

The effectiveness of excimer laser angioplasty to treat coronary in-stent restenosis with peri-stent calcium as assessed by optical coherence tomography



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KEYWORDS

- calcified stenosis
- in-stent restenosis
- laser
- optical coherence tomography

Abstract

Aims: We aimed to evaluate the effectiveness of excimer laser coronary angioplasty (ELCA) to treat in-stent restenosis (ISR) due to peri-stent calcium-related stent underexpansion as assessed by optical coherence tomography (OCT).

Methods and results: We studied 81 patients (81 lesions with ISR, stent underexpansion, and peri-stent calcium >90°) who underwent OCT imaging both pre and post percutaneous coronary intervention and compared lesions treated with ELCA (n=23) vs. without ELCA (n=58). ELCA use was associated with more calcium fracture (ELCA: 61%, non-ELCA: 12%, p<0.01), larger final minimum lumen area (ELCA: 4.76 mm² [3.25, 5.57], non-ELCA: 3.46 mm² [2.80, 4.13], p<0.01), and a larger previously implanted stent area (ELCA: 6.15 mm² [4.83, 7.09], non-ELCA: 4.65 mm² [3.84, 5.40], p<0.01). In the multivariable model, ELCA use was associated with peri-stent calcium fracture (odds ratio 46.5, 95% confidence interval: 6.8, 315.9, p<0.001) that, in turn, was associated with final larger lumen and stent dimensions. Finally, contrast injection during ELCA was associated with multiple calcium fractures and fractures even in thicker calcium.

Conclusions: ELCA is effective for treating ISR with underexpansion by disrupting peri-stent calcium, facilitating better expansion of the previously implanted stent.

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Abbreviations

ELCA	excimer laser coronary angioplasty
ISR	in-stent restenosis
IVUS	intravascular ultrasound
MLA	minimum lumen area
MSA	minimum stent area
OAS	orbital atherectomy system
OCT	optical coherence tomography
PCI	percutaneous coronary intervention
RA	rotational atherectomy

Introduction

Stent underexpansion is one of the most frequent causes of stent failure, especially within one year of stent implantation¹⁻³. Stent underexpansion is related to poor vessel compliance, especially in severely calcified lesions⁴. Although calcified lesion preparation with rotational atherectomy (RA), the orbital atherectomy system (OAS), or excimer laser coronary angioplasty (ELCA) modifies calcium to prevent stent underexpansion, these devices are underutilised.

The predominant ELCA effect is rapid conversion of water into exploding vapour bubbles, thereby modifying the plaque⁵. Although the use of ELCA when treating in-stent restenosis (ISR) and stent underexpansion due to peri-stent calcium has been reported in previous case series⁶⁻⁸, its efficacy and mechanism have not been well studied.

Intravascular optical coherence tomography (OCT) can penetrate and characterise calcium with great resolution (10 μm)⁹. We used OCT to assess the mechanism of ELCA use before conventional high-pressure ballooning when treating ISR lesions with peri-stent calcium-related stent underexpansion.

Methods

STUDY POPULATION

This was a retrospective observational study at two sites (St. Francis Hospital, Roslyn, NY; NewYork-Presbyterian Hospital, New York, NY, USA). From May 2011 to April 2017, there were 139 patients who underwent OCT imaging during percutaneous coronary intervention (PCI) of 149 ISR lesions and peri-stent calcium $>90^\circ$ ^{9,10}. Operators decided whether to use (1) ELCA before conventional high-pressure ballooning, (2) contrast or saline flush during ELCA, and (3) additional new stent implantation. All lesions were treated by xenon-chlorine (excimer) pulsed laser (Turbo-Elite™ catheter; Spectranetics Corporation, Colorado Springs, CO, USA). The size of the laser catheter, fluency, and repetition rate were left to the operator's discretion.

After excluding 68 lesions, 81 ISR lesions in 81 patients were included (**Figure 1**). The primary analysis was a comparison of angiographic and OCT acute outcomes between lesions with versus without ELCA. A secondary subgroup comparison was performed for lesions treated with or without new stent implantation.

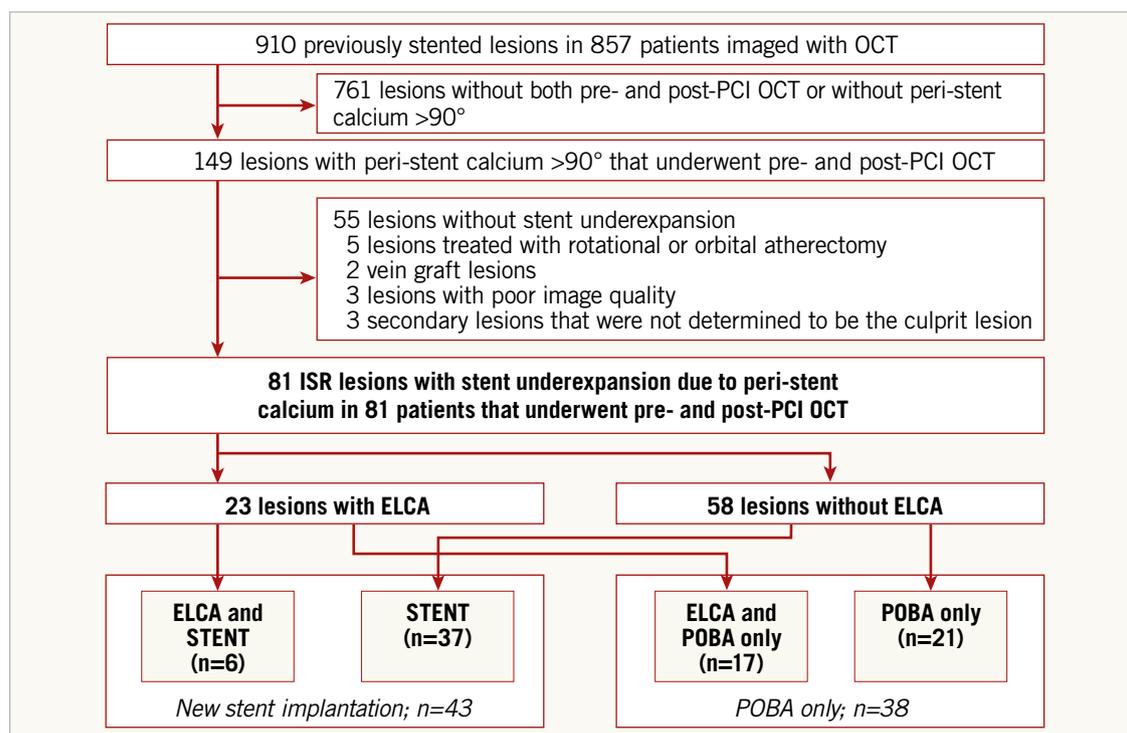


Figure 1. Study flow diagram. Overall, 81 in-stent restenosis (ISR) lesions (81 patients) with stent underexpansion due to peri-stent calcium $>90^\circ$ underwent pre- and post-PCI OCT and were divided into the following groups: (1) with or without excimer laser coronary angioplasty (ELCA) treatment and (2) with or without new stent implantation. POBA: plain old balloon angioplasty

CORONARY ANGIOGRAPHIC ANALYSIS

Off-line quantitative coronary angiography was performed using QAngio XA (Medis medical imaging systems, Leiden, the Netherlands) without knowledge of clinical and OCT information. The minimum lumen diameter, reference diameter, and lesion length were measured, and the restenosis pattern was classified¹¹.

OCT IMAGE ACQUISITION AND ANALYSIS

OCT images were acquired using frequency-domain OCT: C7-XR™ or ILUMIEN™ OPTIS™ system (Abbott Vascular, Santa Clara, CA, USA) and a 2.7 Fr OCT imaging catheter (C7 Dragonfly™, Dragonfly™ Duo, or Dragonfly™ OPTIS™; Abbott Vascular). An OCT catheter was advanced distal to the lesion, and contrast media was injected at a flush rate of 3.0-4.0 mL/s through the guiding catheter with automatic pullback at a frame interval of 0.1-0.2 mm. Using previously validated criteria for OCT plaque characterisation¹², off-line analysis was performed using proprietary software (Abbott Vascular) by two experienced investigators (T. Lee and A. Maehara) who were blinded to the angiographic findings and one of whom (A. Maehara) was blinded to ELCA usage.

All cross-sectional OCT frames were evaluated; stent and lumen areas were measured at the minimum lumen area (MLA)

site, including old stent MSA (minimum stent area) and new stent MSA (if implanted). Calcium was defined as a region with sharply delineated borders, and peri-stent calcium was defined as calcium outside and/or inside the stent (i.e., calcified neointima) (Figure 2, Figure 3, Moving image 1-Moving image 4). Calcium fracture was a slit or complete break in the calcium plate that was identified in the final OCT¹³; it was considered as multiple fractures when >1 calcium fracture was observed in a single frame (Figure 2, Figure 3, Moving image 1-Moving image 4)¹⁴. Fractured calcium thickness was measured at the edge of the fracture. The maximum peri-stent calcium angle was measured, and the minimum and maximum peri-stent calcium thicknesses were measured in the frame with maximum peri-stent calcium. Stent expansion was the MSA (old or new stent) divided by the average of the proximal and distal reference lumen areas; underexpansion was stent expansion <0.8 and MSA <5.0 mm²^{1,15}.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS, Version 22.0 (IBM Corp., Armonk, NY, USA). Categorical data were expressed as frequencies and compared using the χ^2 or Fisher's exact test, as appropriate. Because most values were not normally distributed, continuous variables were expressed as

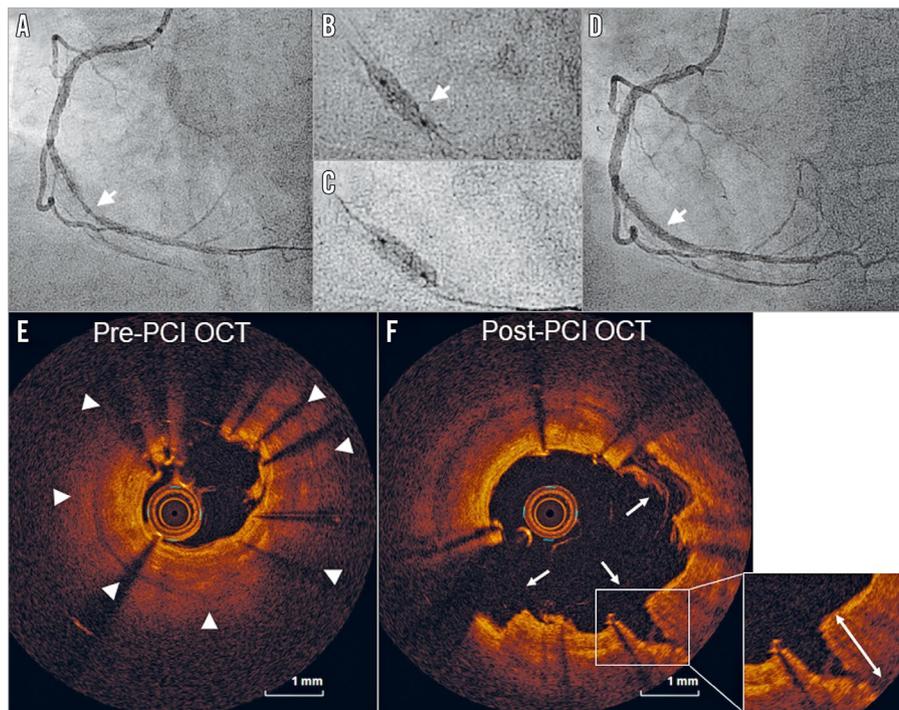


Figure 2. Representative case of ELCA treatment of in-stent restenosis. A) Pre-PCI angiogram showed severe in-stent stenosis in the distal right coronary artery (white arrow). B) Non-compliant ballooning (3.5 mm in diameter) at 22 atm showing indentation (white arrow). ELCA was then performed. C) After ELCA, non-compliant ballooning (3.75 mm in diameter) at 22 atm showing no balloon indentation. D) Final angiogram showing no residual stenosis. E) OCT before ELCA showing old stent underexpansion (stent area 3.25 mm²) due to diffuse circumferential peri-stent calcium (white arrowheads). F) Post-PCI OCT showed good expansion of the old stent (stent area 7.99 mm²) with multiple peri-stent calcium fractures (white arrows at 2, 5, and 8 o'clock). Fractured calcium thickness was 0.82 mm (inset, double-headed arrow).

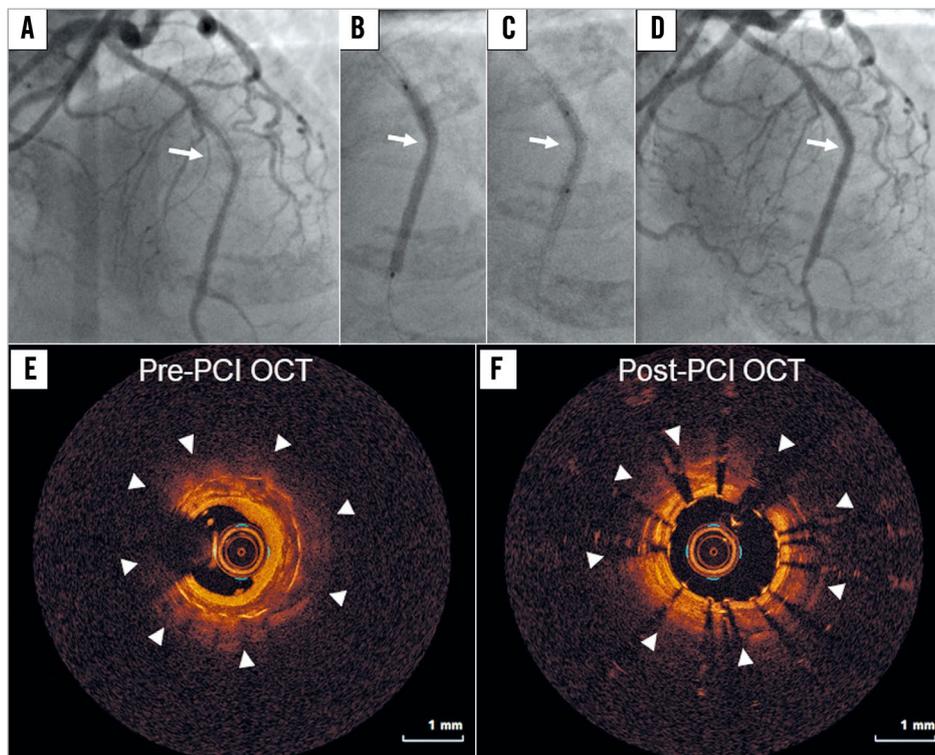


Figure 3. Representative case of PCI without ELCA treatment. A) Pre-PCI angiogram showed severe in-stent stenosis in the mid left anterior descending coronary artery (white arrow). B) New stent implantation with balloon indentation (white arrow). C) Balloon dilation at 30 atm after new stent implantation. D) Final angiogram showed mild residual stenosis in the middle of the stent (white arrow). E) Pre-PCI OCT imaging showing diffuse circumferential peri-stent calcium (white arrowheads) and old stent underexpansion (stent area 4.00 mm²). F) Post-PCI OCT imaging showing poor expansion of the newly implanted stent (stent area 4.27 mm²) without peri-stent calcium fracture.

median (interquartile range) and compared using the Mann-Whitney U test. The effect of ELCA in creating calcium fracture was tested using a multivariable logistic regression model. The effect of ELCA on acute OCT-derived outcomes (i.e., final MLA or MSA) was tested using a multivariable linear regression model after adjusting for OCT-derived morphological characteristics based on the results (**Table 1-Table 3**) along with known clinical risk factors^{4,16,17} including multiple stent layers, peri-stent maximum calcium angle, peri-stent minimum calcium thickness, pre-PCI old stent MSA, mean reference lumen area, maximum balloon pressure, scoring balloon use, and balloon/artery ratio. Qualitative and quantitative inter- and intra-observer variability was tested using kappa statistics and intra-class correlation coefficient (ICC), respectively. A p-value <0.05 was considered statistically significant.

Results

CLINICAL, ANGIOGRAPHIC, AND OCT CHARACTERISTICS

Among 81 ISR lesions, 23 were treated with ELCA and 58 were treated with just high-pressure balloon inflation (**Figure 1**). Mean ELCA catheter size, fluency, and repetition rate were 1.3±0.2 (0.9 mm in six lesions, 1.4 mm in 15 lesions, and 1.7 mm in two lesions), 66±9 mJ/mm², and 64±8 Hz, respectively. Contrast

flush was used during ELCA in 35% (8/23). A new stent was implanted in 53% (43/81).

There was no significant difference in clinical characteristics between patients treated with versus without ELCA (**Table 1**). In the angiographic analysis (**Table 2**), pre-PCI findings were similar between the two groups. Post PCI, lesions treated with ELCA showed a larger angiographic minimum lumen diameter and a smaller diameter stenosis than those not treated with ELCA, even though new stent implantation was less frequent in lesions treated with ELCA (26.1%) versus those treated without ELCA (63.8%).

There was good concordance both of inter- and intra-observer agreement for the diagnosis of calcium fracture (κ=0.85, 0.95), maximum calcium angle (ICC=0.83, 0.91), maximum calcium thickness (ICC=0.88, 0.88), and minimum calcium thickness (ICC=0.77, 0.89), respectively. Peri-stent calcium was located only outside the stent (calcium in the native plaque) in 93% (75/81), and both inside (i.e., neointimal calcium) and outside the stent in 7% (6/81). Time from stent implantation was longer in lesions with neointimal calcium compared with only calcium outside the stent: 9.2 (8.3, 11.3) years versus 2.3 (0.8, 5.6) years, p=0.002. In the pre-PCI OCT analysis, the maximum peri-stent calcium angle and thickness measured 273° (median

Table 1. Patient characteristics.

	Lesions with ELCA (n=23)	Lesions without ELCA (n=58)	p-value
Age, years	72 (60, 76)	68 (61, 74)	0.60
Male sex	20 (87.0)	37 (63.8)	0.06
Stable angina	11 (47.8)	22 (37.9)	0.41
Acute coronary syndrome	12 (52.2)	36 (62.1)	0.41
STEMI	1 (4.3)	1 (1.7)	0.49
Non-STEMI	0 (0.0)	4 (7.0)	0.32
Unstable angina	11 (47.8)	31 (53.4)	0.65
Diabetes mellitus	15 (65.2)	29 (50.0)	0.32
Insulin-treated	5 (21.7)	12 (20.7)	1.00
Hypertension	19 (82.6)	53 (91.4)	0.27
Dyslipidaemia	19 (82.6)	52 (89.7)	0.46
Current smoker	3 (13.0)	4 (6.9)	0.40
Previous myocardial infarction	11 (47.8)	22 (37.9)	0.41
Previous CABG	10 (43.5)	15 (25.9)	0.12
Renal insufficiency*	11 (47.8)	23 (40.4)	0.54
Haemodialysis	2 (8.7)	5 (8.8)	1.00

Values are n (%) or median (interquartile range). * Estimated glomerular filtration using Modification of Diet in Renal Disease study equation <60 mL/min/1.73 m². CABG: coronary artery bypass grafting; ELCA: excimer laser coronary angioplasty; STEMI: ST-segment elevation myocardial infarction

and 0.70 mm (median), respectively; the old stent MSA measured 3.47 mm² (median) without any difference between the ELCA and non-ELCA groups. Irrespective of new stent implantation, the final old stent MSA (6.15 mm² [4.83, 7.09] versus 4.65 mm² [3.84, 5.40], p<0.01) and the acute gain of the old stent MSA (2.15 mm² [1.34, 3.55] versus 0.93 mm² [0.39, 1.57], p<0.001) were larger in lesions treated with ELCA versus without ELCA along with more peri-stent calcium fracture (61% versus 12%, p<0.001) (**Table 3**). Among 23 lesions treated with ELCA, there were 13 lesions with pre-intervention, post-ELCA (but before post-dilation with high pressures), and final OCT imaging. Calcium fracture was observed in one lesion post ELCA, while in nine lesions (69%) calcium fracture was observed post dilation or after new stent implantation (p=0.004). Accordingly, the Δ MLA was greater from post ELCA to final (1.91±0.45 mm²) than pre-intervention to post ELCA (0.70±0.83 mm², p=0.02). In non-calcified segments, dissections were small without difference between lesions with versus without ELCA (dissection angle, 38 [0, 52] versus 0 [0, 29]°, p=0.09).

All peri-stent calcium fractures were observed in calcium outside the stent. This was consistent in six lesions with calcium both inside and outside of the stent (prevalence of peri-stent calcium fracture: 2/2 with ELCA versus 0/4 without ELCA, p=0.07) or in 75 lesions with calcium only outside the stent (12/21=57% with ELCA versus 7/54=13% without ELCA, p<0.001).

Table 2. Angiographic findings.

	Lesions with ELCA (n=23)	Lesions without ELCA (n=58)	p-value
Target vessel			
Left anterior descending	11 (47.8)	24 (41.4)	0.62
Left circumflex	5 (21.7)	19 (32.8)	
Right	7 (30.4)	15 (25.9)	
Lesion location			
Ostium	1 (4.3)	4 (6.9)	0.94
Proximal	8 (34.8)	15 (25.9)	
Mid	11 (47.8)	30 (51.7)	
Distal	1 (4.3)	3 (5.2)	
Branch	2 (8.7)	6 (10.3)	
In-stent restenosis pattern			
Focal	20 (87.0)	46 (79.3)	0.43
Diffuse	3 (13.0)	8 (13.8)	
Proliferative	0 (0.0)	4 (6.9)	
Pre-PCI			
Lesion length, mm	9.3 (6.2, 13.0)	9.1 (6.2, 13.0)	0.76
Total old stent length, mm	27.2 (21.2, 34.1)	28.6 (23.1, 36.4)	0.51
Reference vessel diameter, mm	2.71 (2.18, 3.04)	2.43 (2.21, 2.65)	0.14
Minimum lumen diameter, mm	1.03 (0.80, 1.33)	0.97 (0.72, 1.42)	0.46
Diameter stenosis, %	57.7 (52.1, 63.8)	56.6 (47.3, 70.0)	0.79
Post-PCI			
Minimum lumen diameter, mm	2.48 (2.11, 2.72)	2.18 (1.97, 2.42)	0.03
Diameter stenosis, %	14.6 (11.2, 26.6)	24.6 (15.9, 31.3)	0.01
Acute gain, mm	1.37 (0.97, 1.77)	1.15 (0.77, 1.61)	0.14
Procedure characteristics			
Cutting balloon use	0 (0.0)	3 (5.2)	0.55
Scoring balloon use	13 (56.5)	23 (39.7)	0.22
New stent implantation	6 (26.1)	37 (63.8)	0.003
Maximum balloon diameter, mm	3.50 (3.25, 3.75)	3.00 (3.00, 3.50)	0.003
Balloon to artery ratio	1.29 (1.17, 1.45)	1.29 (1.13, 1.43)	0.73
Maximum balloon pressure, atm	20 (20, 24)	20 (20, 24)	0.41

Values are n (%) or median (interquartile range). PCI: percutaneous coronary intervention

IMPACT OF CONTRAST INJECTION DURING ELCA

Irrespective of new stent implantation, 35% (8/23) of ELCA procedures used contrast flush, and 65% (15/23) used saline flush.

Table 3. Optical coherence tomography findings.

	Lesions with ELCA (n=23)	Lesions without ELCA (n=58)	p-value
Pre-PCI			
Maximum peri-stent calcium angle, °	289 (231, 360)	258 (210, 307)	0.09
Maximum peri-stent calcium thickness, mm	0.74 (0.66, 0.87)	0.66 (0.56, 0.78)	0.056
Minimum peri-stent calcium thickness, mm	0.43 (0.37, 0.52)	0.33 (0.27, 0.40)	0.001
MLA, mm ²	1.96 (1.31, 2.59)	1.77 (1.36, 2.14)	0.39
Old stent MSA, mm ²	3.24 (2.28, 4.60)	3.51 (3.11, 4.20)	0.41
Multiple old stent layers at MSA site	9 (39.1)	17 (29.3)	0.44
Post-PCI			
MLA, mm ²	4.76 (3.25, 5.57)	3.46 (2.80, 4.13)	0.004
Delta minimum lumen area, mm ²	2.16 (1.45, 3.73)	1.66 (0.93, 2.37)	0.01
Old stent MSA, mm ²	6.15 (4.83, 7.09)	4.65 (3.84, 5.40)	0.001
Δ old stent MSA, mm ²	2.15 (1.34, 3.55)	0.93 (0.39, 1.57)	<0.001
Old stent expansion	1.05 (0.92, 1.24)	0.84 (0.74, 0.93)	<0.001
Peri-stent calcium fracture	14 (60.9)	7 (12.1)	<0.001
Multiple peri-stent calcium fracture	7 (30.4)	1 (1.7)	<0.001
Dissection	11 (47.8)	21 (36.2)	0.34
Maximum angle, °	38 (0, 52)	0 (0, 29)	0.09
Length, mm	0.6 (0.0, 2.2)	0.0 (0.0, 1.2)	0.16
Values are n (%) or median (interquartile range). MLA: minimum lumen area; MSA: minimum stent area; PCI: percutaneous coronary intervention			

ELCA procedures performed with contrast flush more often had multiple calcium fractures (63% versus 13%, $p=0.03$), even though lesions treated with contrast flush had greater peri-stent calcium (and thicker calcium) versus lesions treated using saline flush (360° [301, 360] versus 266° [206, 294], $p=0.01$). Fractured calcium was thicker in lesions treated by ELCA with contrast (0.73 mm) versus ELCA without contrast (0.45 mm) or without ELCA (0.32 mm), but not between lesions treated by ELCA with versus without contrast (**Figure 4**).

IMPACT OF NEW STENT VERSUS BALLOON DILATION ALONE

We performed subgroup comparison between lesions treated with versus without ELCA in lesions with or without new stent implantation (i.e., balloon only), separately (**Table 4**). The effect of ELCA (more peri-stent calcium fractures resulting in a greater increase in the old stent MSA and a larger final MLA) was consistent in both

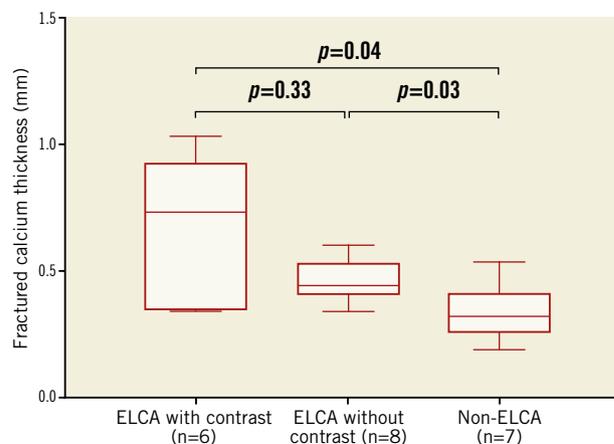


Figure 4. Calcium fracture thickness among lesions without ELCA, ELCA without contrast, and ELCA with contrast. In lesions treated using ELCA with contrast, fractured calcium was thicker than in the other two groups.

subgroups with a greater difference in lesions treated with a new stent versus balloon only.

CLINICAL AND OCT CHARACTERISTICS ASSOCIATED WITH CALCIUM FRACTURE AND IMPROVED OLD STENT EXPANSION

In a multivariable logistic regression analysis to predict peri-stent calcium fracture (seen in 26%, 21/81), ELCA (odds ratio [OR] 46.5, 95% confidence interval [CI]: 6.8, 315.9, $p<0.001$), maximum peri-stent calcium angle per quadrant (OR 5.1, 95% CI: 1.46, 17.9, $p=0.01$), and minimum peri-stent calcium thickness per 0.1 mm (OR 0.99, 95% CI: 0.98, 0.99, $p=0.01$) were independently associated with peri-stent calcium fracture. Because there were only 21 calcium fractures, only three covariates were entered into the model.

In a multivariable linear regression model to predict (1) MLA increase, (2) old stent MSA increase, and (3) post-PCI old stent expansion, ELCA and scoring balloon use were significantly associated with all three endpoints, whereas multiple stent layers of old stents and maximum peri-stent calcium angle were associated with lesser stent expansion (**Table 5**).

There was one coronary perforation and one coronary dissection requiring additional stent implantation in patients treated without ELCA, one dissection requiring additional stent implantation in a patient treated with ELCA without contrast, and no coronary perforation or dissection requiring additional stent implantation in patients treated with ELCA with contrast flush.

Discussion

OCT provided insights into the mechanism of the efficacy of ELCA for ISR lesions due to OCT-documented peri-stent calcium. The major findings were as follows: (1) ELCA created more calcium fractures even if the calcium was thicker, and this effect was

Table 4. Optical coherence tomography findings between lesions with ELCA and non-ELCA among lesions with new stent implantation and those without.

	ELCA and stent (n=6)	Non-ELCA and stent (n=37)	p-value	ELCA and POBA (n=17)	Non-ELCA and POBA (n=21)	p-value
Pre-PCI findings						
Maximum peri-stent calcium angle, °	301 (266, 360)	258 (216, 321)	0.34	284 (224, 360)	257 (197, 295)	0.18
Maximum peri-stent calcium thickness, mm	0.75 (0.70, 0.87)	0.64 (0.54, 0.77)	0.08	0.74 (0.65, 0.94)	0.68 (0.61, 0.79)	0.69
Minimum peri-stent calcium thickness, mm	0.49 (0.41, 0.55)	0.32 (0.27, 0.36)	0.005	0.42 (0.36, 0.50)	0.34 (0.27, 0.42)	0.12
Minimum lumen area, mm ²	2.65 (1.28, 2.96)	1.66 (1.28, 2.03)	0.19	1.78 (1.34, 2.52)	2.03 (1.62, 2.27)	0.69
Old stent MSA, mm ²	4.12 (2.92, 4.96)	3.51 (3.09, 4.37)	0.57	3.18 (2.25, 4.52)	3.51 (3.15, 4.06)	0.42
Multiple old stent layers at MSA site	0 (0.0)	9 (24.3)	0.32	9 (52.9)	9 (38.1)	0.51
Final OCT findings						
Minimum lumen area, mm ²	5.60 (4.83, 7.99)	3.45 (2.80, 4.14)	<0.001	4.35 (3.10, 5.05)	3.53 (2.90, 4.11)	0.19
ΔMLA, mm ²	3.77 (1.64, 5.08)	2.01 (0.92, 2.44)	0.038	2.12 (1.37, 3.08)	1.59 (0.95, 2.14)	0.06
Old stent MSA, mm ²	7.22 (6.63, 9.94)	4.61 (3.85, 5.36)	0.001	5.73 (4.60, 6.64)	4.68 (3.83, 5.62)	0.10
Δ old stent MSA, mm ²	3.71 (2.15, 4.96)	0.95 (0.33, 1.48)	0.01	2.07 (1.31, 3.29)	0.90 (0.58, 1.85)	0.007
Old stent expansion	1.25 (0.98, 1.43)	0.85 (0.75, 0.91)	0.005	1.02 (0.91, 1.13)	0.80 (0.67, 0.99)	0.036
New stent MSA, mm ²	7.22 (6.63, 9.94)	4.61 (3.85, 5.36)	–	–	–	–
New stent expansion	1.04 (0.66, 1.21)	0.65 (0.55, 0.75)	0.006	–	–	–
Peri-stent calcium fracture	4 (66.7)	5 (13.5)	0.01	10 (58.8)	2 (9.5)	0.002
Multiple peri-stent calcium fracture	2 (33.3)	1 (2.7)	0.047	5 (29.4)	0 (0.0)	0.01

Values are n (%) or median (first quartile, third quartile). ELCA: excimer laser coronary angioplasty; MSA: minimum stent area; OCT: optical coherence tomography; PCI: percutaneous coronary intervention; POBA: plain old balloon angioplasty

Table 5. Procedural and lesion characteristics associated with ΔMLA, Δ old stent MSA, and stent expansion.

	ΔMLA		Δ Old stent MSA		Old stent expansion	
	Regression coefficient (95% CI)	p-value	Regression coefficient (95% CI)	p-value	Regression coefficient (95% confidence interval)	p-value
Excimer laser coronary angioplasty	1.20 (0.63, 1.78)	<0.001	1.62 (1.05, 2.20)	<0.001	0.25 (0.15, 0.35)	<0.001
Multiple stent layers	-1.04 (-0.49, -1.59)	<0.001	-1.29 (-0.72, -1.86)	<0.001	-0.19 (-0.10, -0.28)	<0.001
Scoring balloon use	0.72 (0.20, 1.25)	0.008	0.63 (0.10, 1.16)	0.02	0.13 (0.04, 0.21)	0.005
Maximum peri-stent calcium angle per quadrant	–	–	–	–	-0.09 (-0.03, -0.15)	0.004
Pre-PCI old stent MSA	–	–	-0.60 (-0.30, -0.91)	<0.001	–	–
Mean reference lumen area	0.46 (0.29, 0.64)	<0.001	0.57 (0.38, 0.75)	<0.001	–	–

Values are n (%) or median (interquartile range). CI: confidence interval; PCI: percutaneous coronary intervention

more pronounced with contrast flush; (2) ELCA resulted in larger final lumen dimensions and better stent expansion compared with high-pressure balloon dilation alone.

ELCA was introduced two decades ago to treat complex coronary artery disease, including ISR and calcified lesions. Even in the drug-eluting stent (DES) era, stent underexpansion remains an important risk factor for stent thrombosis and restenosis³, and management of ISR lesions with an underexpanded stent due to severe peri-stent calcium remains a technical challenge. Although

treatment of stent underexpansion due to severe calcium is a niche application for ELCA, alternatives for these patients are limited and include coronary artery bypass graft surgery, RA, or OAS, all with their own potential problems (burr entrapment, distal embolisation of microparticles, and vessel damage). There is limited published clinical experience^{18,19}.

Mintz et al²⁰ reported that ELCA in non-stented lesions increased lumen area by both atheroablation and vessel expansion without a reduction in lesion calcium, and superficial

fibrocalcific deposits developed a fragmented appearance when imaged by intravascular ultrasound (IVUS). Another IVUS study showed that lumen enlargement from ELCA during the treatment of ISR was the result of neointimal tissue ablation²¹. Even though the efficacy of ELCA to treat an underexpanded restenotic stent has been reported⁷, the precise mechanisms have not been well understood. Because IVUS is unable to penetrate calcium with a limited resolution compared with OCT, it is difficult to assess the efficacy of ELCA treatment using IVUS, especially when treating ISR lesions. We demonstrated that ELCA-treated lesions had more calcium fracture, especially in more severely calcified lesions with greater calcium thickness where calcium fracture was necessary to correct stent underexpansion. This current study also highlighted the value of contrast flush during ELCA, including multiple calcium fractures even in the setting of more severe peri-stent calcium. Blood and radiographic contrast absorb 308 nm light avidly, and the presence of either of these two liquids exacerbates vapour bubble explosion while preventing light from reaching the tissue²². While ELCA with saline flush is recommended to reduce complications such as coronary dissection and perforation due to high-pressure waves, in cases of underexpanded stents where the stents are protective, contrast medium flush could optimise the ELCA effect⁶⁻⁸. Contrast injection during ELCA should be reserved for thick, extensive, and resistant peri-stent calcium^{5,6}.

In two studies, chronic stent underexpansion persisted after high-pressure balloon inflation and a third stent implantation for recurrent ISR^{23,24}. In line with these studies, the current analysis suggested that multiple layers of underexpanded stents not only triggered recurrent stent failure, but also constituted a challenging substrate for reintervention. Therefore, it is important to correct stent underexpansion even when treating the first ISR event, especially when implanting a second stent and before the problem becomes magnified during a second or third ISR episode.

Case reports have indicated the effectiveness of RA for lesions with non-dilatable calcified neointima²⁵. One IVUS study reported that calcified neointima was associated with increased calcium outside the stent²⁶. ELCA treatment may be effective to treat undilatable calcified neointima because these lesions also typically have heavy calcium outside the stent struts.

In the present study, approximately 60% of ISR lesions showed stent underexpansion as a main cause of stent restenosis. Contrary to the bare metal stent era, stent underexpansion appeared to be the main cause of DES restenosis because of suppressed neointimal hyperplasia compared with bare metal stents²⁷. IVUS-guided PCI can minimise stent underexpansion²⁸. The importance of stent underexpansion has been substantiated in OCT studies².

Limitations

This was a retrospective observational study. The number of patients was relatively small, precluding subgroup analysis,

especially the number of lesions treated with ELCA, probably causing selection bias.

Conclusions

ELCA is effective for treating ISR with underexpansion due to peri-stent calcium. OCT clarifies the mechanism showing that ELCA disrupts peri-stent calcium facilitating better expansion of the previously implanted stent.

Impact on daily practice

ELCA use to treat ISR due to peri-stent calcium-related stent underexpansion was associated with better acute outcomes (larger lumen and stent area). Lesions treated using ELCA had more fracture of peri-stent calcium detected by OCT, especially using ELCA with contrast flush.

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Conflict of interest statement

G. Mintz declares receiving honoraria from Boston Scientific/Philips. A. Maehara declares receiving grant support from Boston Scientific and Abbott Vascular. Z. Ali declares receiving grant support from Cardiovascular Systems Inc, Abbott Vascular, and ACIST Medical, and being a consultant to Boston Scientific, Abbott Vascular, and ACIST Medical. A. Jeremias declares being a consultant to and receiving honoraria from Boston Scientific. L. Song declares receiving a research grant from Boston Scientific. The other authors have no conflicts of interest to declare.

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Supplementary data

Moving image 1. Pre-PCI OCT. ELCA treatment of in-stent restenosis (same lesion as Figure 2). OCT before ELCA showing old stent underexpansion due to diffuse circumferential peri-stent calcium.

Moving image 2. Post-PCI OCT. ELCA treatment of in-stent restenosis (same lesion as Figure 2). Post-PCI OCT showed good expansion of the old stent with multiple peri-stent calcium fractures.

Moving image 3. Pre-PCI OCT. PCI without ELCA treatment (same lesion as Figure 3). Pre-PCI OCT imaging showing diffuse circumferential peri-stent calcium and old stent underexpansion.

Moving image 4. Post-PCI OCT. PCI without ELCA treatment (same lesion as Figure 3). Post-PCI OCT imaging showing poor expansion of the newly implanted stent without peri-stent calcium fracture.

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