Clinical Application of Intravascular Ultrasound in Coronary Artery Disease: An Update

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Intravascular ultrasound (IVUS) employs a miniature ultrasound probe positioned at the tip of a coronary catheter to emit ultrasound signal which is reflected from surrounding tissue and then reconstructed into a real-time tomographic gray-scale image. IVUS directly images the vessel inside, allowing measurement of plaque morphology, distribution and exact vessel composition. Recent technical developments enable processing of the backscattered ultrasound radiofrequency signal underlying the gray-scale image. Therefore, IVUS can now provide more accurate measurement of tissue properties than traditional gray-scale images by different methods of tissue characterization. Thin-cap fibroatheroma by virtual histology was a proved risk factor for future cardiac events. Clinical trials disclosed significant improvement in patient outcome and reduced complications by IVUS-guided percutaneous coronary intervention (PCI), which can also provide more information in angiographic ambiguous lesions. 3-4 mm² for non-left main (LM) lesion or 5.9-7.5 mm² for LM lesion are considered the cut-off minimal lumen areas to identify significant stenosis. After stenting, in-stent minimal area ≥ 90% of the average reference lumen area or ≥ 100% of the lumen area of the reference segment with the lowest lumen area are IVUS-acceptable. In conclusion, IVUS is a powerful imaging modality which can provide more information before, during and after PCI to facilitate the procedure. Therefore, it should be used more widely in order to improve clinical outcomes and quality of our interventions.

Key Words: Coronary artery disease • Intravascular ultrasound • Percutaneous coronary intervention • Tissue characterization

INTRODUCTION

Even though there have been major advances in diagnosis and treatment, coronary artery disease (CAD) remains a leading cause of morbidity and mortality in the developed world, and it is also a growing cause of death in developing countries. Traditionally, quantitative coronary angiography (QCA) was the major imaging modality used to assess the severity of CAD and to determine the process of coronary atherosclerosis. However, many studies have questioned its accuracy and reproducibility. During the last two decades, technical advances made slender catheters that generate real-time intraluminal ultrasound images of the coronary arteries possible. This new imaging modality, intravascular ultrasound (IVUS), can evaluate the severity of CAD directly inside the vessel and can easily detect the progression and regression of atherosclerotic plaque during serial follow-up. Angiography evaluates the coronary anatomy as a planar silhouette of the lumen (lumenogram). Ultrasound, on the other hand, directly images the vessel in it, allowing measurement of plaque morphology, distribution and exact vessel composition. By using this new modality during percutaneous coronary intervention...
(PCI), many clinical trials have disclosed significant improvement in patients’ outcomes and reduced complications. Meanwhile, plenty of clinical pharmacological trials employ IVUS to demonstrate their beneficial effects because it offers great value in precisely quantifying atherosclerosis progression or regression. This new imaging modality can change our viewpoint in the treatment and evaluation of CAD.

LIMITATIONS OF CORONARY ANGIOGRAPHY

Mason Sones, Jr. performed the world’s first coronary angiography in 1958 at the Cleveland Clinic, starting the modern era of percutaneous cardiovascular treatment. Although coronary angiography has contributed greatly to clinical cardiology, this imaging modality may have misled us regarding the true nature of the atherosclerotic process. Angiography is a lumenogram obtained by injecting contrast media into coronary arteries in order to detect atherosclerotic disease and predict coronary events. However, coronary disease is largely not a disease of the lumen itself but an abnormality of the vessel wall. In fact, most major coronary events occur at insignificantly and not highly stenotic lesions. Once the plaque ruptures and a thrombus develops, a patient could experience unstable angina, acute myocardial infarction (AMI), or sudden cardiac death. Therefore, the size of the lumen and severity of narrowing are not good predictors of cardiac events.

Angiography depicts arteries as a planar silhouette of the contrast-filled lumen. Since the angiogram is a lumenogram, inadequate angiographic projection may mislead interpretations of the luminal narrowing. Furthermore, the assessment of lesion severity requires a comparison of the diseased lumen diameter and normal segment, which might not always be truly normal if only diagnosed with angiography.

In 1987, Glagov et al. proposed a new paradigm for atherogenesis. They suggested that initial atherosclerotic plaque growth leads to compensatory expansion of the vessel wall (positive or expansive remodeling). In later phases, after the remodeling fails to compensate for the accumulation of plaque, lumen narrowing occurs, and it is at this time that angiography can help. Because of this process, angiography cannot detect early atherosclerotic changes because no lumen narrowing can be detected until further plaque growth. Moreover, in a diffuse atherosclerotic lesion, angiography may fail to evaluate the severity of lumen narrowing since there is no truly “normal” segment that can act as a reference site.

MECHANISM

IVUS is a miniature ultrasound probe positioned at the tip of a coronary catheter. The probe emits ultrasound frequencies, typically at 20-45 MHz, and the signal is reflected from surrounding tissue and reconstructed into a real-time tomographic gray-scale image. The probe is inserted over the guiding wire and then pushed beyond the lesion; the ultrasound catheter is then withdrawn slowly for the imaging process. Ultrasound waves are reflected at the interface of two different tissues. In coronary arteries, there are two clear borders which can be defined: the lumen-intimal border and the media-external elastic membrane (EEM) border (Figure 1). Blood speckle in the lumen reflects more weakly than the echo signal from the intima, allowing for a clear lumen-intimal border next to the IVUS catheter. At the same time, the media is echolucent (faint echo signal), which is manifest on the gray-scale image as a dark ring outside the intima. The other clear border, the media-EEM border, is between the dark media and echodense (bright echo signal) adventitia. Manual or computer-assisted planimetry of these two borders allows precise measurement of coronary artery dimensions.
measurements of the lumen area, intima-media area, and EEM area. On the basis of the backscattered echo signal from various tissues, we can distinguish different tissues from each other based on brightness in the gray-scale image. In addition, recent approaches that use image-processing technology to analyze the radiofrequency of backscattered echo signals can make tissue characterization more objective and detailed, which may influence decision-making in daily practice, especially decisions in acute coronary syndrome cases.

**EQUIPMENT**

The equipment required to obtain such tomographic images is comprised of three major components: a catheter with a miniaturized probe at the tip, a pullback device, and a console to reconstruct real-time images. The use of a motorized pullback device at a constant speed permits volumetric evaluation of the lesion and plaque dimensions after longitudinal or 3-dimensional reconstruction. IVUS catheters currently available range from 2.6 to 3.5 French (outer diameter, 0.87-1.17 mm), are suitable for examining distal coronary lesions and permit examination of most stenotic lesions before PCI. Most IVUS catheters are monorail system, which can facilitate rapid exchange and can be placed through a 6-French guiding catheter. For some specific probes, even a 5-French guiding catheter can be used. Two different approaches to transducer design are commonly used: (1) mechanical rotating devices and (2) electronically switched multi-element array system.

Mechanical rotating probes use a driving cable to rotate at 1800 rpm (30 images per second). The probes emit an ultrasound beam perpendicular to the catheter and vessel. In this system, the imaging transducer is protected in a transparent sheath, which facilitates smooth and uniform pullback. During IVUS examination, the sheath as well as the probe is advanced beyond the lesion or the segment of interest and the probe is then pulled back within the sheath either manually or motorized (usually 0.5 mm/s). However, small air bubbles between the probe and protective sheath can significantly deteriorate image quality, and saline flushing is required to provide a fluid environment for the ultrasound beam before the probe is inserted in a coronary artery. Because of the probe’s rotating nature, a common artifact, “non-uniform rotational distortion (NURD)” can develop (Figure 2). NURD is a result of the uneven drag of the rotating transducer, resulting in cyclical oscillations in rotational speed. NURD is a visible distortion of the image, which may be due to excessive tightening of the hemostatic valve, a highly tortuous vessel, bending of the guiding catheter, kinking of the imaging catheter, or a too small lumen of the guiding catheter. One should avoid images with NURD in doing measurements.

In phased array system, on the other hand, multiple transducer elements in an annular array are activated sequentially, generating the image without any rotation. The phased array can be programmed so that one set of elements transmits while a second set simultaneously receives information. Because there is no protective sheath needed, repeated saline flushing is not necessary for electronic systems and the profile of the distal shaft is smaller than in the mechanical system; however, such differences have been reduced in recent years. Owing to the phased array but non-rotating and long monorail design, NURD and guide-wire artifacts, respectively, do not develop in electronic system. Furthermore, shorter transducer-to-tip design can facilitate better visualization of distal anatomy than the mechanical rotating system. However, the ultrasound frequency of the electronic sys-

![Figure 2. NURD, non-uniform rotational distortion (arrow).](image-url)
tem is only 20 MHz, which means that it has poorer image resolution than mechanical system.

**ADVANTAGES OF ULTRASOUND IMAGING**

The basic advantage of IVUS over angiography is the penetrating nature of ultrasound, which allows direct evaluation of not only the lumen but also the surrounding vessel wall. Unlike angiography, IVUS can directly assess an atherosclerotic plaque and the remodeling of arterial wall as well as diffuse lesions. Hence, it is more sensitive than angiography for detecting vascular lesions, especially in the early phase. An IVUS study of the hearts of cardiac transplant donors revealed significant coronary plaques even in very young (< 20 y/o) patients. This means that atherosclerotic risk factors begin affecting coronary arteries many decades before symptoms appear, and IVUS, not angiography, can easily detect such damage. In almost all CAD patients, IVUS detects more diffuse and extensive plaques within coronary arteries than angiography. Therefore, IVUS provides more information regarding CAD than angiography does.

IVUS can also detect plaques that have a high risk of spontaneous rupture or the ruptured plaque with insignificantly angiographic finding. Some typical morphologic criteria, such as echolucent area located in the positive remodeling segment covered by a thin fibrous cap, can be identified by IVUS. However, most of these studies were cross-sectional, which limited their ability to identify real causal relationships. Recently, the preliminary results of the first prospective IVUS virtual histology follow-up study were announced, which suggested the combination of large plaque burden and a large necrotic core with thin cap identified by virtual histology are risk factors for future adverse cardiovascular events.

Despite the invasive nature of IVUS, its safety is well established. Complication rates vary from 1% to 3%, and the most frequently reported adverse event is transient coronary spasm, which can be easily resolved by administering nitroglycerin. Major complications are vessel dissection and closure, and these complications occur in < 0.5% of cases; most of these events develop during PCI.

**IVUS-BASED DETECTION OF PLAQUE COMPOSITION**

The IVUS probe generates an ultrasound signal and receives the backscattered signal from tissue; this signal is processed in real-time into a tomographic gray-scale image. This image provides useful information for the determination of vessel and lumen diameters and the severity and distribution of plaques. The gray-scale IVUS image can also be used to characterize coronary plaque composition on the basis of the echogenicity of different structures. However, owing to the basic features of the gray-scale images, such as operator-dependent interpretation, equipment settings, and limited resolution, gray-scale IVUS is a suboptimal tool for accurately and reproducibly identifying plaque composition. However, recent technical developments enable processing of the backscattered ultrasound radiofrequency (RF) signal underlying the gray-scale image. Therefore, IVUS can now provide more accurate measurement of tissue properties than traditional gray-scale images. There are three different RF data analysis methods now available: autoregressive (AR) modeling, fast Fourier transform (FFT), and a newly designed pattern recognition algorithm and mathematically defined spectral similarity system (Table 1).

<table>
<thead>
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<th>Table 1. The comparison of different tissue characterization models</th>
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<td><strong>Mechanism</strong></td>
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AR, autoregressive; FFT, fast Fourier transform; IB, integrated backscatter; IVUS, intravascular ultrasound; VH, virtual histology.
**Autoregressive modeling**

After the IVUS-RF data are obtained from coronary arteries during pullbacks, AR modeling converts these data into a spectrum graph that plots the strength of the backscattered signal against frequency. The averaged spectrum is then normalized and parameters are identified from it within the bandwidth 17-42 MHz. A classification tree is used to characterize atherosclerotic coronary plaques, and this tree has the following parameters: (1) y-intercept, (2) maximum power, (3) mid-band fit, (4) minimum power, (5) frequency at maximum power, (6) frequency at minimum power, (7) slope of regression line, and (8) integrated backscatter. Atherosclerotic coronary plaques can be characterized into four different categories on the basis of their components: fibrotic, fibro-fatty, necrotic, and calcified. An in vivo IVUS mapping study generated 87-97% accurate predictions after results were compared with histological sections obtained by directional coronary atherectomy. However, in another in vivo study, IVUS had only 38-58% diagnostic accuracy for assessing 60 lesions in an atherosclerotic porcine model. Therefore, we still need large-scale in vivo studies to validate this modeling method. Meanwhile, electrocardiogram-gating is required by this method, which may limit its clinical convenience.

**Fast Fourier transform modeling**

Another tissue characterization method is direct mapping of the region of interest, using its integrated backscatter (IB) value. IB was calculated as the average power of the ultrasound backscattered signal by using FFT measured in decibels (dB). A color-coded tissue map based on the IB values for different plaque components was then constructed. Unlike AR modeling, FFT modeling divides tissues into 5 categories on the basis of IB value: (1) calcification (-30 dB to -23 dB), (2) mixed lesion (-55 dB to -30 dB), (3) fibrous tissue (-63 dB to -55 dB), (4) lipid core or intimal hyperplasia (-73 dB to -63 dB), and (5) thrombus (-88 dB to -80 dB). High diagnostic sensitivity (84% for lipid pool, 94% for fibrotic, and 100% for calcification) was also found in another autopsy study of 42 coronary arteries. However, such FFT modeling tissue characterization is only available in Japan, and large-scale studies to confirm this method’s accuracy remain to be performed.

**Spectral similarity system**

Recently, a newly designed pattern recognition algorithm was used to predict the tissue type of a given region of interest by comparing its RF spectrum against a database (library) and also estimating the confidence of prediction. Conceptually, this system characterizes a tissue type by comparing the spectrum from a vessel with spectra of known tissue types, using a mathematically defined measure to determine the similarity between the two spectra. Therefore, this system can provide the average confidence level for each tissue type within the frame or entire lesion, which is a capability that previous tissue characterization systems lack. This system classifies plaques into four different tissue types: fibrotic, necrotic, lipidic, and calcified. One example of such system is shown in Figure 3. Recently, by the first...
clinical study that used this system reported a large proportion of necrotic tissue in the culprit lesion of an acute coronary syndrome (ACS) patient with high confidence levels and no reflow phenomenon. Since this mapping modality is a newly developed system, further studies are needed before it can be used in clinical settings.

**IVUS-GUIDED PCI**

IVUS-guided stenting has been proved to lead to a 21% reduction (from 18.7% to 15%) in major cardiac adverse events as compared to angiographic-guided stenting in a meta-analysis. This result was mainly because of a 38% reduction in target vessel revascularization in the IVUS-guided arm. According to the 2005 update of the PCI guidelines of the American College of Cardiology/American Heart Association/Society of Cardiovascular Angiography and Interventions, there is no class I indication for IVUS in PCI; however, several class IIa indications are recommended: (1) to assess the adequacy of stent expansion, including the extent of stent apposition and the minimal luminal diameter within the stent; (2) to determine the mechanism of stent re-stenosis, such as under-expansion or neointimal hyperplasia, and to guide selection of appropriate therapy (repeat balloon expansion or vascular brachytherapy); (3) to evaluate undetermined coronary lesions, which are difficult to image with angiography because of their location; (4) to assess a suboptimal angiographic result after PCI; (5) to establish the distribution and presence of coronary calcium for which adjunctive rotational atherectomy is considered; and (6) to determine the plaque location and circumferential distribution for guidance of directional coronary atherectomy. In addition, color-coded tissue mapping of a specific pattern of culprit plaques in ACS patients can predict notorious slow flow or no reflow phenomenon before intervention. Furthermore, by tissue characterization, it is possible to identify “vulnerable plaques”, lipid-rich necrotic cores covered by a thin fibrous cap (TCFA, thin-cap fibroatheroma), before rupture. Strategies for IVUS-guided PCI are summarized in Figure 4.

**Before intervention**

IVUS is a powerful tool for evaluating plaques themselves and the surrounding anatomy before PCI. Clear identification of the characteristics of culprit plaques...
plaque and vessels can help to improve clinical outcomes after interventions. Usually, the monorail-system IVUS probe should be advanced at least 10 mm beyond the culprit lesion after adequate systemic heparinization and intracoronary administration of 100-200 μg nitroglycerin. During motorized or manual pullback at a constant speed, the image is recorded to a videotape or a hard disk. Automatic pullback is usually recommended, because we are able to obtain volumetric data. The entire imaging process should be continued until back to the aorta in all cases, and disengaging the guiding catheter from the coronary artery is mandatory if an aorto-coronary lesion is suspected.

**Lesion length**

Determining adequate lesion length and stent landing zone is crucial for PCI, especially in long and diffuse lesions. In a quantitative IVUS analysis from the SIRIUS trial, inadequate lesion coverage may contribute to edge restenosis after deploying a sirolimus-eluting stent. The baseline maximal reference plaque area was significantly larger in the edge restenosis group than in the non-restenosis group (60.5% vs. 48.58%). Therefore, it is reasonable to choose a stent-landing zone with a plaque area of < 50%.

At least three methods exist to determine the lesion length for further PCI planning. (1) Time-counting method: Since the motorized pullback occurs at a constant speed and detailed imaging time is also simultaneously recorded, the lesion length can be easily determined with the following equation: (pullback speed) × (time taken by the probe to travel from the distal reference site to the proximal reference site). (2) Long-view method: Almost all IVUS consoles can yield a reconstructed longitudinal view during and after the imaging process. By identifying the proximal and distal reference sites, the lesion length can be rapidly determined. (3) Marking technique: In some pullback devices, the pullback distance can be manually reset. In such circumstances, whenever the distal reference site is identified by angiography and IVUS, one can obtain precise lesion length on the pullback device after resetting the distance to zero and manually pulling back the device to the proximal reference site.

**Lesion diameter**

The lumen and EEM cross-sectional area (CSA) of the distal, proximal reference site and lesion site should be evaluated during or online immediately after the pullback. Negative remodeling is frequently encountered at the lesion site, especially in chronic total occlusion (CTO) cases, making lesion sizing difficult. It is reasonable to size the stent to 0.8- to 0.9-folds of the minimal diameter of the EEM at the distal reference site. In the Multicenter Ultrasound Stenting in Coronaries study (MUSIC) trial, in-stent minimal area ≥ 90% of the average reference lumen area or ≥ 100% of the lumen area of the reference segment with the lowest lumen area was suggested.

**Intermediate lesions**

Although coronary angiography has been considered the gold standard for evaluating the stenosis of coronary arteries, indeterminate lesions are commonly encountered despite multiple angiographic projections because of vessel overlapping, tortuosity, eccentricity, ostial/bifurcation, or severe calcification. A study of 70 de novo coronary lesions [not including the left main (LM) coronary artery] used 4.0 mm² as the cut-off minimal lumen area (MLA) to identify significant stenosis when compared with stress myocardial perfusion scan results; it revealed 80% sensitivity and 90% specificity. Another study of 51 non-LM lesions used 3.0 mm² as the MLA criteria for maximizing the sensitivity (83%) and specificity (92.3%) when a value of fractional flow reserve (FFR) < 0.75 was considered as significant in determining inducible ischemia.

It is more difficult and unreliable to assess the severity of LM lesions, making further revascularization plans difficult. In an autopsy study, it has been demonstrated that angiographically significant lesions were often mildly diseased. Similar to non-LM stenosis, IVUS provided a tomographic viewpoint of LM stenosis and was more sensitive in detecting vessel wall characteristics and atherosclerosis than angiography. When FFR < 0.75 was used as the gold standard for detecting significant LM stenosis, a study of 55 patients showed highest sensitivity and specificity by using an MLA of 5.9 mm² and minimal lumen diameter (MLD) of 2.8 mm as IVUS indicators. Another LM study with clinical end-points has suggested that an MLA of 7.5 mm² should be used as the cut-off value for performing revascularization.
Pre-treatment before PCI

Several plaque characteristics such as the severity and extent of calcification, arterial remodeling, plaque distribution, and the presence of dissection or thrombi can affect the decision to use a particular treatment before PCI. Some studies have reported that IVUS imaging before PCI can influence operators’ decision making and treatment strategy. With regard to calcified lesions, IVUS is more sensitive than angiography for determining the distribution of calcification as circumferential or non-circumferential. During high-pressure balloon or stent inflation, vessel expansion tends to develop at compliant sites if heterogeneous materials are involved. It means that in a non-circumferential calcified lesion, vessel dissection or even rupture may occur at the junction of calcified and non-calcified plaques if high-pressure inflation is used. In such a scenario, dilatation followed by stenting may be prepared before PCI. With regard to circumferential calcified lesions, especially superficial calcified plaques, the delivery and expansion of balloons and stents may be difficult. Plaque modification by rotablation or cutting balloon before intervention is reasonable and can facilitate procedure success and also prevent balloon/stent under-expansion.

With regard to bifurcation lesions, IVUS can detect the distribution of plaques not only in the main branch but also in the ostium of the side branch (SB). One study revealed that SB occlusion occurred in 35% of the plaque-containing lesions at the SB ostium after PCI as compared to the 8.2% occlusion rate of plaque-free lesions at the SB ostium. Therefore, wiring the SB to protect it before PCI should be considered if IVUS reveals plaque involvement at the SB ostium.

In ACS patients, no reflow phenomenon during PCI leads to an unfavorable outcome. Clinical factors associated with this phenomenon include age, male sex, hyperglycemia, increased white blood cell count, and absence of pre-infarction angina. The most consistent risk factors for this phenomenon, determined by gray-scale IVUS, are the presence of an attenuated plaque, thrombus, large plaque burden, lipid pool-like imaging, and positive vessel remodeling. Color-coded tissue characterization has been proved to predict such phenomena before PCI if lesions are observed to have a higher percentage of necrotic core component and a smaller percentage of fibrous component. Thrombus aspiration or distal protection device deployment before PCI is recommended if such lesions are found. Furthermore, sometimes interventionists may encounter multiple borderline angiographic lesions without critical narrowing during ACS intervention. IVUS as well as tissue characterization may play an important role in locating the culprit lesion where plaque rupture or TCFA has developed.

After intervention

In the era of bare metal stent (BMS), post procedure MLD has been proved to be one of the predictors of restenosis by angiography. By IVUS, the MUSIC trial has suggested that adequate stenting results in favorable clinical and angiographic outcomes. Such strategy includes the following: (1) complete apposition of the stent over its entire length against the vessel wall; (2) in-stent minimal area ≥ 90% of the average reference lumen area or ≥ 100% of the lumen area of the reference segment with the lowest lumen area; and (3) symmetric stent expansion defined by a minimal lumen diameter/maximal lumen diameter of ≥ 0.7.

Under-expansion and incomplete stent apposition (ISA) (Figure 5)

Stent expansion refers to the in-stent minimal area after the stent is deployed, and stent apposition refers to a condition in which the stent is in complete contact with the vessel wall. In the bare-metal stent era, neointimal hyperplasia and suboptimal stent expansion were strong factors for restenosis. In the Can Routine Ultrasound Influence Stent Expansion (CRUISE) trial, larger MLD and MLA were obtained in the IVUS-guided group than in the angiographic-guided group. Such improved expansion with IVUS-guided stenting resulted in a clinical benefit at the 9-month follow-up in terms of target vessel revascularization. In the drug-eluting stent (DES) era, neointimal hyperplasia was largely suppressed, making stent under-expansion the major mechanism for restenosis. In a prospective study, the post-procedural minimal stent area remained a strong predictor of restenosis. Meanwhile, ISA has been proved to be a major cause of acute/subacute stent thrombosis (ST). Moreover, late/very late ST of DES was also observed in patients with ISA. In that study,
the incidence of ISA was 77% in the very late ST group and only 12% in the control group. Therefore, higher pressure with larger balloon should be recommended for post-dilation in order to obtain adequate stent expansion and apposition.

Complication survey

After PCI, IVUS is commonly used to detect the morphological effects of angioplasty and complication such as slow flow/no reflow, dissection, intramural hematoma, plaque prolapsed, or spasm. Six morphological patterns after angioplasty have been proposed by researchers using IVUS. Meanwhile, coronary dissection is a common reason for acute closure during or after PCI. According to the depth of the dissection, a classification of intimal, medial, and adventitial dissection was proposed. IVUS is more sensitive than angiography for detecting dissection and can also clearly identify the extent of dissection to guide further stenting if flow-limiting dissection develops, which usually requires a longer stent than angiographic-guided stenting. At the same time, intramural hematoma, defined as an accumulation of blood within the medial space and displacement of the internal elastic membrane inward and the EEM outward, can be accurately evaluated with IVUS. Intramural hematoma may accompany dissection and associated with higher rate of non-Q-wave MI, repeated revascularization and sudden cardiac death.

APPLICATION OF CLINICAL RESEARCH

Because IVUS is more sensitive than angiography for evaluating coronary plaque even in “angiographically normal” arteries, it has become a powerful tool for evaluating plaque progression or regression trials with various pharmacological interventions such as statins and angiotensin-converting enzyme inhibitor. In the Reversal of Atherosclerosis with Aggressive Lipid...
Lowering (REVERSAL) trial, IVUS demonstrated a significant lower plaque progression rate in the intensive lipid control arm than the moderate-treatment arm. In A Study to Evaluate the Effect of Rosuvastatin on Intravascular Ultrasound-Derived Coronary Atheroma Burden (ASTEROID) trial, IVUS showed significant atheroma volume regression after high-dose statin treatment. In a substudy of the Comparison of Amlodipine vs. Enalapril to Limit Occurrences of Thrombosis (CAMELOT) trial, IVUS showed atheroma progression in the placebo group, a trend toward progression in the enalapril group, and no progression in the amlodipine group.

**IVUS VERSUS OPTICAL COHERENCE TOMOGRAPHY (OCT)**

Intravascular OCT is a high-resolution optical intravascular imaging modality, which is approximately 10 times higher in resolution than IVUS. It uses near-infrared light rather than ultrasound, which may allow evaluation of not only intravascular microanatomy but also neointimal formation and stent apposition. However, there are some limitations of OCT in clinical use. First, blood cells can interfere with OCT imaging; therefore, vessel occlusion with a balloon, followed by continuous flushing with lactated Ringer’s solution, is mandatory for OCT examination. Second, limited visual depth is a limitation of OCT; it prohibits the assessment of large coronary vessels and deeper structures, so that IVUS is still more useful in terms of assisting PCI. Recently, new generation frequency-domain OCT (FD-OCT) has demonstrated some advantage over conventional time-domain OCT (TD-OCT) and has been developed for clinical use (Table 2).

**FUTURE DIRECTIONS OF IVUS USAGE IN TAIWAN**

IVUS-guided PCI accounts for approximately 5%-8% of procedures in the United States, and the number in our country is likely lower than that. Since IVUS has been proved to improve clinical outcomes in various studies, it should be used more frequently in daily practice. In order to do so, the crossing ability, pushing ability, tracking ability, and image quality should be improved; it should be made more easy to use; and the system interface should be more user-friendly. Meanwhile, the cost of the system is also a key point influencing decisions about performing IVUS-guided PCI, especially if it is not covered by national health insurance. Reducing the cost of IVUS-guided PCI is another critical issue that needs to be addressed if this procedure is to be popularized. Furthermore, holding IVUS-specific workshops or conferences with experts will also help.

**SUMMARY**

IVUS provides more detailed information than conventional angiography. Its safety and significant influence on daily decision-making in the catheterization laboratory have been proved. IVUS evaluation before and after PCI can improve clinical outcome and resolve doubts about ambiguous lesions. Tissue characterization is a new technique that is based on signal analysis, which provides further information for lesion survey and complication prevention. IVUS is also a powerful tool for atherosclerotic evaluation for pharmacological treatment. OCT is another tomographic modality for evaluating coronary anatomy in more detail. However, increased procedure difficulty and limited visual depth

| Table 2. The differences between intravascular ultrasound (IVUS), time-domain optical coherence tomography (TD-OCT) and frequency-domain optical coherence tomography (FD-OCT) |
|---------------------------------|-----------------|-----------------|-----------------|
| **Mechanism**                  | **IVUS**         | **TD-OCT**      | **FD-OCT**      |
| Axial resolution (µm)          | 100-150          | 10-20           | 10-20           |
| Lateral resolution (µm)        | 150-300          | 20-40           | 20-40           |
| Frame rate (image/sec)         | 30               | 15.6            | 100             |
| Catheter size (inches)         | 0.08-0.12        | 0.016           | 0.016           |
| Pullback speed (mm/sec)        | 0.5              | 1.0-2.0         | 20              |
restrain its clinical use. Finally, the use of IVUS in our country remains low because of various reasons. System improvements, reduction in costs, and frequent IVUS-specific conferences could lead to IVUS being used more widely, thus improving clinical outcomes and the quality of our interventions.

REFERENCES

29. Sathyanarayana S, Carlier S, Li W, Thomas L. Characterisation of


