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Intracoronary Imaging

Takashi Kubo and Takashi Akasaka

About us Wakayama Medical University is located in the southwestern part of Japan. Areas of our expertise are intracoronary imaging (OCT, IVUS, NIRS, CT, and MRI) and coronary physiology (CFR and FFR). We have participated in a number of international clinical trials and worked as an imaging core laboratory. We will continue our efforts to elucidate the mechanisms of coronary atherosclerosis and establish the clinical significance of imaging- and physiology-oriented percutaneous coronary intervention.

Introduction

Intravascular imaging provides a valuable opportunity to assess coronary atherosclerosis in living people and to guide percutaneous coronary intervention (PCI). Several catheter-based, invasive, intravascular imaging methods are currently available for research and clinical purposes. Intravascular ultrasound (IVUS) and optical coherence tomography (OCT) are commonly used intravascular imaging methods in our daily clinical practice.

IVUS

Grayscale IVUS

- IVUS uses high-frequency (20–60 MHz) sound waves and produces cross-sectional, monochrome images of a coronary vessel with a resolution of 100–200 μm. IVUS enables visualization of not only the lumen of the coronary arteries but also the atherosclerotic plaque within the vessel wall, which cannot be seen by angiography.
- In the IVUS image, the coronary artery wall is visualized as three layers. Moving outward from the lumen, the first layer includes a complex of intima, plaque, and internal elastic membrane. The second layer includes the media with external elastic membrane (EEM), which is usually less echogenic than the intima. The third and outer layer includes the adventitia and periadventitial tissues.
- The plaque is classified into high, iso, or low echo-reflectance type. The high echoic plaque is usually regarded as "hard" or "calcified"; the iso echoic plaques as "fibrotic"; and the low echoic plaques as "soft" or "lipid rich."
- The low or iso echoic plaque with ultrasound attenuation behind the plaque, in the absence of calcification, is described as "attenuated plaque." This is considered to be atheroma with a lipid-rich necrotic core. However,

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T. Kubo (✉) · T. Akasaka
Department of Cardiovascular Medicine, Wakayama Medical University, Wakayama, Japan
e-mail: takakubo@wakayama-med.ac.jp; akasat@wakayama-med.ac.jp

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diagnostic accuracy of grayscale IVUS for plaque tissue characterization is modest.
- For guiding PCI, IVUS is useful to assess angiographically ambiguous lesions including intermediate lesions of uncertain stenotic severity, aneurysmal lesions, ostial stenoses, tortuous vessels, diffuse disease, left main lesions, bifurcation stenosis, sites with plaque rupture, stent edge dissection, intraluminal filling defects, angiographically hazy lesions, and angiographically foreshortened vessels.
- In addition, IVUS is capable of measuring lumen and vessel diameter, plaque and stent area, and plaque eccentricity and vascular remodeling index, which are helpful information to determine balloon and stent size (Figs. 14.1 and 14.2).

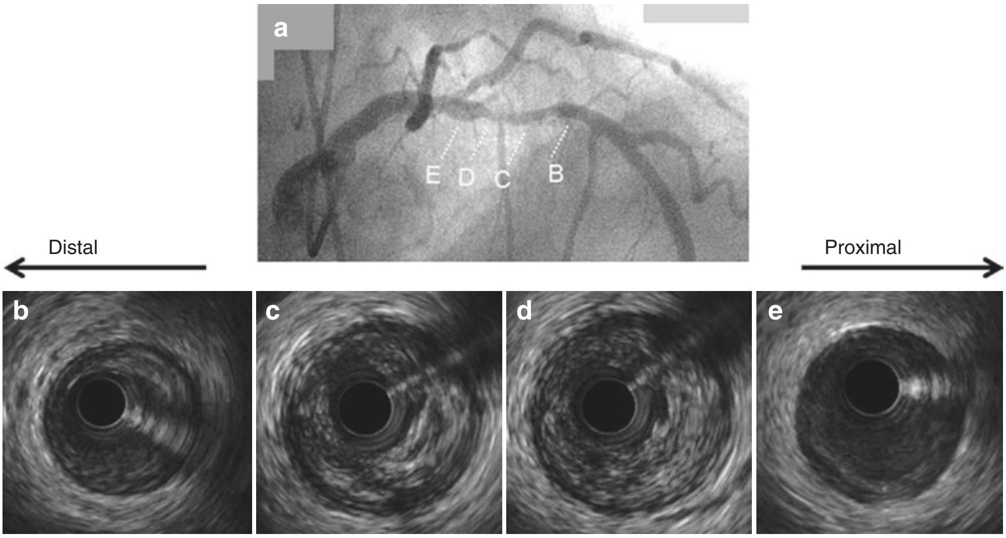

Fig. 14.1 Positive vessel remodeling. Coronary angiography shows an intermediate lesion in the proximal left anterior descending coronary artery (**a**). Grayscale IVUS demonstrates that the lesion EEM area (**c** and **d**) is greater than the reference EEM area (**b** and **e**)

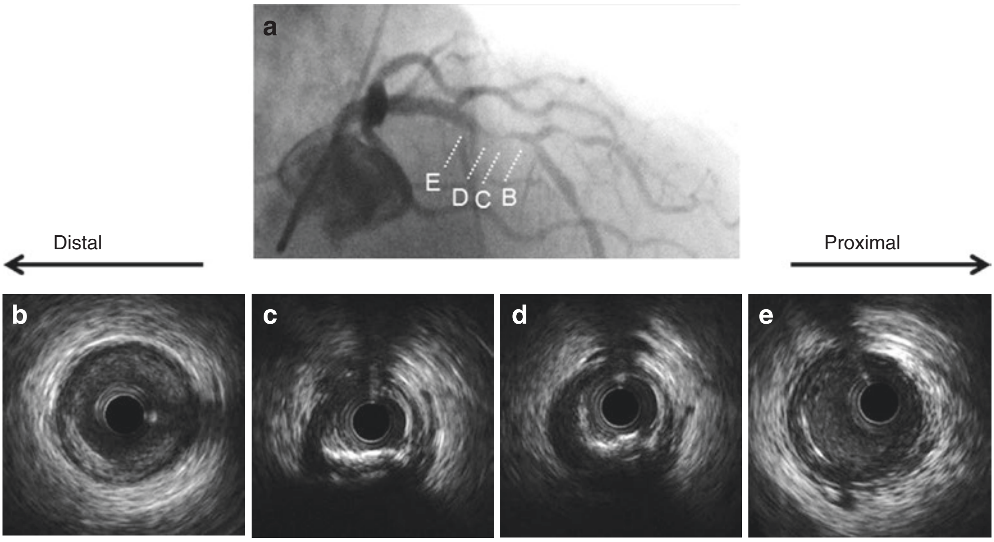

Fig. 14.2 Negative vessel remodeling. Coronary angiography shows a severe stenosis lesion in the proximal left anterior descending coronary artery (**a**). Grayscale IVUS demonstrates that the lesion EEM area (**c** and **d**) is smaller than the reference EEM area (**b** and **e**). The plaque in the lesion (**c** and **d**) is usually regarded as "calcified"

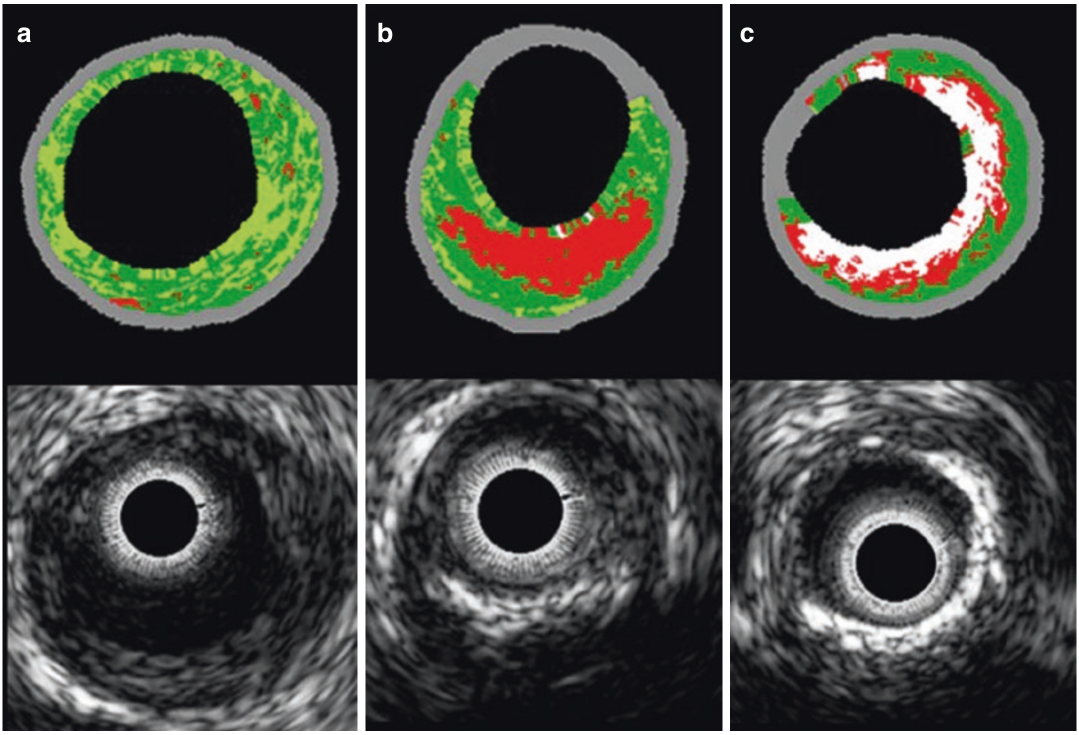

Fig. 14.3 Plaque type classification by VH-IVUS. VH-IVUS shows pathological intimal thickening (**a**), thin-capped fibroatheroma (**b**), and fibrocalcific plaque (**c**)

Virtual Histology (VH)-IVUS

- Based on the radiofrequency analysis of ultrasound backscattered signals, VH-IVUS allows automatic assessment of plaque tissue composition.
- VH-IVUS identifies four different tissue types and produces a color-coded map of the plaque (fibrous = green, fibro-fatty = yellow green, dense calcium = white, and necrotic core = red).
- In the VH-IVUS image, the plaque is classified into pathological intimal thickening, thin-capped fibroatheroma (TCFA), thick-capped fibroatheroma, fibrotic plaque, or fibrocalcific plaque (Fig. 14.3).
- Pathological intimal thickening consists of mainly a mixture of fibrous and fibro-fatty tissue with <10% confluent necrotic core and <10% confluent dense calcium.
- VH-derived TCFA is defined as a fibroatheroma (>10% confluent necrotic core) without evidence of a fibrous cap (necrotic core abutting the lumen >30°) because the resolution of IVUS is insufficient for detecting the thin fibrous cap of <65 μm determined by pathology.
- Thick-capped fibroatheroma is defined as a fibroatheroma with a definable fibrous cap. Fibrotic plaque consists of mainly fibrous tissue with <10% confluent necrotic core, <15% fibro-fatty tissue, and <10% confluent dense calcium.
- Fibrocalcific plaque is composed of nearly all fibrous tissue and dense calcium with <10% confluent necrotic core.
- In the stent-treated lesion, stent struts exhibit a VH-IVUS appearance of white surrounded by a red “halo” and neointima within the stent is indicated predominantly by a mixture of fibrous and fibro-fatty tissue.

OCT

- OCT is an optical analog of IVUS using near-infrared light (wavelength: 1250–1350 nm). OCT provides an extraordinarily high-resolution (10–20 μm) image.

- However, the visible range of OCT is limited in the vessel surface because the depth of penetration of near-infrared light is shallow (<2 mm, depended on the tissue type).
- OCT enables visualization of the intima (high-signal-intensity inner layer), media (low-signal-intensity middle layer), and adventitia (high-signal-intensity outer layer) in the coronary artery wall.
- OCT is capable of differentiating three types of coronary plaque: fibrous, calcified, and lipidic.
- The OCT images of fibrous plaque are characterized by a homogeneous, signal-rich region; fibrocalcific plaque by a well-delineated, signal-poor region with sharp border; and lipid-rich plaque by a signal-poor region with diffuse border.
- OCT delineates unstable plaque features including plaque rupture, erosion, and calcified nodule(s) in the culprit lesion of an acute coronary syndrome.
- Plaque rupture is characterized by the presence of fibrous-cap discontinuity with a clear cavity formed inside the plaque (Fig. 14.4); OCT-derived erosion by the presence of attached thrombus overlying an intact plaque (Fig. 14.5); and OCT-derived calcified nodule by the fibrous-cap disruption over a calcified plaque with protruding calcification, superficial calcium, and substantive calcium proximal and/or distal to the lesion (Fig. 14.6).
- Furthermore, OCT has the potential to detect key features of vulnerable plaque such as TCFA, macrophage accumulation, cholesterol crystals, and the vasa vasorum. The high resolution of OCT can directly identify the thin fibrous cap of <65 μm overlying a lipid-rich necrotic core.
- OCT-derived macrophage accumulation is characterized by signal-rich, distinct, or confluent punctuate regions with shadowing; cholesterol crystal by a thin, linear region of high signal intensity within the lipid plaque; and vasa vasorum by a signal-poor, well-delineated void within plaque. Microchannels in chronic total occlusions give a "lotus root" appearance on OCT (Fig. 14.7).
- The high resolution of OCT is beneficial for guidance of PCI. The clear image of OCT permits automated quantitative analyses, which provides accurate and highly reproducible measurements of lumen.

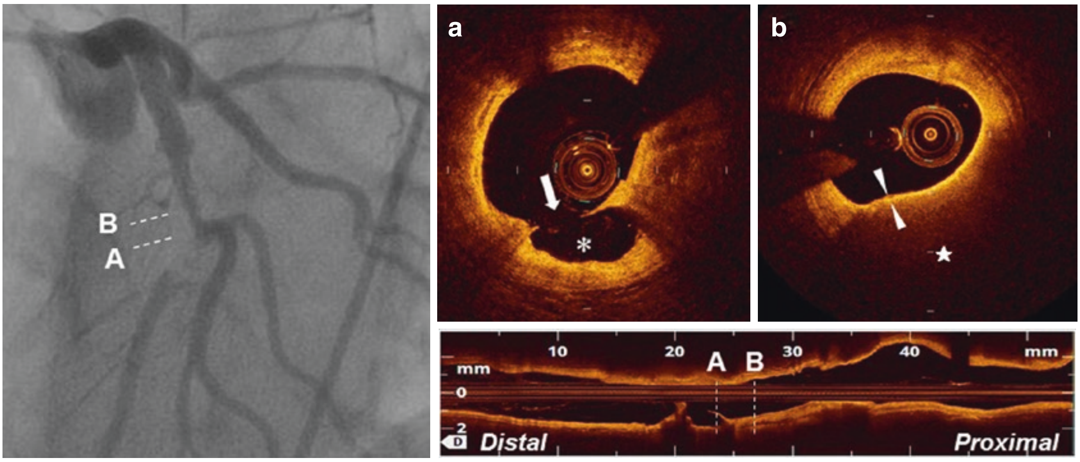

Fig. 14.4 Plaque rupture. Images were obtained from a 72-year-old female with ST-segment-elevation myocardial infarction. Coronary angiography showed an occlusion in the proximal left anterior descending coronary artery. OCT after aspiration thrombectomy demonstrated fibrous-cap disruption (arrow) and core cavity (star) (**a**), and thin-capped fibroatheroma (fibrous cap = arrowheads, and lipid core = asterisk) (**b**)

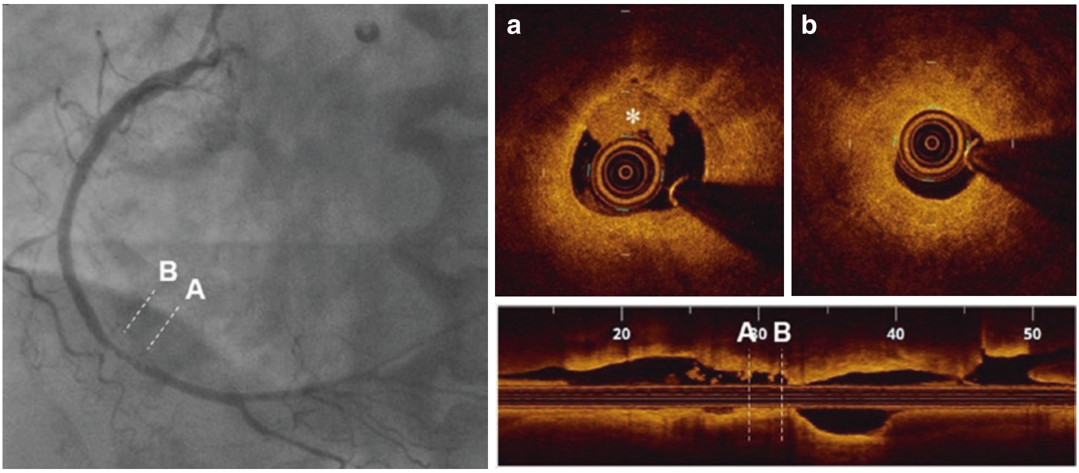

Fig. 14.5 Erosion. Images were obtained from a 63-year-old female with ST-segment-elevation myocardial infarction. Coronary angiography showed a lesion with haziness and a filling defect in mid-right coronary artery. OCT demonstrated a probable erosion which was characterized by intracoronary thrombosis (**a**, asterisk) overlying a fibrous plaque (**b**)

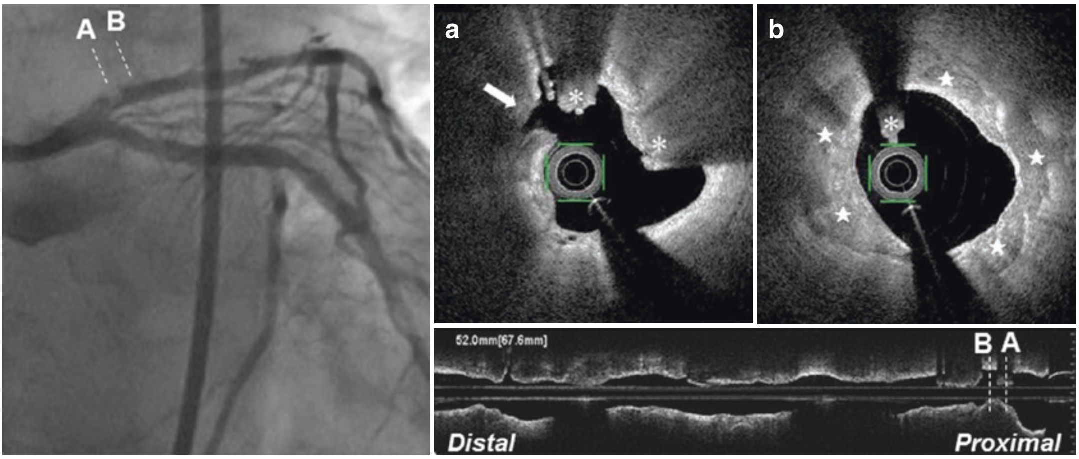

Fig. 14.6 Calcified nodule. Images were obtained from a 78-year-old male with non-ST-segment-elevation myocardial infarction. Coronary angiogram showed a filling defect and haziness in the ostial left anterior descending coronary artery. OCT demonstrated a calcified nodule, which was characterized by thrombus (**a**, asterisks) and rupture (**a**, arrow) of calcified plaque (**b**, stars) without lipid (courtesy of Dr. Kadotani. Kakogawa Central City Hospital, Kakogawa, Japan)

- OCT identifies stent malapposition, tissue protrusion, and stent-edge dissection immediately after PCI and detects thin neointima over drug-eluting stents and neoatherosclerosis (defined as a development of atherosclerosis in the neointima) at late follow-up. Furthermore, in the case of bioresorbable scaffolds, OCT provides information regarding the time course of scaffold dissolution.

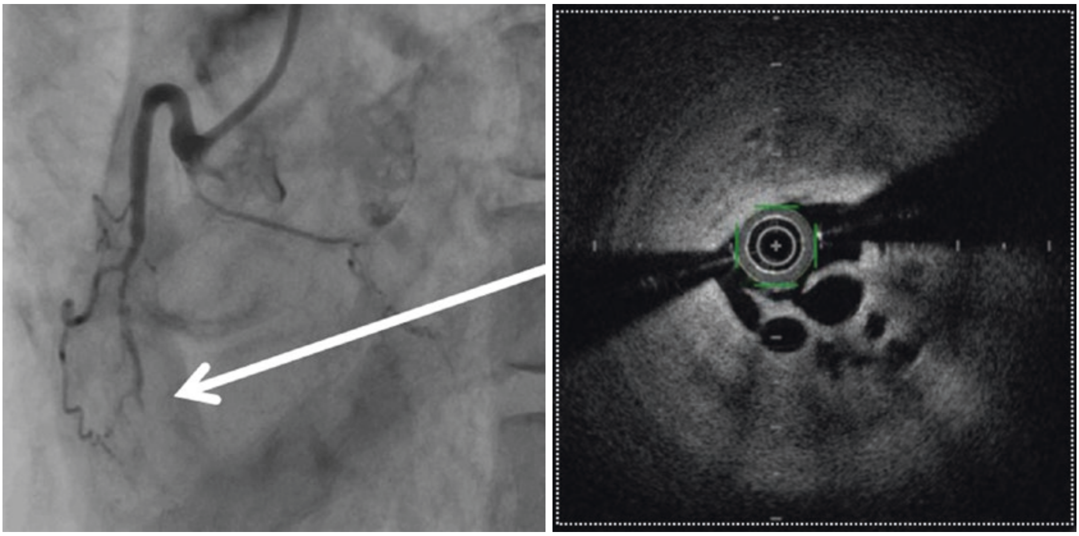

Fig. 14.7 Lotus root appearance in chronic total occlusion. Coronary angiography shows an occlusion in the mid-right coronary artery. OCT after pre-dilatation with a small balloon demonstrates multiple channels within the lesion

IVUS Versus OCT

- Each method has advantages and disadvantages in technology.
- Advantages of IVUS are deeper signal penetration that allows visualization of the whole vessel wall and longer pullback distance that permits assessment from distal coronary artery to aorto-ostial junction. However, IVUS has had no fundamental advances in the technology in more than a decade.
- Advantages of OCT are higher resolution image that is easy to interpret and faster pullback speed that enables 3-dimensional reconstruction of coronary arteries.
- However, for reliable image acquisition, OCT requires injection of contrast media to displace blood from the vessel lumen because the OCT signal is attenuated by the presence of red blood cells. Therefore, OCT is not suited for assessing coronary artery ostia and totally or subtotally occluded lesions.

Indications for Use

- Both IVUS and OCT are powerful tools for research. These methods increase our knowledge of the nature of atherosclerosis, pathophysiology of vulnerable plaques, and mechanism of restenosis and thrombosis following PCI.
- In addition, IVUS and OCT are widely used in daily clinical practice. These methods provide valuable information that has a great influence on the procedural strategy for lesion preparation and stent optimization especially in PCI to complex lesions.
- However, routine use of intravascular imaging in PCI may be limited by the cost of the imaging catheter and the extra time for imaging procedures in addition to angiography guidance alone.

Evidence Base

IVUS

- A plaque burden of at least 70%, a minimal luminal area of 4.0 mm^2 or less, and the presence of VH-derived TCFA were independent risk factors of subsequent major adverse cardiovascular events [1].
- Increase of plaque volume is associated with increased risk of future cardiac event. Decrease of plaque volume is observed during intensive statin treatment.

- IVUS is useful for the assessment of angiographically intermediate left main stenosis: IVUS-measured minimum lumen area of <4.8 mm^2 is reported to be the cutoff for predicting myocardial ischemia [2].
- Stent under-expansion is associated with stent restenosis and stent thrombosis: IVUS-measured minimum stent area of <5.3–5.5 mm^2 is reported to be the cutoff for predicting late restenosis in second-generation drug-eluting stents [3].
- Optimal stent-edge landing zone is a segment with less plaque: IVUS-measured residual plaque burden of >55% in the stent-edge segment is reported to be the cutoff for predicting stent-edge restenosis [4].
- Attenuated plaque and VH-derived fibro-fatty tissue are associated with angiographic slow flow during PCI and periprocedural myocardial infarction (MI).
- Late-acquired stent malapposition is often observed in very late drug-eluting stent thrombosis. IVUS is helpful for guidance of coronary stent implantation, particularly in cases with long stenting (stent length >28 mm) [5] or left main coronary artery stenting [6]. Several studies have demonstrated that IVUS-guided PCI reduced major adverse cardiac events including stent thrombosis, MI, and target-lesion revascularization after drug-eluting stent implantation compared with angiography-guided PCI [7].

OCT

- OCT-derived TCFA and vasa vasorum are potential predictors of subsequent plaque progression and lumen narrowing.
- Increase of fibrous-cap thickness and decrease of lipid arc and macrophage density are observed during lipid-lowering therapy with statin and/or eicosapentaenoic acid.
- OCT-derived TCFA and lipid-rich plaque (lipid arc >180°) are associated with angiographic slow flow during PCI and periprocedural MI [8].
- A registry study reported that OCT-derived irregular tissue protrusions as well as small minimal stent area were associated with target-lesion revascularization within 1 year after PCI (Fig. 14.8) [9].
- Optimal stent-edge landing zone is a segment with less lipidic plaque: OCT-measured lipid arc of >180° in the stent-edge segment is reported to be the cutoff for predicting stent-edge restenosis [10].

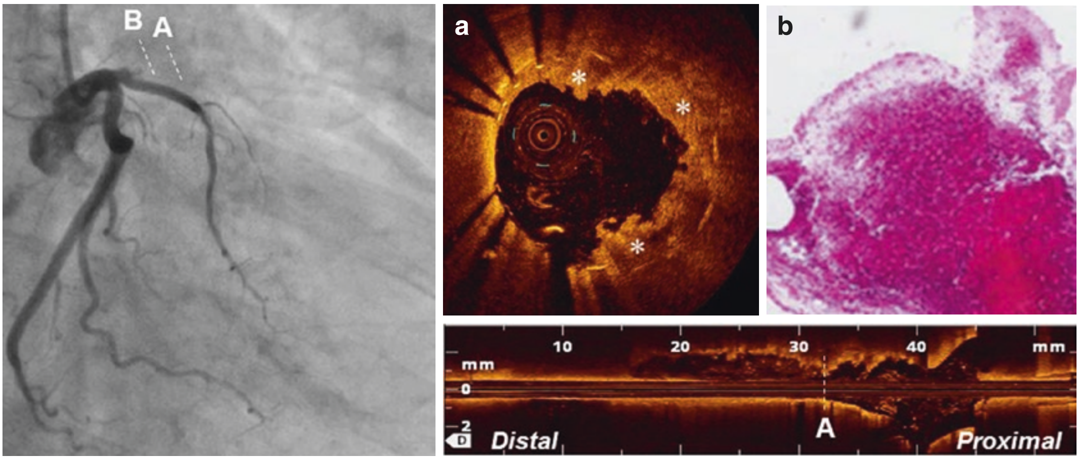

Fig. 14.8 Early stent thrombosis. Images were obtained from a 63-year-old male with stent thrombosis 13 days after second-generation drug-eluting stent implantation. Coronary angiography showed an occlusion in the previously stented segment in the proximal left anterior descending coronary artery. OCT demonstrated in-stent thrombus (**a**, asterisks). After OCT imaging, red thrombi, which consisted mainly of red blood cells, were obtained from the infarct-related lesion by aspiration thrombectomy (**b**)

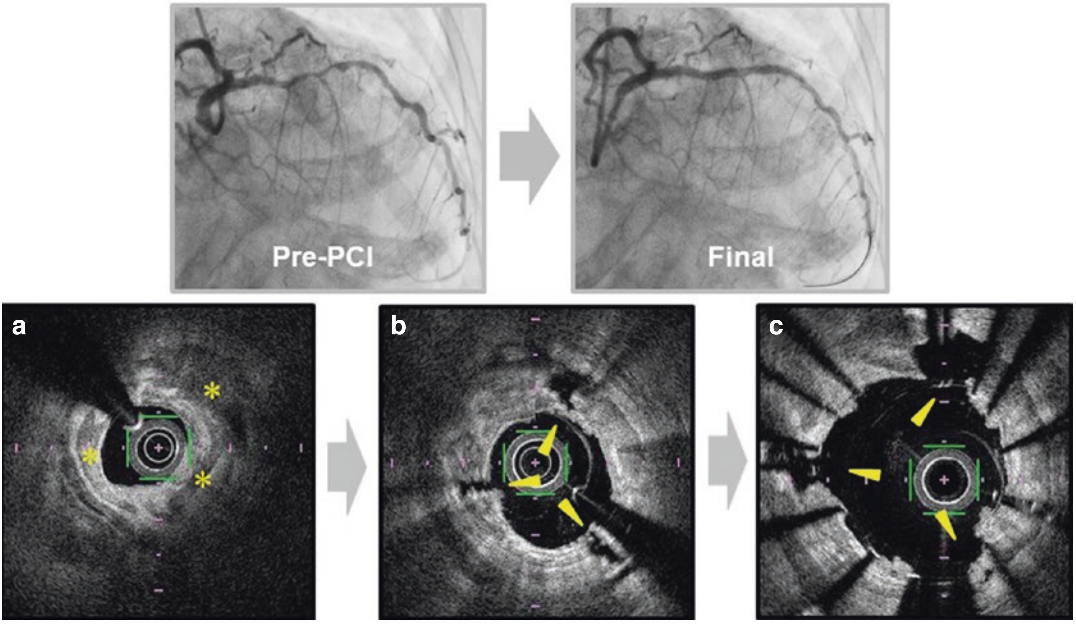

Fig. 14.9 Calcium fracture. Coronary angiography showed a significant stenosis in the proximal left anterior descending coronary artery. OCT before PCI demonstrated circumferential calcium in the lesion (**a**, asterisks). We used a cutting balloon for lesion preparation and successfully induced calcium fracture (**b**, arrowheads). We then implanted a stent and achieved adequate lumen expansion (**c**)

- In bifurcation PCI, OCT-measured small side-branch angle (<50°) and long carina-tip length (>1.7 mm) are predictors of side-branch occlusion after main-vessel stenting [11]. The guidance with 3-dimensional OCT imaging is helpful in bifurcation PCI for guide wire recrossing into the jailed side branch after main-vessel stenting.
- In circumferentially calcified lesions, if the calcium is thin (OCT-measured minimum calcium thickness <500 μm), high-pressure ballooning or cutting balloon angioplasty before stenting is effective for inducing calcium fracture which is associated with adequate stent expansion and favorable late outcomes (Fig. 14.9); and if it is thick (>500 μm), use of rotablator is recommended [12].
- In small-vessel stenting (≤2.5 mm), OCT-measured minimum stent area of <3.5 mm^2 is reported to be the cutoff for predicting late restenosis in second-generation drug-eluting stents [13].
- There is no evidence demonstrating direct relationship between OCT-identified stent strut without neointimal coverage and very late stent thrombosis.
- In in-stent restenosis with OCT-derived homogenous signal-rich neointima, drug-coated balloon therapy is reported to be effective for preventing repeat revascularization [14].
- Late-acquired stent malapposition and OCT-derived neoatherosclerosis are often observed in very late drug-eluting stent thrombosis (Fig. 14.10). Only one registry study demonstrated that OCT-guided PCI reduced cardiac death and MI compared with angiography-guided PCI [15].

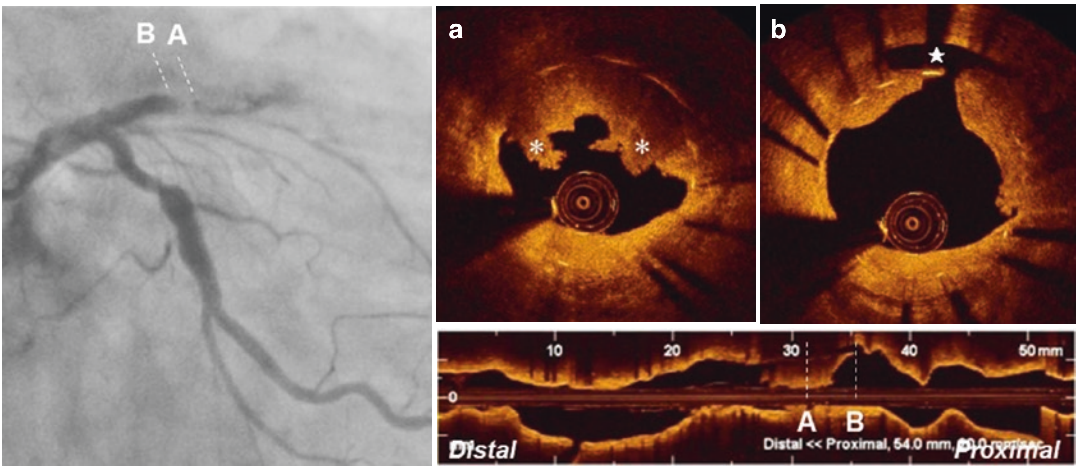

Fig. 14.10 Very late stent thrombosis. Images were obtained from a 71-year-old male with stent thrombosis 5 years after first-generation drug-eluting stent implantation. Coronary angiography showed an occlusion in the previously stented segment in the proximal left anterior descending coronary artery. OCT demonstrated in-stent thrombus (**a**, asterisks) and late-acquired stent malapposition (**b**, star)

Conclusion

IVUS and OCT are useful in assessing coronary atherosclerosis, guiding and optimizing PCI, and determining mechanisms of stent failure. Use of intravascular imaging in addition to angiography has a potential to improve clinical outcomes in patients undergoing PCI.

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