CHAPTER 12

Intracoronary Imaging-I: Step-by-Step Technique for Intravascular Ultrasound (IVUS)

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Introduction

Intravascular ultrasound (IVUS) imaging has evolved as an adjunct to coronary angiography for understanding coronary pathology. This technique has enhanced the ability to characterize intracoronary plaque morphology and guide intervention. When compared with two – dimensional coronary angiography, IVUS has the advantage of providing three – dimensional information about the coronary arteries, including lesion quantification (vessel dimensions, lesion size, severity and volume) and anatomical architecture (arterial remodeling, thrombus, and dissection). It can also be used to assess atherosclerotic plaque composition, such as extent of calcification, which can help guide an interventional strategy and optimize results after drug eluting stent (DES) deployment. IVUS provides information about stent expansion and apposition, which may help decrease occurrence of stent thrombosis (ST) and in-stent restenosis (ISR) down the line. In this chapter, we discuss the indications for IVUS, various types of IVUS catheters, and procedural technique including challenges.

Use

Indications for IVUS

Table 1 demonstrates the indications for IVUS according to the 2011 ACCF (American College of Cardiology)/AHA (American Heart Association)/SCAI (Society of Coronary Angiography and Intervention)

guidelines for percutaneous coronary intervention (PCI).[1] In addition, IVUS helps to: (i) estimate lesion severity including detection of restenosis, evaluation of lesions deemed "intermediate" by coronary angiography and lesions in a diffusely diseased or bifurcating vessel; (ii) identify lesion morphology including extent of plaque, type of plaque and presence of pseudoaneurysms; (iii) guide treatment regarding optimal entry site into the true lumen for CTOs, optimal balloon size and stent optimization; and (iv) manage complications including edge dissection following coronary intervention. Prior studies have demonstrated that IVUS is safe with a reported major complication rate of 0.1 - 0.5%,[2] the most reported complication being coronary vasospasm reported in 2.9% of cases.

Contraindications to IVUS

In general, any contraindication for performing coronary angiography applies to IVUS as well.

IVUS types

There are two types of IVUS systems: the mechanical and the electronic systems.[1, 3] Both are commercially available and create an axial image of the vessel wall and lumen at the catheter tip by transmitting ultrasound waves which cover 360 degrees of the vessel wall. There is a separate console that the catheters are connected to which allows recording and display of still images and video loops. Vessel measurements including diameter, circumference, and area can be performed on this console. Most coronary IVUS catheters can be passed through 5–6 French sheaths.

Mechanical systems use a single rotating ultrasound transducer mounted at the tip of a flexible high-torque catheter which is driven at 30 revolutions/second at approximately 1° increments, and sends and receives ultrasound signals to visualize the vessel in cross-section. They have the advantage of a simple design with greater signal to power output and good image quality. However, these catheters are less flexible and more difficult to use in tortuous vessels due to the central drive shaft, which decreases

flexibility and prevents the simultaneous use of a central guidewire. Frequent saline flushing of these catheters is necessary to provide a fluid pathway for the US beam and to eliminate accumulation of air bubbles which can create image artifacts. Volcano Corporation (Rancho Cordova, CA), Boston Scientific Corporation (Natick, MA), HD-IVUS and Acist Medical Systems Inc. (Eden Prairie, MN) and Terumo Corporation (Tokyo, Japan) all manufacture this type of catheter.

Electronic systems use multiple phased array of small crystals positioned in a circumferential fashion around the tip of the catheter programmed such that there is simultaneous transmission by one set of elements and receiving by a second set, followed by processing into real time imaging. A central guidewire is required to remain in the vessel for these catheters. They do not require rotation to acquire images nor do they need continuous flushing with saline. Volcano Corporation (Rancho Cordova, CA) manufactures phased array catheters.

Frequency and resolution

The frequency of an IVUS system determines its resolution. Low frequency catheters have lower proximal image resolution and an expanded imaging field, whereas high frequency catheters have higher proximal image resolution but a narrower imaging field. Axial resolution of IVUS catheters may vary depending on the manufacturer, ranging from 38-170 microns. Frequencies of 8 and 12 MHz are best suited for imaging large vessels (e.g. aorta, inferior vena cava); around 20 MHz for smaller vessels like the carotids and vessels of the lower extremity (e.g. femoropopliteal arteries); and higher frequencies around 45 MHz for imaging of very small vessels (e.g. coronary arteries).

Procedure details

This section describes the technical approach to IVUS.

1. An important prerequisite before inserting an IVUS catheter is to ensure that the patient is on therapeutic anticoagulation.
2. A high frequency IVUS catheter (40-60 MHz) has suitable image resolution in the coronary vasculature. Unless contraindicated, intracoronary nitroglycerine should be given before inserting the IVUS catheter to avoid coronary vasospasm.
3. Following standard PCI techniques, the selected coronary artery is engaged with a guide catheter and a guidewire is passed into the target artery.
4. Mechanical IVUS catheters require fastidious flushing of the sheath to remove any air to prevent air embolization and poor image quality, while multiple array catheters require flushing of the wire port prior to insertion in the body.
5. The IVUS catheter is then connected to the image console. When the system is ready, it can be introduced into the target vessel through the guide over a guidewire under fluoroscopic guidance. If resistance is met, it is important not to push the IVUS catheter but to remove, reassess and perform adequate steps such as vessel dilation prior to reinsertion.
6. Once the IVUS catheter is at the desired location, imaging is performed by a slow pullback using a manual technique or by mechanical pullback sleds with rates of pullback of 0.5 or 1.0 mm/sec.
7. After imaging is complete, the catheter can be withdrawn, images reviewed and measurements made.
8. A final angiogram is performed after removing the IVUS catheter to ensure there was no injury to the artery.

<u>Interpretation of IVUS images</u>

Appearance of normal coronary artery

Ultrasound (US) waves are reflected when they encounter an interface of different acoustic impedance which is dependent on tissue density. The wall of the coronary vessel has three layers from inside to outside - intima, media made up of smooth muscle cells, and adventitia made up of multiple collagen fibers. US waves from the transducer are reflected by the intima; those waves not reflected pass through to the media and through it with minimal reflection to the adventitia where they are highly reflected. Thus, the IVUS image in a normal coronary artery (**Figure 1**) would consist of an area of bright echo from the intima, followed by an area of dark zone due to the media, followed by areas of multiple bright echoes from the adventitia.

IVUS measurements

Both quantitative and qualitative measurements are performed with IVUS.

Quantitative: The leading edge of the image boundaries is used to perform all IVUS measurements, not the trailing edge. Lumen measurements are performed using the interface between the lumen and the leading edge of the intima. Other commonly used measurements include: (i) lumen cross sectional area (CSA) which is the area bounded by the luminal border, (ii) minimum and maximum lumen diameters which are the shortest and longest diameters through the center point of the lumen respectively, and (iii) lumen area stenosis which is reference lumen CSA minus minimum lumen CSA.

Qualitative: IVUS is a reliable tool in identification of various coronary pathologies including thrombus, intimal hyperplasia, soft plaques, fibrous plaques and coronary calcifications. These characteristics are demarcated by differences in echogenicity – soft plaques, fibrous plaques and calcific lesions have low, intermediate and high echogenicity on IVUS imaging, respectively. Similarly, intimal hyperplasia associated with early ISR is associated with low echogenicity while that associated with late ISR is associated with high echogenicity. Thrombus can be sometimes difficult to identify with IVUS and is usually recognized as an intracoronary lesion that is relatively echolucent and often has a

pedunculated or a layered appearance. In addition, IVUS can also be used for assessment of extent of coronary dissection and differentiation between true and false lumen.

IVUS for diagnostic evaluation

Assessment of angiographically indeterminate coronary artery stenosis

Though IVUS provides high resolution images of the coronary arteries, it does not assess for the physiologic significance of a lesion like FFR or IFR or stress imaging. However, mean luminal area (MLA) can be used as a rough guide for this purpose.

Left main disease

In the evaluation of indeterminant LM disease, a mean luminal diameter (MLD) < 2.8 mm and a MLA < 5.9 mm^2 are most accurate to determine lesion significance. Lesions with MLA >7.5 mm^2 can be safely deferred. Lesions with MLA of 6 mm^2 – 7.5 mm^2 may require another form of physiological assessment such as FFR.[1, 4, 5]

Non-left main disease

Indeterminant lesions in non-LM major coronary arteries with a MLD > 2mm and MLA of >4 mm^2 are not hemodynamically significant and correlate with low event rates.[6] Lesions < 4 mm^2 may be significant but require confirmation by another physiological assessment such as FFR or IFR. In small diameter arteries < 3mm^2, FFR is a more accurate evaluation of significant stenosis.[7] Overall, IVUS studies have demonstrated a high negative-predictive value but low positive-predictive value and hence, an intervention can be deferred based on MLA size in the appropriate clinical situation. However, IVUS alone should not be used to justify interventions.

Post-cardiac transplantation surveillance of CAD

IVUS evaluation of the coronary vasculature 4 to 6 weeks and 1 year after cardiac transplantation can be used to identify donor CAD, demonstrate rapidly progressive cardiac allograft vasculopathy, and provide prognostic information.[1] IVUS is a better modality than angiography for early detection of cardiac allograft vasculopathy.[8]

Determination of the etiology of in-stent restenosis and stenosis thrombosis

It is important to understand the etiology of ISR and ST to successfully treat and avoid their recurrence. IVUS can be used to evaluate the mechanical causes of stent failure including the degree of neointimal hyperplasia in ISR[9] as well as stent underexpansion or malapposition, which are associated with thrombosis.[1, 10]

<u>IVUS for optimizing stent implantation</u>

After stent deployment, IVUS can be used to identify stent placement, expansion, apposition, and edge dissection. Inadequate stent expansion [minimal stent areas (MSA) of 80% to 90% of the reference areas] is known to increase the risk of ISR or ST, more so with BMS than DES and may justify further IVUS guided balloon dilation.[11] To prevent ISR within a BMS, an IVUS measured minimal stent area (MSA) threshold of 6.4–6.5 mm^2 has been reported in studies; meanwhile a post-procedural MSA cutoff of 5.3–5.5 mm^2 has been reported to prevent ISR within newer generation DES.[12] Inadequate stent apposition (struts not touching the lumen interface and “free floating” in the lumen) was previously considered a risk factor for stent thrombosis.[12] Identification of tissue prolapse into the stent struts and edge dissection is paramount, as these pathologies may also impact clinical outcomes and management. Tissue prolapse is managed by serial balloon inflations while edge dissection requires deployment of an additional stent.

IVUS for CTO interventions

There are several potential roles for IVUS with CTO interventions due to its high resolution cross sectional imaging of the coronary vessels. IVUS can help direct crossing total occlusions by showing the location of the wire in plaque, media/adventitia, or extravascular locations. These may lead to choosing alternative approaches through the lesion and whether or not to attempt balloon inflations. IVUS can be used for identification of the precise site of occlusion for stumpless lesions, antegrade and retrograde tracking of the guidewire, CART or reverse CART techniques, and optimal balloon sizing and dilatation. The short-tip phased array catheter may be helpful in this regard due to the short distance from tip to IVUS sensor, although other smaller IVUS catheters can be inserted directly without the need for pre-dilation. In addition, IVUS substantially decreases the use of contrast and radiation exposure.
The major limitation is the presence of calcium that impairs the detection of the true lumen. Due to the side looking nature of the image, the IVUS should be inserted into the occlusion to adequately image the vessel.[13]

IVUS artifacts

Several artifacts have been described during IVUS use, for which the operator has to be keenly aware of while interpreting images.[3, 14]

Non-uniform rotational distortion (NURD)

This artifact may be seen with mechanical systems secondary to mechanical binding of the drive cable that rotates the transducer. This can be due to multiple reasons including vessel tortuosity, tortuous shapes/ kinking/too small a lumen of guide catheters, kinking of the imaging sheath, and changes in position between diastole and systole. Artifacts can also occur when a wire channel lies

adjacent to the transducers, which can be eliminated by positioning the guide wire central to the transducer elements. Some catheters have an automatic software correction to minimize NURD artifact.

Near field artifacts

These include ring down artifacts and blood speckle artifacts.

a. Ring-down artifacts (**Figure 5**):

   These artifacts are seen as bright halos around the guiding catheter and occur from high-amplitude ultrasound signals from the transducer. Time gain compensation (TGC) and digital subtraction of a reference mask can be used to reduce this artifact.

b. Blood speckle artifacts:

   These artifacts occur with increasing transducer frequency and decreasing blood flow velocity, thereby limiting the ability to distinguish lumen from tissue. Flushing contrast or saline to clear the lumen of the guiding catheter can help identify tissue borders in these cases. TGC manipulation and computer based imaging algorithms can be applied to decrease blood speckle.

Side lobe artifacts

Side lobe artifacts (**Figure 6**) are seen as bright round lines that occur adjacent to a hyperechoic structure. They occur when low-energy sound beams are reflected outside the central beam and are erroneously assigned to the main beam parallel to the false location.

<u>Virtual histology IVUS (VH-IVUS)</u>

Virtual histology (**Figure 7**) is an IVUS-based-post-processing modality that can create color-coded images of the coronary plaque and vessel lumen. Plaque is classified as (i) White: dense calcium,

(ii) Dark green: fibrous tissue, (iii) Light green: fibrofatty plaque and (iv) Red: necrotic core. Components are reported as percentages of total plaque areas and volumes.[15, 16]

VH-IVUS can currently be obtained using a 45 MHz 3.2 French rotational catheter or a 20 MHz, 2.9 French phased-array transducer catheter, and the post-processing analysis is performed using a proprietary software.[15] The imaging technique is similar to gray-scale IVUS using distal and proximal fiduciary points with a gradual pull back of the catheter after administration of intracoronary nitroglycerine.

Three studies including – VIVA (VH-IVUS in Vulnerable Atherosclerosis), sub-study of the PROSPECT and ATHEROREMO-IVUS Study (The European Collaborative Project on Inflammation and Vascular Wall Remodeling in Atherosclerosis - Intravascular Ultrasound Study) – demonstrated that VH-IVUS can identify high-risk plaques even among non-culprit lesions and can be a useful tool in identification of dynamic changes in plaque morphology.[17-20] However, these studies were non-randomized and combined VH-IVUS and gray-scale IVUS, rather than independently investigating the utility of VH-IVUS.

The role of VH-IVUS in evaluating the pharmacological effects on coronary atherosclerosis was evaluated in the STABLE (Statin and Atheroma Vulnerability Evaluation) study.[21] This prospective double-blind randomized controlled trial (312 patients) demonstrated that rosuvastatin significantly decreased plaque necrotic core volume and frequency of thin-capped fibroatheroma at 12 months follow up. Additional utility of VH-IVUS include its role of predicting distal embolization during PCI and assessing plaque composition in CTOs.[22, 23]

VH-IVUS suffers from several limitations. One major concern is its diagnostic accuracy and external validity regarding its ability to perform accurate measurements. A recent study in a porcine model utilizing VH-IVUS demonstrated poor accuracy for identifying fibrous (58%), fibrofatty (38%), and necrotic core (38%) plaque. Furthermore, there was no significant correlation of necrotic core size

between VH-IVUS and histology.[24] VH-IVUS can be prone to artifacts, especially in the presence of dense calcium, thrombus, and stent struts. Poor axial and longitudinal resolution can limit the comparison between baseline and follow up images. Despite its several limitations, VH-IVUS is a valuable tool to further our understanding of the coronary plaque structure. Currently, this technology has limited clinical application on its own and must be combined with additional gray-scale IVUS or OCT in the appropriate patient.

Clinical Outcomes with IVUS imaging

One prospective, multicenter trial including 1,448 patients who received DES showed that IVUS-guidance significantly improved clinical outcomes, including target-vessel failure (hazard ratio [HR]: 0.530; 95% confidence interval [CI]: 0.312 to 0.901; p=0.019) and target-vessel revascularization including stent failure (HR: 0.407; 95% CI: 0.188 to 0.880; p=0.018) at 1 year follow up compared with angiography.[25] Another metanalysis including 17,882 patients from 31 clinical trials demonstrated that, when compared with angiography, IVUS-guided PCI reduced risk of all-cause death by 36%, MI by 38%, target lesion revascularization by 36%, and stent thrombosis by 48%.[26] Therefore, it is imperative that current practicing interventional cardiologists as well as trainees become adept at the use of IVUS imaging.

Conclusion

IVUS is a useful tool not only to obtain additional information regarding lesion severity, lesion length, and plaque characteristics, but also to plan optimal treatment strategies. Larger studies are required to further determine the clinical impact and cost of IVUS guidance in complex coronary lesions.

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Tables

Table 1: Indications for IVUS use

Indications for IVUS Use
Class IIa
1. Assessment of angiographically indeterminant left main CAD. *(Level of Evidence: B)*
2. Four 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)*
3. To determine the mechanism of stent restenosis. *(Level of Evidence: C)*
Class IIb
1. Assessment of non–left main coronary arteries with angiographically intermediate coronary stenoses (50% to 70% diameter stenosis). *(Level of Evidence: B)*
2. For guidance of coronary stent implantation, particularly in cases of left main coronary artery stenting. *(Level of Evidence: B)*
3. To determine the mechanism of stent thrombosis. *(Level of Evidence: C)*
Class III: NO Benefit
1. Routine lesion assessment with IVUS is not recommended when revascularization with PCI or CABG is not being contemplated. *(Level of Evidence: C)*

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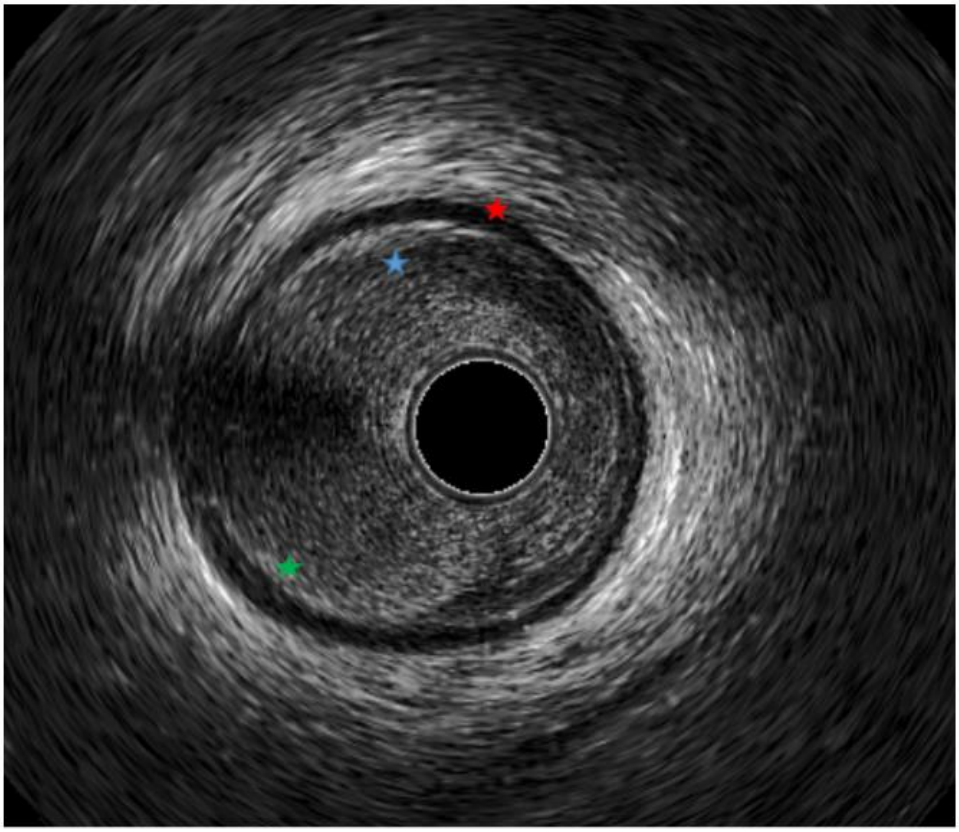
Figures

Figure 1: Normal anatomy



★Intima, ★Media, ★Adventitia.

Figure 2: Stent struts within coronary lumen

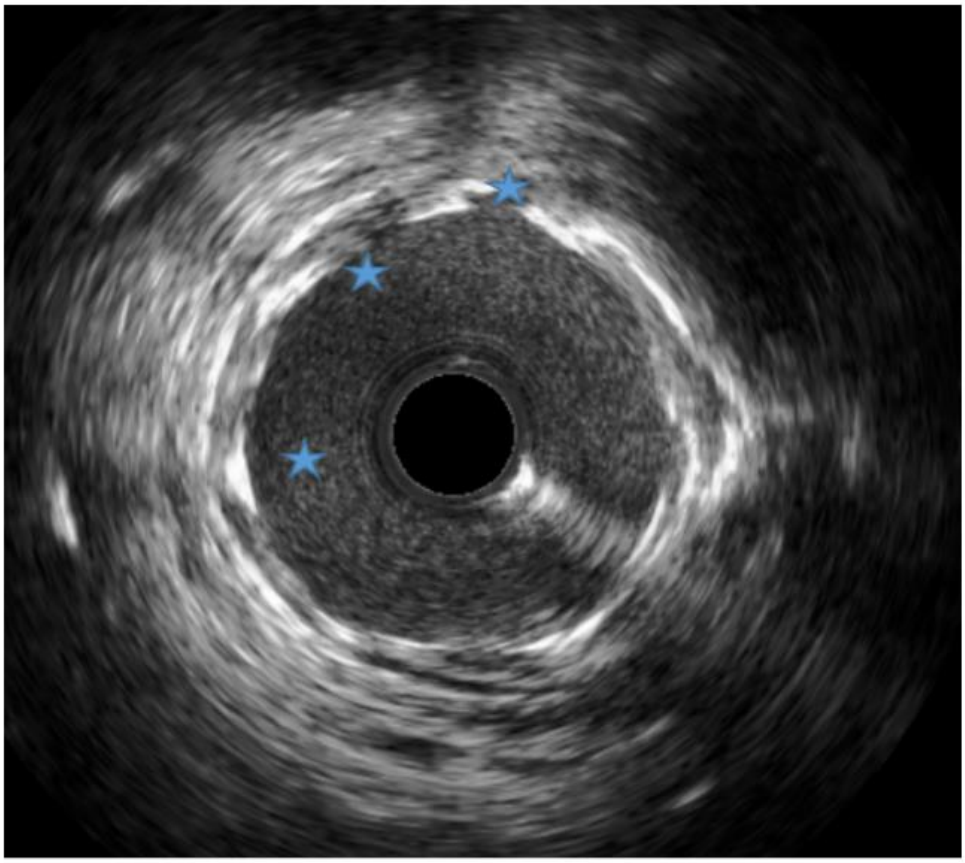


Figure 3: Coronary calcium

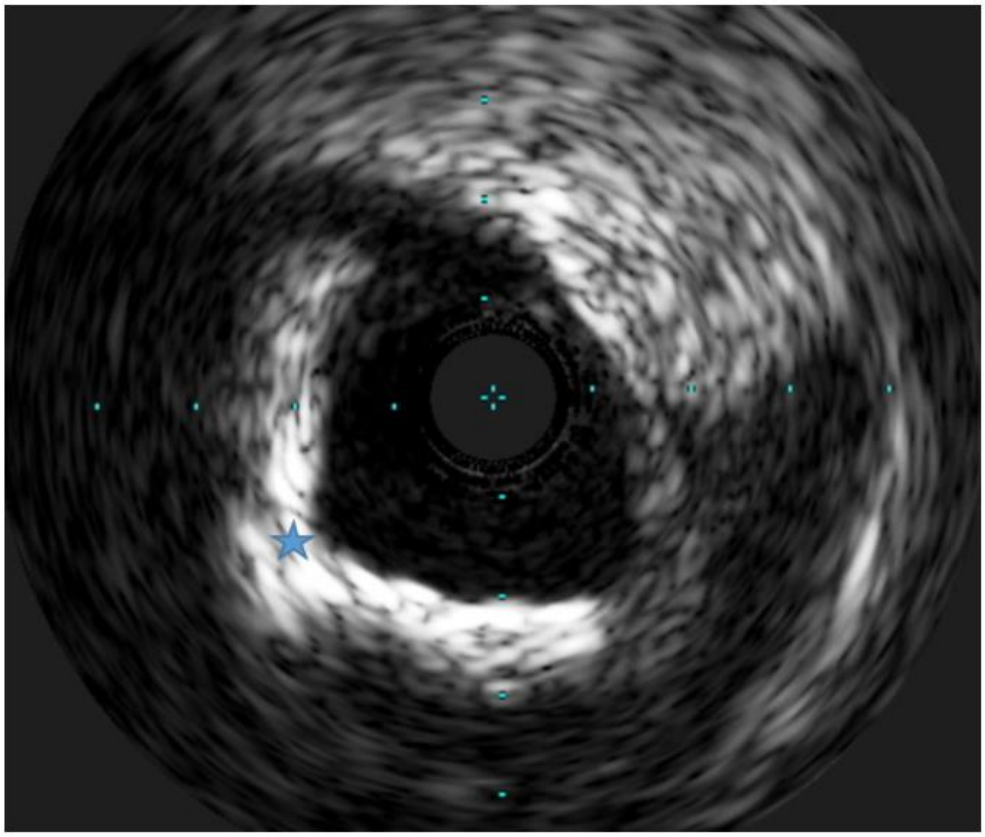


Figure 4: Guidewire artifact

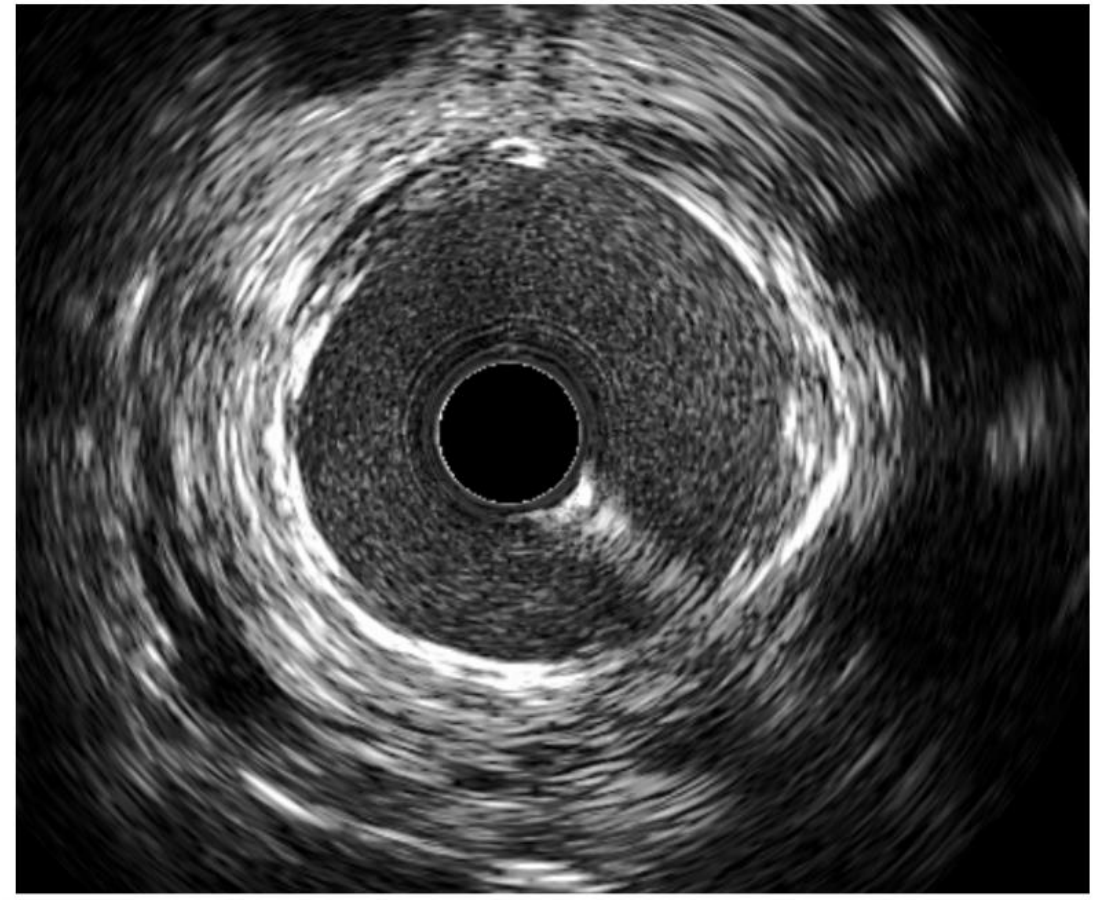


Figure 5: Ringdown artifact

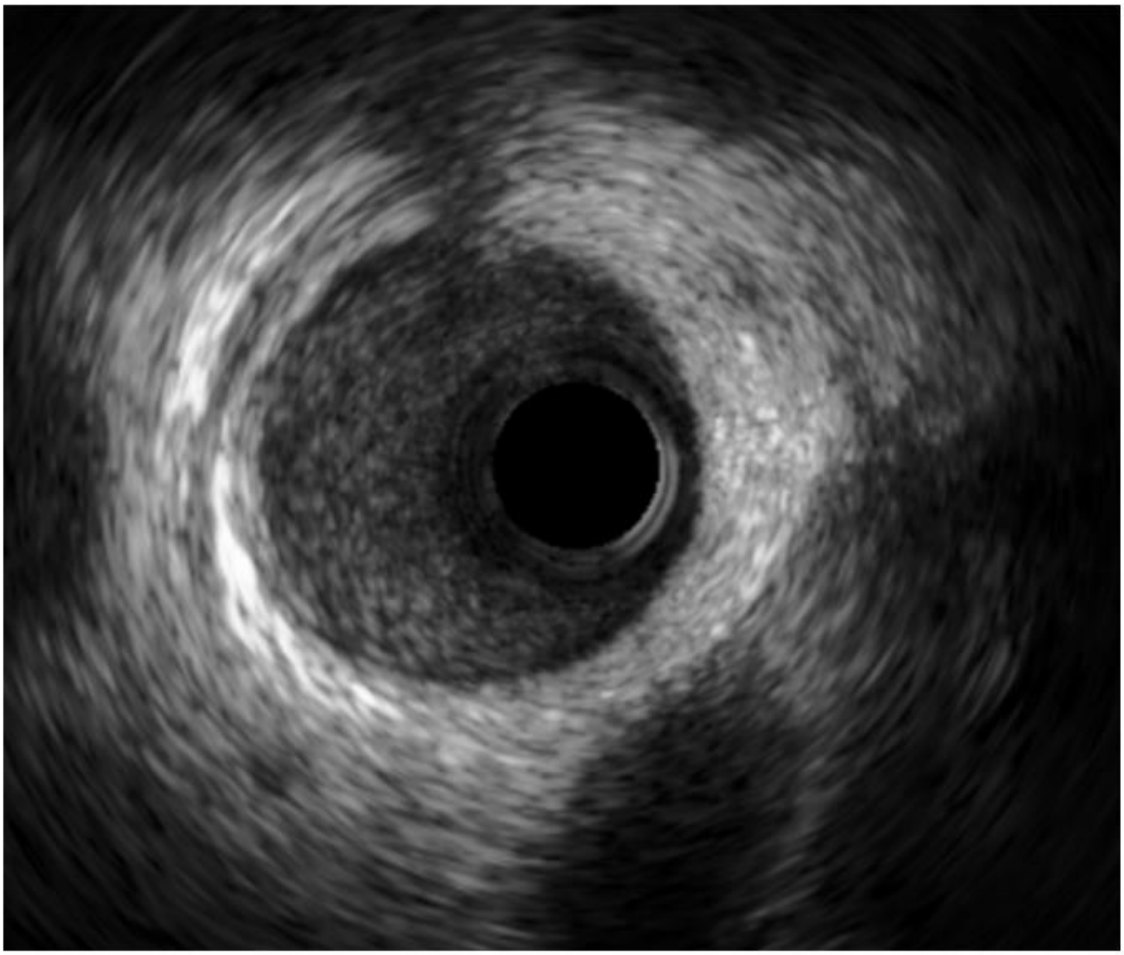


Figure 6: Sidelobe artifact

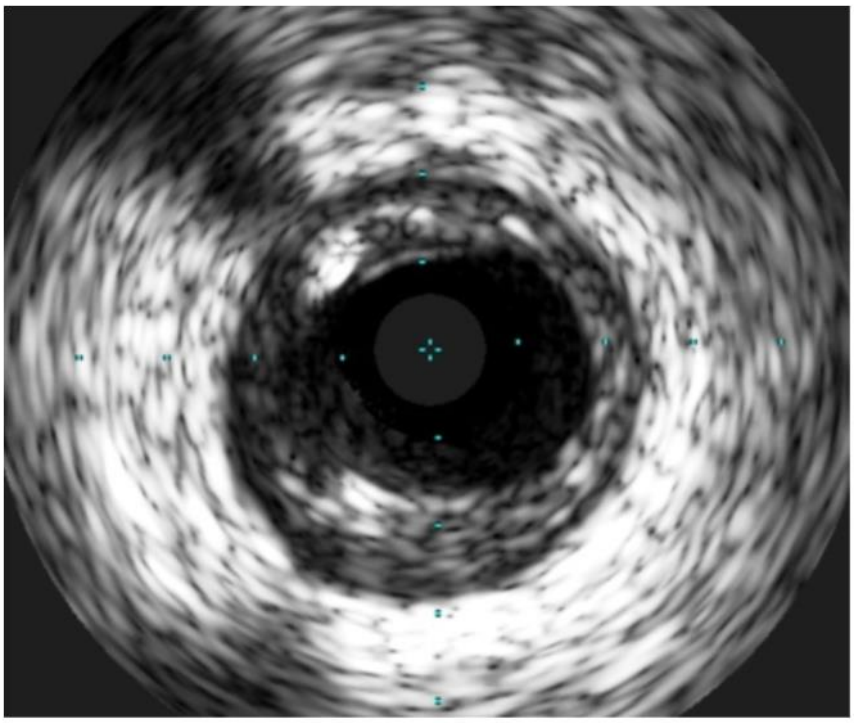
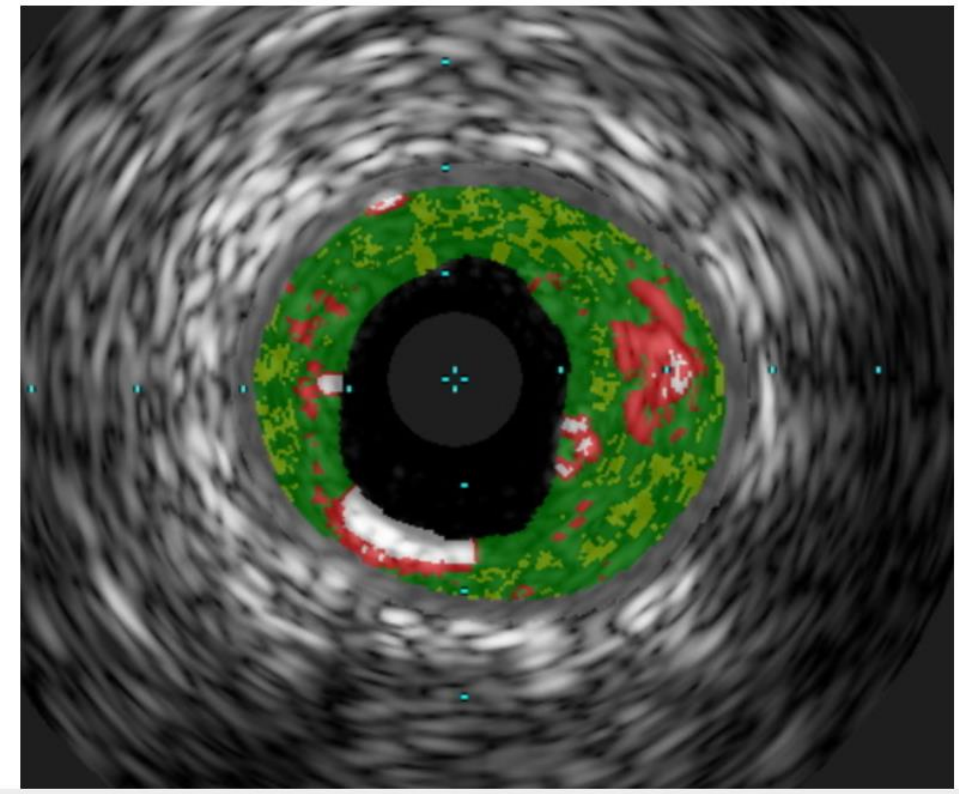


Figure 7: Virtual histology



Light green- fibrofatty tissue, Dark green- fibrous tissue, Red- necrotic core, White- dense calcium

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