Optical Coherence Tomography Characterization of Shockwave IVL for Treatment of Calcified Coronary Lesions

Patient-level Pooled Analysis of the Disrupt CAD OCT Sub-studies

Ziad A. Ali, MD DPhil

Department of Cardiology, St. Francis Hospital & Heart Center

Roslyn, New York

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
Consulting Fees	Abbott Vascular Inc
Consulting Fees	Boston Scientific Corporation
Consulting Fees	Shockwave Medical
Stock Shareholder/Equity	Shockwave Medical

Individual Patient-data Pooled Analysis

Disrupt CAD I-IV: OCT Sub-studies

	CAD I	CAD II	CAD III	CAD IV	Pooled
Enrollment	Dec 2015 – Sep 2016	May 2018 – Mar 2019	Jan 2019 – Mar 2020	Nov 2019 – Apr 2020	Dec 2015 – Apr 2020
Study design	Prospective, multi-center, single-arm				
ITT (N)	60[1]	120[3]	384[4]	64[5]	628[6]
OCT Analysis* (N)	28[2]	57	106†	71†	**262**
OCT core laboratory	Cardiovascular Research Foundation New York, NY				
Target lesions	Severely calcified*, *de novo* coronary artery lesions				
Target lesion RVD	2.5mm – 4.0mm				
Target lesion stenosis	≥50% and <100%	≥50% and <100%	≥70% and <100%	≥70% and <100%	

*Patient enrollment in OCT sub-studies was open to all sites participating in the Disrupt CAD studies that routinely perform OCT imaging. †Includes patients from the roll-in cohort.

Consistent OCT core laboratory evaluation across all OCT sub-studies

[1]Brinton et al. Circulation 2019;139:834-836, [2]Ali et al. J Am Coll Cardiol Img 2017;10:897-906, [3]Ali et al. Circ Cardiovasc Interv 2019;12:e008434, [4]Hill et al. J Am Coll Cardiol 2020;76:2635-46, [5]Saito et al. Circ J 2021;85(6):826-33, [6]Kereiakes et al., J Am Coll Cardiol Intv 2021;14:1337-48

Baseline Clinical & Lesion Characteristics

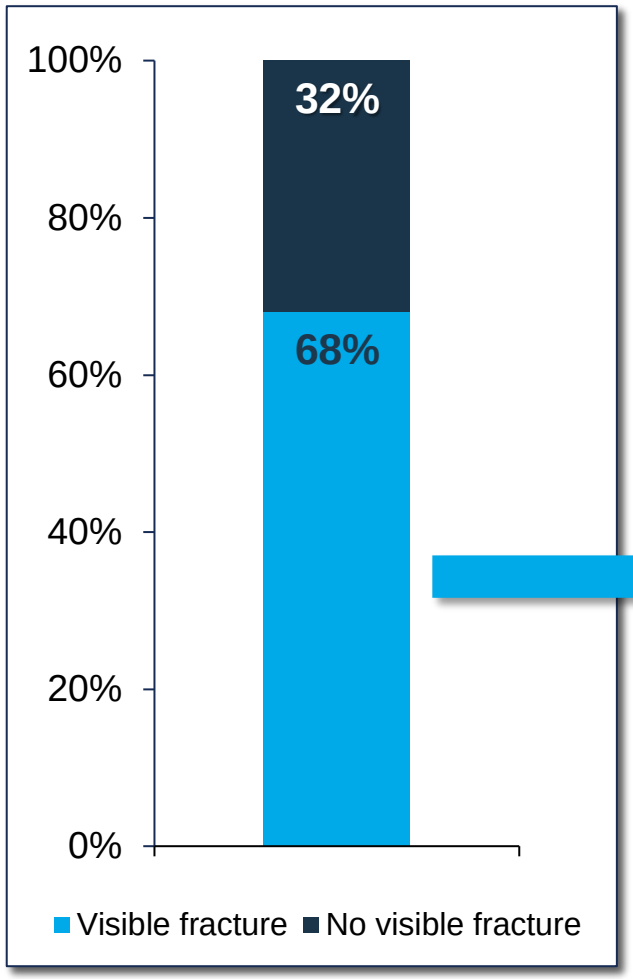
Characteristic	N = 248
Age, yrs	72 ± 9
Male, %	77.1
Diabetes mellitus, %	37.8
Hyperlipidemia, %	84.0
Hypertension, %	83.2
Prior MI, %	24.0
Prior CABG, %	5.7
Renal insufficiency	22.1

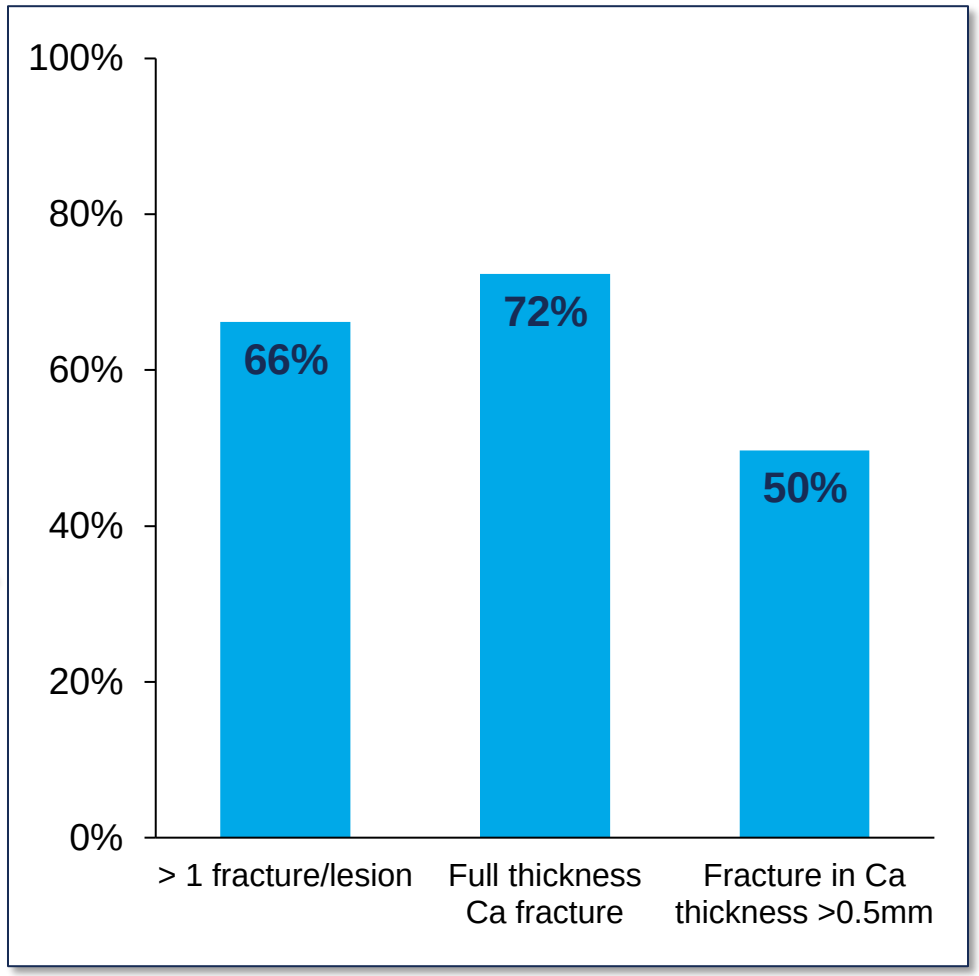
Core Lab Analysis		N = 248
Target vessel	LAD	67.3%
	LCx	7.7%
	RCA	24.2%
	LM	0.8%
Reference vessel diameter, mm		3.0 ± 0.5
Minimum lumen diameter, mm		1.1 ± 0.4
Diameter stenosis		63.2 ± 11.5%
Lesion length, mm		25.8 ± 11.3
Calcified length, mm		42.8 ± 21.2
Severe calcification		98.4%
Bifurcation lesion		31.5%

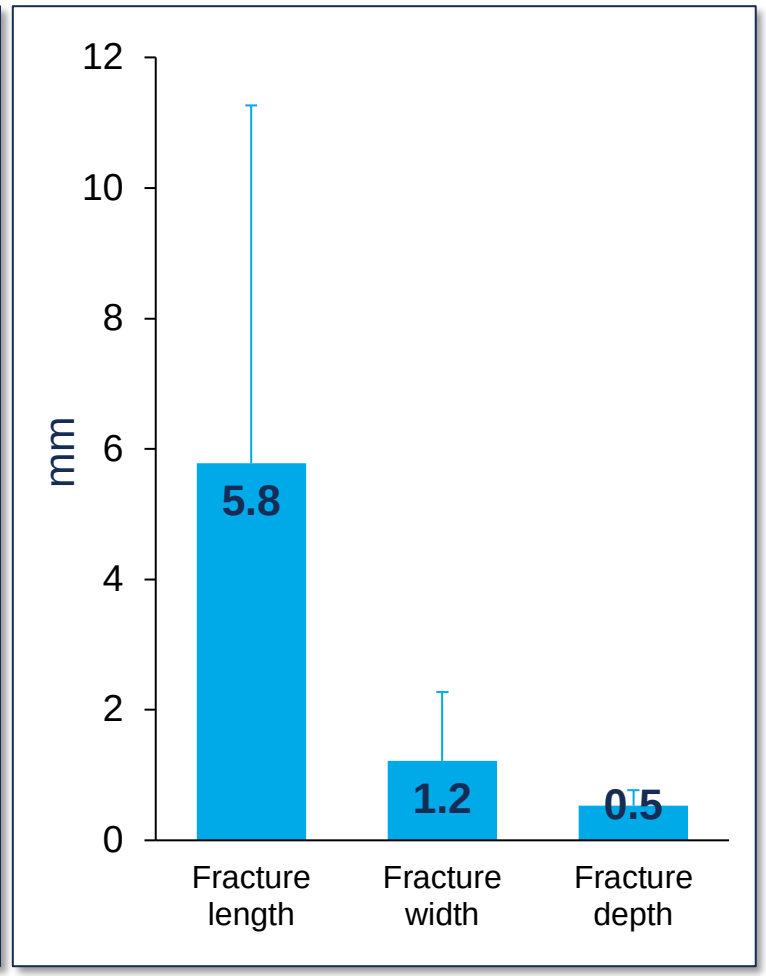
Procedural Characteristics

Characteristic	OCT Pooled N=262
Procedure time, min	70 ± 24
Contrast volume, ml	207 ± 75
Pre-dilatation	34%
IVL catheters per patient	1.4 ± 0.8
Max IVL inflation pressure	6.0 ± 0.6
IVL balloon to artery ratio	1.3 ± 0.2
Pulses delivered	87 ± 51
Post-IVL dilatation	9%
Stents placed per patient	1.3 ± 0.5
Post-stent dilatation	96%

Visible Calcium Fracture Characteristics

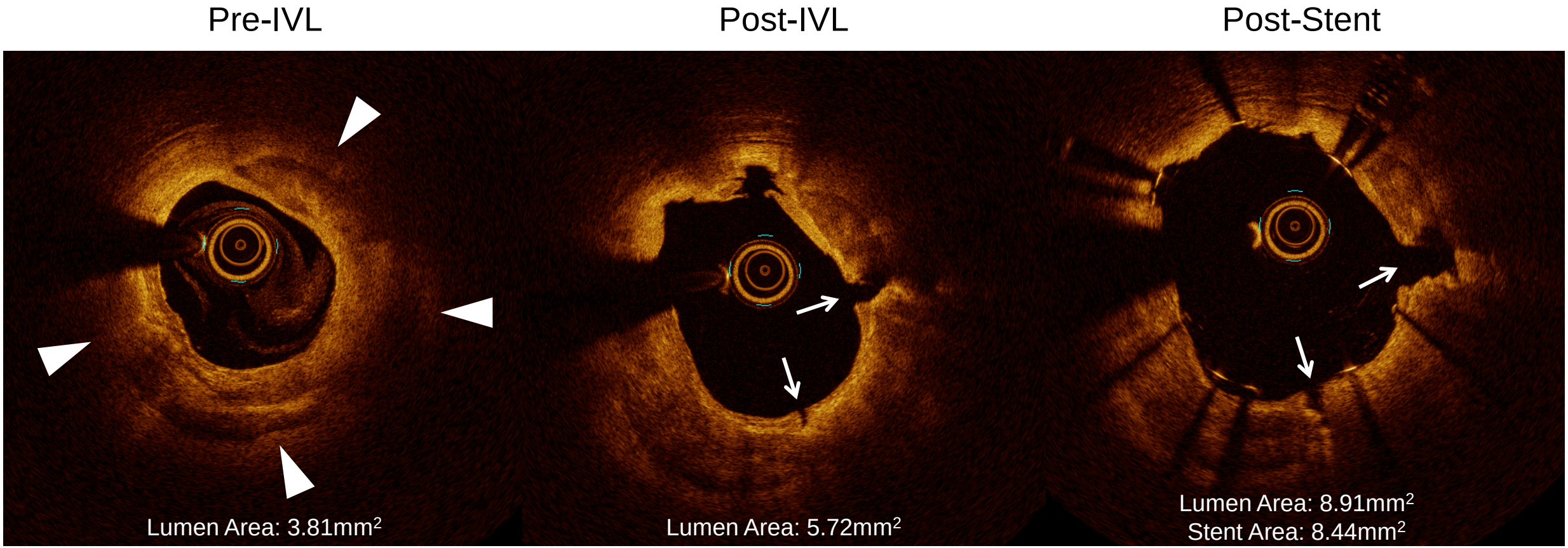






Average of **3.2 fractures per lesion** demonstrated by OCT

MLA Not Co-located with Pre-Procedural Max Calcium Site



Lesion Characteristics and Stent Deployment Outcomes

	Pre-IVL N=248	Post-stent N=245
MLA, mm^2	2.1 ± 1.0	6.2 ± 1.9*
Area stenosis @MLA site, %	72 ± 12	18 ± 20
Calcium arc @max calcium site, °	270 ± 81	
Calcium thickness @max calcium site, mm	0.96 ± 0.25	
MSA, mm^2		6.0 ± 1.9
Mean stent area, mm^2		7.9 ± 2.3
Stent expansion @max calcium site, %		103 ± 29
Mean stent expansion, %		107 ± 29
Any malapposition strut, %		3.9 ± 4.6

*MLA was never co-localized with the pre-IVL maximum calcification

Predictors of Stent Expansion

Variable	Regression coefficient (95%CI)	p-value
Number of visible calcium fractures × fracture length	-0.26 (-1.36, 0.85)	0.65
Max calcium thickness at max continuous calcium site	5.25 (-9.54, 20.04)	0.49
Max superficial continuous calcium arc	-0.03 (-0.09, 0.03)	0.38
Length of continuous calcium ≥270°	0.61 (-0.97, 2.20)	0.45
Circumferential (360°) calcium	3.93 (-9.43, 17.30)	0.56
Number of pulses	0.06 (-0.01, 0.14)	0.11
Balloon to artery ratio*, per 0.1	4.51 (2.57, 6.45)	<0.0001
Maximum balloon pressure*, atm	-0.28 (-1.74, 1.18)	0.71

*Balloon to artery ratio and maximum balloon pressure derived from the largest post-dilatation or stent balloon used during the procedure.

Good stent expansion achieved regardless of calcium burden or visible calcium fracture

Final Angiographic and 30-day Clinical Outcomes

Core Lab Assessment	OCT Pooled N=262
Final in-stent diameter stenosis	12.2 ± 6.8%
Acute gain, mm	1.6 ± 0.4
Any serious angiographic complications	0.0%
Perforation	0.0%
Abrupt closure	0.0%
Slow flow	0.0%
No reflow	0.0%
Distal embolization	0.0%

CEC Adjudicated	OCT Pooled N=262
30-d MACE	4.6%
Cardiac death	0.0%
All MI	4.6%
NQWMI	4.6%
Q-wave MI	0.0%
TVR	0.4%
Target lesion failure	4.6%
Stent thrombosis (definite or probable)	0.4%

Safety of IVL treatment in calcified coronary lesions

Conclusions

- The present individual patient data pooled analysis of 4 studies (N=262) represents the largest evaluation of IVL by OCT
- No serious angiographic complications were observed confirming the safety of IVL for the treatment of severely calcified coronary lesions
- OCT demonstrated extensive calcium fracture after IVL treatment with excellent stent expansion of severely calcified lesions
- Visible calcium fracture and calcium characteristics were not predictors of stent expansion following treatment with IVL

OCT Characterization of Eccentric Versus Concentric Calcium Treated with Shockwave IVL

Angiographic Lesion Characteristics

Core Lab Analysis		≤ 180° N=56	181° - 270° N=56	271° - 359° N=51	360° N=66	*P* value
Target vessel	LAD	66.1%	75.4%	64.7%	68.2%	0.62
	LCx	8.9%	1.8%	9.8%	6.1%	0.27
	RCA	23.2%	21.1%	25.5%	25.8%	0.93
	LM	1.8%	1.8%	0.0%	0.0%	0.59
Reference vessel diameter, mm		2.9 ± 0.5	3.0 ± 0.5	2.9 ± 0.5	3.1 ± 0.5	0.26
Minimum lumen diameter, mm		1.1 ± 0.4	1.1 ± 0.4	1.1 ± 0.4	1.1 ± 0.4	0.93
Diameter stenosis		61.4 ± 10.9%	62.9 ± 12.8%	61.3 ± 12.3%	62.8 ± 10.5%	0.93
Lesion length, mm		24.3 ± 10.1	24.8 ± 9.1	25.6 ± 13.3	27.9 ± 11.4	0.24
Calcified length, mm		35.3 ± 19.4	44.6 ± 18.7	42.8 ± 20.2	49.9 ± 23.0	0.002
Severe calcification		96.4%	100%	100%	98.5%	0.45
Bifurcation lesion		32.1%	24.6%	35.3%	31.8%	0.66

Pre-IVL OCT Characteristics

Core Lab Analysis	≤ 180° N=56	181° - 270° N=56	271° - 359° N=51	360° N=66	*P* value
Minimum lumen area, mm^2	2.0 ± 1.1	2.1 ± 1.0	2.0 ± 0.8	2.1 ± 0.9	0.85
Area stenosis, %	72.4 ± 10.5	70.1 ± 11.2	72.7 ± 10.3	73.1 ± 12.5	0.24
Max continuous calcium arc*, °	131.1 ± 30.4	225.3 ± 27.3	309.3 ± 23.6	360.0 ± 0.0	<0.0001
Calcium index, ° x mm	1660 ± 803	3069 ± 1074	3794 ± 1423	5522 ± 2291	<0.0001
Max calcium thickness, mm	0.93 ± 0.27	0.92 ± 0.21	1.01 ± 0.27	0.97 ± 0.25	0.21
Min calcium thickness, mm	0.41 ± 0.13	0.35 ± 0.13	0.28 ± 0.14	0.27 ± 0.13	<0.0001

*Continuous calcium angle was defined as the maximum uninterrupted calcium angle observed in the lesion and was used to define the category assignment.

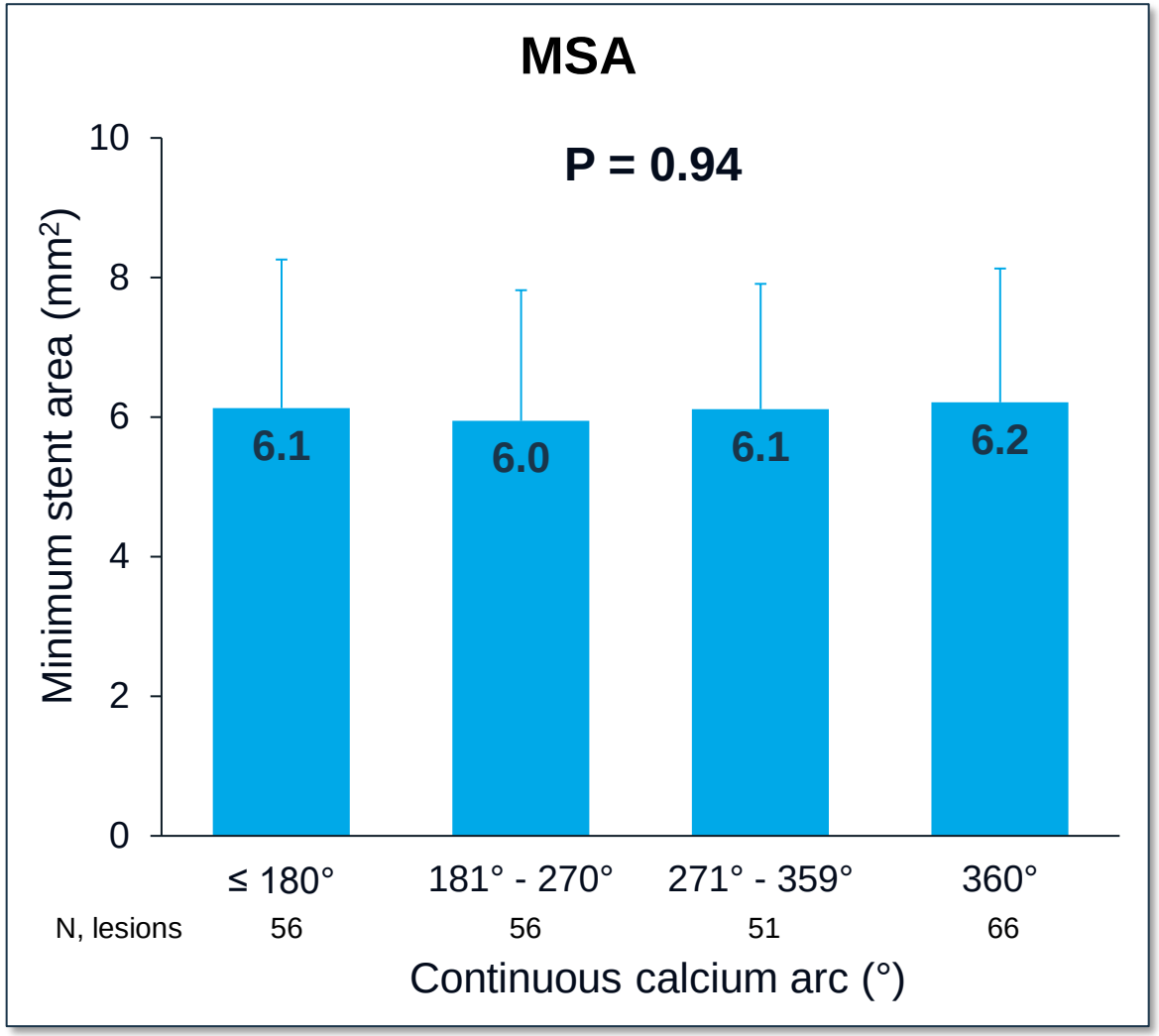
Divided into ~quartiles based on maximum continuous calcium angle

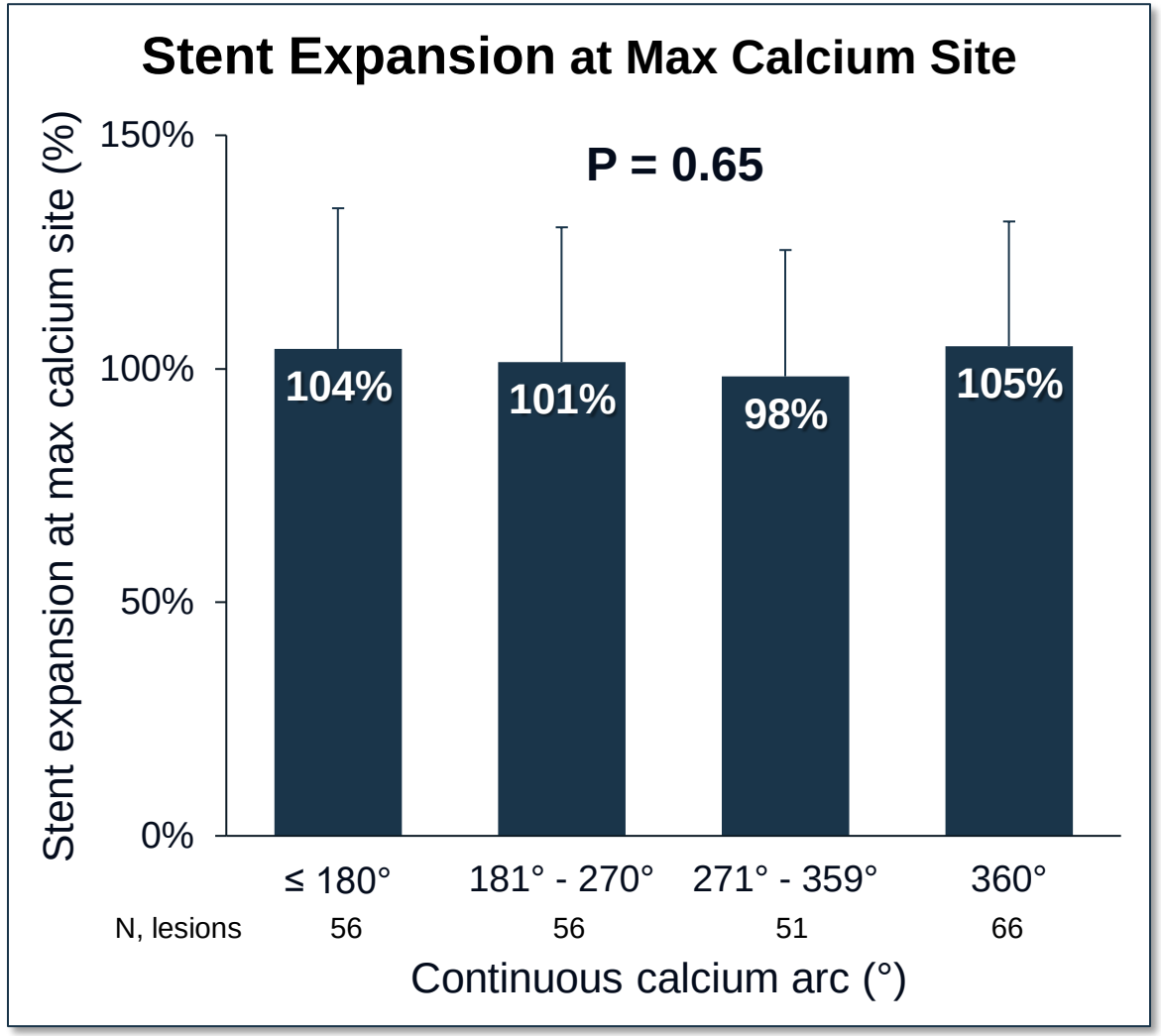
Procedural Characteristics

Core Lab Analysis	≤ 180° N=56	181° - 270° N=56	271° - 359° N=51	360° N=66	*P* value
Procedure time, min	70.1 ± 31.1	65.8 ± 31.6	67.6 ± 30.0	69.7 ± 31.9	0.87
Contrast volume, ml	215.5 ± 89.6	198.1 ± 76.4	208.5 ± 68.6	206.6 ± 65.8	0.68
Pre-dilatation, %	21.4%	29.8%	25.5%	39.4%	0.15
IVL catheters per patient	1.3 ± 0.6	1.4 ± 0.9	1.5 ± 0.8	1.5 ± 0.6	0.47
Max IVL inflation pressure	6.0 ± 0.3	6.0 ± 0.6	6.0 ± 0.8	6.0 ± 0.6	0.92
IVL balloon to artery ratio	1.3 ± 0.2	1.2 ± 0.2	1.3 ± 0.2	1.3 ± 0.2	0.87
Pulses delivered	86.6 ± 44.6	87.8 ± 60.6	83.3 ± 49.8	90.9 ± 38.1	0.91
Post-IVL dilatation, %	3.6%	8.8%	5.9%	10.6%	0.47
Stents placed per patient	1.3 ± 0.5	1.3 ± 0.6	1.4 ± 0.6	1.4 ± 0.5	0.80
Post-stent dilatation	94.6%	98.2%	96.1%	98.5%	0.57

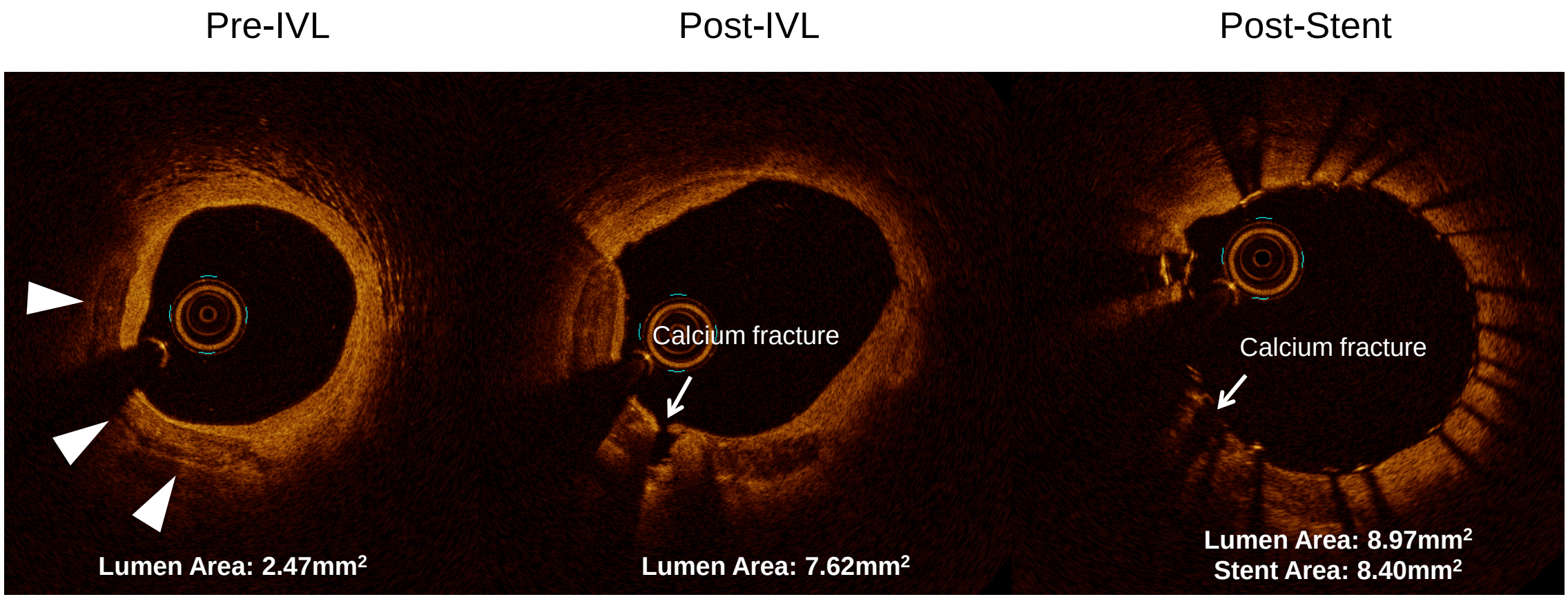
Similar procedural approach across calcium angle quartiles

Consistent Outcomes in Eccentric and Concentric Calcium



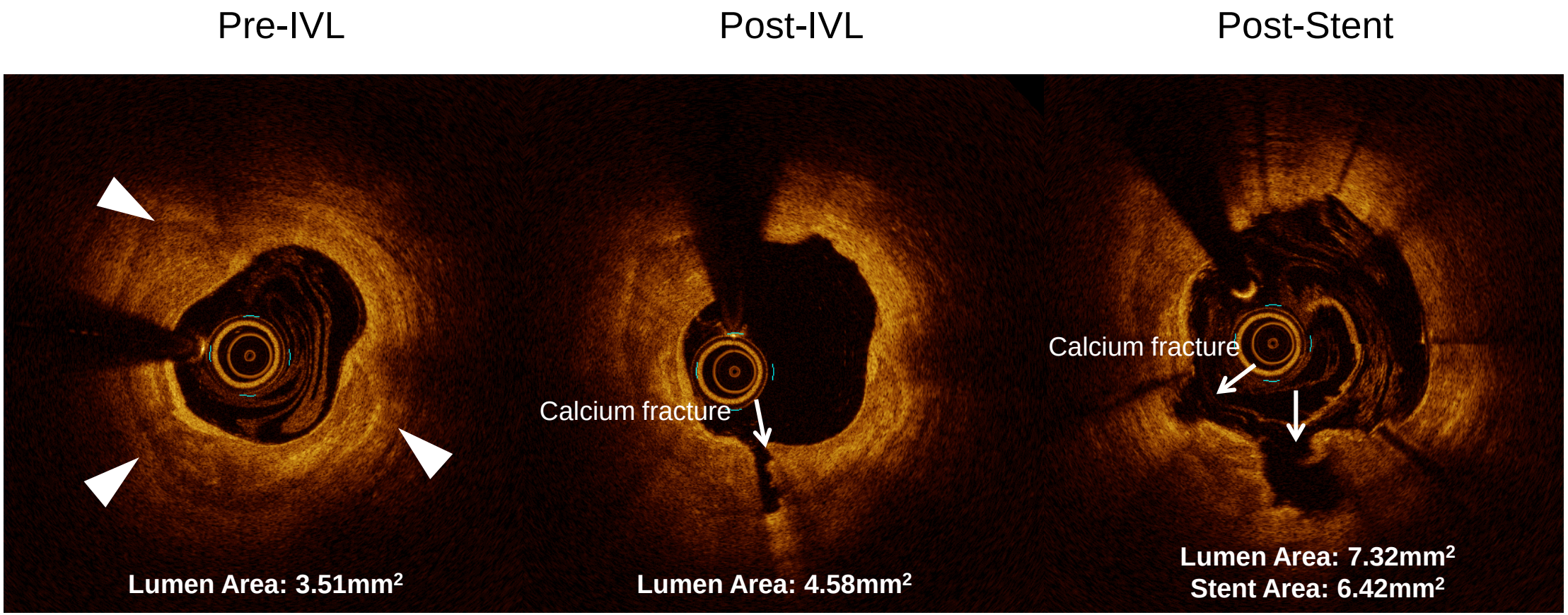


Impact of IVL Treatment in Eccentric Calcification



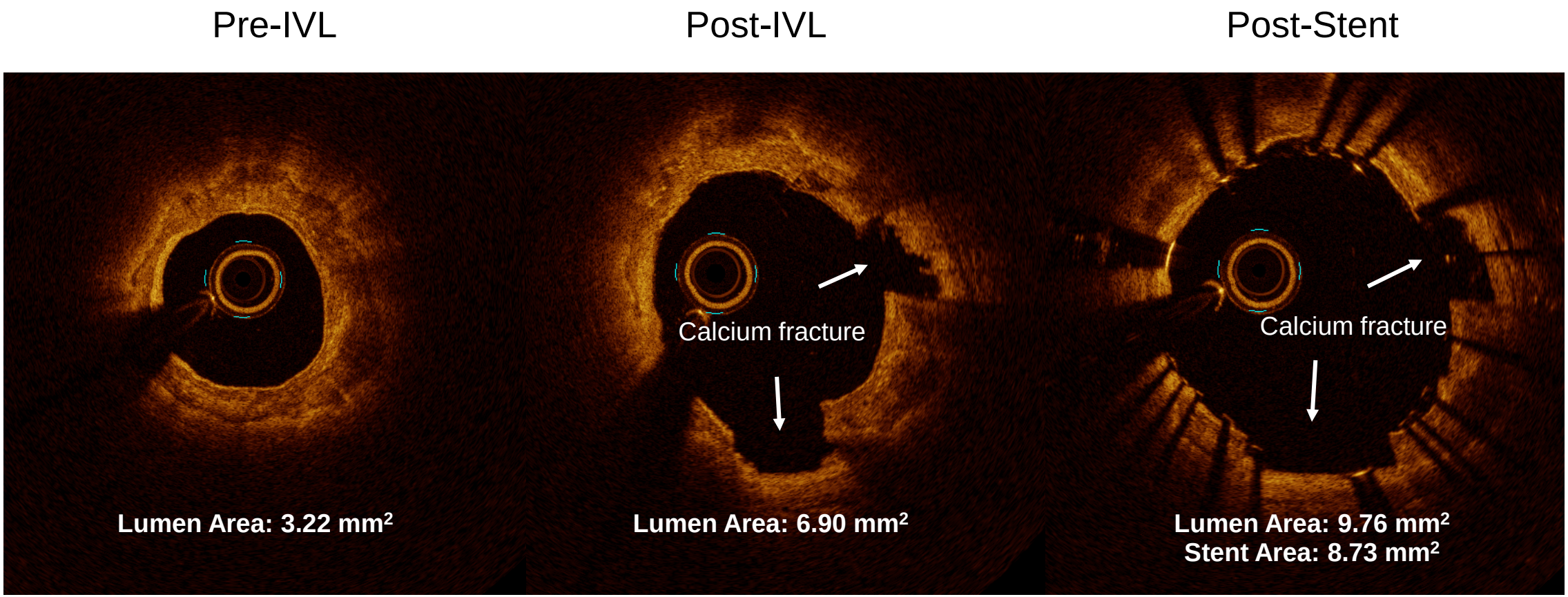
Good luminal gain following IVL treatment (continuous calcium angle: <180°)

Impact of IVL Treatment in Concentric Calcification



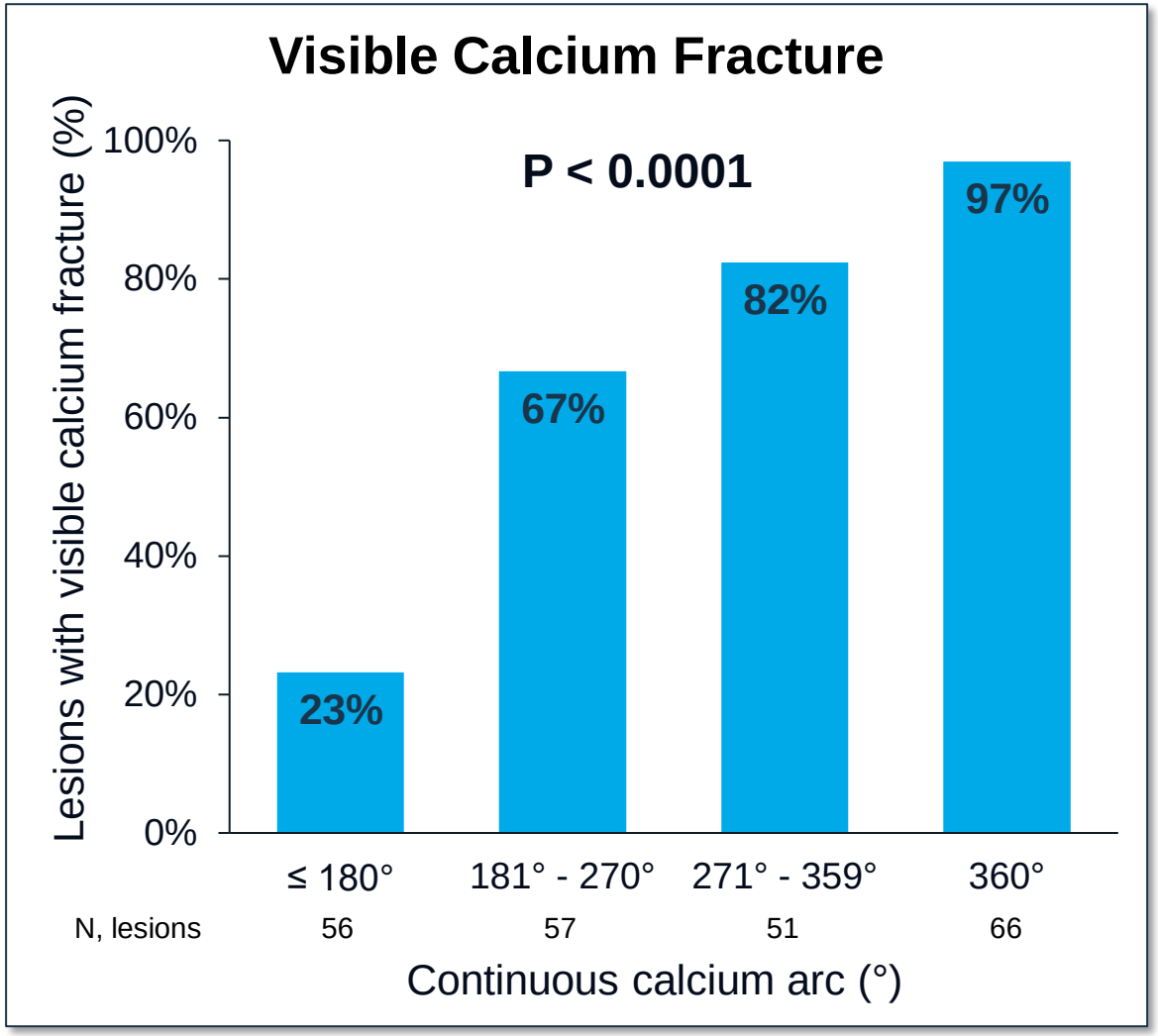
Good luminal gain following IVL treatment (continuous calcium angle: 181° to 270°)

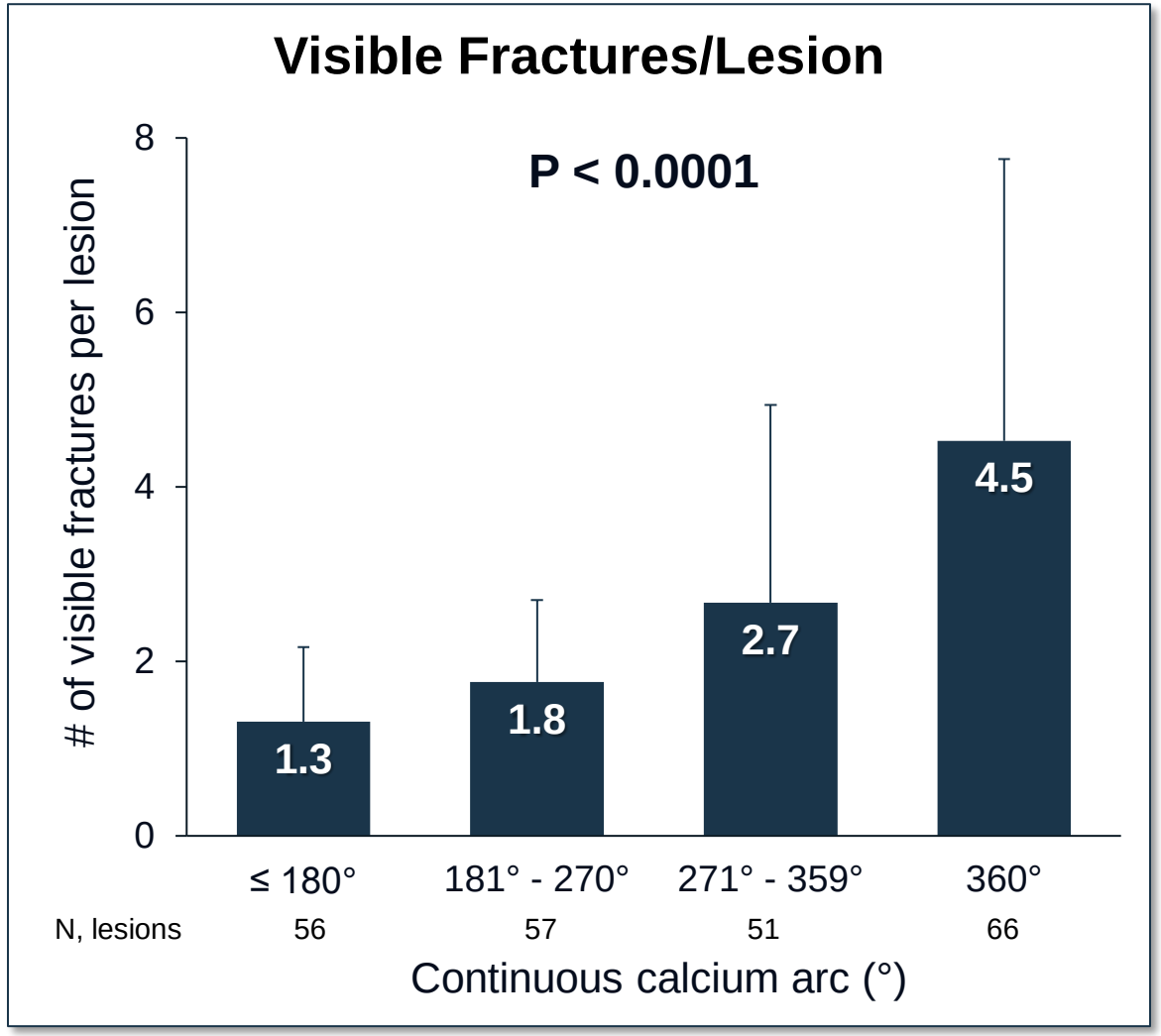
Impact of IVL Treatment in 360° Coronary Calcification



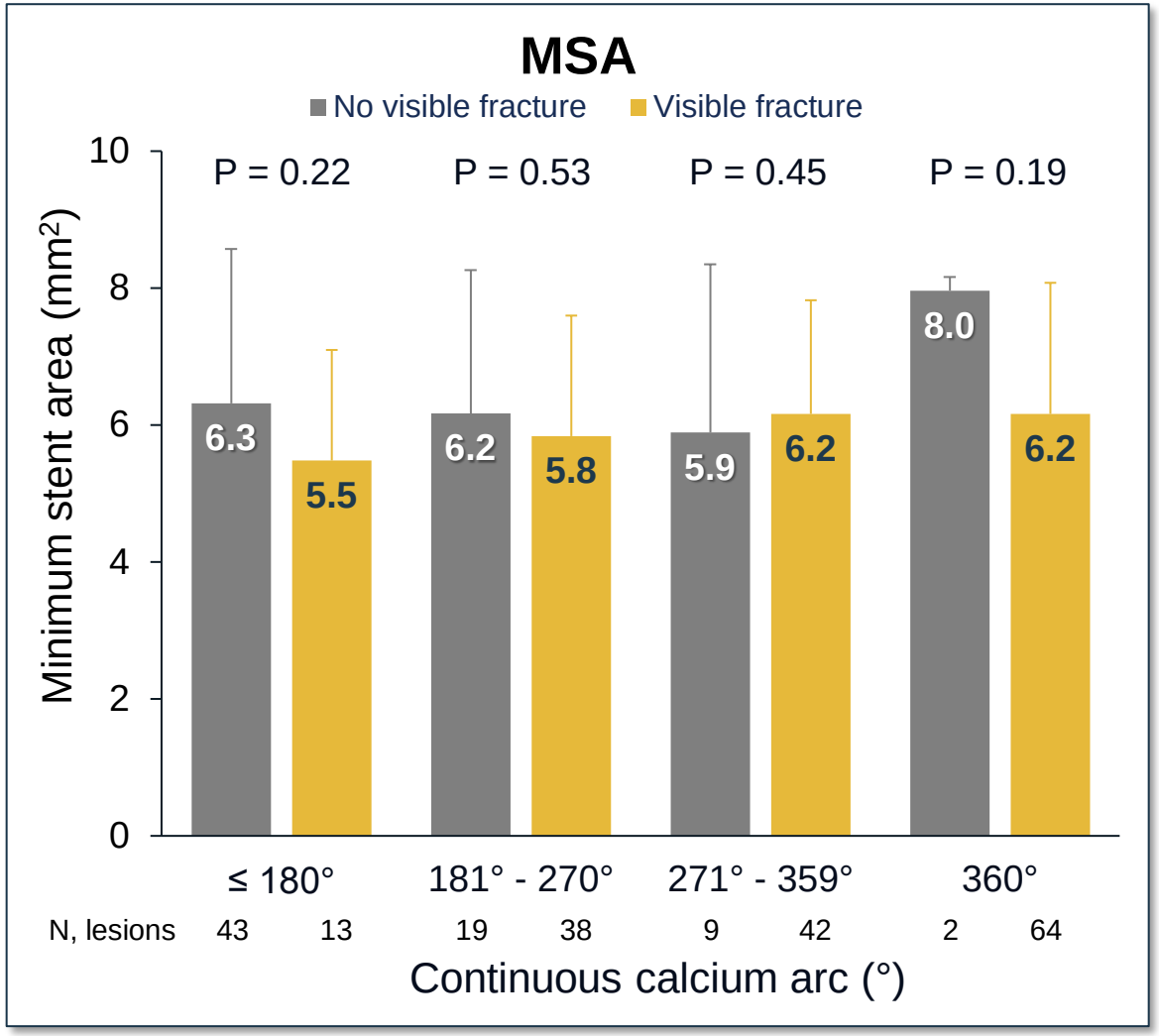
Good luminal gain following IVL treatment (continuous calcium angle: 360°)

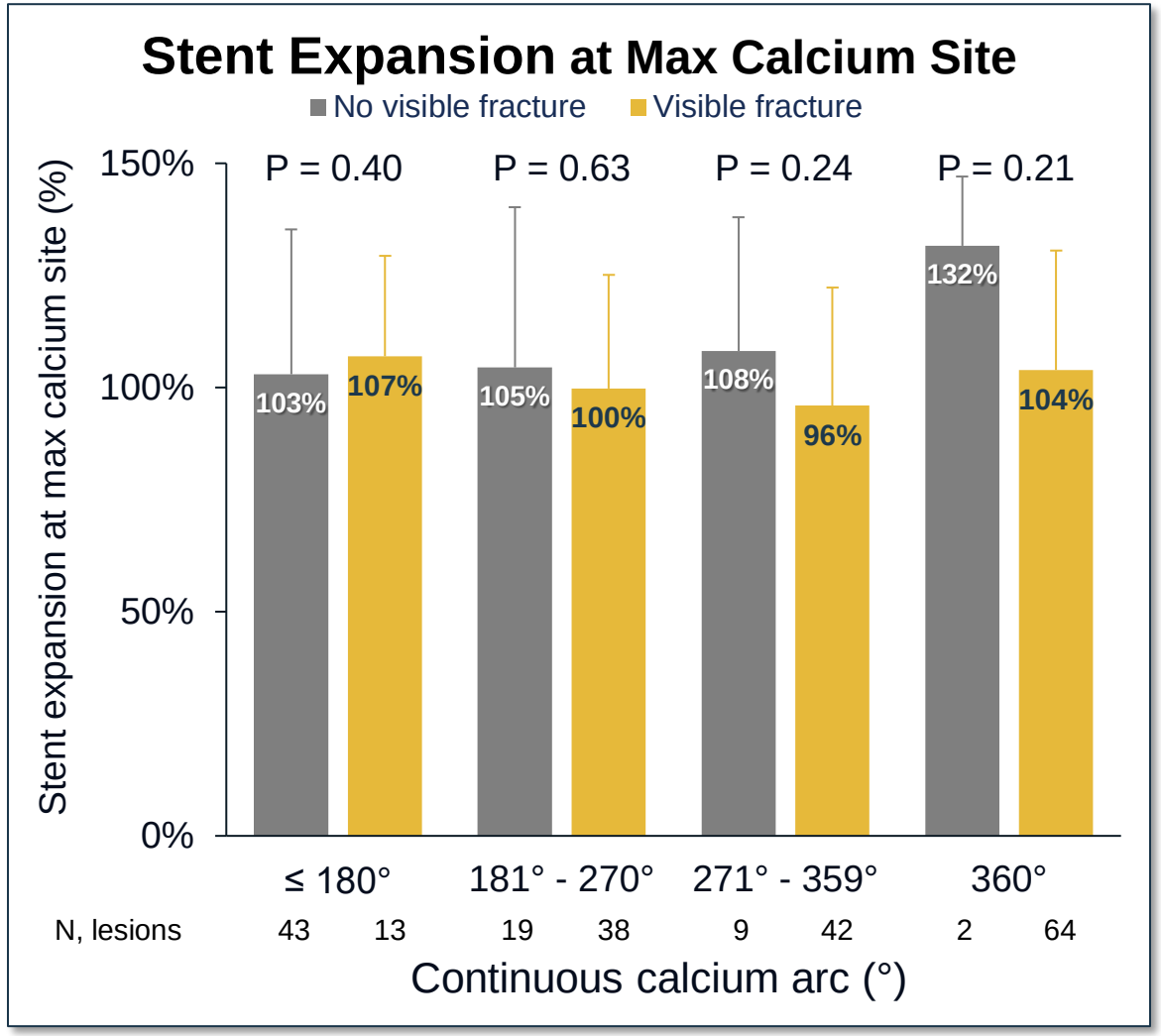
Increased Calcium ⇨ Increased Visible Fracture





Consistent MSA and Stent Expansion Regardless of Visible Fracture





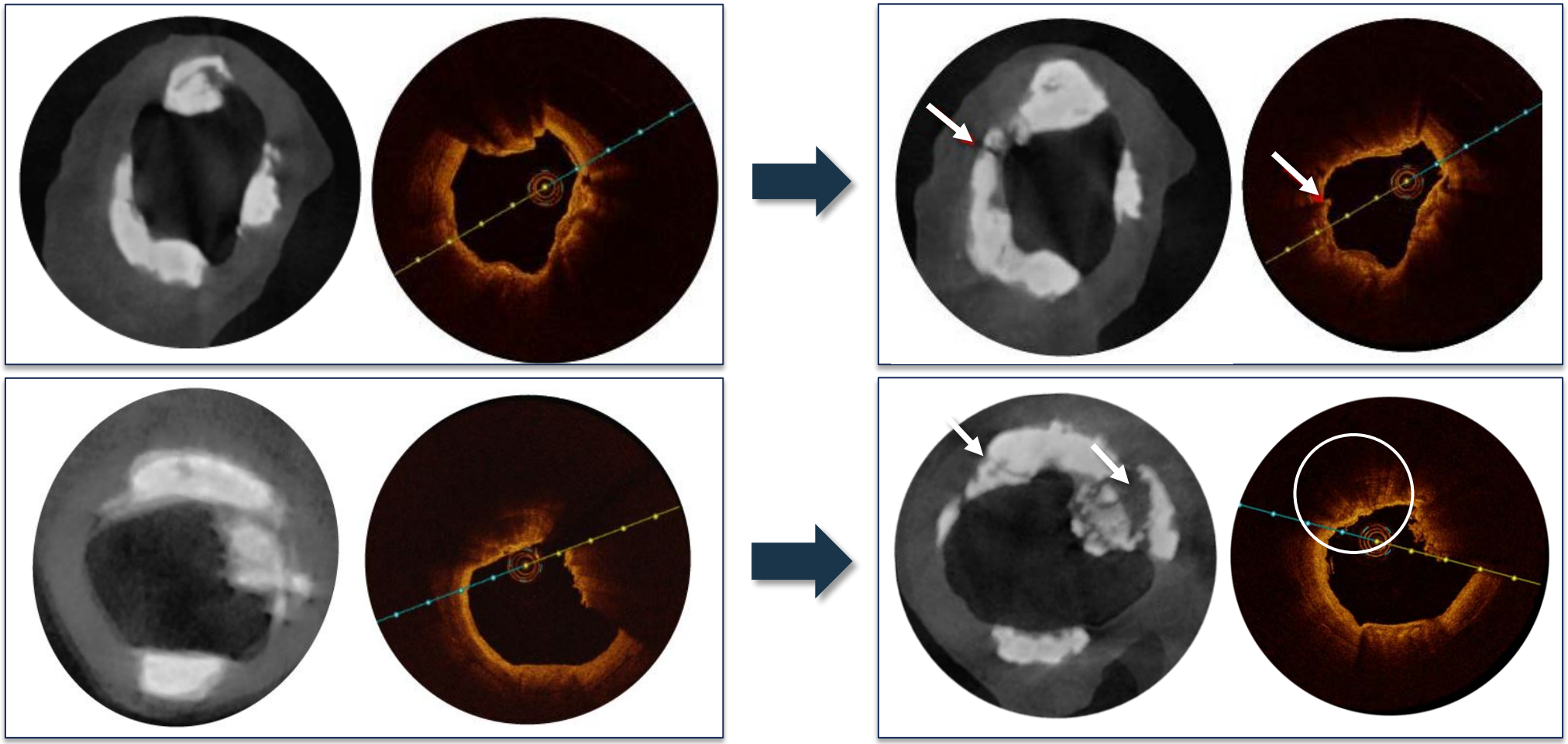
CRF TCT

OCT may not detect subtle micro-fractures in calcific plaque

Micro-fracture Visualization by MicroCT

Pre-IVL

Post-IVL



Imaging	Fracture Visualization
MicroCT	Yes
OCT	Yes

Imaging	Fracture Visualization
MicroCT	Yes
OCT	No

OCT may not detect subtle micro-fractures in calcific plaque

Virmani R., CVPath Institute

Post-stent OCT outcomes

Core Lab Analysis	≤ 180°	181° - 270°	271° - 359°	360°	*P* value
Minimum lumen area*, mm^2	6.1 ± 2.1	6.1 ± 1.9	6.2 ± 1.8	6.4 ± 1.9	0.78
Acute lumen gain at MLA site, mm^2	4.1 ± 1.7	4.0 ± 1.6	4.2 ± 1.6	4.4 ± 1.8	0.73
Mean lumen area, mm^2	8.1 ± 2.6	8.1 ± 2.1	8.2 ± 2.3	8.7 ± 2.2	0.22
Mean stent area, mm^2	8.0 ± 2.7	7.8 ± 2.1	7.8 ± 2.1	8.3 ± 2.3	0.67
Mean stent expansion, mm^2	110.6 ± 30.8	108.1 ± 24.8	100.9 ± 24.1	105.1 ± 22.0	0.36
Any malapposition strut, %	1.9 ± 2.5	3.0 ± 3.5	4.8 ± 6.2	5.2 ± 4.5	<0.0001

Consistent outcomes regardless of calcium angle

Conclusions

- OCT demonstrated consistent MSA and stent expansion outcomes in eccentric and concentric calcium
- Increased IVL-induced calcium fracture was observed in proportion to the amount of calcium
- Consistent MSA and stent expansion outcomes were observed regardless of the presence of visible calcium fracture
  - Micro-CT imaging suggests OCT may not detect subtle micro-fractures in calcific plaque