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7.1 Introduction

Although the coronary angiography (CAG) can visualize the improvement of luminal narrowing after stent implantation in coronary atherosclerotic lesions, it only provides indirect vessel information using contrast medium because of a shadow image at stented segments as well as adjacent reference segments. Intravascular ultrasound (IVUS) is capable of generating a cross-sectional anatomy of the vessel wall comparable to corresponding histologic image, resulting in providing more information of atherosclerotic coronary plaque either quantitatively or qualitatively. On the other hand, stent struts appear as focal, bright spots at cross-sectional and longitudinal images owing to a strong echoreflexion by ultrasound beam. Thus, it allows detailed information regarding stent strut expansion, intrastent luminal condition, and plaque characteristics at adjacent reference vessel area [1]. The routine use of IVUS in daily practice is still a matter of debate in current drug-eluting stent (DES) era, however, stent optimization by IVUS immediately after stent deployment has reported to improve clinical outcomes, especially during

complex percutaneous coronary intervention (PCI) [2, 3]. This chapter reviews important IVUS findings after stent implantation and its clinical relevance.

7.2 Evaluation of Stent Symmetry and Eccentricity

Symmetry index (SI) defines minimum stent diameter/maximum stent diameter (Fig. 7.1) [4]. Asymmetry index (AI) also can be used to express the stent symmetry: $(1 - \text{minimum stent diameter}/\text{maximum stent diameter})$ [5]. Because maximum and minimum stent diameters are the values throughout an entire stented segment, these diameters can derive from different cross section in the stented segment. A stent was characterized as asymmetric when the value of AI was over 0.3 (which corresponds to SI of 0.70 from the MUSIC study). Post-procedural asymmetry of device was associated with unfavorable clinical outcomes [6].

Eccentricity index (EI) was calculated as minimum stent diameter/maximum stent diameter to show the circularity of the cross section. Therefore, the calculation of minimum and maximum stent diameters were derived from the same cross section frame by frame and value was expressed as an average. A stent with $EI \geq 0.7$ was defined as concentric while $EI < 0.7$ was

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defined as eccentric [7, 8]. The eccentricity of DES had been previously considered as one of the factors for restenosis, because of the higher possibility of the uneven diffusion of the drug into the arterial wall [9]. However, subsequent reports showed that eccentricity of DES did not have any clinical impact because DES powerfully suppressed the neointimal formation [8, 10].

7.3 Measurement of Minimal Stent Area

Minimal stent area (MSA) of bare metal stent (BMS) for long-term patency was considered as 6.4–6.5 mm² [11, 12], and adequate post-interventional MSA of DES was 5.0–5.7 mm² (Fig. 7.2) [13–15]. In left main lesions, optimal

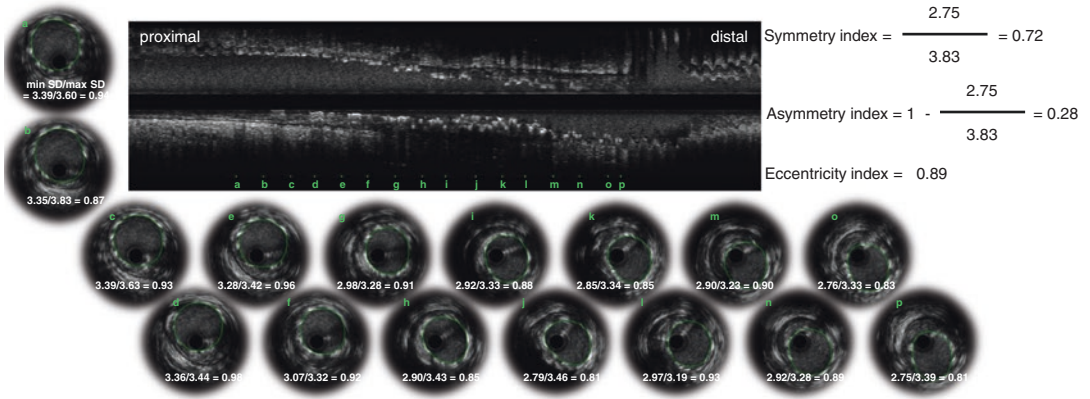


Fig. 7.1 A representative images showing stent symmetry and eccentricity. Minimum and maximum stent diameters with 1 mm interval over the length of the device were

shown. Stent (Xience alpine, 3.5 × 15 mm) showed symmetric and concentric expansion

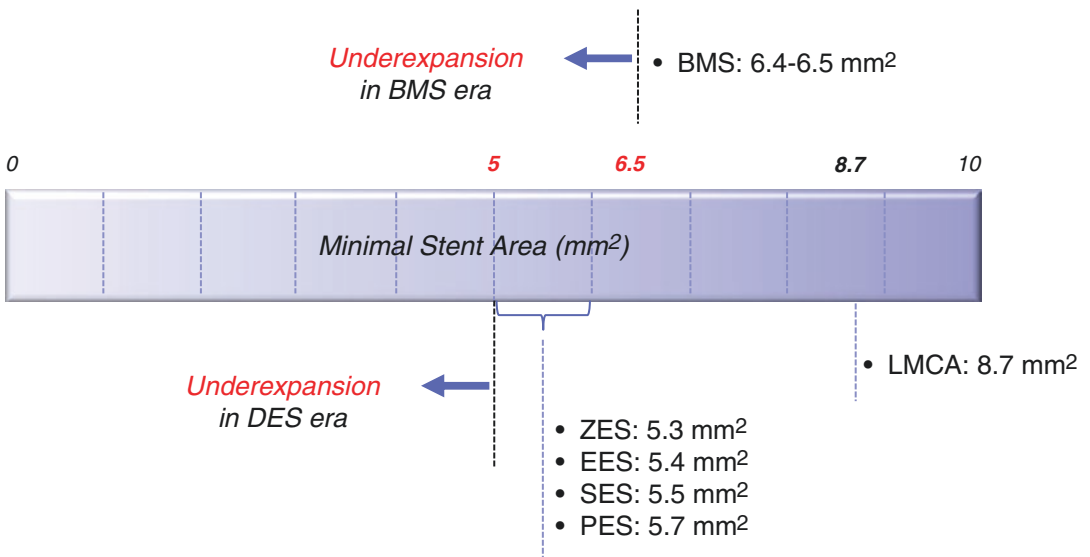
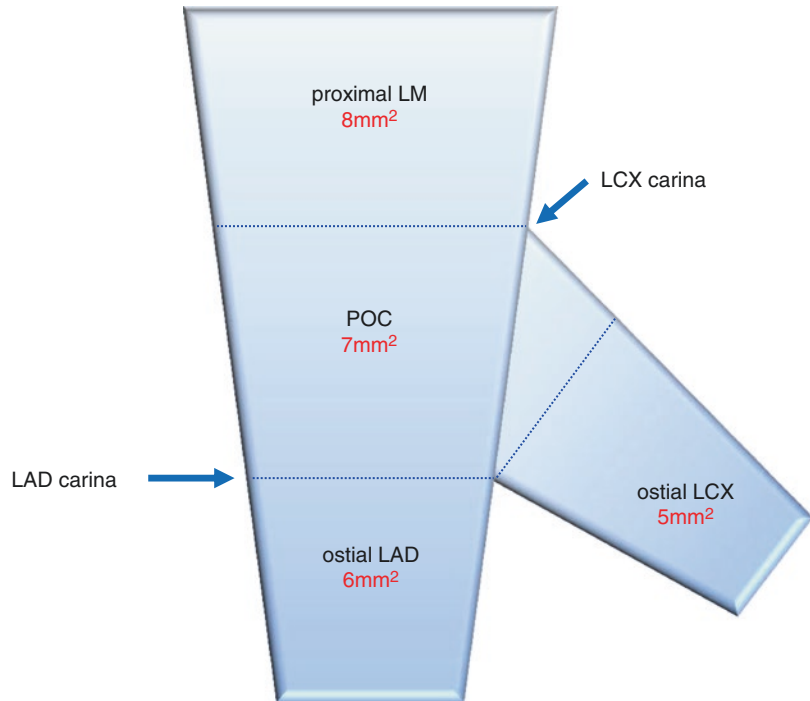


Fig. 7.2 Minimal stent area (MSA) to prevent in-stent restenosis or target vessel revascularization. Best cutoff of bare metal stent (BMS) was 6.4–6.5 mm² and the value of

drug-eluting stent (DES) was 5.0–5.7 mm². In case of left main coronary artery (LMCA), 8.7 mm² was suggested

Fig. 7.3 Minimal stent area (MSA) for left main bifurcation lesion. Considering 4 segments of left main bifurcation, the best MSA criteria were 5.0 mm² (ostial left circumflex artery), 6.3 mm² (ostial left anterior descending artery), 7.2 mm² (polygon of confluence [POC]), and 8.2 mm² (proximal left main artery above the POC)



MSA was reported as 8.7 mm² in the MAIN-COMPARE (revascularization for unprotected left main coronary artery stenosis: comparison of percutaneous coronary angioplasty versus surgical revascularization) study [2]. Considering 4 segments of left main bifurcation, the best minimal stent area criteria to predict angiographic restenosis were 5.0 mm² (ostial left circumflex artery), 6.3 mm² (ostial left anterior descending artery), 7.2 mm² (polygon of confluence [POC]), and 8.2 mm² (proximal left main artery above the POC) (Fig. 7.3) [16].

7.4 Evaluation of Stent Expansion (Well Expansion vs. Underexpansion)

In the BMS era, MUSIC study (multicenter ultrasound stenting in coronaries study) defined adequate expansion as >90% of the average reference cross-sectional area (CSA), or >100% of a smaller reference CSA with complete apposition and symmetric expansion [4]. CRUISE (Can Routine

Ultrasound Influence Stent Expansion) study showed better stent expansion of IVUS-guided PCI than angiography-guided PCI, especially in terms of target vessel revascularization (TVR), but not in mortality or myocardial infarction [17]. In contrast to the BMS era, early studies of IVUS-guided PCI with DES had no significant benefit in terms of TVR or clinical events. AVIO (Angiography Versus IVUS Optimization) study which defined optimal stent expansion as final minimum stent CSA of at least 70% of the hypothetical CSA of the fully inflated balloon used for post-dilatation did not show any difference in clinical outcome [18]. However, attention should be paid to avoid stent underexpansion. Several evidences indicate that stent underexpansion is one of the major causes of stent failure such as stent restenosis or stent thrombosis (Table 7.1) [14, 19–21]. ADAPT-DES (Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents) study showed reduction in stent thrombosis, myocardial infarction, and major adverse cardiac events by IVUS-guided optimization of stent expansion and apposition [22]. Representative

Table 7.1 Underexpansion as the predictor of DES thrombosis and restenosis

Study	Stent type	No. of lesion	Minimal stent area
Fujii K, et al. [19]	Sirolimus-eluting stent (Cypher)	15 in ST group vs. 45 in control group	$4.3 \pm 1.6 \text{ mm}^2$ in ST group vs. $6.2 \pm 1.9 \text{ mm}^2$ in control group
Okabe T, et al. [20]	Sirolimus-eluting stent (Cypher), paclitaxel-eluting stent (Taxus)	14 in ST group vs. 30 in control group	$4.6 \pm 1.1 \text{ mm}^2$ in ST group vs. $5.6 \pm 1.7 \text{ mm}^2$ in control group
Liu X, et al. [21]	Sirolimus-eluting stent (Cypher), paclitaxel-eluting stent (Taxus)	20 in ST group vs. 50 in ISR group vs. 50 in control group	$3.9 \pm 1.0 \text{ mm}^2$ in ST group vs. $5.0 \pm 1.7 \text{ mm}^2$ in ISR group vs. $6.0 \pm 1.6 \text{ mm}^2$ in control group
Hong MK, et al. [14]	Sirolimus-eluting stent (Cypher)	21 in ISR group vs. 522 in control group	$5.1 \pm 1.5 \text{ mm}^2$ in ISR group vs. $6.5 \pm 1.9 \text{ mm}^2$ in control group

DES drug-eluting stent, ST stent thrombosis, ISR in-stent restenosis

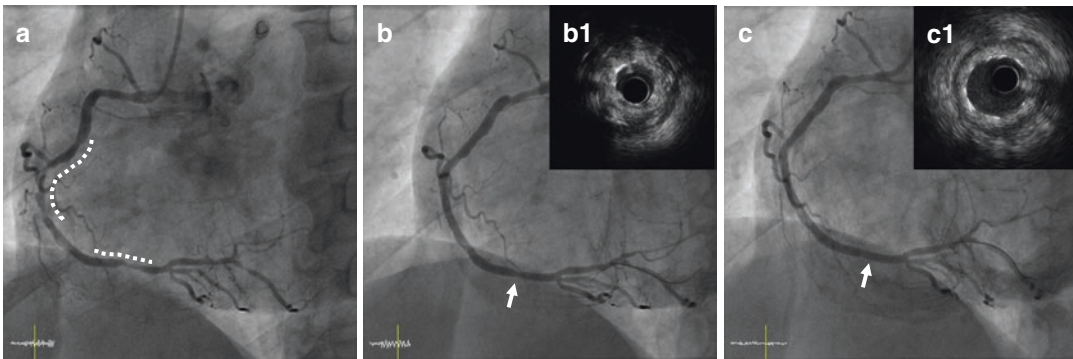


Fig. 7.4 A representative images of stent underexpansion and well expansion. A 53-year-old man was admitted with stable angina. The coronary angiogram (CAG) showed significant stenosis (*dotted line*) on mid and distal right coronary artery (RCA) (**a**). Two drug-eluting stents (Ultimaster 3.0×33 mm on mid RCA and Ultimaster 2.75×18 mm on distal RCA) were implanted separately

and CAG after stent implantation showed stent underexpansion on distal RCA (**b**, *arrow*). Corresponding intravascular ultrasound image showed minimal stent area (MSA) of 2.57 mm^2 (**b1**). After additional dilation with noncompliant balloon, CAG showed well expansion of distal stent (**c**, *arrow*) and MSA was increased as 5.06 mm^2 (**c1**)

IVUS images of underexpansion and well expansion are shown in Fig. 7.4.

7.5 Detection of Stent Edge Dissection

Stent edge dissection is a tear in the plaque parallel to the vessel wall with visualization of blood flow in the false lumen <5 mm to a stent edge. The incidence of edge dissections by IVUS is approximately 10–20% and 40% of the IVUS-identified dissections was not detected by angiography [23–25]. Significant (major) edge dissections, defined by IVUS as lumen area $< 4 \text{ mm}^2$ or dissection

angle $\geq 60^\circ$, have been associated with early stent thrombosis [26]. However, minor non-flow-limiting dissection at the edge of stent may not be associated with an increased incidence of clinical events although no consensus exists on an optimal strategy. Figure 7.5 is an example of stent edge dissection.

7.6 Detection of Acute Incomplete Stent Apposition

Incomplete stent apposition (ISA), synonymous with stent malapposition, was defined as the absence of contact between at least one strut and

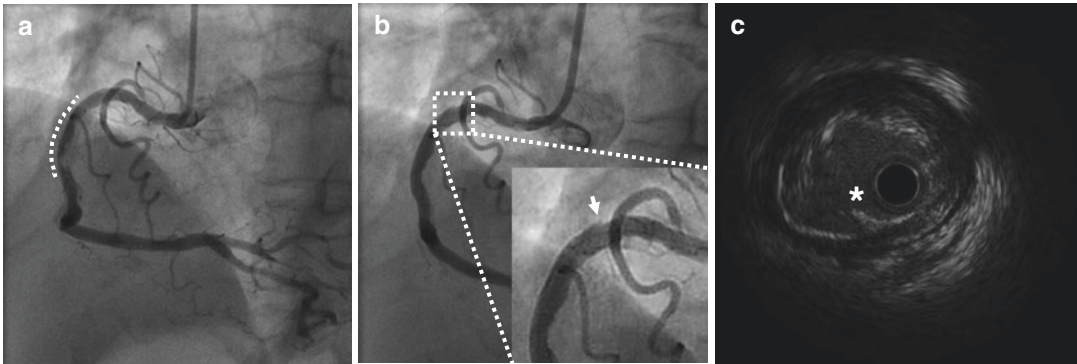


Fig. 7.5 A case of stent edge dissection. A 60-year-old woman with stable angina showed calcified stenotic lesion (dotted line) on mid-right coronary artery (a). The coronary angiogram after drug-eluting stent implantation

showed small dissection on proximal stent edge (b, arrow). Dissection flap (asterisk) was observed by intravascular ultrasound (c)

the lumen wall that did not overlap a side branch with evidence of blood speckle behind the strut and can occur acutely after stent implantation (acute ISA) or develop over time (late-acquired ISA). Acute ISA is almost due to suboptimal stent deployment. The frequency of acute ISA has been reported to be nearly 10% and it appears not to be associated with increased cardiac events [27, 28].

7.7 Detection of Tissue Protrusion (Plaque Prolapse and Intra-stent Thrombus)

Tissue protrusion (TP) was defined as a visible tissue extrusion through the stent struts by IVUS (Fig. 7.6) [29, 30]. Although thrombus was characterized by heterogeneous echodensity tissue with a sparkling pattern by IVUS [31], the accurate discrimination of atherosclerotic plaque and thrombus within stent is very difficult because of limited resolution of IVUS. Thus, TP includes plaque and/or thrombus extrusion within stent [32]. The incidence of TP has been reported in various ranges between 20% and 73%, depended on characteristics of enrolled patients (Table 7.2) [29, 30, 32–36]. In fact, TP is likely to develop in patients with acute coronary syndrome, especially ST-segment elevation myocardial infarction owing to a higher

chance of thrombus or friable plaque compared to stable patients [32, 35] and receiving longer stent probably caused by unequal distribution of inflation pressure during stent deployment [30, 34]. Other predictors of TP are larger reference lumen area, greater plaque burden, more plaque rupture, attenuated plaque, positive vascular remodeling, and virtual histology thin-cap fibroatheroma by IVUS [30, 32]. The clinical impact of TP remains a controversy. Previous studies suggested that TP after stent implantation may increase the risk of stent thrombosis [26, 37]. Other studies, however, have been failed to show this relationship [29, 32, 38].

Although some investigators demonstrated greater cardiac enzyme elevation after stent implantation in patients with TP, it did not translate into the increased risk of stent thrombosis or periprocedural myocardial infarction [30, 32]. An IVUS substudy from ADAPT-DES reported the 2-year clinical outcomes of TP after stenting. At 2-year clinical follow-up, there was no difference in the rate of major adverse cardiac events between patients with or without TP. Interestingly, patients with TP showed a less frequency of clinically driven target lesion revascularization at 2 years (1.9% vs. 4.0%, $p = 0.008$), probably due to larger minimal stent area at the end of procedure [32]. Taken together, TP may influence the early clinical phase rather than late clinical stage after

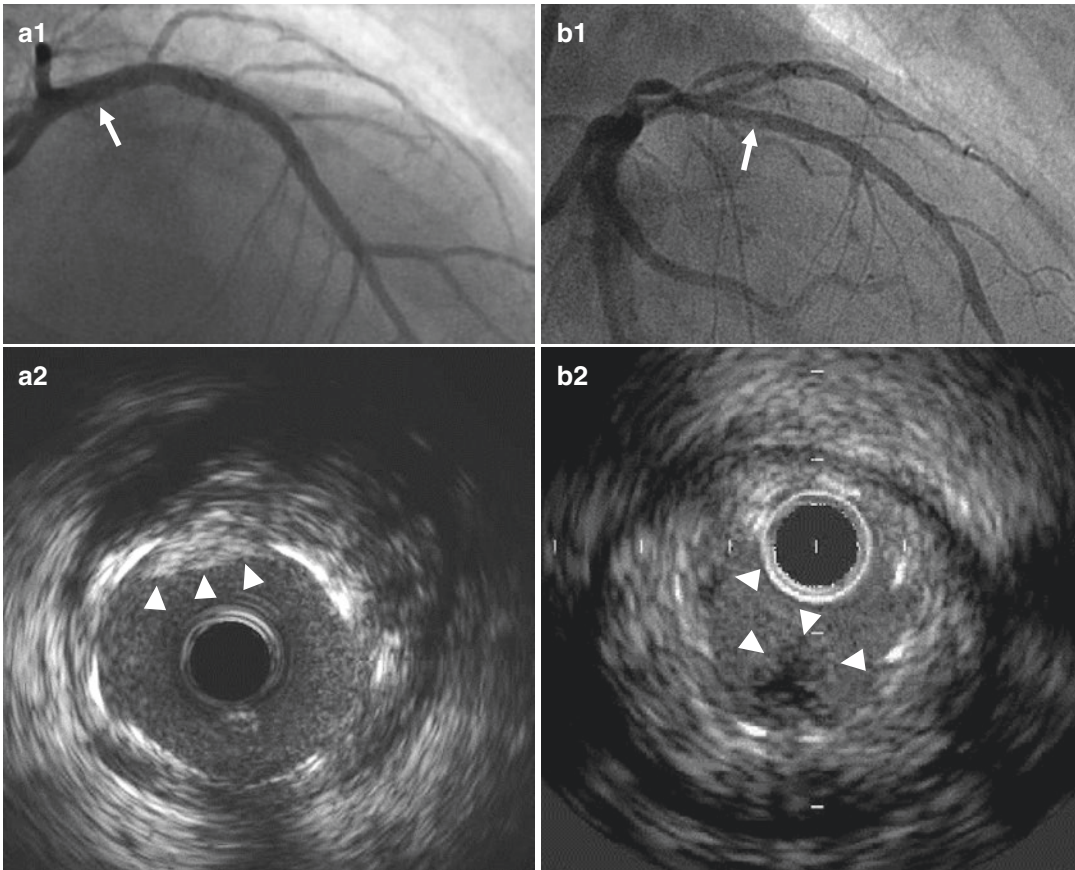


Fig. 7.6 Representative cases of tissue protrusion. A 65-year-old man was admitted with ST-segment elevation myocardial infarction (**a**). The coronary angiogram (CAG) after drug-eluting stent (DES) implantation showed no luminal narrowing within stented segments (*a1*, arrow). Correspondingly, intravascular ultrasound (IVUS) revealed tissue protrusion (plaque and/or throm-

bus) between stent struts (*a2*, arrowheads). A 55-year-old woman was admitted with ST-segment elevation myocardial infarction (**b**). The CAG after DES implantation showed mild luminal narrowing within stented segments (*b1*, arrow). Correspondingly, IVUS revealed tissue protrusion (most likely thrombus) between stent struts (*b2*, arrowheads)

stent implantation even though its clinical significance is still uncertain.

7.8 Evaluation of Full Lesion Coverage

IVUS can assess plaque amount in atherosclerotic coronary lesion, enabling to determine reference segment during stent implantation. Based on IVUS examination, reference segment is defined as <40% of plaque burden at cross-sectional image adjacent to the lesion [39]. Early IVUS study has demonstrated that angiographi-

cally normal looking segments, namely reference vessel segments, have 30–50% of plaque burden at cross-sectional image [40]. Several studies have shown that a reference segment that has >50% of plaque burden at cross-sectional area may increase the risk of target lesion revascularization or restenosis at follow-up after DES implantation (Fig. 7.7) (Table 7.3) [41–43]. Recent study also reported plaque burden with a cutoff value of 54.7% at less than 1 mm from proximal stent edge as a predictor of stent edge restenosis after everolimus-eluting stent implantation [43]. During or after stent deployment, thus, estimation of plaque amount at landing

Table 7.2 Summary of tissue protrusion after stent implantation

Study	Patients/lesions	% of TP	% of ACS (% of STEMI)	Cardiac enzyme elevation	% of peri-procedural MI	% of stent thrombosis	Clinical outcomes (TP vs. non-TP)
Sohn J, et al. [29]	38/40	45%	65.8% (18.4%)	Yes	5.3%	0%	2-year MACE: no difference
Choi SY, et al. [26] (HORIZON-AMI IVUS substudy)	401/401	73.6%	100% (100%)	NA	NA	Early: 3.4%	1-year clinical events: no difference
Hong YJ, et al. [37]	418/418	34%	100% (37.1%)	Yes	NA	Acute: 3.5% Subacute: 4.2%	1-year cardiac death, MI, TVR: no difference
Maehara A, et al. [48]	286/286	27.3%	39.1% (0%)	NA	NA	NA	NA
Qiu F, et al. [32] (ADAPT-DES)	2072/2446	34.3%	58.5% (17.9%)	Yes	1.8%	0.6%	2-year cardiac death, MI, ST: no difference
Shimohama T, et al. [36]	183/199	19.1%	12.7% (NA)	NA	NA	NA	9-month TLR: 3.3%

TP tissue protrusion, ACS acute coronary syndrome, STEMI ST-segment elevation myocardial infarction, MACE major adverse cardiac events, TVR target vessel revascularization, ST stent thrombosis, TLR target lesion revascularization

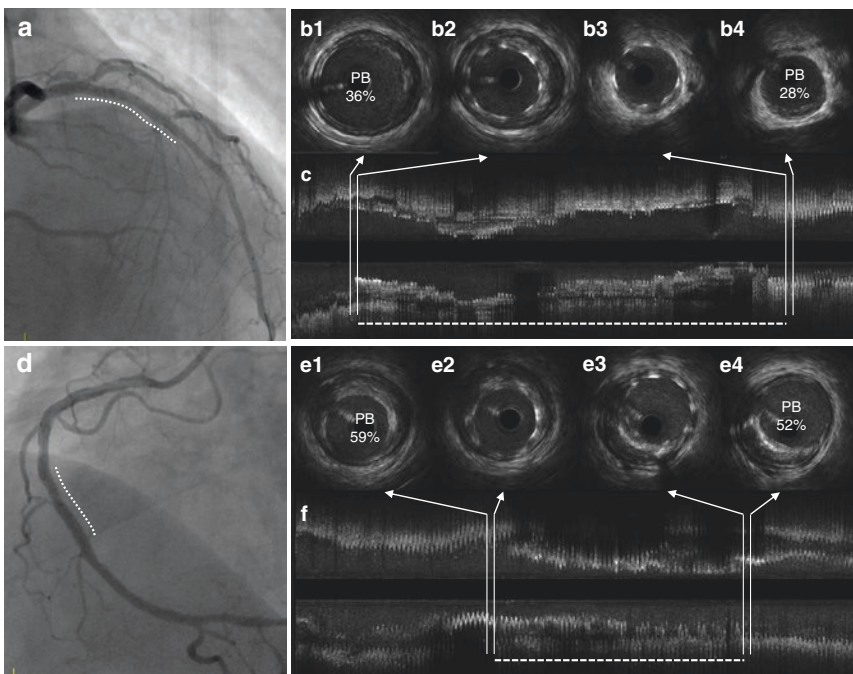


Fig. 7.7 Representative cases of appropriate (a–c) and inappropriate (d–f) location of drug-eluting stent (DES) based on post-stenting intravascular ultrasound findings. A 49-year-old man with acute myocardial infarction was treated with a second-generation DES 3.0×30 mm (dotted line) at mid to proximal left anterior descending artery (a). There is a well-expanded and apposed struts at the proximal (b2) and distal (b3) edges of stent. In addition, less than 50% of plaque burden is observed at proximal (b1)

and distal (b4) reference segments, suggesting that the location of deployed stent is appropriate. A 68-year-old man with stable angina was treated with a second-generation DES 3.0×16 mm (dotted line) at mid right coronary artery (d). There is a well-expanded and apposed struts at the proximal (e2) and distal (e3) edges of stent. However, more than 50% of plaque burden is observed at proximal (e1) and distal (e4) reference segments, suggesting that the location of deployed stent is inappropriate

Table 7.3 Suggestive IVUS criteria for stent optimization

Completely apposed struts
Apposition of stent struts to the vessel wall, not surrounded by lumen
Well expanded struts
Minimal stent area (MSA) at least
<ul style="list-style-type: none"> • 5.0–5.5mm² (non-LM) & 8.7 mm² (LM) for DES • 6.5–7.5 mm² for BMS (not in small vessels) • >90% of distal reference segment LA or >80% of average reference segment LA
No edge dissection
Post-procedure IVUS for evaluation of edge dissection
Full lesion coverage
Reference site with plaque burden of <50%

IVUS intravascular ultrasound, LM left main, DES drug-eluting stents, BMS bare metal stents, LA lumen area

point determined by IVUS can assess future clinical outcomes.

7.9 Evaluation of Plaque Characteristics at Stented or Reference Segments

IVUS can provide qualitative and quantitative change of plaque characteristics at stented segments as well as adjacent reference segments by serial IVUS examination. Analysis of radiofrequency backscatter signals of IVUS allows us to understand whether stent strut is placed underlying necrotic core or not at reference segments due to capability of tissue characterization at adjacent segment to the stent [44]. One investigator reported that a higher frequency of plaque vulnerability behind the stent strut as well as at reference segments in DES-treated lesions compared to BMS by virtual histology IVUS (VH-IVUS) [44]. Another long-term serial VH-IVUS study demonstrated similar change of neointimal tissue characterization beyond 3 years between DES and BMS [45]. On the other hand, a recent study suggested that decrease in plaque located behind the stent area may be associated with neointimal proliferation at follow-up after BMS implantation [46].

7.10 Impact on Final Procedure During Stent Deployment

The most important utility of IVUS after stent implantation is that it can provide information whether additional procedure is needed or not. An IVUS substudy from ADAPT-DES showed that the operator changed the PCI strategy based on IVUS findings in three fourth of 3349 patients including the use of a larger stent or balloon (38%) and a longer stent (22%), higher inflation pressure (23%), additional post-stent dilatation due to underexpansion (13%) or incomplete apposition (7%), and additional stent implantation (8%) [22]. Among them, post-stenting IVUS was performed in 93% of patients (Fig. 7.8). A study by Kim et al. also reported that post-stenting IVUS findings contributed to performance of additional balloon inflation or stent implantation [47].

7.11 Summary

Since stent optimization has been reported to be associated with clinical events, IVUS assessment after stent implantation might be important in a clinical point of view. Although the clinical relevance of stent eccentricity, acute stent malapposition, and tissue protrusion was a matter of debate, numerous studies have shown that smaller MSA, stent underexpansion, and major edge dissection were independent predictors of poor clinical outcomes. Even in the current era of bioresorbable scaffold, improved procedural results under IVUS guidance still contribute to avoidance of early scaffold failure. In conclusion, post-stenting IVUS can offer qualitative as well as quantitative information within and adjacent stented segments that may expand our comprehensive understanding during procedure. Importantly, the major role of IVUS after stent implantation is that IVUS-driven suboptimal procedure results can provide a clue of whether operator should perform additional intervention during stenting procedure for making better acute and long-term clinical outcomes.

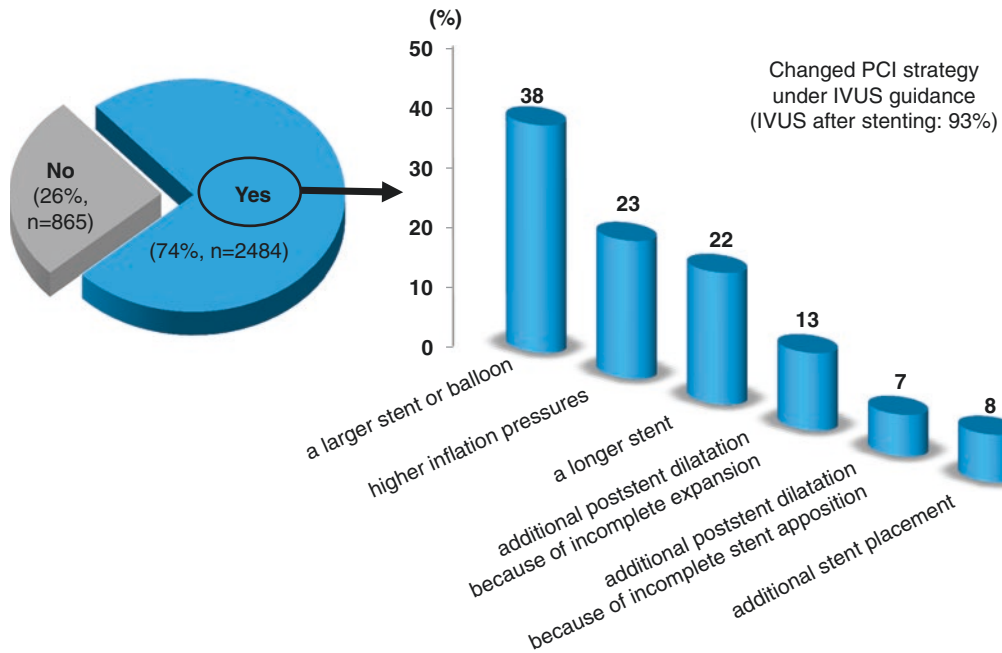


Fig. 7.8 The frequency and detailed information of changed the percutaneous coronary intervention (PCI) strategy after procedural intravascular ultrasound use (data from ADAPT-DES study) [22]. The operator changed the PCI strategy in 74% (2484/3349) of patients to choose (1) a larger stent or balloon (in 38% [943/2484]

of cases); (2) higher inflation pressures (in 23% [564/2484] of cases); (3) a longer stent (in 22% [546/2484] of cases); (4) additional post-stent dilatation because of incomplete expansion (in 13% [329/2484]) or incomplete stent apposition (in 7% [166/2484]); and/or (5) additional stent placement (in 8% [197/2484])

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