ESC European Society of Cardiology

European Heart Journal (2018) **0**, 1–20
doi:10.1093/eurheartj/ehy285

FASTTRACK CLINICAL RESEARCH
Coronary artery disease

Clinical use of intracoronary imaging. Part 1: guidance and optimization of coronary interventions. An expert consensus document of the European Association of Percutaneous Cardiovascular Interventions

Endorsed by the Chinese Society of Cardiology

Lorenz Räber[1], Gary S. Mintz[2], Konstantinos C. Koskinas[1], Thomas W. Johnson[3], Niels R. Holm[4], Yoshinubo Onuma[5], Maria D. Radu[6], Michael Joner[7,8], Bo Yu[9], Haibo Jia[9], Nicolas Menevau[10,11], Jose M. de la Torre Hernandez[12], Javier Escaned[13], Jonathan Hill[14], Francesco Prati[15], Antonio Colombo[16], Carlo di Mario[17], Evelyn Regar[18], Davide Capodanno[19], William Wijns[20], Robert A. Byrne[21], and Giulio Guagliumi[22]*

Coordinating editor: Prof Patrick W. Serruys, MD, PhD, Imperial College, London, UK

Document Reviewers: Fernando Alfonso[23], Ravinay Bhindi[24], Ziad Ali[25], Rickey Carter[26]

[1]Department of Cardiology, Bern University Hospital, Bern, Switzerland; [2]Cardiovascular Research Foundation, New York, NY, USA; [3]Bristol Heart Institute, University Hospitals Bristol NHSFT, Bristol, UK; [4]Department of Cardiology, Aarhus University Hospital, Aarhus, Denmark; [5]Department of Interventional Cardiology, Cardialysis, Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands; [6]The Heart Center, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; [7]Deutsches Herzzentrum München, Technische Universität München, Munich, Germany; [8]DZHK (German Center for Cardiovascular Research), partner site Munich Heart Alliance, Munich, Germany; [9]Department of Cardiology, 2nd Affiliated Hospital of Harbin Medical University, The Key Laboratory of Myocardial Ischemia, Chinese Ministry of Education, Harbin, China; [10]Department of Cardiology, University Hospital Jean Minjoz, 25000 Besancon, France; [11]EA3920, University of Burgundy Franche-Comté, Besancon, France; [12]Department of Cardiology, IDIVAL, Hospital Universitario Marques de Valdecilla, Santander, Spain; [13]Hospital Clinico San Carlos IDISSC and Universidad Complutense, Madrid, Spain; [14]Department of Cardiology, King's College Hospital, London, UK; [15]Department of Cardiology, San Giovanni Hospital, Rome, Italy & CLI Foundation, Rome, Italy; [16]Interventional Cardiology Unit, Cardio-Thoracic-Vascular Department, San Raffaele, Scientific Institute, Milan, Italy; [17]Structural Interventional Cardiology, Careggi University Hospital, Florence, Italy; [18]Department of Cardiovacular Surgery, Zürich University Hospita, Zürich, Switzerland; [19]Division of Cardiology, Cardio-Thoraco-Vascular and Transplant Department, CAST, Rodolico Hospital, AOU "Policlinico-Vittorio Emanuele", University of Catania, Catania, Italy; [20]The Lambe Institute for Translational Medicine and Curam, National University of Ireland Galway, Saolta University Healthcare Group, Galway, Ireland; [21]Deutsches Herzzentrum München, Technische Universität München, Munich, Germany; [22]Cardiovascular Department, Ospedale Papa Giovanni XXIII, Bergamo 24127, Italy; [23]Department of Cardiology Hospital Universitario de la Princesa, Madrid, Spain; [24]Royal North Shore Hospital, The University of Sydney, Sydney, Australia; [25]Columbia University Medical Center, New York, USA; and [26]Department of Health Sciences Research, Mayo Clinic, Rochester, USA

Received 4 April 2018; revised 16 April 2018; editorial decision 30 April 2018; accepted 16 May 2018

This Consensus Document is the first of two reports summarizing the views of an expert panel organized by the European Association of Percutaneous Cardiovascular Interventions (EAPCI) on the clinical use of intracoronary imaging including intravascular ultrasound (IVUS) and optical coherence tomography (OCT). The first document appraises the role of intracoronary imaging to guide percutaneous coronary interventions (PCIs) in clinical practice. Current evidence regarding the impact of intracoronary imaging guidance on cardiovascular outcomes is summarized, and patients or lesions most likely to derive clinical benefit from an imaging-guided intervention are identified. The relevance of the use of IVUS or OCT prior to PCI for optimizing stent sizing (stent length and diameter) and planning the procedural strategy is discussed. Regarding post-implantation imaging, the consensus group recommends key parameters that characterize an optimal PCI result and provides cut-offs to guide corrective measures and optimize the stenting result. Moreover, routine performance of

* Corresponding author. Tel: +39 035 2673452; Fax: +39 035 2674964, Email: guagliumig@gmail.com

intracoronary imaging in patients with stent failure (restenosis or stent thrombosis) is recommended. Finally, strengths and limitations of IVUS and OCT for guiding PCI and assessing stent failures and areas that warrant further research are critically discussed.

Keywords Intracoronary imaging • Optical coherence tomography • Intravascular ultrasound • Percutaneous coronary intervention (PCI) • Coronary artery disease

Preamble

This Consensus Document, which is the first of two reports summarizing the views of an expert panel organized by the European Association of Percutaneous Cardiovascular Interventions (EAPCI), appraises current evidence on clinical indications for intracoronary imaging and provides consensus opinion regarding use, strengths, and limitations of intravascular ultrasound (IVUS) and optical coherence tomography (OCT) based also on the best current practice.

Expert committee: selection criteria, organization, and consensus development

The consensus group was selected by the Scientific Documents and Initiatives Committee of the EAPCI based on the acknowledged expertise in intracoronary imaging and the origin from different geographical areas. During the first meeting in August 2017, the expert committee discussed the documents content, the perspectives and scopes, the methods of data searching and assigned lead authors for each document. Authors conducted literature searches [peer review literature with special attention to the publications in the last 5 years, existing level of evidence, randomized clinical trials, meta-analyses, registries, including a systematic research for the derivation of the meta-analysis (*Figure 1*)] and drafted the document outline. Consensus on the final document was found during several meetings and conference calls as well as two revisions of the draft document by all expert committee members. The key points of each chapter are summarized in summary boxes. The relationships and industry information for all members, writing committee, and peer reviewers are published in the Supplementary Material.

Introduction

Coronary angiography is the traditional imaging modality for visual evaluation of coronary anatomy and guidance of percutaneous coronary interventions (PCIs). However, the derived two-dimensional lumenogram cannot depict the arterial vessel wall, and thus evaluate vessel dimensions and plaque characteristics, nor directly assess the result of stent implantation. Intracoronary imaging by means of IVUS and OCT provides valuable incremental information that can be used clinically to optimize stent implantation and minimize stent-related problems.[1,2] Pre-procedural measurement of lumen and vessel dimensions and lesion characterization can facilitate accurate stent sizing and guidance of the stenting strategy. Post-procedural imaging provides strut-level evaluation of the stent result and guides optimization measures. There is growing evidence from observational studies,[3] randomized controlled trials (RCTs),[4] and meta-analyses[5,6] that intravascular imaging guidance by IVUS not only enhances the acute procedural result, but also improves clinical outcomes. In spite of this, the adoption of intracoronary imaging remains limited in routine clinical practice and highly heterogeneous according to geographic region.[7] Over the past decades, IVUS and OCT have progressively evolved with respect to technical performance (higher resolution imaging), and procedural aspects (faster pullback, automatic vessel/lumen and plaque burden detection and measurements, and co-registration with angiography). This has enabled their use as clinical tools used routinely or in selected cases.[7]

Does intracoronary imaging improve clinical outcomes following percutaneous coronary intervention?

Intravascular ultrasound vs. angiography

In the era of bare metal stents (BMS), several RCTs showed significant favourable effect of IVUS guidance over angiographic guidance alone on restenosis and target lesion revascularization (TLR) rates, with a neutral effect on mortality and myocardial infarction (MI) (Supplementary material online, *Table S1*).[8–11]

With respect to PCI with drug-eluting stents (DES), eight RCTs have compared IVUS-guided with angiography-guided PCI to date (Supplementary material online, *Table S1*).[4,12–18] Among these trials, the IVUS-XPL[4] (lesion length >28 mm), and CTO-IVUS[12] (chronic total occlusions) trials showed significant reductions in major adverse cardiac events (MACE) with IVUS guidance. The benefit was driven by a reduction in repeat revascularization for restenosis in both trials. A meta-analysis of seven RCTs (3192 patients) including only DES-treated patients confirmed the superiority of IVUS guidance vs. angiographic guidance alone in reducing MACE [odds ratio (OR) 0.60; 95% confidence interval 0.46–0.77], cardiovascular mortality [OR 0.46 (0.21–1.00)] and stent thrombosis [OR 0.49 (0.24–0.99)].[5] The duration of follow-up in these studies ranged between 12 and 24 months. These findings were confirmed in a subsequent patient-level meta-analysis including 2345 patients from RCTs of new-generation DES.[19] Significant reduction in MACE, TLR, and TVR was also shown in a meta-analysis of RCTs specifically in patients with complex lesions.[20] An updated meta-analysis performed by the present group including eight RCTs (3276 patients) confirmed the superiority of IVUS-guided PCI for reduction of MACE and ischaemia-driven TLR following DES implantation (*Figure 1*).

Several points require consideration when interpreting these findings. First, the fact that most individual RCTs with DES showed a directionally favourable trend but no significant superiority of routine IVUS guidance (despite achieving larger post-intervention stent dimensions) is likely explained by the limited power of the individual studies. The inclusion of non-complex lesions, and at least in part the absence of pre-

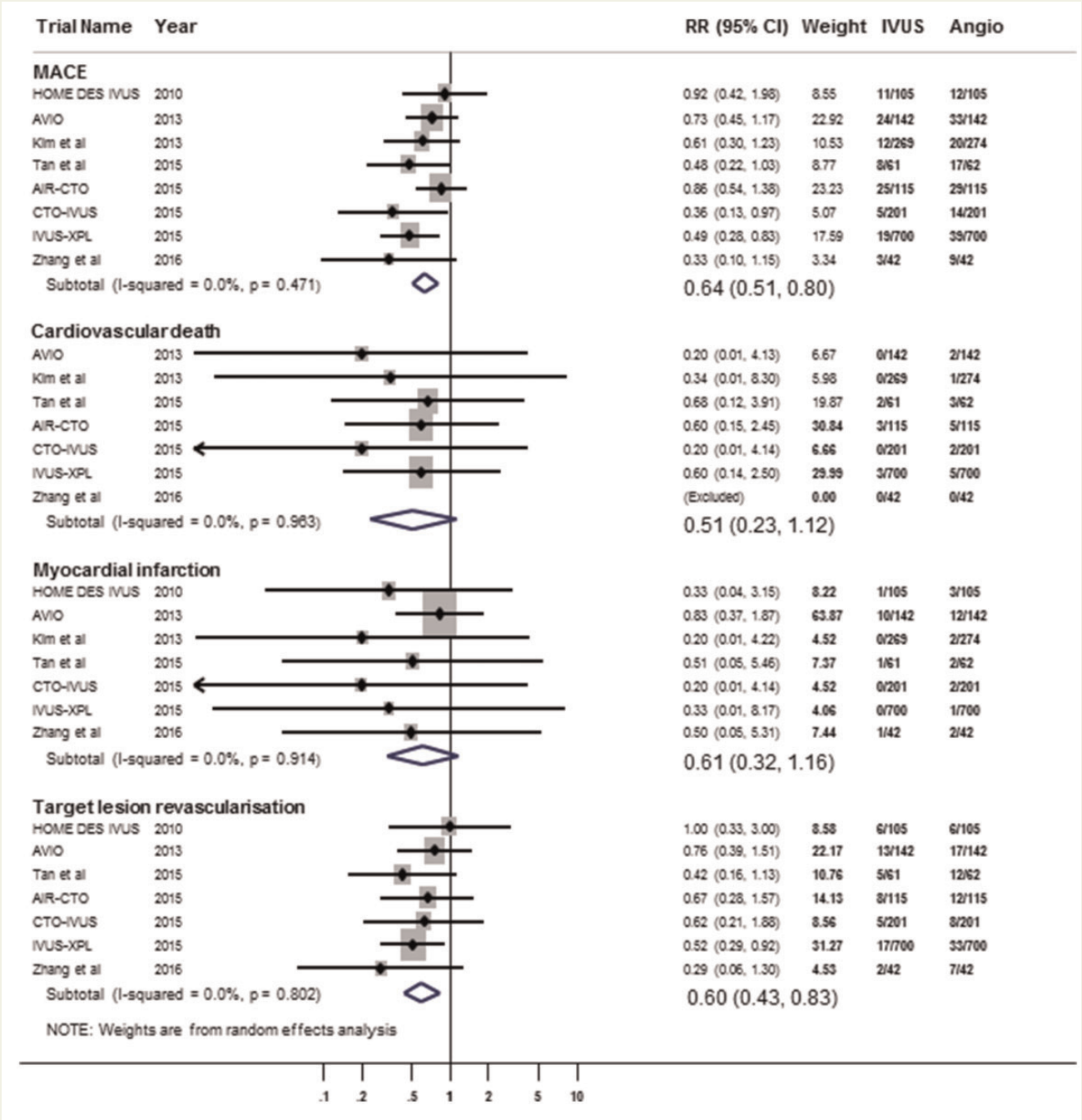


Figure 1 Forrest plot summarizing the effects of intravascular ultrasound-guided percutaneous coronary intervention as compared with angiography-guided percutaneous coronary intervention on cardiovascular outcomes.

specified guidance protocol represent additional limitations. Indeed, significant MACE reduction was observed in studies assessing patients with long lesions and chronic total occlusions,[12] as well as in meta-analyses of all available RCTs.[5] Notwithstanding these benefits, the effects of the use of intracoronary imaging in an all comers setting remains to be established.

Notably, the pooled benefit emerged despite the fact that predefined stent optimization targets were not reached in many of the enrolled patients (*Figure 2*). It should also be noted that, although pre-specified expansion targets in imaging-guided PCI are not always achievable, it is reasonable to assume that these targets do guide operators in attempting to achieve the goals and potentially result in increasing minimum stent area (MSA). Whether a higher rate of acute procedural optimization or alternative optimization targets might result in an incremental improvement in clinical outcomes is unclear. Another unknown factor is the potential effect of a systematic implementation of quantitative coronary analysis to assist angiography-guided PCI as compared to visual estimation alone.

Observational studies of IVUS-guided PCI with DES reported consistent reductions in ischaemic outcomes.[21] Owing to the lack of

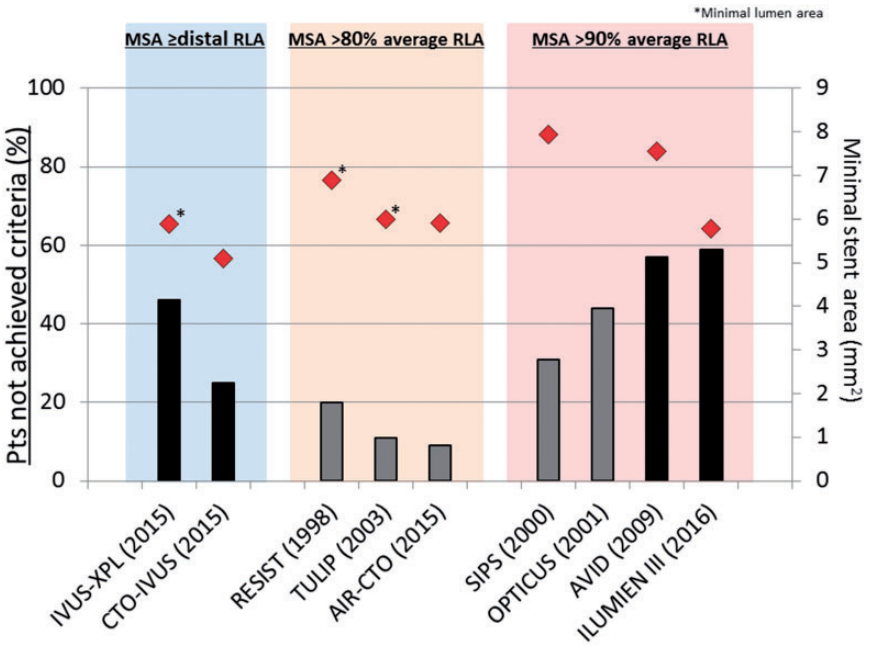


Figure 2 Effects of intravascular ultrasound-guidance and optical coherence tomography-guidance on stent expansion. Proportion of patients who did not achieve predefined criteria of stent expansion in selected randomized trials of intravascular ultrasound-guided and optical coherence tomography-guided interventions are shown by bars and the achieved minimal stent area (or lumen area indicated by asterisks) as indicated by the red diamonds. Trials are grouped according to the predefined stent expansion criteria. Black bars represent drug-eluting stents and grey bars represent bare metal stents. Minimum stent area values are means with the exception of ILUMIEN 3 (median). RLA, reference lumen area.

randomization, considerable differences in patient and lesion characteristics were observed at baseline. Moreover, additional unmeasured confounding factors are also likely to be differentially distributed between the comparison groups. The largest observational study including 8583 'all-comer' patients (ADAPT DES) showed most pronounced benefit of IVUS guidance in patients with acute coronary syndromes (ACS) and complex lesions.[3] In a meta-analysis of 20 studies (including three RCTs),[22] the benefit of IVUS guidance with respect to mortality and MACE was particularly pronounced in ACS patients or complex lesions (left main, bifurcation, CTO, or long lesions).

Intravascular ultrasound-guided left main percutaneous coronary intervention

The clinical value of IVUS-guided PCI has been studied in one small RCT[17] including 123 elderly patients (age >70 years) undergoing revascularization with second-generation DES. At 2 years, IVUS guidance resulted in a lower risk of MACE, which was driven by a significant reduction in TLR.[17] Extensive evidence exists to support IVUS-guided left main PCI in non-randomized studies. In the largest study including 1670 patients with left-main lesions treated with DES, propensity score-matched analyses showed that IVUS guidance was associated with reduced MACE (cardiac death, MI, or TLR) within 3 years (11.3% vs. 16.4%, $P = 0.04$).[23] MACE reduction was largely driven by all-cause mortality and not by MI or TLR, leaving open the question regarding the mechanism of the observed survival benefit. Larger stents with better expansion, more frequent stent post-dilatation and less use of two-stent techniques in IVUS-guided interventions were also observed in this study, which identified IVUS-guided revascularization as independently associated with MACE reduction, predominantly in the subgroup of patients with distal left-main lesions [hazard ratio (HR) 0.54 (0.34–0.90)].[23] In the observational MAIN-COMPARE study, a trend for lower mortality was demonstrated, yet again without a difference in MI or TLR.[24] A meta-analysis of 10 studies showed significantly lower risk of all-cause death, cardiac death and stent thrombosis for IVUS-guided left-main interventions.[25] The observed reduction in mortality without clear mechanistic explanation suggests that the results in these studies may be influenced by the presence of residual confounding factors.

Optical coherence tomography vs. angiography

Currently, there are relatively limited data for OCT-guided interventions and there is no RCT of clinical outcomes with OCT-guided vs. angiography-guided PCI. One registry study reported a reduced rate of cardiac death and MACE in patients who underwent OCT-guided interventions.[26] Additional observational studies showed larger final in-stent minimum lumen diameter (MLD)[27] and a reduction in the number of stents used with OCT-guided primary PCI.[28] The importance of pre-stent assessment by OCT was highlighted in the non-randomized ILUMIEN-I study.[29] Pre-stenting imaging changed the PCI strategy more frequently (57%) compared with imaging performed after stent implantation (27% of cases).

In the randomized DOCTORS trial[30] including 240 patients with non-ST-segment elevation ACS, OCT-guided PCI was associated with a small but significant improvement in the primary endpoint,

post-procedural fractional flow reserve (FFR) compared with angiography-guided PCI. This benefit was mainly driven by improved stent expansion. In the OCTACS study, 100 ACS patients were randomized to either OCT-guided or angiography-guided implantation of newer-generation DES; OCT-guidance resulted in a lower proportion of uncovered struts at 6 months (4.3% vs. 9.0%, $P < 0.01$).[31] Similarly, the DETECT OCT study showed a superior stent coverage at 3 months (7.5% vs. 9.9%, $P = 0.009$) when OCT-guidance PCI was applied in 894 stable CAD patients.[32] The randomized ILUMIEN-III trial[33] compared the effects of OCT-guided, IVUS-guided, and angiography-guided PCI on stent expansion. The study was not powered for clinical outcomes, and the primary efficacy endpoint was post-PCI minimum stent area (MSA). Non-inferiority of OCT vs. IVUS and superiority of OCT vs. angiography was tested. OCT was not found to be superior to angiography with respect to MSA but led to significantly improved minimum and mean stent expansion and fewer untreated dissections and persisting major malapposition.[33] These results have to be interpreted against the background of relatively simple lesion morphology and the efforts to optimize the results in all three groups by experienced operators. The impact of OCT-guided vs. angiography-guided PCI is being investigated further in RCTs currently underway ILUMIEN-IV (NCT0350777/) and OCTOBER trials (NCT03171311).

Intravascular ultrasound vs. optical coherence tomography

Recently, two dedicated RCTs directly compared OCT-guided vs. IVUS-guided PCI with respect to surrogate[33] and clinical endpoints.[34] ILUMIEN-III addressed the question whether OCT-guided PCI using a specific optimization protocol is comparable to IVUS-guided PCI.[33] A total of 450 patients were enrolled (median lesion length 15.5 mm; exclusion of left-main and CTO lesions; 36% ACS patients). The primary endpoint, MSA, was non-inferior following OCT-guided vs. IVUS-guided PCI. Minimum and mean stent expansion with OCT-guided PCI was comparable to IVUS-guided PCI and significantly improved vs. angiography-guided PCI. Untreated major dissections [OCT 14% vs. IVUS 26% vs. angiography 19%, P (OCT vs. IVUS) = 0.009, P (OCT vs. angio) = 0.25] and major malapposition [11% vs. 21% vs. 31%, respectively; P (OCT vs. IVUS) = 0.02, P (OCT vs. angiography) <0.0001] were less frequent in the OCT group compared with the IVUS and angiography groups. Post-dilatation was required to achieve a stent expansion of at least 90% in both the proximal and distal halves of the stent relative to the respective reference segment—a unique OCT criterion introduced in this trial.[33] Notably, the protocol-mandated expansion target was achieved in only 41% of OCT-guided cases and the difference in MSA was minimal compared with the IVUS group, in which no expansion criteria were predefined.

The OPINION RCT included 829 patients with relatively simple lesions (lesion length 18 mm) and tested whether OCT-guided PCI using a lumen-based approach was non-inferior to IVUS-guided PCI with respect to the clinical endpoint of target vessel failure within 12 months post-PCI.[34] It is thus the first OCT study formally powered for a clinical endpoint. The primary endpoint did not differ between groups (5.2% vs. 4.9%, P for non-inferiority <0.05). In addition, in-stent MLD as assessed by quantitative coronary angiography at 8 months was similar and binary restenosis was identical between groups.[34]

Critical appraisal of current evidence: intracoronary imaging (intravascular ultrasound or optical coherence tomography) vs. angiography

The ILUMIEN-III and OPINION trials consistently showed that OCT is non-inferior to IVUS for PCI guidance with respect to the acute procedural result, as well as mid-term clinical outcomes. Although a dedicated RCT is required to address the superiority of OCT-guidance vs. angiography-guidance, the aforementioned studies suggest that the superior clinical outcomes defined by RCTs on IVUS guidance[5] in selected patients are likely applicable to OCT-guidance. Consistent with this, a recent network meta-analysis including 17 882 patients who underwent angiography-, IVUS-, or OCT-guided implantation in 17 RCTs and 14 observational studies demonstrated that IVUS- or OCT-guidance was associated with significant reductions in MACE and cardiovascular mortality vs. angiographic guidance, without efficacy differences between IVUS and OCT.[6]

It is the consensus opinion of this expert group that IVUS and OCT are equivalent (and superior to angiography) in guiding and optimizing most PCI procedures. Both modalities can identify features of optimal stent implantation (expansion, apposition, and complications), as well as mechanisms of stent failure that cannot be captured using coronary angiography alone. However, the benefits and limitations of each modality require consideration (*Table 1*).[2]

Owing to lower tissue penetration, especially in lipid-rich tissue, OCT is limited for assessing plaque burden and detecting vessel size [as delineated by the external elastic membrane (EEM)] in the presence of diffuse disease—an approach used for IVUS-guided stent sizing. IVUS is the preferred modality for assessment and treatment of ostial left-main lesions (due to frequent inability of OCT to visualize the ostium as proper blood clearance may be challenging), CTO lesions and patients with renal insufficiency (due to the potential for lower volume or minimal contrast PCI).[35,36] In contrast, due to its higher resolution, OCT is more accurate for detecting lumen or stent-related morphologies with potential clinical impact, including thrombus and culprit plaque identification in patients with suspected ACS; residual edge dissection, incorrect wire positions and stent malapposition immediately after stenting. Whether the higher accuracy in the detection of aforementioned findings has the potential to translate into improved cardiovascular outcomes remains unknown. Optical coherence tomography is more user-friendly as the pullback acquisition is faster, and reliable automatic analyses are made available immediately. Furthermore, stent-related findings are easier to interpret with OCT.

The results of available studies should be interpreted in the context of best clinical practice standards. First, newer-generation DES and technical refinements of stenting procedures have resulted in overall improvements of the safety and efficacy of coronary interventions. The SYNTAX II study reported the outcomes in patients prospectively enrolled and treated with a combined protocol incorporating coronary physiology-based revascularization, IVUS-guided stenting, thin strut stent implantation, and contemporary CTO revascularization techniques. The primary analysis showed improved clinical outcomes in comparison with historical control.[37] Although the contribution of IVUS-guided PCI cannot be exactly defined, it may have contributed to the excellent outcomes in this high risk population (likely in combination with a favourable effect of physiological assessment). Second,

Table 1 Advantages and disadvantages of intravascular ultrasound and optical coherence tomography for PCI guidance and optimization

IVUS	OCT
Advantages	*Advantages*
• Extensive clinical experience → IVUS has been used clinically for almost three decades	• 10× higher resolution compared with IVUS → OCT can detect fine details which are missed by IVUS (edge dissections, tissue coverage of stent struts, and malapposition that is below the resolution of IVUS)
• Pre-intervention imaging is possible in most patients without pre-dilation	• Better tissue characterization (calcium)
• Penetration to the adventitia allows mid-wall or true vessel stent sizing	• Better suited for thrombus detection
• Extensive research regarding impact of IVUS guidance of the procedural result as well as clinical outcomes	• Images are clearer and easier to interpret
• IVUS predictors of restenosis are well established	• OCT predictors of restenosis and stent thrombosis are well established
• Better guidance for CTO techniques (e.g. wire re-entry)	• More user friendly due to rapid availability of reliable automatic analyses (i.e. accurate lumen profile)
Disadvantages	*Disadvantages*
• Images can be difficult to interpret	• Additional contrast
• Tissue characterization is limited	• Flushing is necessary to clear the lumen of blood to visualize the vessel wall
• Thrombus detection is challenging	• Pre-dilation may be necessary pre-intervention to allow blood to be flushed from the lumen
• Assessment of stent-strut tissue coverage not possible (low resolution)	• Limited penetration of OCT
• Assessment of strut malapposition is limited	• Compared with IVUS, there is limited research evidence on OCT-guided vs. angiography-guided PCI with respect to surrogate endpoints and no RCT powered for clinical outcomes
• Low-resolution of the longitudinal view	

although RCTs are of greater value for shaping recommendations in the hierarchy of evidence, practical limitations of performing large, adequately powered RCTs comparing imaging-guided vs. conventional PCI should be taken into account. Along these lines, IVUS was associated with a significant clinical benefit in the largest of the available RCTs[12] and in pooled analyses of all individual RCTs.[5] Third, the benefits of intracoronary imaging depend largely on the interpretation and the operators' reaction to these findings. Image acquisition alone will not be sufficient to impact on outcomes. Positive impact will require proper technique, correct imaging interpretation and adequate reaction to the findings. Therefore, it is important to implement quantitative measurements, and develop practical algorithms to allow stent guidance and optimization based on standardized criteria. The frequent failure to achieve stent expansion cut-off values (by the study protocols) suggest how relevant pre-stent imaging is to guide appropriate lesion preparation.

Which patients and lesions should be considered for intracoronary imaging during percutaneous coronary intervention?

Guidance of procedural strategy and optimization of the stenting result are major clinical indications for intracoronary imaging. This is in accordance with current guidelines,[38] and in agreement with the views of interventional cardiologists (see *Box 1*).[7]

Box 1 Clinical indications and expected effects of intravascular ultrasound- or optical coherence tomography-guided PCI

- IVUS-guided PCI improves clinical outcomes in selected patients with long lesions and CTOs. Limited data from RCTs suggest that IVUS and OCT-guided PCI are equally effective in achieving these benefits.
- Patients with left-main lesions should be considered for imaging-guided interventions by means of IVUS, or OCT in non-ostial left main lesions, due to particular challenges in angiographic evaluation and procedural complexity, and because of the clinical sequelae of a suboptimal result in this context.
- There is stronger evidence on the advantages of intravascular imaging to guide stenting in complex lesion morphology and in patients presenting with ACS, with less benefit in simpler lesions or patients with more stable clinical presentation.
- OCT for guidance of PCI is more user-friendly as the interpretation is simpler and automatic analyses are available immediately.
- Additional indications favouring OCT include identification of mechanisms of documented stent failure (stent thrombosis and restenosis), and guidance of BRS implantation (*Table 2*).
- Patients at high risk of developing contrast-induced acute kidney injury can benefit from IVUS-guided PCI due to the potential for lower volume of contrast.[37]

Table 2 Recommendations on the adjunctive use of intravascular imaging for diagnostic evaluation of coronary artery disease, guidance and optimization of PCIs

• **Diagnostic assessment of coronary lesions**
Consensus opinion
Angiographically unclear/ambiguous findings (e.g. dissection, thrombus, calcified nodule)
Assessment of left main stenosis
Complex bifurcation lesions
Suspected culprit lesion of ACS
• **PCI guidance and optimization**
RCT evidence
Long lesions
Chronic total occlusions
Consensus opinion
Patients with acute coronary syndromes
Left main coronary artery lesions
Two stents bifurcation
Implantation of bioresorbable scaffolds
Patients with renal dysfunction (IVUS)
• **Identification of mechanism of stent failure**
Restenosis
Stent thrombosis

How to perform intracoronary imaging and which criteria should be used for stent implantation and optimization with intravascular ultrasound and optical coherence tomography?

Image acquisition

Intravascular imaging-guided PCI should start, if possible, prior to stent implantation. Prior to stenting, intravascular imaging can assess plaque composition and distribution (calcification, lipid-rich plaque) and identify the need for more aggressive (rotational atherectomy, cutting, or scoring balloons to induce calcium fractures) or less aggressive (direct stenting to avoid lipid embolization) lesion preparation, and facilitate choice of stent size (diameter and length).[3,29,30] Imaging is recommended to be performed using a motorized pullback device, with continued control of the image quality during acquisition. Occasionally, a manual pullback is required with IVUS to verify focal and specific findings detected during the automatic pullback. Low profile, open lumen imaging catheters require purging to exclude air and to ensure optimal image quality. The imaging run should start at least 20 mm distal to the lesion and end at the left main or RCA ostium to include the longest vessel segment possible; using OCT the survey mode (75 mm) is thus preferable for pre-PCI imaging. If the imaging catheter does not cross the lesion prior to stenting, or if the flush is insufficient to clear blood from the lumen (in OCT cases), balloon pre-dilatation may be used to facilitate image acquisition. Establishing a correlation of the intracoronary imaging findings and the angiogram is important for further angiography-guided actions like identification of stent landing zones. Co-registration of IVUS or OCT images with angiography is the ideal technique for this purpose. IVUS and OCT allow the assessment of reference lumen and reference vessel dimensions (as delineated by the EEM) at the proximal and distal, non-diseased, reference sites; IVUS can also assess the vessel dimensions (delineated by the EEM) at the site of minimal lumen diameter. The term EEM is used throughout this document to describe the interface between media and adventitia.

Plaque composition

Calcific plaque

Coronary angiography has low sensitivity, but a relatively high positive predictive value for detection of calcific plaque.[39] Intravascular ultrasound and particularly OCT are valuable for detection, localization, and quantification of coronary calcification. OCT can visualize calcified plaque without artefacts,[40] penetrate calcium to a certain degree, and thus evaluate its thickness more accurately than IVUS.[41,42] Extensive target lesion calcification may adversely impact the PCI procedure by affecting the ability for effective dilatation of a coronary stenosis and is associated with greater likelihood of stent underexpansion. In lesions with maximum circumferential extension of calcium >180° by IVUS, greater calcific burden was associated with a smaller stent area and greater stent eccentricity.[43] The presence of OCT-detected fractures following lesion preparation was associated with greater stent expansion in a small-scale observational study.[44] Similarly, an OCT-based study suggested that lesions with calcium pools with a maximum angle >180°, maximum thickness >0.5 mm, and length >5 mm are at increased risk for stent under-expansion,[45] but there is no evidence of an impact of lesion calcification on clinical PCI outcomes.

Lipid-rich plaque

Stenting of attenuated plaque as assessed by greyscale IVUS,[46–49] or lipid-rich plaques as assessed by IVUS-virtual histology,[50] OCT,[51] and near infrared spectroscopy (NIRS) has been consistently associated with a higher risk of post-procedural MI, distal embolization, and no reflow phenomenon. The clinical implications of these observations

Box 2 Pre-PCI detection of calcium and lipid plaque by optical coherence tomography and intravascular ultrasound

- OCT, in contrast to IVUS, can often assess calcium thickness.
- Total calcium arc >180° and increased calcium thickness >0.5 mm are associated with greater risk of stent underexpansion.
- Evidence of calcium fractures following lesion preparation is associated with improved stent expansion.
- In case of large (>180°) calcium pools and absence of calcium fracture following the initial lesion preparation, a more aggressive lesion preparation should be considered.
- Although stenting of lipid-rich plaques is related to an increased risk of peri-procedural MI and no reflow, the procedural consequences of lipid/necrotic pool detection by OCT or IVUS prior to PCI remain unclear.

nonetheless remain unclear. The use of a distal protection filter in NIRS-detected lipid rich lesions did not reduce peri-procedural MI rates in the randomized CANARY study (potentially because of issues caused by the insertion of filters *per se*).[52]

Selection of optimal stent sizing

Stent diameter

Stent underexpansion is a powerful predictor of early stent thrombosis and restenosis after DES implantation according to numerous IVUS studies,[53–56] pointing to the importance of appropriate stent sizing and expansion. Several potential approaches have been proposed for selection of stent diameter (*Figure 3*). More conservative approaches advocate a stent diameter based on the smallest reference lumen dimensions. Progressively larger stent diameters would be chosen by accounting for the mean (average of proximal and distal) reference lumen dimension; the largest reference lumen dimensions (proximal or distal); or considering the smallest reference EEM area (by IVUS or OCT). Even more aggressive approaches by IVUS (not applicable to OCT) are based on a media-to-media (or mid-wall approach) at the site of the minimal lumen diameter (*Figure 3*). From a practical standpoint, the use of the distal lumen reference (either EEM or lumen based) represents a straightforward approach to safely apply, with subsequent post-dilatation of the mid- and proximal part of the stent. When applying a lumen based approach, the use of the mean lumen diameter with up rounding the stent diameter for 0–0.25 mm was recommended in the OPINION study. When applying an EEM based approach, the use of the mean EEM diameter (derived from two orthogonal measurements, or only from one measurement in case the visibility of the EEM is limited to approximately 180°) was recommended with down rounding the stent diameter to the nearest 0.25 mm. In terms of feasibility, the distal EEM was visible for >180° in 77% of patients included in the ILUMIEN 3 study. An important exception to this strategy may be long lesions with large diameter changes (e.g. mid-LAD to LM lesion).

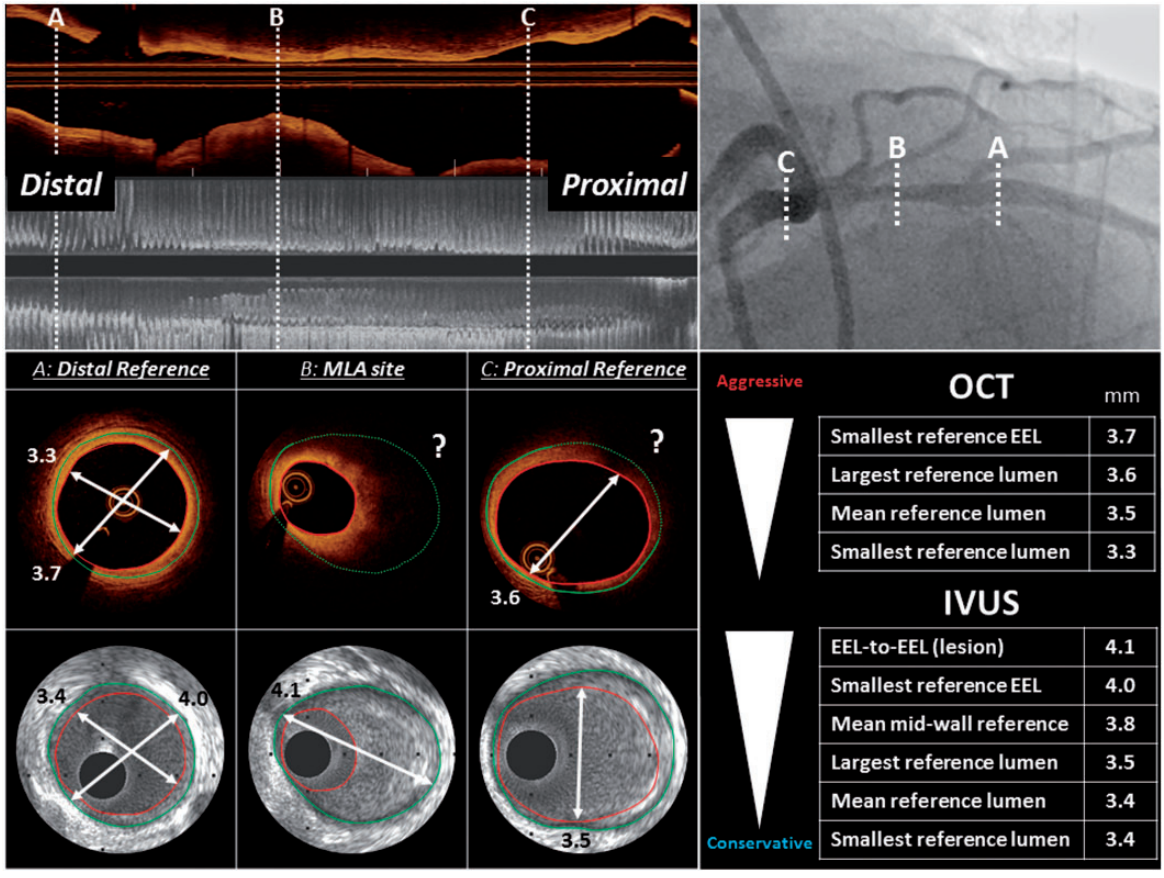


Figure 3 Intravascular ultrasound- and optical coherence tomography-based stent sizing approaches. Illustrative case of a proximal LAD stenosis as displayed by angiography and longitudinal views of intravascular ultrasound and optical coherence tomography. The cross section at the distal reference, the minimal lumen area site and the proximal reference are depicted for intravascular ultrasound and optical coherence tomography. The measurements of various sizing approaches are provided in the lower right panel. The external elastic membrane distance or the mid-wall to mid-wall approach can be used by intravascular ultrasound at the position of the minimum lumen area, whereas optical coherence tomography often fails to visualize the vessel boundaries at this position (?), due to the limited penetration depth in lipid tissues. An external elastic membrane-based approach at the proximal and/or distal reference segment can be used by intravascular ultrasound. The use of optical coherence tomography for such a strategy depends on the visibility of the external elastic membrane within the external elastic membrane segment. A lumen-based approach is similarly feasible for both intravascular ultrasound and optical coherence tomography.

In certain lesion subsets (e.g. long stenoses, vessels located distal to a CTO or location involving a myocardial bridge), assessment of vessel size may be important to rule out negative vessel remodelling, and to ensure that the selected stent size does not imply a risk of vessel rupture.

Criteria for stent sizing need to be viewed in light of certain differences in lumen detection by means of IVUS vs. OCT: minimum lumen area (MLA) derived by OCT is smaller (~10%) compared with IVUS, which may affect lesion severity assessment.[57,58] Similarly, lumen dimension assessment at the reference site results in smaller measurements by OCT vs. IVUS[59] (with the exception of one study[57]) and this may affect stent diameter selection.[58,59]

Intravascular ultrasound guidance results in larger stent diameter, greater angiographic MLD and MSA, and implantation of more and longer stents compared with angiographic guidance.[5,21,60] When comparing IVUS vs. OCT guidance, the largest available study including 809 patients in Japan[34] (OPINION) reported a small but significant difference in the average stent size (OCT 2.92 ± 0.39 mm vs. IVUS 2.99 ± 0.39 mm, $P = 0.005$) when applying a lumen-based stent sizing approach. However, this did not translate into differences in angiographic in-stent MLD immediately after stent implantation or at 8-month angiographic follow-up. In the OPINION imaging sub-study including 103 patients, the lumen-based OCT strategy was associated with a trend for non-significantly smaller minimal and mean stent area.[61] In the ILUMIEN III study, in which an EEM based distal reference sizing approach was applied, no difference in the stent diameter was observed.[33]

Stent length

The importance of proper selection of stent length is highlighted by the consistent identification of incomplete lesion coverage as a one of the predictors of stent failure (stent thrombosis or restenosis)[1,62,63] and MACE.[64] Avoidance of definition of the landing zone within an area of residual plaque burden (e.g. >50%[63]) and particularly lipid-rich plaque is clinically important, as this has been linked to subsequent stent edge restenosis following new-generation DES implantation.[65–67] In addition, incomplete stent coverage of lipid pools has been associated with an increased risk of post-procedural MI.[68]

Co-registration of intracoronary imaging and angiography is an important tool to facilitate stent length selection and precise implantation. This technique is available for clinical practice[69] and simplifies imaging-guided stent deployment.

Percutaneous coronary intervention optimization after stent implantation

Following stent implantation, IVUS/OCT can detect correctable abnormalities related to the stent and underlying vessel wall, such as underexpansion, geographic plaque miss, strut malapposition, and stent edge dissection; these abnormalities have been associated with adverse PCI outcomes.[1] Findings that represent possible targets for stent optimization are shown in *Figure 4 and Take home figure*.

While both techniques can be used in this context, OCT has proven to be superior in the detection of malapposition and stent edge dissections.[33] Optical coherence tomography as compared to IVUS has a unique value for detecting thrombus, which is often indicative of mechanical or anticoagulation problems.

Box 3 Stent sizing by intracoronary imaging

- The beneficial effect of imaging-guided PCI does not appear to be strictly linked to the algorithm used for stent sizing by IVUS or OCT.
- From a practical standpoint, a distal lumen reference based sizing may represent a safe and straightforward approach with subsequent optimization of the mid and proximal stent segments. Specifically, the mean distal lumen diameter with up rounding stent (0–0.25 mm) may be used (e.g. 3.76 → 4.0 mm), or the mean EEM (2 orthogonal measurements) with down rounding to the nearest 0.25 mm stent size (e.g. 3.76 → 3.5 mm).
- When using OCT, an EEM reference based sizing strategy appears feasible, although more challenging than a lumen based approach for routine clinical practice.
- Appropriate selection of the landing zone is crucial as residual plaque burden (<50%) and particularly lipid rich tissue at the stent edge is associated with subsequent restenosis.
- Co-registration of angiography and IVUS or OCT is a useful tool to determine stent length and allows for precise stent placement.

Stent expansion

Stent underexpansion is established as a major predictor of stent failure.[70,71] Stent expansion describes the minimum stent cross-sectional area either as an absolute measure (*absolute* expansion), or compared with the predefined reference area, which can be the proximal, distal, largest, or average reference area (*relative* expansion). In principle, greater absolute stent expansion has been associated with better long-term stent patency, better clinical outcomes and a lower risk of stent failure[55,71–73] and appears to be a better predictor of future stent patency than relative expansion. Intravascular ultrasound studies have been relatively consistent in showing that a stent cross-sectional area of 5.5 mm^2 best discriminates subsequent events in non-left main lesions.[71,73] Consistently, in the DOCTORS trial the optimal cut-off to predict post-procedural FFR >0.90 was >5.44 mm^2 by OCT[30] and data from the CLI-OPCI registries identified an MLA of 4.5 mm^2 as a threshold for discriminating patients with MACEs.[74] For LM lesions, cut-offs values are higher (e.g. >7 mm^2 for distal LM and >8 mm^2 for proximal left main by IVUS). Several points require consideration in this respect. Firstly, this cut-off may not be achievable in small vessels or may result in stent undersizing in large vessels. Secondly, there is a step-wise decrease in event rates with larger MSAs. Thirdly, evidence exists that cut-offs of absolute stent expansion that predict future events differ between BMS and DES.[55] Finally, different criteria apply in the case of left main lesions (larger cut-offs).

With respect to relative stent expansion, there are no uniform criteria regarding recommended targets for PCI optimization in clinical practice. The pre-specified criteria used for stent expansion in currently available IVUS and OCT studies are summarized in Supplementary material online, *Tables S1* and *3*, respectively. Different targets for stent optimization include either MSA greater than the distal reference lumen area; or >80% or >90% of the

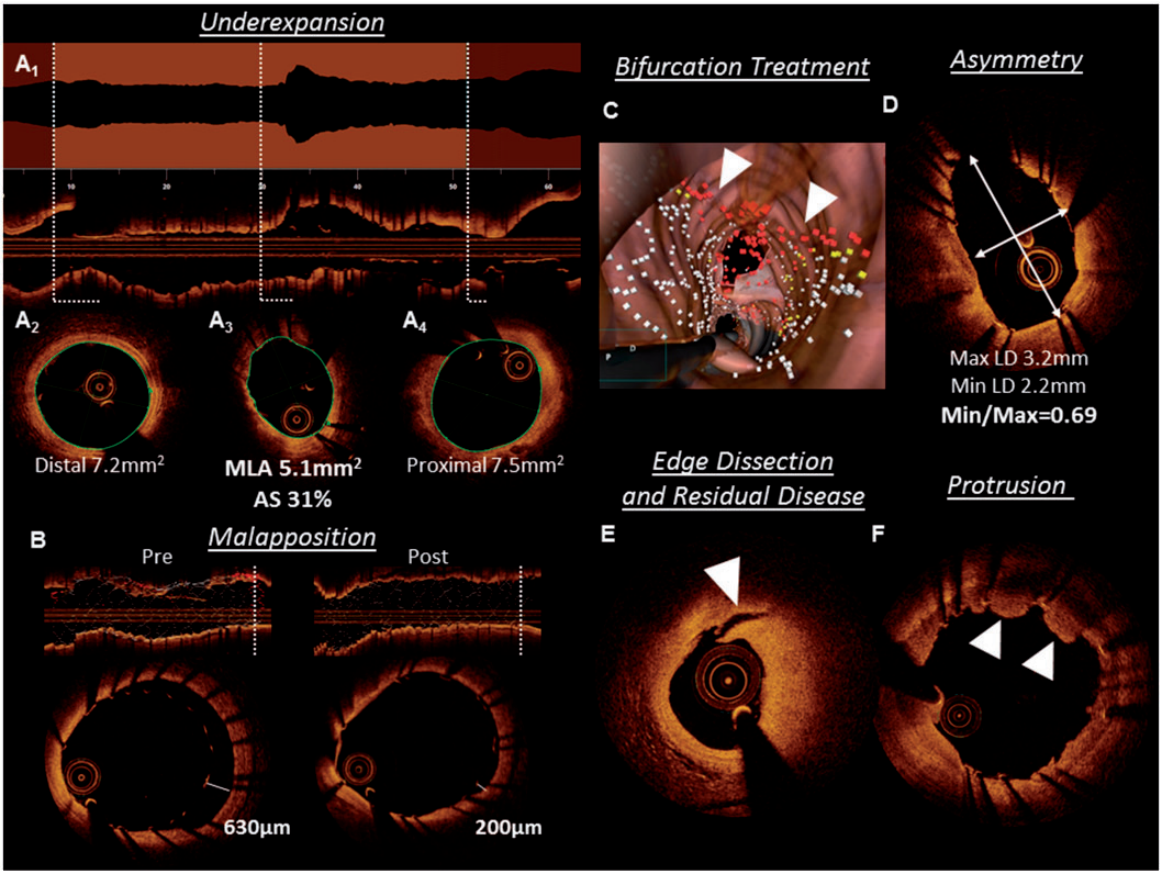


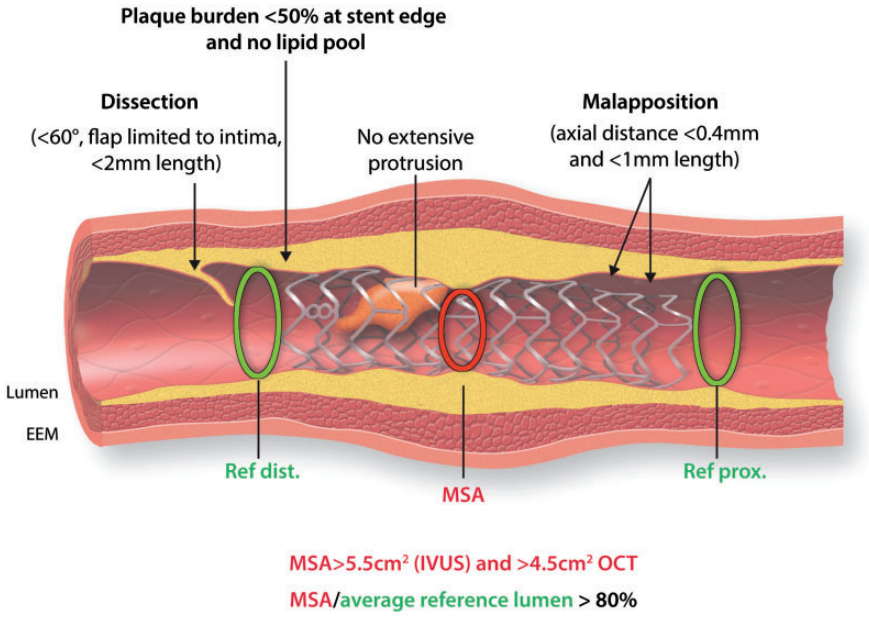
Figure 4 Targets for intracoronary imaging-guided percutaneous coronary intervention. (*A*) Avoidance of stent underexpansion represents the most relevant target for percutaneous coronary intervention guidance. The use of an automated lumen profile, provided by online optical coherence tomography software, allows detection of the minimal lumen area site. (*A1*) Graphical representation of the luminal area for every frame and facilitates assessment of stent expansion through operator selection of distal (*A2*) and proximal (*A4*) reference boundaries, and automated detection of the minimum lumen area (*A3*) are shown. In this illustrative case, a residual lumen area stenosis of 31%, required additional post-dilatation. (*B*) Online optical coherence tomography software allows automatic detection of stent struts, and therefore, identification of acute malapposition according to operator-defined strut distance from the vessel wall (white dots in longitudinal view for apposed and red dots for malapposed struts in *C*). Indication of malapposed struts may be especially helpful in bifurcation treatment as shown in this case of LAD-D1 bifurcation in which the fenestration of the first diagonal (ostium shown in the upper part) was erroneously performed under the LAD stent without taking note angiographically. The red dots (white arrows) in the three-dimensional reconstruction indicate a grossly malapposed LAD stent despite perfect angiographic result (not shown). (*D*) Stent asymmetry can be assessed by the quotient of minimal and maximal lumen diameter. (*E*) Edge dissections (in the context of residual disease burden) and (*F*) irregular tissue protrusion have both been associated with adverse outcomes.

average (proximal and distal) reference area. In recent IVUS trials, the presence of a MSA greater than the distal reference lumen area was associated with a very low adverse event rate (1.5% within 1 year).[1] Considering that the requirement for achieving >90% expansion was frequently out of reach (*Figure 2*), this expert group believes that the cut-off >80% for the MSA (relative to average reference lumen area) appears to be a reasonable approach to adopt in clinical practice. In the DOCTORS study, the optimal cut-off value of stent expansion able to predict FFR >0.90 was >79.4%.[30]

Malapposition

In contrast to underexpansion (i.e. MSA that is substantially smaller than the average reference lumen areas), malapposition refers to the lack of contact of stent struts with the vessel wall. Stent malapposition and underexpansion can co-exist or occur independently. Malapposition can occur either in the acute, post-procedural period, or it may develop later, possibly as a result of an underlying vascular process of inflammation and positive (outwards) remodelling of the vessel wall. When malapposition is identified at follow-up, it may represent either persistent (i.e. ongoing since the time of implantation), or late acquired malapposition; a differentiation of these two entities is not possible in the absence of imaging immediately post stenting.

While stent underexpansion is a major IVUS predictor of early stent thrombosis or restenosis, no clear link exists between acute malapposition (in the absence of underexpansion) and subsequent stent failure, as acute malapposition may subsequently resolve. Malapposition can be more reliably detected by OCT compared with



Take home figure Summary of post-percutaneous coronary intervention optimization targets. The most relevant targets to be achieved following stent implantation in non-LM lesions are shown. These include optimal stent expansion (absolute as well as relative to reference lumen diameter); avoidance of landing zone in plaque burden >50% or lipid rich tissue; avoidance of large malapposition regions, irregular tissue protrusion, and dissections. Thresholds provided reflect the consensus of this group. Some are based on consistent and robust prospective data (e.g. stent expansion, landing zone) and others are less established (e.g. malapposition).

IVUS, translating into a higher proportion of malapposed stent struts identifiable by OCT[33] (up to 50% of stents implanted under OCT evaluation) vs. IVUS (about 15% of stents implanted under IVUS evaluation). Prospective studies have shown little or no relationship between malapposition that is detected during routine imaging and subsequent events. Acute malapposition did not emerge as an independent predictor of stent thrombosis in studies with imaging immediately after stent placement.[75,76] Still, on the basis of the investigated populations a protective effect of optimal stent apposition in high-risk populations cannot be excluded. In contrast, studies of stents presenting with thrombosis have consistently identified malapposition as a frequent underlying stent abnormality and showed a higher incidence and extent of malapposition in stent segments with vs. without thrombus. Three recent registries performed OCT in patients with definite stent (BMS or DES) thrombosis.[77–79] In two studies (PRESTIGE[77] and PESTO[78]) malapposition (unclear whether persistent or late acquired) emerged as a frequent finding: 27% and 60%, respectively, in acute stent thrombosis (within 24 h of implantation), 6% and 44%, respectively in subacute stent thrombosis (1–30 days,) and 10% and 44%, respectively in late stent thrombosis (between 30 days and 1 year post-PCI). These observations were consistent with smaller OCT registries.[80–82] Moreover, malapposition was among the three leading mechanisms in studies investigating patients with very late stent thrombosis[77–79] (>1 year following stent implantation). In line with these observations, malapposition has been associated with increased thrombogenicity in *in vitro* studies.[83]

Notwithstanding current uncertainties regarding the clinical relevance and potential sequelae of different modes of malapposition, the findings of large stent thrombosis registries, in concert with *in vitro* investigations, suggest that extensively malapposed struts should be avoided following stent implantation and should be corrected when anatomically feasible. As it relates to clinical guidance (corrective treatment or not), malapposition is not merely a binary (yes/no) phenomenon, as has been addressed in most studies, but can be quantified in a two-dimensional (or even a three-dimensional) fashion. Regarding thresholds for corrective post-dilatation, although there are no robust data, there is informative evidence to provide some guidance. One consideration is the association between the axial distance of incomplete stent apposition (ISA) and the subsequent integration by neointimal tissue; in determining the axial extent of ISA, differences in strut thickness across different stents should also be considered. Serial OCT studies observed that struts with ISA distance <0.35 mm undergo full neointimal integration at follow-up.[84–86] In agreement with this observation, a detailed analysis of patients with very late stent thrombosis reported minimal ISA distance within the thrombosed segments ranging between 0.3 and 0.6 mm, and longitudinal length between 1.0 and 2.1 mm.[79] The risk for extensive acute malapposition is increased in bifurcation PCI, a situation in which visualization by three-dimensional OCT may be helpful (*Figure 4D*). As complex bifurcation stenting requires rewiring of freshly implanted stents, malapposition constitutes a particular problem due to the risk of accidental abluminal rewiring.

Tissue prolapse

Tissue prolapse (typically defined as tissue extrusion from inside the stent area) may include either lesion protrusion or, in the

Box 4 Criteria to assess optimal stent result

- A relative stent expansion of >80% (MSA divided by average reference lumen area) should be obtained in routine clinical practice.
- An MSA of >5.5 mm^2 by IVUS and > 4.5 mm^2 by OCT should be achieved in non-left main lesions.
- The clinical relevance of acute malapposition is uncertain. Nonetheless, extensive malapposition after stent implantation should be avoided and corrected, if anatomically feasible. Early strut coverage may be promoted by full apposition.
- Acute malapposition of <0.4 mm with longitudinal extension <1 mm or malapposition should not be corrected as spontaneous neointimal integration is anticipated. This cut-off requires prospective validation.
- Late acquired malapposition represents an established cause of late and very late stent thrombosis.
- Tissue prolapse in ACS as compared with stable CAD is adversely related to outcomes, likely because of differences in the composition of the protruding tissue.
- Large dissections detected by IVUS or OCT are independent predictors of MACE. Presence of residual plaque burden, extensive lateral (>60°), and longitudinal extension (>2 mm), involvement of deeper layers (medial or adventitia) and localization distal to the stent increase the risk for adverse events.
- Stent edge haematoma may be detected by IVUS or OCT in case of angiographic appearance of a residual stent edge stenosis.

context of ACS, protrusion of athero-thrombotic material. Optical coherence tomography enables clearer and more frequent visualization of tissue prolapse compared with IVUS[33]. Tissue prolapse after stent implantation has been identified as an OCT predictor of early stent thrombosis and has been related to adverse short-term prognosis following PCI.[53,87–89] The volume of prolapsed tissue by OCT has been associated with unstable plaque morphology as well as with post-PCI myocardial injury.[90] In a large multicenter OCT registry including 780 patients (50% with ACS), irregular protrusion was more common in patients treated for MI and was an independent predictor of 1-year clinical outcomes, primarily driven by TLR.[91] Evidence exist that tissue prolapse in the context of ACS is more likely to have consequences than in more stable (non-ACS) clinical setting as suggested by the CLI-OPCI and HORIZONS-AMI substudies.[53]

Dissection

Large edge dissections by IVUS have been reported as correlates of early stent thrombosis and these dissections were commonly characterized by their depth (at least disrupting the medial layer), their lateral extension (>60°) as well as their length (>2 mm).[53,87] Owing to its higher resolution, OCT can identify less-extensive edge dissections which are missed by IVUS. Therefore, the incidence of OCT-reported edge dissections is at least two-fold higher compared with IVUS-reported dissections; this was confirmed in the OCT vs. IVUS arms of the ILUMIEN-3 trial.[33] In the CLI-OPCI II Study, dissections >200 μm at the distal (but not proximal) stent edge by OCT emerged as an independent predictor of MACE (HR 2.5).[74] In contrast, in an observational study including 780 patients who underwent post-procedural OCT, stent edge dissections (detected in 28.7% of lesions) or in-stent dissections were not associated with adverse 1-year clinical outcomes. In line with IVUS studies, stent edge dissections are considered among OCT-defined predictors of early stent thrombosis. However, subtle abnormalities (i.e. minor edge dissection) are unlikely to be clinically significant and possibly do not require correction.[92,93] Detection of intra-and extramural haematomas by IVUS or OCT may be relevant, as these findings usually appear as edge stenosis by angiography and can be misdiagnosed as stent vessel mismatch or spasm. The progression of uncovered haematoma may lead to early stent thrombosis.

Optimization of bioresorbable scaffold implantation

In contrast to permanent metallic stents, where optimal implantation techniques have been investigated extensively in imaging studies, intracoronary imaging was not routinely recommended for bioresorbable vascular scaffold implantation. Notably, due to inherent mechanical limitations of bioresorbable materials, and radio-lucency of devices, accurate lesion preparation, device sizing and procedure optimization (i.e. complete expansion without fracture or malapposition) may be even more critical when implanting bioresorbable scaffolds.[94,95] Retrospective analyses demonstrated that post-procedural lumen eccentricity and asymmetry are related to target lesion failure.[96] Intracoronary imaging is of importance to detect structural abnormality such as acute disruption and discontinuities at follow-up which are not detectable on angiography due to radio-lucency of devices. Although not shown in prospective trials, malapposition at the time of implantation may adversely impact subsequent tissue coverage and incorporation of the scaffold into the vessel wall, which in turn may create a thrombogenic nidus during the process of scaffold dismantling.[95]

Assessment of mechanisms of stent failure

This expert panel highly recommends intracoronary imaging in the setting of stent failure. Imaging facilitates identification of the mechanisms of restenosis or stent thrombosis, guides appropriate treatment, minimizes the risk of subsequent stent failure events, and raises awareness of any potential device related concerns.

Restenosis and stent thrombosis in metallic drug-eluting stents

Identifiable causes of restenosis other than intimal hyperplasia include chronic underexpansion (in approximately 18–40%[54,97]) stent fracture (<5%), and neoatherosclerosis (i.e. >1 year of DES

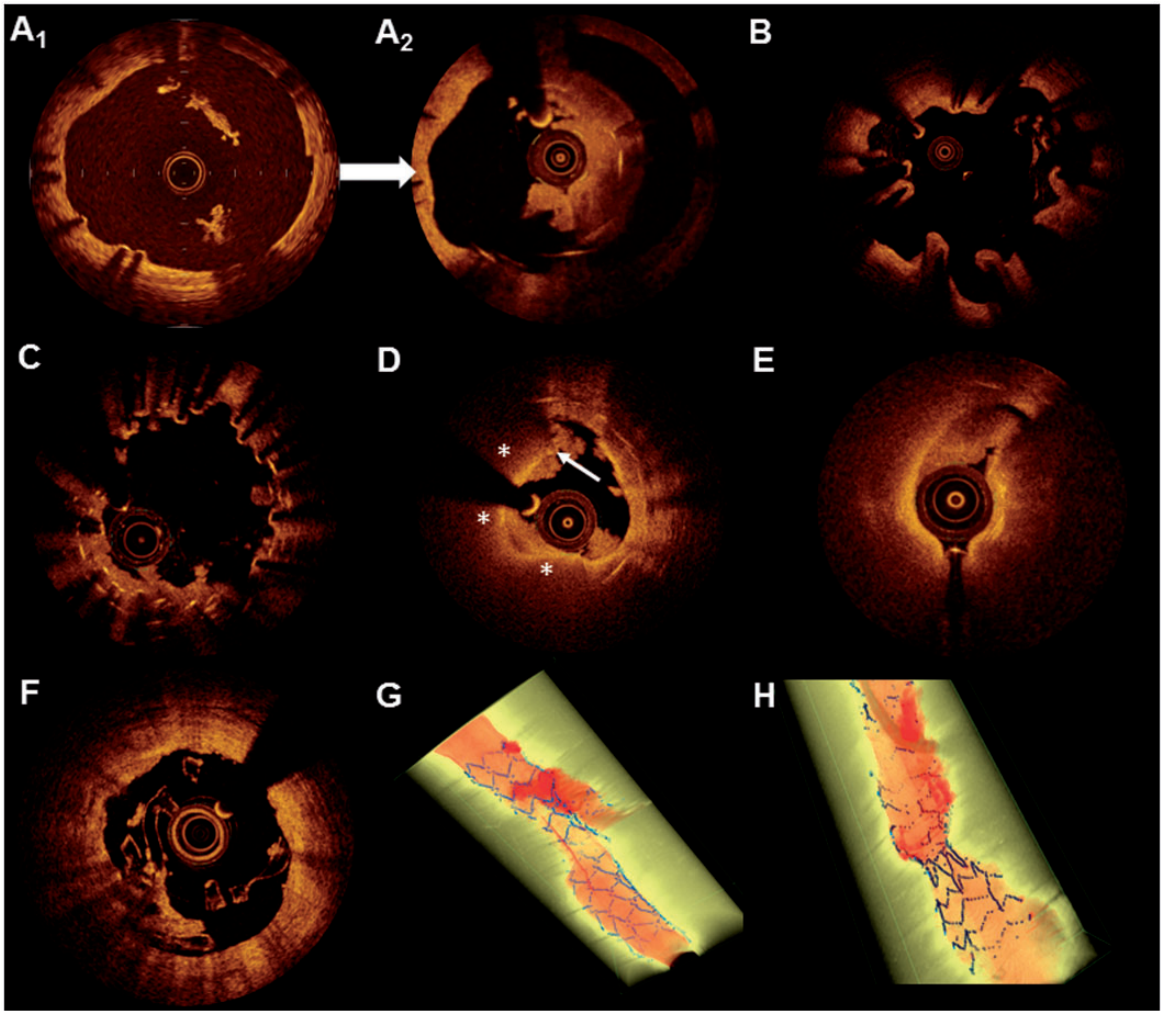


Figure 5 Optical coherence tomography and intravascular ultrasound findings in the context of stent and scaffold thrombosis. (*A*) A significantly undersized stent suggestive of persistent malapposition 1 year after implantation (A_1) was demonstrated. This finding was left uncorrected. Two years later (A_2), an occlusive stent thrombosis occurred after cessation of aspirin. (*B*) Extensive evaginations as an indicator of positive vessel wall remodelling in a Cypher stent implanted 4 years previously. No thrombus is visible as thrombolysis was administered prior optical coherence tomography. (*C*) Uncovered stent struts in the region of multiple overlapping stents with small multiple protruding thrombi. (*D*) A typical in-stent fibroatheroma (6–12 o'clock, stars) with a ruptured cap (arrow) and white thrombus is depicted, suggestive of neoatherosclerosis. Disease progression at the stent edge may be a trigger of stent thrombosis (*E*). Although most mechanisms of scaffold thrombosis are identical with metallic drug-eluting stents, stent discontinuity (i.e. previously apposed scaffold struts that subsequently migrate into the lumen) represents a specific finding in scaffold thrombosis (*F*). (*G*) A stent thrombosis occurring at a bifurcation lesion (three-dimensional, thrombus red, and stent blue) is illustrated and (*H*) a markedly underexpanded stent with thrombus distal to the underexpanded segment. (*I*) 'Pros and Cons' of intravascular ultrasound and optical coherence tomography in the assessment of stent thrombosis is illustrated. The longitudinal view is illustrated on the left hand and cross sections from outside (I_1) and inside (I_2) the thrombotic region. In the longitudinal view and I_2, the thrombus mass is attenuating the light and stent struts are no longer visible (dotted red line and ?) whilst intravascular ultrasound readily depicts the struts. Also, the outer vessel wall (green line), which is indicative of positive remodelling, can only be seen by intravascular ultrasound. Conversely, subtle details like stent strut coverage and peri-strut low intensity regions can only be depicted by optical coherence tomography (I_1).

implantation). The first two abnormalities can be readily detected by IVUS or OCT, whereas the latter is a finding defined by OCT.[98] Regarding stent fracture, this can be identified more readily by means of three-dimensional OCT imaging compared with two-dimensional imaging alone. For approximately 60% of restenosis cases, the leading mechanism cannot be assessed beyond the (expected) presence of neointimal hyperplasia. In contrast, stent thrombosis has multiple underlying mechanisms and most of these are recognizable by intracoronary imaging (*Figure 5*).[53,91,99,100] Optical coherence tomography, as opposed to IVUS, can distinguish thrombus from other tissue components, and is therefore, considered the preferred imaging technique for stent thrombosis.

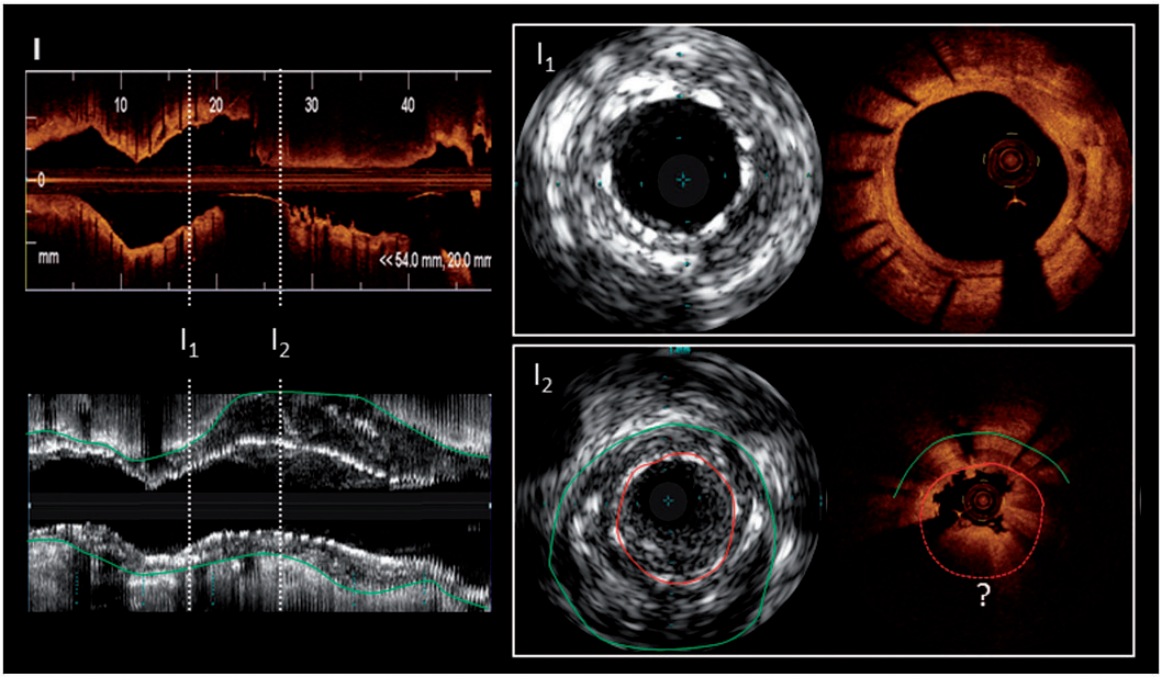


Figure 5 Continued.

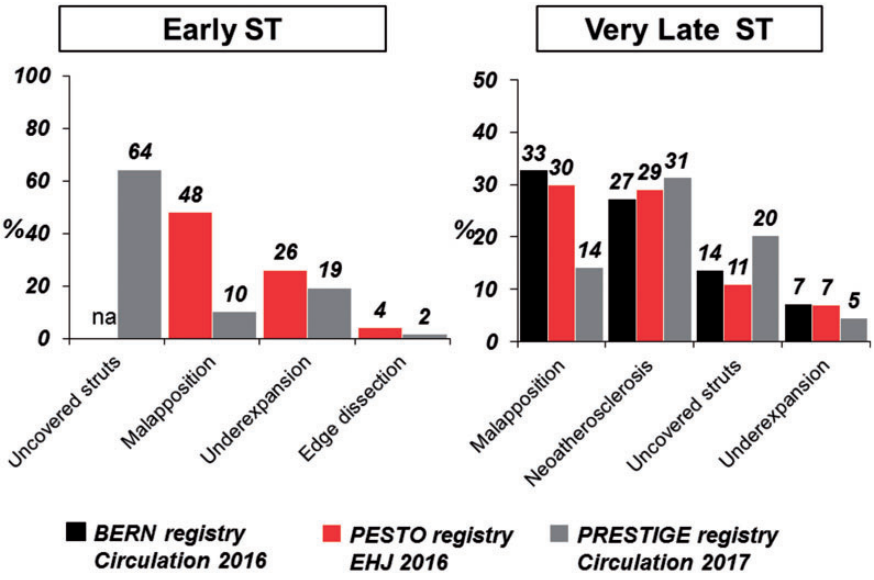


Figure 6 Frequency of presumable causes of early and very late metallic drug-eluting stent thrombosis as assessed in three optical coherence tomography registries.

However, in some cases the presence of large amounts of thrombus can make the assessment of stent struts and the outer vessel wall challenging by OCT due to light attenuation, and IVUS may be preferred (*Figure 5* I). Restoration of TIMI III flow with subsequent administration of GP IIb/IIIa inhibitors and staged OCT represents a strategy previously applied to enhance analysis of the underlying stent thrombosis aetiology.[78] Three recent cohort studies investigated correlates of stent thrombosis occurring at various time points after stent implantation.[77–79] One or several leading mechanisms responsible for thrombus formation could be identified in

Box 5 Stent/scaffold failure analyses by intracoronary imaging

- Analysis of stent restenosis and stent thrombosis by intracoronary imaging is essential to understand mechanisms of failure and is highly recommended.
- Although prospective data are lacking, tailored treatment strategies based on the exact failure mechanisms appear reasonable (e.g. post-dilatation only in case of malapposition/underexpansion induced stent thrombosis vs. stent implantation in presence of neoatherosclerosis).
- OCT is the preferred technique to study in-stent restenosis and stent thrombosis.
- Intracoronary imaging should be mandatory in case of any investigational device failure to expedite the identification of potential safety concerns and is recommended for evaluation of any new DES or BRS.
- OCT findings from stent thrombosis registries propose the following correctable targets for PCI guidance: malapposition, residual disease burden at stent edge, dissections and stent underexpansion.

the majority of patients (>90%). Reassuringly, the interpretations of the operating physicians were in agreement with those of experts in 70% of cases in the PESTO registry. The main causes for stent thrombosis in the DES subgroups are reported in *Figure 6*. In patients with early stent thrombosis, malapposition, underexpansion, and edge dissections were the predominant abnormalities. At variance to previous IVUS studies, malapposition was a relatively frequent finding by OCT. In patients with very late DES thrombosis, malapposition, neoatherosclerosis, uncovered struts and underexpansion were frequently observed. A tailored treatment approach according to the specific OCT findings (e.g. additional stent in case of neoatherosclerosis, post-dilatation in case of underexpansion or malapposition) appears clinically reasonable, although prospective data to support such a treatment strategy are lacking. The 2014 ESC guidelines on myocardial revascularization, which were published prior to publication of the three OCT registries, considered a Class IIa C recommendation for the performance of intracoronary imaging in stent failure by IVUS or OCT.[38]

Scaffold thrombosis

The Absorb BVS scaffold is the only bioresorbable device that has undergone extensive scientific evaluation in adequately powered RCT's. Individual studies[101] and meta-analyses[102,103] suggested an increased risk of scaffold thrombosis at all-time points following implantation and particularly beyond one year. Although many experts acknowledge the potential for intracoronary imaging-guided scaffold implantation to mitigate scaffold failures, no RCT to date has addressed the relevance of imaging-guided scaffold implantation and one was stopped prematurely (OPTICO BVS; NCT02683356) following retraction of ABSORB BVS. None of the conducted clinical trials on ABSORB BVS was convincingly able to provide insights into the failure mechanisms. Of note, OCT analyses of scaffold thrombosis by means of OCT within the first year after implantation identified underexpansion and malapposition (due to undersizing or lack of adequate expansion) as predominant findings.[94,104]

The largest cohort study on very late ABSORB BVS scaffold thrombosis studied by OCT—the Independent OCT Registry on Very Late Bioresorbable Scaffold Thrombosis (INVEST)[105]—included 36 patients with available OCT at the time point of the thrombotic event; 31% of patients had serial OCT imaging. The leading associated finding was a new bioresorption-specific phenomenon called strut discontinuity (43%). Strut discontinuity or dismantling is present (according to study definition) when struts are dislocated into the lumen despite initial full apposition, and even despite some degree of tissue coverage as shown by intercurrent OCT recordings, or in case of acute malapposition with subsequent discontinuity or in presence of acute scaffold fracture.[95,105] The newly described mechanism of Absorb BVS failure has not been observed with metallic DES and potentially explains the increased risk of very late scaffold thrombosis. Unravelling of a resorption-specific failure mechanism may permit the development of treatment strategies and provide guidance for improvements in the design of newer-generation devices. Device failures of newer-generation scaffolds should systematically undergo evaluation by intracoronary imaging, preferably OCT.

Potential limitations of intravascular imaging

The clinical value of intracoronary imaging for PCI guidance is widely acknowledged,[1] but potential limitations should be considered. One of the key limitations of intracoronary imaging is the additional time required for imaging. The cost of IVUS and OCT is a notable consideration, and is acknowledged as a potential limitation by practicing interventional cardiologists.[7] A dedicated analysis addressing the cost-effectiveness of IVUS during PCI with DES showed that IVUS-guided interventions are cost-effective, particularly when used in patients at a greater risk of restenosis.[106] In view of substantial geographic variability in the clinical use of IVUS and/or OCT in daily practice, ranging from routine use in Japan to selected use in most other countries[7] to very limited use in countries with no reimbursement, we recommend and encourage imaging-guided PCI primarily in settings with the most robust evidence of a clinical benefit (*Table 3*). Adequate training in the acquisition of images and interpretation of findings is an additional essential factor that may be addressed by integrating training in structured interventional fellowships and by ensuring basic imaging skills for all coronary interventionists and advanced experience with IVUS and/or OCT in at least selected operators in each medium and large-volume interventional catheterization laboratory. With current small diameter imaging device iterations, complications directly related to imaging are exceedingly rare, as shown in a systematic review.[60] In a large registry of patients undergoing

Table 3 Summary of randomized trials comparing optical coherence tomography vs. angiography and/or intravascular ultrasound for percutaneous coronary intervention guidance

Study	Year of publication	Number of patients	Age (years)	ACS (%)	Follow-up (months)	Stent type	Optimization criteria	Number of patients/ lesions not achieved criteria
ILUMIEN 3	2016	146/146/158[a]	67/66/66	34/36/36	1	DES	MSA of at least 90% in both the proximal and distal halves of the stent relative to the closest reference segment	82/140 (58.6%)
OPINION	2017	405/412	69/68	13/11	12	DES	(1) In-stent MLA ≥90% of the average reference lumen area. (2) Complete apposition of the stent. (3) Symmetric stent expansion defined by minimum lumen diameter/maximum lumen diameter ≥0.7. (4) No plaque protrusion, thrombus, or edge dissection with potential to provoke flow disturbances	NA
DOCTORS	2016	120/120	60/61	100/100	6	DES or BMS	(1) In-stent MLA >80% of reference lumen area. (2) Additional stent implantation(s) were to be performed to rectify incomplete lesion coverage. (3) 3. Use of GP IIb/IIIa inhibitors and aspiration thrombectomy were to be considered systematically if thrombus was present.	NA
OCTACS	2015	50/50	62/63	100/100	6	DES	(1) MSA ≥90% of the distal/proximal reference vessel lumen area. (2) No significant malapposition defined as ≥3 struts per CSA detached >140 μm from the underlying vessel wall. (3) No significant edge dissection (causing minimum lumen area <4 mm^2). (4) 4. No significant residual stenosis (causing minimum lumen area <4 mm^2)	NA

CSA, cross sectional area; NA, not available.
[a]Angiography/IVUS/OCT arm.

OCT-guided or IVUS-guided PCI (>3600 procedures), imaging-related complications were infrequent (0.6%), self-limiting or easily treatable with no major adverse events.[107] One potential limitation is the deliverability of imaging catheters in some complex lesion subsets, e.g. heavily calcified, tortuous, angulated anatomies, where accurate imaging could be of potential benefit. Refinements in imaging technology such as co-registration [angiography and intracoronary imaging (roadmap)], lower-profile and more deliverable catheters with faster pullbacks, higher resolution technology (IVUS), and fully automated software to support pre- and post-stent assessment are expected to further improve the ease of use and therefore penetration in daily clinical practice.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

Acknowledgements

The authors thank Georgios Siontis, MD PhD, for assistance in conducting the meta-analysis included in this document and Yasushi Ueki, MD, for assistance in preparing the figures.

Conflict of interest: Dr. F. Alfonso has nothing to disclose. Dr. Z. Ali reports grants from Cardiovascular System Inc, Abbott Vascular, personal fees from Cordis, Canon USA, Abbott Vascular, Boston

Scientific, Acist Medical, Opsens. Dr. R. Bhindi reports grants from National Heart Foundation of Australia, personal fees from Bristol Myers Squibb, Astra Zeneca, Medtronic. Dr. R. Byrne reports grants from HeartFlow, Boston Scientific, personal fees from Boston Scientific, Biotronik, B.Braun. Dr. D. Capodanno reports personal fees from Bayer, Daiichi Sankyo, Pfizer, Astra Zeneca, Abbott, Direct Flow Medical. Dr. R. Carter has nothing to disclose. Dr. A. Colombo has nothing to disclose. Dr. J.M. de La Torre Hernandez reports grants from Boston Scientific, Medtronic, Biotronik, Abbott Vascular. Dr. C. Di Mario reports grants from Volcano, Abbott, Medtronic, Shockwave. Dr. J. Escaned reports personal fees from Astra Zeneca, Philips Volcano, Abbott, Medtronic, Orbus Neich, Boston Scientific. Dr. G. Guagliumi reports grants from Boston Scientific, Abbott, personal fees from Abbott, Boston Scientific. Dr. J. Hill reports grants from Boston Scientific, Abbott Vascular, personal fees from Boston Scientific, Abbott Vascular, Abiomed. Dr. N.R. Holm reports grants from Abbott, Terumo Inc, REVA Medical, Medis medical imaging, Abbott, Boston Scientific, personal fees from REVA Medical, Abbott, Terumo Inc. Dr. H. Jia has nothing to disclose. Dr. T. Johnson reports personal fees from Boston Scientific, Terumo Inc, Abbott Vascular, Daiichi Sankyo, Astra Zeneca. Dr. M. Joner reports grants from European Society of Cardiology, personal fees from Orbus Neich, Biotronik, Astra Zeneca. Dr. K. Koskinas reports personal fees from Amgen, Sanofi Aventis. Dr. N. Meneveau reports grants from Abbott Vascular, Daiichi Sankyo, personal fees from BMS/Pfizer, Abbott Vascular, Boehringer-Ingelheim, Daiichi Sankyo, Bayer Healthcare, Edwards Life Sciences. Dr. G. Mintz reports grants from Boston Scientific, Volcano, Abbott Vascular, personal fees from Boston Scientific, Volcano, Infraredx, Abbott Vascular. Dr. Y. Onuma reports personal fees from Abbott Vascular. Dr. F. Prati reports personal fees from Abbott. Dr. L. Rõber reports grants from Abbott, Sanofi Aventis, personal fees from Abbott, Amgen, Astra Zeneca, Biotronik, CSL Behring, Sanofi Aventis. Dr. M. Radu reports personal fees from Abbott. Dr. E. Regar reports grants from Abbott, personal fees from Abbott. Dr. W. Wijns reports grants from Abbott Vascular, MICELL, Microport, personal fees from Microport. Dr. B. Yu has nothing to disclose.

References

1. Mintz GS, Guagliumi G. Intravascular imaging in coronary artery disease. *Lancet* 2017;**390**:793–809.
2. Koskinas KC, Ughi GJ, Windecker S, Tearney GJ, Räber L. Intracoronary imaging of coronary atherosclerosis: validation for diagnosis, prognosis and treatment. *Eur Heart J* 2016;**37**:524–535.
3. Witzenbichler B, Maehara A, Weisz G, Neumann F-J, Rinaldi MJ, Metzger DC, Henry TD, Cox DA, Duffy PL, Brodie BR, Stuckey TD, Mazzaferri EL, Xu K, Parise H, Mehran R, Mintz GS, Stone GW. Relationship between intravascular ultrasound guidance and clinical outcomes after drug-eluting stents: the Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents (ADAPT-DES) Study. *Circulation* 2014;**129**:463–470.
4. Hong S-J, Kim B-K, Shin D-H, Nam C-M, Kim J-S, Ko Y-G, Choi D, Kang T-S, Kang W-C, Her A-Y, Kim YH, Kim Y, Hur S-H, Hong B-K, Kwon H, Jang Y, Hong M-K. Effect of intravascular ultrasound-guided vs angiography-guided everolimus-eluting stent implantation: the IVUS-XPL Randomized Clinical Trial. *JAMA* 2015;**314**:2155–2163.
5. Elgendy IY, Mahmoud AN, Elgendy AY, Bavry AA. Outcomes with intravascular ultrasound-guided stent implantation: a meta-analysis of randomized trials in the era of drug-eluting stents. *Circ Cardiovasc Interv* 2016;**9**:e003700.
6. Buccheri S, Franchina G, Romano S, Puglisi S, Venuti G, D'Arrigo P, Francaviglia B, Scalia M, Condorelli A, Barbanti M, Capranzano P, Tamburino C, Capodanno D. Clinical outcomes following intravascular imaging-guided versus coronary angiography-guided percutaneous coronary intervention with stent implantation: a systematic review and Bayesian network meta-analysis of 31 studies and 17,882 patients. *JACC Cardiovasc Interv* 2017;**10**:2488–2498.
7. Koskinas KC, Nakamura M, Räber L, Colleran R, Kadota R, Capodanno D, Wijns W, Akasaka T, Valgimigli M, Guagliumi G, Windecker S, Byrne RA. Current use of intracoronary imaging in interventional practice: results of a European Association of Percutaneous Cardiovascular Interventions (EAPCI) and Japanese Association of Cardiovascular Interventions and Therapeutics (CVIT) clinical practice survey. *EuroIntervention* 2018 (published ahead of print).
8. Schiele F, Meneveau N, Vuillemenot A, Zhang DD, Gupta S, Mercier M, Danchin N, Bertrand B, Bassand J-P. Impact of intravascular ultrasound guidance in stent deployment on 6-month restenosis rate: a multicenter, randomized study comparing two strategies–with and without intravascular ultrasound guidance. RESIST Study Group. REStenosis after Ivus guided STenting. *J Am Coll Cardiol* 1998;**32**:320–328.
9. Frey AW, Hodgson JM, Müller C, Bestehorn HP, Roskamm H. Ultrasound-guided strategy for provisional stenting with focal balloon combination catheter: results from the randomized Strategy for Intracoronary Ultrasound-guided PTCA and Stenting (SIPS) trial. *Circulation* 2000;**102**:2497–2502.
10. Oemrawsingh PV, Mintz GS, Schalij MJ, Zwinderman AH, Jukema JW, van der Wall EE. Intravascular ultrasound guidance improves angiographic and clinical outcome of stent implantation for long coronary artery stenoses: final results of a randomized comparison with angiographic guidance (TULIP Study). *Circulation* 2003;**107**:62–67.
11. Parise H, Maehara A, Stone GW, Leon MB, Mintz GS. Meta-analysis of randomized studies comparing intravascular ultrasound versus angiographic guidance of percutaneous coronary intervention in pre-drug-eluting stent era. *Am J Cardiol* 2011;**107**:374–382.
12. Kim B-K, Shin D-H, Hong M-K, Park HS, Rha S-W, Mintz GS, Kim J-S, Kim JS, Lee S-J, Kim H-Y, Hong B-K, Kang W-C, Choi J-H, Jang Y. Clinical impact of intravascular ultrasound-guided chronic total occlusion intervention with zotarolimus-eluting versus biolimus-eluting stent implantation: randomized study. *Circ Cardiovasc Interv* 2015;**8**:e002592.
13. Kim J-S, Kang T-S, Mintz GS, Park B-E, Shin D-H, Kim B-K, Ko Y-G, Choi D, Jang Y, Hong M-K. Randomized comparison of clinical outcomes between intravascular ultrasound and angiography-guided drug-eluting stent implantation for long coronary artery stenoses. *JACC Cardiovasc Interv* 2013;**6**:369–376.
14. Jakabcin J, Spacek R, Bystron M, Kvasnák M, Jager J, Veselka J, Kala P, Cervinka P. Long-term health outcome and mortality evaluation after invasive coronary treatment using drug eluting stents with or without the IVUS guidance. Randomized control trial. HOME DES IVUS. *Catheter Cardiovasc Interv* 2010;**75**:578–583.
15. Chieffo A, Latib A, Caussin C, Presbitero P, Galli S, Menozzi A, Varbella F, Mauri F, Valgimigli M, Arampatzis C, Sabate M, Erglis A, Reimers B, Airoldi F, Laine M, Palop RL, Mikhail G, Maccarthy P, Romeo F, Colombo A. A prospective, randomized trial of intravascular-ultrasound guided compared to angiography guided stent implantation in complex coronary lesions: the AVIO trial. *Am Heart J* 2013;**165**:65–72.
16. Tian N-L, Gami S-K, Ye F, Zhang J-J, Liu Z-Z, Lin S, Ge Z, Shan S-J, You W, Chen L, Zhang Y-J, Mintz G, Chen S-L. Angiographic and clinical comparisons of intravascular ultrasound- versus angiography-guided drug-eluting stent implantation for patients with chronic total occlusion lesions: two-year results from a randomised AIR-CTO study. *EuroIntervention* 2015;**10**:1409–1417.
17. Tan Q, Wang Q, Liu D, Zhang S, Zhang Y, Li Y. Intravascular ultrasound-guided unprotected left main coronary artery stenting in the elderly. *Saudi Med J* 2015; **36**:549–553.
18. Znang JQ, Shi R, Pang W, Guo Q, Xuz Y, Zhang J, Yang Q, Li Y, Mei JP, Jiang TM, Li YM. Application of intravascular ultrasound in stent implantation for small coronary arteries. *J Clin Invasive Cardiol* 2016;**3**:1–8.
19. Shin D-H, Hong S-J, Mintz GS, Kim J-S, Kim B-K, Ko Y-G, Choi D, Jang Y, Hong M-K. Effects of intravascular ultrasound-guided versus angiography-guided new-generation drug-eluting stent implantation: meta-analysis with individual patient-level data from 2,345 Randomized Patients. *JACC Cardiovasc Interv* 2016;**9**: 2232–2239.
20. Bavishi C, Sardar P, Chatterjee S, Khan AR, Shah A, Ather S, Lemos PA, Moreno P, Stone GW. Intravascular ultrasound-guided vs angiography-guided drug-eluting stent implantation in complex coronary lesions: meta-analysis of randomized trials. *Am Heart J* 2017;**185**:26–34.
21. Jang J-S, Song Y-J, Kang W, Jin H-Y, Seo J-S, Yang T-H, Kim D-K, Cho K-I, Kim B-H, Park YH, Je H-G, Kim D-S. Intravascular ultrasound-guided implantation of drug-eluting stents to improve outcome: a meta-analysis. *JACC Cardiovasc Interv* 2014;**7**:233–243.
22. Zhang Y-J, Pang S, Chen X-Y, Bourantas CV, Pan D-R, Dong S-J, Wu W, Ren X-M, Zhu H, Shi S-Y, Iqbal J, Gogas BD, Xu B, Chen S-L. Comparison of intravascular ultrasound guided versus angiography guided drug eluting stent implantation: a systematic review and meta-analysis. *BMC Cardiovascular Disorders* 2015;**15**:153.

23. de la Torre Hernandez JM, Baz Alonso JA, Gómez Hospital JA, Alfonso Manterola F, Garcia Camarero T, Gimeno de Carlos F, Roura Ferrer G, Sanchez Recalde A, Martínez-Luengas ÍL, Gomez Lara J, Hernandez Hernandez F, Pérez-Vizcayno MJ, Cequier Fillat A, Perez de Prado A, Gonzalez-Trevilla AA, Jimenez Navarro MF, Mauri Ferre J, Fernandez Diaz JA, Pinar Bermudez E, Zueco Gil J. Clinical impact of intravascular ultrasound guidance in drug-eluting stent implantation for unprotected left main coronary disease: pooled analysis at the patient-level of 4 registries. *JACC Cardiovasc Interv* 2014;**7**:244–254.
24. Park S-J, Kim Y-H, Park D-W, Lee S-W, Kim W-J, Suh J, Yun S-C, Lee CW, Hong M-K, Lee J-H, Park S-W. Impact of intravascular ultrasound guidance on long-term mortality in stenting for unprotected left main coronary artery stenosis. *Circ Cardiovasc Interv* 2009;**2**:167–177.
25. Ye Y, Yang M, Zhang S, Zeng Y. Percutaneous coronary intervention in left main coronary artery disease with or without intravascular ultrasound: a meta-analysis. *PLoS One* 2017;**12**:e0179756.
26. Prati F, Di Vito L, Biondi-Zoccai G, Occhipinti M, La Manna A, Tamburino C, Burzotta F, Trani C, Porto I, Ramazzotti V, Imola F, Manzoli A, Materia L, Cremonesi A, Albertucci M. Angiography alone versus angiography plus optical coherence tomography to guide decision-making during percutaneous coronary intervention: the Centro per la Lotta contro l'Infarto Optimisation of Percutaneous Coronary Intervention (CLI-OPCI) study. *EuroIntervention* 2012;**8**:823–829.
27. Sheth TN, Kajander OA, Lavi S, Cantor WJ, Cheema AN, Stankovic G, Niemelä K, Natarjan MK, Shestakovska O, Tittarelli R, Meeks B, Jolly SS. Optical coherence tomography-guided percutaneous coronary intervention in ST-segment-elevation myocardial infarction: a prospective propensity-matched cohort of the thrombectomy versus percutaneous coronary intervention alone trial. *Circ Cardiovasc Interv* 2016;**9**:e003414.
28. Iannaccone M, D'Ascenzo F, Frangieh AH, Niccoli G, Ugo F, Boccuzzi G, Bertaina M, Mancone M, Montefusco A, Amabile N, Sardella G, Motreff P, Toutouzas K, Colombo F, Garbo R, Biondi-Zoccai G, Tamburino C, Omedè P, Moretti C, D'Amico M, Souteyrand G, Meieir P, Lüscher TF, Gaita F, Templin C. Impact of an optical coherence tomography guided approach in acute coronary syndromes: a propensity matched analysis from the international FORMIDABLE-CARDIOGROUP IV and USZ registry. *Catheter Cardiovasc Interv* 2017;**90**:E46–E52.
29. Wijns W, Shite J, Jones MR, Lee SW-L, Price MJ, Fabbiocchi F, Barbato E, Akasaka T, Bezerra H, Holmes D. Optical coherence tomography imaging during percutaneous coronary intervention impacts physician decision-making: ILUMIEN I study. *Eur Heart J* 2015;**36**:3346–3355.
30. Meneveau N, Souteyrand G, Motreff P, Caussin C, Amabile N, Ohlmann P, Morel O, Lefrançois Y, Descotes-Genon V, Silvain J, Braik N, Chopard R, Chatot M, Ecarnot F, Tauzin H, Van Belle E, Belle L, Schiele F. Optical coherence tomography to optimize results of percutaneous coronary intervention in patients with non-ST-elevation acute coronary syndrome: results of the multicenter, randomized DOCTORS Study (Does Optical Coherence Tomography Optimize Results of Stenting). *Circulation* 2016;**134**:906–917.
31. Antonsen L, Thayssen P, Maehara A, Hansen HS, Junker A, Veien KT, Hansen KN, Hougaard M, Mintz GS, Jensen LO. Optical coherence tomography guided percutaneous coronary intervention with Nobori stent implantation in patients with non-ST-segment-elevation myocardial infarction (OCTACS) trial: difference in strut coverage and dynamic malapposition patterns at 6 months. *Circ Cardiovasc Interv* 2015;**8**:e002446.
32. Lee SY, Kim JS, Yoon HJ, Hur SH, Lee SG, Kim JW, Hong YJ, Kim KS, Choi SY, Shin DH, Nam CM, Kim BK, Ko YG, Choi D, Jang Y, Hong MK. Early strut coverage in patients receiving drug-eluting stents and its implications for dual antiplatelet therapy: a randomized trial. *JACC Cardiovasc Imaging* 2018 (published ahead of print).
33. Ali ZA, Maehara A, Généreux P, Shlofmitz RA, Fabbiocchi F, Nazif TM, Guagliumi G, Meraj PM, Alfonso F, Samady H, Akasaka T, Carlson EB, Leesar MA, Matsumura M, Ozan MO, Mintz GS, Ben-Yehuda O, Stone GW. Optical coherence tomography compared with intravascular ultrasound and with angiography to guide coronary stent implantation (ILUMIEN III: oPTIMIZE PCI): a randomised controlled trial. *Lancet* 2016;**388**:2618–2628.
34. Kubo T, Shinke T, Okamura T, Hibi K, Nakazawa G, Morino Y, Shite J, Fusazaki T, Otake H, Kozuma K, Ioji T, Kaneda H, Serikawa T, Kataoka T, Okada H, Akasaka T. Optical frequency domain imaging vs. intravascular ultrasound in percutaneous coronary intervention (OPINION trial): one-year angiographic and clinical results. *Eur Heart J* 2017;**38**:3139–3147.
35. Ali ZA, Karimi Galougahi K, Nazif T, Maehara A, Hardy MA, Cohen DJ, Ratner LE, Collins MB, Moses JW, Kirtane AJ, Stone GW, Karmpaliotis D, Leon MB. Imaging- and physiology-guided percutaneous coronary intervention without contrast administration in advanced renal failure: a feasibility, safety, and outcome study. *Eur Heart J* 2016;**37**:3090–3095.
36. Mariani J, Guedes C, Soares P, Zalc S, Campos CM, Lopes AC, Spadaro AG, Perin MA, Filho AE, Takimura CK, Ribeiro E, Kalil-Filho R, Edelman ER, Serruys PW, Lemos PA. Intravascular ultrasound guidance to minimize the use of iodine contrast in percutaneous coronary intervention: the MOZART (Minimizing cOntrast utiliZation With IVUS Guidance in coRonary angioplasTy) randomized controlled trial. *JACC Cardiovasc Interv* 2014;**7**:1287–1293.
37. Escaned J, Collet C, Ryan N, Luigi De Maria G, Walsh S, Sabate M, Davies J, Lesiak M, Moreno R, Cruz-Gonzalez I, Hoole SP, Ej West N, Piek JJ, Zaman A, Fath-Ordoubadi F, Stables RH, Appleby C, van Mieghem N, van Geuns RJ, Uren N, Zueco J, Buszman P, Iñiguez A, Goicolea J, Hildick-Smith D, Ochala A, Dudek D, Hanratty C, Cavalcante R, Kappetein AP, Taggart DP, van Es G-A, Morel M-A, de Vries T, Onuma Y, Farooq V, Serruys PW, Banning AP. Clinical outcomes of state-of-the-art percutaneous coronary revascularization in patients with de novo three vessel disease: 1-year results of the SYNTAX II study. *Eur Heart J* 2017;**38**:3124–3134.
38. Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, Filippatos G, Hamm C, Head SJ, Jni P, Kappetein AP, Kastrati A, Knuuti J, Landmesser U, Laufer G, Neumann FJ, Richter DJ, Schauerte P, Sousa Uva M, Stefanini GG, Taggart DP, Torracca L, Valgimigli M, Wijns W, Witkowski A. 2014 ESC/EACTS Guidelines on myocardial revascularization: the Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J* 2014;**35**:2541–2619.
39. Wang X, Matsumura M, Mintz GS, Lee T, Zhang W, Cao Y, Fujino A, Lin Y, Usui E, Kanaji Y, Murai T, Yonetsu T, Kakuta T, Maehara A. *In vivo* calcium detection by comparing optical coherence tomography, intravascular ultrasound, and angiography. *JACC Cardiovasc Imaging* 2017;**10**:869–879.
40. Tearney GJ, Regar E, Akasaka T, Adriaenssens T, Barlis P, Bezerra HG, Bouma B, Bruining N, Cho J-M, Chowdhary S, Costa MA, de Silva R, Dijkstra J, Di Mario C, Dudeck D, Falk E, Feldman MD, Fitzgerald P, Garcia H, Gonzalo N, Granada JF, Guagliumi G, Holm NR, Honda Y, Ikeno F, Kawasaki M, Kochman J, Koltowski L, Kubo T, Kume T, Kyono H, Lam CCS, Lamouche G, Lee DP, Leon MB, Maehara A, Manfrini O, Mintz GS, Mizuno K, Morel M-A, Nadkarni S, Okura H, Otake H, Pietrasik A, Prati F, Räber L, Radu MD, Rieber J, Riga M, Rollins A, Rosenberg M, Sirbu V, Serruys PWJC, Shimada K, Shinke T, Shite J, Siegel E, Sonada S, Suter M, Takarada S, Tanaka A, Terashima M, Troels T, Uemura S, Ughi GJ, van Beusekom HMM, van der Steen AFW, van Es G-A, van Soest G, Virmani R, Waxman S, Weissman NJ, Weisz G. Consensus standards for acquisition, measurement, and reporting of intravascular optical coherence tomography studies: a report from the International Working Group for Intravascular Optical Coherence Tomography Standardization and Validation. *J Am Coll Cardiol* 2012;**59**:1058–1072.
41. Mehanna E, Bezerra HG, Prabhu D, Brandt E, Chamié D, Yamamoto H, Attizzani GF, Tahara S, Van Ditzhuijzen N, Fujino Y, Kanaya T, Stefano G, Wang W, Gargesha M, Wilson D, Costa MA. Volumetric characterization of human coronary calcification by frequency-domain optical coherence tomography. *Circ J* 2013;**77**:2334–2340.
42. Kume T, Okura H, Kawamoto T, Yamada R, Miyamoto Y, Hayashida A, Watanabe N, Neishi Y, Sadahira Y, Akasaka T, Yoshida K. Assessment of the coronary calcification by optical coherence tomography. *EuroIntervention* 2011;**6**:768–772.
43. Hoffmann R, Mintz GS, Popma JJ, Satler LF, Kent KM, Pichard AD, Leon MB. Treatment of calcified coronary lesions with Palmaz-Schatz stents. An intravascular ultrasound study. *Eur Heart J* 1998;**19**:1224–1231.
44. Kubo T, Shimamura K, Ino Y, Yamaguchi T, Matsuo Y, Shiono Y, Taruya A, Nishiguchi T, Shimokado A, Teraguchi I, Orii M, Yamano T, Tanimoto T, Kitabata H, Hirata K, Tanaka A, Akasaka T. Superficial calcium fracture after PCI as assessed by OCT. *JACC Cardiovasc Imaging* 2015;**8**:1228–1229.
45. Fujino A, Mintz GS, Matsumura M, Lee T, Kim SY, Hoshino M, Usui E, Yonetsu T, Haag ES, Shlofmitz RA, Kakuta T, Maehara A. A new optical tomography-based calcium scoring system to predict stent under-expansion. *EuroIntervention* 2018;**13**:e2182–e2189.
46. Okura H, Taguchi H, Kubo T, Toda I, Yoshida K, Yoshiyama M, Yoshikawa J. Atherosclerotic plaque with ultrasonic attenuation affects coronary reflow and infarct size in patients with acute coronary syndrome: an intravascular ultrasound study. *Circ J* 2007;**71**:648–653.
47. Lee SY, Mintz GS, Kim SY, Hong YJ, Kim SW, Okabe T, Pichard AD, Satler LF, Kent KM, Suddath WO, Waksman R, Weissman NJ. Attenuated plaque detected by intravascular ultrasound: clinical angiographic, and morphologic features and post-percutaneous coronary intervention complications in patients with acute coronary syndromes. *J Am Coll Cardiol Interv* 2009;**2**:65–72.
48. Wu X, Mintz GS, Xu K, Lansky AJ, Witzenbichler B, Guagliumi G, Brodie B, Kellett MA, Dressler O, Parise H, Mehran R, Stone GW, Maehara A. The relationship between attenuated plaque identified by intravascular ultrasound and no-reflow after stenting in acute myocardial infarction: the HORIZONS-AMI

(Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial. *J Am Coll Cardiol Intv* 2011;**4**:495–502.
49. Claessen BE, Maehara A, Fahy M, Xu K, Stone GW, Mintz GS. Plaque composition by intravascular ultrasound and distal embolization after percutaneous coronary intervention. *JACC Cardiovasc Imaging* 2012;**5**:S111–S118.
50. Hong YJ, Jeong MH, Choi YH, Ko JS, Lee MG, Kang WY, Lee SE, Kim SH, Park KH, Sim DS, Yoon NS, Youn HJ, Kim KH, Park HW, Kim JH, Ahn Y, Cho JG, Park JC, Kang JC. Impact of plaque components on no-reflow phenomenon after stent deployment in patients with acute coronary syndrome: a virtual histology-intravascular ultrasound analysis. *Eur Heart J* 2011;**32**:2059–2066.
51. Tanaka A, Imanishi T, Kitabata H, Kubo T, Takarada S, Tanimoto T, Kuroi A, Tsujioka H, Ikejima H, Komukai K, Kataiwa H, Okouchi K, Kashiwaghi M, Ishibashi K, Matsumoto H, Takemoto K, Nakamura N, Hirata K, Mizukoshi M, Akasaka T. Lipid-rich plaque and myocardial perfusion after successful stenting in patients with non-ST-segment elevation acute coronary syndrome: an optical coherence tomography study. *Eur Heart J* 2009;**30**:1348–1355.
52. Stone GW, Maehara A, Muller JE, Rizik DG, Shunk KA, Ben-Yehuda O, Genereux P, Dressler O, Parvataneni R, Madden S, Shah P, Brilakis ES, Kini AS. Plaque characterization to inform the prediction and prevention of periprocedural myocardial infarction during percutaneous coronary intervention: the CANARY Trial (Coronary Assessment by Near-infrared of Atherosclerotic Rupture-prone Yellow). *JACC Cardiovasc Interv* 2015;**8**:927–936.
53. Choi S-Y, Witzenbichler B, Maehara A, Lansky AJ, Guagliumi G, Brodie B, Kellett MA, Dressler O, Parise H, Mehran R, Dangas GD, Mintz GS, Stone GW. Intravascular ultrasound findings of early stent thrombosis after primary percutaneous intervention in acute myocardial infarction: a Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) substudy. *Circ Cardiovasc Interv* 2011;**4**:239–247.
54. Kang S-J, Ahn J-M, Song H, Kim W-J, Lee J-Y, Park D-W, Yun S-C, Lee S-W, Kim Y-H, Lee CW, Mintz GS, Park S-W, Park S-J. Comprehensive intravascular ultrasound assessment of stent area and its impact on restenosis and adverse cardiac events in 403 patients with unprotected left main disease. *Circ Cardiovasc Interv* 2011;**4**:562–569.
55. Sonoda S, Morino Y, Ako J, Terashima M, Hassan AHM, Bonneau HN, Leon MB, Moses JW, Yock PG, Honda Y, Kuntz RE, Fitzgerald PJ. Impact of final stent dimensions on long-term results following sirolimus-eluting stent implantation: serial intravascular ultrasound analysis from the Sirius Trial. *J Am Coll Cardiol* 2004;**43**:1959–1963.
56. Song H-G, Kang S-J, Ahn J-M, Kim W-J, Lee J-Y, Park D-W, Lee S-W, Kim Y-H, Lee CW, Park S-W, Park S-J. Intravascular ultrasound assessment of optimal stent area to prevent in-stent restenosis after zotarolimus-, everolimus-, and sirolimus-eluting stent implantation. *Catheter Cardiovasc Interv* 2014;**83**:873–878.
57. Bezerra HG, Attizzani GF, Sirbu V, Musumeci G, Lortkipanidze N, Fujino Y, Wang W, Nakamura S, Erglis A, Guagliumi G, Costa MA. Optical coherence tomography versus intravascular ultrasound to evaluate coronary artery disease and percutaneous coronary intervention. *JACC Cardiovasc Interv* 2013;**6**:228–236.
58. Kubo T, Akasaka T, Shite J, Suzuki T, Uemura S, Yu B, Kozuma K, Kitabata H, Shinke T, Habara M, Saito Y, Hou J, Suzuki N, Zhang S. OCT compared with IVUS in a coronary lesion assessment: the OPUS-CLASS study. *JACC Cardiovasc Imaging* 2013;**6**:1095–1104.
59. Okamura T, Onuma Y, Garcia-Garcia H, van Geuns R-J, Wykrzykowska J, Schultz C, van der Giessen W, Ligthart J, Regar E, Serruys P. First-in-man evaluation of intravascular optical frequency domain imaging (OFDI) of Terumo: a comparison with intravascular ultrasound and quantitative coronary angiography. *EuroIntervention* 2011;**6**:1037–1045.
60. Ahn J-M, Kang S-J, Yoon S-H, Park HW, Kang SM, Lee J-Y, Lee S-W, Kim Y-H, Lee CW, Park S-W, Mintz GS, Park S-J. Meta-analysis of outcomes after intravascular ultrasound-guided versus angiography-guided drug-eluting stent implantation in 26,503 patients enrolled in three randomized trials and 14 observational studies. *Am J Cardiol* 2014;**113**:1338–1347.
61. Otake H, Kubo T, Takahashi H, Shinke T, Okamura T, Hibi K, Nakazawa G, Morino Y, Shite J, Fusazaki T, Kozuma K, Ioji T, Kaneda H, Akasaka T. Optical frequency domain imaging versus intravascular ultrasound in percutaneous coronary intervention (OPINION Trial): results from the OPINION imaging study. *JACC Cardiovasc Imaging* 2018;**11**:111–123.
62. Mintz GS. Intravascular ultrasound and outcomes after drug-eluting stent implantation. *Coron Artery Dis* 2017;**28**:346–352.
63. Choi S-Y, Maehara A, Cristea E, Witzenbichler B, Guagliumi G, Brodie B, Kellett MA, Dressler O, Lansky AJ, Parise H, Mehran R, Mintz GS, Stone GW. Usefulness of minimum stent cross sectional area as a predictor of angiographic restenosis after primary percutaneous coronary intervention in acute myocardial infarction (from the HORIZONS-AMI Trial IVUS substudy). *Am J Cardiol* 2012;**109**:455–460.
64. Calvert PA, Brown AJ, Hoole SP, Obaid DR, West NEJ, Bennett MR. Geographical miss is associated with vulnerable plaque and increased major adverse cardiovascular events in patients with myocardial infarction. *Catheter Cardiovasc Interv* 2016;**88**:340–347.
65. Kang S-J, Cho Y-R, Park G-M, Ahn J-M, Kim W-J, Lee J-Y, Park D-W, Lee S-W, Kim Y-H, Lee CW, Mintz GS, Park S-W, Park S-J. Intravascular ultrasound predictors for edge restenosis after newer generation drug-eluting stent implantation. *Am J Cardiol* 2013;**111**:1408–1414.
66. Ino Y, Kubo T, Matsuo Y, Yamaguchi T, Shiono Y, Shimamura K, Katayama Y, Nakamura T, Aoki H, Taruya A, Nishiguchi T, Satogami K, Yamano T, Kameyama T, Orii M, Ota S, Kuroi A, Kitabata H, Tanaka A, Hozumi T, Akasaka T. Optical coherence tomography predictors for edge restenosis after everolimus-eluting stent implantation. *Circ Cardiovasc Interv* 2016;**9**:e004231.
67. Liu J, Maehara A, Mintz GS, Weissman NJ, Yu A, Wang H, Mandinov L, Popma JJ, Ellis SG, Grube E, Dawkins KD, Stone GW. An integrated TAXUS IV, V, and VI intravascular ultrasound analysis of the predictors of edge restenosis after bare metal or paclitaxel-eluting stents. *Am J Cardiol* 2009;**103**:501–506.
68. Imola F, Occhipinti M, Biondi-Zoccai G, Di Vito L, Ramazzotti V, Manzoli A, Pappalardo A, Cremonesi A, Albertucci M, Prati F. Association between proximal stent edge positioning on atherosclerotic plaques containing lipid pools and postprocedural myocardial infarction (from the CLI-POOL Study). *Am J Cardiol* 2013;**111**:526–531.
69. van der Sijde JN, Guagliumi G, Sirbu V, Shimamura K, Borghesi M, Karanasos A, Regar E. The OPTIS Integrated System: real-time, co-registration of angiography and optical coherence tomography. *EuroIntervention* 2016;**12**:855–860.
70. Fujii K, Carlier SG, Mintz GS, Yang Y-M, Moussa I, Weisz G, Dangas G, Mehran R, Lansky AJ, Kreps EM, Collins M, Stone GW, Moses JW, Leon MB. Stent underexpansion and residual reference segment stenosis are related to stent thrombosis after sirolimus-eluting stent implantation. *J Am Coll Cardiol* 2005;**45**:995–998.
71. Hong M-K, Mintz GS, Lee CW, Park D-W, Choi B-R, Park K-H, Kim Y-H, Cheong S-S, Song J-K, Kim J-J, Park S-W, Park S-J. Intravascular ultrasound predictors of angiographic restenosis after sirolimus-eluting stent implantation. *Eur Heart J* 2006;**27**:1305–1310.
72. Morino Y, Honda Y, Okura H, Oshima A, Hayase M, Bonneau HN, Kuntz RE, Yock PG, Fitzgerald PJ. An optimal diagnostic threshold for minimal stent area to predict target lesion revascularization following stent implantation in native coronary lesions. *Am J Cardiol* 2001;**88**:301.
73. Doi H, Maehara A, Mintz GS, Yu A, Wang H, Mandinov L, Popma JJ, Ellis SG, Grube E, Dawkins KD, Weissman NJ, Turco MA, Ormiston JA, Stone GW. Impact of post-intervention minimal stent area on 9-month follow-up patency of paclitaxel-eluting stents: an integrated intravascular ultrasound analysis from the TAXUS IV, V, and VI and TAXUS ATLAS Workhorse, Long Lesion, and Direct Stent Trials. *J Am Coll Cardiol Intv* 2009;**2**:1269–1275.
74. Prati F, Romagnoli E, Burzotta F, Limbruno U, Gatto L, La Manna A, Versaci F, Marco V, Di Vito L, Imola F, Paoletti G, Trani C, Tamburino C, Tavazzi L, Mintz GS. Clinical impact of OCT findings during PCI. The CLI-OPCI II Study. *JACC Cardiovasc Imaging* 2015;**8**:1297–1305.
75. Guo N, Maehara A, Mintz GS, He Y, Xu K, Wu X, Lansky AJ, Witzenbichler B, Guagliumi G, Brodie B, Kellett MA, Dressler O, Parise H, Mehran R, Stone GW. Incidence, mechanisms, predictors, and clinical impact of acute and late stent malapposition after primary intervention in patients with acute myocardial infarction: an intravascular ultrasound substudy of the Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) trial. *Circulation* 2010;**122**:1077–1084.
76. Romagnoli E, Gatto L, La Manna A, Burzotta F, Taglieri N, Saia F, Amico F, Marco V, Ramazzotti V, Di Giorgio A, Di Vito L, Boi A, Contarini M, Castriota F, Mintz GS, Prati F. Role of residual acute stent malapposition in percutaneous coronary interventions. *Catheter Cardiovasc Interv* 2017;**90**:566–575.
77. Adriaenssens T, Joner M, Godschalk T, Malik N, Alfonso F, Xhepa E, De Cock D, Komukai K, Tada T, Cuesta J, Sirbu V, Feldman LJ, Neumann FJ, Goodall AH, Heestermans T, Buysschaert I, Hlinomaz O, Belmans A, Desmet W, Ten Berg JM, Gershlick AH, Massberg S, Kastrati A, Guagliumi G, Byrne RA; Prevention of Late Stent Thrombosis by an Interdisciplinary Global European Effort (PRESTIGE) Investigators. Optical coherence tomography findings in patients with coronary stent thrombosis: a report of the PREvention of Late Stent Thrombosis by an Interdisciplinary Global European Effort (PRESTIGE) Consortium. *Circulation* 2017;**136**:1007–1021.
78. Souteyrand G, Amabile N, Mangin L, Chabin X, Meneveau N, Cayla G, Vanzetto G, Barnay P, Trouillet C, Rioufol G, Rangé G, Teiger E, Delaunay R, Dubreuil O, Lhermusier T, Mulliez A, Levesque S, Belle L, Caussin C, Motreff P. Mechanisms of stent thrombosis analysed by optical coherence tomography: insights from the national PESTO French registry. *Eur Heart J* 2016;**37**:1208–1216.
79. Taniwaki M, Radu MD, Zaugg S, Amabile N, Garcia-Garcia HM, Yamaji K, Jørgensen E, Kelbæk H, Pilgrim T, Caussin C, Zanchin T, Veugeois A, Abildgaard U, Jüni P, Cook S, Koskinas KC, Windecker S, Räber L. Mechanisms of very late drug-eluting stent thrombosis assessed by optical coherence tomography. *Circulation* 2016;**133**:650–660.

80. Guagliumi G, Sirbu V, Musumeci G, Gerber R, Biondi-Zoccai G, Ikejima H, Ladich E, Lortkipanidze N, Matiashvili A, Valsecchi O, Virmani R, Stone GW. Examination of the in vivo mechanisms of late drug-eluting stent thrombosis: findings from optical coherence tomography and intravascular ultrasound imaging. *JACC Cardiovasc Interv* 2012;**5**:12–20.
81. Parodi G, La Manna A, Di Vito L, Valgimigli M, Fineschi M, Bellandi B, Niccoli G, Giusti B, Valenti R, Cremonesi A, Biondi-Zoccai G, Prati F. Stent-related defects in patients presenting with stent thrombosis: differences at optical coherence tomography between subacute and late/very late thrombosis in the Mechanism Of Stent Thrombosis (MOST) study. *EuroIntervention* 2013;**9**:936–944.
82. Cuesta J, Rivero F, Bastante T, García-Guimaraes M, Antuña P, Alvarado T, Navarrete G, Benedicto A, Alfonso F. Optical coherence tomography findings in patients with stent thrombosis. *Rev Esp Cardiol (Engl Ed)* 2017;**70**:1050–1058.
83. Foin N, Lu S, Ng J, Bulluck H, Hausenloy D, Wong P, Virmani R, Joner M. Stent malapposition and the risk of stent thrombosis: mechanistic insights from an in-vitro model. *EuroIntervention* 2017;**13**:e1096–e1098.
84. Gutierrez-Chico JL, Wykrzykowska J, Nuesch E, van Geuns RJ, Koch KT, Koolen JJ, di Mario C, Windecker S, van Es G-A, Gobbens P, Juni P, Regar E, Serruys PW. Vascular tissue reaction to acute malapposition in human coronary arteries: sequential assessment with optical coherence tomography. *Circ Cardiovasc Interv* 2012;**5**:20–29, S1–8.
85. Shimamura K, Kubo T, Akasaka T, Kozuma K, Kimura K, Kawamura M, Sumiyoshi T, Ino Y, Yoshiyama M, Sonoda S, Igarashi K, Miyazawa A, Uzui H, Sakanoue Y, Shinke T, Morino Y, Tanabe K, Kadota K, Kimura T. Outcomes of everolimus-eluting stent incomplete stent apposition: a serial optical coherence tomography analysis. *Eur Heart J Cardiovasc Imaging* 2015;**16**:23–28.
86. Sotomi Y, Onuma Y, Dijkstra J, Miyazaki Y, Kozuma K, Tanabe K, Popma JJ, de Winter RJ, Serruys PW, Kimura T. Fate of post-procedural malapposition of everolimus-eluting polymeric bioresorbable scaffold and everolimus-eluting cobalt chromium metallic stent in human coronary arteries: sequential assessment with optical coherence tomography in ABSORB Japan trial. *Eur Heart J Cardiovasc Imaging* 2018;**19**:59–66.
87. Cheneau E, Leborgne L, Mintz GS, Kotani J, Pichard AD, Satler LF, Canos D, Castagna M, Weissman NJ, Waksman R. Predictors of subacute stent thrombosis: results of a systematic intravascular ultrasound study. *Circulation* 2003;**108**:43–47.
88. Hong YJ, Jeong MH, Ahn Y, Sim DS, Chung JW, Cho JS, Yoon NS, Yoon HJ, Moon JY, Kim KH, Park HW, Kim JH, Cho JG, Park JC, Kang JC. Plaque prolapse after stent implantation in patients with acute myocardial infarction: an intravascular ultrasound analysis. *J Am Coll Cardiol Imaging* 2008;**1**:489–497.
89. Hong YJ, Jeong MH, Choi YH, Song JA, Kim DH, Lee KH, Yamanaka F, Lee MG, Park KH, Sim DS, Yoon NS, Yoon HJ, Kim KH, Park HW, Kim JH, Ahn Y, Cho JG, Park JC, Kang JC. Impact of tissue prolapse after stent implantation on short- and long-term clinical outcomes in patients with acute myocardial infarction: an intravascular ultrasound analysis. *Int J Cardiol* 2013;**166**:646–651.
90. Sugiyama T, Kimura S, Akiyama D, Hishikari K, Kawaguchi N, Kamiishi T, Hikita H, Takahashi A, Isobe M. Quantitative assessment of tissue prolapse on optical coherence tomography and its relation to underlying plaque morphologies and clinical outcome in patients with elective stent implantation. *Int J Cardiol* 2014;**176**:182–190.
91. Soeda T, Uemura S, Park S-J, Jang Y, Lee S, Cho J-M, Kim S-J, Vergallo R, Minami Y, Ong DS, Gao L, Lee H, Zhang S, Yu B, Saito Y, Jang I-K. Incidence and clinical significance of poststent optical coherence tomography findings. One-year follow-up study from a Multicenter Registry. *Circulation* 2015;**132**:1020–1029.
92. Kawamori H, Shite J, Shinke T, Otake H, Matsumoto D, Nakagawa M, Nagoshi R, Kozuki A, Hariki H, Inoue T, Osue T, Taniguchi Y, Nishio R, Hiranuma N, Hirata K-I. Natural consequence of post-intervention stent malapposition, thrombus, tissue prolapse, and dissection assessed by optical coherence tomography at mid-term follow-up. *Eur Heart J Cardiovasc Imaging* 2013;**14**:865–875.
93. Radu MD, Räber L, Heo J, Gogas BD, Jørgensen E, Kelbæk H, Muramatsu T, Farooq V, Helqvist S, Garcia-Garcia HM, Windecker S, Saunamäki K, Serruys PW. Natural history of optical coherence tomography-detected non-flow-limiting edge dissections following drug-eluting stent implantation. *EuroIntervention* 2014;**9**:1085–1094.
94. Karanasos A, Van Mieghem N, van Ditzhuijzen N, Felix C, Daemen J, Autar A, Onuma Y, Kurata M, Diletti R, Valgimigli M, Kauer F, van Beusekom H, de Jaegere P, Zijlstra F, van Geuns R-J, Regar E. Angiographic and optical coherence tomography insights into bioresorbable scaffold thrombosis: single-center experience. *Circ Cardiovasc Interv* 2015;**8**:e002369.
95. Räber L, Brugaletta S, Yamaji K, O'Sullivan CJ, Otsuki S, Koppara T, Taniwaki M, Onuma Y, Freixa X, Eberli FR, Serruys PW, Joner M, Sabaté M, Windecker S. Very late scaffold thrombosis: intracoronary imaging and histopathological and spectroscopic findings. *J Am Coll Cardiol* 2015;**66**:1901–1914.
96. Suwannasom P, Sotomi Y, Ishibashi Y, Cavalcante R, Albuquerque FN, Macaya C, Ormiston JA, Hill J, Lang IM, Egred M, Fajadet J, Lesiak M, Tijssen JG, Wykrzykowska JJ, de Winter RJ, Chevalier B, Serruys PW, Onuma Y. The impact of post-procedural asymmetry, expansion, and eccentricity of bioresorbable everolimus-eluting scaffold and metallic everolimus-eluting stent on clinical outcomes in the ABSORB II Trial. *JACC Cardiovasc Interv* 2016;**9**:1231–1242.
97. Goto K, Zhao Z, Matsumura M, Dohi T, Kobayashi N, Kirtane AJ, Rabbani LE, Collins MB, Parikh MA, Kodali SK, Leon MB, Moses JW, Mintz GS, Maehara A. Mechanisms and patterns of intravascular ultrasound in-stent restenosis among bare metal stents and first- and second-generation drug-eluting stents. *Am J Cardiol* 2015;**116**:1351–1357.
98. Kang S-J, Mintz GS, Akasaka T, Park D-W, Lee J-Y, Kim W-J, Lee S-W, Kim Y-H, Whan Lee C, Park S-W, Park S-J. Optical coherence tomographic analysis of in-stent neoatherosclerosis after drug-eluting stent implantation. *Circulation* 2011;**123**:2954–2963.
99. Alfonso F, Suárez A, Angiolillo DJ, Sabaté M, Escaned J, Moreno R, Hernández R, Bañuelos C, Macaya C. Findings of intravascular ultrasound during acute stent thrombosis. *Heart* 2004;**90**:1455–1459.
100. Lee CW, Kang S-J, Park D-W, Lee S-H, Kim Y-H, Kim J-J, Park S-W, Mintz GS, Park S-J. Intravascular ultrasound findings in patients with very late stent thrombosis after either drug-eluting or bare-metal stent implantation. *J Am Coll Cardiol* 2010;**55**:1936–1942.
101. Wykrzykowska JJ, Kraak RP, Hofma SH, van der Schaaf RJ, Arkenbout EK, IJsselmuiden AJ, Elias J, van Dongen IM, Tijssen RYG, Koch KT, Baan J, Vis MM, de Winter RJ, Piek JJ, Tijssen JGP, Henriques JPS. Bioresorbable scaffolds versus metallic stents in routine PCI. *N Engl J Med* 2017;**376**:2319–2328.
102. Ali ZA, Serruys PW, Kimura T, Gao R, Ellis SG, Kereiakes DJ, Onuma Y, Simonton C, Zhang Z, Stone GW. 2-year outcomes with the Absorb bioresorbable scaffold for treatment of coronary artery disease: a systematic review and meta-analysis of seven randomised trials with an individual patient data substudy. *Lancet* 2017;**390**:760–772.
103. Ali ZA, Gao R, Kimura T, Onuma Y, Kereiakes DJ, Ellis SG, Chevalier B, Vu M-T, Zhang Z, Simonton CA, Serruys PW, Stone GW. Three-year outcomes with the absorb bioresorbable scaffold: individual-patient-data meta-analysis from the ABSORB randomized trials. *Circulation* 2018;**137**:464–479.
104. Cuculi F, Puricel S, Jamshidi P, Kallinikou Z, Toggweiler S, Weissner M, Münzel T, Cook S, Gori T. Optical coherence tomography findings in bioresorbable vascular scaffolds thrombosis. *Circ Cardiovasc Interv* 2015;**8**:e002518.
105. Yamaji K, Ueki Y, Souteyrand, Daemen J, Wiebe J, Nef H, Adriaenssens T, Loh JP, Lattuca B, Wykrzykowska JJ, Gomez-Lara J, Timmers L, Motreff P, Hoppmann P, Abdel-Wahab M, Byrne RA, Meincke F, Boeder N, Honton B, O'Sullivan CJ, Ielasi A, Delarche N, Christ G, Lee JKT, Lee M, Amabile N, Karagiannis A, Windecker S, Räber L. Mechanism of very late scaffold thrombosis. *J Am Coll Cardiol* 2017;**70**:2330–2344.
106. Alberti A, Giudice P, Gelera A, Stefanini L, Priest V, Simmonds M, Lee C, Wasserman M. Understanding the economic impact of intravascular ultrasound (IVUS). *Eur J Health Econ* 2016;**17**:185–193.
107. van der Sijde JN, Karanasos A, van Ditzhuijzen NS, Okamura T, van Geuns RJ, Valgimigli M, Ligthart JM, Witberg KT, Wemelsfelder S, Fam JM, Zhang B, Diletti R, de Jaegere PP, van Mieghem NM, van Soest G, Zijlstra F, van Domburg RT, Regar E. Safety of optical coherence tomography in daily practice: a comparison with intravascular ultrasound. *Eur Heart J Cardiovasc Imaging* 2017;**18**:467–474.