Title

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Intravascular Ultrasound Imaging

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Intravascular ultrasound imaging is a useful and promising modality that is capable of demonstrating the structure of blood vessel walls. It also provides a quantitative assessment of the amount of atheroma present that cannot be visualized by angiography. This article reviews the basic principles of intravascular ultrasound imaging and describes the clinical studies after balloon angioplasty evaluated by intravascular ultrasound imaging. (Trends Cardiovasc Med 1991; 1:305–311)

Coronary arteriography has been the standard method to evaluate the characteristics and significance of atherosclerotic lesions. Recent advances in catheter-based interventions, such as balloon angioplasty, mechanical atherectomy, placement of expandable stents, and laser angioplasty, have required a more precise method to assess arterial anatomy before and after these procedures. Although contrast angiography is relatively safe and easy to perform, an angiogram is a two-dimensional projection image of an irregular three-dimensional structure. Even when multiple projections are obtained, angiograms tend to underestimate the extent of atherosclerotic disease compared with histologic examination (Vlodaver et al. 1973). Angioscopy is another technique that has been used to evaluate atherosclerosis. Angioscopy identifies ulcerated plaques, intraluminal thrombus, and intimal flaps, but it does not provide quantitative information about the vessel structure beneath the inner surface, the extent of atheroma, or the thickness of the arterial wall (Forrester et al. 1987). An alternative technique that can quantify the amount of atherosclerosis and analyze plaque composition is high-

frequency ultrasound, which can be adapted to obtain cross-sectional images of the arterial wall. Epicardial echocardiography with a 12-MHz probe has been used to obtain cross-sectional arterial images (Hiratzka et al. 1986; Sahn et al. 1982; Yao et al. 1984). However, this technique is useful only in an open-chest preparation, which limits further clinical application. Catheter-based, intravascular ultrasound is a unique and promising modality that provides an alternative approach to obtain high-resolution images of the structure of blood vessel walls (Mallery et al. 1988; Pandian et al. 1988; Yock et al. 1988). These high-quality ultrasound images enable quantitative assessment of the extent of atheroma involvement of arterial walls as well as the characteristics of the arterial tissue with a lateral resolution accuracy of 0.4 mm and an axial resolution of 0.1 mm.

• General Description of the Catheters

There are four major devices that are currently available from the following companies: Cardiovascular Imaging Systems Incorporated (CVIS), Diasonics (in association with Boston Scientific Corporation), Endosonics, and InterTherapy Incorporated.

The CVIS catheter has a fixed 20-MHz ultrasound transducer with a mechanically driven rotating reflector system

that generates an image perpendicular to the longitudinal plane of the catheter. The ultrasound beam is reflected onto a rotating mirror revolving at 1500 rpm. The rotating reflector is shielded from the vessel by an acoustically translucent housing. The catheter is guided as a monorail system over a standard coronary angioplasty wire. The imaging electronics provide a 360° image of the vessel at frame rates between 15 and 30/s, depending on image depth.

The Diasonics device provides a 5-Fr disposable catheter enclosing a mechanically rotating driveshaft with an imaging console adapted for 20-MHz operation and 360° scans. The driveshaft rotates at 900 rpm to provide images at 15 frames/s. The catheter is passed over a guidewire as in a monorail system.

The Endosonics ultrasound catheter has a maximal diameter of 5.5 Fr (1.83 mm) at the tip with reduction to a 4.5-Fr shaft. This technology differs significantly from the other devices because the ultrasound transducer is a synthetic aperture 64-element phased-array system. The image is electronically produced by alternating the transducer elements, which operate at a frequency of 20 MHz. Because there are no rotating parts, the central lumen accommodates a 0.014-in. angioplasty guidewire.

The ultrasound imaging catheter used in the following studies was developed in conjunction with InterTherapy Inc., Costa Mesa, California. It consists of a single 20-MHz transducer on the distal end with a mirror at 45°, which reflects the beam perpendicular to the long axis of the catheter (Figure 1). This design permits imaging up to the surface of the catheter, since the initial transducer oscillations occur in the space between the transducer and the mirror. The catheter is connected to a motor-driven unit that rotates at 1800 rpm to provide real-time cross-sectional images at 30 frame/s. The 1.2-mm-diameter transducer subassembly is inserted through a 1.6-mm plastic introducing sheath to protect the arterial lumen from injury during movement of the catheter. Images are displayed in a two-dimensional format on a video monitor in real time and stored on a Super VHS videotape or archived onto a computer disk. A graphic display system with automatic calibration allows measurements of the vessel structures.

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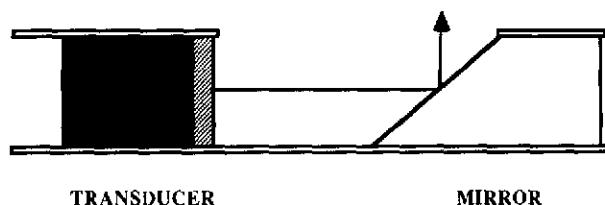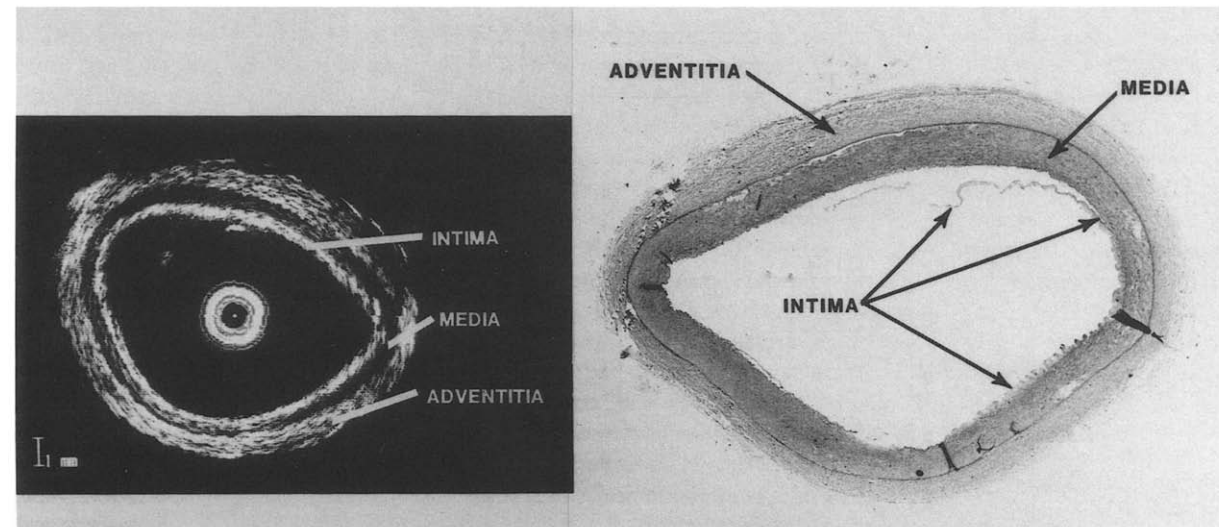
Figure 1. A schematic representation of the tip of the intravascular ultrasound imaging catheter transducer and mirror is shown. A single 20-MHz ultrasound transducer is located at the distal end of the catheter so that the ultrasound energy is transmitted against a mirror that deflects the sound waves perpendicular to the long axis of the catheter.

• Arterial Wall Thickness

In normal vessels, the lumen is seen as an echolucent space, whereas the arterial wall usually exhibits a three-layered appearance, which includes a highly reflective intima, an echolucent media, and a moderately reflective adventitia. Figure 2 shows an ultrasound cross-sectional image from a normal human carotid artery with an H&E histologic section of the same artery. The echolucent media is outlined centrally by a strong echo, which corresponds to the internal elastic lamina. The evidence that this bright echo is due to the internal elastic lamina is based on the observation that, in arteries with small to moderate eccentric atheroma, the bright echo is seen to extend behind the base of the atheroma but adjacent to the echolucent muscular media, which corresponds to the location of the internal elastic lamina on histologic examination. If this bright echo were produced by the tissue–fluid interface, it would be expected to be imaged persistently in front of the plaque where the tissue–fluid interface was present. Since this bright echo line is observed behind the plaque when an atheroma is present, it follows that this bright echo in normal arteries is caused by reflections from the internal elastic lamina and not the fluid–tissue interface. In a study of 17 human artery segments, each arterial cross section was measured in four orthogonal quadrants. The mean ultrasound and histologic measurements are compared in Table 1. There was a close correlation of intima thickness measured by the ultrasound catheter and histology ($r=0.91$). These results indicate the accuracy of ultrasound images compared with histology for measuring arterial intima, media, and total wall thickness. In certain situations, the ultrasound images cannot identify the plaque–media interface. This occurs in elastic arteries such as the aorta, where elastic fibers in the media reflect the echo signals. Inability to see the media also occurs in muscular arteries when the presence of severe atherosclerosis destroys the media (Nishimura et al. 1989). If the media cannot be identified, the thickness or cross-sectional area of the atheroma cannot be measured, but the images are still useful for measuring the cross-sectional lumen area.

• Tissue Characterization

Calcification is identified as very intense echo reflections of ultrasound with shadowing (that is, dropout of echo signals) of the distal wall. Fibrotic, noncalcified plaques are identified as intimal thickening of at least 0.25 mm without echo shadowing. Fibrous plaque is not as brightly reflective as calcium, and does not generate shadowing. Figure 3 demonstrates an ultrasound image from a diseased human carotid artery. The eccentric intimal plaque contains a small region of calcification at its base, which causes shadowing or dropout of echo information. The echolucent media is seen circumferentially. The corresponding histologic section shows a small area of dense calcium (thick arrow). The thin internal elastic membrane (thin arrow) generates a highly echogenic signal that

Figure 2. The ultrasound cross-sectional image from a normal human carotid artery is represented on the **left**. The central artifact corresponds to the intravascular catheter, which is surrounded by a black echolucent lumen. The intima is the first bright echoreflectant structure that overrepresents the thin intimal layer as seen on the accompanying histologic section. The muscular media layer of the artery is echolucent separating intima from adventitia. Adventitia consists of all echos originating peripheral to the media. From Tobis et al. (1989). Reprinted with permission from the AHA.

Table 1. Comparison of arterial wall measurements		
	Histology[a]	*Ultrasound*[a]
Intima	0.9 ± 0.8	1.2 ± 0.8
Media	0.4 ± 0.2	0.5 ± 0.2
Total wall thickness	1.7 ± 0.8	2.4 ± 0.8

[a]Mean ± SD in millimeters.

overestimates the true thickness of this structure.

Regions of necrotic liquid or lipid pools are identified as large echolucent areas within the plaque and are distinguished from calcium-induced dropout because the area is surrounded by tissue reflections. An ultrasound image from a severely diseased artery (Figure 4) demonstrates a large echolucent region bounded around its perimeter by echo reflections from the atheroma (arrow). The companion gross specimen shows the corresponding large space to the right of the lumen that contained liquid necrotic material (arrow). These studies indicate that intravascular ultrasound images can correctly identify various types of tissue within the arterial wall.

- **Ultrasound Imaging During Interventions: Balloon Angioplasty**

An ultrasound imaging catheter was used before and after balloon dilation in 13 human atherosclerotic artery segments in vitro, and the ultrasound and histologic images were analyzed for plaque tears and dissection. The postdilation image (Figure 5) demonstrates a plaque tear identified as a fracture of the intimal plaque with separation of the torn ends. The balloon dilation also appears to have created a new lucency separating the intimal plaque from the media. The corresponding histologic cross section from the artery segment demonstrates the intimal plaque fracture with sepa-

ration of the torn ends as well as separation of the plaque from the media. In most arteries studied, balloon dilation created a tear through the plaque, which typically was located through the thinnest region of the atheroma or at the junction of the plaque and normal artery wall. In 85% of the artery segments, the ultrasound images also demonstrated a dissection plane between the plaque and the internal elastic membrane. The artery was stretched in this torn region of the plaque, which resulted in enlargement of the internal lumen. Intimal flaps, where the torn atheroma projected into the lumen, were occasionally seen. The results from these studies suggest that intravascular ultrasound is capable of visualizing and quantifying human atherosclerosis before and after an intervention such as balloon angioplasty.

- **Clinical Trials**

Several clinical studies are now in progress by various research groups using intracoronary ultrasound to obtain images in patients who undergo balloon or excimer laser angioplasty, atherectomy, or stent implants. An intravascular ultrasound cross-sectional image from the mid-LAD is shown in Figure 6. The central white band represents the 1.6-mm plastic introducing sheath and encompasses the ultrasound catheter,

Figure 3. This photograph of an ultrasound image **(left)** and the corresponding histologic cross section **(right)** demonstrates calcium as a very echodense reflector with dropout of the echo signal behind the calcium at the base of the plaque. From Tobis et al. (1989). Reprinted with permission from the AHA.
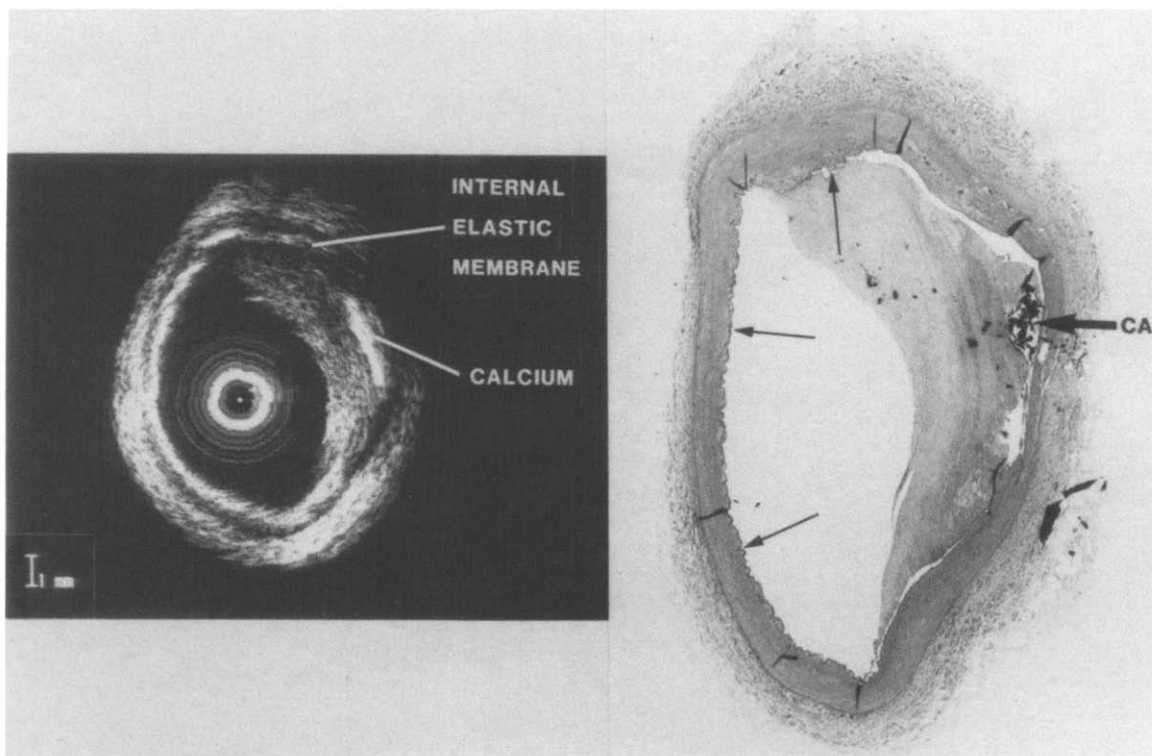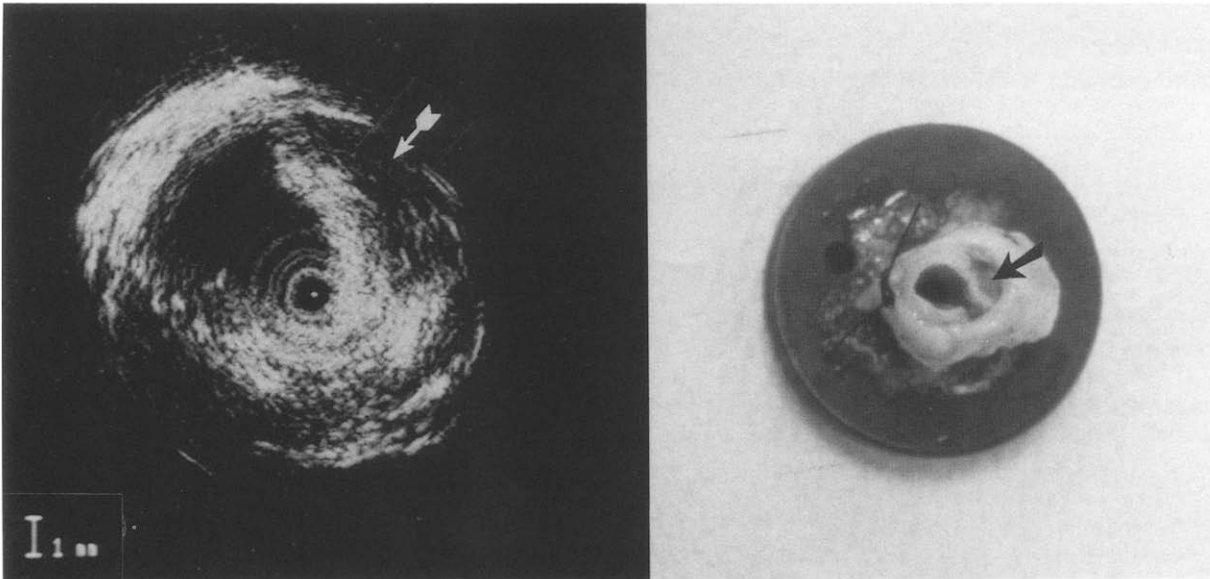
Figure 4. The ultrasound characteristics of necrotic liquid that was found within a human iliac artery. There is a large echolucent area bounded by fibrotic plaque and adventitia echoes. The companion gross specimen **(right)** shows the location of this material that was liquid, even at the room temperature. From Tobis et al. (1989). Reprinted with permission from the AHA.

which corresponds to the central black area. The lumen of the artery is demonstrated as a dark, echolucent area that surrounds the plastic sheath. The atheroma appears as a mildly eccentric plaque around the entire circumference of the artery with more intense echo reflections between 9 and 12 o'clock and at 5 o'clock. Based on the findings of the prior in vitro histologic studies, these intense echo reflections represent fibrosis with a small amount of calcification. The acoustic shadowing behind the echodense material at 5 and 12

o'clock is typical of calcification. The media is shown as an echolucent area (~0.2 mm wide) that surrounds the

echogenic atheroma. Beyond the media, we can see echogenic structures corresponding to adventitia, with poor distinction between the adventitia and surrounding tissues.

Figure 7 shows the angiogram and selected intravascular ultrasound images from a left circumflex artery. This patient had balloon angioplasty per-

Figure 5. The results of balloon angioplasty on a densely calcified and fibrotic human iliac artery. **(Left)** The ultrasound image before angioplasty demonstrates dense fibrocalcific plaque with dropout of echogenic information distal to the atheroma. There is an artifact at the base of each ultrasound image corresponding to the acoustic reference needle placed on the outside wall of the artery. **(Right)** The postangioplasty ultrasound image demonstrates dilatation of the lumen with tearing of the edges of the plaque and separation of the torn edges. In addition, there is a new echolucent area behind the dense fibrocalcific plaque at the top right-hand corner. This plane of dissection was also observed on the histologic cross section to extend behind the atheromatous plaque. The area of the atheroma that was torn was the thinnest section of the plaque, ~3–4 o'clock on the image. From Tobis et al. (1989). Reprinted with permission from the AHA.
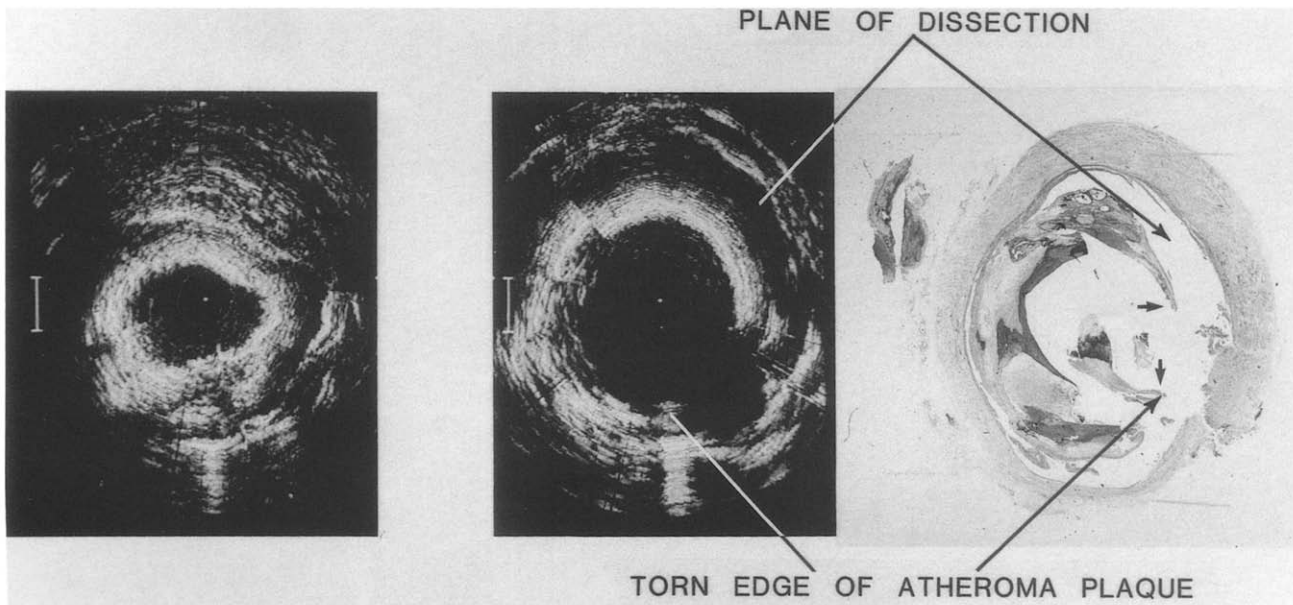
formed at the middle segment of the artery. The angiogram shows a successful balloon angioplasty result with the dilated region widely patent. At the angioplasty site, however, intravascular ultrasound imaging reveals a large amount of residual atheroma with a compromised lumen and a dissection behind the atherosclerotic plaque. In the two images of the proximal segments, a thin rim of intima can be seen. In the top right image, an eccentric atheroma is demonstrated despite the fact that this segment appears normal by angiography.

These preliminary studies demonstrate that intravascular ultrasound devices provide real-time cross-sectional images of human coronary arteries in vivo. Not only is it possible to observe the eccentricity of the plaque relative to the cross-sectional area of the artery, but it is also feasible to quantify the cross-sectional area of the lumen and the atheroma plaque. As noted during the in vitro studies, the in vivo ultrasound images are capable of distinguishing certain characteristics such as fibrous tissue, calcification, and lipid or necrotic material within the atheroma plaque. Angiography does not provide this kind of cross-sectional analysis. Even if an
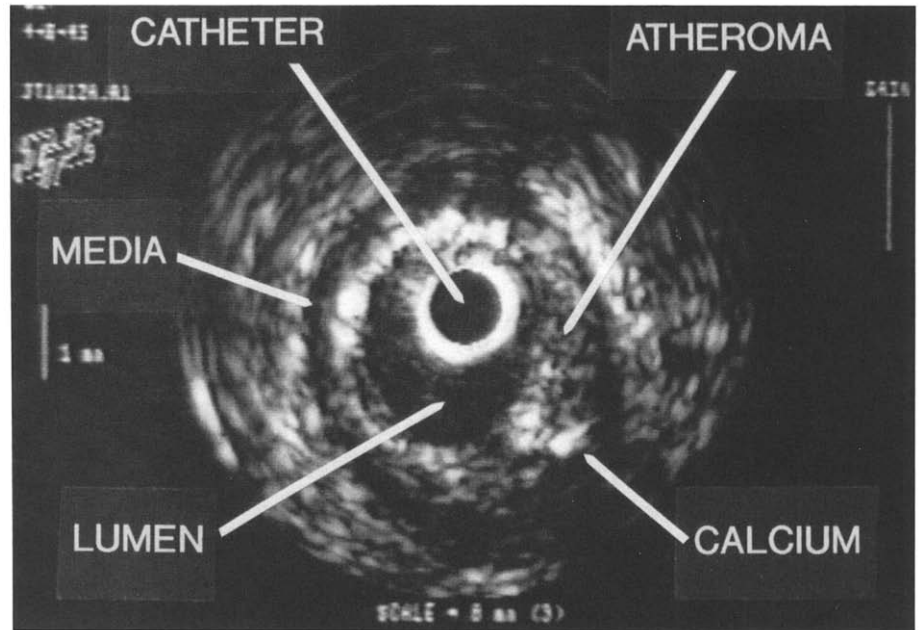
Figure 6. A representative intravascular ultrasound image from the mid-LAD from a patient who underwent balloon angioplasty. This ultrasound image was taken from a section of the artery that appeared normal on angiography. From Tobis et al. (1989). Reprinted with permission from the AHA.

Figure 7. Composite angiogram and ultrasound images from a left circumflex artery after balloon angioplasty. The two images on the **left** show a thin rim of intima at the proximal segment. In the **top right** image, an eccentric atheroma is seen despite the fact that the segment appeared normal by angiography. Significant residual atheroma with a compromised lumen and dissection plane behind the atheroma is demonstrated by ultrasound imaging.
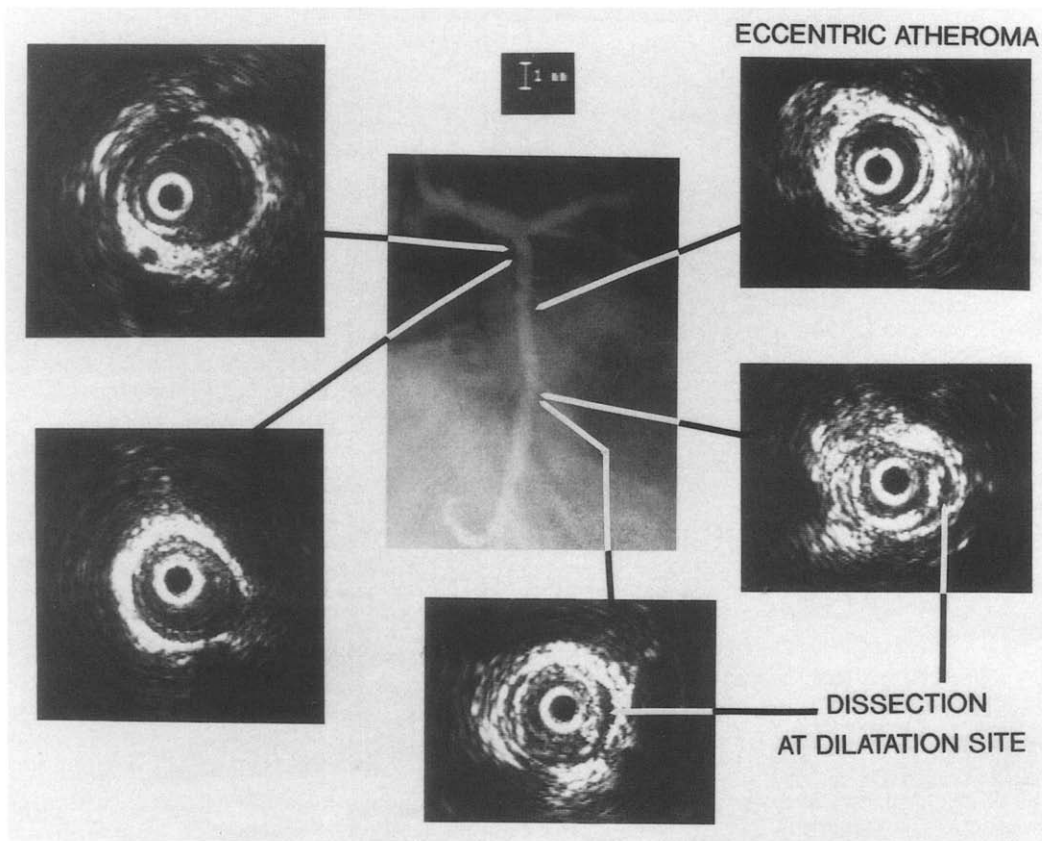
	Lumen cross-sectional area	Atheroma area	% Stenosis
Dilated site (n=40)	4.9 ± 2.2 mm²	8.2 ± 3.4 mm²	61.8 ± 16.0
Nondilated site (n=45)	9.2 ± 6.0 mm²	5.6 ± 3.8 mm²	40.9 ± 20.3

angiogram appears normal, the ultrasound images often reveal atheromatous involvement of the wall. It is common to recognize a small amount of calcification within the atheroma by ultrasound, but not by angiography. The images taken by intravascular ultrasound at areas of dissection are complimentary to angiography and often provide further information than is apparent by angiography. In addition, the sites at which angiography show a hazy appearance often correspond to the presence of dissection and reveal a much smaller cross-sectional lumen on ultrasound imaging than was demonstrated by angiography.

Angiography underestimates the amount of atheroma compared to cross-sectional ultrasound images. In the segments of the artery that were considered normal on angiography, the ultrasound images demonstrated that atheroma plaque encompassed a mean of 41% of the cross-sectional area. These findings from the ultrasound images in vivo are consistent with previous pathologic studies that suggest that angiography underestimates the amount of atherosclerosis within the arterial wall (Waller and Roberts 1980). The results of these intravascular ultrasound studies may explain why angiography is not reliable in predicting the subsequent progression to occlusion in arteries with mild-to-moderate disease as defined by angiography (Little et al. 1988).

• **Clinical Problems and Future Directions**

The information derived from the ultrasound images might alter the operator's decision regarding further intervention. If intravascular ultrasound images demonstrate a more compromised lumen than is appreciated on angiography, the operator might choose to perform further balloon dilatation or use another method of intervention. Table 2 shows the measure-

ments of the lumen and atheroma cross-sectional area documented by ultrasound in 40 patients. Intravascular ultrasound images revealed a large amount of residual atheroma at the site of balloon angioplasty in all cases. In this study, the mean cross-sectional area of the atheroma post dilation was 8.2 ± 3.4 mm², which represented 61.8 ± 16.0% of the available arterial cross-sectional area inside of the media. The present type of intravascular imaging devices have several limitations. The diameter is currently 1.6 mm, which is adequate for imaging small structures such as coronary arteries following balloon dilation. However, this device would be occlusive for most symptomatic stenoses before dilation. Much effort is now being devoted to construction of an ultrasound assembly that is 1.0 mm in diameter and can fit into a 1.3-mm sheath. In addition, a rapid-exchange catheter system (similar to the Monorail) is being developed. Because the presence of thrombus or minute air bubbles between the transducer and the mirror severely impairs image quality, frequent flushes with warm saline are required to prevent adherence of blood or air bubbles. Future models will be able to record the position of the ultrasound catheter during fluoroscopy simultaneously with the ultrasound images on the same video monitor to assist in correlating the cross-sectional images with the position on the angiogram from which they were derived.

Refinement in ultrasound catheter technology is directed toward development of lower profile, flexible catheters for coronary imaging, as well as slightly larger catheters with a lower frequency for intracardiac imaging. The combination of imaging with various therapeutic modalities such as balloons, atherectomy, and lasers is being developed (Aretz et al. 1989; Yock et al. 1989). Production of not only a side-viewing, but also a forward-looking, ultrasound catheter could be very useful in assessing the characteris-

tics of the atheroma in front of the catheter tip without crossing the lesion. It is also necessary to continue to improve image resolution and reduce signal artifacts. In addition, three-dimensional reconstruction of vessel segments is progressing with the use of current computer image-processing technology (Burrell et al. 1990).

• **Conclusion**

Intravascular ultrasound imaging is feasible and promising as a method for distinguishing normal and diseased arterial wall structures. High-quality ultrasound images enable not only quantitative assessment of the extent of atheromatous involvement of arterial walls, but also qualitative analysis of the tissue characteristics. Development of this technique, which can be performed percutaneously in the catheterization laboratory, is the dawn of a new era that will supplement traditional angiographic methods for evaluating the severity of coronary, carotid, or peripheral artery disease.

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