Journal of Cardiology and Cardiovascular Research

Mody R, et al., 2022- J Cardiol Cardiovasc Res Review Article

Intracoronary Imaging-Can It Make Difference in State of the Art PCI?

Rohit Mody^{1*}, Debabrata Dash², Bhavya Mody³, Anand Reddy Maligireddy⁴, Ankit Agarwal⁵, Lakshay Rastogi⁶ and Inderjeet Singh Monga⁷

Abstract

There is an anatomy and there is an anatomy. Angiography is a rough method used for estimating dimensions. By completing the intervention with intracoronary imaging, one can directly characterize lesion composition, elucidate pathophysiology, and luminal size measurement. This review describes patients and lesions where imaging may be most beneficial, along with up-todate evidence of the impact induced on cardiovascular events by the intracoronary imaging. It summarizes the importance of organizing procedural strategies and the use of various imaging methods such as optical coherence tomography or intravascular ultrasound for percutaneous coronary intervention (PCI) to improve stent optimization. Further, various advantages and disadvantages are associated with the use of imaging methods OCT and IVUS in the management of PCI and the elucidation of the causes of stent failure are discussed. It also explains the use of OCT or IVUS in various severe pathological conditions such as severe kidney disease (CKD), left main disease, bifurcation lesion, acute coronary syndrome (ACS), and patients present with high bleeding risk. It also describes diagnostic imaging of patients with vulnerable plaques. We will also talk about various other advanced imaging methods such as investigational Microoptical Coherence Tomography and near-infrared spectroscopy (NIRS).

¹Department of Cardiology, MD, DM, MAX Super specialty hospital, Bathinda, Punjab, India

²Department of Cardiology, MD, DM, FICC, FAPSC, FCCP, FSCAI, Aster Hospital, Dubai, Al Quasis, UAE

³Department of Medicine, MBBS, Kasturba Medical College, Manipal, Karnataka, India

⁴Department of Cardiology, Mayo Clinic, 13400 E Shea Blvd, Scottsdale, AZ 85259, USA

⁵Department of Cardiology, Cleveland Clinic, 9500 Euclid Avenue Cleveland, Ohio 44195, USA

⁶Department of Cardiology, Kasturba Medical College, Manipal, India

⁷Department of Cardiology, MBBS, DNB, DM, FSCAI, Command Hospital Chandimandir, Panchkula, Haryana, India

*Corresponding Author: Rohit Mody, Department of Cardiology, MD, DM, MAX Super specialty hospital, Bathinda, Punjab, India.

Received Date: 09-05-2022 Accepted Date: 09-21-2022 Published Date: 10-12-2022

Copyright© 2022 by Mody R, et al. All rights reserved. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Keywords: Intracoronary Imaging; OCT; IVUS.

Abbreviation: ACS: Acute Coronary Syndrome; ATM: Ataxia Telangiectasia Mutated; CFA: Common femoral artery; CTO: Chronic Total Occlusion; DAPT: nDual Antiplatelet Therapy; DES: Drug-Eluting Stent; EHL: Electrohydraulic Lithotripsy; ESWL: Extracorporeal Shockwave Lithotripsy; PAD: Peripheral Arterial Disease;

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article **Citation:** Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37. **DOI:** https://doi.org/10.37191/Mapsci-JCCR-3(3)-066 PCI: Percutaneous Coronary Intervention; RVD: Reference Vessel Diameter; TVR: Target Vessel Revascularization; µOCT: Micro-Optical Coherence Tomography; ACS: Acute Coronary Syndrome; ADAPT-DES: Assessment of Dual Antiplatelet Therapy with Drug-Eluting Stents; ADR: Antegrade Dissection and Reentry; BMS: Bare Metal Stents; BRS: Bioresorbable Scaffolds; CAC: Coronary Artery Calcium; CAD: Coronary Artery Disease; CAG: Coronary Artery Angiography; CKD: Chronic Kidney Disease; CLI: OPCI- I'Infarto-Optimisation of Percutaneous Coronary Intervention; CTO: Chronic Total Occlusion; DAPT: Dual antiplatelet therapy; DCS: Drug-Coated Stent; DES: Drug-eluting Stent; EEL: External Elastic Lamina; EEM: external elastic membrane; EES: Everolimus-eluting stents; FFR: Fractional Flow Reserve; GM: Gray Matter; HBR: Heart Beat Rate; ISR: In-stent Restenosis; IVUS: Intravascular Ultrasound; KAMIR: Korea AMI Registry-National Institute of Health Database ; LAD: left anterior descending artery; LCX: left circumflex artery ; LM: Left Main; LMCA: Left Main Coronary Artery; LMT: Left Main Trunk; MACE: Major Adverse Cardiovascular Events; MI: yocardial Infarction; MLA: Minimum Lumen Area; MSA: Minimum stent area; MUSIC: Multicenter Ultrasound Stenting in Coronaries ; NIRS: Near-infrared Spectroscopy; OCT: Optical Coherence Tomography; PCI: Percutaneous Coronary Intervention; POC: Point of Care; POT: Proximal Optimization Technique ; RCP: Respiratory Care Practitioner; RCT: Resynchronization Therapy; RNCP: Registered Nutritional Consulting Partner; RVD: Right Ventricular Dysfunction; SCA: Sudden Cardiac Arrest; SES: sirolimus-eluting stents; SMC: smooth muscle cells; STEMI: ST-elevation MI; SVG: Saphenous vein grafts; TCFA: Thin-cap fibroatheroma; TL: Target Lesion Revascularization; TVF: Tactile vocal fremitus; TVR: Tricuspid Valve Replacement; VANQWISH: Veterans Affairs Non-Q-Wave Infarction Strategies In-Hospital; ZES: zotarolimus-eluting stents.

Introduction

In addition to angiography, certain patients are required to undergo further intracoronary assessment, intermediate lesions may be subjected to the following physiological assessment such as fractional flow reserve (FFR). Stent thrombosis and restenosis is reduced by the intracoronary imaging method in PCI which is guite beneficial effect associated with it. Assessment after highpressure balloon inflation and of small vessels, long lesions, bifurcations, left main (LM) is feasible [1]. When assessing a baremetal stent, a larger minimal lumen area (MLA) reduces angiographic restenosis and revascularization within the stent. With drugeluting stents (DES), intracoronary imaging (Matrix registry) reduced the incidence of deaths, myocardial infarction (MI) and major cardiovascular adverse events (MACE) that occurred after 30 days, 1 and 2 years. [2]. Coronary angiography is a benchmark. However, it has various limitations because of providing anatomical intravascular data and also it doesn't offer insight into physiological correlation. Intracoronary imaging provides precise and accurate measurements and reduces interobserver variability. It can be informative about vessel anatomy, the severity of disease and morphology as well as sizing. Furthermore, vessel precise determination of dimensions of the vessel, the composition of plaque, extent of narrowing in the vessels can be done by using advanced intracoronary imaging systems such as intravascular sound (IVUS) and optical coherence tomography (OCT) which facilitate the selection of the best suitable intervention method such as the use of atheroblative devices, stent sizing, and stent deployment optimization with the objective

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

to provide the best clinical outcomes to the patients. Due to such advantages, enormous understanding growth in the pathophysiology of coronary artery disease is made by the development of invasive intracoronary imaging modalities such as IVUS, OCT and NIRS [3]. It especially helps in complex procedures, especially the LM and bifurcation disease and can be useful in patients with stent failures [4-6]. Also, imaging can be used to identify vulnerable plaques and to guide about the future Various advanced research. imaging technologies are in the development phase. With the objective to demonstrate that clinical outcomes are improved by the intracoronary imaging tools, robust clinical trials need to be conducted [7]. Considering all aspects, objective of this review article is to discuss about the various available advanced intravascular imaging devices and their applications, the role of these devices in the identification of pathophysiological characteristics of the atherosclerotic plaque, objectives of stent optimization and stent sizing.

Learning objectives

- How the difference among the various intravascular imaging devices
- To understand about method of using the available intravascular imaging devices
- To understand about the improvement in clinical outcomes induced by the stent optimization
- To understand about the evolving role in management of vulnerable plaque played by the intravascular imaging methods

• To understand the evolving role of micro-OCT in humans.

Comparison of IVUS with OCT

- In ILUMEN-III trial, OCT-guided PCI method was compared with IVUS guided by PCI guided by minimal stent area (MSA) is the primary end point of this study which was noninferior in both arms. In the OCT group, the significant dissections and malposition's were found to be less [8]. In OPINION Resynchronization Therapy (RCT), failure of the target vessel at 12 months follow-up of PCI was considered as the clinical endpoint which was found to be noninferior in OCT guided PCI in comparison to the IVUS guided PCI Also, the binary restenosis was identical in two groups [9]. With OCT, we are able to determine vessel size. stent under expansion, dissection, and thrombus. We can have а better assessment of intermediate lesions. which is sometimes not clear on using the coronary angiography.
- IVUS has the advantage that it penetrates about 8 mm inside the vessel, whereas OCT can penetrate only 3 mm. Also, IVUS has the superior role as no contrast is used and also in patients in which ostial lesions require assessment. OCT has a better resolution as compared to IVUS in general. But recently used high definition IVUS gives resolution comparable to OCT. OCT shows the ability to visualize intrastent tissue,

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

Citation: Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37. DOI: https://doi.org/10.37191/Mapsci-JCCR-3(3)-066

hence it is useful in new classification systems for in-stent restenosis (ISR). OCT can differentiate between a ruptured plaque and non-ruptured thin cap fibroatheroma (TCFA), while lumen area and plaque burden is evaluated by the IVUS and has the ability to discriminate TCFA [10]. The composition of the plaque and the structural details are better delineated by OCT which may not be seen in IVUS. The comparison of CAG, IVUS and OCT in different PCI situations is shown in Table 1 [11]. The relative advantages and disadvantages of IVUS and OCT in PCI optimization are discussed in table 2 [12] and table 3 [12].

Clinical feature	Angiography	IVUS	ОСТ
Appraisal of LMCA stenosis	+	+++	+
Appraisal of non-LMCA stenosis	++	++	+++
Localize the culprit lesion	+	++	+++
Finding the vulnerable plaque	0	++ (VH-IVUS)	+++
Clinch the possibility of MI during procedure and risk of			
distal embolization	0	+++ (VH-IVUS)	++
Size the vessel undergoing stent implantation	++	+++	+++
Optimize stent results	+	+++	+++
Evaluate stent thrombosis or restenosis	+	++	+++

Table 1: Analyzing CAG, IVUS and OCT in different PCI situations [11]. o: no data; +: less data; ++: moderate data; +++: extensive data; + LMCA: Left Main Coronary Artery; IVUS: Intravascular Ultrasound; OCT: Optical Coherence Tomography; MI: Myocardial Infarction; PCI: Percutaneous Coronary Intervention; CAG: Coronary Angiogram.

IVUS	OCT	
Superiority	Superiority	
	10 times higher clarity compared from IVUS à It can	
	detect very minute observations which IVUS can	
More experience à Usage of IVUS is prevalent since 30	miss Malposition, neointima on struts of stent,	
years	dissections	
Imaging can be done without pre-dilatation in most	More characterization of plaque and vessel wall like	
of cases.	calcium	
IVUS penetrate adventitia which allows exact sizing of	Thrombus can be detected more often and its	
vessel and stent	varieties	
IVUS has been studied extensively and various trials		
give indications that it can guide the procedure. Also,		
clinical outcomes are well studied	It is clearer and interpretation is easy	
IVUS shows predicted evidence of restenosis which is	The tissue characters of OCT in ISR and ST are well	
well documented	studied	
	Gives more accurate measurements because of	
In CTO PCI there is better help	availability of automatic AI enabled OCT	

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

Inferiority	Inferiority
There can be difficulty in clarifying the images	Intravenous contrast required
The characterization of tissue can be challenging	Flushing required
Evaluation of coverage of struts by neointima cannot	
be done	preparation of bed before OCT frequently required
Evaluation of Malposition is less clear	Less penetration of OCT is a handicap
	There are limited trails of OCT guidance as
	compared to angiography and no RCT which
Less clarity on views which are longitudinal	compares the clinical outcome

 Table 2: Superiority and inferiority of IVUS and OCT for PCI facilitation and optimization [12].

 + IVUS: Intravascular Ultrasound; OCT: Optical Coherence Tomography; CTO: Chronic Total Occlusion;

 PCI: Percutaneous Coronary Intervention; AI: Artificial Intelligence; ISR: In-Stent Restenosis.

	Frequency Domain OCT	IVUS
Wavelength	1.3 µm	35-80 µm
Axial resolution	10-15 µm	150 µm
Lateral resolution	40-90 µm	250 µm
Penetration in tissue	2-3.5 μm	7 mm
Field of view	< 10 mm	15 mm
Maximal frame rate	100-200 fps	30 fps
Maximal pullback speed	20-40 mm/s	1 mm/s

 Table 3: Comparison of basic OCT and IVUS features [12].

† fps: frames per second; IVUS: Intravascular Ultrasound; OCT: Optical Coherence Tomography.

The non-inferiority of OCT vs IVUS for aiding during PCI in context to acute outcomes and long-term results have been seen in ILUMIEN-III and OPINION trials. Similarly, recently network meta-analysis of 17 RCT's and 14 observational studies demonstrated that IVUS or OCT guidance leads to a severe reduction in various MACE or cardiovascular mortality as compared to the angiographic guidance, with similar efficacy [13].

In the cases of diffuse disease, the OCT imaging method is unable to assess the various parameters such as plaque burden evaluation and measuring the size of the vessel due to its lower penetration power in the tissue, especially in tissues having high lipid content. In patients present with ostial

LM lesions, chronic total occlusion (CTO) and renal insufficiency, IVUS is the preferred modality [14]. In contrast, OCT is more advantageous in the characterization of plaque, and in the detection of morphologies that are related to stents or its lumen. incorrect wire position or malposition and dissections. The SYNTAX II study reported outcomes better than historical controls because protocols included coronary physiology-based revascularization and IVUS guided stenting. Till now IVUS guided PCI in RCT's have demonstrated superior clinical outcomes. However, proper technique and correct imaging interpretation are of paramount importance in influencing the clinical outcomes [15,16].

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

Citation: Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37.

The recommendations for Intravascular imaging method adjunctive uses for diagnostic evaluations and optimization of PCI and the guidelines are described in table 4 [17] & 5 [18,19] and figure 1.

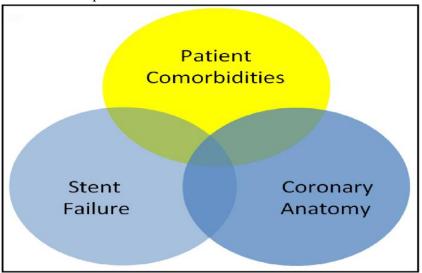


Figure 1: Which patient's benefits from imaging guidance?

	Appraisal of Coronary arteries		
	The lesions such as dissections, thrombus or calcified.		
	Also, if there is equivocal finding		
	Appraisal of LMCA stenosis		
Mostly agreed	Appraisal of stenosis involving bifurcations Assessment of culprit vessel in MI		
	PCI facilitation and stent optimization		
Randomized trial	In lesions which are long		
evidence	In CTO PCI		
	Patients sustaining MI		
	LMCA stenosis		
	Deployment of bioresorbable devices		
Mostly agreed	CKD patients especially (IVUS)		
	To find out cause of stent failure		
	ISR		
ST			

Table 4: Use of Intracoronary Imaging for appraisal of CAD, PCI facilitation and stent optimization [17].+ LMCA: Left Main Coronary Artery; MI: Myocardial Infarction; CTO: Chronic Total Occlusion; PCI:Percutaneous Coronary Intervention; CKD: Chronic Kidney Disease; IVUS: Intravascular Ultrasound; ISR:
In-stent Restenosis.

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article **Citation:** Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37. **DOI:** https://doi.org/10.37191/Mapsci-JCCR-3(3)-066

IVUS/OCT in 2018 ESC/EACTS Guidelines		
Recommendations		Level
With the objective to predict the intermediate grade stenosis hemodynamic		
relevance, FFR or iwFR is recommended especially when the ischemia evidence is		
not available.	Ι	А
In the patients present with the muti vessel disease undergoing PCI, FFR-guided PCI		
should be recommended	IIa	В
For the assessment of severity of the unprotected left main lesions, IVUS should be		
recommended.	IIa	В
IVUS/OCT in 2021 ACC/AHA/SCAI guidelines		
Recommendations	Class	Level
With the objective to reduce various ischemic events in the patients present with the		
left main or complex coronary artery stenting who are undergoing coronary stent		
implantation, to provide procedural guidance IVUS can be used	2a	B-R
Further, OCT imaging method is the alternative method to the IVUS method for		
procedural guidance in the patients undergoing coronary stent implnataion, expect		
in the patient present with the ostial left main disease		B-R
To evaluate the mechanism behind the failure of stent in the patient present with		
		I
the stent failure, both imaging method IVUS or OCT are the promising imaging		

 Table 5: IVUS/OCT in the Guidelines [18,19].

† CTO: Chronic Total Occlusion; PCI: Percutaneous Coronary Intervention; IVUS: Intravascular Ultrasound; FFR: fractional flow reserve; iFR: instantaneous wave-free ratio; OCT: Optical Coherence Tomography.

OCT patterns of ISR

In the era of drug-eluting stent understanding the morphological characteristics of infrequent stent restenosis is a serious clinical challenge. A piece of evidence is provided by the clinical studies that based on the geometry of the stent, reduced concentration of the local drug might be the reason for the in-stent restenosis [20,21].

In-stent restenosis process is considered as quite stable process, in early phase of this process hyperplasia is observed. The optical coherence tomography (OCT) is the high-resolution imaging method which is associated with huge advantage to demonstrate the differential morphological pattern of the restenosis tissue after stenting [24]. The technical & biological mechanisms of ISR are described in figure 2 [19]. Current OCT findings demonstrated that neointima, thrombi and neointimal rupture are the morphological characteristics present in the in-stent TCFA (thin-cap fibroatheroma) in DES failure patients present with ISR [25]. The layered appearance of the restenosis tissue (figure 3) occurred due to variations in

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

the morphological and anatomical features of tissues present further from the lumen which appears heterogenous and homogenous visualization of the inner luminal border [26].

Micro-vessels in restenosis can be recognized by using the OCT as suggested by postmortem histological data [27,28]. Furthermore, in comparison to the greyscale IVUS, neointimal rupture and thrombi detected in restenosis tissue were higher in comparison to the OCT due to its high spatial resolution [29]. The OCT patterns of ISR in a patient presenting with stable and unstable angina are shown in figure 4 [30]. Accordingly, the treatment strategy of ISR can be guided by Intracoronary imaging (Table 6).

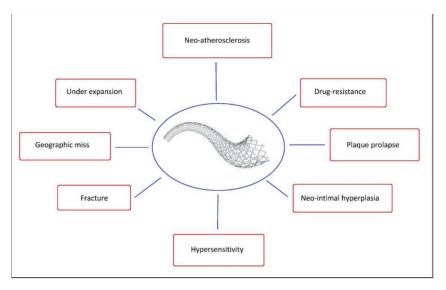


Figure 2: Technical & Biological Mechanisms of ISR [19].

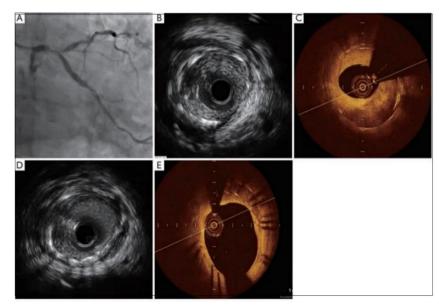


Figure 3: ISR patterns as evaluated by IVUS and OCT.

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article **Citation:** Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37. **DOI:** <u>https://doi.org/10.37191/Mapsci-JCCR-3(3)-066</u>

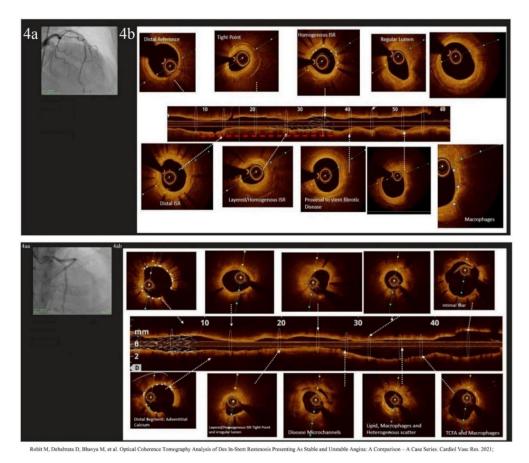


Figure 4: OCT patterns of ISR in different situations [30].

ISR Mechanism	Potential Treatments	
Unstented/gap segment	BA, DES	
Severe neointimal hyper-plasia	BA, laser, DES	
Stent fracture	BA, DES, brachytherapy	
Undersized	BA high pressure, scoring balloon, larger DES	
	BA high pressure inflation, scoring balloon, laser,	
Underexpansion	atherectomy, DES	
>layers of stent	Laser, brachytherapy, outside US-DCB	

Table 6: Intravascular Imaging: Critical for guiding ISR treatment strategy.+ DES: Drug Eluting Stent; DCB: Drug Coated Balloon.

Down the road Intracoronary Imaging

OCT has emerged as a benchmark imaging method that has overcome many limitations of angiography and IVUS. OCT has provided unique insight into atherosclerotic plaque along with the ability to understand the tissue response underlying stent implantation. The upcoming growth in OCT is filled with a lot of opportunities for interventional cardiologists. The recent developments can increase the clinical use of OCT. To name a few:

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

- In pulmonary hypertension, enhanced neointimal formation detection [31].
- Vasculopathy induced by transplantation.
- Improving imaging time as well as quality.
- There can be a better depiction of the character of the fibrous cap with the use of different cellular targeting substances which are tagged with fluorophore [32].

The microstructures at cellular and subcellular levels can be visualized by using micro-OCT, as studied in animal models.

Lesion Significance & Stent Sizing

For the stent sizing or optimal procedure endpoints which can guide implantation of stent, there are no criteria which can be standardized either we utilize OCT or IVUS. The ongoing large, randomized trials-the IMPROVE (Impact on Revascularization-Outcomes of IVUS Guided Treatment of Complex Lesions and Economic Impact) trial (NCT04221815) and the RENOVATE (Randomized Controlled Trial of Intravascular Imaging Guidance versus Angiography-Guidance on Clinical Outcomes After Complex Percutaneous Coronary Intervention) trial (NCT03381872)-will guide us regarding the outcomes of IVUS vs Angiography guided interventions [33].

The MUSIC (Multicenter Ultrasound Stenting in Coronaries) Study criteria [34] were created in order to obtain optimal stent implantation, which included complete stent apposition and adequate expansion of the stent. The

criteria for optimization were fulfilled in only 56% of cases. As a result, a simpler way can be utilized in stent sizing and optimization. In OCT we can rely on external elastic membrane (EEM) quantifications. It can result in similar sizing of the stent to that used with guidance of IVUS to (avert) target vessel failure (TVF). The minimal stent area (MSA) that predicted (prediction) ISR at 9 months remained the same across different stent types like sirolimus-eluting stents (SES), zotarolimus-eluting stents (ZES), everolimuseluting stents (EES) [5.5, 5.3, and 5.4mm2, respectively] [35]. The landing zone, which has plaque more than 50% by IVUS [36] or lipid rich lesions seen by OCT are associated with complications like MI, ISR and edge dissection which should be avoided. Also, the calcification with an arch and TCFA at stent edge can also be the predictor of stent edge dissection [37].

In the Centro per la Lotta Contro l'Infartoof Percutaneous Optimisatio Coronary (CLI-OPCI) Intervention study [38], suggested various guidelines to achieve optimal stent deployment such as having mean reference lumen area of MSA> 90% stent malapposition) with a distance of <200µm, edge dissections with a width of less than 200µm, and narrowing of the lumen edge with a lumen area plaque protrusion inside a stent are not clinically pertinent when detected by OCT.

Stent Sizing

To summarize stent sizing

• Stent sizing should be based on the distal reference dimension. The optimization of proximal and mid

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

Citation: Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37.

DOI: https://doi.org/10.37191/Mapsci-JCCR-3(3)-066

regions suggests a straightforward as well as safe approach. Especially, the up rounding of the stent with mean lumen diameter (o-o.25mm), or the EEM to EEM quantification associated with down computing to the o.25 mm stent size may be utilized.

- EEM reference-based sizing strategy appears practical while utilizing OCT. Selection of the landing zone in appropriate way is quite important (<50% plaque) As subsequent restenosis is associated with presence of the tissue having high lipid content at the edge of the stent
- To determine stent length and perfect placement, co-registration of angiography and OCT or IVUS is convenient.

Post-Intervention predictors of clinical outcomes

Imaging criteria for adequate results

- >80% in relation to the distal vessel is a must in clinical practice.
- In non-LM lesions, MSA of >5.5mm² by IVUS and >4.5mm² with OCT is targeted. They are the cutoff to predict future events.
- If anatomically viable, gross malposition after stent implantation should be corrected. Complete apposition might promote early endothelization of stent struts.
- When malposition is less than 0.5 mm which extends up to 1 mm, the

correction, is not recommended. This might attract neointimal formation. However, this needs to be validated in RCTs.

- Variations in the protruding tissue composition is the reason of various adverse outcomes when it is compared to tissue prolapse in ACS with stable CAD
- Late and very late stent thrombosis is majorly caused by the delayed acquired malposition
- In scenarios of a residual stent edge stenosis, the Imaging with either IVUS or OCT can demonstrate hematoma as a cause of residual stent edge stenosis.
- IVUS or OCT detected large dissections are considered as the independent predictors of MACE.

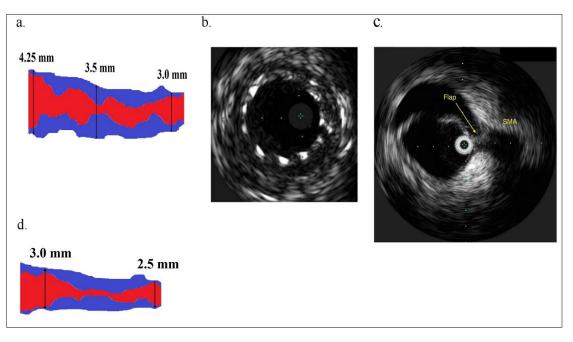
Remaining burden of the plaque, lateral or lengthwise plaque extension, involvement of medial or adventitial layer and extension across the distal end of the stent, potentiate the risk of various future events.

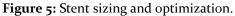
Goals of stent optimization

- Largest possible minimum stent area (>5mm² or >90% reference area)
- Avoid landing in significant plaque burden (>50%)
- Avoid gross malapposition (>1.0mm)
- Correct edge dissections (where involving media and >3mm in length) figure 5.

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

Citation: Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37.





Plaque Composition (Lipid, Thrombus and Calcium)

- OCT is better at assessing calcium thickness
- The risk of under expansion of the stent increases if calcium arc and thickness are more than 180° and 0.5 mm respectively.
- Improved stent expansion is often linked with calcium fractures is evident on post-lesion preparation.
- A combined approach might be prudent in cases, where there are large calcium pools that fail to demonstrate calcium fracture after the initial bed preparation.
- During stenting of plaques rich in lipid content, risk of various adverse outcomes such as no-reflow phenomenon or peri-procedural MI increased. Whether detecting a lipidcontaining lesion or a necrotic plaque

by OCT or IVUS before embarking on PCI, impacts clinical outcomes needs to be demonstrated.

 Post PCI adequate expansion should be achieved with additional dilatation with higher balloon diameters. Optimal stent expansion was defined as an MSA >90% of the distal reference lumen or an MSA ≥5 mm² in ULTIMATE [50].

In this study, the 1.5% event rate was achieved with optimal stent expansion. However, even after IVUS or OCT guidance, the optimization was achieved in only approximately 50% of cases.

The problems related to stent edge occur secondary to expansion of stent as stent problems related to stent edge occur secondary to expansion of stent related events predictors. The factors which require additional stent implantation are as follows:

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

- Intramural hematomas
- Geographic miss
- Significant stent edge dissections i.e., that have a reduced effective area of lumen (<4.5 mm²), extending to the media or more than 3mm in length associated with a dissection arc of >90°.

There is a misinterpretation of whether any adverse outcomes are induced by acute stent malapposition [51]. It is seen in approximately 15% and 50% of DES using IVUS and OCT respectively. Adverse events are not induced by acute malapposition in the absence of under expansion of stent.

It requires treatment when located at the proximal edge so that rewiring during future intervention become easier. In this event, it should be corrected by using a larger diameter balloon. In case of thrombosis within the stent or tissue prolapse inside the stent, the additional stent is required only if the effective lumen area is reduced, or it is causing acute coronary syndrome (ACS) [52-54]. During stenting, myonecrosis and plaque rupture can occur if TCFAs are detected [55]. OCT or NIRS can detect TCFAs, large lipidplaque and plaque rupture can be detected by both imaging methods IVUS and OCT.

There have been various publications assessing intravascular imaging-guided DES implantation, comprising 20 RCTs, 65 registries and 30 meta-analyses that revealed the mortality advantage of IVUS guidance when compared with angiographic guidance [56] Further, at 1 year follow-up IVUS guidance halved the rate of adverse events demonstrated by the findings of the one of the largest RCTs. [53]. At five years follow-up, the positive results continued, and improvements were seen beyond 1 year of follow up. The data with OCT is sparse but a Bayesian network meta-analysis showed similar results as that of IVUS guidance [57]. OCT and IVUS characteristics of plaque are seen in figure 6 & 7 respectively [58].

Plaque composition in special populations

OCT imaging method can be used to visualize the external elastic lamina in the presence of fibrotic plaque or normal vessel. whereas the presence of necrotic core or lipid attenuates light and makes EEL unclear. With IVUS the attenuation caused by lipid is not as much when compared with OCT, making an exception in the attendance of a large necrotic core containing TCFA.

OCT method is recommended method for the determination of TCFA, due to its higher resolution and ability to assess fibrous cap, while lipid characterization is best with the dual-modality device having NIRS with IVUS.

Thrombus is best assessed with OCT as it can distinguish white from red thrombus. OCT is superior for providing an accurate assessment of calcium thickness when compared to IVUS, as it penetrates calcium better. However, both the modalities assess arc and length of calcium equally good and are better as compared to angiography.

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

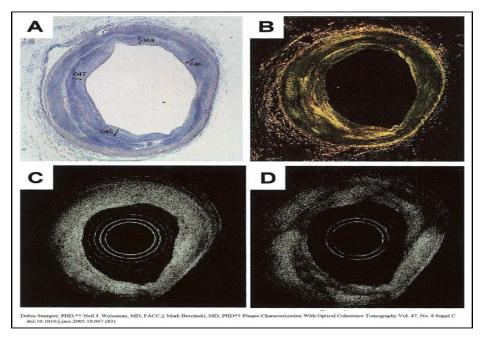


Figure 6: OCT characters of plaque [58].

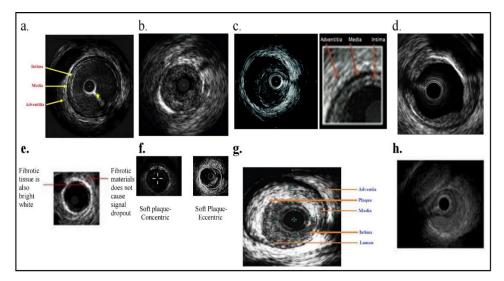


Figure 7: IVUS characters of plaque.

In the assessment of an angioplasty balloon to fracture the calcium, a vital role is played by the thickness of calcium, which is quite useful in achieving the optimum expansion of stent in heavily calcified lesions [59]. An OCTbased score came into the limelight with the objective to predict the expansion of the stent and requirement for the modification of the calcium. It has been suggested that adjunctive techniques like atherectomy or lithotripsy should be included in the presence of calcium with an arc greater than 180° along with thickness >0.5 mm, also length >5 mm [60]. Similarly, a IVUS score has been created,

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

suggesting the arc of calcium >270° and >5.0 mm in length, presence of circumferential calcium or a calcified nodule and vessel size. By OCT, the plaques, which are remodeled positives adjunctive techniques mainly fracture the plaque of harder superficial calcium with only minor debulking and are not useful in the absence of superficial calcium.

Goals in therapy in CAC

Crossing the lesion/modifying Plaque

- Crossing the Lesion
- Enables the access for upscaling balloons and stents

Plaque modification

• Debulking calcific plaque

- Inducing calcium fracture
- Maximizing luminal gain (stent expansion)

Summary and conclusion

Angiographic severe calcification leads to various adverse outcomes such as higher tactical vocal fremitus rates and stent under expansion. In the presence of angiographic severe calcification, an algorithmic approach, utilizing intravascular imaging, can guide optimal therapy.

Device selection is dependent on the intravascular imaging findings. Calcium fracture (or nodular debulking) should be identified for (DES) deployment. Various types of CAC and treatment modalities are shown in figure 8 & figure 9.

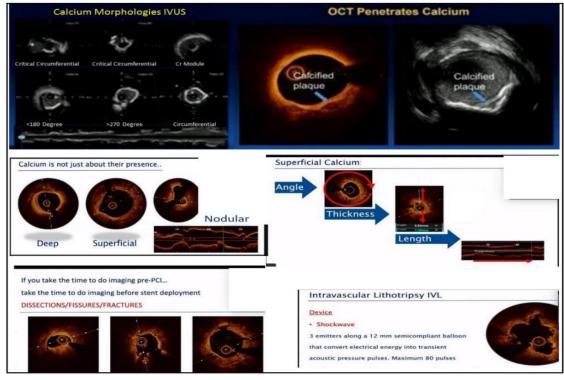


Figure 8: Types of CAC and treatment.

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article **Citation:** Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37. **DOI:** https://doi.org/10.37191/Mapsci-JCCR-3(3)-066

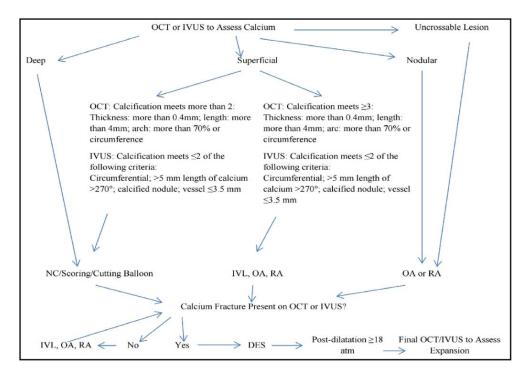


Figure 9: Imaging in CAC.

Special Populations

Acute coronary syndromes (ACS)

Various pathological studies have suggested certain culprit lesions in patients succumbing suddenly to ACS: mainly plaque rupture in 65%, followed by erosions in 30% and calcified nodule in approx. 5%, leading finally to a common thrombus formation. Though they might be clinically evident, VANQWISH (Veterans Affairs Non-Q-Wave Infarction Strategies In-Hospital) study demonstrated no or multiple culprits in 50% of cases [61].

The major characteristics feature of the atherosclerotic plaque was the maximum lipid core burden index of more than 400 within the 4 mm long segment which demonstrate about the plaques induced ST-elevation MI an evidence provided by the another study but it was not observed in the

patients presents with calcified nodules or talostubos cardiomyopathy, coronary artery dissections (SCAD).Rupturing of the plaque in half of the patients present with STEMI is detected by the imaging method OCT and IVUS. However, detection of the ruptured plaques is done by OCT in quite better way. Moreover, erosion can also be detected by OCT method. This is proposed by the some of the authors that erosions in most of the culprits are caused by an intact fibrous cap and are more stable than plaque rupture, so it may be possible to avoid stenting [62-64].

Further, identification of the SCAD and calcified nodules can be done by using both imaging methods IVUS and OCT. The online KAMIR (Korea AMI Registry-National Institute of Health database) registry of 11,731 patients with STEMI undergoing primary PCI suggested mortality advantage of IVUS or

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

OCT over angiographic guidance, demonstrated decreased patient or deviceoriented clinical events [65]. Healing and rupturing of the plaques are frequent findings reported in the patients present with STEMI or non-Q wave infraction, though it lacks any evidence to be treated actively. Culprit lesions in atherosclerotic lesions and nonatherosclerotic causes are depicted in figure 10.

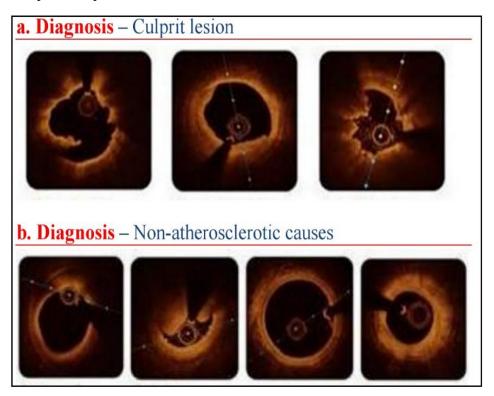


Figure 10: Culprit lesions in ACS.

LM Disease and Bifurcation

Intracoronary imaging of LM Stenosis Severity

The IVUS parameter which is a key determinant for deciding the need for intervention is the MLA. A value of less than or equal to 6mm2 is accepted for the LM. Jasti, et al [66] initially came up with the cut off utilizing FFR as an indicator of significant physiological ischemia. Moreover, by using FFR along with IVUS for analyzing functional severity of LM stenosis, is also a prognostic indicator. While doing IVUS interrogation of

LM, it is critical for the operator to disengage the guiding catheter and maintain a conjoining relation between IVUS catheter and LM ostium. Thereafter, the pullback should be performed to the LM from both LAD (Left Anterior Descending Artery) and LCX (left circumflex artery) sequentially. The smaller MLA on the two pullbacks is most accurate and pullback from both arteries provides a complete and accurate assessment of plaque distribution [67]. IVUS criteria for stent optimization in LM are depicted in figure 11 [68].

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

Citation: Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37.

DOI: <u>https://doi.org/10.37191/Mapsci-JCCR-3(3)-066</u>

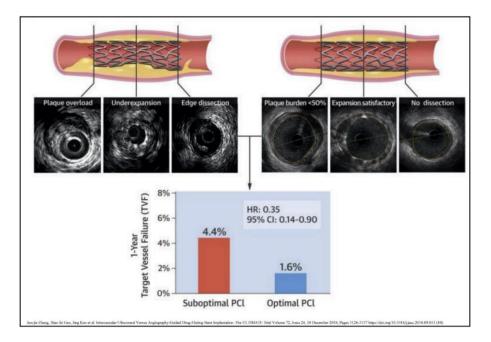


Figure 11: IVUS criteria for stent optimization [68].

Procedure Planning and Optimization -IVUS Step by Step

Imaging in LM can be performed to indicate whether the lesion requires modification as in calcified lesions and also the distribution of plaque (single vs two stents), ostial location, a stent size and length, landing zones and vessel size. IVUS is recommended as the useful modality for the optimization of the stent. The plaque distribution can be seen with angiography is different from that evaluated by IVUS (figure 12) [69].

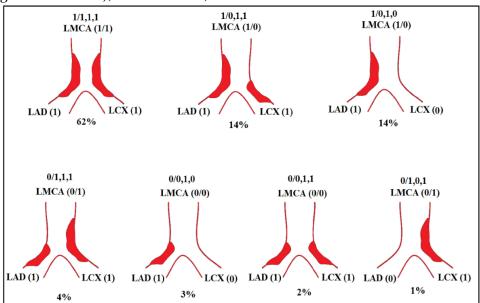


Figure 12: IVUS classification for LMCA bifurcation plaque distribution [69].

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article **Citation:** Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37. **DOI:** https://doi.org/10.37191/Mapsci-JCCR-3(3)-066

Qualitative Assessment of Lesion Calcium

In LM lesions, calcium is commonly present. [70].

IVUS or OCT can define the extent of calcium and the need for lesion modification with atherectomy or lithotripsy, to decrease complications of stent under expansion [71]. The modification devices should be utilized for heavy calcification and calcified nodule [72,73].

Stent Sizing

IVUS can provide accurate information pertaining to stent length and diameter. It can assess. balloon size for the proximal optimization technique (POT). IVUS use in LM bifurcation is shown in Table 7.

Pre-PCI
Pullback from MB (LAD), check entry of SB (LCX)
Pullback from SB (LCX) if possible
During the procedure
Check guidewire position after re-crossing the guidewire through stent struts
Check if IVUS catheter is going smoothly
Check the guidewire position at the side of crossing (middle or distal crossing)
Final IVUS from both MB and SB to Ostium to check
Incomplete stent apposition, stent deformation
Dissection/injury in SB following KBT
Injury in LMT to guiding catheter

Table 7: IVUS use in LM bifurcation.

+ MB: Main Branch; SB: Side Branch; LAD: Left Anterior Descending Artery; LCX: Left Circumflex Artery; IVUS: Intravascular Ultrasound; KBT: Kissing Balloon Technique; LMT: Left Main Trunk; ISR: In-stent Postenosis

Restenosis.

One-Stent versus Two-Stent Strategy

According to the European bifurcation Club, the provisional approach involves stenting the LM to LAD with a reference diameter of LAD and post dilating the LM according to intravascular imaging assessment. If LCX is large and diseased, a provisional stent to LCX can be deployed (inverse provisional approach). Side branch rewiring should be done through the distal strut after the performance of adequate POT [74]. Kissing balloon inflation (KBI) is essential followed by final POT in case of two stent techniques. During the provisional stenting, need of second stent can be assessed by measuring the plaque burden of the side branch or can be predicted by pre-procedural ostial LCX MLA of <3.7 mm² or a pre-procedural ostial LCX plaque burden of >50% [75]. This predicts the post stent crossover FFR of <0.80 in the LCX. Rewiring the side branch through the particular proximal or distal struts can be ascertained by imaging as shown in figure 13 [76].

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

Citation: Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37.

DOI: https://doi.org/10.37191/Mapsci-JCCR-3(3)-066

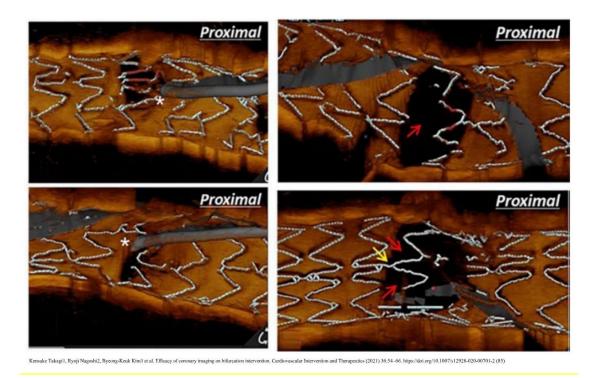


Figure 13: Imaging wire position during crossing side branch [76].

Stent Optimization

Malapposition in LMCA PCI is not common. Treatment is not essential as it is not associated with further cardiac events [77,78]. The only exception is when the patient requires rewiring which can be reduced by proper POT using the large balloon sized to inter intimal dimension can be used to reduce the rewiring One should look for significant edge dissection and geographical miss, if significant should be treated with the deployment of another stent [79]. The criteria of LM IVUS-guided optimization are depicted in figure 14.

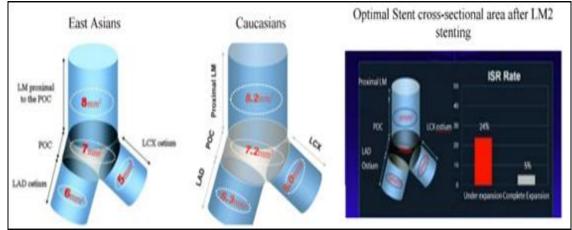


Figure 14: Criterions for LM IVUS-guided Optimization.

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article **Citation:** Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37. **DOI:** <u>https://doi.org/10.37191/Mapsci-JCCR-3(3)-066</u>

Side Branch Compromise

Patients who are particularly at risk of carina shift towards the side branch, due to high plaque burden or significant calcium [80] should be treated with KBI to restore flow. In case of significant shift, two stent strategies should be embarked on from the beginning. The eyebrow sign can be particularly of high importance to predict side branch closure after main branch stenting (figure 15) [81].

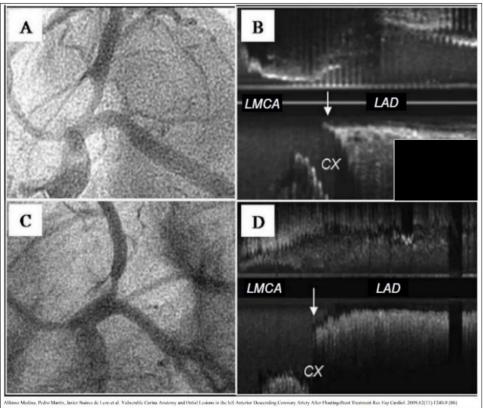


Figure 15: Eyebrow sign to predict side branch closure [81].

IVUS vs. OCT in LM PCI

IVUS may provide a better assessment of LM ostium because contrast injection does not require to be cleared from the lumen as in OCT. Also, the manual pullback allows specific imaging in the focal area of interest. OCT is superior in the assessment of various parameters such as malapposition, edge dissections, and geographic miss. But practical application of OCT in prediction of various clinical outcomes needs to be demonstrated.

Clinical Outcomes Using IVUS for LMPCI

Observational Studies

Evidence is provided by various observational studies that various long term and short-term adverse outcomes like stent thrombosis, mortality, and myocardial infraction are being reduced by IVUS-guided PCI particularly in patients present with complex coronary lesions. Recently, Kubo T et al enrolled 100 patients present with the coronary artery disease in the OPUS-class

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

study to demonstrate the reliability of the IVUS for the measurement of the lumen diameter in comparison to the other techniques frequency domain optical coherence tomography (FD-OCT) and quantitative coronary angiography (QCA). Results of the study suggested that the lumen area evaluated by the IVUS was significantly higher in comparison to the other techniques [82]. Further, findings of another observational study KAMIR (Korean acute myocardial infraction registry data) including 16264 patients suggested that various major adverse clinical outcomes MI, and stent thrombosis occurred less frequently in IVUS guided PCI group of patients after one-year follow-up [83].

Meta-Analyses

Benefits of IVUS guidance over the angiographic guidance in reducing the various short-term and long-term adverse outcomes have been demonstrated by multiple meta-analyses particularly in patients present with complex atherosclerotic lesions.

- A meta-analysis by Ahn JM, et al. of 3 randomized and 14 observational studies (26503 patients) indicated that risk of various adverse clinical outcomes like revascularization of the target lesion, stent thrombosis and myocardial infraction are reduced by the IVUS-guided PCI in comparison to the PCI guided by angiography method after the implantation of the drug-eluting stent [84].
- A meta-analysis by Frederik TW of a total of 9 studies (8 observational and

I randomized controlled trial) with a total of 838,902 patients (796,953 Angio-guided PCI, 41,949 IVUSguided PCI) demonstrated that all adverse clinical outcomes like mortality, myocardial infraction occurred less frequently in IVUSimaging method guided patients' group [85]. A meta-analysis by Yang RR, et al. of total 5 studies including 7830 patients present with coronary bifurcation lesion were included. In early follow-up, incidence of major adverse clinical outcomes was less in the IVUS-guided PCI group of patients. Furthermore, in long-term follow up study, incidence of cardiac death was reported lower in IVUSguided PCI group of patients [86].

• Findings of a meta-analysis of 19 studies by Fahed Darmoch et.al in which 27,637 patients were included demonstrated that the risk of cardiovascular death and MI was less in the IVUS-guided PCI group of patients in comparison to the computed angiography alone [87].

RCTs

Favorable clinical outcomes of the IVUSguided PCI have been demonstrated by the various smaller, single-center randomized clinical trials. 1400 patients having long coronary lesions were randomized by Hog SJ et al to either IVUS guided LM PCI or angiography [88]. In this study, in comparison to the angiography-guided PCI group (5.8%), in the IVUS-guided PCI group of patient's rates of major adverse cardiac events (2.9%) were lower at the 1-year follow

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

Citation: Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37. DOI: https://doi.org/10.37191/Mapsci-JCCR-3(3)-066

up. Another recent randomized trial by the Chieffo A, et al. randomized 284 patients present with the complex lesions to either angiographic or IVUS guidance [89]. Major cardiac adverse events combined with the revascularization of the target vessel target at the 1,6, 9,12 and 24 months were considered as the secondary endpoints of this study and primary end point of this study was the postprocedure lesion minimal lumen diameter. A significant difference in favour of the IVUS group was reported in the primary endpoint. However, at the follow-up of 24 months, in between the two groups, no marked difference was seen in the occurrence of major adverse cardiac events.

The summary of conclusion is summarized in Table 8. The future MACE risk was found to be higher in patients to have presence of four high risk plaque findings on OCT, in CLIMA registry [90].

- Plaque at the entry of a side branch and "Eyebrow sign" on the longitudinal view are the good predictors for side branch occlusion.
- Plaque distribution in LMT bifurcation is not always related to angiographic classification. Carina always spared and the disease in diffuse rather than focal.
- 2nd wire position is important to obtain good stent expansion without stent deformation.
- Use longitudinal view to check guidewire passage to the SB (proximal, middle, or distal?)
- Try to achieve 5-6-7-8mm² endpoint to minimize ISR.

Table 8: Take home messages for imaging of LM interventions.

 + SB: Side Branch; LMT: Left Main Trunk; ISR: In-stent Restenosis.

OCT has strong ability to identify the patients who are at the huge risk of subsequent adverse cardiovascular events confirmed by the registry. The pre-defined morphologies on OCT with the simultaneous presence of four plaque with huge risk findings were adopted as pre-defined endpoints [91]. During the first year follow up, major adverse coronary event was experienced by the 20% of the patient, and 3.6% of non-culprit plaques had high risk features [92]. The event-free survival was seen in 3.5% of patients with the combination of MLA <3.5 mm², FCT <75 mm, lipid arc extension >180, and OCT-defined macrophage infiltration. Thus, limited sensitivity was exhibited by the OCT-based classification, but for various primary end point it exhibited high specificity and for 1year events it remained an independent predictor. A fivefold greater risk of MACE was observed in diabetic patients who have more than 1 FFR negative lesion, TCFA positive which represented 25% of the population. The risk of future events in diabetic populations shows a paradigm shift due to the discrepancy between effect induced by the ischemia and vulnerable plaque.

PCI in Chronic Renal Insufficiency

The patients have a high rate of TLR post PCI if they suffer from chronic renal insufficiency. These types of patients, especially on dialysis,

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

have diffuse and calcified CAD. IVUS has the preference over OCT because IVUS can be done with low contrast and even zero contrast [94,95]. However, without using any contrast media or dextran injection, OCT has been performed.

CTO intervention

In CTO interventions the IVUS imaging in addition to being used for stent optimization has been used in other indications [97]. It can determine the entry point during antegrade approach when the proximal cap is ambiguous. It can be useful in navigating guidewire from sub-intimal space by reentering the true lumen. It can also be used to evaluate that if the guidewire is presence in true or false lumen, both proximally and distally. This helps to avoid the deployment of the stent in the false lumen. IVUS imaging may be useful in retrograde navigation of guidewire into the antegrade true lumen. IVUS does not propagate the dissection as it occurs during OCT imaging. IVUS reduces the event rate at 1 year by 75% over angiography alone in CTO PCI [98]. The IVUS in different situations in CTO interventions is shown in figure 16.

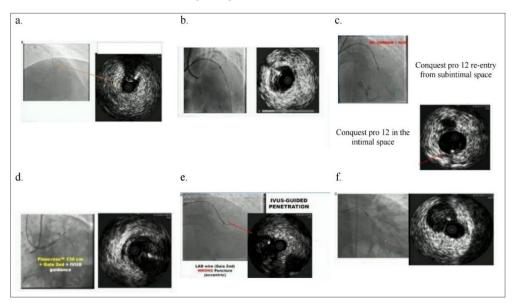


Figure 16: Use of IVUS in different situations in CTO interventions.

ISR and ST

The stent failure occurs in the form of stent restenosis or stent thrombosis [99]. It can be evaluated by intracoronary imaging and the exact mechanism of failure can be ascertained. It is a highly recommended indication of imaging. In event of under expansion or malapposition post dilatation alone may be sufficient instead of implantation of another stent. OCT imaging method is recommended method to study the stent failure reason and necessary corrective action if required. OCT plays in a pivotal role in edge dissection, under expansion and malapposition. The cause and mechanism of stent thrombosis after DES implantation can be ascertained by OCT imaging (figure 17) [100].

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article **Citation:** Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37. **DOI:** https://doi.org/10.37191/Mapsci-JCCR-3(3)-066

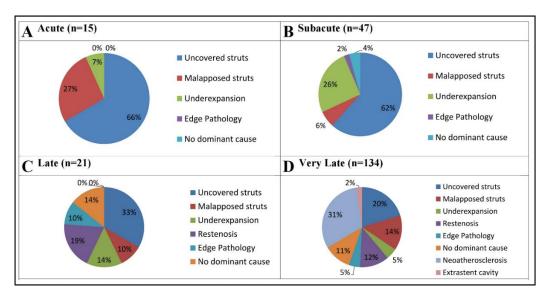


Figure 17: OCT imaging after DES implantation [100].

Stent failure & optimization

- Useful insights are provided by the OCT method to understand the mechanism of failure of stent.
- Stent failure is multi-factorial
- CT and IVUS are equivalents and detailed assessment post-stenting is required to achieve optimal results
- The best treatment of stent failure=Avoidance of under expansion.

High Bleeding Risk

More intravascular Imaging to accurately treat high bleeding risk (HBR) patients must be used. Most of the short dual antiplatelet therapy (DAPT) trials exclude complex lesion(B₂/C), CTOs, low EF <30%, Acute MI, SVG saphenous vein grafts (SVG)) lesions, ISR, multiple overlapping stents etc. Most patients with HBR have complex coronary anatomy due to age, diabetes, and chronic renal sufficiency. The application of intravascular imaging has demonstrated clear short term and long-term data to improve TLR and MACE rates for all patients, including HBR.

Current Stent/Short DAPT trials for HBR-Intravascular Imaging NOT Mandated. Onyx One- Biolimus vs Resolute ZES, non-inferior with one month of DAPT, however high event rates *17% MACE, *1.5% ST-imaging NOT mandated! SENIOR – Biodegradable Polymer DES in > 75-year-old patients better than BMS (low rate of ST 0.5% in 1 year, but high CVA rate 2%). LEADERS FREE-DCS (Drug-Coated Stent) stent vs BMS (Bare Metal Stents) for 30 days in HBR (Heartbeat Rate), excluded highrisk patients. Xience 28/90 (open-label trial, imaging not mandated, very low rates of ST).

New Stent/Vessel Technology

High-Definition imaging is crucial with new technology and/or shorter DAPT therapy. Angioplasty BMS, DES, Bioresorbable Scaffolds (BRS). The movement toward using a shorter DAPT regimen. Challenge: Imaging is essential for use of BRS technology. First-

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

generation (bulky): Not as deliverable as metallic stents can oversize by 0.5mm only. Absorb III-3-year data concern* (higher TVMI and thrombosis rate). STOPDAPT2 (Japanese Trial) 1-month DAPT non-inferior to 12 months DAPT >95% of cases used Intracoronary imaging. The healing process after stent implantation is important in ascertaining that the DAPT can be stopped if healing has occurred.

Intravascular Plaque Imaging-Vulnerable Atherosclerotic Plaque

IVUS can be used as an imaging tool for assessing plaque morphology. The greyscale

is constructed by processing a backscatter signal. It can give many signs of vulnerability [101]. The various signs like positive vessel plaque burden, remodeling, spotty calcification, and presence of an echo lucent core, which represents a lipid-rich core. There is the limitation of the IVUS that it cannot tell us about the fibrous cap thickness but these limitations have been overcome by virtual histology IVUS (VH-IVUS). With VH-IVUS we can define plaque as having four components of fibrous fatty, necrotic and calcified. Thin cap fibroatheroma can also be differentiated by this method (Figure 18) [102].

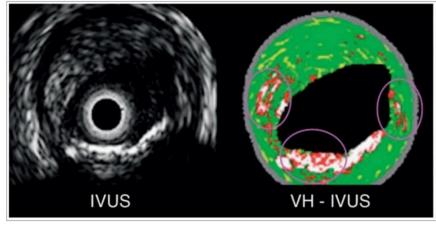


Figure 18: Virtual histology on IVUS imaging showing vulnerable plaque [102].

Validation of virtual histology was done against the histology studies which is having the specificity of 93%. The finding of TCFA by VH-IVUS core related to the risk of future events. When it is combined with other parameters like plaque burden and higher necrotic core, core related with future events in PROSPECT trial [103]. OCT is an imaging modality, which can have greater resolution and therefore can recognize features of vulnerability more accurately like plaque rupture, cap thickness, erosion, and thrombus. It can also detect subintimal lipid deposition. OCT also can quantitate the macrophage content of the cap [104].

In comparison to the IVUS, OCT can provide better imaging of the ruptured atherosclerotic plaque with visible intimal flap and mixed thrombus at the arrow (figure 19) [102].

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

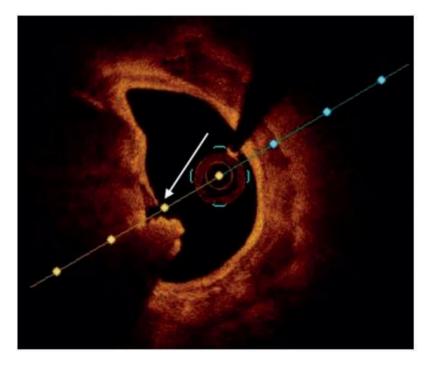


Figure 19: OCT showing ruptured atherosclerotic plaque with visible intimal flap and mixed thrombus at arrow [102].

Another imaging method is the near-Infrared Spectroscopy (NIRS) which used near-infra red-light specific absorption patterns by cholesterol molecules. This way it can detect and also can quantify the presence of lipid in plaque. It is mounted on IVUS and maps a picture called "Chemogram". It is found to be superior then IVUS alone to detect lipid cores [105]. There are reports of combining OCT with NIRS, which may further improve the accuracy of detection of lipid (Figure 20) [106,107].

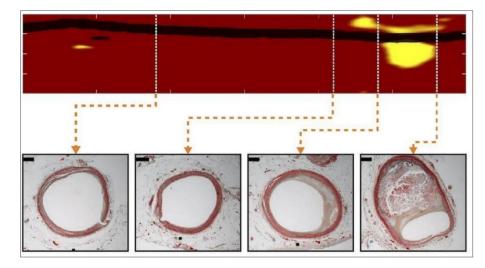


Figure 20: Intracoronary Imaging Backed in Hunt for Vulnerable Plaques with NIRS [107].

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article **Citation:** Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37. **DOI:** <u>https://doi.org/10.37191/Mapsci-JCCR-3(3)-066</u> The 14% cardiac events occur over four years among 900 patients in untreated benign nonflow-limiting lesions detected angiographically, as is reported in PROSPECT II trial [107]. The question is, how to treat these plaques? This is being addressed in FITTER and YELLOW III trials for PCKS9 inhibitors and local stenting in PREVENT trial [108-110]. The answer to treating nonflow-limiting lesions can depend upon the characteristic of the patient. It can vary according to the anatomy of the individual patient.

Also, the number of non-culprit lesions with vulnerable plaque could be accounted for the plaque composition can be important and the therapy can be a combination of different therapies tailored to different needs. In PROSPECT-II trials the lesions which were highly lipidic on NIRS and those who showed heavy plaque burden higher than 70% on IVUS and MLA of less than 4.0mm² were responsible for future events. Huge plaque burden was reported in such lesions with 7% MACE in each lesion followed for 4 years and patients who have both characteristics had a 13% risk of MACE. The analysis of this study had suggested that PCI on such vulnerable plaque was safe and effective also. However, the authors pointed out that unless these are studied in large, randomized trials the treatment of vulnerable plaques which are not ischemia producing remains controversial and whether to treat it with intensified pharmacotherapy or focal intervention remains to be seen [111].

Even limited imaging, however, appears tothprovide a glimpse into an individual patient'sfaunderlying atherosclerosis morphology. ThebeMody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

presence of one high-risk plaque implies the existence of others. What happens if these high-risk plaques do not cause mortality or MI? Plaque rupture and repair are frequently silent and repeated, resulting in lesion development and the requirement for revascularization rather than mortality or MI. Furthermore, serial intravascular imaging investigations have demonstrated that plaque shape can alter over time without inducing plaque rupture, particularly in stable patients taking high doses of statins. Finally, the stented lesions had a very low occurrence rate (2.6% over 2 years). Although no information regarding the stent implantation process was available, we believe the treatments were OCT-guided because the average 1-year event rate was identical to that reported in IVUS-XPL IVUS-optimized patients (Impact of Intravascular Ultrasound Guidance on Outcomes of Xience Prime Stents in Long Lesions) [112]. High risk of eventual ACS is associated with non-culprit plaques identified as both LRP and TCFA by the OCT imaging method at the lesion level. OCT may thus be beneficial in detection of vulnerable plaque [113].

Micro OCT

High-resolution imaging of the luminal microstructures of various biological tissues is offered by a new evolving imaging method known as Micro-Optical Coherence Tomography (µOCT) at both cellular and subcellular levels. A better understanding of various parameters such as coronary atherosclerosis natural history and healing of the vessel after the revascularization is facilitated by this technique. Initially, a bench-top microscopy system was used for

the implementation of this technology which has shown broad applications in the in-vivo and ex-vivo studies. Recently, intracoronary catheter and single fibre optic OCT probe have been developed with the objective of implementation of μOCT at the clinical level in an efficient way. Intravascular µOCT catheter imaging potential is demonstrated by the atherosclerotic rabbit aortae in vivo and human cadaver coronary arteries ex-vivo. Furthermore, this technique plays marked role in the development of coronary atherosclerotic lesions due to its strong potential of typing the leukocytes and macrophages at cellular and intracellular levels. [114,115].

There is a case report of a flexible endoscopic μ OCT probe that acquires three-dimensional images of the arterial microstructures via helical scanning in rabbits. It could image a cellular level feature with a rabbit artery with high-risk atheroma. In spite of various advantages, certain drawbacks such as reduced penetration depth due to its use at low wavelength and huge strain induced on data acquisition sensitivity by the huge amount of data collected in this technology are some of the drawbacks associated with it. This endoscopic μ OCT can be a useful tool for imaging CAD plaques and stent histology (figure 21) [16].

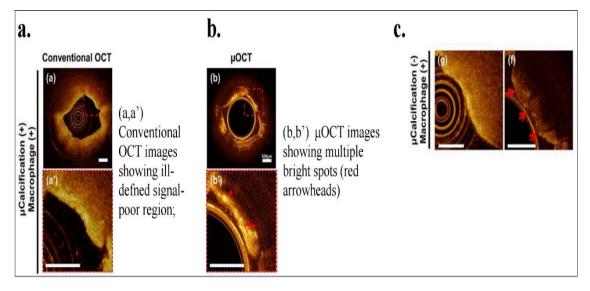


Figure 21: analogy between clinical OCT and µOCT of a vulnerable plaque with microcalcifcation [116].

Conclusion

This review article describes about the patients and lesions where imaging may be most beneficial, along with up-to-date evidence for the effect of intracoronary imaging on cardiovascular outcomes. The IVUS and OCT can be used interchangeably in clinical practice although one has

advantages and disadvantages over the others. Imaging is required in a wide array of the clinical spectrum including stent failure, LM disease, CTO & high bleeding risk patients and so on. Especially the usefulness of investigational tools like Micro-OCT and NIRS are evolving.

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article **Citation:** Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37. **DOI:** https://doi.org/10.37191/Mapsci-JCCR-3(3)-066

Acknowledgment

I thank Ms. Nikita and Mr. Rohit for assisting me to finalize the review article. Figures are edited by Jiwan Singh.

Author Contributions

The lead author of the review is Dr Rohit Mody. Dr Debabrata Dash, Dr Bhavya Mody, Dr Anand Reddy Maligireddy, Dr Annkit Agrawal, and Dr Lakshay Rastogi and Dr. Inderjeet Singh Monga had equal and substantial contributions in the formation of this review article. They were involved in conceptualization, data curation, formal analysis, resources, software, validation, visualization, writing-original draft, Writing, review & editing.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Ethical approval was not required since it is an accepted procedure.

Consent for Publication

Written consent has been obtained to publish the review article from the guardian. The consent copy is available with the authors and ready to be submitted if required.

References

- Park SJ, Kim YH, Park DW, Lee SW, Kim WJ, Suh J, et al. Impact of intravascular ultrasound guidance on longterm mortality in stenting for unprotected left main coronary artery stenosis. Circ Cardiovasc Interv. 2009;2(3):167-77. <u>PubMed | CrossRef</u>
- 2. Claessen BE, Henriques JP, Jaffer FA, Mehran R, Piek JJ, Dangas GD. Stent thrombosis: a clinical perspective. JACC Cardiovasc Interv. 2014;7(10):1081-92. <u>PubMed | CrossRef</u>
- 3. Imola F, Mallus MT, Ramazzotti V, Manzoli A, Pappalardo A, Di Giorgio A, et al. Safety and feasibility of frequency domain optical coherence tomography to guide decision making in percutaneous coronary intervention. EuroIntervention. 2010;6(5):575-81. <u>PubMed | CrossRef</u>
- 4. Kim JS, Hong MK, Ko YG, Choi D, Yoon JH, Choi SH, et al. Impact of intravascular ultrasound guidance on longterm clinical outcomes in patients treated with drug-eluting stent for bifurcation lesions: data from a Korean multicenter bifurcation registry. Am Heart J. 2011;161(1):180-7. <u>PubMed | CrossRef</u>
- 5. Kubo T, Shinke T, Okamura T, Hibi K, Nakazawa G, Morino Y, et al. Optical frequency domain imaging vs. intravascular ultrasound in percutaneous coronary intervention (opinion trial): one-year angiographic and clinical results. Eur Heart J. 2017;38(42):3139-47. <u>PubMed | CrossRef</u>
- 6. Mehran R, Dangas G, Abizaid AS, Mintz GS, Lansky AJ, Satler LF, et al. Angiographic patterns of in-stent restenosis: classification and implications for long-term outcome. Circulation. 1999;100(18):1872-8. <u>PubMed</u> | <u>CrossRef</u>
- 7. Batty JA, Subba S, Luke P, Gigi LW, Sinclair H, Kunadian V. Intracoronary imaging in the detection of vulnerable plaques. Curr Cardiol Rep. 2016;18(3):1-2. <u>PubMed | CrossRef</u>
- 8. Ali ZA, Maehara A, Généreux P, Shlofmitz RA, Fabbiocchi F, Nazif TM, et al. 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(10060):2618-28. <u>PubMed | CrossRef</u>
- 9. Kubo T, Shinke T, Okamura T, Hibi K, Nakazawa G, Morino Y, et al. Optical frequency domain imaging vs. intravascular ultrasound in percutaneous coronary intervention (opinion trial): one-year angiographic and clinical results. Eur Heart J. 2017;38(42):3139-47.PubMed | CrossRef

Mody R | Volume 3; Issue 3 (2022) | Mapsci-ICCR-3(3)-066 | Review Article

- 10. Tian J, Ren X, Vergallo R, Xing L, Yu H, Jia H, et al. Distinct morphological features of ruptured culprit plaque for acute coronary events compared to those with silent rupture and thin-cap fibroatheroma: a combined optical coherence tomography and intravascular ultrasound study. J Am Coll Cardiol. 2014;63(21):2209-16. PubMed | CrossRef
- Saia F, Lemos PA, Sianos G, Degertekin M, Lee CH, Arampatzis CA, et al. Effectiveness of sirolimus-eluting stent implantation for recurrent in-stent restenosis after brachytherapy. Am J Cardiol. 2003;92(2):200-3. <u>PubMed</u> | <u>CrossRef</u>
- 12. Mintz GS, Ali Z, Maehara A. Use of intracoronary imaging to guide optimal percutaneous coronary intervention procedures and outcomes. Heart. 2021;107(9):755-64. <u>PubMed | CrossRef</u>
- 13. Buccheri S, Franchina G, Romano S, Puglisi S, Venuti G, D'Arrigo P, et al. 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(24):2488-98. PubMed | CrossRef
- 14. Ali ZA, Karimi Galougahi K, Nazif T, Maehara A, Hardy MA, Cohen DJ, et al. 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(40):3090-5. <u>PubMed | CrossRef</u>
- 15. Escaned J, Collet C, Ryan N, Luigi De Maria G, Walsh S, Sabate M, et al. 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(42):3124-34. <u>PubMed | CrossRef</u>
- 16. Kim BK, Shin DH, Hong MK, Park HS, Rha SW, Mintz GS, et al. Clinical impact of intravascular ultrasoundguided chronic total occlusion intervention with zotarolimus-eluting versus biolimus-eluting stent implantation: Randomized study. Circ Cardiovasc Interv. 2015;8(7):e002592. <u>PubMed | CrossRef</u>
- 17. Räber L, Mintz GS, Koskinas KC, Johnson TW, Holm NR, Onuma Y, et al. 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. EuroIntervention. 2018;39(35):3281-300. <u>PubMed</u> | <u>CrossRef</u>
- Lawton JS, Tamis-Holland JE, Bangalore S, Bates ER, Beckie TM, Bischoff JM, et al. 2021 ACC/AHA/SCAI guideline for coronary artery revascularization: executive summary: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;79(2):197-215. <u>PubMed | CrossRef</u>
- 19. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, et al. 2018. ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J. 2019;40(2):87-165. <u>PubMed | CrossRef</u>
- 20. Lemos PA, Saia F, Ligthart JM, Arampatzis CA, Sianos G, Tanabe K, et al. Coronary restenosis after sirolimuseluting stent implantation: morphological description and mechanistic analysis from a consecutive series of cases. Circulation. 2003;108(3):257-60. <u>PubMed | CrossRef</u>
- 21. Van Beusekom HM, Saia F, Zindler JD, Lemos PA, Hoor SL, Van Leeuwen MA, et al. Drug-eluting stents show delayed healing: paclitaxel more pronounced than sirolimus. Eur Heart J. 2007;28(8):974-9. PubMed | CrossRef
- 22. Kimura T, Yokoi H, Nakagawa Y, Tamura T, Kaburagi S, Sawada Y, et al. Three-year follow-up after implantation of metallic coronary-artery stents. N Engl J Med. 1996;334(9):561-7. <u>PubMed | CrossRef</u>
- 23. Schatz RA, Palmaz JC, Tio FO, Garcia F, Garcia O, Reuter SR. Balloon-expandable intracoronary stents in the adult dog. Circulation. 1987;76(2):450-7. <u>PubMed | CrossRef</u>
- 24. Gonzalo N, Serruys PW, Okamura T, van Beusekom HM, Garcia-Garcia HM, van Soest G, et al. Optical coherence tomography patterns of stent restenosis. Am Heart J. 2009;158(2):284-93. <u>PubMed | CrossRef</u>
- 25. Kang SJ, Mintz GS, Akasaka T, Park DW, Lee JY, Kim WJ, et al. Optical coherence tomographic analysis of instent neoatherosclerosis after drug-eluting stent implantation. Circulation. 2011;123(25):2954-63. <u>PubMed</u> | <u>CrossRef</u>
- 26. Van Beusekom HM, Van der Giessen WJ, Van Suylen RJ, Bos E, Bosman F, Serruys PW. Histology after stenting of human saphenous vein bypass grafts: observations from surgically excised grafts 3 to 320 days after stent implantation. J Am Coll Cardiol. 1993;21(1):45-54. <u>PubMed | CrossRef</u>

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

Citation: Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37.

DOI: https://doi.org/10.37191/Mapsci-JCCR-3(3)-066

- 27. Kang SJ, Mintz GS, Akasaka T, Park DW, Lee JY, Kim WJ, et al. Optical coherence tomographic analysis of instent neoatherosclerosis after drug-eluting stent implantation. Circulation. 2011;123(25):2954-63. <u>PubMed</u> | <u>CrossRef</u>
- 28. Habara M, Terashima M, Nasu K, Kaneda H, Inoue K, Ito T, et al. Difference of tissue characteristics between early and very late restenosis lesions after bare-metal stent implantation: an optical coherence tomography study. Circ Cardiovasc Interv. 2011;4(3):232-8. <u>PubMed</u> | <u>CrossRef</u>
- 29. Kubo T, Imanishi T, Takarada S, Kuroi A, Ueno S, Yamano T, et al. Assessment of culprit lesion morphology in acute myocardial infarction: ability of optical coherence tomography compared with intravascular ultrasound and coronary angioscopy. J Am Coll Cardiol. 2007;50(10):933-9. <u>PubMed | CrossRef</u>
- 30. Rohit M, Debabrata D, Bhavya M. Optical Coherence Tomography Analysis of Des In-Stent Restenosis Presenting As Stable and Unstable Angina: A Comparison-A Case Series. Cardiol Vasc Res. 2021;5(2):1-4.
- 31. Hou J, Qi H, Zhang M, Meng L, Han Z, Yu B, et al. Pulmonary vascular changes in pulmonary hypertension: optical coherence tomography findings. Circ Cardiovasc Imaging. 2010;3(3):344-5. <u>PubMed | CrossRef</u>
- 32. Tahara N, Imaizumi T, Virmani R, Narula J. Clinical feasibility of molecular imaging of plaque inflammation in atherosclerosis. J Nucl Med. 2009;50(3):331-4. <u>PubMed | CrossRef</u>
- 33. Leesar MA, Hage FG. IVUS Guidance on Optimal Stent Deployment: New Insights and Perspectives. JACC Cardiovasc Interv. 2022;15(2):217-9. <u>PubMed | CrossRef</u>
- 34. De Jaegere P, Mudra H, Figulla H, Almagor Y, Doucet S, Penn I, et al. Intravascular ultrasound-guided optimized stent deployment: immediate and 6 months clinical and angiographic results from the Multicenter Ultrasound Stenting in Coronaries Study (MUSIC Study). Eur Heart J. 1998;19(8):1214-23. <u>PubMed | CrossRef</u>
- 35. Song HG, Kang SJ, Ahn JM, Kim WJ, Lee JY, Park DW, et al. 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(6):873-8. <u>PubMed | CrossRef</u>
- 36. Choi SY, Maehara A, Cristea E, Witzenbichler B, Guagliumi G, Brodie B, et al. 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(4):455-60. PubMed | CrossRef
- 37. Chamié D, Bezerra HG, Attizzani GF, Yamamoto H, Kanaya T, Stefano GT, et al. Incidence, predictors, morphological characteristics, and clinical outcomes of stent edge dissections detected by optical coherence tomography. JACC Cardiovasc Interv. 2013;6(8):800-13. PubMed | CrossRef
- 38. Prati F, Di Vito L, Biondi-Zoccai G, Occhipinti M, La Manna A, Tamburino C, et al. 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(7):823-9. PubMed | CrossRef
- 39. Liu X, Doi H, Maehara A, Mintz GS, de Ribamar Costa J, Sano K, et al. A volumetric intravascular ultrasound comparison of early drug-eluting stent thrombosis versus restenosis. JACC Cardiovasc Interv. 2009;2(5):428-34. PubMed | CrossRef
- 40. Kang SJ, Ahn JM, Song H, Kim WJ, Lee JY, Park DW, et al. 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(6):562-9. <u>PubMed</u> | <u>CrossRef</u>
- 41. Doi H, Maehara A, Mintz GS, Yu A, Wang H, Mandinov L, et al. 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. JACC Cardiovasc Interv. 2009;2(12):1269-75. <u>PubMed | CrossRef</u>
- 42. Song HG, Kang SJ, Ahn JM, Kim WJ, Lee JY, Park DW, et al. Intravascular ultrasound assessment of optimal stent area to prevent in-stent restenosis after zotarolimus, everolimus, and sirolimus-eluting stent implantation. Catheter Cardiovasc Interv Catheter Cardiovasc Interv. 2014;83(6):873-8. <u>PubMed | CrossRef</u>
- 43. Choi SY, Witzenbichler B, Maehara A, Lansky AJ, Guagliumi G, Brodie B, et al. Intravascular ultrasound findings of early stent thrombosis after primary percutaneous intervention in acute myocardial infarction: a Harmonizing Mody R | Volume 3; Issue 3 (2022) | Mapsci-ICCR-3(3)-066 | Review Article

Citation: Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37.

DOI: https://doi.org/10.37191/Mapsci-JCCR-3(3)-066

Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) substudy. Am J Cardiol. 2011;4(3):239-47. <u>PubMed | CrossRef</u>

- 44. Fujii K, Carlier SG, Mintz GS, Yang YM, Moussa I, Weisz G, et al. Stent underexpansion and residual reference segment stenosis are related to stent thrombosis after sirolimus-eluting stent implantation: an intravascular ultrasound study. J Am Coll Cardiol. 2005;45(7):995-8. <u>PubMed</u> | <u>CrossRef</u>
- 45. Choi SY, Witzenbichler B, Maehara A, Lansky AJ, Guagliumi G, Brodie B, et al. 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(3):239-47. <u>PubMed | CrossRef</u>
- 46. Soeda T, Uemura S, Park SJ, Jang Y, Lee S, Cho JM, et al. Incidence and clinical significance of poststent optical coherence tomography findings: one-year follow-up study from a multicenter registry. Circulation. 2015;132(11):1020-9. PubMed | CrossRef
- 47. Prati F, Romagnoli E, Burzotta F, Limbruno U, Gatto L, La Manna A, et al. Clinical impact of OCT findings during PCI: the CLI-OPCI II study. JACC Cardiovasc Imaging. 2015;8(11):1297-305. <u>PubMed | CrossRef</u>
- 48. Ali ZA, Maehara A, Généreux P, Shlofmitz RA, Fabbiocchi F, Nazif TM, et al. 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(10060):2618-28. <u>PubMed | CrossRef</u>
- 49. Kobayashi N, Mintz GS, Witzenbichler B, Metzger DC, Rinaldi MJ, Duffy PL, et al. Prevalence, features, and prognostic importance of edge dissection after drug-eluting stent implantation: an adapt-des intravascular ultrasound substudy. Circ Cardiovasc Interv. 2016;9(7):e003553. PubMed | CrossRef
- 50. Zhang J, Gao X, Kan J, Ge Z, Han L, Lu S, et al. Intravascular ultrasound versus angiography-guided drug-eluting stent implantation: the ultimate trial. J Am Coll Cardiol. 2018;72(24):3126-37. <u>PubMed | CrossRef</u>
- 51. Wang B, Mintz GS, Witzenbichler B, Souza CF, Metzger DC, Rinaldi MJ, et al. Predictors and long-term clinical impact of acute stent malapposition: an assessment of Dual Antiplatelet Therapy with Drug-Eluting Stents (ADAPT-DES) intravascular ultrasound substudy. J Am Heart Assoc. 2016;5(12):e004438. <u>PubMed | CrossRef</u>
- 52. De Ribamar Costa Jr J, Mintz GS, Carlier SG, Costa RA, Fujii K, Sano K, et al. Intravascular ultrasonic assessment of stent diameters derived from manufacturer's compliance charts. Am J Cardiol. 2005;96(1):74-8. <u>PubMed</u> | <u>CrossRef</u>
- 53. Hong SJ, Kim BK, Shin DH, Nam CM, Kim JS, Ko YG, et al. Effect of intravascular ultrasound-guided vs angiography-guided everolimus-eluting stent implantation: the IVUS-XPL randomized clinical trial. JAMA. 2015;314(20):2155-63. PubMed | CrossRef
- 54. Prati F, Romagnoli E, Gatto L, La Manna A, Burzotta F, Limbruno U, et al. Clinical impact of suboptimal stenting and residual intrastent plaque/thrombus protrusion in patients with acute coronary syndrome: The CLI-OPCI ACS Substudy (Centro per la Lotta Contro L'Infarto-Optimization of Percutaneous Coronary Intervention in Acute Coronary Syndrome). Circ Cardiovasc Interv. 2016;9(12):e003726. <u>PubMed | CrossRef</u>
- 55. Kini AS, Motoyama S, Vengrenyuk Y, Feig JE, Pena J, Baber U, et al. Multimodality intravascular imaging to predict periprocedural myocardial infarction during percutaneous coronary intervention. JACC Cardiovasc Interv. 2015;8(7):937-45. <u>PubMed | CrossRef</u>
- 56. Gao XF, Wang ZM, Wang F, Gu Y, Ge Z, Kong XQ, et al. Intravascular ultrasound guidance reduces cardiac death and coronary revascularization in patients undergoing drug-eluting stent implantation: results from a metaanalysis of 9 randomized trials and 4724 patients. Int J Cardiovasc Imaging. 2019;35(2):239-47. <u>PubMed</u> | <u>CrossRef</u>
- 57. Otake H, Kubo T, Shinke T, Hibi K, Tanaka S, Ishida M, et al. OPtical frequency domain imaging vs. Intravascular ultrasound in percutaneous coronary Intervention in patients with Acute Coronary Syndrome: Study protocol for a randomized controlled trial. Eur Heart J. 2020;76(3):317-21. <u>PubMed | CrossRef</u>
- 58. Stamper D, Weissman NJ, Brezinski M. Plaque characterization with optical coherence tomography. J Am Coll Cardiol. 2006;47(8S):C69-79. PubMed | CrossRef

- Fujino A, Mintz GS, Lee T, Hoshino M, Usui E, Kanaji Y, et al. Predictors of calcium fracture derived from balloon angioplasty and its effect on stent expansion assessed by optical coherence tomography. JACC Cardiovasc Interv. 2018;11(10):1015-7. <u>PubMed</u> | <u>CrossRef</u>
- 60. Fujino A, Mintz GS, Matsumura M, Lee T, Kim SY, Hoshino M, et al. A new optical coherence tomography-based calcium scoring system to predict stent underexpansion. EuroIntervention. 2018;13(18):e2182-9. <u>PubMed</u> | <u>CrossRef</u>
- 61. Kerensky RA, Wade M, Deedwania P, Boden WE, Pepine CJ. Veterans Affairs Non-Q-Wave Infarction Strategies in-Hospital (VANQWISH) Trial Investigators. Revisiting the culprit lesion in non-Q-wave myocardial infarction: results from the VANQWISH trial angiographic core laboratory. J Am Coll Cardiol. 2002;39(9):1456-63. <u>PubMed</u> | <u>CrossRef</u>
- 62. Prati F, Uemura S, Souteyrand G, Virmani R, Motreff P, Di Vito L, et al. OCT-based diagnosis and management of Stemi associated with intact fibrous cap. JACC Cardiovasc Imaging. 2013;6(3):283-7. <u>PubMed | CrossRef</u>
- 63. Jia H, Dai J, Hou J, Xing L, Ma L, Liu H, et al. Effective anti-thrombotic therapy without stenting: intravascular optical coherence tomography-based management in plaque erosion (the EROSION study). Eur Heart J. 2017;38(11):792-800. PubMed | CrossRef
- 64. Hu S, Zhu Y, Zhang Y, Dai J, Li L, Dauerman H, et al. Management and outcome of patients with acute coronary syndrome caused by plaque rupture versus plaque erosion: an intravascular optical coherence tomography study. J Am Heart Assoc. 2017;6(3):e004730. <u>PubMed</u> | <u>CrossRef</u>
- 65. Kim N, Lee JH, Jang SY, Bae MH, Yang DH, Park HS, et al. Intravascular modality-guided versus angiographyguided percutaneous coronary intervention in acute myocardial infarction. Catheter Cardiovasc Interv. 2020;95(4):696-703. <u>PubMed | CrossRef</u>
- 66. Jasti V, Ivan E, Yalamanchili V, Wongpraparut N, Leesar MA. Correlations between fractional flow reserve and intravascular ultrasound in patients with an ambiguous left main coronary artery stenosis. Circulation. 2004;110(18):2831-6. <u>PubMed | CrossRef</u>
- 67. Oviedo C, Maehara A, Mintz GS, Araki H, Choi SY, Tsujita K, et al. Intravascular ultrasound classification of plaque distribution in left main coronary artery bifurcations: where is the plaque really located? Circ Cardiovasc Interv. 2010;3(2):105-12. PubMed | CrossRef
- 68. Zhang J, Gao X, Kan J, Ge Z, Han L, Lu S, et al. Intravascular ultrasound versus angiography-guided drug-eluting stent implantation: the ultimate trial. J Am Coll Cardiol. 2018;72(24):3126-37. <u>PubMed | CrossRef</u>
- 69. Oviedo C, Maehara A, Mintz GS, Araki H, Choi SY, Tsujita K, et al. Intravascular ultrasound classification of plaque distribution in left main coronary artery bifurcations: where is the plaque really located? Circ Cardiovasc Interv. 2010;3(2):105-12. PubMed | CrossRef
- 70. Mercado N, Moe TG, Pieper M, House JA, Dolla WJ, Seifert L, et al. Tissue characterisation of atherosclerotic plaque in the left main: an in vivo intravascular ultrasound radiofrequency data analysis. EuroIntervention. 2011;7(3):347-52. PubMed | CrossRef
- Hendry C, Fraser D, Eichhofer J, Mamas MA, Fath-Ordoubadi F, El-Omar M, et al. Coronary perforation in the drug-eluting stent era: incidence, risk factors, management and outcome: the UK experience. EuroIntervention. 2012;8(1):79-86. <u>PubMed | CrossRef</u>
- 72. Barbato E, Carrié D, Dardas P, Fajadet J, Gaul G, Haude M, et al. European expert consensus on rotational atherectomy. EuroIntervention. 2015;11(1):30-6. <u>PubMed | CrossRef</u>
- 73. Mintz GS, Popma JJ, Pichard AD, Kent KM, Satler LF, Chuang YC, et al. Patterns of calcification in coronary artery disease: a statistical analysis of intravascular ultrasound and coronary angiography in 1155 lesions. Circulation. 1995;91(7):1959-65. PubMed | CrossRef
- 74. Mintz GS, Lefevre T, Lassen JF, Testa L, Pan M, Singh J, et al. Intravascular ultrasound in the evaluation and treatment of left main coronary artery disease: a consensus statement from the European Bifurcation Club. EuroIntervention. 2018;14(4):e467-74. PubMed | CrossRef
- 75. Kang SJ, Ahn JM, Kim WJ, Lee JY, Park DW, Lee SW, et al. Functional and morphological assessment of side branch after left main coronary artery bifurcation stenting with cross-over technique. Catheter Cardiovasc Interv. 2014;83(4):545-52. PubMed | CrossRef

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

- 76. Takagi K, Nagoshi R, Kim BK, Kim W, Kinoshita Y, Shite J, et al. Efficacy of coronary imaging on bifurcation intervention. Cardiovascular Intervention and Therapeutics. 2021;36(1):54-66. <u>PubMed | CrossRef</u>
- 77. Kang SJ, Ahn JM, Song H, Kim WJ, Lee JY, Park DW, et al. 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(6):562-9. <u>PubMed | CrossRef</u>
- 78. R\u00e4ber L, Mintz GS, Koskinas KC, Johnson TW, Holm NR, Onuma Y, et al. 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. Eur Heart J. 2018;39(35):3281-300. PubMed | CrossRef
- 79. Kobayashi N, Mintz GS, Witzenbichler B, Metzger DC, Rinaldi MJ, Duffy PL, et al. Prevalence, features, and prognostic importance of edge dissection after drug-eluting stent implantation: an ADAPT-DES intravascular ultrasound substudy. Circ Cardiovasc Interv. 2016;9(7):e003553. <u>PubMed | CrossRef</u>
- 80. Sato K, Naganuma T, Costopoulos C, Takebayashi H, Goto K, Miyazaki T, et al. Calcification analysis by intravascular ultrasound to define a predictor of left circumflex narrowing after cross-over stenting for unprotected left main bifurcation lesions. Cardiovasc Revasc Med. 2014;15(2):80-5. <u>PubMed | CrossRef</u>
- Medina A, Martín P, de Lezo JS, Amador C, de Lezo JS, Pan M, et al. Vulnerable carina anatomy and ostial lesions in the left anterior descending coronary artery after floating-stent treatment. Rev Esp Cardiol. 2009;62(11):1240-9. <u>PubMed | CrossRef</u>
- 82. Kubo T, Akasaka T, Shite J, Suzuki T, Uemura S, Yu B, et al. OCT compared with IVUS in a coronary lesion assessment: the OPUS-CLASS study. JACC Cardiovasc Imaging. 2013;6(10):1095-104. <u>PubMed | CrossRef</u>
- 83. Lee HW, Choi JH, Jang HY, Ahn JH, Kim JH, Park JS, et al. Benefit of IVUS-guided PCI in diabetic patients presented with acute myocardial infarction-from Korea acute myocardial infarction registry. Eur Heart J. 2013;34(1). <u>CrossRef</u>
- 84. Ahn JM, Kang SJ, Yoon SH, Park HW, Kang SM, Lee JY, et al. 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(8):1338-47. <u>PubMed | CrossRef</u>
- 85. Groenland FT, Neleman T, Kakar H, Scoccia A, des Plantes AC, Clephas PR, et al. Intravascular ultrasoundguided versus coronary angiography-guided percutaneous coronary intervention in patients with acute myocardial infarction: A systematic review and meta-analysis. Int J Cardiol. 2022;353:35-42. <u>PubMed | CrossRef</u>
- 86. Yang RR, Lv YH, Guo C, Li M, Zhang MB, Wang ZL, et al. Intravascular ultrasound-guided percutaneous coronary intervention for patients with coronary bifurcation lesions: A systematic review and meta-analysis. Medicine. 2020;99(37):e20798. <u>PubMed</u> | <u>CrossRef</u>
- 87. Darmoch F, Alraies MC, Al-Khadra Y, Moussa Pacha H, Pinto DS, Osborn EA. Intravascular ultrasound imagingguided versus coronary angiography-guided percutaneous coronary intervention: a systematic review and metaanalysis. J Am Heart Assoc. 2020;9(5):e013678. <u>PubMed</u> | <u>CrossRef</u>
- 88. Hong SJ, Kim BK, Shin DH, Nam CM, Kim JS, Ko YG, et al. Effect of intravascular ultrasound-guided vs angiography-guided everolimus-eluting stent implantation: the IVUS-XPL randomized clinical trial. JAMA. 2015;314(20):2155-63. PubMed | CrossRef
- 89. Chieffo A, Latib A, Caussin C, Presbitero P, Galli S, Menozzi A, Varbella F, et al. 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(1):65-72. <u>PubMed | CrossRef</u>
- 90. Prati F, Romagnoli E, Gatto L, La Manna A, Burzotta F, Ozaki Y, et al. Relationship between c oronary pl aque morphology of the left anter i or descending artery and 12 m onths clinic al outcome: the clima study. Eur Heart J. 2020;41(3):383-91. <u>PubMed | CrossRef</u>
- 91. Prati F, Gatto L, Romagnoli E, Limbruno U, Fineschi M, Marco V, et al. In vivo vulnerability grading system of plaques causing acute coronary syndromes: an intravascular imaging study. Int J Cardiol. 2018;269:350-5. <u>PubMed | CrossRef</u>
- 92. Naghavi M, Libby P, Falk E, Casscells SW, Litovsky S, Rumberger J, et al. From vulnerable plaque to vulnerable patient: a call for new definitions and risk assessment strategies: Part I. Circulation. 2003;108(14):1664-72. <u>PubMed | CrossRef</u>

Mody R | Volume 3; Issue 3 (2022) | Mapsci-JCCR-3(3)-066 | Review Article

Citation: Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37.

DOI: https://doi.org/10.37191/Mapsci-JCCR-3(3)-066

- 93. Kedhi E, Berta B, Roleder T, Hermanides RS, Fabris E, IJsselmuiden AJ, et al. Thin-cap fibroatheroma predicts clinical events in diabetic patients with normal fractional flow reserve: the combine oct-ffr trial. Eur Heart J. 2021;42(45):4671-9. <u>PubMed | CrossRef</u>
- 94. Mariani J, Guedes C, Soares P, Zalc S, Campos CM, Lopes AC, et al. 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(11):1287-93. PubMed | CrossRef
- 95. Ali ZA, Karimi Galougahi K, Nazif T, Maehara A, Hardy MA, Cohen DJ, et al. 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(40):3090-5. <u>PubMed | CrossRef</u>
- 96. Gore AK, Shlofmitz E, Karimi Galougahi K, Petrossian G, Jeremias A, Sosa FA, et al. Prospective comparison between saline and radiocontrast for intracoronary imaging with optical coherence tomography. JACC Cardiovasc Imaging. 2020;13(9):2060-2. <u>PubMed | CrossRef</u>
- 97. Galassi AR, Sumitsuji S, Boukhris M, Brilakis ES, Di Mario C, Garbo R, et al. Utility of intravascular ultrasound in percutaneous revascularization of chronic total occlusions: an overview. JACC Cardiovasc Interv. 2016;9(19):1979-91. <u>PubMed | CrossRef</u>
- 98. Kim BK, Shin DH, Hong MK, Park HS, Rha SW, Mintz GS, et al. Clinical impact of intravascular ultrasoundguided chronic total occlusion intervention with zotarolimus-eluting versus biolimus-eluting stent implantation: Randomized study. Circ Cardiovasc Interv. 2015;8(7):e002592. <u>PubMed</u> | <u>CrossRef</u>
- 99. Räber L, Mintz GS, Koskinas KC, Johnson TW, Holm NR, Onuma Y, et al. 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. EuroIntervention. 2018;39(35):3281-300. <u>PubMed</u> | <u>CrossRef</u>
- 100. Adriaenssens T, Joner M, Godschalk TC, Malik N, Alfonso F, Xhepa E, et al. Optical coherence tomography findings in patients with coronary stent thrombosis: a report of the Prestige Consortium (Prevention of Late Stent Thrombosis by an Interdisciplinary Global European Effort). Circulation. 2017;136(11):1007-21. <u>PubMed</u> | <u>CrossRef</u>
- 101. Kotani JI, Mintz GS, Castagna MT, Pinnow E, Berzingi CO, Bui AB, et al. Intravascular ultrasound analysis of infarct-related and non-infarct-related arteries in patients who presented with an acute myocardial infarction. Circulation. 2003;107(23):2889-93. <u>PubMed | CrossRef</u>
- 102. Spacek M, Zemanek D, Hutyra M, Sluka M, Taborsky M. Vulnerable atherosclerotic plaque-a review of current concepts and advanced imaging. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2018;162(1). <u>PubMed</u> | <u>CrossRef</u>
- 103. Stone GW, Maehara A, Lansky AJ, De Bruyne B, Cristea E, Mintz GS, et al. A prospective natural-history study of coronary atherosclerosis. N Engl J Med. 2011;364(3):226-35. <u>PubMed | CrossRef</u>
- 104. Rathore S, Terashima M, Matsuo H, Kinoshita Y, Kimura M, Tsuchikane E, et al. Association of coronary plaque composition and arterial remodelling: a optical coherence tomography study. Atherosclerosis. 2012;221(2):405-15. PubMed | CrossRef
- 105. Kang SJ, Mintz GS, Pu J, Sum ST, Madden SP, Burke AP, et al. Combined IVUS and NIRS detection of fibroatheromas: histopathological validation in human coronary arteries. JACC Cardiovasc Imaging. 2015;8(2):184-94. <u>PubMed | CrossRef</u>
- 106. Fard AM, Vacas-Jacques P, Hamidi E, Wang H, Carruth RW, Gardecki JA, et al. Optical coherence tomographynear infrared spectroscopy system and catheter for intravascular imaging. Optics express. 2013;21(25):30849-58. <u>PubMed | CrossRef</u>
- 107. Erlinge D, Maehara A, Ben-Yehuda O, Bøtker HE, Maeng M, Kjøller-Hansen L, et al. Identification of vulnerable plaques and patients by intracoronary near-infrared spectroscopy and ultrasound (prospect II): a prospective natural history study. Lancet. 2021;397(10278):985-95. <u>PubMed | CrossRef</u>

Citation: Mody R, Dash D, Mody B, Maligireddy AR, Agarwal A, Rastogi L, Monga IS. Intracoronary Imaging-Can It Make Difference in State of the Art PCI? J Cardiol Cardiovasc Res. 2022;3(3):1-37. DOI: https://doi.org/10.37191/Mapsci-JCCR-3(3)-066

- 108. Robert Jan van Geuns, MD, PhD Functional Improvement of Coronary Artery Narrowing by Cholesterol Reduction with a PCSK9 Antibody (fitter) Clinical Trials. Gov identifier (NCT number): NCT04141579. Study ongoing.
- 109. Annapoorna Kini, MD, Effect of Evolocumab on Coronary Plaque Characteristics (yellow III) Clinical Trials. Gov Identifier: NCT04710368. Study ongoing.
- 110. Gregg Stone, MD. The Preventive Coronary Intervention on Stenosis with Functionally Insignificant Vulnerable Plaque (prevent) Clinical Trials. Gov Identifier: NCT02316886. Study ongoing.
- 111. Erlinge D, Maehara A, Ben-Yehuda O, Bøtker HE, Maeng M, Kjøller-Hansen L, et al. Identification of vulnerable plaques and patients by intracoronary near-infrared spectroscopy and ultrasound (prospect II): a prospective natural history study. Lancet. 2021;397(10278):985-95. <u>PubMed | CrossRef</u>
- 112. Mintz GS. Predicting the vulnerable patient using intravascular imaging. J Am Coll Cardiol. 2017;69(20):2514-6. <u>PubMed | CrossRef</u>
- 113. Kubo T, Ino Y, Mintz GS, Shiono Y, Shimamura K, Takahata M, et al. Optical coherence tomography detection of vulnerable plaques at high risk of developing acute coronary syndrome. Eur Heart J Cardiovasc Imaging. 2021;22(12):1376-84. <u>PubMed | CrossRef</u>
- 114. Liu L, Gardecki JA, Nadkarni SK, Toussaint JD, Yagi Y, Bouma BE, et al. Imaging the subcellular structure of human coronary atherosclerosis using micro-optical coherence tomography. Nat Med. 2011;17(8):1010-4. <u>PubMed</u> | <u>CrossRef</u>
- 115. Chinetti-Gbaguidi G, Colin S, Staels B. Macrophage subsets in atherosclerosis. Nat Rev Cardiol. 2015;12(1):10-7. <u>PubMed | CrossRef</u>
- 116. Kim J, Kim S, Song JW, Kim HJ, Lee MW, Han J, et al. Flexible endoscopic micro-optical coherence tomography for three-dimensional imaging of the arterial microstructure. Sci Rep. 2020;10(1):1-1. <u>PubMed | CrossRef</u>