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Lasers in Cardiology and Cardiothoracic Surgery

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Abstract

History and rationale for laser in the treatment of cardiovascular diseases.

Early applications, growing expectations and the development of realistic perspectives.

Current indications and applications: coronary, peripheral, TMR, EP.

Technique of lasing and catheter technology.

Adverse outcomes.

Future potential.

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Keywords

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Calcified coronary lesions
Coronary thrombus · Saphenous vein grafts
Coronary stents · Intracoronary imaging

Box 1: Introduction

- History and rationale for laser in the treatment of cardiovascular diseases
- Laser catheter design and technology
- Early clinical applications, growing expectations and the development of realistic perspectives
- Current cardiovascular indications and applications: coronary, peripheral, TMLR, electrophysiology
- Future potential

Introduction

Utilization of lasers in cardiovascular medicine began some two decades after the first therapeutic application of medical lasers had occurred in the field of dermatology. The 1980s heralded the introduction of lasers for the treatment of atherosclerotic vascular disease, initially exploited for the treatment of critical limb ischaemia [1]. It was the absorption properties of laser light by

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atherosclerotic material that created the hypothesis that laser could treat a variety of coronary and peripheral occlusions that were considered "non ideal" for standard balloon angioplasty [2]. The concept of using laser to debulk or ablate coronary atherosclerosis followed and laser gained momentum as a potential method to remove atherosclerosis and reduce the rate of vessel restenosis and occlusion that accompanied coronary balloon angioplasty [3]. Initial studies predicted that laser would render coronary bypass surgery an unnecessary operation as preliminary experience reported successful plaque removal [4–6].

Publication of several large scale successful clinical trials during early experience with laser led to a conviction that laser had established a prominent role in interventional cardiology [7, 8]. However, the application of the device in cardiac catheterization laboratories was limited by technical difficulties. The devices were very large, cumbersome to handle and necessitated lengthy warm up and calibration time. The laser catheters were also very rigid restricting their deliverability to the lesion particularly when sited more distally or within tortuous vessel segments. Lasing technique was basic with a tendency for rapid advancement of the catheters across the target lesions which did not permit adequate absorption of the laser energy within the irradiated plaque and thus did not yield the maximum ablative potential of the device.

Therefore, although initial laser experience in cardiovascular medicine was positive, limitations in laser catheter technology and an incomplete understanding of laser-tissue interaction combined with the inevitable early frequency of significant complications including abrupt vessel closure, thrombosis and vessel dissection, dampened the expansion of this therapy [9, 10]. However, despite concurrent development of coronary stents that solved some deficiencies of balloon angioplasty, there remained a desire amongst enthusiasts to develop laser in the field of coronary intervention. Refinements in catheter design permitting smaller laser generators [11] and introduction of safe lasing techniques emphasizing slow debulking and concomitant injections of saline [12, 13] led to significant improvement in clinical outcomes [14]. With better understanding of laser as a treatment modality, numerous indications were soon established for utilization within the field of cardiovascular medicine.

In contemporary percutaneous coronary intervention (PCI) practice laser is used in the cardiac catheterization suite for treatment of coronary atherosclerotic vascular disease, for peripheral vascular disease, surgically for trans-myocardial revascularization and for pacemaker/AICD lead removal in electrophysiology laboratories. There are emerging technologies utilizing laser for atrial fibrillation ablation.

How Lasers Work in Cardiovascular Medicine

Laser devices harness light of a specific wavelength to generate a unidirectional beam of high-intensity light that can be directed towards on object of interest. The wavelength of the emitted light is used to categorize the type of laser (Table 9.1). The depth of penetration of the laser is directly related to its wavelength, with laser in the ultraviolet range (shorter wavelength) having less depth of penetration, less heat production, and less unwanted tissue damage. The excimer (excited dimer) laser emits light at 308 nm with a typical absorption depth of 50 µm (Fig. 9.1). The original Nd-YAG and Argon medical lasers emitted infra-red light continuously, which resulted in excess heat production and tissue injury and inflammation, explaining the high rates of throm-

Table 9.1 Different types of laser categorized by emitted light wavelength

XeCl[a] (Excimer)	308	0.05	Protein-lipids
Nd:YAG[b]	1060	2.0	Protein-water
Dye	480	0.5	Protein
Argon	488	0.5	Protein
Ho:YAG[c]	2060	0.3	Water
Nd:YAG	1320	1.25	Water

[a]Xenon chloride
[b]Neodymium-doped yttrium aluminium garnet
[c]Holmium yttrium aluminium garnet

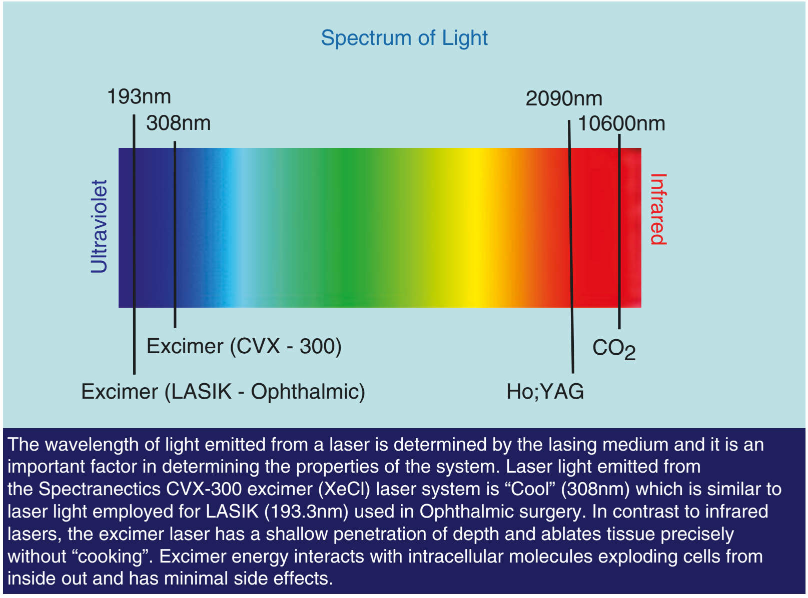

Fig. 9.1 Wavelengths of medical lasers. A figurative representation of the spectrum of light demonstrating the wavelength of light used in Excimer laser systems (308 nm for the CVX-300 used in coronary intervention) relative to that used in OCT (1300 nm—within the infra-red spectrum), and other forms of industrial Laser (Ho;YAG and CO2)

bosis and vessel damage/dissection. The newer excimer laser systems deliver the light in short bursts or 'pulses' during a period of between 5 and 10 s. This approach minimizes heat production and allows the emitted energy to disperse during the "off" period. The number of pulses generated during 1 s (known as the frequency) can be modified at the operator's discretion. Fluence refers to the amount of energy delivered in mJ/mm^2 and the frequency relates to the on/off repetition rate per second. These values are typically presented as numerical values with fluence first and frequency second e.g. 60/40.

Excimer laser tissue ablation within the cardiovascular system is mediated through three distinct mechanisms: photothermal, photochemical, and photomechanical. UV light is rapidly and effectively absorbed by intravascular tissue and thrombus, and the absorbed light breaks carbon bonds so weakening the structure of the cells (photochemical). Delivery of UV light aggravates molecular bonds, which elevates the temperature of intracellular water, eventually producing water vapour causing the cells to rupture. The generation of a vapour bubble cloud at the tip of the catheter enables controlled disruption of the atherosclerotic material (photothermal). Expansion and implosion of these vapour bubbles generates the photomechanical effect as the pressure is released from the vapour bubble, further disrupting the obstructive intravascular material as well as sweeping the freed particles downstream (photomechanical). The vast majority of the fragments released during laser atherectomy are >10 μm in diameter and are easily filtered by the reticuloendothelial system downstream which avoids microvascular obstruction and no-reflow phenomena.

Excimer Laser Equipment and General Technique

The majority of cardiovascular applications of laser utilize excimer laser technology; therefore we will focus on this modality. The only available excimer laser coronary atherectomy (ELCA) system is manufactured by Spectranetics, Inc. Colorado, USA. The excimer laser light is produced by a transportable generator that is powered by mains electricity with a standard plug suitable for each country (Fig. 9.2). There are a several catheters available in a variety of sizes that are tailored to the relevant clinical application (Fig. 9.3). The catheters are available as

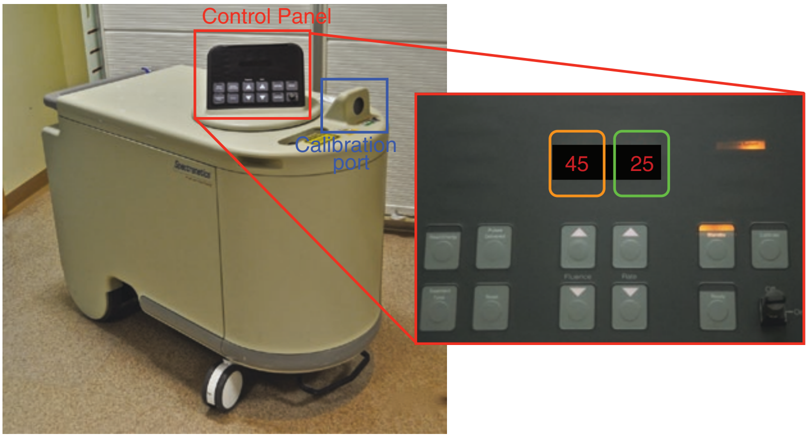

Fig. 9.2 Excimer laser generator (Spectranetics® Colorado Springs, CO, USA). The Spectranetics CVX-300 system system which is a portable unit 89 cm high, 124 cm long and 61 cm wide weighing approximately 295 kg. The system can emit laser energy from 30–80 mJ/mm² (indicated within the orange panel) with repetition rate from 25 to 80 Hz (indicated in green) and a pulse width range of 125–200 ns (nominal 135), altered via the control panel (red). Prior to introduction of the laser catheter, it should be calibrated by pointing the tip of the catheter towards the energy detector (highlighted in blue) on the CVX 300 unit itself and activating the laser by pressing the foot pedal for 5 s. The laser calibrates automatically and enters standby mode

RX	0.9mm	0.9mm X-80	1.4mm	1.7mm	1.7mm Eccentric	2.0mm	2.0mm Eccentric
Model Number	110-003	110-004	114-009	117-016	117-205	120-009	120-008
Guidewire Compatibility (in)	0.014	0.014	0.014	0.014	0.014	0.014	0.014 / 0.018
Guide Catheter Compatibility (F)	6	6	6 / 7	7	7	8	8
Minimum Vessel Diameter (mm)	1.5	2.0	2.2	2.5	2.5	3.0	3.0
Max Tip Outer Diameter (in)	0.038	0.038	0.057	0.069	0.066	0.080	0.079
Max Shaft Outer Diameter (in)	0.049	0.049	0.062	0.072	0.072	0.084	0.084
Working Length (cm)	130	130	130	130	130	130	130
Fluence (mJ / mm²)	30-60	30-80	30-60	30-60	30-60	30-60	30-60
Repetition Rate (Hz)	25-40	25-80	25-40	25-40	25-40	25-40	25-40
Laser On / Off Time (sec)	5 / 10	10 / 5	5 / 10	5 / 10	5 / 10	5 / 10	5 / 10

OTW	0.9mm	0.9mm X-80
	110-001	110-002
	0.014	0.014
	6	6
	1.5	2.0
	0.038	0.038
	0.049	0.049
	130	130
	30-60	30-80
	25-40	25-80
	5 / 10	10 / 5

Fig. 9.3 Sizes of laser catheters commercially available for human use. Table of excimer laser catheters produced by Spectranetics® Colorado Springs, CO, USA

over-the-wire or monorail (rapid exchange) devices and laser fibre arrangement is either eccentric or concentric (Fig. 9.4), each having relevant applications. Specific catheters will be referred to in subsequent sections of this chapter. Safety is paramount and therefore prior to the excimer laser being activated all persons in the room, including the patient, MUST wear protective spectacles to minimize the risk of retinal exposure and all windows should be covered and the doors should be locked. Following this safety checklist, the laser unit is warmed up and then the selected catheter is plugged into the generator and calibrated prior to being introduced into the body. Laser catheter size selection is primarily based on (a) the severity of the lesion, (b) the reference vessel diameter, and (c) consistency of the target material [15].

In general the 0.9 mm X80 catheter is used in non-crossable, non-dilatable fibrocalcific lesions given its excellent deliverability characteristics and because this catheter can emit the most power (80 mJ/mm²) at the highest repletion rate (80 Hz) necessary for 'balloon resistant' coronary lesions.

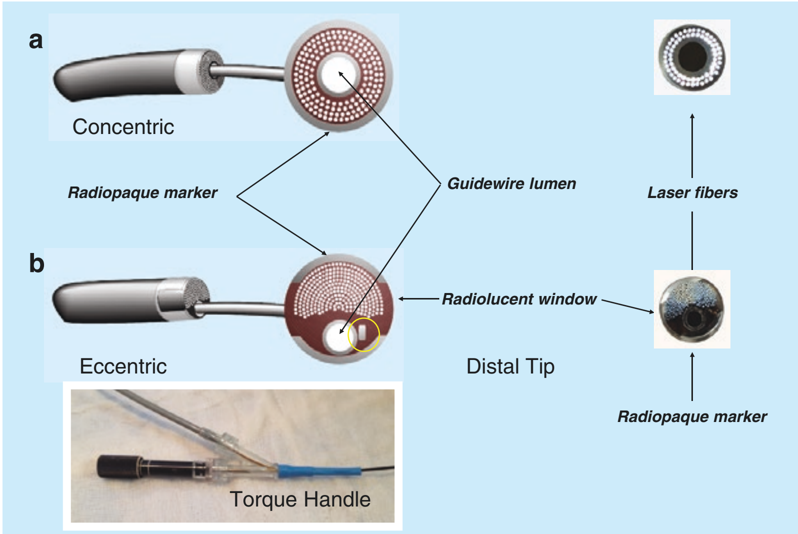

Fig. 9.4 Currently, each disposable ELCA catheter contains a bundle of very pure fused silica (synthetic quartz) fibres since ordinary glass or polymer fibres such as that used for telecommunications will not conduct UV light at useful power levels. Up to 250 individual fibres are used in each catheter with a fibre diameter of 50–140 mm. The use of these multiple fibres is preferable since it permits catheter flexibility and improves deliverability. At the distal end of the concentric catheter the fibres are potted in epoxy around a guide-wire lumen and polished to an optical finish. At the proximal end of the catheter, a laser coupler holds the fibres in a bundle to receive the laser beam. At the proximal end of the eccentric catheter (Illustrated in panel **b**i), a torque handle allows rotation of the device around the torque wire (highlighted within the yellow circle), and with catheter manipulation enabling systematic quadratic tissue ablation

The larger (1.4–2.0 mm) catheters are used in larger diameter vessels with straight segments and are therefore particularly useful when dealing with heavy intra-coronary thrombus or in the treatment of saphenous venous grafts (SVG). In some circumstances more than one catheter may be required, gradually increasing size based on the result obtained from the initial laser procedure. For intravascular applications, the laser catheter is delivered to the appropriate clinical site via a percutaneous guiding catheter and intravascular wire. In the coronary circulation the laser catheter is compatible with any standard 0.014″ guidewire which is a major advantage over alternative atherectomy systems that require a dedicated guidewire.

The guide catheter must then be flushed with 15–20 mL of normal saline to remove all contrast and blood prior to lasing. The laser catheter is positioned a few millimeters proximal to the lesion and using a foot pedal it is activated and slowly advanced forward under fluroscopic guidance. For the coronary catheters the duration of each lasing train is preset so for the standard catheters activation will automatically stop after 5 s with a 10 s rest period before the next laser train can commence. The X80 0.9 mm catheter permits 10 s activation and 5 s rest period reflecting its use in more complex lesions subsets. In contrast to the coronary catheters those used in the peripheral circulation (Turbo Elite™) do not have automatic preset timings and permit continuous laser activation with the operator determining the duration of each lasing train.

The excimer laser energy is delivered in pulses as the catheter is slowly (0.5 mm/s) advanced through the lesion. Since the depth of the excimer laser penetration is shallow (35–50 μm) the slow advancement along the target lesion provides adequate absorption of the emitted light energy into the lesion and subsequent ablation of the atherosclerotic plaque and thrombus. Upon completion of several trains of emission along antegrade laser propagation the laser catheter should perform retrograde lasing particularly in severe lesions when there is resistance for antegrade crossing. Continuous saline flushes accompany all stages of the procedure to reduce adverse augmentation of acoustic shock waves from interaction between the contrast media or blood and the laser light. Application of laser in blood or contrast media is rarely performed in certain specific situations, but should only be undertaken by experienced operators (see later sections).

Current Indications

Table 9.2 presents the current indications for use of laser in cardiovascular medicine. Careful case selection is integral to ensuring successful laser procedures. In acute coronary syndromes (ACS) or acute myocardial infarction (AMI) caused by obstructive plaque and associated thrombus, restoration of normal antegrade coronary flow is crucial for preservation of the myocardium. As the laser devices interact uniquely with plaque and thrombus, they can be successfully applied in these patients [16, 17]. An important advantage of laser PCI (both holmium:YAG [18] and excimer laser) is its safe application in patients with depressed left ventricular ejection fraction (LVEF). When the outcome of ELCA and stenting was compared in patients with depressed ejection fraction [mean LVEF = 28 ± 6%] versus those with preserved ejection fraction [LVEF = 53 ± 8%], successful debulking and thrombus removal was achieved irrespective of baseline ventricular function [19].

Table 9.2 Current indications for use of laser in cardiovascular medicine

1. Percutaneous treatment of atherosclerotic coronary artery disease
(a) Acute myocardial infarction, especially with large thrombus burden
(b) Chronic total occlusions
(c) Non-crossable or non-dilatable stenoses
(d) Degenerative saphenous vein grafts
(e) In-stent restenosis
(f) Under-expanded metallic stents
(g) Fibrotic aorto-ostial plaques
2. Cardiac electrophysiology
(a) Extraction of pacemaker and defibrillator leads
(b) Atrial fibrillation ablation
3. Cardiac surgical treatment of refractory angina
(a) Transmyocardial laser revascularization (TMLR)
4. Peripheral arterial disease
(a) Superficial femoral artery occlusions
(b) Popliteal artery occlusions
(c) Below the knee arterial occlusions
(d) Renal artery stenosis
(e) Stent restenosis

The Specific Effects of Laser on Thrombus

Thrombus is an integral factor in the pathophysiology of ACS and AMI. The presence of intracoronary thrombus is associated with an increased complication rate both during and after PCI. Laser energy interacts with two essential components of thrombus: fibrin and platelets. Pulsed wave lasers such as the mid infrared holmium: YAG and the ultraviolet excimer create acoustic shock waves that propagate along the irradiated vessel. These waves carry a dynamic pressure front toward the fibrin mesh within the thrombus. This process disrupts and breaks the fibrin fibers resulting in fibrinolysis and thereby reduces thrombus size [17]. Clinically, the excimer laser has been found to be a useful interventional tool for targeted thrombus removal strategy [18]. This laser also alters the aggregation kinetics of platelets leading to reduced platelet force development and inhibition of platelet activity. This phenomenon of platelets stunning is dose dependent and most pronounced at high fluence levels such as 60 mJ/mm^2 [19].

Contraindications

Laser coronary atherectomy can be safely performed in PCI centers without on-site cardiothoracic surgery but as with all PCI procedures, arrangements for offsite surgical cover must be in place. Other than lack of informed consent and unprotected left main disease [a relative contraindication] there are no absolute coronary contraindications to laser. As for peripheral laser applications, the presence of poor flow in a sole remaining vessel to the lower limb constitutes a contraindication.

Laser Induced Complications and Adverse Outcome

Several procedural and clinical complications can occur with either percutaneous or surgical laser application. These complications, though rare, relate almost without exception to faulty lasing techniques and mistakes in judgment by the operators [10]. Perforation, dissection, acute closure thrombosis, distal embolization and spasm have been reported. There is a clear inverse relationship between complication rate and operator volume.

Box 2: Key Points of Cardiovascular Lasing Technique

- Eccentric and concentric laser catheters are available with rapid exchange and over the wire systems
- The more severe the target stenosis—the smaller the initial catheter size
- Laser catheter should be advanced slowly, do not exceed 0.5 mm/s
- Saline flush should be used each laser-lesion interaction to reduce augmentation of laser induced acoustic shock waves
- Antegrade lasing should be followed by retrograde lasing along the target

Specific Coronary Clinical Applications and Lesion Subsets Suitable for Laser

Acute Coronary Syndromes and Myocardial Infarction

Patients presenting with AMI represent a medical emergency and frequently exhibit unstable hemodynamic parameters. These patients have marked activation of the clotting cascade with production of large amounts of platelet and fibrin rich thrombus within the coronary arterial vasculature. In most developed countries the recommended treatment for AMI associated with ST segment elevation on the electrocardiogram is immediate emergent PCI (Primary PCI) [20, 21] ELCA is a potentially beneficial revascularization modality given the potential for effective thrombus removal [22], promotion of fibrinolysis [23], platelet stunning effects [24], and concomitant plaque debulking [25] (Fig. 9.5).

However, randomised clinical data regarding for the use of ELCA in AMI is extremely limited. The largest study to date, The CARMEL [Cohort of Acute Revascularization of Myocardial infarction with Excimer Laser] [19] multicenter registry, enrolled 151 AMI patients from 6 centers in the USA, 1 in Canada and 1 in Germany. One in five cases involved a SVG, 13% patients presented in cardiogenic shock and large thrombus burden was present in the infarct related vessel (IRA) in 65% of the patients. Adjunctive glycoprotein IIb/IIIa inhibitor (GPI) was administered in 52% of the cases. Following ELCA, TIMI flow grade was significantly increased from 1.2 to 2.8, along with reduction in angiographic stenosis diameter from 83% to 52%. Overall a 91% procedural success rate, a 95% device success rate and a 97% angiographic success rate were reported [19]. There was a low rate (8.6%) of associated major adverse coronary events (MACE) with a 3% dissection and only 0.6% distal embolization rate encountered. There were no laser induced perforations. Mortality of those presenting in cardiogenic shock was 30%. Importantly, maximal laser effect was observed in lesions laden with a heavy thrombus burden. Separate analysis of the study's data base demonstrated maximal laser luminal gain among those patients who presented with an already established Q wave MI, an ongoing ST segment elevation and large-extensive thrombus burden in the IRA [26]. Further data has suggested that ELCA is capable of removing as much as 80% of the thrombus burden from the treated targets [27]. The first Laser AMI study is the only completed randomized trial of ELCA in acute MI and included just 27 patients. The study demonstrated safety and feasibility but was not powered to determine superiority over conventional treatments [28]. Two other small registries examining the effects of ELCA in ACS suggested a greater outcome with regards to TIMI flow and myocardial blush grade compared with manual thrombus aspiration devices [29, 30]. A second, larger Italian Laser AMI study is currently recruiting up to 194 patients treated with Primary PCI with 1:1 randomization to either ELCA or manual thrombus aspiration followed by standard PCI strategies. The primary endpoint in this study will be MACE at 6 months follow-up.

Non-crossable and Non-expansible Lesions

In contemporary PCI and with an expanding elderly patient cohort, it is not unusual to find that a coronary lesion can be crossed with a 0.014″ guidewire but either a low profile balloon fails to cross or once across the lesion fails to fully expand. ELCA can successfully be applied in this situation (Fig. 9.6). The success rate in uncrossable or undilatable stenoses is high, approaching 90%. However, when these targets are calcified, the response is less favorable to laser debulking than that of non calcified lesions [79% vs. 96%, $p < 0.05$] [31]. In the past, lasers utilizing a wide range of wavelengths encountered difficulties in recanalization of these stenoses. However, following Rentrop's invention of a high energy level excimer laser catheter [capable of producing fluence up to 80 mJ/mm^2 at 80 Hz frequency] for calcified lesions, the device was introduced to the field as the 0.9 mm X-80 catheter and improved results have been reported with this technology [32].

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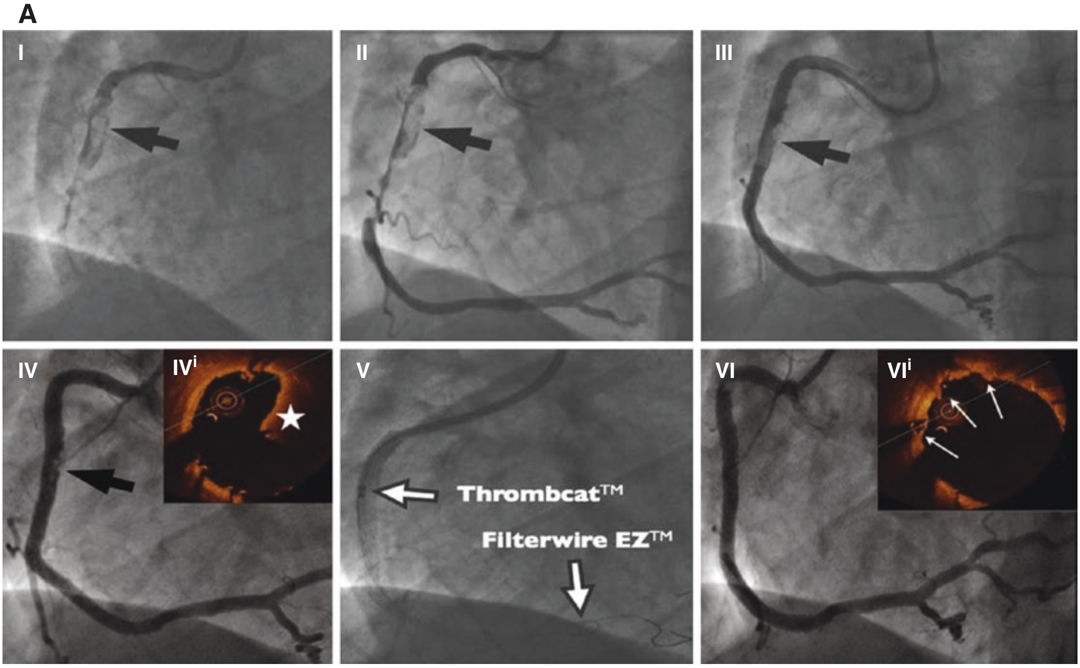

Fig. 9.5 (**A**) Series of angiographic stills that demonstrate: (I) Occluded dominant right coronary artery with a massive intracoronary thrombus (Black arrrows). (II) Establishment of TIMI 2 flow following excimer laser atherectomy. (III) Final result after treatment with three drug-eluting stents with proximal thrombus still evident (Black arrows). (IV) Evidence of proximal red thrombus remains (black arrow), shown to overly stent struts (Panel di—Star indicating residual thrombus). (V) Passage of Thromcat device over distal protection device. (VI) Final angiographic and Optical CT (panel fi) result, with almost complete thrombus resolution (white arrows showing small volume of red thrombus remains adherent to stent struts). (**B**) Contempory management of intracoronary thrombus: 25 year old male presenting with anterior STEMI. (I) Massive thrombus in the LAD, evident on OCT (II). ELCA with excellent effect to reduce thrombus burden angiographically (III), with the underlying lesion treated with an appropriately sized bioresorbable scaffold (final angiographic result—panel (IV) and (V), OCT result (VI) and (VII))

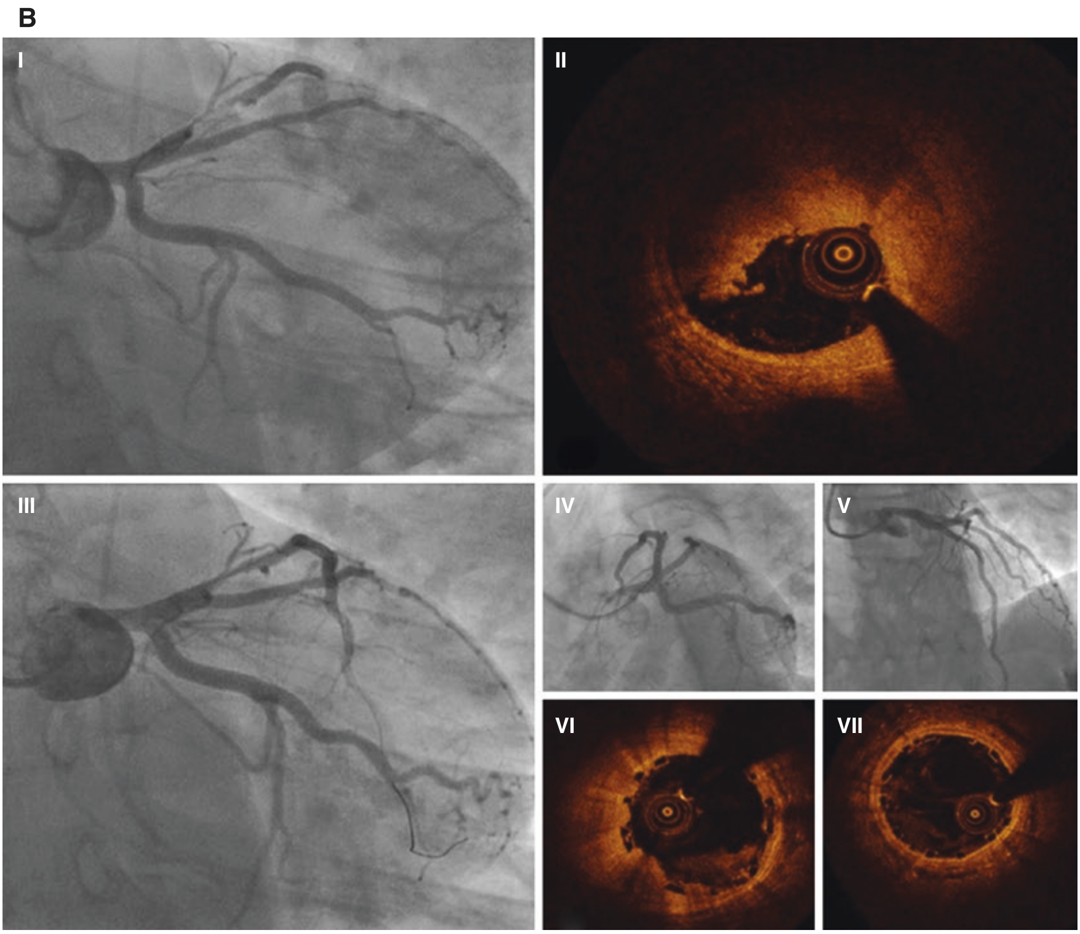

Fig. 9.5 (continued)

In this situation for the non-ELCA operator, rotational atherectomy (RA) would be considered the treatment of choice. Even for the proficient ELCA user, RA would be preferred if there was heavy calcification as it is more effective at debulking. However, this technique requires delivery of a dedicated 0.009″ guidewire which is less deliverable and may not be possible either independently or through a micro-catheter exchange system when the lesion is very stenotic. The combination of ELCA upstream to modify the lesion and create a channel through which a Rotawire™ can be delivered distally and subsequently permit RA was described by our group as Raser (Fig. 9.6). This technique is particularly effective for non-crossable, non-dilatable calcified stenosis and has been demonstrated to have a low complication rate in experienced hands [33, 34].

Chronic Total Occlusions

Chronic total occlusions (CTO) are challenging atherosclerotic stenoses that are frequently difficult to traverse with a guide wire, respond unfavorably to balloon angioplasty and resist stent deployment. There have been significant advances in CTO techniques in recent years with adoption of antegrade dissection re-entry (ADR) systems [35] and increasing utilization of retrograde approach [36]. An extensive array of equipment has been developed to support the CTO techniques and ELCA is considered amongst expert CTO operators to be very helpful within the CTO toolbox to debulk these lesions and facilitate adjunct balloon and stenting [37] (Fig. 9.7). A success rate of 86–90% for ELCA in CTO cases has been reported [38]. From a technical perspective saline is often not used at the

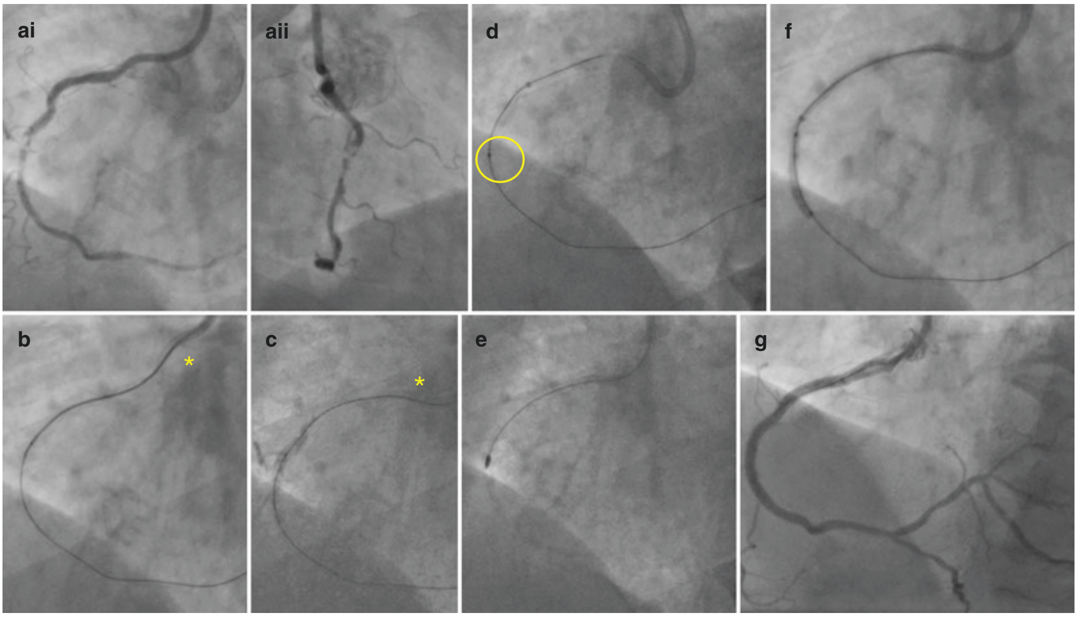

Fig. 9.6 The Uncrossable lesion. Angiographic Panel **ai** and AII demonstrate a severe complex calcific lesion in the RCA. Wire passage was challenging, requiring corsair support. Neither corsair (panel **b**) nor a low profile balloon (panel **c**) would cross the lesion, with multiple balloons bursting within the lesion (panel **d**). After further lasing, rotawire passage was possible. After extensive rotational atherectomy, balloon inflation and stent deployment was possible (panels **e** and **f**)

laser-lesion interface for CTO cases as antegrade injections are usually not desirable in case of hydraulic pressure extending sub-intimal planes leading to hematoma formation.

A CTO is by definition a long standing lesion that contains layers of old, well organized thrombus within calcified and fibrotic plaques. In sub-total occlusions fresh thrombus can form in the area heavily disease with near-occlusive fibrocalcific atheromatous plaque material producing acute-on-chronic occlusion. ELCA can be used successfully to modify the fresh thrombus in addition to facilitating the recanalization of the sub-total chronic occlusion [22].

Under-Expanded Stents

Under-expanded stents represent a high potential for stent thrombosis and in-stent restenosis. There are few PCI options available when confronted with these cases and in most situations where this is encountered, maximal balloon dilatation in terms of diameter and pressure have already been undertaken without success. RA although, an option, risks metal fragment embolization and stalling of the burr. In contrast ELCA is both a safe and effective therapy (Fig. 9.8). Usually the mechanism of under-expansion is fibro-calcific plaque impinging on the stent struts to obstruct full expansion during deployment. Whilst having no impact on the calcification itself, ELCA modifies the plaque behind the stent which weakens the overall resistance, thus enabling subsequent complete stent expansion [39–42]. From a technical perspective this is also an indication for delivering laser energy in contrast or blood (rather than saline) [39–42].

Instent Restenosis

In-stent restenosis (ISR) is caused by focal or diffuse neo-intimal and neo-atherosclerotic tissue growth. Laser debulking of this re-stenotic material may become a preferred treatment over simple tissue displacement by standard balloon angioplasty [43]. Mehran et al. compared excimer laser with adjunctive balloon angio-

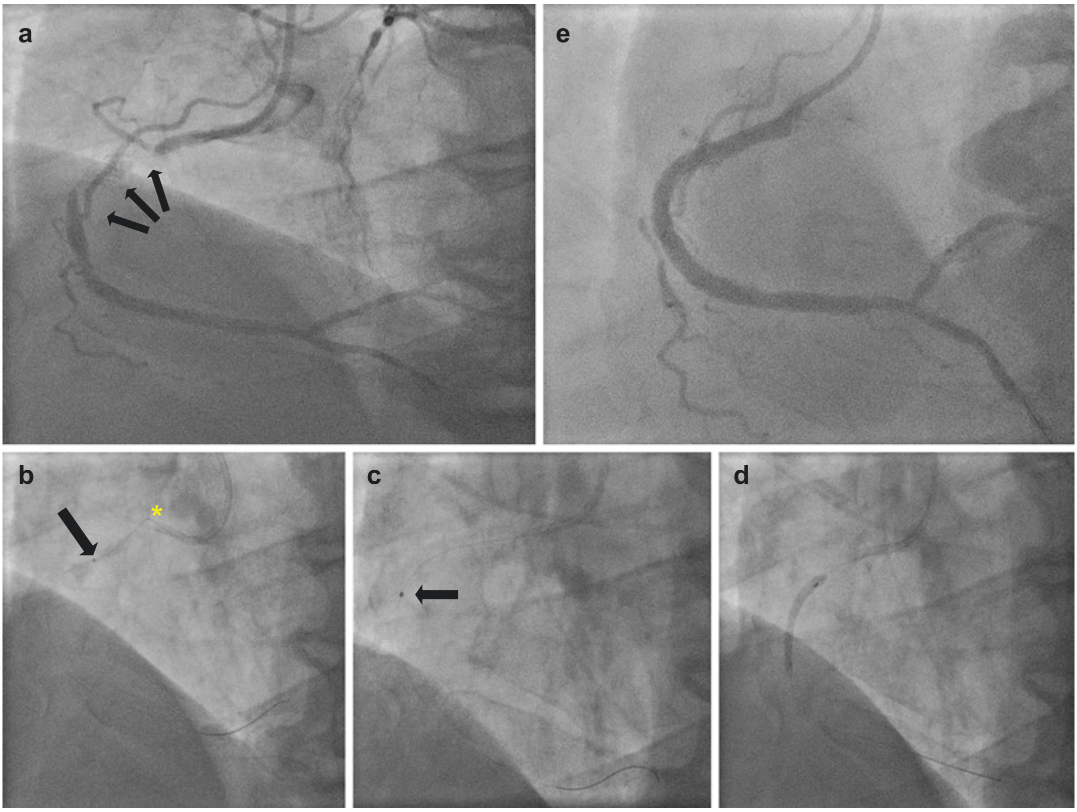

Fig. 9.7 The use of ELCA in CTO intervention. (**a**) Demonstrates the CTO in RCA which appears to be heavily calcified (arrows). (**b**) Failure to advance a low-profile 0.85 × 10 mm balloon (arrow) across the CTO resulting in 'buckling' of the guide-wire and disengagement of the guide-catheter (asterisk). (**c**) 0.9 mm X-80 ELCA catheter is used to debulk, crossing the proximal cap and establishing position within the true lumen. A 2.5 × 20 mm non-compliant balloon is used to pre-dilate the lesion (**d**) and the final result can be seen (**e**), after deployment of overlapping DES

plasty to balloon angioplasty alone and concluded that (a) no complications were associated with the use of laser, and (b) laser resulted in greater luminal gain, greater ablation of intimal hyperplasia, and a tendency toward less frequent subsequent target vessel revascularization [44]. The use of Eccentric laser catheters in treatment of diffuse in-stent restenosis may offer advantages over standard concentric equipment as they can be reorientated in increments of 90° thus providing progressive quadrantic tissue ablation [45] (Fig. 9.9).

Saphenous Vein Grafts

Occlusions in old saphenous vein grafts frequently consist of diffuse or multifocal plaques often containing thrombus. These lesions are degenerative and prone to distal embolization leading to the microvascular obstruction and the no reflow phenomenon, which is associated with adverse clinical outcomes. Despite the presence of a large thrombus burden within these vessels, a success rate of 94% was reported with both ELCA and mid-infrared holmium: YAG laser [46, 47]. The considerable capability of laser to provide safe debulking of these grafts even in the setting of AMI and in the presence of a heavy thrombus burden has been documented [29, 48]. Furthermore, the remarkably low rate of distal embolization during ELCA of degenerative bypass grafts (1–5%) precludes the need for adjunct distal protection device (DPD) in the

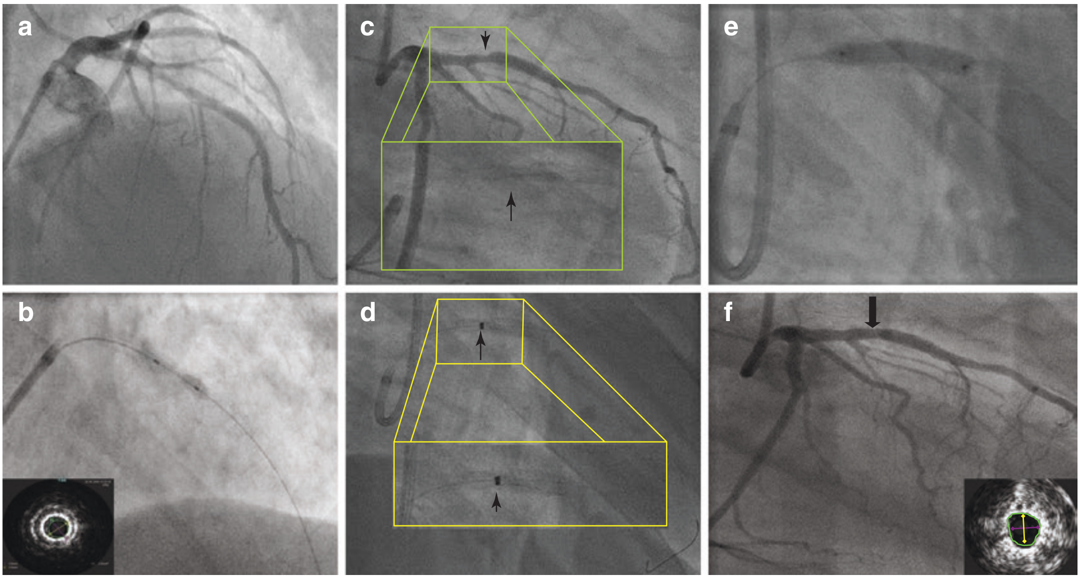

Fig. 9.8 Panel (**a**) illustrates a heavily calcified lesion in the proximal LAD. Despite extensive lesion preparation, including the use of rotational atherectomy (2 burrs), extensive use of non compliant, cutting, and double layer balloons, the lesion remains un-dilated (panel **b**, with IVUS of lesion within the inlay). A stent also failed to deploy, with an under expanded stent is visualised in the proximal LAD. (**d**) A 2.0 mm ELCA catheter is seen within the stent (arrow). The under expanded stent has been magnified in the in set (arrow head). (**e**) Successful balloon dilatation with a 4.25 x 10 mm balloon. (**f**) Final result

majority of cases where the excimer laser is used. However, when OCT has been used to visualize the effects of ELCA in SVG PCI, it is clear that there remain friable fragments that could embolise and cause no reflow [49] (Fig. 9.10). Indeed, one application of ELCA in SVG PCI is purely to create a small channel to deliver a DPD easily to complete the PCI in contrast to full debulking strategy with a larger diameter laser catheter.

Left Main Stem PCI

The role of PCI for unprotected left main coronary artery (LMCA) disease remains a hot topic of debate. Many Cardiologists agree that outcomes of PCI in ostial and mid-body LMCA disease are comparable to those with CABG, however the trial data for distal LMCA bifurcation disease somewhat favours CABG although a number of trials to report imminently look set to challenge that. A role for laser in LMCA PCI has emerged. In a series of 20 symptomatic patients with severe LMCA disease, the ELCA was used for pre-stent debulking (Fig. 9.11). Traditionally, performing a safe percutaneous intervention in the LMCA requires at least partial myocardial protection by patent bypass grafts (protected LMCA). However, in this series patent grafts were present in only 20% of cases with the majority having no distal protection or poor protection from a diseased graft. Nevertheless, successful intervention was achieved in 95% of the patients. The investigators concluded that small size laser catheters, when used with proper lasing technique and adjunct stenting can lead to successful debulking strategy in select patients with left main stenosis [50].

Aorto-Ostial Disease

These resistant atherosclerotic obstructions are usually focal, almost universally fibrotic, and often calcified. Precise laser debulking enables subsequent stenting. The success rate with laser and adjunct balloon angioplasty in two series of patients have been reported as high as 94% [51, 52], thus, far exceeding the relatively low 74–80% success rate for standard balloon angioplasty.

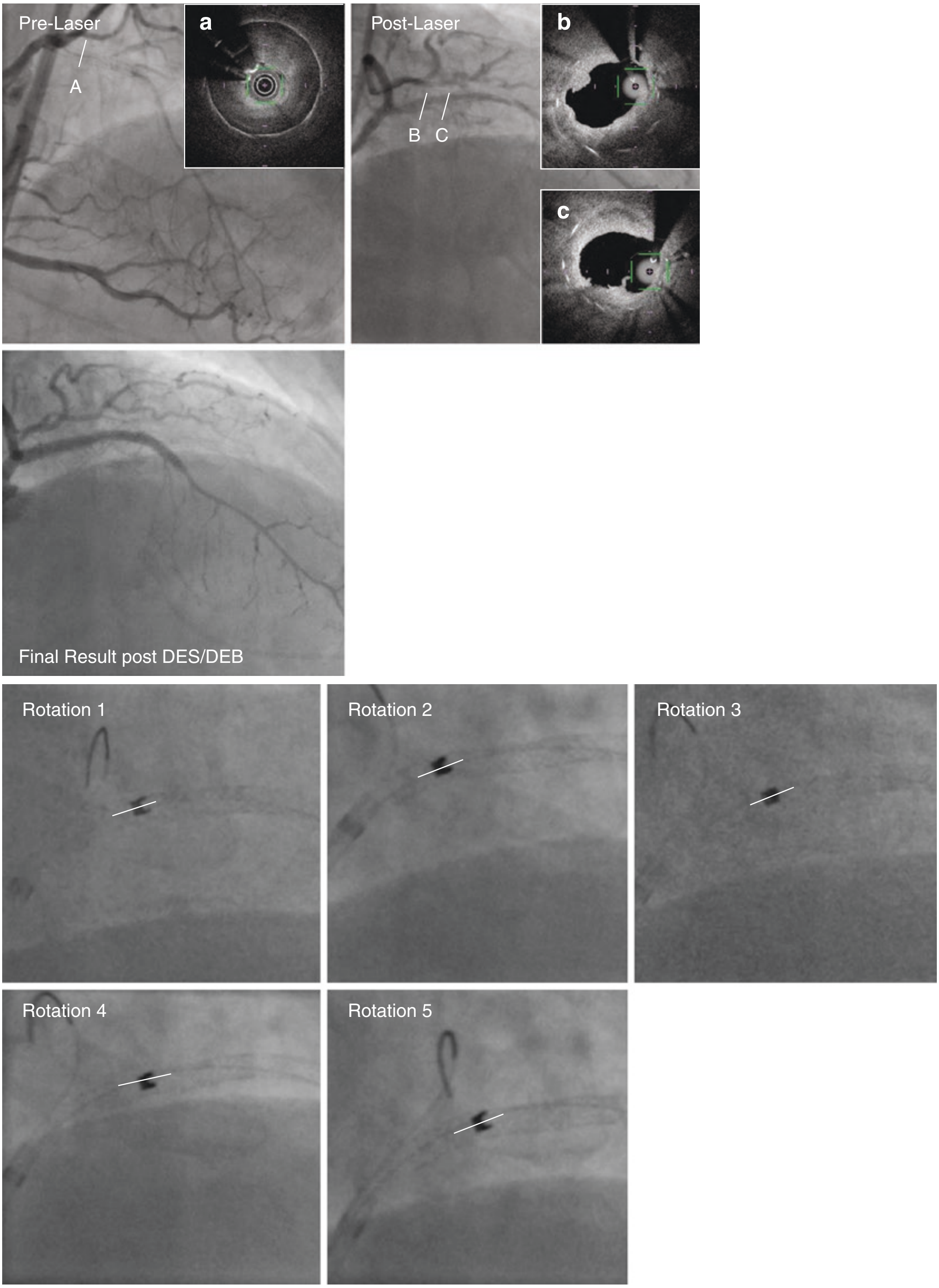

Fig. 9.9 (**a**) Severe concentric In-stent restenosis with near obliteration of the true lumen, with the appropriately sized stent clearly shown on the OFDI image. (**b**) Mid stent after passage of eccentric ELCA catheter, with evidence of tissue having been denuded from the stent surface (white circle). (**c**) Distal stent with a clear eccentric cavity having been created through tissue ablation from the ELCA catheter passage. The case is completed with a combination of new distal edge DES plus drug eluting balloons to the main LAD

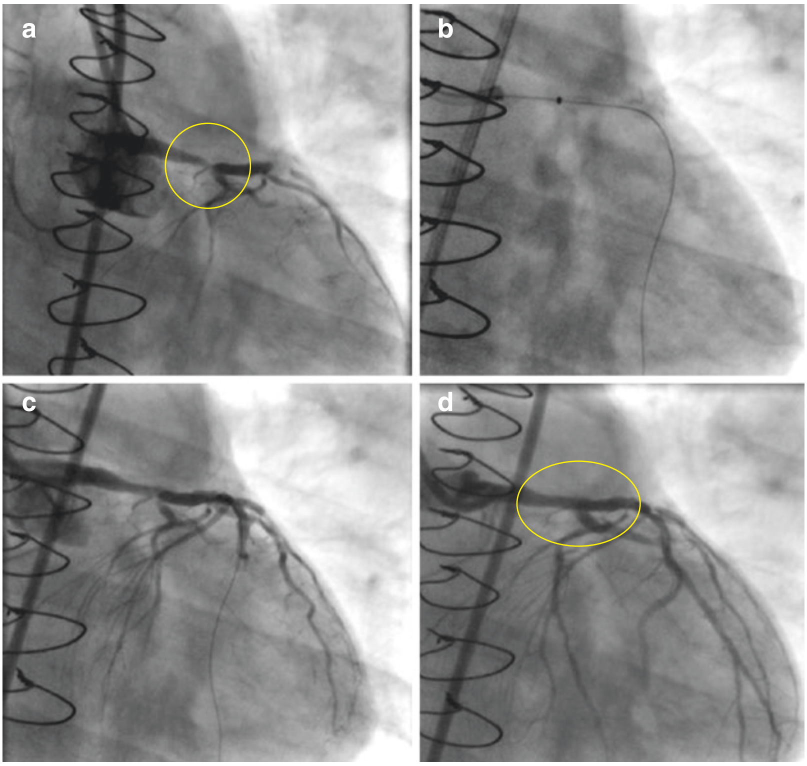

Fig. 9.10 Application of excimer laser in left main coronary artery disease in a patient with unstable angina following recent coronary artery bypass surgery, just 4 weeks prior to presentation. Two saphenous vein grafts had occluded with only the left internal mammary artery remaining patent. (**a**) The critical stenosis at the distal segment of the left main coronary artery (highlighted), with a strategy of performing PCI to the LMS bifurcation. (**b**) Activation of a 0.9 mm X-80 excimer laser [Spectranetics, Colorado Springs, CO] catheter [The radio-opaque tip highlighted and visible], successfully traversing the lesion. (**c**) Adequate recanalization post laser debulking, with maintenance of TIMI flow. (**d**) Final angiographic results post adjunct stenting: patent left main artery is present with good flow into the Circumflex artery. The patient's symptoms were completely relieved

Specific Non-coronary Clinical Applications for Laser

Trans Myocardial Laser Revascularization [TMLR]

This unique revascularization concept is based on the diversion of arterial blood flow into regions of the myocardium that do not receive adequate perfusion as a result of severe atherosclerotic coronary arterial disease. The technique predates coronary bypass grafting and coronary balloon angioplasty [53]. The aim of TMLR procedure is to create multiple 1 mm intramyocardial laser channels [TMLR] within the viable ischemic myocardium. The creation of these channels then promotes angiogenesis with growth of microvessels that provides an alternative blood supply to the treated area of myocardium [54]. The increase in microvessels significantly correlates with the expression of matrix metalloproteinases −2 and platelet-derived endothelial cell growth factor [55]. A specific indication for TMLR is the treatment of patients with refractory angina pectoris who are unable to undergo coronary bypass surgery for pain relief. TMLR has also been incorporated as an adjunct surgical treatment for those who undergo coronary bypass surgery but need further intraoperative revascularization of myocardial regions that cannot be reached with bypass grafts. The TMLR application involves application of specially designed laser catheters under direct vision or under fluo-

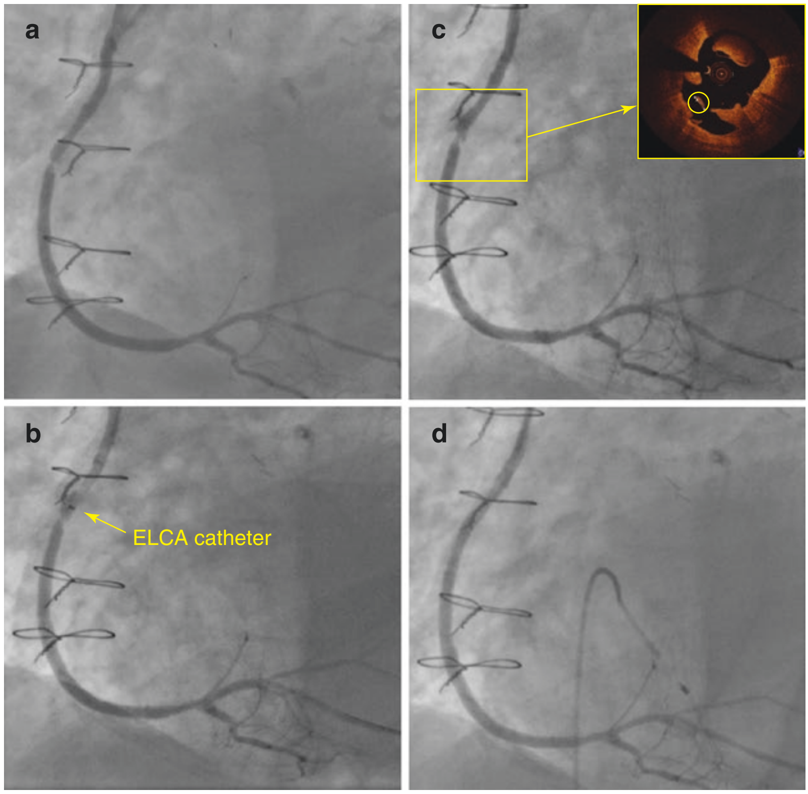

Fig. 9.11 Series of angiographic stills illustrating the role of ELCA in vein graft intervention. Panel **a** demonstrates a severe lesion in the mid SVG. Given its severity, distal protection device passage was not possible, to the lesion was treated with LECA (panel **b**). Panel **c** shows the angiographic and OCT result post ELCA. Crucially, given the soft nature of the plaque contained within SVGs, large fragments (~600 μm) are visible (yellow circle), and use of distal protection devices should be encouraged where possible to minimise any embolic complications. The case was completed with a pericardial stent (panel **d**)

roscopy guidance. These catheters are placed in direct contact against the epicardium and activated with emission of laser fluence inward toward the myocardium. Various laser sources such as CO2, excimer and holmium:YAG have been used for TMLR either surgically or percutaneously for treatment of patients with refractory angina [56]. TMLR has been shown in randomized studies to improve subjective symptoms of angina [57, 58] promote increased exercise time [59] and improve quality of life as compared with maximal medical therapy [60]. Recently it has been proposed that combining TMLR with cell therapy delivered through direct myocardial injections is a safe strategy which may act synergistically to reduce myocardial ischemia and improve functional capacity [61]. However, the precise functional mechanism of angina relief in TMLR remains unclear, and its effect is often transient in many cases [62]. One suggested punitive mechanism, that laser induced thermal damage to cardiac nerves resulting in denervation and subsequent angina relief, has been refuted [63]. Furthermore, whether TMLR results in improved cardiac function remains a controversial issue. It is a procedure that is now rarely undertaken, as both interventional revascularisaton and medical therapy for advanced intractable angina has advanced considerable since the techniques inception.

Laser for Revascularization of Heart Transplant Allograft Vasculopathy

Coronary allograft vasculopathy is a leading cause of late death in heart transplant recipients. Given the surgical complexity of repeat heart transplant, these patients are frequently not considered to be good candidates for the procedure. Hence, endovascular treatment in general, is the preferred, practical management option. However, this strategy has encountered difficulties with balloon angioplasty, directional atherectomy, and direct stenting having all been applied but with results that have been disapointing and less successful than in native vessels [64]. The application of excimer laser through low profile laser catheters appear to provide a unique advantage for revascularization in these challenging target lesions [65, 66]. As long term reduction of restenosis is not expected from the laser alone, adjunct stenting with drug eluting stents is indicated, and may offer reasonable long results.

Laser for Congenital Heart Disease

In certain congenital cardiac defects, the laser can provide means of critical revascularization. For example, the prognosis of infants with pulmonary atresia and intact ventricular septum is poor and presents a major management challenge. Mechanical penetration of the atretic pulmonary valve is an applicable option for decompression of the right ventricle to reduce critically high pressure and improve overall left ventricular function. Percutaneous excimer laser induced ablation of the atretic pulmonary valve can be accomplished safely by a "step by step" technique whereby the tip of the laser catheter is advanced before a guide wire. This recanalization then enables insertion and deployment of a peripheral balloon leading to life saving reopening of the main pulmonary artery. The laser fluence does not damage the surrounding cardiac tissue along this application [67].

Laser in Peripheral Revascularization

Peripheral atherosclerotic arterial disease is a major cause of lower extremity ischemia and limb loss. While several lasers have been investigated for peripheral revascularization [Holmium:YAG, Nd:YAG and excimer], initial experience by Isner and Rosenfield indicated that more favorable clinical results are obtained with the ultraviolet excimer laser [68]. Over the last decade, the excimer laser has gained a recognized role in the treatment of superficial femoral occlusions, popliteal artery stenoses and infra popliteal lesions. These targets cause chronic or critical limb ischemia, claudication and non-healing ulcers. The laser provides safe and efficacious lesion debulking, thrombus removal and facilitates stenting in such targets [69–71]. As for the technique of peripheral lasing Biamino and colleagues have described a gradual "step by step" approach for arterial recanalization with excimer laser. The long occlusions are reached by a guide wire and an over the wire laser catheter. The lesion is traversed by the laser catheter while the guide wire inside the catheter provides stable support. Then as the laser catheter debulks a portion of the obstructive plaque, the guide wire is advanced a few millimeters distally into the occlusion and the laser is reactivated to follow it with debulking [72]. Then the process is repeated until the entire length of the lesion is recanalized [64].

Specific Electrophysiological Clinical Applications for Laser

Device Lead Extraction

Until recently the only option for removal of intracardiac pacemaker or defibrillator leads were either by surgical procedure or traction; however both approaches carried significant risk and complications. The development and application of the excimer laser sheath technology [Spectranetics, Colorado Springs, CO] that delivers ultraviolet light has revolutionized the lead extraction procedure. The energy interacts and ablates the encasing fibrotic tissue surrounding the pacemaker or defibrillator leads making extraction of the entire lead possible without disruption of the myocardium and vascular structures. This results in a predictably high success rate and markedly low complication rate [73]. Furthermore, the excimer laser has been shown to be safe and effective in the removal of device leads associated with central venous obstruction, and in crossing device related subclavian vein occlusion where wire escalation techniques have failed without damaging the in situ lead insulation [74, 75].

AF Ablation/Pulmonary Vein Isolation

Over recent years ablative strategies for atrial fibrillation have grown hugely. These procedures have typically been performed using radiofrequency energy with electro-anatomical mapping. Recently, visually guided laser ablation (VGLA) has been developed which incorporates an endoscope, a laser and a semi-compliant balloon in a system that enables direct visualization of the left atrium and pulmonary veins and delivery of a

980 nm diode laser to isolate the pulmonary veins [76]. This technology appears to be effective with acceptable peri-procedural complications.

Future Potential

Renal Artery Interventions

Since the excimer laser effectively removes coronary and peripheral plaques, conceptually it could also be applied for renal artery stenosis. In an early experience, this technology was found safe and effective in debulking of severe-critical renal artery stenosis. The application of laser energy facilitated adjunct stenting and preserved renal integrity. Improved hypertension control and management of congestive heart failure were observed. This was accompanied by preservation of renal function [77].

Stroke

Thrombus plays a crucial role in the pathophysiology of intracranial stroke. As lasers enhance the effect of thrombolytic agents and favorably interact with thrombus and platelets they may become a unique treatment option for enhanced thrombolysis in selected acute stroke patients [78, 79].

Venous System

Based on the abovementioned description of the favorable interaction between laser light and thrombus and fibrotic tissues, conceivably, selected patients with acute or chronic venous obstructions or thrombosis will benefit from laser treatment.

Summary

Cardiovascular lasers with various wavelengths produce intense electromagnetic energy. This may be utilised in a variety of applications throughout the cardiovascular sstem. Currently, the most common application remains the ablation and removal of coronary and peripheral atherosclerotic plaques. The ultraviolet pulsed wave excimer laser [308 nanometer wavelength] is currently the only laser approved by the FDA for peripheral and coronary interventions in the context of acute and chronic ischemic syndromes. This laser has been shown to effectively debulk atherosclerotic and fibrotic plaques and remove associated thrombus burden. Within the coronary circulation, data would currently support the use of excimer laser in "uncrossable" lesions and the treatment of an under-expanded and re-stenotic stent. The holmium:YAG laser is currently approved for surgical TMLR. Careful case selection, proper utilization of the laser equipment and incorporation of a safe, efficacious lasing technique plays a crucial role in successful laser interventions.

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