



Review Article

Imaging during percutaneous coronary intervention for optimizing outcomes

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ABSTRACT

Angiography is the current gold standard for imaging during percutaneous coronary interventions but has significant limitations. Catheter-based intravascular imaging techniques such as intravascular ultrasound and the more recent optical coherence tomography have the potential to overcome these limitations and thus optimize clinical outcomes. In this update, we discussed the current applications of the available imaging techniques, existing evidence, continuing unmet needs, and potential areas for further research.

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1. Introduction

Advances in equipment, stents, techniques, and pharmacological therapy have significantly improved short- and long-term clinical outcomes after percutaneous coronary intervention (PCI) over the past few decades.¹ Imaging guidance during PCI is one of the key determinants of procedural outcomes because it is an integral part of every stage of PCI including assessment of lesion severity, preprocedural planning (selection of appropriate stenting strategy, stent size, landing zones), optimization (stent expansion, malapposition, lumen gain), and management of immediate complications (dissection, thrombus, tissue prolapse, side-branch compromise). During follow-up, imaging helps in identification and management of mechanisms of stent failure (restenosis, thrombosis).²

Till date, angiography has been the imaging modality of choice during PCI despite significant limitations (Table 1).³ Furthermore, selection of stent size and length may not be optimal as angiography assesses only the lumen (luminology) and not the entire vessel wall.³ For example, with diffuse disease, the reference vessel diameter as assessed by angiography may be significantly lower than the actual vessel size. Also, plaques are not visualized unless they produce luminal narrowing, which makes it difficult to choose appropriate landing zones for stent placement.

Intravascular imaging techniques with the ability to visualize both vessel wall structures and lumen provide valuable additional information and promise to cover the shortfalls of conventional angiography.⁴

There are two catheter-based intravascular imaging techniques which are currently in use: intravascular ultrasound (IVUS) and optical coherence tomography (OCT). IVUS uses ultrasound waves to visualize the vessel wall while the relatively newer OCT uses near-infrared light. OCT has better spatial resolution (10–15 μm) when compared with IVUS (100–150 μm) but has poorer penetration. Consequently, OCT is able to visualize superficial structures of vessel wall with much higher resolution than IVUS which can visualize the entire vessel wall albeit with poor resolution.^{5,6} Two types of OCT systems are available: (1) time domain (TD) OCT (first-generation) systems, and (2) Fourier domain (FD) OCT (second-generation) systems that differ mainly with respect to the method used to calculate the electric field amplitude.⁵ The development of FD-OCT has enabled faster image acquisition of longer coronary segments compared with TD-OCT.⁵ The differences between the IVUS and OCT are enlisted in Table 2.⁷ The safety of both these techniques is well documented.^{1,8,9}

1.1. IVUS guidance for PCI

The most important predictor of adverse outcomes (thrombosis and restenosis) after stent implantation is the degree of stent expansion achieved.^{10–15} By achieving greater stent expansion, IVUS guidance has been associated with improved event-free survival compared with angiographic guidance alone (Fig. 1).^{4,13,16,17}

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Table 1
Limitations of conventional angiography.

Limitations of angiography
Intermediate coronary lesions (40–70%)
Complex lesions
Bifurcation lesions
Diffuse disease
Thrombus
Left main disease
Complex clinical settings
Acute coronary syndromes
Uncertain/unclear settings
Biovascular scaffolds

Table 2
Comparison: optical coherence tomography versus intravascular ultrasound.

	OCT	IVUS
Frame rate (s)	100	30
Pullback speed (mm/s)	20	0.5–1.0
Lines per frame	500	256
Axial resolution (μm)	12–15	150
Scan diameter in contrast (mm)	10	15–20
Tissue penetration (mm)	1.0–2.0	10
Ease of use	++	++/+++
Need for contrast or dextran	Yes	No
Detection of lipid	+++	+/+++
Detection of fibrous cap	+++	+
Detection of thrombus	++	+
Detection of calcium	++	+++
Dissection	+++	++
Malapposition	+++	++
Stent strut surface coverage	+++	+

IVUS, intravascular ultrasound; OCT, optical coherence tomography.

Other reasons such as stent malapposition, edge dissection, inadequate coverage of plaque and so forth for a suboptimal result after PCI which cannot be identified with angiography alone can be picked up by IVUS in the immediate postprocedure period, thereby prompting corrective steps which lead to improved procedural and clinical outcomes (Fig. 2).¹⁸

Use of IVUS to optimize PCI reduces target vessel revascularization as well as other outcomes including major adverse cardiac events (MACEs) when compared with angiography alone both in bare-metal stent (BMS) and drug-eluting stent (DES) eras.^{16,17,19–23} Recent guidelines have endorsed the use of IVUS for specific situations (Table 3).^{2,22–24}

Several meta-analyses which have included randomized trials, registries, and observational studies have been published on the role of IVUS during PCI with BMS and DES.^{16,17,19–21,25–29} The most recent of these meta-analyses by Steinvil et al concluded that IVUS-guided PCI was associated with better overall clinical outcomes than angiography-guided DES implantation. However, in a meta-analysis of only randomized controlled trials (RCTs), this benefit was mainly driven by reduced rates of revascularizations.^{21,30}

Most of these meta-analyses are limited by the lack of uniform criteria for IVUS use and lack of homogeneity with regard to clinical scenarios. Further research with adequately powered RCTs is needed in specific subgroups [bifurcation lesions, left main disease, chronic total occlusions (CTOs)] in which routine imaging guidance in addition to angiography is expected to significantly alter decision-making during PCI.

1.2. OCT guidance for PCI

The clear visualization of surface of vessel lumen with high resolution is the main strength of OCT over IVUS. OCT can therefore image lumen-vessel wall and lumen-stent interface better than

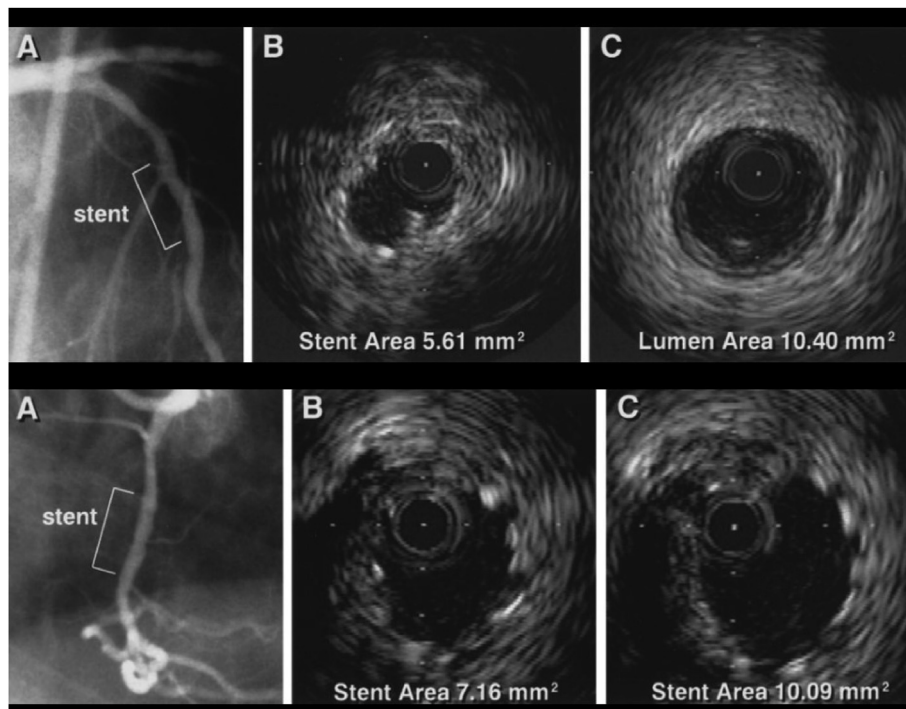


Fig. 1. Top, angiographically guided stent implantation. Despite acceptable angiographic appearance (A), IVUS demonstrates underdeployment, achieving MSA of only 5.61 mm² (B) Compared with proximal reference segment of 10.40 mm² (C). Bottom, both angiographically and IVUS-guided stent implantation. Angiogram after stent deployment in mid right coronary artery with 3.5-mm balloon inflated at 16 atm shows acceptable result (A). Initial IVUS (B) shows underdeployment. IVUS image after further dilatation with 4.0-mm balloon at 16 atm demonstrates substantial improvement in MSA (C).¹³ IVUS, intravascular ultrasound; MSA, minimal stent area.

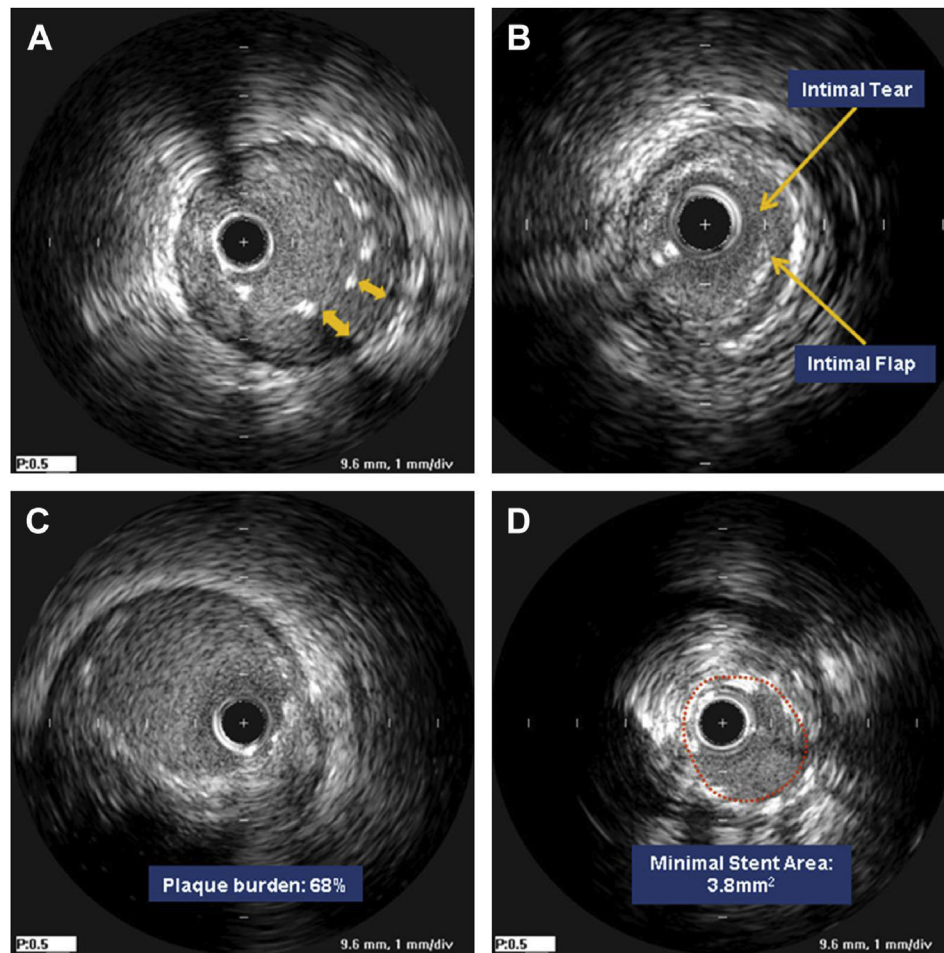


Fig. 2. Suboptimal stent results seen with IVUS. (A) Acute incomplete stent apposition underexpansion, (B) edge dissection, (C) large edge plaque burden, and (D) underexpansion.¹⁸

IVUS. This means better identification of mechanisms of stent failures (e.g., stent malapposition, dissection, tissue protrusion, and thrombus) and also, culprit lesions in acute coronary syndromes (Figs. 3 and 4). However, OCT cannot measure plaque burden because of its shallow penetration depth (1–2 mm).¹

The Centro per la Lotta contro l'Infarto–Optimisation of Percutaneous Coronary Intervention (CLI-OPCI) observational study, which showed that angiographic plus OCT guidance was associated with a significantly lower risk of cardiac death or myocardial infarction.¹ Importantly, for the first time, the CLI-OPCI study

Table 3
Current guidelines for IVUS use.

Guideline	Year	Recommendation	Class of recommendation	Level of evidence
ESC/EACTS Guideline ²³	2014	1. IVUS in selected patients to optimize stent implantation	II a	B
		2. IVUS to assess severity and optimize treatment of unprotected left main lesions	II a	B
		3. IVUS to assess mechanisms of stent failure (restenosis and stent thrombosis)	II a	C
ACCF/AHA/SCAI Guideline ²⁴	2011	1. IVUS is reasonable for the assessment of angiographically indeterminate left main coronary artery disease	II a	B
		2. IVUS and coronary angiography are reasonable 4–6 wk and 1 y after cardiac transplantation to exclude donor coronary artery disease, detect rapidly progressive cardiac allograft vasculopathy and provide prognostic information	II a	B
		3. IVUS is reasonable to determine the mechanism of stent restenosis	II a	C
		4. IVUS may be reasonable for the assessment of nonleft main coronary arteries with angiographically intermediate coronary stenoses (50%–70% diameter stenosis)	II b	B
		5. IVUS may be considered for guidance of coronary stent implantation, particularly in cases of left main coronary artery stenting	II b	B
		6. IVUS may be reasonable to determine the mechanism of stent thrombosis	II b	C
		7. IVUS for routine lesion assessment is not recommended when revascularization with PCI or CABG is not being contemplated	III	C

ACCF, American College of Cardiology Foundation; AHA, American Heart Association; CABG, coronary artery bypass graft; ESC, European Society of Cardiology; EACTS, European Association for Cardiothoracic Surgery; IVUS, intravascular ultrasound; SCAI, Society of Cardiovascular Angiography and Interventions.

addressed the question of how to interpret OCT findings by setting specific quantitative criteria to identify suboptimal stent deployment. Suboptimal stent deployment was defined as the presence of at least 1 of the OCT findings given in Table 4 below.

Retrospective analysis of clinical outcomes in patients undergoing end-procedural OCT assessment in the CLI-OPCI II study showed that suboptimal stent deployment was associated with an increased risk of MACE during follow-up.³⁶

A multicenter study, ILUMIEN I, involving 418 patients evaluated the impact of pre-PCI and post-PCI OCT on clinical decision-making during PCI. Altogether, OCT impacted the PCI procedure in 65% of the patients pre-PCI and/or post-PCI.³⁷ Operators changed their strategy based on pre-PCI OCT in 57% of cases; mostly involving change in number, length, or diameter of stents used. Post-PCI OCT findings during optimization stage (edge dissection, malapposition, thrombus, underexpansion) influenced strategy in 27% of cases. A drawback of this study was that there were no upfront rules on how to interpret pre-PCI OCT.³⁷ Further studies are needed on OCT parameters that predict short- and long-term clinical outcomes. The current guidelines for use of OCT are summarized in Table 5.

OCT is still a relatively newer imaging modality and therefore lacks adequate data and standardization to identify suboptimal stent deployment, stent lumen, and minimal lumen areas. In fact,

lumen dimensions measured by OCT were smaller than those measured by IVUS as reported by several studies.^{40–44} Using IVUS criteria during PCI with OCT guidance may therefore lead to suboptimal stent expansion and poor clinical outcomes.

Furthermore, reliable image acquisition with OCT systems requires injection of contrast media to displace blood from vessel wall lumen because OCT signal is attenuated by the presence of red blood cells. This increases the risk of contrast nephropathy which then may lead to poor clinical outcomes, especially in patients with underlying renal dysfunction. Hence, a substitute for contrast is necessary to further improve outcomes when using OCT.

Despite unmatched resolution with OCT, underestimation of reference vessel diameter resulting in smaller luminal diameters after stent implantation has been reported by few studies including the OPINION trial.^{37,43,44} The principle reason being the measurement of lumen diameter as reference instead of vessel wall diameter especially in the presence of significant plaque burden and diffuse disease. The ILUMIEN II study, a post hoc analysis of two prospective studies (ILUMIEN and ADAPT-DES), showed that OCT and IVUS guidance resulted in a comparable degree of stent expansion.⁴⁵ In the ILUMIEN III study, the authors used a novel OCT-based stent-sizing strategy by measuring proximal and distal reference mean external elastic lamina diameters and using the

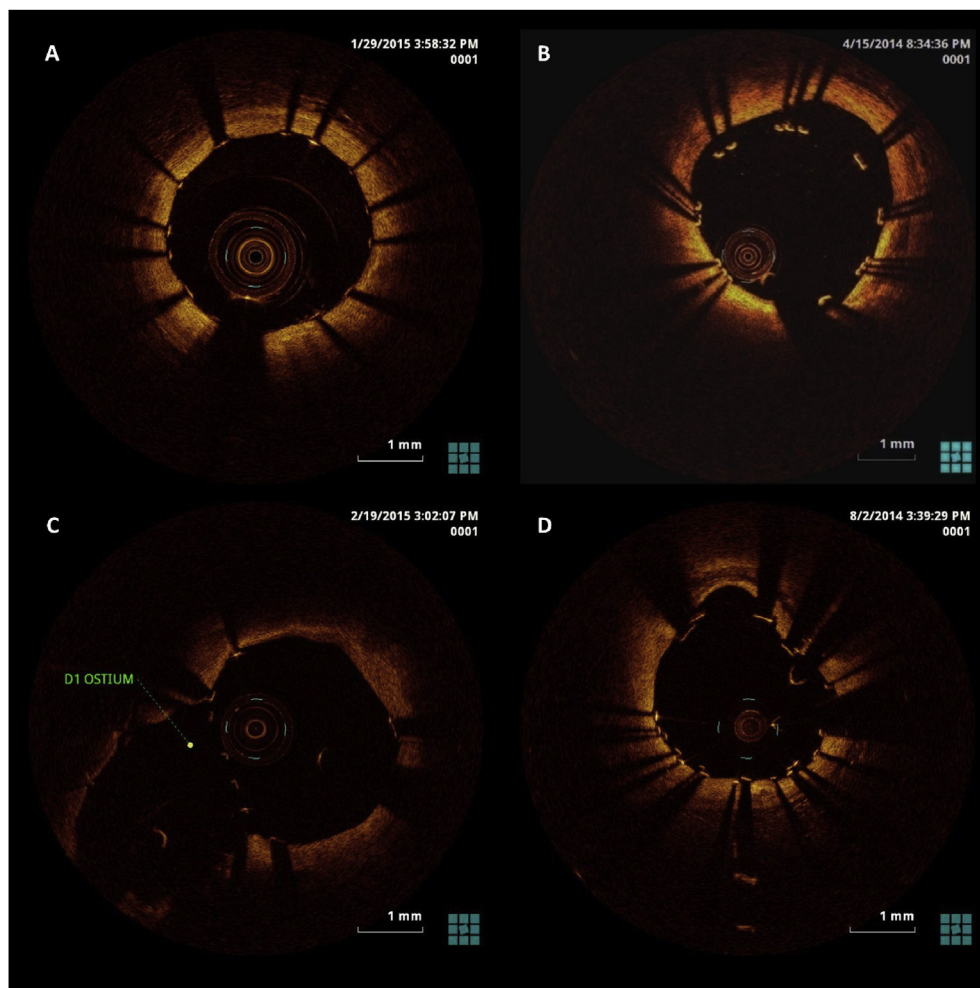


Fig. 3. OCT guidance during PCI. (A) OCT after stent placement showing well-apposed stent. B, Malapposed stent struts visualized with OCT which led to postdilatation with a larger balloon. C, Stent struts visualized at ostium of the first diagonal branch of the left anterior descending coronary artery. For bifurcation angioplasty, OCT guidance can be used to select the distal most cell for passing guidewire. D, Two layers of well-apposed stent struts visualized after bifurcation angioplasty with Crush technique. OCT, optical coherence tomography

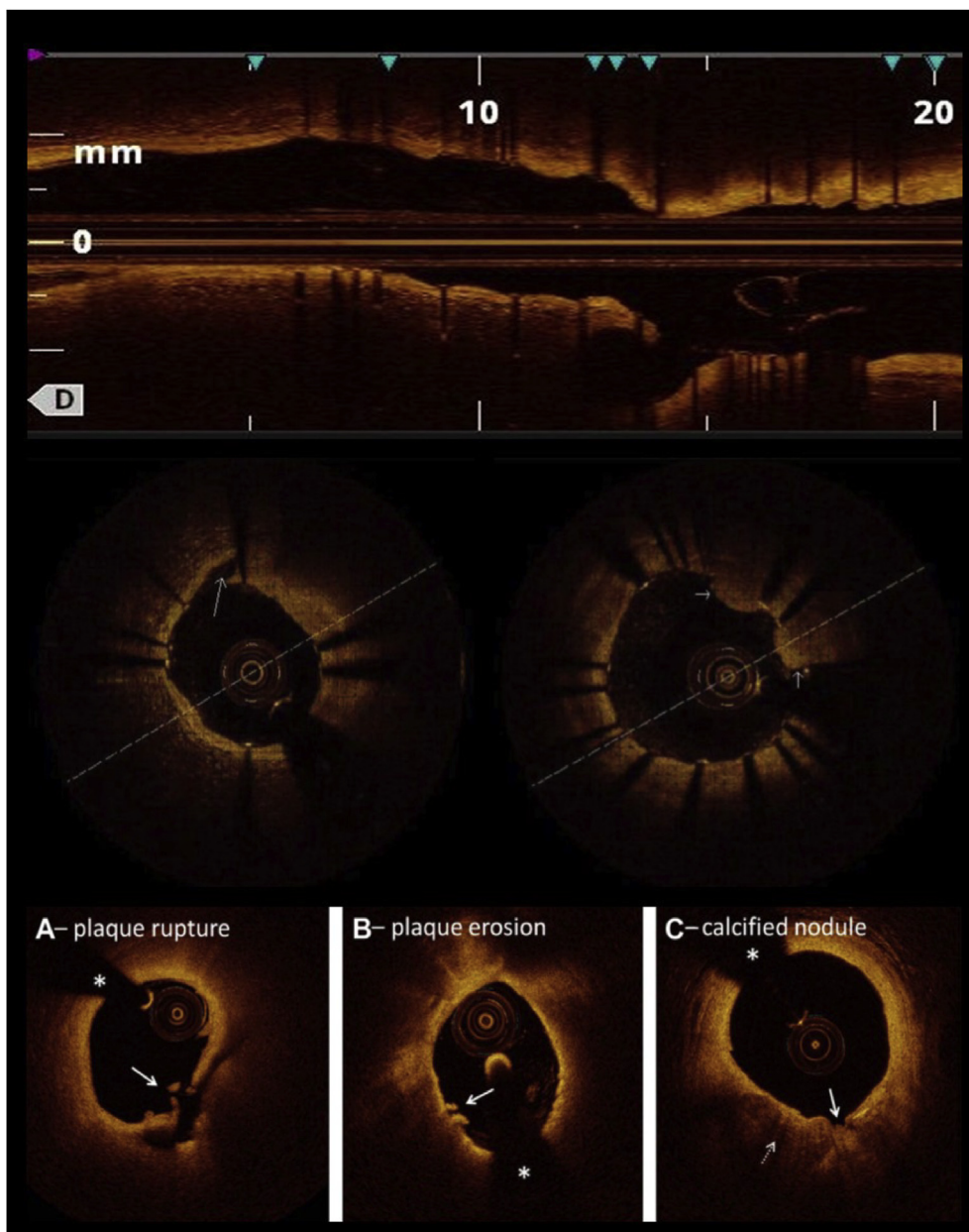


Fig. 4. Top, OCT pullback after stenting showing longitudinal view of the vessel. Stent length can be measured and side-branch ostium visualized. The same view can be used pre-PCI to decide stent length and landing zones. Middle left, stent edge dissection as seen on OCT (long arrow). Middle right, tissue prolapse through stent struts (short arrows). Bottom, OCT findings in acute coronary syndrome. (A) Plaque rupture is defined as a lipid plaque with fibrous cap discontinuity (arrow) and cavity formation inside the plaque. (B) Definite plaque erosion is defined by the presence of attached thrombus (arrow) overlying an intact and visualized plaque. (C) Calcified nodules are defined by fibrous cap disruption (solid arrow) with underlying calcified plaque (dotted arrow) characterized by protruding calcification, superficial calcification, or the presence of significant calcium adjacent to the lesion. The asterisks denote guidewire shadow artifact. OCT, optical coherence tomography.

smaller of these diameters rounded down to the nearest 0.25 mm to determine stent diameter. This strategy resulted in a similar minimum stent area compared with IVUS-guided PCI.⁴⁶

2. Imaging guidance in specific subgroups

Additional imaging guidance are expected to improve outcomes in interventions involving specific subgroups such as bifurcation lesions, left main coronary artery (LMCA) lesions, chronic total occlusions, calcified lesions, and in-stent restenosis which are considered to be complex or high risk where the results tend to be poorer.

2.1. Left main coronary artery lesions

There has been a recent surge in LMCA interventions, hitherto considered to be a cardiovascular surgeon's domain.^{47–52} Short vessel length, lack of normal reference segment, streaming of contrast agent, and aortic cusp calcification hinder assessment of true lumen size and lesion morphology of LMCA lesions by angiography alone.⁵³ Therefore, IVUS assessment can be helpful in detecting significant stenosis, selecting stent with appropriate length and diameter, and help guide optimal stent placement and expansion.^{53–56} Both the recently published EXCEL and NOBLE trials have used IVUS extensively during unprotected LMCA PCI.

Table 4
Definitions of OCT findings.^{31–35}

Findings	Definition
Edge dissection	Linear rim of tissue with a width >0.2 mm and a clear separation from the vessel wall or underlying plaque that was adjacent (<5 mm) to a stent edge. Longitudinal extension >2 mm, lateral extension >60° and involvement of deeper layers (medial or adventitia) are considered large dissections.
Intrastent plaque/thrombus protrusion	Tissue prolapsing between stent struts extending inside a circular arc connecting adjacent struts or intraluminal mass >0.5 mm in thickness with no direct continuity with the surface of the vessel wall or highly backscattered luminal protrusion in continuity with the vessel wall and resulting in signal-free shadowing.
Reference lumen narrowing	Lumen area <4.5 mm ² in the presence of significant plaque adjacent to stent endings.
Stent malapposition	Stent-adjacent vessel lumen distance >0.4 mm with longitudinal extension >1 mm.
In-stent minimal luminal cross-sectional area (MLA)	In-stent MLA <4.5 mm ² and <70% of the average reference lumen area is considered significant.

OCT, optical coherence tomography.

Table 5
Current guidelines for OCT use.

Guideline	Year	Recommendation	Class of recommendation	Level of evidence
ESC/EACTS guidelines on myocardial revascularization ²³	2014	1. OCT can be used in select patients to optimize stent implantation 2. OCT can be used to assess the mechanisms related to stent failure	II b II a	C C
ESC guidelines on the management of stable CAD ³⁸	2013	1. OCT can be considered to further characterize the target lesions 2. OCT can be considered to improve stent deployment	II b II b	B B
SCAI Consensus Statement ²⁹	2014	1. OCT is “probably beneficial” to determine optimal stent placement (sizing, apposition, and lack of edge dissection) 2. OCT is “possibly beneficial” for assessing plaque morphology	NA	NA

ESC, European Society of Cardiology; EACTS, European Association for Cardiothoracic Surgery; NA, not applicable; OCT, optical coherence tomography; SCAI, Society of Cardiovascular Angiography and Interventions.

While the EXCEL trial investigators concluded that PCI is non-inferior to coronary artery bypass graft (CABG), the NOBLE trial showed CABG to be better after 3 years of follow-up. Nonetheless, both studies demonstrated safety and immediate procedural success with the use of IVUS.^{57,58}

An IVUS-derived minimal luminal cross-sectional area (MLA) cutoff of 6 mm² for revascularization has correlated well with outcomes in intermediate LMCA lesions on angiography (30–60%).⁵⁹ However, in light of several nonrandomized trials recommending different MLA cutoffs, a recent review proposed that revascularization can be recommended when MLA is < 4.5 mm² on IVUS. For LMCA lesions with MLA between 4.5 and 6 mm², fractional flow reserve or noninvasive stress test is to be considered before revascularization.^{60–63}

Several studies have suggested that IVUS-guided stent implantation for LMCA disease is associated with improved survival during long-term clinical follow-up.^{64,65} This led to a class IIa recommendation for the use of IVUS for LMCA intervention in the recent ESC/EACTS guidelines.²³

Studies are underway for the use of OCT in LMCA interventions especially involving its bifurcation. However, OCT is not a good choice for left main ostial disease due to difficulty in achieving a blood-less field required for optimal OCT imaging. Therefore, IVUS is the imaging modality of choice in this subgroup.

2.2. Bifurcation lesions

Bifurcation lesions are particularly difficult to assess by angiography alone because overlapping side branches often obscure the lesion. PCI of bifurcation lesions is technically challenging due to multiple factors that include bifurcation angle, bifurcation site, plaque burden and morphology, branch diameter, and also dynamic variability during PCI because of plaque shifts, dissections causing side-branch compromise.^{66–68} Intravascular imaging guidance during bifurcation PCI is useful in assessing side-branch ostium,

selecting sizes of stents, and appropriate stenting strategy and after stenting to assess stent expansion, malapposition, dissection, and side-branch ostium. Studies evaluating the impact of IVUS and OCT guidance for bifurcation PCI have shown mixed results.^{69–76} Intravascular imaging has also been used to identify mechanisms and predictors of side-branch pinching. In this regard, the “eyebrow sign” or the “spiky carina” is a powerful predictor of ostial side-branch damage after stent implantation in the main branch in bifurcation coronary lesions without plaque involving the side branch.^{77,78} Furthermore, 3D OCT has been used to guide accurate distal cell rewiring at side-branch ostium which leads to improved procedural results.^{79,80} The OCTOBER trial, ongoing multicenter European trial, is comparing 2-year clinical outcomes after OCT-guided vs standard-guided revascularization of patients requiring complex bifurcation stent implantation.

Left main bifurcation lesions are high-risk complex lesions in which intravascular imaging guidance may be indispensable. Even in the era of DES, the left main bifurcation location is a major determinant of adverse outcomes.^{81,82} Kang et al found that the best IVUS predictors of angiographic restenosis were minimal stent areas (MSAs) of <8.2 mm² in the proximal left main, <7.2 mm² in the polygon of confluence, <6.3 mm² in the ostial left anterior descending, and <5.0 mm² in the ostial left circumflex. When adequate expansion was defined as stent areas above these thresholds at all four locations, angiographic restenosis was greater with “underexpansion” compared with “adequate expansion”. More importantly, freedom from major adverse events was higher in patients with adequate stent expansion compared with underexpansion.⁸³

2.3. Chronic total occlusion

PCI of CTO is still challenging even with the current advancement in equipment and techniques and has been associated with poor clinical outcomes.^{84–87} Using IVUS guidance is one way to

improve overall PCI outcomes although there have been only a few studies in this area.

A randomized study by Kim et al.⁸⁸ showed that IVUS guidance did not significantly reduce cardiac mortality when compared with angiography guidance but did demonstrate an improvement in MACE at 12 months.

To facilitate the passage of guidewires across CTOs, intravascular imaging guidance using IVUS has been used, and several successful techniques have emerged. Important examples include crossing stumpless CTO lesions, reverse controlled antegrade and retrograde subintimal tracking technique for complex CTO, and novel techniques such as transvenous placement of IVUS catheter to facilitate guidewire passage.^{89–92} IVUS is also useful to assess the true vessel size distal to the CTO as negative remodeling is very common in chronically underfilled vessels. Although recommending such strategies for routine practice needs larger randomized trials demonstrating effectiveness, it gives us a glimpse of the possibilities that IVUS guidance can bring to the table in such complex coronary interventions.

Use of OCT in CTO intervention has been limited to evaluation of results after stenting to look for malapposition, dissection, and during follow-up to evaluate mechanisms of stent failure.⁹³

OCT and IVUS are currently limited to lateral imaging as forward-looking catheters are not yet commercially available. Forward-looking catheters which will facilitate direct visualization of proximal cap of CTO and passage of guidewires under direct visual guidance can make CTO interventions safer and more successful.^{94,95}

2.4. Calcified lesions

Intravascular imaging studies, mostly using IVUS, and more recently studies using OCT, have been instrumental in understanding the relationship between calcium and coronary atherosclerosis, the predictors, the natural history, and the impact on treatment.⁹⁶

Severe calcification as assessed by intravascular imaging limits stent expansion, and severe stent underexpansion can be associated with adverse events including restenosis and stent thrombosis.^{97–101} Treating stent underexpansion in a heavily calcified lesion is more difficult than preventing underexpansion.¹⁰²

Lesion preparation can involve the use of a cutting or scoring balloon, excimer laser angioplasty, or rotational or orbital atherectomy. IVUS and OCT have been used to evaluate the effectiveness of such techniques, to help optimize stent expansion, and also to predict postprocedural complications based on the pattern of calcification. OCT can be used to assess the depth of calcium and therefore has an edge over IVUS which only the superficial arc.¹⁰³

IVUS and OCT studies have shown that excimer laser coronary angioplasty does not decrease lesion-associated calcium but causes dissections and, especially, fragmentation of calcific deposits^{98,104} and that rotational (and probably) orbital atherectomy ablate calcium to cause fissuring or cracks within the ablated calcium.^{100,101}

However, there are a lack of systematic, consistent, conclusive confirmatory data with any intravascular imaging technique (IVUS or OCT) in a large number of patients in PCI of calcific lesions.

2.5. Stent thrombosis and in-stent restenosis

IVUS-guided PCI has the potential for accurate measurement of lesion length and minimal stent diameters and areas, allowing for adequate stent expansion and coverage, thereby preventing stent thrombosis and in-stent and edge restenosis.^{105–108} Finally, IVUS may be useful to ensure full stent-vessel wall apposition, although this is of less importance than stent underexpansion and lesion

coverage. In fact, stent malapposition may lead to inadequate drug delivery and DES failure and has been associated with late stent thrombosis.¹⁰⁹ The reductions in restenosis and stent thrombosis achieved may reduce the impact of routine IVUS guidance on revascularization rates.¹⁰⁵

In patients who present with suspected stent thrombosis, IVUS and OCT are helpful in identifying the underlying mechanism such as stent underexpansion, malapposition, neoatherosclerosis, uncovered stent struts, and lesions at stent edges and in guiding PCI to achieve optimal results.^{110–112} Most of these aforementioned causes are potentially preventable by using intravascular imaging guidance during the index procedure.

The mechanism of in-stent restenosis (ISR) has been studied in new light using IVUS and OCT and has helped us understand the pathophysiology behind ISR.^{113,114} The most common underlying causes of ISR are intimal hyperplasia and stent underexpansion.¹¹⁵ Time course, patterns (focal, multifocal, diffuse, stent edge), and mechanism of ISR is different for BMS and DES. Some studies have reported differences between different generations of DES.¹¹⁶ IVUS and OCT not only identify the causes but also guide the interventionist to take appropriate corrective measures to address them effectively.^{116,117}

2.6. Long coronary artery stenoses

In the BMS era, a randomized trial has shown that IVUS guidance when treating long lesions improves immediate- and long-term angiographic and clinical outcomes.¹¹⁸ In the DES era, initial studies using IVUS guidance for stent implantation in long lesions did not improve the 1-year MACE rates. However, IVUS use per operator decision was associated with improved results.¹¹⁹ But IVUS-XPL trial published in 2015 showed a significant reduction in MACE at 1 year when IVUS guidance was used for stent implantation compared with angiographic guidance alone.³⁰

2.7. Other subgroups

Other subgroups in which intravascular imaging guidance during PCI has the potential to improve clinical outcomes are acute coronary syndromes, small vessel disease, bypass graft occlusions, bioresorbable vascular scaffolds, and so on. Ongoing research will provide us with more evidence to successfully use IVUS and OCT guidance to optimize clinical outcomes in these difficult-to-treat subgroups.^{120–122}

Conflicts of interest

All authors have none to declare.

Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.ihj.2018.08.012>.

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