

Application of a New Phased-Array Ultrasound Imaging Catheter in the Assessment of Vascular Dimensions

In Vivo Comparison to Cineangiography

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Tomographic imaging techniques such as ultrasound can provide important information in the evaluation of vascular anatomy. Recent technical advances have permitted fabrication of a small (1.83 mm), phased-array, intravascular ultrasonic imaging catheter capable of continuous real-time, cross-sectional imaging of blood vessels. We used this imaging catheter to compare intraluminal ultrasound with cineangiography in the measurement of vascular dimensions in animals and to assess the intraobserver and interobserver variability of the technique. Segmental deformation of vessel anatomy was produced by stenoses created with a tissue ligature or by balloon dilation. The mean value for measurements of vessel diameter was 5.6 mm by cineangiography and 5.7 mm by intravascular ultrasound. The correlation between cineangiography and ultrasound was close ($r=0.98$). Mean cross-sectional area by angiography was 28.8 mm^2 and 29.6 mm^2 ($r=0.96$) by ultrasound. Percent diameter reduction produced by the stenoses averaged 48.4% by cineangiography and 40.1% by ultrasound, and the two methods correlated closely ($r=0.89$). Correlation between cineangiography and ultrasound for vessel diameter and area before balloon dilation was closer ($r=0.92$ and 0.88) than after balloon dilation ($r=0.86$ and 0.81). This difference reflected an increase in measured vessel eccentricity following balloon dilation. These data demonstrate that intravascular ultrasound is an accurate and reproducible method for measurement of vascular diameter and cross-sectional area in vivo. Intravascular ultrasound is capable of accurately identifying and quantifying segmental deformation of vascular dimensions produced by either stenoses or balloon dilation. (*Circulation* 1990;81:660–666)

Tomographic imaging by ultrasound techniques has played an important role in defining vascular anatomy for carotid and peripheral arterial atherosclerosis. However, attenuation of high frequency ultrasonic energy and limited resolution have prevented percutaneous ultrasound from visualizing small vessels within the thorax and abdomen. Recent developments in microelectronic and piezoelectric technology have permitted the fabrication of ultrasound devices capable of intraluminal tomographic imaging of vessels. In fact, technical advances have now enabled the miniaturization of a multiele-

ment ultrasonic transducer to fit on a 5.5F catheter (Figure 1). These devices offer the promise of precise definition of both intravascular size and anatomy of the vessel wall.

Despite the enormous potential of intraluminal ultrasound, few data exist regarding the feasibility and accuracy of these techniques in defining vascular anatomy, particularly *in vivo*. Therefore, the following study was undertaken to define the ability of an intravascular ultrasound catheter system to quantify the cross-sectional size of peripheral arteries *in vivo*. Specifically, we compared diameter and cross-sectional area (CSA) measurements of peripheral vessels in experimental animals obtained by an ultrasound imaging catheter with those provided by direct cineangiography.

Methods

Animal Preparation

Studies were performed in eight mongrel dogs and two minipigs weighing 15–30 kg. Although it was

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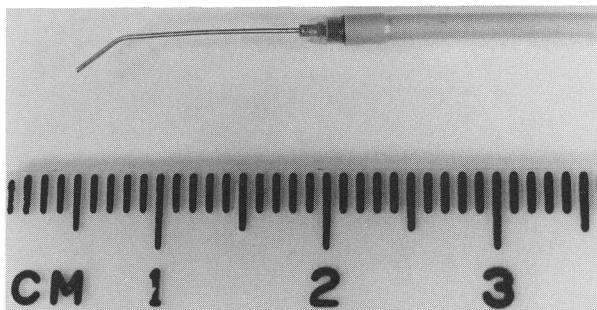


FIGURE 1. Photomicrograph of intravascular imaging catheter. A 0.014 in. steerable angioplasty guidewire is shown extending beyond catheter tip. Ultrasonic transducer elements are seen just proximal to catheter tip.

planned to use dogs for all experiments, their limited availability necessitated the use of minipigs, which were more readily obtained. The animals were anesthetized with morphine and chloralose-urethane or pentobarbital, mechanically ventilated, and anticoagulated with heparin (200 units/kg). A 6–8F sheath was placed in the femoral or carotid artery via a surgical cutdown. In five animals, an extensive dissection was performed exposing the iliac artery or aorta, and stenoses were produced by banding the vessel with a tissue ligature fashioned from femoral nerve. Tension was placed on the two ends of the ligature until a stenosis was produced that was fixed by securing the ends of the nerve segment with a hemostat. In five dogs, an 8F Fogarty balloon catheter was inflated in the iliac artery to produce a localized dilation of the vessel.

Angiographic Methods

A contrast angiogram was obtained for each vessel site imaged with the ultrasonic catheter (Figure 2). Cineangiography was performed during hand injection of 1–5 ml iodinated contrast (Renografin-76[®]) via either the arterial sheath or an angiographic catheter placed proximal to the imaging site. The radiographic system consisted of an image intensifier with a 5-in. field of view and a 35-mm camera operating at 30 frames/sec. A radiographic dose of approximately 30 μ R/ frame was used. A standard radiographic grid was filmed to correct for radiographic magnification. For balloon dilation sites, an angiogram was performed before and after balloon inflation (Figure 3).

Intravascular Ultrasound

In this study, we used a 32-element array, 5.5F (1.83 mm) intravascular ultrasound catheter system (Endosonics Corp, Rancho Cordova, California). The prototype catheter incorporates a central lumen that accommodates a 0.014-in. steerable angioplasty guidewire to facilitate safe positioning (Figure 1). Operating at a frequency of 20 MHz, the catheter transducer is capable of displaying real-time (12 frames/sec), 360° intravascular ultrasound images on a video monitor and transferring these images to a

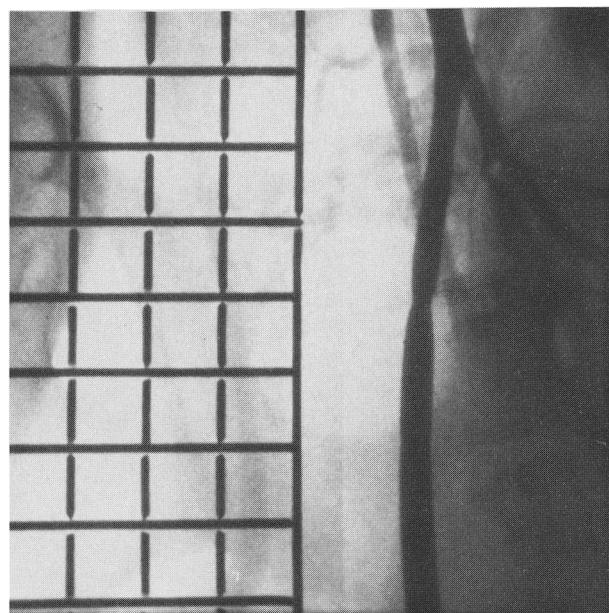


FIGURE 2. Contrast angiogram of iliac artery in a dog with an artificially produced stenosis. The radiographic grid used to correct for magnification is also shown. Each small square represents 10 mm.

½-in. videocassette for archiving. This phased-array device differs from other intravascular ultrasound devices now undergoing preliminary testing that employ mechanical rotation of the ultrasound beam.^{1–5}

Operator-selectable controls were available to alter the gray scale of the ultrasound image and to



FIGURE 3. Contrast angiogram of iliac artery in a dog following balloon angioplasty. Deformed ectatic area of the vessel is apparent.

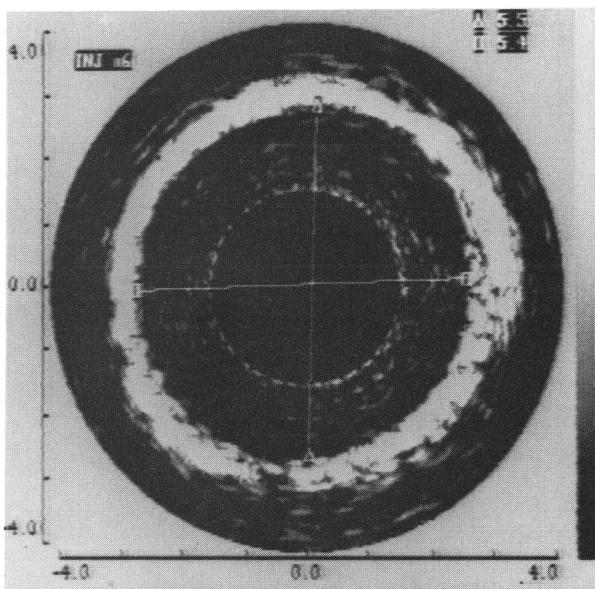


FIGURE 4. Representative image obtained *in vivo* from phased-array intravascular catheter. Bright central circle is a catheter transducer artifact. Larger outer circle represents the artery.

permit frame-averaging to improve image quality. Frame-averaging did not appear to substantially augment image quality and was therefore not employed during measurements for this study. In general, operator adjustments resulted in only small modifications of the image obtained.

The ultrasound catheter was inserted via one of the arterial sheaths under fluoroscopic guidance. A 0.014-in. angioplasty guidewire, inserted through a central lumen, was advanced beyond the tip. The guidewire facilitated manipulation of the catheter and maintenance of an optimal orientation to the vessel wall. Movement of the catheter and guidewire to a position as near as possible to the center of the vessel was frequently required to obtain a high quality 360° image (Figure 4). When an acceptable image was obtained, it was archived on ½-in. videotape for subsequent review.

For the extrinsic stenoses, the catheter was positioned under ultrasonic guidance at the point of minimum vessel diameter and in an adjacent normal segment and images were recorded (Figure 5). At vascular sites subjected to balloon dilation, ultrasound images were acquired at the selected site before balloon inflation. This site was then tagged with a radiopaque marker and an ultrasound was obtained from the same site following one or more balloon inflations (Figure 6).

Ultrasound Calculations

When a satisfactory image was obtained with the intravascular ultrasound catheter, a video freeze-frame was acquired. The vessel diameter was measured in three separate planes that bisected the vessel by visually placing a cursor on opposite sides of

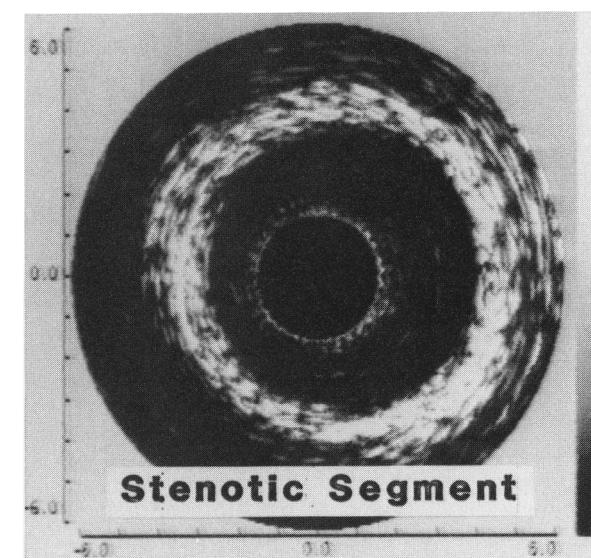
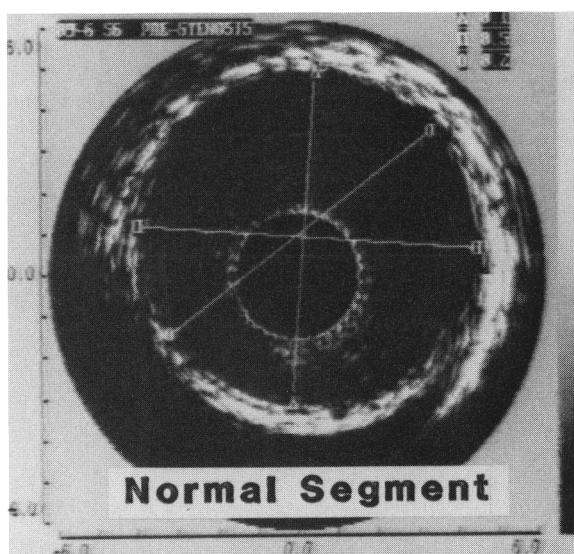


FIGURE 5. Vessel appearance by intravascular ultrasound for stenotic segment and normal adjacent segment. This stenosis represents a 22% diameter reduction and a 39% cross-sectional area reduction.

the artery. These three measurements were averaged to obtain a mean vessel diameter. CSA was determined by tracing the inner border of the endothelium with a trackball. Measurements of diameter at 11 vascular sites were evaluated by a single observer on three separate occasions to evaluate intraobserver variability. At 11 other locations, the vessel diameter was evaluated by three separate observers.

Angiographic Measurements

For each vascular site, the cineangiograms were projected on a ground glass screen using a back projection method without rotating mirrors or other potentially distorting optical devices. Vessel diameter was measured using calipers to the nearest 0.5 mm. Because the ultrasound catheter was radiopaque, it

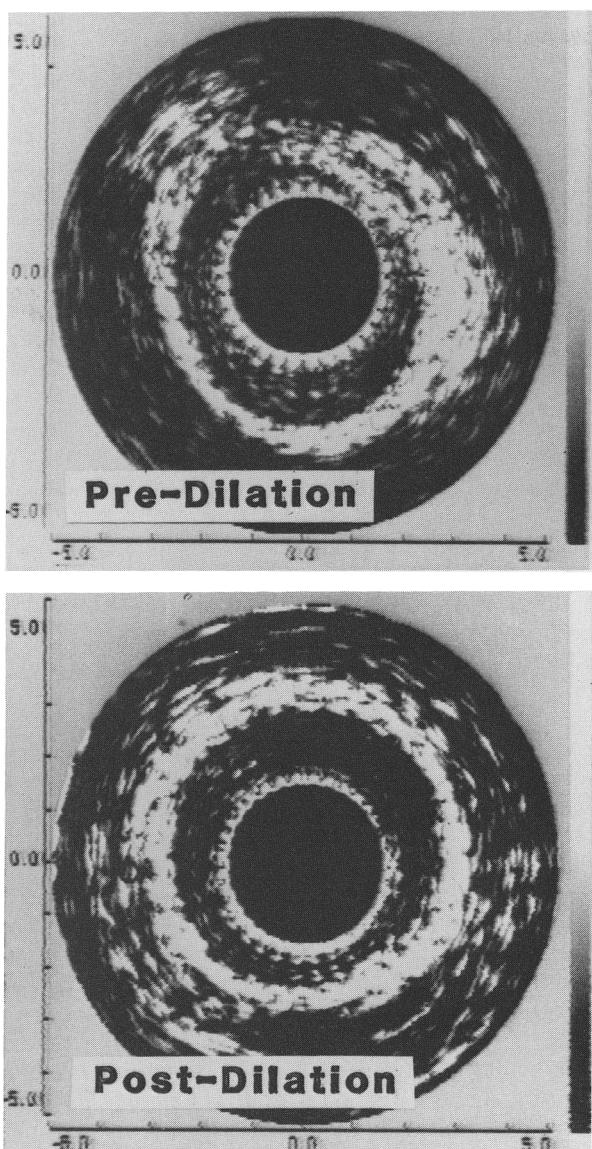


FIGURE 6. Representative intravascular ultrasound of a vascular site before and after balloon angioplasty.

was possible to make ultrasonic and angiographic measurements at the identical site. In the case of stenoses, angiographic diameter was measured both at the stenosis and the normal adjacent vessel segment. For the balloon dilation sites, vessel diameter by cineangiography was measured before and after bal-

loon inflation. In addition to angiographic measurement of diameter, CSA was calculated geometrically using the formula area = πr^2 (where r = radius).

Statistical Analysis

Mean values for vessel diameter and CSA derived from the ultrasonic catheter and cineangiography were compared using linear regression analysis. The mean difference in the measurement of vessel size between intravascular ultrasound and cineangiography was also determined. As a measurement of intraobserver and interobserver variability, each of the three diameter measurements were compared and a standard deviation was computed. For the stenoses, measurements of diameter and CSA reduction by angiography were compared with ultrasound by linear regression analysis. For animals subjected to balloon dilation, vessel diameter and CSA by ultrasound and cineangiography were compared by linear regression analysis before and after dilation.

Results

The ultrasound catheter was easily introduced, readily manipulated, and images were successfully obtained in all animals. No untoward effects were noted during manipulation of the catheter. The image quality was variable and dependent on catheter orientation in the vessel. The best images were obtained with the catheter centrally located in the vessel and orthogonally positioned with reference to the vessel long axis. Advancement of the central lumen guidewire several centimeters beyond the catheter tip was frequently helpful in stabilizing the catheter position and enhancing image quality.

Intraobserver and Interobserver Variability

Intraobserver and interobserver variability were measured for 11 arterial sites. For vessel diameter, the average of the standard deviation for three measurements by the same observer was 0.10 mm. For observations of vessel diameter performed by three separate observers, the standard deviation between observers averaged 0.12 mm.

Vessel Dimensions

Vessel diameter ranged from 3.1 mm to 11.0 mm (mean, 5.6 mm) by cineangiography, and ranged from 3.4 to 10.7 mm (mean, 5.7 mm) by intravascular ultrasound (Figure 7). Linear regression analysis

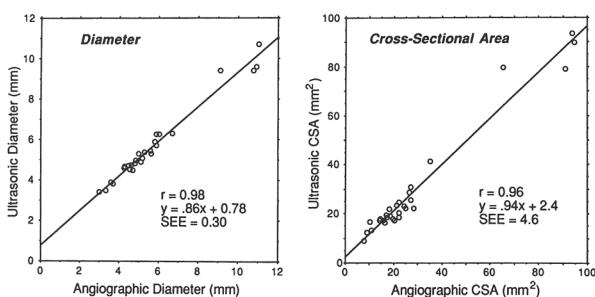


FIGURE 7. Plots of linear regression analysis comparing diameter and cross-sectional area by intravascular ultrasound to similar measurements performed by angiography.

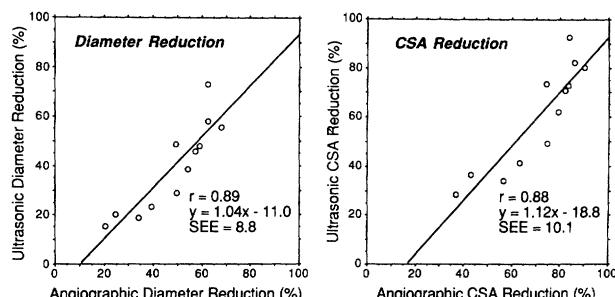


FIGURE 8. Plots of linear regression analysis comparing luminal diameter and area reduction by intravascular ultrasound and angiography for artificially induced stenoses.

revealed a close correlation between cineangiography and ultrasound ($r=0.98$). The regression equation was close to the line of identity ($y=0.86x+0.78$), and the standard error of the estimate (SEE) was small (0.3 mm). The mean difference between cineangiography and intravascular ultrasound was small (0.28 mm), a difference that represented a discrepancy of $\pm 5.0\%$.

CSA measurement by cineangiography ranged from 7.6 mm² to 94.9 mm² (mean, 28.8 mm²), while intravascular ultrasound yielded values of 9.1 mm² to 89.9 mm² (mean, 29.6 mm²). The correlation between cineangiographic and ultrasonic measurement of CSA was close ($r=0.96$), the regression equation was near to the line of identity ($y=0.94x+2.4$), and the SEE was 4.6 mm² (Figure 7).

Vessel Stenoses

For 12 stenoses, the diameter by cineangiography was 20.6–68.2% (mean, 48.4%), and by ultrasound was 15.3–72.9% (mean, 40.1%). There was a close correlation between angiographic and ultrasonic lesion severity ($r=0.89$) (Figure 8). The regression equation was close to the line of identity ($y=1.04x - 11.0$; SEE, 8.8%).

CSA reduction ranged from 36.9% to 89.9% (mean, 69.9%) by angiography and 28.3% to 92.7% by ultrasound (mean, 60.4%). The correlation between angiography and ultrasound in the measurement of CSA reduction was also close ($r=0.88$; $y=1.12x - 18.8$; SEE, 10.1%).

Balloon Dilation

Mean vessel size before balloon dilation was 5.3 mm by cineangiography with a range of 4.3–6.6 mm. The same sites measured by ultrasound had a mean diameter of 5.4 mm with a range of 4.5–6.3 mm. There was a close correlation between cineangiographic and ultrasonic diameter measurements before balloon dilation, $r=0.92$ (Figure 9). CSA before balloon dilation averaged 22.6 mm² by cineangiography with a range of 14.7–35.5 mm². Area by ultrasound for these same preangioplasty sites averaged 22.9 mm² with a range of 15.9–30.8 mm². The correlation for CSA preangioplasty between cineangiography and intravascular ultrasound was close

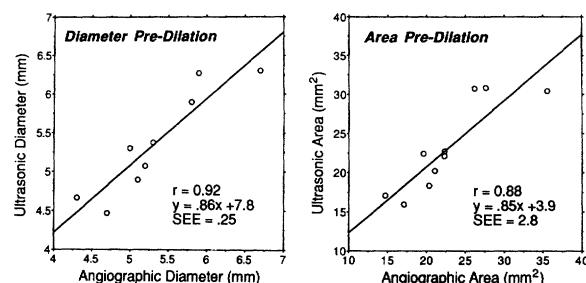


FIGURE 9. Plots of the comparison of vascular diameter and area by intravascular ultrasound and angiography before balloon dilation.

($r=0.88$) (Figure 9). After balloon dilation, the mean diameter increased to 6.6 mm with a range of 5.6–7.4 mm by cineangiography, while the mean diameter by ultrasound was 6.7 mm with a range of 5.7–7.7 mm. The correlation for diameter measurements between cineangiography and intravascular ultrasound after balloon dilation was $r=0.86$ (Figure 10). After dilation, mean CSA by cineangiography increased to 35.6 mm² with a range of 25.2–46.2 mm². CSA at these same sites by intravascular ultrasound increased to a mean of 34.0 mm² with a range of 24.3–43.8 mm². The correlation between cineangiography and intravascular ultrasound for CSA after balloon dilation was $r=0.81$ (Figure 10).

The correlation for vessel size was closer before than following balloon dilation. Examination of the images indicated an increase in vessel eccentricity after balloon dilation. The mean difference between measurements of the largest and smallest vessel dimension by ultrasound was 0.34 mm before dilation and 0.57 mm after dilation ($p<0.05$). This increased eccentricity was easily detected by intravascular ultrasound, but represented a confounding variable for single-plane cineangiography, and may account for the slightly lower correlation between cineangiography and ultrasound after dilation.

Discussion

Tomographic imaging techniques such as ultrasound provide additional information to contrast radiography in the definition of vascular structures, including the ability to visualize the lumen circumference and the vessel wall. However, few data are currently available regarding the applicability of these devices. The results of our studies establish both the feasibility of this approach to *in vivo* intravascular imaging and the accuracy of the measurements of intraluminal size, which are derived.

A variety of approaches have been taken in the development of intravascular ultrasound instruments. One approach uses the catheter tip transducer that is mechanically rotated to obtain a 360° cross-sectional scan of the vessel.^{1–5} Depending on the rotational speed and image processing capability of the acquisition device, these mechanical systems may be capable of continuous real-time display or may present images reconstructed on a delayed basis.

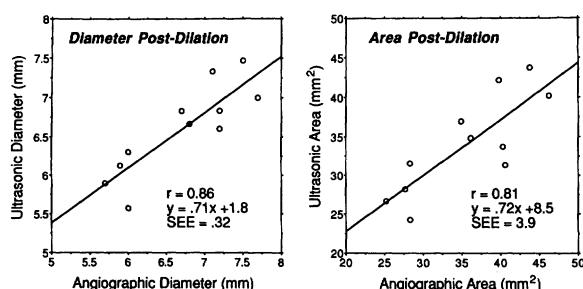


FIGURE 10. Plots of the comparison of vascular diameter and cross-sectional area by ultrasound and angiography after balloon dilation.

An alternate approach uses a multielement array to produce an intravascular image.⁶⁻⁷ In this study, we used a new 32-element, 5.5F array ultrasound catheter. The system accommodates a steerable angioplasty guidewire for vascular placement and provides a continuous real-time, cross-sectional display of the vessel under examination.

In this study, we compared *in vivo* measurements of intraluminal dimensions by ultrasound with those obtained by cineangiography. Previous studies have described limitations in the ability of cineangiography to assess vascular anatomy, particularly in the presence of eccentric atherosclerotic obstructions.⁸⁻¹¹ However, in the present study, we avoided these limitations of cineangiography by studying normal vessels free of significant curves. Further, we used high quality angiographic equipment in small animals so that impediments to radiographic transmission were avoided. Therefore, the radiographic images with which intravascular ultrasound data were compared in this study are representative of optimal cineangiographic performance.

Our initial experience in the manipulation and positioning of the nonmechanical intravascular ultrasonic catheter revealed that the device was generally comparable with standard catheters of similar diameters. Thus, the catheter was readily advanced and positioned within the vessels studied. In contrast to excellent maneuverability, we encountered difficulties in continuously visualizing vessel walls during catheter movement. To obtain high quality images, it was necessary for the ultrasound beam to be perpendicular to the vessel wall. The sensitivity of imaging to beam orientation was related to the low energy level of the high frequency signal. This observation was substantiated by the difficulties encountered in imaging vessels larger than 12 mm in diameter. Nevertheless, the imaging capability proved adequate for localization of minimal and maximal vessel diameter in stenotic and dilated arterial segments, respectively.

The ability to reproducibly determine the borders of structures is fundamentally related to the quality of any imaging system. The intraobserver and interobserver variability for the measurement of vascular diameter by ultrasound catheters observed in this study was low. These data demonstrate that the

images provided consistent localization of endothelial borders and that the technique is highly reproducible.

The accuracy of intravascular ultrasound in the measurement of vascular dimensions was assessed by comparing ultrasonic and cineangiographic images obtained at identical vascular sites in normal vessels. Vessel diameter measurements derived from the ultrasound catheter correlated closely with those obtained by cineangiography over a range of values. Area measurements derived directly from ultrasound compared favorably to those computed geometrically from cineangiography. This finding was probably related to the fact that normal circular vessels were imaged in which diameter enabled accurate calculation of area.

The ability of intravascular ultrasound to quantify vascular dimensions was also assessed in the presence of segmental distortions of vessel size induced by stenosis or dilatation. The correlation of ultrasonic and cineangiographic measures of luminal reduction produced by a tissue ligature (femoral nerve) was close for diameter ($r=0.89$) and CSA ($r=0.88$). Localized balloon dilation was used to produce segmental increases in intraluminal size. Again, measurements of vessel diameter and CSA obtained by intravascular ultrasound and cineangiography correlated well, although the relation was closer before than following dilation. This lower correlation following dilation probably reflects the eccentric shape of the vessel induced by balloon dilation detected in this study. These data suggest that intravascular ultrasound may be superior to cineangiography in defining intravascular size in the setting of distortions of lumen shape.

Based on the accuracy of the ultrasonic catheter in the measurement of vascular size demonstrated in this study, the technique may have several important clinical applications. Intraluminal ultrasound may be of value in obviating difficulties in the quantitation of vascular stenoses manifested by angiography and may prove to be the most precise measure of intraluminal size available. Intravascular ultrasound could then be used to establish the significance of stenotic lesions judged to be of borderline magnitude by cineangiography. Intravascular ultrasound has the potential to be the most sensitive technique by which to define the progression or regression of atherosclerosis, and to study the response of intravascular size to pharmacologic agents. The use of ultrasonic catheters also holds the enormous potential for anatomic definition of the vessel wall, and the possible assessment of the extent and composition of atherosclerotic plaque.

A variety of improvements in intravascular ultrasound technology will likely occur in the future. Efforts are underway to increase the ultrasonic energy used by this device, and to increase the piezoelectric elements from 32 to 64. Efforts are also underway to reduce the size of the catheter to approximately 3.5F. The results of this study document the feasibility and accuracy of intravascular ultrasound in assessing in

vivo intraluminal size. The ultimate clinical role of intravascular ultrasound in the coronary bed will be dependent on the technological refinements that can be achieved in the future.

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