Intravascular Lithotripsy for Treatment of Severely Calcified Coronary Artery Disease: The Disrupt CAD III OCT Sub-study

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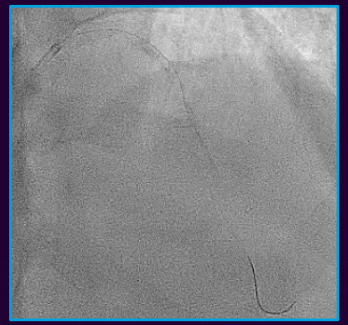
Disclosure Statement of Financial Interest

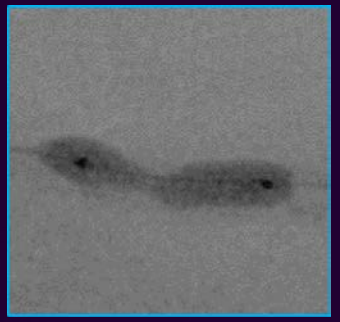
Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
Consultant	Shockwave Medical, Inc.

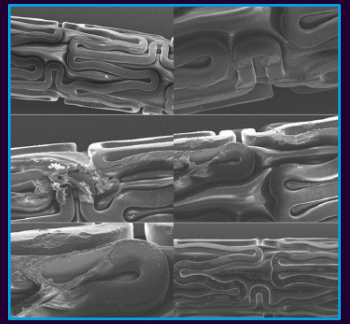
Impact of Coronary Calcification on PCI



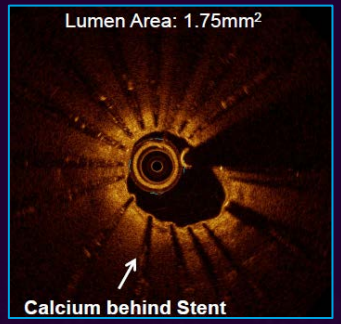
Impairs
device crossing



Insufficient
balloon force



Stent
Delamination



Stent
under expansion

Intravascular Lithotripsy

- Expanding and collapsing vapor bubble creates a short burst of **acoustic pressure waves**
- Acoustic pressure waves travel through the vessel tissue with an effective pressure of **~50 atm**
- A **localized field effect** within the vessel fractures both **superficial and deep** calcium

Coronary IVL Clinical Programs

	Disrupt CAD I	Disrupt CAD II	Disrupt CAD III	Disrupt CAD IV
Status	Enrollment completed	Enrollment completed	Enrollment completed	Enrollment completed
Study design	Single arm, safety & feasibility	Single arm, post-market, safety & effectiveness	Single arm, IDE, safety & effectiveness	Single arm, pre-market safety & effectiveness
# of patients	60	120	384	64
# of sites	7	15	47	8
Regions	AU, EU	EU	U.S., EU	Japan
OCT Sub-study	N=31	N=47	N=100	N=72

Disrupt CAD I and II: OCT Sub-studies

DISRUPT CAD III

Optical Coherence Tomography Characterization of Coronary Lithoplasty for Treatment of Calcified Lesions

First Description

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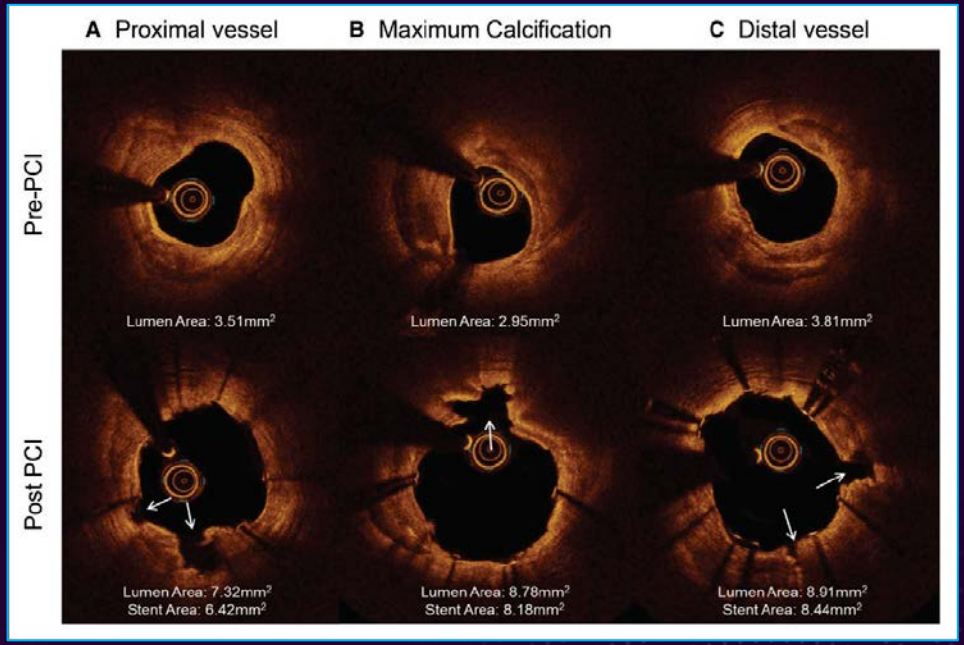
Circulation: Cardiovascular Interventions

ORIGINAL ARTICLE

Safety and Effectiveness of Coronary Intravascular Lithotripsy for Treatment of Severely Calcified Coronary Stenoses

The Disrupt CAD II Study



CAD I & II: OCT demonstrated multiple circumferential calcium fractures and excellent stent expansion

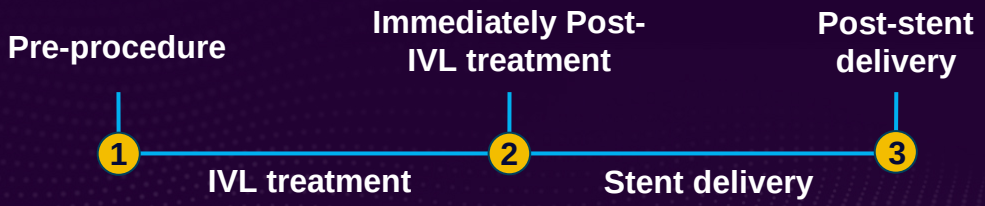
Ali et al. JACC CV Imaging. 2017
Ali et al. Circ Cardiovasc Interv. 2019

Disrupt CAD III: OCT Sub-study

Objective

Further understand the mechanism of action of IVL for the treatment of *de novo*, heavily calcified coronary lesions prior to stent placement using optical coherence tomography (OCT)

OCT Imaging*



*Analyzed by OCT core laboratory at MLA, MSA & Maximum Ca^{++} sites

Heavily calcified†, *de novo* coronary lesions
RVD 2.5-4.0 mm, stenosis ≥50%,
lesion length ≤ 40mm

Patients enrolled from
January 2019 to March 2020
N=431 (Safety Population)

Roll-in Population (N=47)

ITT Population (N=384)

OCT Sub-study (N=100)

†Radiopacities on both sides of the vessel with a calcified length ≥15 mm in the vessel by angiography or calcium angle ≥270° by IVUS or OCT

Baseline Characteristics

	OCT N=100	Non-OCT N=331	*P* Value
Age	70.1 ± 8.6	71.4 ± 8.4	0.17
Male	82%	75%	0.17
Hypertension	84%	91%	0.09
Hyperlipidemia	88%	88%	0.38
Diabetes mellitus	36%	41%	0.46
Current smoker	11%	13%	0.78
Prior MI	18%	19%	1.00
Prior CABG	3%	11%	0.03
Prior Stroke	5%	6%	0.97
Renal insufficiency	19%	29%	0.05

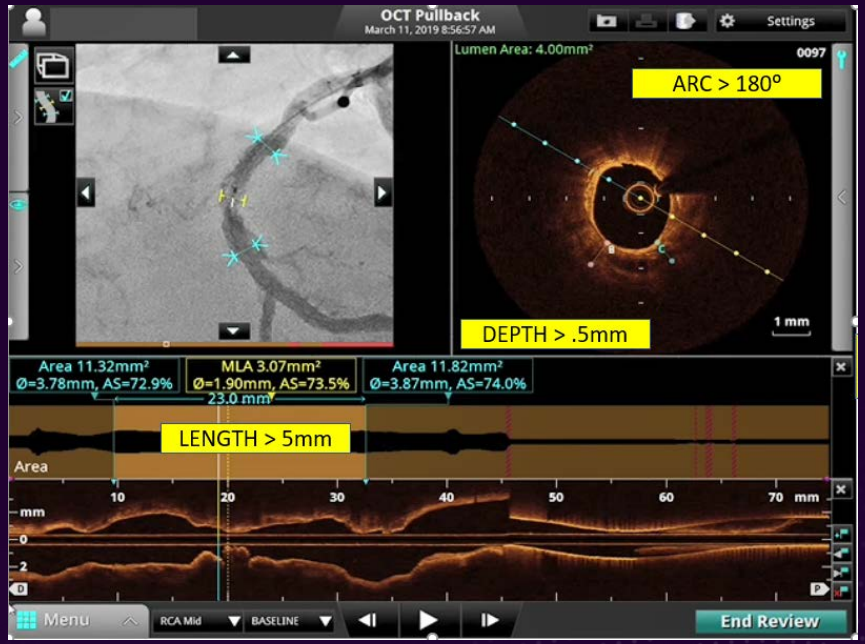
Angiographic Characteristics

	OCT N=100	Non-OCT N=331	*P* Value
Target vessel			0.03
Protected LM	0%	2%	
LAD	67%	54%	
Circumflex	5%	16%	
RCA	28%	28%	
Reference vessel diameter, mm	3.1 ± 0.5	3.0 ± 0.5	0.02
Minimum lumen diameter, mm	1.2 ± 0.4	1.0 ± 0.4	0.001
Diameter stenosis	63 ± 11%	66 ± 11%	0.01
Calcified length, mm	51 ± 20	47 ± 18	0.20
Severe calcification	100%	100%	1.00
Side branch involvement	23%	34%	0.19

Procedural Characteristics

	OCT N=100	Non-OCT N=331	*P* Value
Total procedure time, min	58 ± 24	60 ± 30	0.61
IVL catheters	1.3 ± 0.5	1.2 ± 0.5	0.50
IVL pulses	77 ± 31	67 ± 35	0.01
Max IVL inflation pressure, atm	6.0 ± 0.4	5.8 ± 1.0	0.02
Pre-dilatation	26%	55%	<0.001
Post-IVL dilatation	20%	22%	0.78
Number of stents	1.4 ± 0.5	1.3 ± 0.5	0.15
Post-stent dilatation	99%	99%	1.00

Pre-procedure



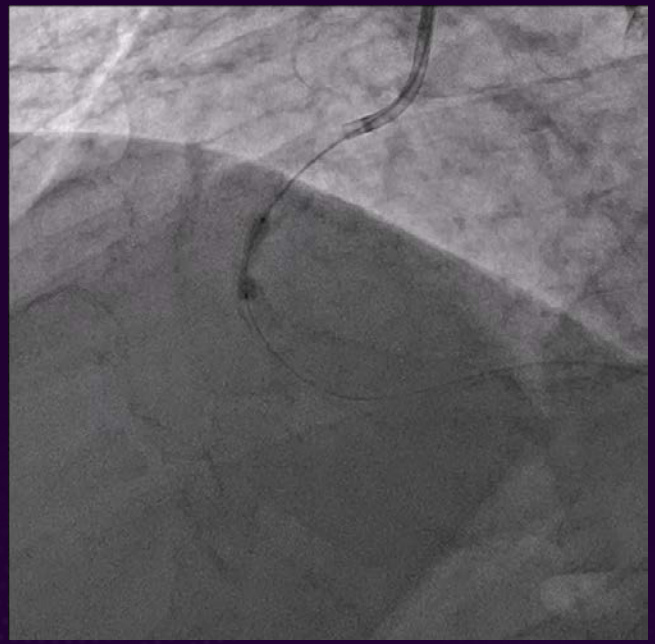
Angiographic Core Lab

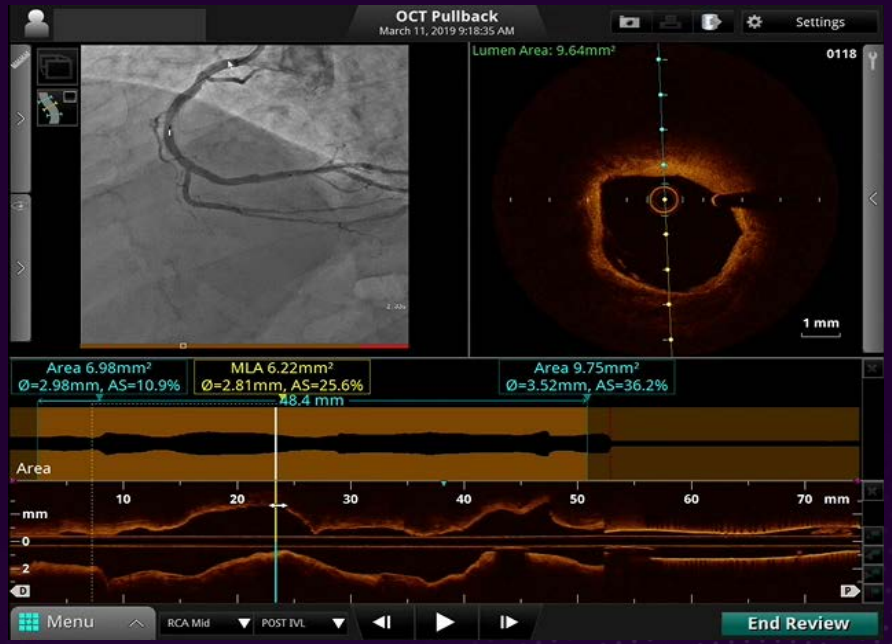
RVD: 3.0 mm
Lesion length: 12.6 mm
Diameter stenosis: 50.7%

OCT Core Lab

MLA: 3.3 mm^2
Area stenosis: 70.6%
Max Ca^{++} angle: 360°, Thickness: 1.05 mm

Post-IVL





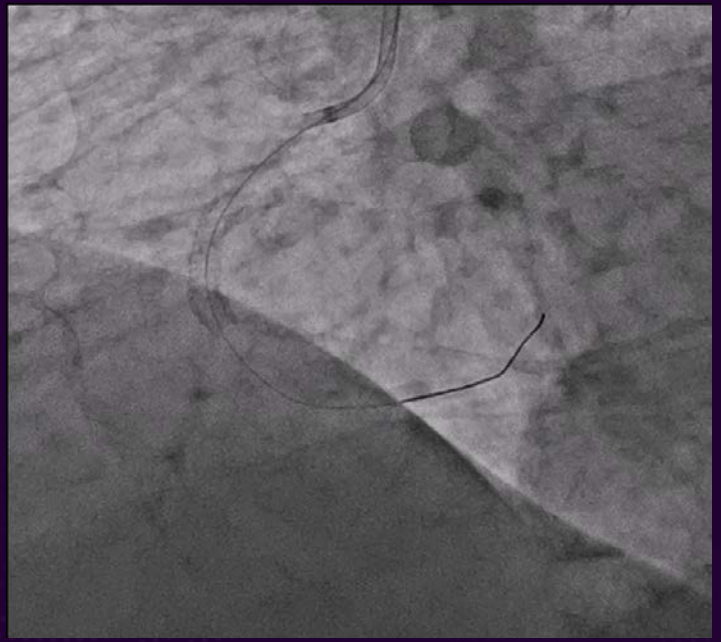
Angiographic Core Lab

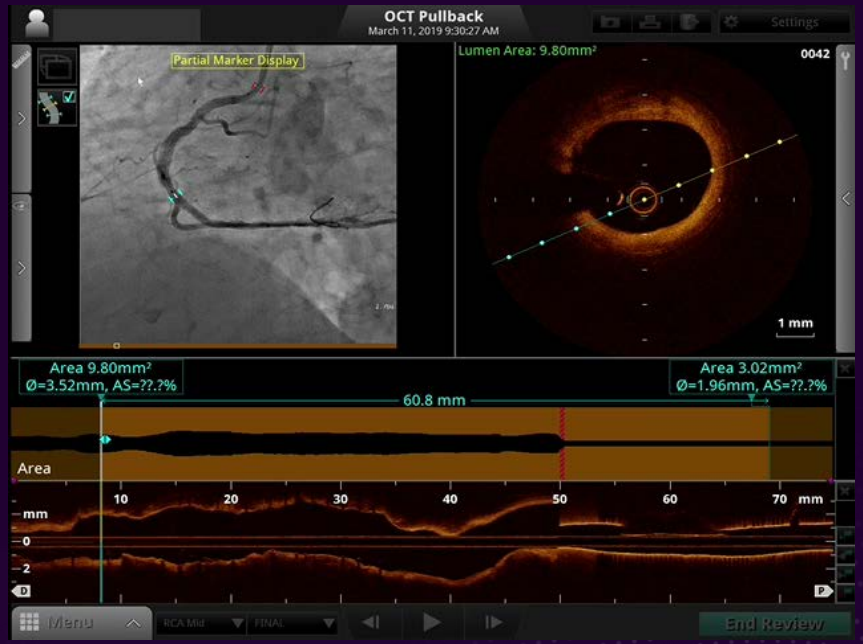
Acute gain: 1.15 mm
Diameter stenosis: 17.1%

OCT Core Lab

MLA: 5.8 mm^2
Area gain: 2.5 mm^2
Multiple Ca^{++} fractures

Post-stent





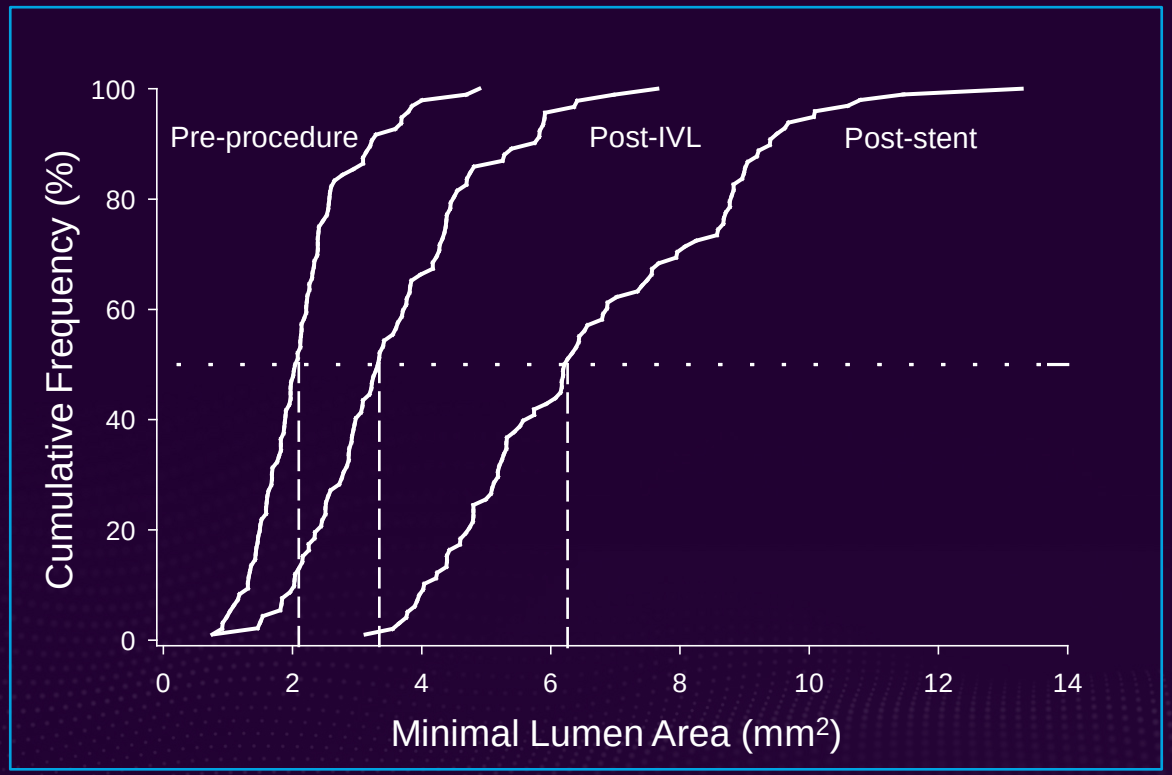
Angiographic Core Lab	In-stent %DS: 7.2% Acute gain: 1.18 mm
OCT Core Lab	MSA: 8.7 mm^2 Stent expansion (Max Ca^{++} site): 79%

Serial OCT Measurements

	Pre-IVL N=97	Post-IVL N=92	Post-stent N=98
At MLA site			
Minimum Lumen area, mm^2	2.2 ± 0.8*	3.6 ± 1.4*	6.5 ± 2.0*
Maximum Area stenosis	72 ± 12%*	56 ± 16%*	22 ± 19%*
At Maximum Ca^{++} site			
Maximum calcium angle, °	293 ± 77		
Maximum calcium thickness, mm	0.96 ± 0.25		
Stent expansion			102 ± 29%
At MSA site			
Minimum stent area, mm^2			6.5 ± 2.1
Any malapposed strut			4.1%

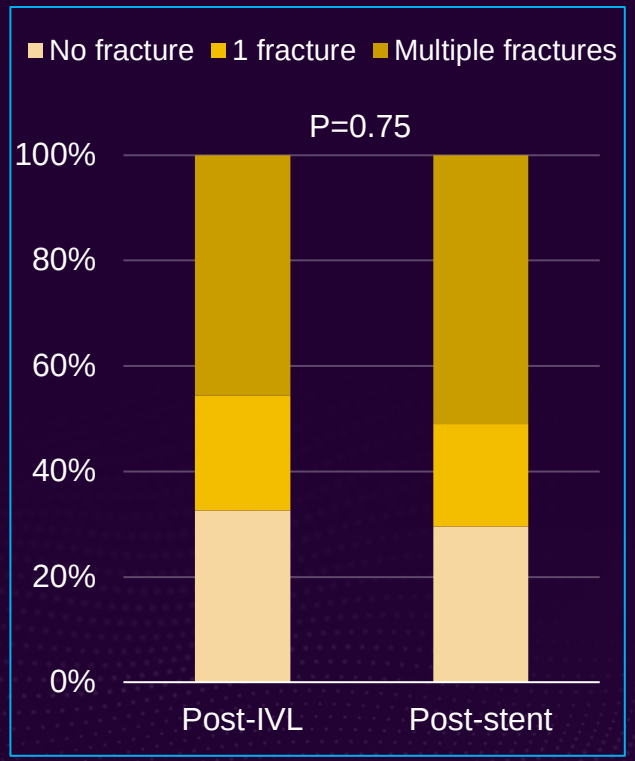
*P<0.01 for all comparisons between pre-IVL, post-IVL, post-stent

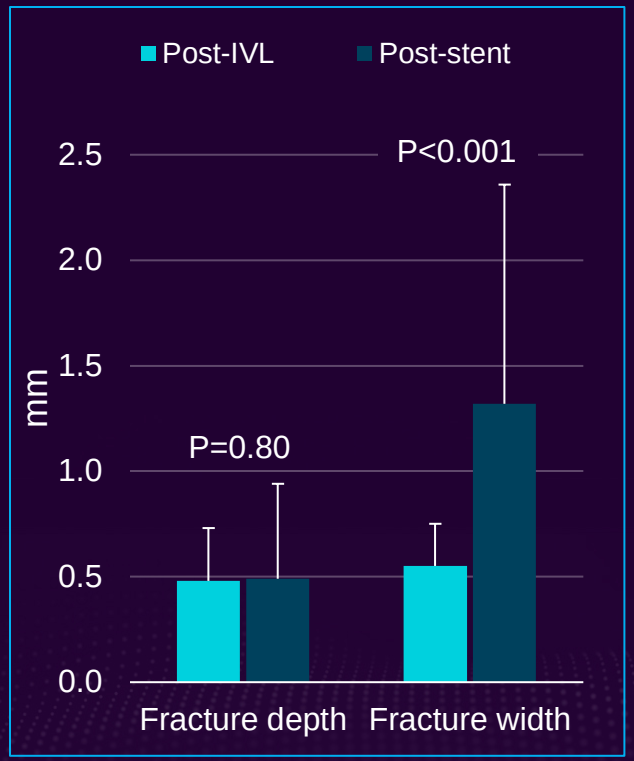
Luminal Area Gain



- Positive MLA shift after IVL with low balloon inflation pressure
- Further increase in MLA after stent placement

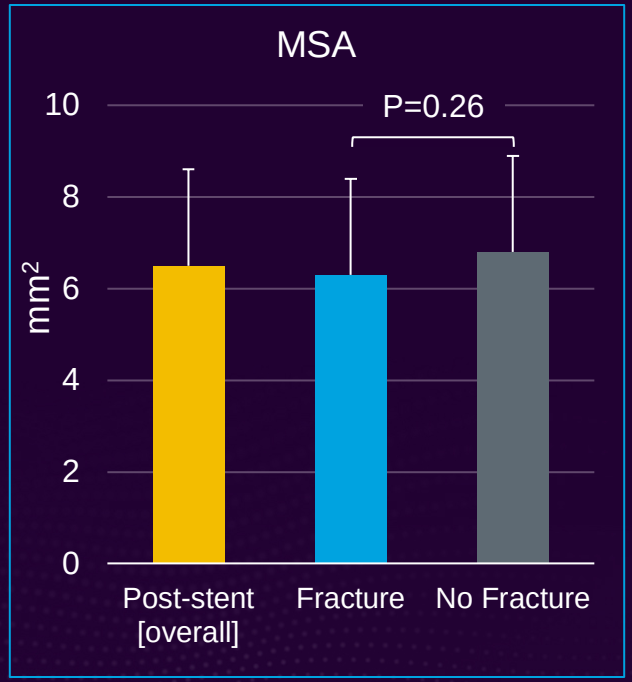
Calcium Fracture Characteristics

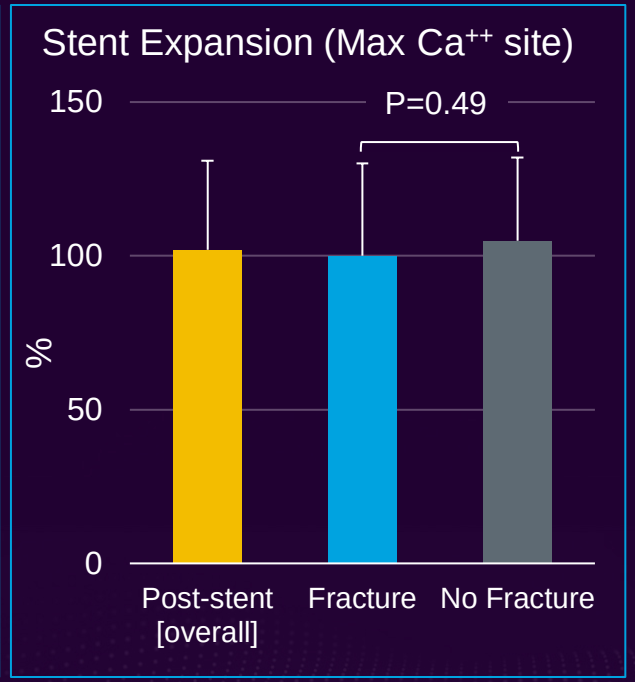


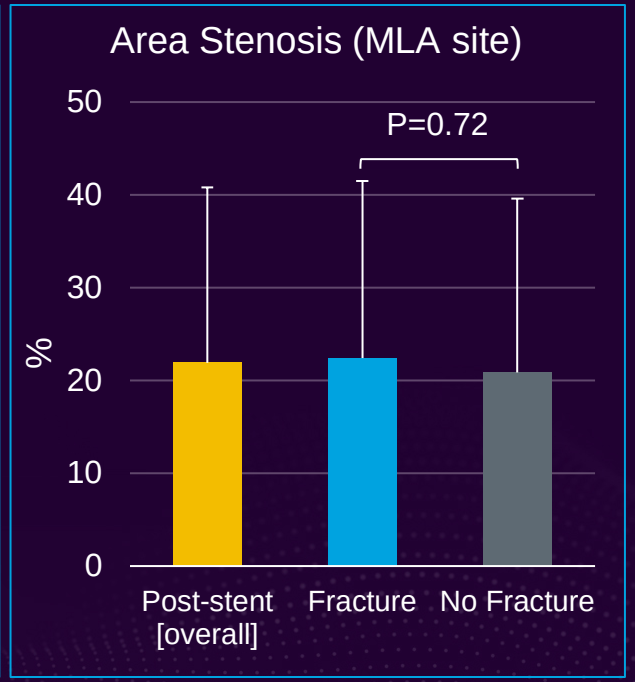


- Ca^{++} fracture observed in 67% of lesions post-IVL
- Minimum angle at fracture site was 192°
- Significant increase in fracture width post-stent
- Ca^{++} microfractures may occur beyond the current resolution limits of OCT

Outcomes by Fracture Visualization







Consistent outcomes regardless of fracture visualization by OCT

Performance and Safety Outcomes

DISRUPT CAD III

Core Lab Analysis	OCT N=100
Device crossing success	100%
Procedural success (<50% RS)	98%
Procedural success (≤30% RS)	98%
Angiographic success	100%
Final in-stent angiographic outcomes	
Minimum lumen diameter, mm	2.8 ± 0.4
Residual diameter stenosis	13 ± 7
Acute gain, mm	1.6 ± 0.4
Diameter stenosis ≤30%	100%

End of Procedure	OCT N=100
Dissections (Type D-F)	0%
Perforation	0%
Abrupt closure	0%
Slow flow	0%
No-reflow	0%

Conclusions

- OCT confirmed the safety of coronary IVL with no severe angiographic complications at the end of the procedure
- OCT demonstrated longitudinal and circumferential calcium fractures in heavily calcified lesions resulting in:
  - Increased vessel compliance
  - Large post-procedural MSA
  - Excellent stent expansion
- MSA, area stenosis, and stent expansion outcomes were excellent regardless of Ca^{++} fracture visualization by OCT and may represent a limitation of OCT to detect subtle micro-fractures or out-of-plane fractures in calcified plaque