



Laser Imaging: Unraveling Laser Atherectomy Mechanisms of Action with Optical Coherence Tomography

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Abstract

Purpose of Review The goal is to review the current data regarding excimer laser coronary atherectomy (ELCA) through optical coherence tomography (OCT) imaging. We aim to reveal the mechanisms of action and principles of use for laser, and to analyze the current supportive data.

Recent Findings ELCA is an adjuvant procedure to percutaneous coronary intervention, aimed at properly preparing coronary lesions to optimize stenting. It is an effective atherectomy device that requires a short period of training and works on a standard 0.014" guidewire. Laser modifies coronary vessels by three distinct mechanisms: photoablation, chemoablation and thermoablation. Accordingly, it plays an important role in the management of lesions that require appropriate debulking, such as in-stent restenosis, chronic coronary occlusions (chronic total occlusion), stent underexpansion, and non-crossable/non-expandable lesions.

Summary OCT imaging of ELCA demonstrates that the most important mechanism of action is tissue debulking, facilitating pressure delivery to the vessel and tissue compression. In addition, laser light pulses weaken the connection between tissues, facilitating expansion. With combined laser use and OCT guidance, procedures may be properly planned to maximize final lumen gain and decrease predictors of restenosis.

Keywords Excimer laser coronary atherectomy (ELCA) · Optical coherence tomography · Percutaneous coronary intervention (PCI) · Restenosis · Intra-coronary thrombus · Underexpanded stents

Introduction

Excimer laser coronary atherectomy (ELCA) is an adjuvant procedure to percutaneous coronary intervention (PCI) designed to properly prepare coronary lesions to optimize

stenting. It is an effective form of atherectomy for complex coronary disease and plays an important role in the management of lesions that require debulking, such as in-stent restenosis (ISR) and chronic coronary occlusions. The major indications for ELCA are acute coronary syndromes (ACS) with thrombotic lesions, uncrossable or undilatable lesions, chronic total occlusion (CTO), stent underexpansion, and ISR [1, 2].

The high resolution of optical coherence tomography (OCT) provides more detailed structural information of the coronary artery wall compared with conventional imaging modalities. Current OCT technology facilitates identification of mechanisms of restenosis and detailed analysis of lesion anatomy. This information informs optimal procedural planning of the procedure to optimize final lumen gain and decrease the risk of restenosis [3].

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ELCA Principles, Materials, and Techniques

Excimer lasers are pulsed gas lasers that utilize high-energy ultraviolet (UV) light to debulk tissues through three different

mechanisms: photochemical, photothermal and photomechanical [2••, 4].

Several modifications of ELCA over the past two decades have improved its safety and efficacy. Adjunctive ELCA devices have been developed, including smaller laser catheters capable of delivering of higher energy with lower heat production (Fig. 1), and techniques such as saline infusion for removing dye to prevent vapor bubble formation, all of which have improved the ELCA procedure [1•, 5].

ELCA Clinical Indications

Laser has demonstrated safety and efficacy throughout different scenarios in current practice, including complex procedures. In this review, we will discuss the role of ELCA in different clinical and anatomic scenarios.

The multicenter ULTRAMAN registry for ELCA [1•] showed that in Japan, the most frequent indication for ELCA has been ACS (53.4%) and the second most frequent indication has been ISR (32.3%). In the USA, the distribution of disease indications for ELCA is different, where laser is primarily used to treat saphenous vein graft (SVG) (33.6%), CTO (26.9%), and calcified lesions (21%). [1•]

Acute Coronary Syndromes

ACS results from sudden luminal narrowing typically caused by thrombosis superimposed on plaque rupture, erosion, or superficial calcified nodule. Of these, plaque rupture is noted most frequently (55% to 60%), followed by plaque erosion (30% to 35%) and superficial calcified nodule (2% to 7%) [6]. OCT has been applied for the assessment of culprit lesion morphologies in patients with ACS. The high resolution of OCT provides histology-grade definition of the microstructures of coronary unstable plaques in vivo. OCT can also visualize unstable lesion morphologies in vivo which have previously only been demonstrated by histological examinations. Thus, OCT allows a greater understanding of the pathophysiology of ACS and may possess potential to guide patient-specific therapeutic approaches. [7]

The advantages of performing ELCA for ACS are the rapid removal of thrombus with the vaporization of procoagulant reactants, promotion of fibrinolysis, reduction of the risk of distal embolization, and debulking underlying plaque, providing excellent immediate and long-term results. In addition, the interaction between ultraviolet beam 308 nm, which is used in ELCA, and platelets has demonstrated a phenomenon of altered aggregation kinetics as manifested by decreased platelet aggregation and reduced platelet force development, the so-called stunned platelets phenomenon. [8]

The Cohort of Acute Revascularization of Myocardial infarction with Excimer Laser (CARMEL) [9] multicenter registry was a multicenter study of 151 patients with AMI who underwent ELCA, and showed an acceptable success rate and low complication rate even in high-risk populations, to include patients in cardiogenic shock [9].

The Laser AMI study, a single randomized trial, included 27 patients and showed that ELCA is feasible and safe for the treatment of patients with ST elevation MI. Procedural results were at least on par with conventional treatment and no procedure-associated complications were observed [10].

The ULTRAMAN registry [1•] demonstrated better success and similarly low complication rates for laser use in ACS (175 patients) as the CARMEL study, perhaps due to technical advances over the intervening decade. ULTRAMAN data showed better rates of laser technical success (92.5% vs. 89%), PCI success (94.5% vs. 93%), mortality (1.7% vs. 4%), perforation (1.1% vs. 0.6%), major dissection (1.1% vs. 5%), and no reflow/slow flow (6.9% vs. 3%) [9].

Plaque rupture can be identified by fibrous cap discontinuity together with cavity formation within plaque, and atheroma with thin-fibrous cap (<65 μm) is thought to be the precursor lesion of plaque rupture. Erosion has an area lacking surface endothelium and occurs over lesions with thick intima. Calcified nodule is a plaque with luminal thrombi showing calcific nodule protruding into the lumen through a disrupted thin fibrous cap [6].

Rich-Thrombus Lesions

The major mechanism of ELCA is the vaporization of thrombus and debulking of plaque. The former is key for treating

Fig. 1 ELCA device and catheter



rich-thrombus lesions including ACS and SVG disease, and the latter is key for treating poor-thrombus lesions including CTO, moderate calcified lesions, and long or bifurcated lesions. The Japanese ULTRAMAN ELCA registry demonstrated a higher incidence of complications, especially slow flow or no-reflow, in a rich-thrombus group compared to a poor-thrombus group, although the laser technical success and the PCI success were similar and excellent (>90%) in both groups. The rates of MACCEs for 1 month after ELCA were also similar and acceptable (3.3% and 1.4%, respectively) in both groups. Overall, the ULTRAMAN registry revealed ELCA to be effective and safe for treating both rich-thrombus and poor-thrombus lesions in patients with various forms of coronary artery disease [1•].

OCT is the best intra-vascular method for identifying thrombus (Fig. 2), with sensitivity of 100% when compared to intravascular ultrasound (IVUS) (33%) [11]. OCT is also a feasible imaging modality in patients with AMI and facilitates identification not only of plaque rupture but also fibrous cap erosion, intracoronary thrombus, and TCFA *in vivo* more frequently compared with conventional imaging techniques [11].

Saphenous Vein Grafts

Occlusions in old SVGs frequently consist of degenerative diffuse plaques often containing thrombus and are prone to distal embolization. Hence, embolic protection devices (EPDs) are advocated when attempting SVG-PCI, although their bulky profile may sometimes prevent distal device delivery [12, 13]. ELCA is a safe alternative, allowing predictable debulking during SVG-PCI. The low rate of distal embolization during ELCA of degenerative bypass grafts (1–5%) may preclude the need for routine distal protection devices in some cases. However, OCT images post-SVG ELCA make it clear that there remain friable fragments in other SVG lesions that may embolize and cause no-reflow [2••, 13]. Therefore, when using ELCA for SVG-PCI, it is still advisable to perform PCI

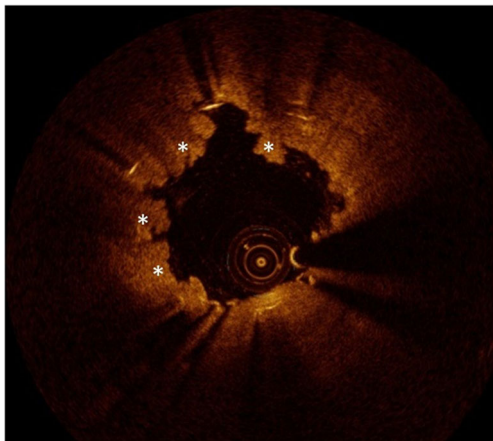


Fig. 2 Thrombus identified by OCT imaging (asterisks)

using EPD to prevent no-reflow. Given recent advances in CTO success, SVG-PCI may be less frequently undertaken as operators choose to treat the occluded native vessel instead. Nonetheless, if SVG-PCI is considered necessary, ELCA remains a useful adjunctive therapeutic intervention [12, 13].

Bifurcation Lesions

Generally, the best treatment for bifurcation lesions is main vessel only stenting approach with preservation of side branch (SB) instead of planned up-front double-stent strategy. However, sometimes it is necessary to stent the SB in large vessels involving extensive SB disease, and in this case ELCA may potentially be useful by debulking the SB lesion to permit more predictable success with the MV-only approach. However, in the few cases in our practice in which we have used this technique, we have discovered SB dissection due to vessel angulation which has necessitated SB stenting—thereby defeating the purpose of using ELCA. In other cases, we have used ELCA successfully to treat SB restenosis (often due to stent underexpansion) guided by intra-coronary imaging with durable results [2••] (Fig. 3).

Chronic Total Occlusion

Another use for ELCA is for CTO treatment. The Multicenter CTO registry of Japan (J-CTO) [14] revealed high procedural success rates for even complex CTO lesions (88.6%) without ELCA. Thus, in Japan, the target diseases for ELCA have been large-vessel lesions (including large thrombi) and a high volume of in-stent tissues. In addition, because glycoprotein IIb/IIIa inhibitors are not readily available in Japan, ELCA is useful to vaporize a thrombus for AMI before the implantation of a stent. Moreover, when drug-coated balloons are not available, the debulking effect of ELCA on the large mass of in-stent tissue in ISR lesions is important [1•].

Underexpanded Stents

Underexpanded stents cause an increased risk for thrombosis and restenosis [15], and there are limited PCI options available in this situation. Maximal balloon dilatation (both diameter and pressure) has often already been undertaken, and rotational atherectomy may cause burr stalling and fragment embolization. ELCA is still the best way to disrupt the underlying resistant atheroma by delivering energy to the abluminal stent surface without modifying the stent architecture. ELCA can modify the plaque behind the stent with no impact on calcification, weakening the overall resistance and enabling complete stent expansion [2••, 16].

In patients with ISR and unexpandable stents, the use of additional stenting should not be routinely advocated and

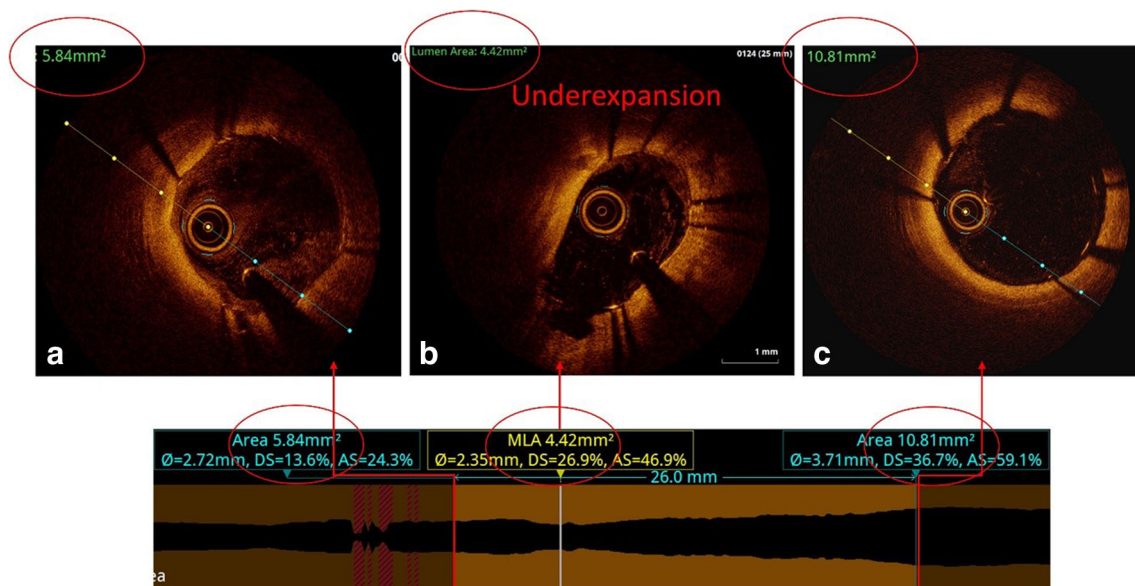


Fig. 3 Underexpanded stent. (a) Distal reference (area = 5.84 mm²); (b) stent underexpansion (area = 4.42 mm²); (c) proximal reference (area = 10.8 mm²)

aggressive attempts to expand the underlying stents is recommended instead.

Intra-Stent Restenosis

Restenosis after PCI has become less frequent in the stent era. However, once ISR occurs, PCI is less effective than it was for the initial procedure [1•, 2••, 3, 4]. Additional stent implantation may provide superior long-term clinical outcomes [6], but there is concern that multiple layers of metal may induce hypersensitivity to polymers. Other devices, such as rotational atherectomy, scoring balloon, and vascular brachytherapy, have been suggested as alternative treatment strategies for ISR. Overall, it is important for ISR treatment to dilate the restenosis lumen as much as possible to reduce the neointimal area.

ISR is becoming increasingly prevalent, representing more than 10% of all coronary interventions [17–19] with a recurrence rate as high as 30% with current therapy [20]. An aging population and higher life expectancy is driving the exponential increase of stent implantations in the USA, with more than 17.5 million PCIs and coronary angiographies performed since the launch of CathPCI in 1998 up to 2017. The rise of PCI is further enhanced by high rates of obesity and diabetes, making it clear that ISR will represent an even more common complication further increasing social and personal burden in addition to higher healthcare costs [21].

ELCA is thought to be advantageous for ISR treatment by removing neointima and allowing adequate new stent expansion. However, angiographic and IVUS studies have shown that conventional therapy is not sufficient to achieve this goal [8–10]. This is attributed to inadequate stent expansion due to

the cushion-like effect of the neointima which diminishes the balloon pressure [3].

ELCA has been demonstrated to be effective as an atherectomy device for lumen enlargement and optimal lesion preparation. In a recent study of 81 patients comparing PCI with and without ELCA, even though ELCA was used for ISR of drug-eluting stent (DES) in significantly more complex lesions, the long-term clinical outcomes were favorable and similar [22].

In the ULTRAMAN registry, the second major target disease of ELCA was ISR [1•]. Mehran et al. also showed a trend for less target vessel revascularization in ELCA compared to traditional POBA: 21% versus 38%, $p = 0.082$ [23]. Dahm et al. [24] reported < lower rates of recurrent ISR and major adverse cardiovascular events with < 30% residual percent diameter restenosis after ELCA. Thus, initial debulking of in-stent tissue is the key to achieving a good clinical course after ELCA procedures [1•].

Dangas et al. demonstrated the strategy for ISR in DES within DES for diffuse-type ISR and debulking or drug-coated balloons for focal-type ISR [19]. Debulking by coronary atherectomy has acceptable results (restenosis rate 25%) for ISR. In the DES era, focal-type ISR is more common than diffuse-type ISR and neointima debulking could provide better elution of the drug from a drug-coated balloon [1•].

Laser Atherectomy Mechanisms of Action with OCT Imaging

Historically, ISR balloon angioplasty achieved adequate luminal gain through tissue compression and previous stent expansion [25, 26], but fell short due to recoil and tissue re-

protrusion into the lumen soon after treatment [27]. With technological advancements, bare metal stents were used to provide structural support, preventing recoil, but created a new problem of a continuous inflammatory stimulus, leading to neointimal hyperplasia [28]. DES aimed to avoid the proliferative neointimal growth characteristic of ISR, but the presence of multiple stent layers adds a lifelong inflammatory stimulus [29]. Despite the important reduction in ISR brought on by current generation standard of care devices [30], rates are still high and need addressing, and constitute a burden on patients, physicians, and the healthcare system.

ELCA has been shown to affect both the abluminal and abluminal sides of stents in ISR segments, clearing abluminal space for additional stent growth. ELCA has advantages over alternative atherectomy interventions through the delivery on a standard 0.014-in. guidewire to perform adequate NIH debulking, with high technical and post-procedural success rates.

Combined ELCA and stent strategy for ISR treatment is possible by three important synergetic mechanisms: tissue ablation (Fig. 4), tissue compression, and previous stent expansion (Fig. 5). OCT imaging can demonstrate that all three of these mechanisms are involved (Fig. 6). The significant reduction in NIH, as well as the growth in lumen area and stent expansion exhibits the successful treatment through this suggested approach [31].

The main technical limitation of laser atherectomy is the presence of extensive calcification. In such cases, other types of atherectomy, such as rotational atherectomy, must be used. However, it is also possible to perform a hybrid procedure, when rotational atherectomy is required but cannot be used due to the impossibility of advancing the dedicated guidewire, and ELCA can create a channel for advancement of the dedicated guidewire and completion of the procedure [32].

Restenosis Predictors

In a large cohort of patients with angiographic surveillance, it was demonstrated that PCI with first-generation DES is a strong independent predictor of lower rates of restenosis as compared with bare-metal stent (BMS), and that less restenosis is predicted following intervention with second-generation DES compared with first-generation DES. Predictors of restenosis were small vessel size, increased stented length, complex lesion morphology, diabetes mellitus, and prior bypass

Fig. 4 ELCA mechanisms of action: tissue ablation

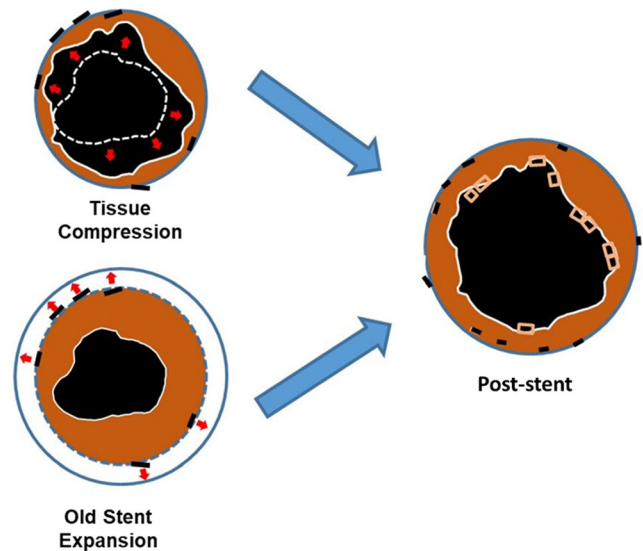
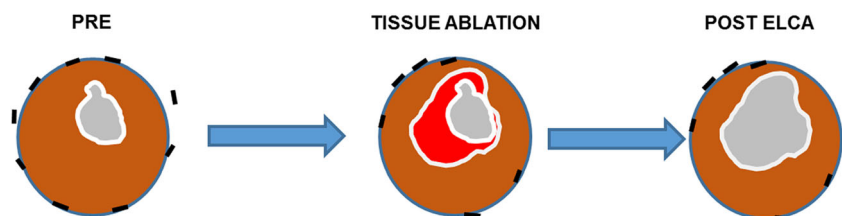


Fig. 5 ELCA mechanisms of action: tissue compression and previous stent expansion

surgery, and remained similar across the spectrum of stent devices [20].

Bioresorbable Scaffolds

Bioresorbable scaffolds were designed to limit stent permanence and provide pharmacological therapy to target lesions. Despite recognized challenges with this new scaffold platform [33, 34], a few studies investigated the use of bioresorbable vascular scaffold (BVS) for ISR cases [35–37], and despite not having enough power to draw a conclusion, they showed that such treatment is feasible with outcomes comparable to current-generation DES. Thus, exploring the combination of ELCA and BVS is a logical next step for optimizing ISR treatment, by integrating a method for lesion preparation that is crucial for the BVS platform [38], potentially leading to reduction in current rates of ISR.

The use of BVS seems attractive because it allows drug delivery combined with transient vessel scaffolding. Several studies have demonstrated that treating DES ISR is even more challenging because of the unfavorable substrate of DES ISR because of the presence of resistant stent underexpansion or neoatherosclerosis that has been shown to be associated with poorer clinical and angiographic outcomes than treating BMS ISR [1•, 2••, 3, 4]. Compared with DEB, BVS achieves excellent acute gain, prevents acute recoil and stabilizes dissections,

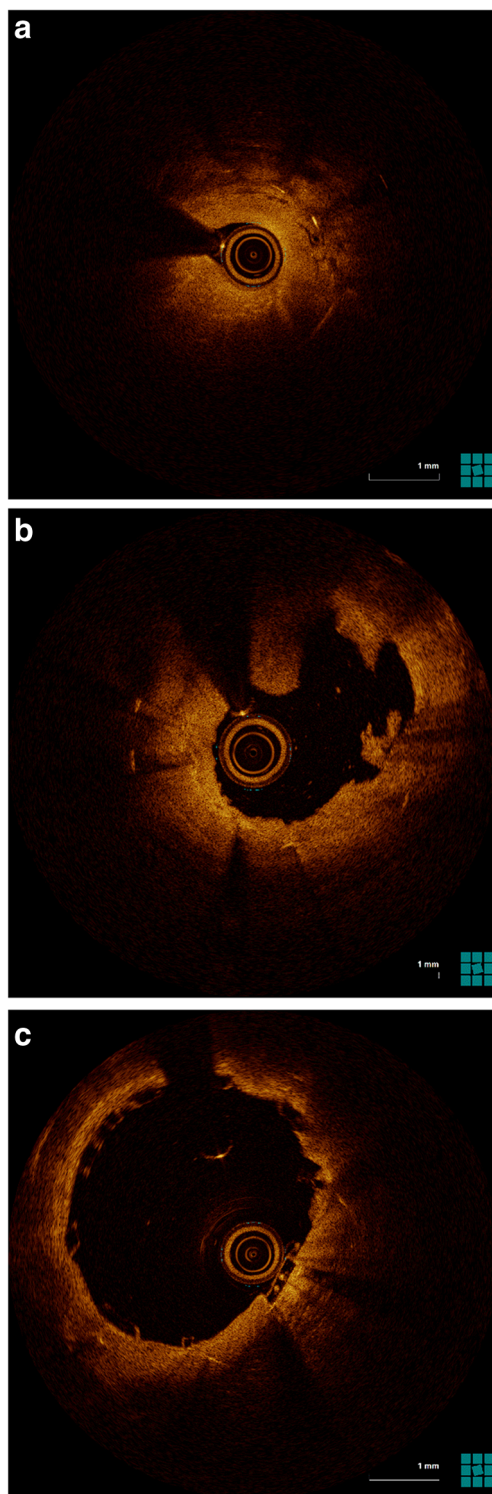


Fig. 6 Combined therapy ELCA and BVS for ISR treatment: tissue ablation, tissue compression, and previous stent expansion mechanisms displayed by OCT images (a) pre-stent, (b) post laser, and (c) final result after BVS implantation

whereas compared with DES, it avoids the addition of a further permanent metallic layer. So, BVS could theoretically reduce the occurrence of long-term clinical events compared with both drug-coated balloons and DES [35].

Regarding long-term results after BVS use in ISR lesions, a large registry demonstrated that among the ISR lesions, the majority were drug-eluting stent ISR (78, 61.6%), de novo ISR (92, 72.4%), and diffuse ISR (81, 63.8%). Procedural success was achieved for all patients, with no in-hospital death, myocardial infarction, or revascularization. The incidence of the device-oriented composite end point after 15 months of follow-up was 9.1%, suggesting that BVS implantation in the BMS and DES ISR lesions scenario might be associated with acceptable long-term clinical outcomes. Larger randomized trials of head-to-head comparison versus contemporary standard of care are strongly needed to fully assess the potential clinical benefit of BVS in ISR lesion treatment [35].

Contraindications and Complications

There are no absolute coronary contraindications for ELCA other than patient refusal or unprotected left main coronary disease (the last being even a relative contraindication). ELCA complications are similar to those that may occur during routine PCI. Interruption of the saline flush or contamination with contrast may generate excessive heat and increase perforation risks. Also, ELCA is not recommended when the interventionalist is aware that there is a long length of sub-intimal guidewire positioning such as may occur with chronic total occlusion or hybrid PCI techniques [2•].

Conclusions

The current indications for the use of Excimer laser atherectomy in modern interventional practice are ACS, non-crossable or non-expandable lesions, CTO, stent underexpansion, and ISR. ELCA technology provides a solution to a variety of problems that may be encountered in clinical practice, including massive intra-coronary thrombus, uncrossable lesions, and stent underexpansion. OCT advanced imaging yields critical information for understanding ELCA mechanisms of action, aiding proper planning of the procedure, aiming to achieve the appropriate debulking of the lesion with optimal lumen gain, thus decreasing restenosis predictors. Careful case selection, intracoronary imaging, proper use of equipment, and safe, efficacious laser technique all play crucial roles in successful ELCA interventions [2•, 20, 39].

As restenosis rates become more common with disease complexity, the absolute number of patients presenting with restenosis remains considerable. Thus, the identification of predictive factors becomes crucial. The impact of device development on antirestenotic efficacy with sequential improvement from BMS to first-generation DES to second-generation DES, as well as appropriate debulking and lesion preparation

such as may be achieved with ELCA, may result in bigger stent expansion and larger lumen size, thus decreasing some of the predictors of restenosis, such as stent underexpansion and small final lumen vessels, thereby improving short- and long-term clinical outcomes [20, 40, 41].

Compliance with Ethical Standards

Conflict of Interest All authors declare no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- Of major importance

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