Fundamentals of Intracoronary Imaging

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Introduction

Intravascular imaging is an important tool in the arsenal of each interventional cardiologist. A multitude of imaging modalities are available to help understand coronary arterial and plaque morphology. While angiography provides a two-dimensional image of a three-dimensional structure, intravascular imaging enhances understanding by providing detailed cross-sectional images. The imaging modalities used often include intravascular ultrasound (IVUS) and Optical Coherence Tomography (OCT). Near-infrared spectroscopy (NIRS) is also available, although not widely used.

While IVUS imaging is based on ultrasound wave reflection, OCT is based on infrared light transmission and reflection through different tissues. Each of these two modalities has utility in diagnostic coronary angiography and percutaneous interventions, both for stable coronary artery disease (CAD) and in cases of acute coronary syndrome (ACS).

Intravascular Ultrasound (IVUS)

IVUS imaging technique has been available in clinical practice for a long time and is the most widely used and studied technique for intravascular imaging. First commercially available in the USA in the 1980's, IVUS is increasingly being used in day-to-day practice [1].

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Principle of IVUS Imaging

- IVUS catheters use the principles of ultrasonic sound wave [20–45 Megahertz (MHz)], transmission and reflection. Sound waves, produced by a piezoelectric crystal in the IVUS catheter, propagate through the different tissues and are reflected according to the acoustic densities of each one of them.
- Imaging with IVUS technique requires a special catheter to be inserted into the coronary arteries. There are two kinds of IVUS catheters available in the USA currently.
  - Phased Array Transducers:
    Consist of multiple transducers arranged circumferentially that are activated sequentially to produce an image. For example, Eagle Eye imaging system from Philips Healthcare (Andover, Massachusetts, USA).
  - Single array (Mechanical) transducers:
    Consist of a single transducer that rotates 360° to create images of the targeted vessel segment. For example: Opticross imaging catheters (Boston Scientific, Marlborough, Massachusetts, USA) and Kodama HD imaging catheter (Acist Medical Imaging, Eden Praire, Minnesota, USA).
- The above-mentioned imaging systems use similar principles of image production and have similar axillary and longitudinal resolutions. Proprietary post-processing software is marketed by each individual company provides further improvement in image quality and definition.

Indications

- IVUS imaging can be used in cases of acute coronary syndrome and stable coronary artery disease. Current guidelines recommend IVUS use in both pre-procedure planning and post-percutaneous intervention (PCI) stent optimization.
- Pre-procedure planning:
  - Reference vessel sizing proximal and distal to the lesion.
  - Lesion characterization: Lesion complexity (e.g., plaque burden, calcification), and length, especially in bifurcations lesions.
  - To assess the need for lesion preparation/ modification.
  - Left main sizing, including assessing the significance of left main lesions. Class IIa, Level of Evidence: B [2]. Left main lumen area of 5.5 mm^2 and non-left main area of 4 mm^2 are considered significant for intervention.
  - Assessment of graft vasculopathy in transplanted hearts.

  - Assessment of Lesions with in-stent restenosis (ISR) needing evaluation for a mechanism of ISR. Class IIa, Level of Evidence: B [2].
  - Integral to performing no-contrast or ultra-low contrast percutaneous interventions in people with renal insufficiency [3].
- Post-percutaneous intervention (PCI):
  - Optimizing stent placement by assessing for under expansion and malapposition.
  - Assess proximal and distal edge for geographical miss and dissection.
  - To assess for minimal stent area (MSA) post-implantation. MSA > 6 mm^2 in non-left main vessels and MSA > 8.5 mm^2 in left main lesions is considered ideal.

Image Characteristics

- IVUS imaging has a resolution of 100–200 μm. It can help discriminate between the lumen–intima interface and, to a lesser degree, the interface between the media and intima.
- The image is acquired as a gray scale (Fig. 9.1).
- Virtual histology (VH) imaging incorporation and ChromaFlow (Eagle Eye catheter, Philips) can help with additional data, however, their interpretation is more specialized and can require advanced imaging experience.

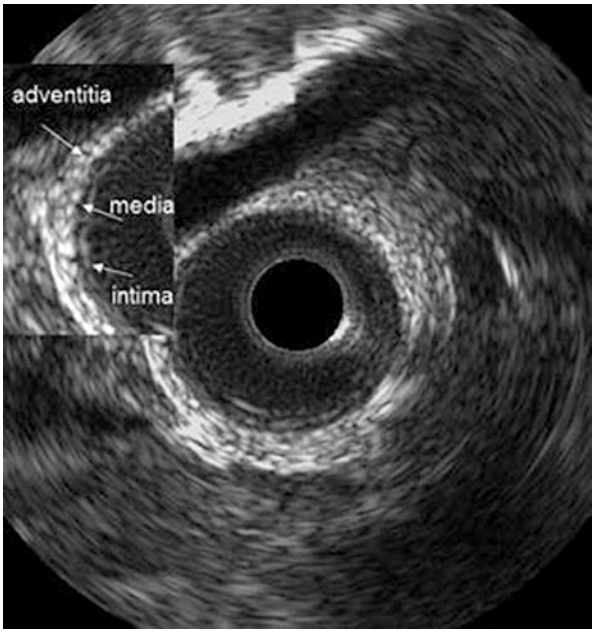

Fig. 9.1 Normal coronary artery

Image Acquisition

- Accurate IVUS image acquisition is essential for correct interpretation. Steps of IVUS imaging are as below.
  - Flush and prepare the IVUS catheter and connect to the imaging console.
  - Coronary artery engagement with the guide catheter. The guide catheter should be ≥5 French (Fr.)
  - Wiring of the desired coronary artery with a 0.014″ guidewire.
  - Flush and prepare the IVUS catheter with heparinized saline/ sterile normal saline.
  - Deliver the IVUS catheter past the targeted area of imaging. Most IVUS catheters are based on a 0.014″ monorail system.
  - Perform manual or mechanical pull back at a consistent speed of 1 m/ sec for imaging.
  - Live images are stored for post-processing and interpretation using vendor-specified software.
  - Remove the IVUS catheter and flush the guide catheter to remove any air from the "Y connector."

Practical Considerations

- Sheath Size: ≥5 French.
- Anticoagulation: Therapeutic with Heparin or bivalirudin for ACT >250 s.
- Administer 100–200 μg of intracoronary nitroglycerin prior to imaging.
- Saline flushing may be needed to clear the vessel of artifact if using a mechanical IVUS catheter.

Limitations

- Catheter deliverability across tortuous and calcified/ stenotic vessels.
- Attenuation across calcified vessel segments.
- Near field imaging is difficult with phased array transducers requiring image processing to clear the ring artifact.
- Inter-observer variability in image interpretation.

Image Characteristic

- IVUS images are gray scale. Various intracoronary plaques are as demonstrated below (Figs. 9.2, 9.3, and 9.4). Reference vessel diameter is measured by considering the average of proximal and distal reference as measured from media to media or lumen-to-lumen.

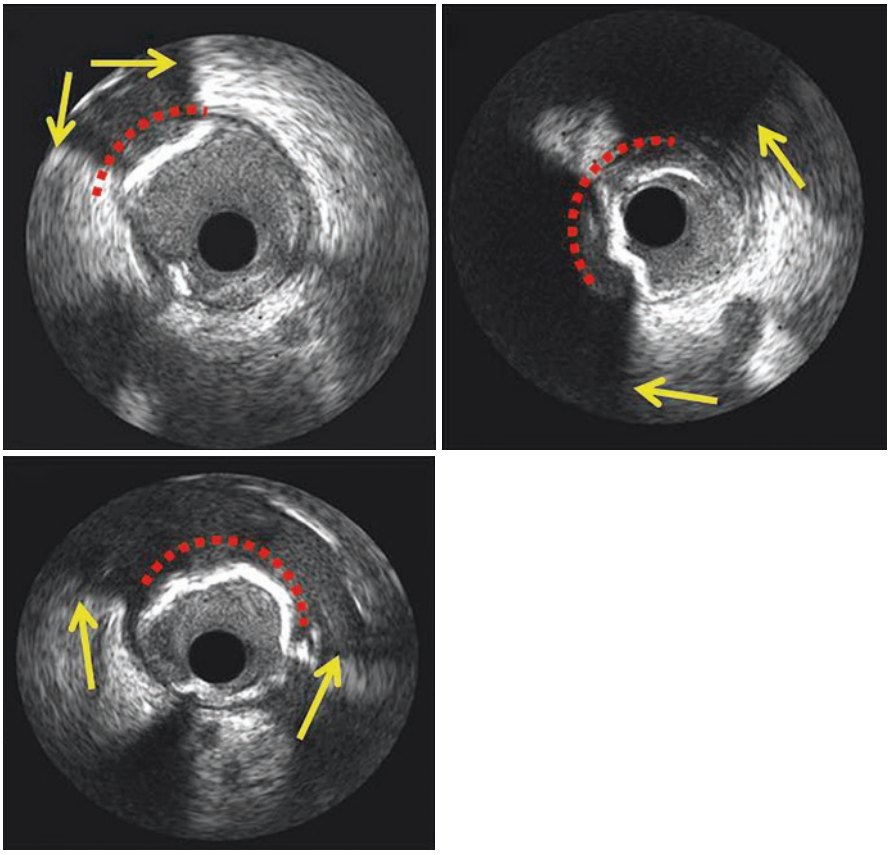

Fig. 9.2 Calcified plaque (hyperechoic) on IVUS (as demarcated by the red dotted line) with tissue attenuation (yellow arrow) beyond calcified segments

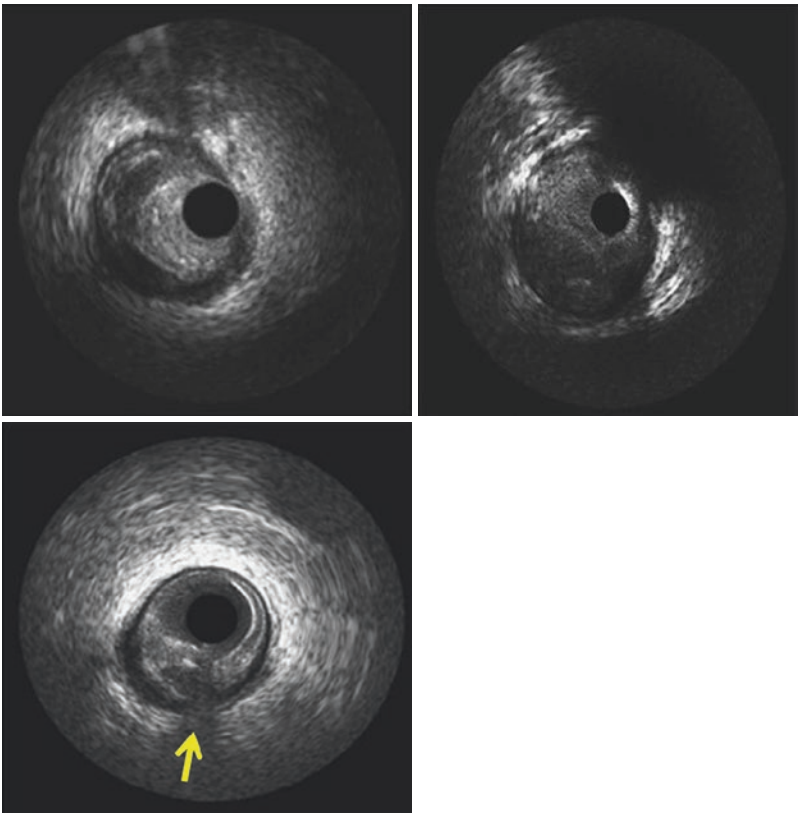

Fig. 9.3 Lipid pool (echo lucent area within plaque) on IVUS

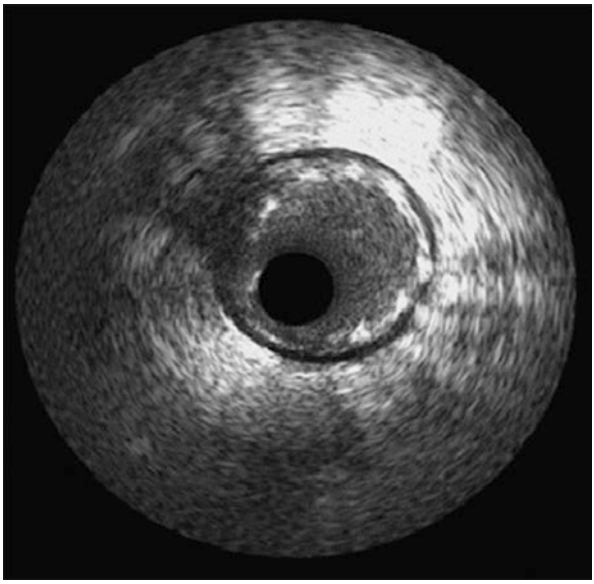

Fig. 9.4 Well-apposed stent struts in a stented coronary artery

Optical Coherence Tomography (OCT)

Optical coherence tomography (OCT) is an intravascular imaging technology for evaluating the cross-sectional and three-dimensional (3D) microstructure of blood vessels at a resolution of approximately 10 μm. It has been commercially available in the USA more recently and is gaining wider acceptance clinically. Abbott Vascular, Minneapolis, Minnesota, manufactures the current catheter (DragonFly OPTIS).

Principles of OCT Imaging

- The OCT catheter utilizes near-infrared light for image acquisition. The lag time of optical echoes reflected or backscattered from subsurface structures in biological tissues helps in discriminating different coronary structures. OCT light source is in the near-infrared (NIR) range, typically with wavelengths of approximately 1.3 μm.
- It has a resolution of nearly 10–20 μm, but tissue penetration is only 1–2 mm due to the short wavelength.

Indications

- OCT and IVUS have overlapping indications in terms of coronary interventions. Some specific circumstances where we prefer OCT imaging to IVUS include plaque characterization and accurate assessment of post-PCI dissections.
- Assessment of plaque morphology (e.g., plaque erosion in ACS) (Figs. 9.5 and 9.6).

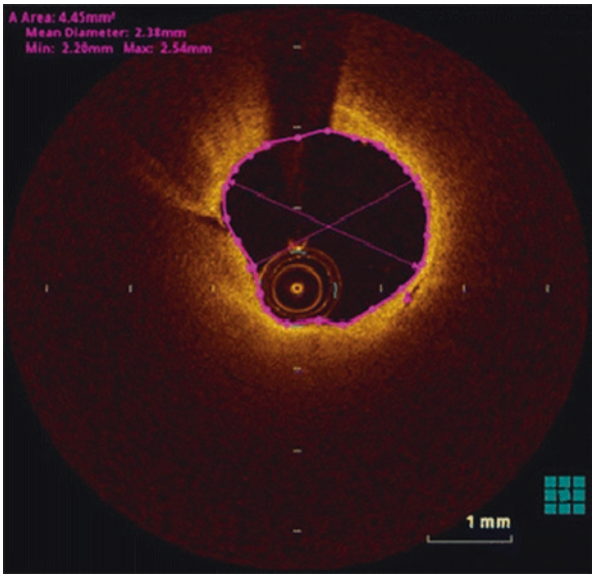

Fig. 9.5 OCT of an LAD lesion. Note the OCT catheter at 7 o'clock

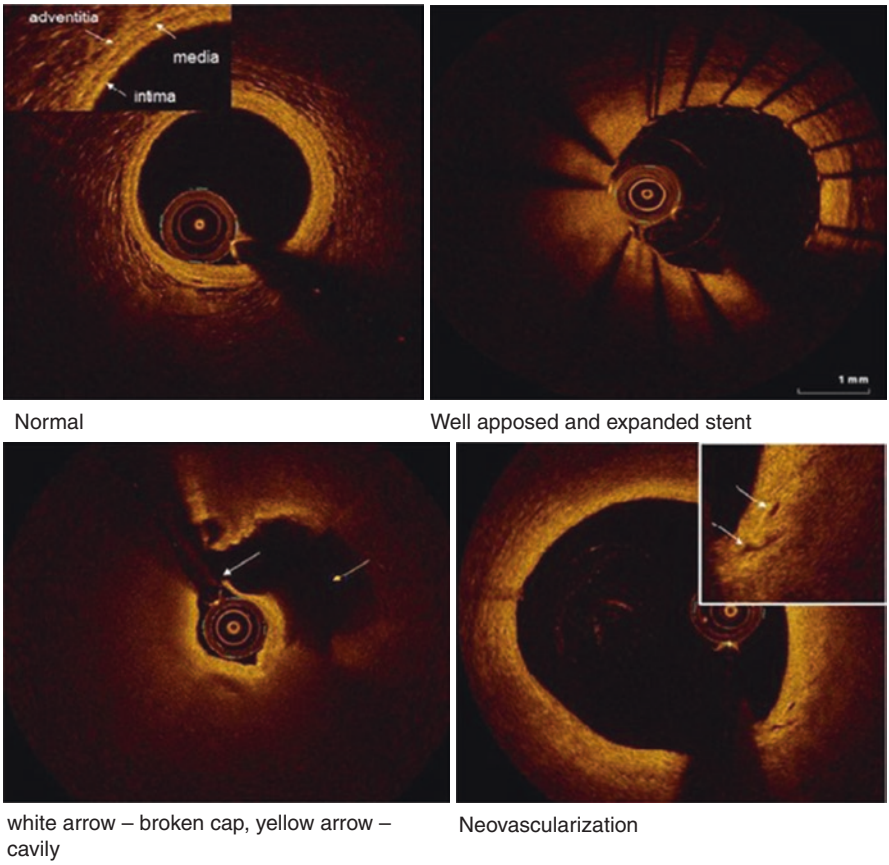

Fig. 9.6 (**a**) OCT cross section of normal vessel. (**b**) OCT of a well-apposed stent. (**c**) Ruptured plaque as seen by OCT. (**d**) Neovascularization of plaque

- Detection of edge dissections (Fig. 9.6). Major dissection defined as dissections >60° or ≥ 3 mm in length) [4].
- Post-PCI stent optimization by exclusion stent malapposition. (Stent malapposition defined as a lumen to stent distance ≥200 μm) [4].

Image Characteristics

- OCT images have a higher resolution than any other intracoronary imaging modality which allows for excellent tissue characterization as well as plaque detection. Therefore, OCT is the only imaging modality used to study/ characterize plaque erosion as an etiology of acute coronary syndromes.
  - Resolution of 10–20 μm.
  - 3-D reconstruction by proprietary software provides real-time visualization of the lumen along different planes.

  - Computer-generated 'rendering' of stent helps identify areas of malapposition that are highlighted as yellow.
  - Automatic measurements of lumen and stent area, with special focus on the minimal stent/ lumen areas.
  - The target vessel needs to be cleared of blood to acquire images using OCT.
  - Universally used automatic pullback at about 25 mm/sec allows for accurate lesion length assessment.

Image Acquisition

- Like any imaging, optimal image acquisition is the first step to accurate image interpretation. To avoid excessive contrast administration with repeated imaging attempts, a protocol based approach to OCT imaging is paramount.
  - Initiate with a sheath size of ≥6 French.
  - Therapeutic anticoagulation with heparin or bivalirudin for ACT >250 s.
  - Engage the target vessel and wire the lesion with a 0.014″ coronary guidewire.
  - Flush and prepare the OCT catheter with attached 3 cc syringe using undiluted contrast to purge air from the catheter.
  - Set the power injector according to the manufacturers' instructions (typically at least 3 milliliters/ second (mL/sec) for a total volume of 12 mL for RCA and 4 mL/sec for a total volume of 14 mL for left coronaries with a pressure of no more than 450 PSI). Consider using a 20 mL syringe in case of manual injection.
  - Check catheter position and blood clearance from the vessel with a test injection.
  - Once assured of position, activate the imaging catheter (preferably with auto-pullback) and inject 100% contrast through the power injector.
  - Remove the imaging catheter from the coronary artery once the imaging pull back is complete.

Equipment and Practical Aspects

- Sheath Size: ≥6 French. Avoid upsizing sheaths after therapeutic anticoagulation.
- Administer 100–200 μg of intracoronary nitroglycerin prior to imaging.
- The 4 P's of successful OCT image acquisition are co-axial catheter positioning, setting up of Power injector, Purging the target vessel of blood, and enabling automated Pull back.
- The length of the vessel acquired is about 75 mm, ensure the catheter is across the target lesion/ segment to be imaged.
- Consider balloon predilation across tight stenosis for catheter delivery.

Limitations

- Tissue penetration is limited, limiting clinical utility to non-left main lesions.

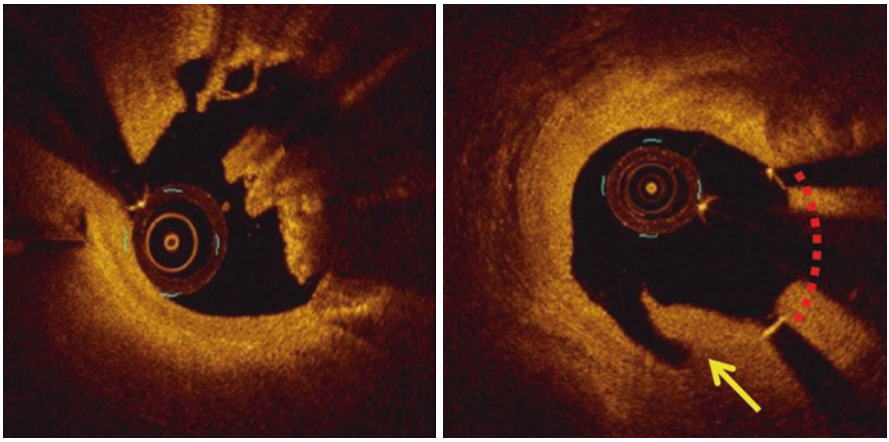

Fig. 9.7 (**a**) OCT showing ruptured plaque with red thrombus, distal attenuation behind thrombus. (**b**) OCT images of stent edge dissection

- Left main and ostial right coronary arterial lesions are not satisfactorily imaged as the blood cannot be cleared adequately with contrast and tissue penetration is limited.
- Catheter deliverability across tortuous and calcified/stenotic vessels.
- Attenuation across lipid-rich plaques.

Image Characteristics

- OCT images are generally crisp and well defined, especially compared to IVUS images. (Fig. 9.5). Some examples of various OCT findings are as below (Figs. 9.6 and 9.7).

Comparing OCT vs IVUS

Intravascular imaging is now considered obligatory for most complex coronary cases, with proven mortality benefits in CTO and long lesions [5, 6].

- The inherent differences in physical principles of either imaging modality (Table 9.1) provide a certain uniqueness to each technique's utility in clinical practice.
- IVUS has also been shown to increase the lumen gain/ post-dilation balloon sizing in various studies especially for complex lesions [5, 6].
- High definition IVUS imaging with mechanical pull-back provides good quality images that help in the optimization of percutaneous interventions, including lesion length, calcification depth, and angle.

- Each imaging modality has some specific scenarios where they are preferred as in Table 9.2.
- An intimal thickness of >0.5 mm in proximal left anterior descending (LAD) is considered a marker for increased rates of major adverse cardiovascular outcomes [7].
- OCT has a superior longitudinal and axial resolution.
- There are well-defined objective definitions of stent malapposition (>200 microns) and major dissection (>60 degrees/ 3 mm) which can further decrease inter-observer variability in image interpretation [4].
- Long-term follow-up for clinical outcomes is lacking but outcomes up to 24 months show decreased MACE rates with either imaging modality [10].
- While there is significant, inter-observer variability in vessel sizing based on angiography alone, such disagreements can be overcome with intracoronary imaging [11].
- It is of paramount importance that each practicing interventional cardiologist is familiar with the practical aspects of both imaging modalities, some of which are listed in Table 9.3.

Table 9.1 Physical characteristics of OCT versus IVUS

	OCT	IVUS
Radiation type	Light	Ultrasound
Wavelength, μm	1.3	35–80
Frequency	190 THz	20–45 THz
Resolution, μm	10–40	100–150
Penetration depth, mm	1–3	4–10
Field-of-view diameter, mm	15	7–10
Frame rate, frames/s	100	30
Pullback speed, mm/s	20	0.5–1
Plaque characterization	Yes	Yes
Fibrous cap measurement	Yes	No
Vessel remodeling	No	Yes
Blood removal required	Yes	No

Table 9.2 Specific scenarios for utility of imaging modalities [3, 7–9, 12]

	OCT	IVUS
No/low contrast PCI	No	Yes
Transplant vasculopathy	No	Yes
Acute stent thrombosis	No	Yes
Delayed in-stent restenosis	Yes	Yes

Table 9.3 Practical aspects of imaging for the interventionalist

	Description
ACT	>250 s before IVUS/ OCT catheter insertion
IVUS	Intimal thickness > 0.5 mm on IVUS consistent with transplant coronary vasculopathy. Left main MLA >6 mm^2, safe to defer stenting.
OCT	Stent malapposition with ≥200 μm distance between vessel wall and stent. Major dissection defined as a dissection >60° or ≥ 2 mm in length.

Near-Infrared Spectroscopy (NIRS): Intravascular Ultrasound (IVUS) Imaging

The imaging system utilizes diffuse reflectance near-infrared spectroscopy (NIRS) , a classic method of analytical chemistry, to characterize the plaque for lipid content [13]. Diffuse reflectance spectroscopy requires scattering and absorption at different wavelengths of the light by the tissue.

How It Works

- The combination of scattering and absorption of near-infrared light by organic molecules in the arterial wall and plaque produces a unique chemical signature.
- An algorithm analyzes the detected signal for signs of cholesterol and provides automated lipid core-containing plaques (LCP) detection without the need for manual image processing (Fig. 9.8).
- In contrast to OCT, NIRS can image through blood, as it does not need light to be directly reflected back to the detector [13].

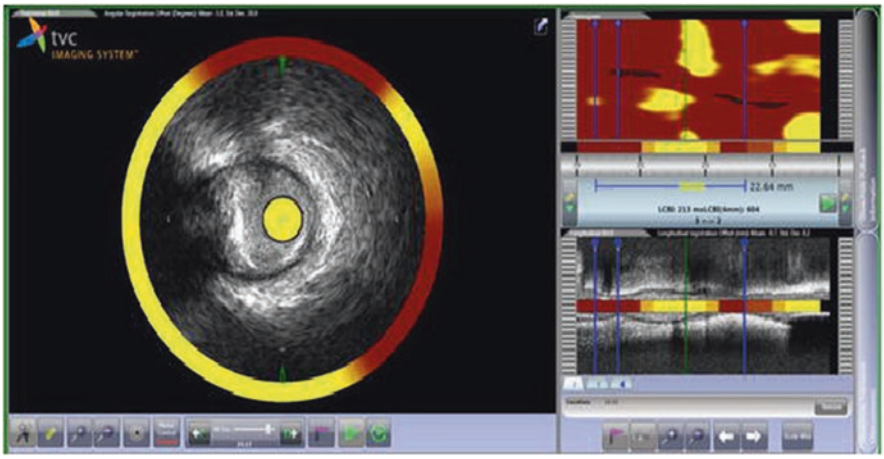

Fig. 9.8 TVC Composite™ view of co-registered near-infrared spectroscopy lipid core plaque with intravascular ultrasound. The chemogram displays low probability of lipid as red and high probability as yellow. The lipid core burden index (LCBI) indicates the amount of lipid in the scanned artery on a 0–1000 scale

Table 9.4 Equipment TVC insight catheter

	Unit
Minimum guide catheter	6 French (2 mm)
Maximum guidewire	0.014 (0.36)
Catheter crossing tip profile	3.2 French (1.1 mm)
Maximum imaging depth	16 mm
Catheter working length	120 mm
Operating frequency	40 MHz

Equipment

- See Table 9.4 for equipment for TVC Insight catheter.

Indications

- The Infraredx TVC Imaging SystemTM is intended for the detection of LCPs using NIRS and IVUS examination of the coronary arteries.
- The combination of NIRS with IVUS in a single catheter combines the benefit of NIRS with the benefits of IVUS.

Limitations

- NIRS–IVUS does not allow detection of non-superficial LCPs and LCPs in large vessels (more than 6 mm diameter) cannot visualize neovascularization.

NIRS–IVUS Numbers to Remember

- Patient with stable coronary artery disease who undergoes PCI of lesions with large lipid core plaques (maxLCBI4 mm ≥500 by NIRS) is associated with a 50% risk of periprocedural MI and a maxLCBI4 mm >400 in the culprit segment is considered significant with STEMI [13, 14]. Statin therapy has been shown to decrease LCBI in lipid-rich plaque demonstrated by NIRS imaging [15].
- Multimodality imaging: correlation of OCT and NIRS–IVUS imaging.
- Combined utilization of OCT and NIRS–IVUS allows to characterize the microstructural features of plaque morphology, such as fibrous cap thickness and neovascularization (OCT) and plaque lipid content (NIRS), and perform robust quantitative measurements of the lumen, vessel, and plaque area (grayscale IVUS) in the same lesion (Table 9.5). Figure 9.9 shows an example of multimodality images of a thin-cap fibroatheroma lesion.

Table 9.5 Comparison of three intravascular imaging modalities for the detection of coronary lipid core plaque

	IVUS	OCT	NIRS–IVUS
Hybrid intravascular imaging	No	No	Yes
Axial resolution, um	200	10	100
Imaging through blood	++	–	++
Need for blood column clearance during image acquisition	No	Yes	No
Imaging through stents	No	Yes	Yes
Imaging through calcium	No	Yes	Yes for NIRS, no for IVUS
Imaging neovascularization	No	Yes	No
Detection of non-superficial LCPs	Yes	No	No
Evaluation of LCP cap thickness	+	++	*
Detection of thrombus	–	+	*
Expansive remodeling	++	–	++
Need for manual image processing for LCP detection	Yes	Yes	No

++ Excellent, + good, – impossible, * potential under investigation, *VHIVUS* virtual histology intravascular ultrasound, *OCT* optical coherence tomography, *NIRS* near-infrared spectroscopy, *LCP* lipid core plaque

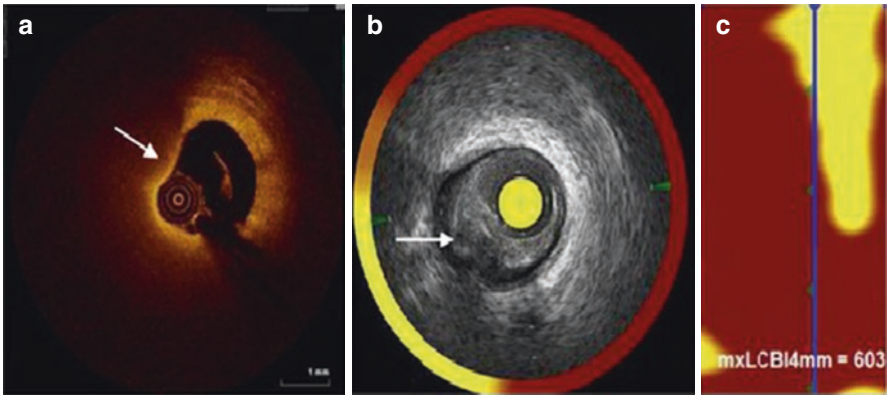

Fig. 9.9 (**a**) OCT image of a thin-cap fibroatheroma (TCFA) lesion with a 60 μm fibrous cap (*arrow*) overlying a large lipid core. (**b**) The lipid pool (*arrow*) is shown in the corresponding IVUS image. (**c**) NIRS chemogram quantifies the lipid content of the lesion

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