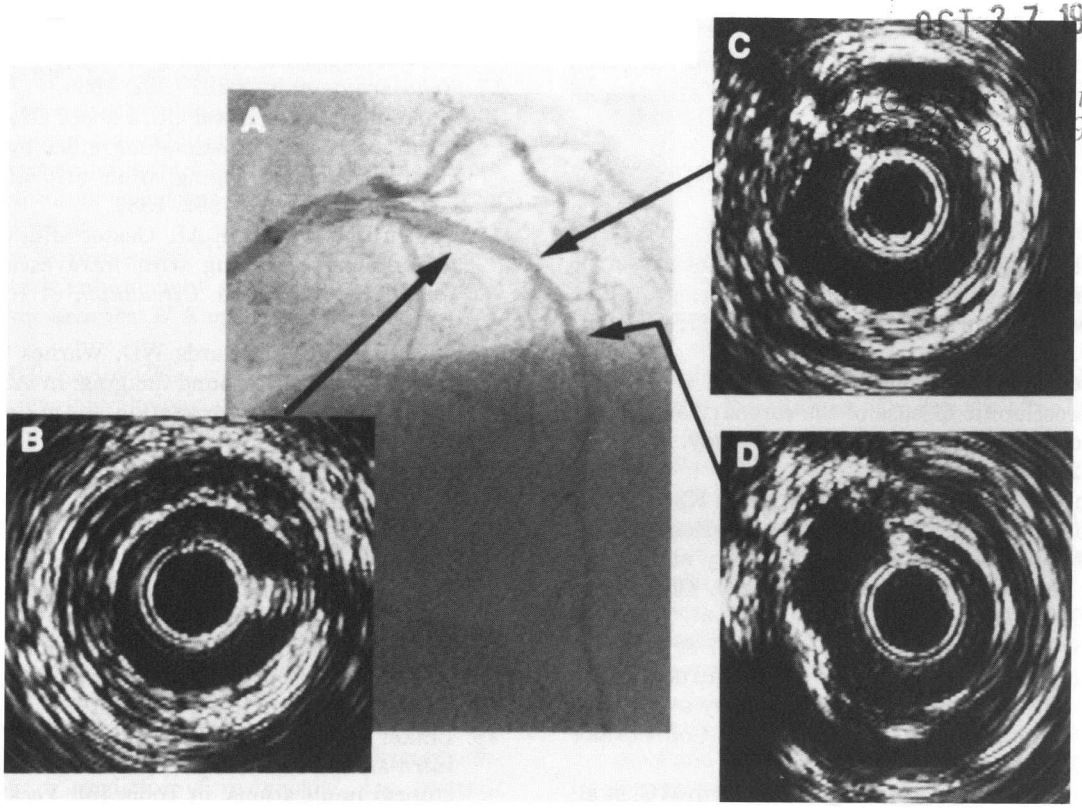

FIGURE 19. Results of an excimer laser angioplasty in a stenosis with a dense concentric atherosclerotic plaque after passage of a 1.7-mm laser probe. There was modest improvement in the vessel lumen both angiographically as well as by intravascular ultrasonography; however, the amount of atheroma ablation was small (see trough at 9 o'clock to 11 o'clock in panel D).

of excimer laser angioplasty is as high (if not greater) than PTCA alone.

CONCLUSIONS

These studies represent a paradigm of how intravascular ultrasonic imaging should be used to assess all technologies that claim to remove or ablate atherosclerotic tissue. The interpretation of angiographic results alone has been misleading and produces excessive enthusiasm, which is not justified when more accurate direct quantitative measurements of plaque area are performed with intravascular ultrasonography. It remains speculative whether eccentrically directed excimer lasers or other types of lasers will have a greater effect, especially if guided by intravascular ultrasonic imaging.

OTHER CLINICAL APPLICATIONS OF INTRAVASCULAR ULTRASONOGRAPHY

As newer interventional techniques are developed, a crucial question to answer is what impact these new technologies will have in alleviating the major problems associated with conventional balloon angioplasty. Intravascular ultrasonic imaging is extremely useful in diagnosing coronary stenoses when the angiographic findings are equivocal. It should be performed when there is a strong clinical suspicion with unclear angiographic findings or when there is a suggestion of stenosis but, due to multiple side branches or other anatomic problems, the stenosis is not completely defined. Poor angiographic results after PTCA can be caused by flaps or thrombus, and intravascular ultrasound may be useful in differentiating these.

Another exciting area of study is the use of this imaging technology to assess atherosclerotic regression prospectively in trials of diet or drug therapy. Because intravascular ultrasound directly visualizes the plaque, it should be more accurate and reveal changes sooner than angiography. It is likely that intracoronary ultrasonic imaging will become invaluable as a clinical tool in identifying specific coronary morphologic patterns that will assist in device selection, in directing therapy of the device, and in assessing the adequacy of the results. As the future of interventional cardiology advances into new technologies, intravascular ultrasound will provide

more insight in assessing in vivo results and should replace angiography as the gold standard for quantitative analysis of coronary atherosclerosis.

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