



A Vision Of Percutaneous Coronary Revascularisation In 2021: How to take advantage of intra-coronary imaging to perform more effective PCI

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Abstract

The use of intracoronary imaging with intravascular ultrasound (IVUS) or optical coherence tomography (OCT) can define vessel architecture and has an established role in guidance and optimisation of percutaneous coronary intervention. Additionally intracoronary imaging has an emerging role in diagnosis, afforded by the ability to depict vessel wall characteristics not seen on angiography alone. Use of intracoronary imaging is recommended by international consensus guidelines from the European Society of Cardiology and two recent expert consensus position statements from the European Association of Percutaneous Coronary Interventions (EAPCI). However, uptake in contemporary practice in the United Kingdom appears to lag behind these recommendations. Imaging is particularly advantageous in complex coronary lesions (such as left main stem coronary artery, bifurcation, or heavily calcified lesions) and in complex patients (acute presentations, atypical presentations, and renal dysfunction). Stent detail to the level of individual struts can be appreciated with intracoronary imaging, which facilitates appropriate stent selection and optimisation of the final stent result. We highlight specific subgroups that benefit from an imaging guided approach to percutaneous coronary intervention. We review the evidence and the role of intracoronary imaging and highlight specific subgroups that show particular benefit from imaging guided percutaneous coronary intervention.

Keywords

Cardiovascular imaging agents/techniques, diagnostic Testing, cardiology, acute myocardial infarction, etiology, cardiology, coronary imaging: angiography/ultrasound/Doppler/CC, diagnostic, testing, cardiology, catheter-based coronary interventions: stents, treatment, cardiology

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Introduction

Invasive coronary angiography remains the gold standard for assessment of coronary artery disease, however it must be acknowledged that the luminal imaging obtained does not define the vessel architecture. The use of intracoronary imaging with IVUS or OCT can provide this additional detail and hence influence treatment decisions, and enhance patient outcomes. Two recent expert consensus position statements from the European Association of Percutaneous Coronary Interventions (EAPCI) outline the role of imaging, firstly in guidance and optimisation of PCI, and secondly in an emerging role of diagnosis in acute coronary syndrome (ACS) and where angiography is ambiguous.^{1,2}

stent results in selected patients. IVUS is recommended to assess lesion severity in left main (LM) coronary artery and to optimise unprotected LM intervention (both Ila B recommendations). Assessment with IVUS or OCT for stent failure also carries a Ila B recommendation.³

In contemporary UK practice the utilisation of intracoronary imaging is observed to lag behind these recommendations, with British Cardiovascular Intervention Society (BCIS) data from 2017–18 demonstrating IVUS use in 8.3% and OCT in just 2.7% of all PCI cases. These rates appear to have plateaued over the last 3 years for which data is available. World-wide there is a vast regional disparity in use, with the highest uptake in Asia, specifically Japan.

Guidelines

Current European Society of Cardiology guidelines recommend IVUS or OCT (Ila B recommendation) to optimise

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Interestingly intra-coronary imaging is more frequently utilised by more experienced operators, particularly those with over 10years experience,⁴ this may reflect an increased awareness of the limitations of angiographic assessment and concerns regarding adequate stent optimisation.

When to use imaging

Complex lesions such as diffuse disease, chronic total occlusions, heavily calcified vessels and bifurcations (particularly the left main stem) benefit from an image-guided approach.¹ Similarly, more complex patient subsets such as ACS presentation, significant renal dysfunction or those with unusual/atypical presentations benefit from enhanced diagnostic ability and optimisation of intervention to minimise the risk of stent failure.² Routine imaging in simple lesions and stable clinical presentations does not provide a clear benefit.

Expert consensus recommends the use of imaging 'upfront' to fully assess the vessel and lesion characteristics prior to stent implantation.² This approach assists in planning the PCI strategy, informs the need for additional lesion preparation or adjunctive treatment, and guides stent selection and placement. The Iliumien I study demonstrated that the combined impact of treatment modification prompted by pre-PCI imaging and image-guided stent optimisation dramatically impacted on procedural/patient outcomes.⁵

Which modality - OCT or IVUS?

IVUS has been available in clinical practice since the 1990s and consequently has achieved greater penetration worldwide than OCT, first commercially available in the late 2000s. The major limitations to adoption of intravascular imaging are cost, extended procedural time and a lack of experience.⁴

Familiarity and availability are most likely to dictate selection of imaging modality; however, it is important to acknowledge that IVUS & OCT have unique capabilities and limitations.

OCT has approximately ten times superior resolution compared with IVUS, so is suited to detailed assessment of lesion characteristics less visible by IVUS. Strut-level detail and automated 3D rendering make OCT the modality of choice for stent visualisation. Compared with IVUS, OCT image acquisition is faster and interpretation is aided by reliable automated analysis of lumen contour. However, image generation by near-infrared light requires blood clearance with contrast injection, limiting the use of OCT in renal insufficiency, aorto-ostial lesions and traumatised vessels at risk of hydraulic dissection.

Despite the lower resolution provided by IVUS, compared with OCT, it offers a greater depth of vessel penetration. Consequently, IVUS provides more accurate assessment of deeper vessel structures, such as the external elastic membrane, delineating vessel size and plaque burden. IVUS is preferred in larger vessels (>5mm) and aorto-ostial lesions as there is no requirement for blood clearance. This makes IVUS well suited to LM lesions, additionally, evidence supports the use of IVUS derived lumen measurements as a marker of severity,² so IVUS can provide a comprehensive anatomical and haemodynamic assessment and guide optimal LM treatment. IVUS is also preferred for CTO lesions and renal insufficiency as there is no reliance on contrast injection. The development of High Definition IVUS allows improved spatial resolution combined with imaging depth. Figure 1 demonstrates comparative images with IVUS and OCT.

Evidence - IVUS

Superiority of IVUS guided PCI over angiography alone has been confirmed in several meta-analyses driven by a

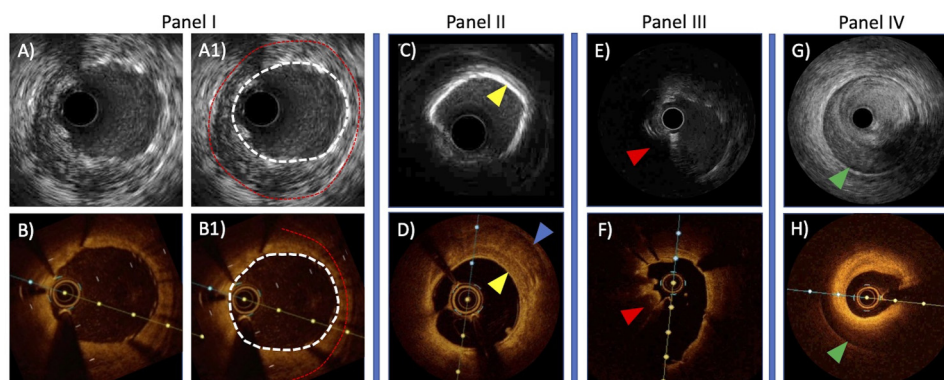


Figure 1. Comparative images using IVUS & OCT panel I: IVUS (A & A1) and OCT (B & B1) demonstrating stented lumen (white dashes) and external elastic membrane contours (red dashes); panel II: IVUS (C) and OCT (D) demonstrating calcification (yellow arrow) with signal loss behind on IVUS, and deep calcific border detectable on OCT (blue arrow); panel III: acute stent thrombosis on IVUS (E) and OCT (F) with red thrombus visible (red arrow); panel IV: haematoma (Green arrow) following stent edge dissection on IVUS (G) and OCT (H).

reduction in MACE and target lesion revascularisation.^{6,7} The most pronounced benefit is seen in ACS and complex lesions (LM, bifurcation, CTO or long lesions).⁸ The most recent meta-analysis suggests reduced cardiac mortality with IVUS guided-PCI (49% relative risk reduction).⁹

The ULTIMATE trial randomised all-comers to IVUS guided versus angiography guided PCI, resulting in a significant reduction in target vessel failure (TVF) at 12 months with IVUS.¹⁰ IVUS criteria for optimal stenting required a minimal stent area >5mm², plaque burden within 5mm of stent edge <50%, and avoidance of medial dissection extending >3mm. TVF included cardiac death, target-vessel MI and clinically-driven target vessel revascularisation. The subset who achieved the pre-specified optimal criteria had an even greater improvement in outcome and the positive results of this study have recently been reported out to 3 years.¹¹ This trial marks a significant step towards routine IVUS use in a real-world cohort.

Evidence - OCT

There are relatively few studies exploring the use of OCT-guided PCI, and no randomised control trials with clinical outcome, although two such trials are ongoing.^{12,13} Registry data suggests a reduction in MACE and cardiac death,¹⁴ and observational data suggests a larger minimum lumen diameter (MLD) and fewer stents used with OCT guided PCI. One randomised trial in NSTEMI-ACS demonstrated higher post-procedure FFR with OCT, driven by improved stent expansion.¹⁵

The randomised Iliumien III study requires more nuanced interpretation, as OCT failed to reach superiority over angiography with respect to minimum stent area (MSA) when PCI was undertaken by experienced operators in relatively simple lesions.¹⁵ However, OCT-guided intervention using an EEM sizing algorithm provided an MSA which was non-inferior to IVUS, and facilitated enhanced detection of acute stent complications including dissection and malapposition, owing to increased axial resolution. The clinical relevance of detection of dissection and malapposition is not yet clear but it is hoped that ongoing studies will provide greater clarity. The Iliumien IV study has recently completed recruitment, enrolling more complex patients and lesions, with greater potential for benefit from an OCT-guided approach to PCI compared against angiographic guidance alone.¹²

Trials incorporating OCT and IVUS suggest that OCT is non-inferior to IVUS both in terms of acute procedural result and clinical outcomes.^{16,17} The favourable clinical outcome data that exists for IVUS is therefore likely applicable to OCT, although RCT data is needed to confirm this view. The expert consensus is that OCT and IVUS are equivalent in guiding PCI, and superior to angiography alone.¹

Image acquisition

To obtain the greatest benefit from intravascular imaging, it is preferred to adopt it from the beginning of the procedure, through to the final optimisation of the stent result. Imaging should usually be performed with an automated pullback beginning at least 20mm distal to the lesion and ideally ending at the ostium. However, it is important to acknowledge that the functionality of the individual imaging devices differ with regards pullback length (Table 1) and the need for blood clearance with OCT (Abbott Vascular) and OFDI (optical frequency domain imaging (OCT by another name), Terumo) can challenge image quality in extended pullbacks. We recommend contrast pump-injection to obtain consistent blood clearance, commonly using 3–4ml/s, with 12–16ml total contrast volume at 300PSI. Co-registration with angiography should be performed to enhance interpretation & minimise the need for additional angiographic acquisitions, reducing the overall contrast volume. Use of saline for OCT image acquisition is feasible and can further limit procedural contrast use.¹⁸ The use of IVUS in patients with severe renal dysfunction has facilitated 'zero-contrast' angiography¹⁹ and should be adopted where concerns exist regarding an elevated risk of contrast induced nephropathy.

Plaque composition

As discussed earlier, OCT & IVUS provide differing evaluation of coronary plaque composition. The penetration depth of IVUS provides deep structure identification, particularly the external elastic membrane, allowing estimation of true vessel size and an appreciation of plaque burden (discussed later). OCT's superior resolution and the specific nature of near-infrared light's interaction with individual tissue components facilitates identification of calcium, macrophage, neovascularisation and lipid/necrotic core (Figure 2).

With recent advances in modification techniques for calcification, there has been an increased focus on identification of calcium and detection of characteristics associated with poor stent results. Specific markers suggesting the need for calcium modification are a calcific arc over 180°, calcium thickness >0.5mm, and length >5mm²⁰ Modification may require use of non-compliant or cutting balloons, rotational atherectomy, intravascular lithotripsy or laser and algorithms are being developed to guide the treatment of severely calcific plaque. It is essential that repeat imaging is undertaken to confirm adequate calcium modification before considering stent implantation, to avoid underexpansion and poor longterm PCI outcomes. The identification of calcium has been enhanced by use of artificial intelligence in the latest software from Abbott Vascular (ULTREONTM) and additional tissue component characterisation is likely to be facilitated in the near future.²¹

Table 1. Intracoronary imaging device specifications. (*NA - data not available).

Modality	IVUS						OCT		
Device	Boston	Opticross	Boston	Opticross HD	Philips Eagle Eye Platinum / Platinum ST	Philips Revolution /Refinity ST	ACIST HDi	Abbott Dragonfly Optis	Terumo Fastview OFDI
Resolution (μm)	100	40	60MHz	60MHz	170	50	40	10	10-20
Wavelength	40MHz	60MHz	NA*	NA*	20MHz	45MHz	60MHz	1.3 μm	1.3 μm
Frame rate (FPS)	30	NA*	NA*	NA*	NA*	NA*	60	180	158
Penetration depth (mm)	6	6	6	10	10	7	>2.5 soft tissue	2.5	2.0
Pullback length (mm)	100	100	100	150	150	135	120	54-75	150
Pullback speed (mm/s)	0.5-1	0.5-1	0.5-1	0.5-1	0.5-1	0.5-1	0.5-10	18 for 54mm 36 for 75mm	40
Compatibility (French)	5 or 6	5 or 6	5 or 6	5	5	6/5	6	5	5
Angio co-registration	No	No	No	Yes	Yes	Yes	No	Yes	Yes

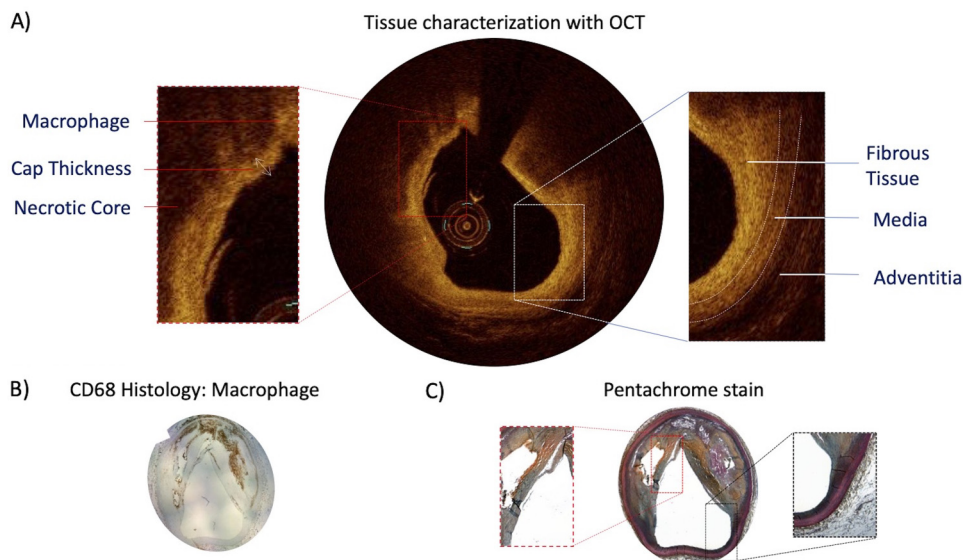


Figure 2. A) tissue characterization with OCT demonstrating pathological (macrophage, fibrous cap, necrotic core) and physiological (fibrous tissue, media, adventitia) vessel architecture; B) CD68 histology used to immunostain macrophages in the vessel wall; C) pentachrome stain highlights vessel constituents (yellow = collagen; red = muscle).

Tissue characterisation with intracoronary imaging requires advanced knowledge and there is significant potential for mis-interpretation.²² Thrombus can obscure underlying plaque components, when using OCT, and additional artefacts exist with both IVUS & OCT technologies. Advances in automated tissue detection are being developed to assist with interpretation. Furthermore, combining imaging modalities can enhance tissue identification, as evidenced by near-infrared spectroscopy-IVUS (NIRS-IVUS) which provides the gold standard method of detecting lipid-rich plaque. The recently reported PROSPECT II trial demonstrated that non-flow limiting plaque with high risk features detected with NIRS-IVUS (plaque burden >70%, MLA <4mm², and lipid core (lipid core burden index_{4mm} ≥324.7) placed patients at especially high risk for future MACE.²³

Bifurcations

Approximately 20% of all PCI involves a bifurcation, and 2D angiographic assessment frequently underestimates the complexity of disease. Imaging clarifies the true nature of bifurcation disease and ensures that the bifurcation technique selected best suits the anatomy. This is particularly important for left main stem bifurcations. Consensus opinion recommends an image guided approach for bifurcations, and further studies are ongoing.²⁴ The October study is testing the role of a dedicated OCT algorithm to guide every step of bifurcation treatment, including the optimal position of wire cross, sizing of vessels and the final stent result; the results are eagerly awaited.¹³

Lesion severity

The minimal lumen area (MLA) in LM lesions detected by IVUS has been acknowledged in ESC guidelines with an IIa recommendation as a marker of severity indicating need for revascularisation. Anatomical measures of severity are inherently linked to patient size and consequently data from Asian and US studies have found significant ischaemia at varying MLA thresholds from 4.5–5.9mm² corresponding to a significant FFR. The consensus recommendation is to revascularize when LMS MLA <4.5 mm², treat conservatively when MLA >6 mm², and to consider physiological assessment for intermediate MLA between 4.5–6 mm².² These values do not apply to measurement with OCT. For non LMS lesions the variation in patient size and subtended myocardium prevents the use of a single threshold value.

Stent selection and optimisation

Use of upfront imaging provides an accurate assessment of lesion length and vessel size. Debate continues regarding the method for vessel sizing, with use of either a lumen measurement or external elastic membrane (EEM) dimensions. Historically, IVUS used the EEM measurement and this has been replicated in the Illumien OCT protocol, with rounding down of the stent size by 0.25mm.¹⁶ However, the OPINION study utilised a lumen measurement for OFDI, without any longterm differences in stent outcome compared against IVUS.¹⁷ Identification of healthy vessel 'landing zones' (<50% plaque burden) are important to avoid unnecessary vessel injury that may

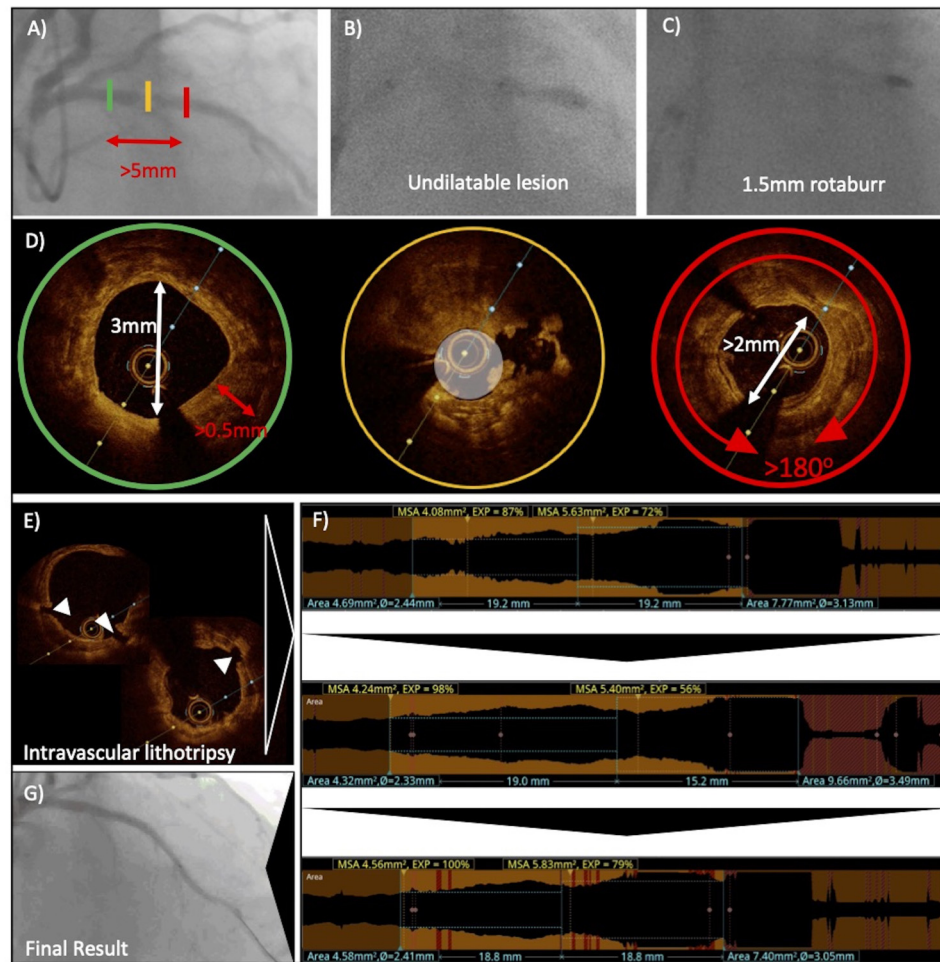


Figure 3. Calcium modification A) discrete severe mid-LAD lesion; B) undilatable lesion with 2.5NC balloon; C) 1.5 mm rotaburr; D) OCT assessment post rotational atherectomy (RA) - demonstrating high burden calcium with $>180^\circ$ arc, calcium thickness >0.5 mm & longitudinal extension >5 mm. Shaded circle demonstrates RA debulking area; E) OCT evidence of calcium disruption (white arrowheads); F) Sequential post-dilatation of 3.0×38 mm DES with 3.0/3.5NC balloons, increasing distal stent segment MSA from 4.08 to 4.56mm² and proximal stent segment MSA from 5.63 to 5.83mm², with an acceptable final angiographic result G).

compromise the longterm result. There are various approaches to stent diameter selection but in general a distal lumen reference approach is advised. The distal lumen diameter should be measured in two orthogonal planes to calculate the mean which is then rounded-up by 0–0.25mm to select the appropriate stent diameter (for instance 3.76 up to 4.0mm). Alternatively, the mean distal reference EEM can be rounded down to the nearest 0.25mm (for instance 4.15 to 4.0mm).¹ A distal vessel EEM measurement appears feasible with OCT, and was possible to obtain in 77% of patients in the Illumien III study.¹⁶ This distal reference strategy may not be appropriate where there is a large difference in calibre from proximal to distal vessel.

Distal landing zones within an area of residual plaque burden $>50\%$ or lipid-rich plaque are associated with stent-edge restenosis, and a landing zone within a lipid pool is associated with increased peri-procedural MI,²⁵ so

these areas should be avoided when determining stent length. On OCT a plaque-free wall angle of >220 degrees predicts an IVUS plaque burden $<40\%$.²⁶

The recommended target stent expansion is $>80\%$, calculated from minimal stent area (MSA) relative to average lumen measurements (mean proximal and distal lumen areas). In the DOCTORS study the optimal threshold stent expansion able to predict FFR >0.90 was $>79.4\%$.¹² Absolute expansion values exist but applicability depends on target vessel size, so there is a risk of under-expansion or over sizing if followed injudiciously. The recommended absolute expansion target is an MSA >5.5 mm² with IVUS or >4.5 mm² with OCT for non-LMS lesions.¹ Figure 3 demonstrates successful use of serial OCT runs to optimise stent expansion in a complex lesion.

IVUS and OCT can detect underexpansion, malapposition, geographic plaque miss, and stent edge dissection which are all associated with adverse PCI outcomes. OCT

is superior at detecting malapposition and stent edge dissections, and has particular utility in detecting plaque protrusion/thrombus which may indicate a mechanical or pharmacological problem.

Malapposition

Malapposition refers to lack of contact of stent struts with the vessel wall and can co-exist with underexpansion or occur independently. Malapposition can occur acutely post-procedure due to inadequate dilatation or acute stent recoil, or may develop later as a result of positive (outwards) remodelling of the vessel (late acquired malapposition), or resolution of thrombus. Acute stent malapposition does not predict stent thrombosis in prospective studies.²⁷ However, late acquired stent malapposition is associated with late and very late stent thrombosis. Extensive malapposition should be corrected where feasible. The treatment targets are an axial distance of <0.4mm and length of <1mm as full neointimal integration of struts is anticipated within these parameters.¹

Dissection

Large edge dissections are markers of MACE, in particular those with lateral extension >60°, length >2mm, or involvement of deeper layers (media or adventitia). Dissection at the distal edge may be clinically more relevant than the proximal edge.²⁸ Haematoma on imaging is an important indicator of dissection which can appear as stent edge stenosis on angiography, with a tendency to be misclassified as spasm or size mismatch. Progression of uncovered haematoma may lead to early stent thrombosis so consideration should be given to correcting this. More minor stent edge dissections and those without haematoma are unlikely to be clinically relevant and may not require correction.

Stent failure

Intracoronary imaging is strongly recommended in stent failure to identify the mechanism and guide appropriate treatment. Mechanisms of stent failure detectable with intracoronary imaging include chronic underexpansion (seen in 18–40%), stent fracture (<5%), and neoatherosclerosis.

OCT is the preferred technique for assessing stent thrombosis, however in large volumes of thrombus the attenuation of OCT signal may prevent strut and deeper vessel wall visualisation. Consideration may be given in this setting to evaluating by IVUS or treating pharmacologically with GP IIb/IIIa inhibitors to restore flow with subsequent staged OCT.

The main markers of early stent thrombosis are underexpansion and edge dissection. Markers of very late stent thrombosis are underexpansion, late acquired stent malapposition, and neoatherosclerosis.²⁹ A tailored treatment strategy based on the observed mechanism of failure is suggested

(post-dilatation for malapposition/underexpansion +/- drug-coated balloon or stent implantation for neoatherosclerosis).

Acute coronary syndrome

Intra-coronary imaging can assist identification of the culprit lesion and understanding of the mechanism of acute coronary syndrome (ACS) where there is clinical uncertainty, including the common scenario of unclear culprit lesion (over 30% of Non-STE ACS).

Imaging can delineate luminal discontinuity, plaque disruption and thrombus which are the hallmarks of a culprit lesion. Confirmation of plaque erosion may have implications for treatment as the aetiology is distinct from plaque rupture. One proof-of-concept study demonstrated successful outcomes at 1month with a conservative approach, avoiding stent implantation, although this was a small and highly selected cohort.³⁰ A 'definite' plaque erosion is confirmed on OCT where there is a fibrous lesion with no evidence of fibrous cap disruption and overlying luminal thrombus.

Eruptive calcific nodules are responsible for up to 7% of ACS, characterised on intracoronary imaging by breaks in the calcific plate with overlying thrombus.³¹ Calcific ACS lesions are associated with higher rates of target lesion revascularisation, and defining this complex anatomy can guide the use of calcium modification techniques.

Myocardial infarction with non-obstructed coronary arteries (MINOCA)

Unobstructed coronary arteries are found in approximately 10% of all ACS presentations and this is not a benign phenomenon, associated with a higher 12month mortality than propensity matched myocardial infarction with obstructive coronary artery disease.³² The causes of MINOCA are diverse, including plaque rupture or erosion with spontaneous recanalization, myocarditis, takotsubo cardiomyopathy, coronary artery spasm, and spontaneous coronary artery dissection.

OCT can detect thrombus or plaque disruption as evidence of type 1 myocardial infarction, which may account for 30% of MINOCA and may have a role in differentiating other causes, and hence informing the correct treatment strategy. In the setting of MINOCA, imaging during the index angiogram is advocated.

SCAD

Spontaneous coronary artery dissection is observed in up to 4% of ACS presentations, more frequently in pre-menopausal women <50 years old. Angiographic appearances vary widely and a working knowledge of these appearances is important. Multi-vessel SCAD is common so careful assessment of the complete coronary anatomy should be made. Both IVUS

and OCT can be utilised to confirm the diagnosis. Imaging should be reserved for cases where the angiographic appearance is ambiguous (Angiographic SCAD type 3 (angiographic appearance mimics coronary artery disease) or recanalised type 4 (dissection associated with abrupt vessel closure)). Intervention should be avoided, where possible, as SCAD PCI is associated with poorer outcomes, however, if necessary, then intracoronary imaging can be very useful to inform peri-procedural decision making.³³

Limitations

The principal limitations with intracoronary imaging are the additional time taken and cost

There is some evidence suggesting cost-effectiveness for IVUS guided PCI when used in patients at high risk of restenosis.³⁴ Additionally, the deliverability of imaging catheters may be difficult in some complex lesions, such as heavily calcified or tortuous vessels. Optimal image acquisition and accurate interpretation requires a level of knowledge and experience, which may also pose a barrier to use. Further refinements such as lower profile, more deliverable devices, with faster image acquisition and automated analysis software may improve uptake.

Conclusions

Imaging provides clarity in ambiguous angiography. Complex lesions and complex patients are known to be at higher risk of adverse outcomes, and imaging is proven to confer improved outcomes in these settings. In particular imaging should be the default strategy for unprotected LM intervention and should be considered mandatory in stent failure. With further improvement in imaging technology and an increasing body of evidence, we anticipate an expanding role for imaging within daily practice.


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