Coronary Intravascular Ultrasound

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Coronary angiography remains an important modality for assessing atherosclerotic coronary artery disease and guiding percutaneous coronary intervention. Intravascular ultrasound (IVUS) is an important adjunct during coronary angiography and has been increasingly used in clinical and research applications in the past decade. It has vastly enhanced our understanding and has provided us with a thorough perspective of the atherosclerotic process. Hyperlinked to this article is a video demonstrating the use of IVUS. Downloadable slides about IVUS are available in the online-only Data Supplement.

Studies done in the 1980s and 1990s helped confirm the Glagov theory of remodeling (expansion of the total arterial size in response to atherosclerotic plaque accumulation) and much of the current understanding of the coronary artery restenotic processes. We now know that acute coronary syndromes are often attributable to plaque rupture from angiographically nonsignificant stenoses, but IVUS studies have demonstrated that these insignificant lesions exhibit the Glagov model of positive remodeling, have the highest volume of lipid-rich plaque, and are thus highly vulnerable to rupture. IVUS studies performed in the 1990s and more recently have helped us understand the restenotic process and underlined the importance of optimal stent deployment to reduce the risk of restenosis and stent thrombosis. Because IVUS can accurately quantify arterial plaque, it is increasingly being used to evaluate newer and evolving strategies for the treatment of coronary artery disease, including high-potency statins, anti-atherosclerotic drugs, and anti-inflammatory therapies.

Rationale for IVUS Use

The advantage of IVUS compared with coronary angiography is its ability to directly image the vessel wall. Coronary angiography has several limitations. Coronary angiogram is a luminogram (images the lumen rather than the vessel wall) and results in significant underestimation or overestimation of lesion severity and extent of atherosclerotic burden. This is attributable to a variety of factors. Coronary angiography is a 2-dimensional imaging modality representing complex lesion anatomy in a simple 2-dimensional luminogram. Hence, several different projections in orthogonal views are required to quantify a lesion. Moreover, even with different projections, lesions that are highly complex or eccentric, ostial lesions, bifurcation lesions, and lesions overlapped by adjacent vessels are often missed. In the presence of a simple concentric lesion, orthogonal angiographic views provide an accurate estimate of lesion severity. However, when the lesion is eccentric, the severity might be underestimated. When the lesion is more complex, multiple orthogonal views may not lead to an accurate assessment of lesion severity and morphology.

Visual estimation of lesion severity based on coronary angiography has wide interobserver and intraobserver variabilities. Although the advent of quantitative coronary angiography has reduced interobserver variability, it has not improved accuracy. In addition, quantification depends on comparison of the lesion with an adjacent normal reference segment, and given the diffuse nature of the atherosclerotic process, defining a normal reference segment is sometimes fraught with errors. Moreover, coronary angiography has limited resolution and is influenced by motion artifacts, contrast streaming, vessel tortuosity, and ectasia. It is also less sensitive at assessing plaque characteristics. Because lumen encroachment is a late phenomenon in the atherosclerotic process (as a result of Glagov remodeling), many nonsignificant lesions (which are culprits for plaque rupture and subsequent acute coronary syndromes) are missed. Histopathological studies have demonstrated that angiographic evidence of stenosis is usually not detected until the cross-sectional area of plaque approaches 40% to 50% of the total cross-sectional area of the vessel because there is a compensatory outward expansion of the external elastic membrane. When the plaque area exceeds 40% to 50% of the external elastic membrane area, the plaque begins to encroach on the lumen and will be detectable on a coronary angiogram as minimal luminal narrowing.

Many of the limitations of coronary angiography are overcome by IVUS; thus, IVUS provides incremental information when used with routine contrast angiography. IVUS images the vessel wall and provides a tomographic view of the entire circumference of the vessel wall. It has a higher axial and lateral resolution compared with angiography and is better able to characterize plaque composition, distribution, morphology, and extent. For a 20- to 40-MHz IVUS transducer, the typical axial resolution is 80 to 100 μm and lateral resolution is 200 to 250 μm. The quantitative measurements with IVUS are precise; hence, IVUS has good intraobserver and interobserver correlations. Moreover, it is helpful in assessing lesion severity...
at sites difficult to image by conventional angiography such as the coronary ostia, bifurcations, tortuous vessels, and highly eccentric plaques. In addition, IVUS provides an estimate of the coronary artery remodeling process and helps identify disease even in apparently normal arteries as assessed by coronary angiography. Coronary angiography is also less sensitive at assessing the adequacy of poststent deployment and procedural complications such as edge dissection.

**Indications for IVUS**

The indications for IVUS use are summarized in the American College of Cardiology/American Heart Association guidelines for percutaneous coronary interventions.16 (Table 1). Of note, there are no Class I indications for IVUS use. Nevertheless, for routine coronary angiography, one third of cases have a clearly identifiable severe stenosis and one third have clearly nonsignificant stenoses, whereas only in another one third of cases is additional information with the use of IVUS potentially necessary for lesion quantification. Although this may be true for diagnostic applications, IVUS is being increasingly used during interventions to ensure adequate stent placement; to assess the effects of intracoronary, catheter-based interventions; and to evaluate postprocedural complications.

The indications for IVUS use can be broadly categorized into diagnostic applications and guidance for intracoronary interventions. IVUS is an important adjunct in the identification of occult atherosclerosis in angiographically normal coronary arteries (eg, cardiac allograft vasculopathy). In an evaluation of 884 angiographically normal reference segments, only 6.8% were normal by IVUS, attesting to the ubiquitous nature of atherosclerosis.17 Similarly, angiography frequently underestimates stenosis severity in vessels with intermediate (50% to 75%) stenosis.18 IVUS is thus an important adjunct to evaluate such lesions. For such lesions, absolute lumen area <4.0 mm² is frequently associated with myocardial ischemia by stress perfusion imaging, whereas a minimal luminal cross-sectional area <2.7 to 3.0 mm² is associated with a physiologically significant stenosis as measured by fractional flow reserve (FFR) or coronary flow reserve measurement. The IVUS criteria for significant stenosis are summarized in Table 2. For ostial lesions, IVUS assists in the estimation of lesion severity and identification of the aorto-ostial junction for accurate stent placement. Similarly, for bifurcation lesions, IVUS aids not only precise quantification of lesion severity but also assessment of the size of the main and side branches for stent placement. It is helpful in device selection for transcatheter procedures. For example, in rotational atherectomy, burr sizing may be influenced by coronary calcium, which IVUS can detect. Similarly, for vein grafts, IVUS may aid in determining lesion severity and helps identify when to use distal protection on the basis of plaque characteristics. IVUS performed before stenting can provide useful information on the extent of the lesion; plaque characteristics, including calcification, dissection extent, and degree of ostial involvement; and the reference vessel size, which is useful in determining the precise stent length and diameter. After stenting, IVUS aids in the identification of stent malapposition, which cannot be easily detected on contrast angiography. In the Optimal Stent Implantation (OSTI) trial, IVUS-guided stent implantation resulted in better in-stent dimensions compared with angiography alone.19 IVUS thus helps to ensure optimal stent deployment and may reduce the risk of restenosis.8 Moreover, IVUS helps identify poststenting complications like edge dissection20 and helps operators better understand the possible mechanical reason for stent thrombosis (sten malapposition, etc).

**Evaluation of Left Main Lesions**

Angiographic assessment of left main lesions is often challenging because in many cases the left main is short and lacks a normal reference segment for comparison. Moreover, estimation of lesion severity at the ostium and the distal bifurcation is challenging. The direction of takeoff of the ostium and contrast in the aortic cusp render precise evaluation of lesion severity at the left main ostium difficult. Similarly, the overlap of the bifurcating branches of left main makes evaluation of the distal segment challenging. In an angiographic-histological correlation study, 71% of the left main lesions were either underestimated or overestimated by angiography.21 Of all the coronary segments, assessment of left main lesion has the greatest intraobserver and interobserver variabilities.22,23 IVUS is therefore increasingly used as an adjunct to aid in the diagnosis of and to guide treatment for such patients.

Suggested IVUS criteria for significant left main stenosis are a minimal luminal cross-sectional area <6 mm² in asymptomatic patients or <7 mm² in symptomatic patients, a minimal luminal diameter <3.0 mm, or an area stenosis >60%. Compared with FFR <0.75 as the gold standard, a minimal luminal cross-sectional area of 5.9 mm² had a sensitivity of 93% and specificity of 95% for determining the functional significance of a left main coronary stenosis, whereas an minimal luminal diameter of 2.8 mm had a sensitivity and specificity of 93% and 98%, respectively.24 In addition, IVUS

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**Table 1. Indications for IVUS Use**

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<tr>
<td>Class Ia</td>
<td>IVUS is reasonable for the assessment of angiographically indeterminate left main CAD. (Level of Evidence, B) IVUS and coronary angiography are reasonable 4 to 6 weeks and 1 year after cardiac transplantation to exclude donor CAD, detect rapidly progressive cardiac allograft vasculopathy, and provide prognostic information. (Level of Evidence, B) IVUS is reasonable to determine the mechanism of stent restenosis. (Level of Evidence, C)</td>
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<tr>
<td>Class Ib</td>
<td>IVUS may be reasonable for the assessment of non–left main coronary arteries with angiographically intermediate coronary stenoses (50% to 70% diameter stenosis). (Level of Evidence, B) IVUS may be considered for guidance of coronary stent implantation, particularly in cases of left main coronary artery stenting. (Level of Evidence, B) IVUS may be reasonable to determine the mechanism of stent thrombosis. (Level of Evidence, C)</td>
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<td>Class III</td>
<td>IVUS for routine lesion assessment is not recommended when revascularization with PCI or CABG is not being contemplated. (Level of Evidence, C)</td>
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From Levine GN et al.16 CAD indicates coronary artery disease; IMUS, intravascular ultrasound; and PCI, percutaneous coronary intervention.
Before insertion of the catheter, anticoagulation with either heparin (unfractionated or low-molecular-weight heparin) or bivalirudin is recommended. With the use of a standard guide catheter (6F) and a standard 0.014-in guidewire, the lesion is crossed. It is recommended that intracoronary nitroglycerin be administered before imaging to prevent vasospasm and to achieve maximal vasodilatation. The IVUS catheter is then advanced over the guidewire so that it is distal to the lesion. It is preferable to start imaging at a site that can be used as a landmark such as a branch vessel. Using automated pullback (usual pullback rate of 0.5 mm/s) for surveillance of the artery and manual pullback for a closer look at sites of interest is recommended. The automated pullback also helps to evaluate the length of the lesion because it enables display of the image in the L mode (longitudinal). For imaging the aorto-ostial segment, it is recommended that the guide catheter be disengaged from the coronary ostium before imaging the ostium. It is vital to ensure that there are no air bubbles in the system to avoid imaging artifacts. Saline/contrast flushes can be used in situations when identification of the false versus true lumen is needed (dissections).

### Equipment

The IVUS system consists of a catheter that has a miniaturized transducer and a console that reconstructs the image. There are 2 types of ultrasound transducers: a mechanical transducer system and a multielement electronic array system (solid-state system). The mechanical transducer system consists of a single piezoelectric crystal transducer mounted at the tip of the catheter driven by a flexible drive cable that rotates it at a speed of 1600 to 1800 rpm. The rotational speed is controlled by an external motor drive. The catheter is introduced in a rapid exchange format with a short monorail at the tip, followed by a 15-cm clear plastic segment, which is the imaging portion, that houses the transducer. Because of this design, guidewire artifacts are routinely seen, and the short monorail design makes it less flexible compared with solid-state transducers. The transducer rotates within the plastic sheath and moves inside the catheter for a 15-cm imaging segment without having to move the entire catheter for imaging.

The multielement electronic array system consists of an annular array of 64 piezoelectric crystals that are activated sequentially to generate a tomographic image. The elements receive the ultrasound signal and are then routed to a computer where the images are reconstructed and presented in real time. Because a central guidewire lumen is used, there are no guidewire artifacts with solid-state transducers. Similarly, because there are no moving parts, no nonuniform rotational distortion is seen either. The mechanical transducers have provided better image quality than the solid-state transducers, but the gap has narrowed. However, mechanical transducers are prone to IVUS artifacts like nonuniform rotational distortion and guidewire artifacts, whereas the multielement transducers are more flexible with fewer artifacts overall but frequently produce ring-down artifacts. The currently available IVUS systems (20–45 Hz) have an axial resolution of 100 μm and lateral resolution of 250 μm.

### Technique

IVUS is performed with standard interventional techniques, is simple to perform, and is associated with a very low complication rate, even in the setting of acute coronary syndromes. Before insertion of the catheter, anticoagulation with either heparin (unfractionated or low-molecular-weight heparin) or bivalirudin is recommended. With the use of a standard guide catheter (6F) and a standard 0.014-in guidewire, the lesion is crossed. It is recommended that intracoronary nitroglycerin be administered before imaging to prevent vasospasm and to achieve maximal vasodilatation. The IVUS catheter is then advanced over the guidewire so that it is distal to the lesion. It is preferable to start imaging at a site that can be used as a landmark such as a branch vessel. Using automated pullback (usual pullback rate of 0.5 mm/s) for surveillance of the artery and manual pullback for a closer look at sites of interest is recommended. The automated pullback also helps to evaluate the length of the lesion because it enables display of the image in the L mode (longitudinal). For imaging the aorto-ostial segment, it is recommended that the guide catheter be disengaged from the coronary ostium before imaging the ostium. It is vital to ensure that there are no air bubbles in the system to avoid imaging artifacts. Saline/contrast flushes can be used in situations when identification of the false versus true lumen is needed (dissections).

### Safety of IVUS

IVUS use is associated with a very low complication rate. The most frequent complication reported is coronary vasospasm (2.9%), and its frequency is likely lower with routine use of intracoronary nitroglycerin before imaging. The risk of acute procedural complications such as occlusion, embolism, dissection, or thrombus is very low (0.4%). There is no reported correlation between adverse events and the size or type of IVUS catheter. The reported rate of adverse events is higher in patients with acute coronary syndromes compared with those with stable angina and in patients undergoing percutaneous coronary intervention compared with those undergoing diagnostic procedures only. Performance of IVUS does not accelerate atherosclerosis.

### Qualitative Analysis of IVUS Images

#### Normal Coronary Artery

The normal coronary artery often appears as a trilaminar structure on IVUS (Figure 1). The innermost layer appears as an echo-reflective zone at the lumen-wall interface. It is relatively echo-reflective compared with the lumen or media and comprises the intima, atheroma, and the internal elastic lamina. The second layer is the media that appears echolucent compared with the innermost layer. The outermost layer is made up of the adventitial and periadventitial layers, which are echo-reflective and more echogenic compared with the...
media. Echo-reflectivity depends on reflection of ultrasound and on the collagen content of the layer. The periadventitial tissue cannot be clearly differentiated from the adventitia because the echo-reflectivity of the 2 structures is similar. In 30% to 50% of cases, the coronary artery trilaminar nature is not seen and the structure appears to be monolaminar. The other normal structures that can sometimes be seen are the pericardium, branch arteries, and venous system.

Atherosclerotic Plaque
Qualitative assessment of coronary artery lesions involves the identification of the proximal and distal reference segments and the lesion itself. The proximal and distal reference segments are the sites with the largest lumen proximal and distal to a stenosis but within the same coronary segment and are usually within 10 mm of the stenosis with no major intervening branches. Qualitative analysis of the lesion involves assessment of plaque characteristics (Figure 2A through 2C). Three types of plaques can be identified: soft plaque, fibrous plaque, and fibrocalcific plaque. Plaque characterization by IVUS is performed by comparing the echo-reflectivity of the plaque with that of the adventitia. Soft plaques have high lipid content and appear as a hypoechoic area compared with the adventitia (Figure 2A). Many times, a fibrous cap (echo-reflective zone) covers the plaque on the luminal surface. The most common type of plaques, the fibrous plaques, have more collagen and elastic tissue and have echogenicity similar to that of adventitia (Figure 2B). Unlike the fibrocalcific plaque, fibrous plaques rarely produce acoustic shadowing. Fibrocalcific plaques are hyperechoic as a result of calcification compared with the adventitia and frequently produce acoustic shadowing (Figure 2C). Besides the plaque type, many plaque characteristics like eccentricity, superficial versus deep calcification, extent of calcification (based on the arc subtended at the center of the lumen), and extent of plaque can be identified.

Stable Versus Unstable Plaque
IVUS can sometimes differentiate stable from unstable plaques on the basis of certain characteristics. Stable plaques have more fibrous tissue or calcification; unstable plaques usually have a large necrotic core (echolucent) covered by a thin fibrous cap with the appearance of mobile echoes consistent with thrombus.

Thrombus
Thrombus appears as an echolucent structure with a variable gray-scale appearance. It usually appears layered, lobulated, or pedunculated. At times, microchannels are present, which can be demonstrated by the injection of saline. The diagnosis of thrombus by IVUS is presumptive, and a definitive diagnosis can often be made with the appropriate combination of clinical history, angiography, and IVUS findings.

Coronary Dissection
Coronary dissection is classified as intimal, medial, adventitial, intramural hematoma, or intrastent on the basis of the extent of the dissection into the vessel wall. It is important to identify the true lumen from the false lumen on IVUS. The true lumen has a trilaminar appearance with communicating branches, whereas in the false lumen, not all layers are present and branches do not communicate with the lumen (Figure 3A). With intramural hematoma, there is accumulation of blood within the medial space. On IVUS, there is displacement of the internal elastic membrane inward and external elastic membrane outward by echolucent material in the media (hematoma) (Figure 3B).

Plaque Rupture
IVUS can help identify plaque rupture. A ruptured plaque usually shows a flap with a fibrous cap and an echolucent zone that represents the soft necrotic core.

Aneurysms
Angiography is less sensitive for differentiating between a true and a false coronary aneurysm. However, because of its superior resolution, IVUS can differentiate between the two. A true aneurysm includes all layers of the vessel wall with an external elastic membrane and lumen diameter ≥50% larger than the proximal reference segment, whereas a pseudoaneurysm does not include all layers of the vessel wall and has evidence of disruption of the external elastic membrane.

Myocardial Bridge
Myocardial bridging occurs when a segment of a coronary artery or its major branch travels through the myocardium instead of on the surface of the myocardium. On coronary angiography, a systolic milking effect, which is systolic compression of the bridge segment of the artery, is seen. On IVUS, systolic compression can be seen in the bridge segment, more often as an eccentric compression. Moreover, a half-moon phenomenon has been described. This consists of an echolucent half-moon–shaped image that exists throughout the cardiac cycle (Figure 4). This half-moon area is located between the epicardial tissue and the bridging coronary segment but not in a normal segment.

Stent Malapposition
With stent malapposition, ≥1 stent struts are clearly separated from the vessel wall with evidence on IVUS of blood speckles behind the strut. Stent malapposition can be attributable to
underdeployment of the stent (early malapposition), absorption of thrombus, or regression of plaque behind a stent, or it can be the result of positive remodeling of the artery with an increase in external elastic membrane area (sometimes caused by drug-eluting stent implantation [late stent malapposition]).

**Quantitative Analysis of IVUS Images**

Quantitative analysis is performed with measurements from leading edge to leading edge. The luminal boundary is drawn at the interface between the lumen and the intimal surface, and the external elastic membrane boundary is drawn at the outer border of the echolucent media. The definitions of various parameters measured on a quantitative analysis are summarized in Table 3. The reference segment should be chosen on the basis of the following definitions:

- Proximal reference: The site with the largest lumen proximal to a stenosis but within the same segment (usually within 10 mm of the stenosis with no major intervening branches).
- Distal reference: The site with the largest lumen distal to a stenosis but within the same segment (usually within 10 mm of the stenosis with no intervening branches).
- Largest reference: The largest of either the proximal or distal reference sites.
- Average reference lumen size: The average value of lumen size at the proximal and distal reference sites.

The reference segment used (proximal, distal, largest, or average) should be reported with quantitative analysis.

**IVUS Artifacts**

**Nonuniform Rotational Distortion**

Nonuniform rotation distortion is seen mainly with mechanical transducers and results from mechanical binding of the drive cable that rotates the transducer (caused by frictional forces), resulting in imperfect 1-to-1 rotation of the driveshaft to the transducer. Such increased frictional forces may be attributable to excessive vessel tortuosity, catheter twisting, calcified arteries, or excessive tightening of the hemostatic valve (O ring). The result of such mechanical binding is smudging of portions of the image that can affect image interpretation. This artifact can be reduced by fixing the underlying problem: by straightening the catheter and motor drive assembly, lessening catheter tension, and loosening the O ring when excessively tight.

**Ring-Down Artifact**

This artifact is produced by acoustic oscillations in the transducer, resulting in bright halos around the catheter. This creates a zone of uncertainty around the transducer, making it difficult to visualize areas immediately around the transducer. This is seen more commonly with multielement array transducers and can be reduced by adjusting the time gain control (ringing down).

**Blood Speckle Artifact**

This artifact is the result of increased transducer frequency or decreased velocity of blood (such as in regions of severe
there is a strong correlation between IVUS measurements and ischemia detected by myocardial perfusion single photon emission computed tomographic imaging, coronary flow reserve, or FFR. The anatomic correlates of function as assessed by ischemia on single photon emission computed tomographic imaging, coronary flow reserve, and FFR are summarized in Table 2. IVUS and FFR should be considered complementary modalities. FFR provides information on functional significance of a lesion, and IVUS provides information on plaque characteristics, sizing of the vessel, presence of ostial disease, poststenting vessel characteristics, and presence of poststenotic complications. Thus, both IVUS and FFR provide useful information for diagnostic and interventional applications.

Disclosures

Dr Bhatt discloses the following relationships - Advisory Board: Elsevier Practice Update Cardiology, Medscape Cardiology; Board of Directors: Boston VA Research Institute, Society of Chest Pain Centers; Chair: American Heart Association Get With The Guidelines Science Subcommitte; Honoraria: American College of Cardiology (Editor, Clinical Trials, Cardiosource), Duke Clinical Research Institute (clinical trial steering committees), Slack Publications (Chief Medical Editor, Cardiology Today’s Intervention), WebMD (CME steering committees); Other: Senior Associate Editor, Journal of Invasive Cardiology; Data Monitoring Committees: Duke Clinical Research Institute, Population Health Research Institute; Research Grants: Amarin, AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, Medtronic, Sanofi Aventis, The Medicines Company; Unfunded Research: FlowCo, PLx Pharma, Takeda. Dr Bangalore reports no conflicts.

References


