Intravascular and Intracardiac Ultrasound Imaging
An Old Concept, Now on the Road to Reality

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Considerable attention is currently being focused on the development of intravascular and intracardiac ultrasound imaging.1-4 Various terms such as “ultrasound angiography,” “intravascular ultrasound imaging,” or “intraluminal ultrasound imaging,” this technique basically refers to the imaging modality of visualizing blood vessels and cardiac structures by an ultrasound transducer placed at the tip of a catheter or catheter-like probe introduced into the vascular system by an arteriotomy or venotomy and advanced to the region of interest. The feasibility of obtaining real-time, two-dimensional images of pulsatile arteries in vivo has been shown recently in intact humans5,6 and animals7-10 and has increased the interest in exploring the potential applications of this technique. In this issue of Circulation, Tobis and coworkers11 extending their previous work,7,12 report on an elegantly performed in vitro study that points to a potential use of intravascular high-frequency ultrasound imaging in identifying atheromatous plaques in coronary arteries and in assessing the distribution, size, and quality of the atheroma before and after balloon angioplasty. Various groups are actively investigating other possible applications.2,6,8,9,13-15 The concept of imaging cardiovascular structures with catheter-based ultrasound transducers is not new. It was attempted in the early sixties and seventies, but interest waned in later years. What is the need for intravascular and intracardiac ultrasound imaging now? Let us examine the original earlier work, the impetus behind current work, the present developments, and the promise of this imaging technique.

Early Work

In the early days of echocardiography, difficulties in obtaining good quality ultrasound signals from transthoracic imaging provided the initial impetus for developing intracardiac and intravascular ultrasound imaging probes. With the use of catheter-mounted transducers, the feasibility of intracardiac unidirectional imaging, measurement of the dimensions of blood vessels and chambers, and identification of abnormalities such as atrial septal defects were shown in the early sixties.16,17 About a decade later, cross-sectional imaging was attempted with multiple transducer elements mounted on a catheter from which images of cardiac chambers were derived.18 Although the feasibility of intravascular imaging was illustrated, the interest in this innovative approach faded because of problems in fabricating catheter devices that allowed rapid acquisition of two-dimensional images with high resolution. Further, the original indication became less important as marked improvements occurred in the image quality obtained by transthoracic two-dimensional echocardiography.

Impetus Behind Current Work

The increasing realization that detailed information on the structure of an atherosclerotic arterial lesion is necessary for optimal performance of interventional therapeutic procedures and for prediction of clinical ischemic syndromes is the stimulus behind current enthusiasm in developing intravascular ultrasound.19-23 For decades, selective coronary arteriography has been the standard method used for evaluation of atherosclerotic coronary artery disease. Selective coronary arteriography has been helpful in the identification of the location and approximate severity of coronary stenoses. When therapeutic options were limited to either medical therapy or coronary artery bypass surgery, this information was deemed sufficient despite the limitations of coronary arteriography. The advances in catheter-based interventional therapy (balloon coronary angioplasty, mechanical atherectomy, and angioplasty using laser and electrical catheter devices) and the problems such as perforations and dissections encountered in the performance of these procedures have emphasized the need for a better assessment of arterial anatomy.19,21,22 Coronary arteriography provides only longitudinal silhouette
The severity of narrowing is assessed primarily by visual inspection of percent reduction in the arterial diameter even though estimation of percent diameter stenosis can be flawed in the setting of eccentric lesions. The accuracy of coronary arteriography in estimating the severity of coronary stenosis and its functional significance is still controversial. Cross-sectional area and the shape of a coronary stenotic lesion cannot be analyzed in the angiograms. Although thrombi and arterial dissections can be identified, there is considerable ambiguity in the angiographic criteria for their diagnosis. Coronary arteriography does not yield information on the size and composition of the atheromatous plaque or on the structure of the diseased vessel wall. The structure of an atherosclerotic lesion, the arterial wall architecture, and the size and shape of luminal cross-sectional area have important diagnostic and prognostic implications. Complicated coronary lesions, characterized by plaque rupture, plaque hemorrhage, and partially occluding or recanalized thrombus have been found to be more dangerous and more likely to become acutely occluded than uncomplicated lesions. When an interventional procedure such as balloon coronary angioplasty is performed, eccentricity of a coronary lesion is a determinant of the primary success of the procedure and of the incidence of complications. The length of intimal tear or dissection, the degree of stenosis, and cross-sectional area after dilatation appear to be independent correlates of ischemic complications after angioplasty. If patients at risk of ischemic complications after angioplasty can be identified, appropriate approaches or devices such as stents can be used in these patients. It is thus desirable, in the assessment of coronary artery disease, to have an imaging technique that complements arteriography and that provides information on the cross-sectional size and shape of the lumen, size, size, shape, and composition of the atheroma (fatty, fibrous, or calcific plaques), integrity of intimal surface, presence or absence of ulcerations, thickness of the arterial wall, and on the presence or absence of dissection, intimal flap, and thrombus. If this information is available in the diagnostic realm, it would aid in selection of patients for interventional procedures, the choice of optimal interventional procedure, the assessment of the efficacy of the interventional procedure, the detection of complications, and in the stratification of the risk.

One technique that has been evaluated is fiberoptic angioscopy. Through the fiberoptic angioscope, the luminal surface of a vessel, protruding atherosclerotic plaques, intraluminal thrombi, and intimal flaps can be visualized. This technique, however, suffers from the following drawbacks: because seeing through blood is not possible, it has to be replaced with a clear transparent medium; because pulsatile blood flow would wash out the clear medium, the vessel has to be occluded with a balloon to keep the transparent solution in front of the angioscope; visualization of multiple segments of a vessel requires multiple occlusions, and these make its use limited in coronary circulation. Calibration problems make precise measurement of luminal area difficult. Furthermore, fiberoptic angioscopy does not provide an understanding of the vessel structure underneath the inner surface, the composition of the atheroma or the thickness of the arterial wall. Thus, the “light at the end of the probe in the tunnel” has not met all the needs. How about “sound at the end of a catheter in the tunnel”? Work with epicardial high-frequency ultrasound probes placed directly over the vessel has shown that high-frequency ultrasound can yield good quality short-axis images of arteries, can define arterial wall thickness, can detect atherosclerotic plaques, and can estimate the severity of arterial stenosis. This technique, however, is useful only in an open-chest situation in the operating room. Catheter-based, intravascular high-frequency ultrasound imaging provides an alternative approach to obtain such information percutaneously in intact humans.

Present Work

Following earlier concepts, both mechanical and phased-array systems are being evaluated to acquire two-dimensional images of vascular and cardiac structures in real time. In the mechanical systems, one or more ultrasound crystals attached to a probe core inside a protective sheath or catheter are rotated to generate a 360° two-dimensional image. In the phased-array system, multiple transducer elements are electronically activated in sequence to produce a two-dimensional image. The ultrasound beam is emitted in an orientation perpendicular to the catheter tip in some systems or with a look-forward angle in some others. The ultrasound probes required for blood vessel imaging need to have higher-frequency (20–40 MHz) transducers, and those for imaging cardiac structures need a relatively lower-frequency (5–20 MHz) transducers. Various catheter designs are being investigated. Some probes require a guiding sheath or catheter, some can be advanced directly, and others are advanced over a guide wire. The images are displayed in a two-dimensional format on a video monitor in real time and can be recorded on a videotape. Calibration in the display system allows measurements of the vessel structure.

In vitro imaging of blood vessels with these probes has yielded high-resolution circumferential images. In normal vessels, the lumen is seen free of any signal while the arterial wall often exhibits a three-layered appearance with clearest delineation of intima, media, and adventitia obtained in muscular arteries. Systematic comparisons of ultrasound images to morphologic analysis have shown excellent correlations in the measurement of luminal diameter and area and of wall thickness. In preliminary reports, in the presence of fibrocalciﬁc or fatty...
plagues in atheromatous arteries, bright echo signals with various gray scale are noted.\textsuperscript{5,6,13} In general, calcific plaques cause the brightest echo reflections. The ability of intravascular ultrasound to assess the site, size, and shape of the plaque and the thickness of the diseased wall has been reported. Changes in the size and shape of the lumen depicted on the intravascular ultrasound image correspond well with morphologic measurements.\textsuperscript{2,8} Preliminary comparisons with external high-frequency ultrasound and anatomic measurements have indicated that intravascular ultrasound can estimate the degree of cross-sectional area stenosis; intravascular imaging before and after mechanical atherectomy has suggested that the extent of plaque removal and increase in luminal area after the procedure can be gauged.\textsuperscript{12,13} The present report by Tobis and associates\textsuperscript{2} further documents the potential value of this imaging technique not only in visualizing the changes in luminal area after an interventional procedure such as balloon angioplasty but also in revealing the mechanism behind such luminal area change.

In vivo investigations using ultrasound catheters in dogs and pigs have shown the feasibility of imaging peripheral and coronary arteries.\textsuperscript{2,5,7,8} Ability to obtain dynamic images, ease of advancing the catheter while continuously imaging, and the lack of complications have been reported. In addition to visualizing normal vessels, intravascular thrombi and arterial dissections have been identified in vivo.\textsuperscript{14,15} Following the experience from studies in animals, the catheter has recently been used in humans, retrograde into the femoral and iliac arteries and antegrade into the distal femoral arteries and has yielded circumferential, two-dimensional, dynamic images of these vessels.\textsuperscript{5,6} This initial experience in humans has shown that regions of atheromatous plaques and arterial stenoses can be identified by this technique. Abnormalities revealed in ultrasound angioscopic images have corresponded well to angiographic sites of arterial disease. It appears that intravascular imaging can detect not only overt lesions in the arterial wall but also abnormalities that may not be recognized on an arteriogram. Studies are now in progress exploring the feasibility and value of intravascular imaging in the coronary circulation of humans.

Intravascular imaging with ultrasound can be extended to visualization of cardiac structures as well. Early attempts using M-mode techniques allowed recording of signals from mitral, aortic, and pulmonic valves and from ventricles and atrium.\textsuperscript{26} Recent investigations in animals with the ultrasound catheter have yielded images of aortic, mitral, and pulmonic valves, left ventricular outflow region, right atrium, right ventricular outflow region, and proximal and distal pulmonary arteries.\textsuperscript{2,5,9,10} Although high-frequency ultrasound catheters may be able to image structures within their range of resolution, probes with relatively lower frequency are needed to image whole valves and chambers. The in vivo experience with intravascular and intracardiac ultrasound, while highly encouraging in general, has also pointed to some of the problems that exist with current instruments being developed and the need for further work in this area.

**Future Directions and Potential Applications**

Intravascular imaging is not yet ready for routine clinical use. At present, it should be considered investigational. Most intravascular ultrasound devices currently being evaluated are prototype catheter probes. Some are usable in vivo whereas others are not. Although in vitro experiments, performed in an optimal setting with careful coaxial positioning of the catheter, allow acquisition of high-resolution images, it is difficult to maintain the catheter in a coaxial orientation inside a pulsatile artery in vivo. Luminal areas are well delineated in vivo, but definition of wall thickness is proving to be difficult.\textsuperscript{2,5,6} Further miniaturization of the catheter and better tip control are required to image distal portions of a coronary artery. Having not only a side-viewing but also a forward-looking capability would be desirable so that the arterial wall around the catheter tip and the segment immediately in front could be imaged. The image quality provided by current devices is variable. Improved image resolution with better gray scale discrimination and suppression of catheter tip signal artifacts are needed. More work has to be performed in the interpretation of the signals arising from normal and abnormal vessels. For intracardiac imaging, catheter probes with a range of lower frequencies need to be developed. Ideally, they should also have Doppler capabilities to record blood flow velocity. Although there are a number of issues to be addressed, they are within the range of practical solutions. If these improvements in instrumentation are brought to fruition, this imaging approach could have numerous potential applications in humans.\textsuperscript{5,27}

Using intravascular ultrasound imaging, accurate measurement of luminal area and, thus, the precise degree of cross-sectional area stenosis could be determined in atherosclerotic arterial disease. Composition of the atherosclerotic wall and atheroma could be determined. Complex lesions could be differentiated from uncomplicated lesions and provide diagnostic and prognostic information. Presence of intraluminal thrombi and arterial dissections and intimal flaps could be identified. The information derived from intravascular imaging could aid in the choice, and guide in the performance, of interventional procedures. The effects of an interventional procedure—the degree of luminal dilatation, the extent to which the atheroma had been removed or resected, and resulting thrombi or dissection—could be gauged. This could help in identifying whether or not adequate atheroma removal has been accomplished, in deciding when to quit and when to continue, in judging which lesions are
likely to develop restenosis, in planning placement of endovascular stents, in avoiding complications, and in detecting problems such as dissection, perforation, and spasm. Use of Doppler modality either separately or incorporated in the imaging catheter can aid in assessing coronary blood flow. The imaging catheter could be incorporated in one of the interventional catheters thus avoiding change of catheters. Intracardiac echocardiography may allow closer visualization of valvular and other cardiac structures. With a catheter placed in the inferior vena cava or in an intracardiac location, continuous monitoring of ventricular function may be performed. Intracardiac imaging may aid as a guide in the performance of balloon valvuloplasty and allow immediate detection of complications such as perforation and tamponade. Other than possible clinical applications, intravascular and intracardiac imaging could serve as valuable research tools in the study of cardiovascular pathophysiology and in the understanding of the natural history of atherosclerotic diseases and therapeutic interventions. Intravascular ultrasound imaging techniques should not be expected to replace arteriography. However, with further refinements in the catheter and imaging technology, intravascular ultrasound imaging is likely to find a valuable and complimentary role in cardiovascular diagnosis and management.

References

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