Editorial Comment

Intravascular Ultrasound
Research Technique or Clinical Tool?

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Intravascular ultrasound is a new technique that allows intraluminal catheter-based vascular imaging. Technological advances in miniaturization have produced 4F to 8F catheters that can be safely maneuvered within coronary and peripheral arteries. Images obtained provide accurate measurements of lumen area as well as high-resolution images of arterial wall components. Histopathological studies have demonstrated the ability of intravascular ultrasound to characterize plaque morphology, and these findings have been extrapolated to provide a novel method of examining plaque morphology in vivo. There has been increasing interest in intravascular ultrasound during the past 5 years, including attempts at tissue characterization and computer-based three-dimensional reconstruction. There subsequently have arisen high expectations of using intravascular ultrasound for overcoming the known limitations of coronary angiography as well as for guiding catheter-based vascular interventions.

See p 64

Despite these high expectations, this new technology has not fulfilled our clinical expectations because of several practical reasons. This invasive procedure has all of the inherent risks that accompany insertion of a catheter into an artery. The catheters are still in the early stages of development. They are relatively large and inflexible and often can only be used in the larger proximal coronary arteries. Hand production techniques and quality control deviations may cause imaging quality to differ from catheter to catheter. Catheter cost is not negligible, and reimbursement has been slow. However, the most important reason is that there are no data demonstrating the benefit of widespread use of this procedure in clinical practice. The one instance in which the catheter has been of clinical value is in delineating the severity of an angiographically equivocal stenosis in a large proximal vessel, but this indication occurs rarely given the available technology in the modern cardiac catheterization.

Nevertheless, these comments should not be misconstrued to suggest that intravascular ultrasound may not become clinically relevant in the future. As with any evolving technology, further innovative developments and experience will be necessary to establish its ultimate role. There already have been major advances in downsizing catheters (3.5F) with better image quality and greater flexibility. Paralleling these technological developments are advances in knowledge of the pathophysiology of coronary artery disease as well as scientific investigation into methods of catheter-based intervention. Animal models, computer modeling, and pathological studies recently have contributed greatly to our understanding of coronary artery disease and the effects of interventions on coronary artery lesions. If these two parallel tracks of investigations can merge together, there may be great potential for clinical applicability of intravascular ultrasound.

Several areas have emerged in which intravascular ultrasound might be combined with the evolving knowledge and understanding of coronary artery disease. Prediction of myocardial infarction has been difficult by conventional coronary angiography, as plaque rupture rather than progression of high-grade stenosis has been found to be the precipitating event. The occurrence of plaque rupture is related to plaque morphology as well as the stress-strain relation of the plaque and adjacent arterial wall, both of which are dependent on the constituents comprising a plaque. Because determination of the composition of the plaque is possible by intravascular ultrasound, identification of high-risk patients may be possible. There has been a recent emphasis on medical intervention in minimally obstructive coronary artery disease. Better quantitation of "plaque load" by intravascular ultrasound should allow a more precise end point for trials evaluating risk factor modifications. Loss of arterial distensibility produces greater shear and intramural wall stresses, which expose intima and plaque to injury. Vessel motion and compliance, which can be evaluated by intravascular ultrasound, thus may provide further understanding of the mechanisms of arterial damage.

Of great interest to the invasive cardiologist would be a technology to improve the results of percutaneous transluminal coronary angioplasty (PTCA). Although initial success rates for coronary angioplasty are over 90% in most institutions, limitations still exist: the risk of abrupt closure and the high rate of restenosis. Again, the parallel knowledge that has been gained from in vitro and pathological studies may provide insight into a potential role for intravascular ultrasound.

It historically was thought that the mechanism of PTCA was compression of atheromatous material with release of fluid constituents of the plaque. From the results of pathological and animal studies, it has become well accepted that PTCA improves lumen area by

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plaque disruption, such as intimal cracking and separation of the intima from the media, as well as by stretching of the adjacent vessel wall.\textsuperscript{16,17} If plaque disruption does not occur, the vessel lumen may enlarge transiently due to stretching of the vessel wall, but it may “recoil” back within minutes to hours; this is one of the causes of “early restenosis.”\textsuperscript{17}

The need to disrupt intimal plaque, however, must be tempered against the potential detrimental effects. A large disruption created at the time of the procedure may cause acute occlusion. Occlusive thrombus formation may occur with plaque disruption, especially if the plaque is associated with a high lipid content.\textsuperscript{18} There has been great interest generated in relating the degree of injury to restenosis, which in some studies approaches 40–50% at 3–6 months.\textsuperscript{19} An excessive cellular proliferation occurs in response to PTCA,\textsuperscript{20} and potential mechanisms include stretching of smooth muscle with stimulation of proliferation and migration of smooth muscle cells, destruction of endothelial protective factors that regulate smooth muscle growth, and injury to subintimal and deep vascular structures.\textsuperscript{21–23} Pathological studies have shown that the highest degree of this excess cellular proliferation occurs in the presence of the greatest degree of disruption caused by PTCA.\textsuperscript{20}

As is evident, a delicate balance must be obtained to achieve optimal results from the use of PTCA. Some disruption of plaque and vessel wall must occur to achieve a reduction in the severity of stenosis, but presently, the degree of injury cannot be predicted. Thus, the risk of acute occlusion or restenosis after PTCA cannot be assessed reliably. It has been speculated that intravascular ultrasound examination before intervention may be used to predict the outcome of balloon inflation in regard to plaque and vessel wall disruption.

In this issue of \textit{Circulation}, Fitzgerald et al\textsuperscript{24} demonstrate that arterial dissection may be predicted on the basis of intravascular ultrasound images, i.e., the presence of calcification areas in areas adjacent to that of dissection. This would fit with previously known biomechanical and pathological studies showing that a disruption would occur at the junction between regions of differing stiffness properties\textsuperscript{12,13} due to nonuniform stress distribution.\textsuperscript{14} Perhaps the degree of calcification seen on intravascular ultrasound could predict not only the ability to disrupt but also the degree to which disruption occurs. Pathological studies have shown that at least a moderate amount of calcification is required to cause partial plaque disruption but that severe calcification may be associated with disruption large enough to cause acute closure.\textsuperscript{18} The ultimate goal of intravascular ultrasound would be the development of catheters small enough to image arterial plaque before a procedure to predict whether plaque disruption would occur and the degree of injury, i.e., risk for acute vessel closure and restenosis.

It also has been proposed that intravascular ultrasound could aid in assisting with decision-making processes during a catheter-based intervention.\textsuperscript{4,10} One of the other predictors of a high rate of restenosis is a smaller residual lumen area.\textsuperscript{19} Intravascular ultrasound can provide a more accurate measurement of lumen area than angiography, especially after PTCA when indistinct angiographic borders occur, and thus may aid in the decision for further intervention.\textsuperscript{4,10} In the homogeneous fibrous plaque resistant to disruption, a bulk removal device may be more beneficial than PTCA alone. Current randomized trials are being conducted to determine whether intravascular ultrasound would be beneficial to the practicing cardiologist in this regard.

Investigation into the use of intravascular ultrasound with other catheter-based interventions is under way. Although directional atherectomy has resulted in a greater reduction in stenosis size than PTCA, this procedure still is plagued by a high restenosis rate. Restenosis is high when there is a suboptimal resection leaving a large amount of residual plaque\textsuperscript{10} as well as when there is deep subintimal and adventitial resection, especially in restenotic lesions and vein grafts.\textsuperscript{25} This higher rate of restenosis in the latter circumstance may be related to an increase of smooth muscle migration in response to deep arterial injury.\textsuperscript{21,25} Whether intravascular ultrasound guidance of atherectomy removal will result in a lower rate of restenosis is a question under investigation. Other possible applicabilities of intravascular ultrasound may be stent sizing and placement and ultrasonic-guided laser therapy.\textsuperscript{10}

The time has not arrived for the routine clinical use of intravascular ultrasound. There certainly are many practical limitations that must be overcome with these catheters to use intravascular ultrasound in the ideal ways described above. However, the accumulation of data, such as that provided by Fitzgerald et al, combined with the parallel investigation in coronary artery disease may allow intravascular ultrasound to become an integral part of the clinical armamentarium of the invasive cardiologist in the future.

References


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