Case 4: Evaluation of IVL – Fractures by Histology, OCT and Micro-CT

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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
Grant/Research Support (*Institutional)*	NIH/NHLBI, Abbott, Philips, Boston Scientific, Abiomed, Opsens, Acist Medical, Medtronic Cardiovascular Systems Inc
Consulting Fees/Honoraria	Amgen, Astra Zeneca, Boston Scientific
Equity	Shockwave Medical

CASE PRESENTATION

Age (years): **70**
Gender: **F**
BMI (kg/m^2): **30.39**

Clinical Presentation

- Patient presents with exertional dyspnea and CP with moderate intensity activities
- 1/2022 – CVA
  - Revealed PAD - PTA of brachiocephalic trunk

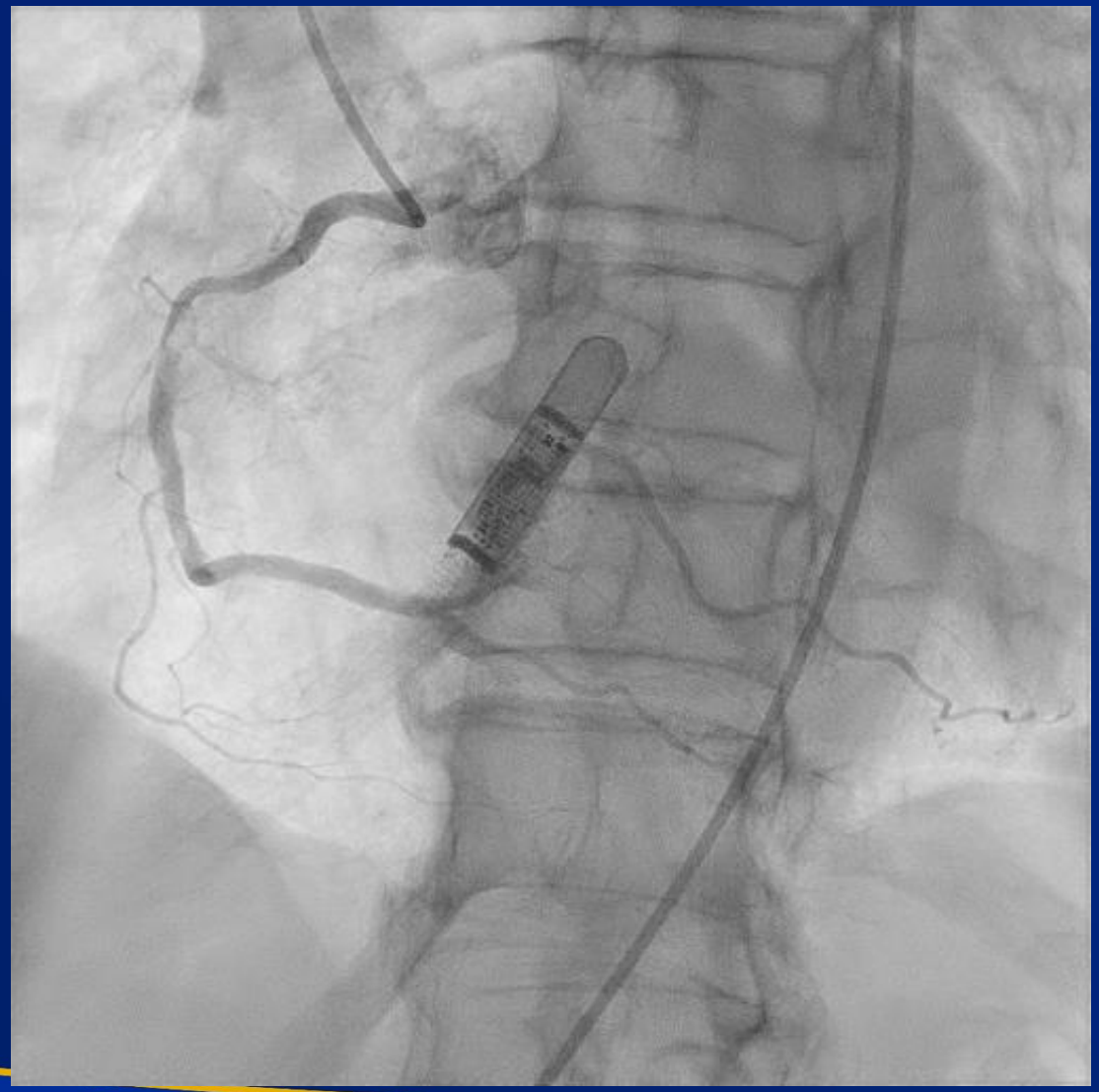
Cardiac History

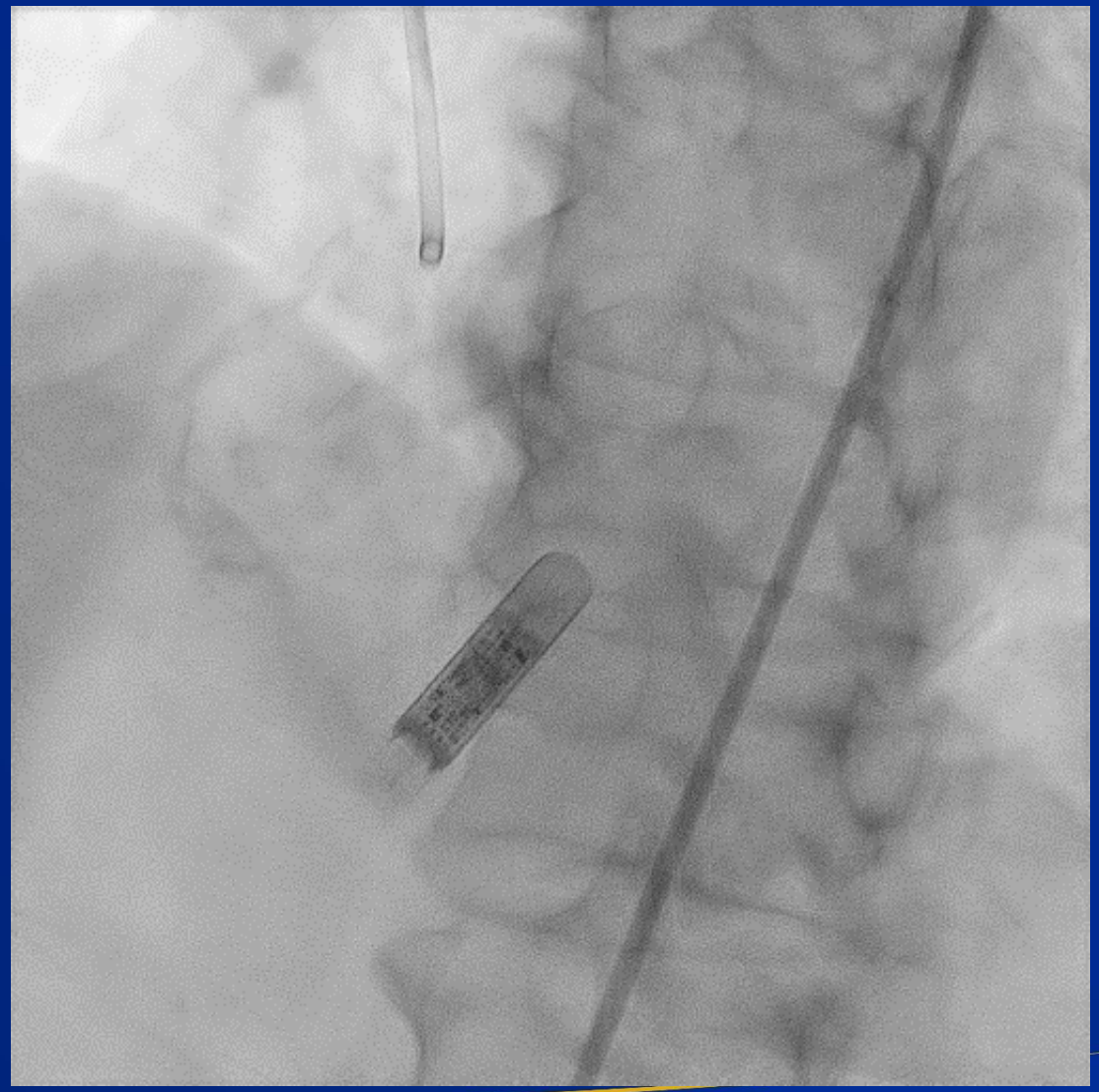
Previous valve disease:	No
Previous coronary disease:	Yes
CHF:	Yes
Atrial fibrillation:	Paroxysmal on OAC
Pacemaker:	No – Loop recorder for AF burden
Previous CV surgery:	NA
Other CV intervention:	Prior PCI (PTCA): OM1
Other:	Pulmonary Hypertension

Co-morbidities

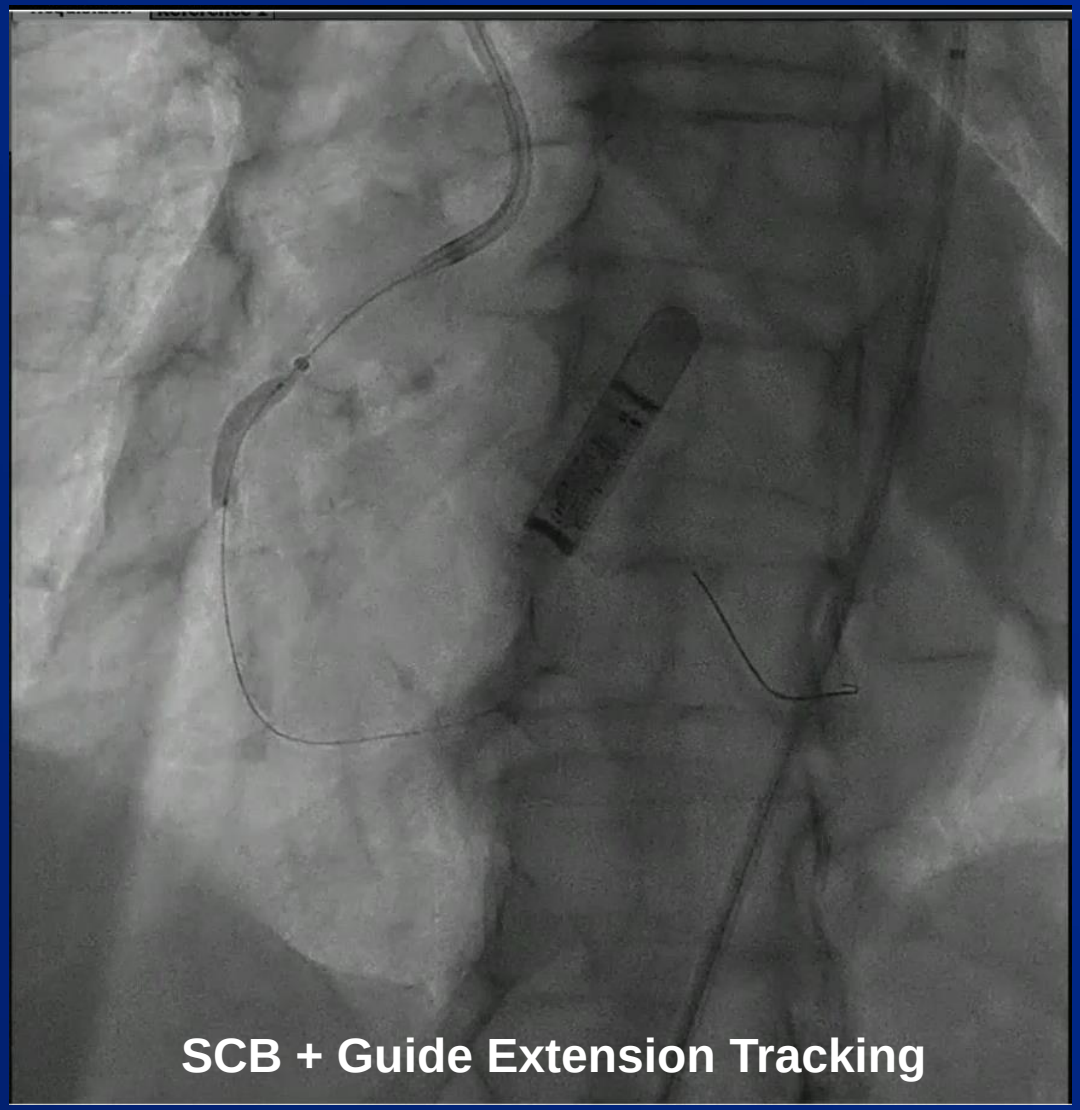
Renal function (Cr: mg/dL, GFR):	Cr: 1.1mg/dL, GFR = 55
Chronic lung disease:	Yes
Prior stroke/TIA:	Yes
Diabetes type II:	Yes
Hypertension:	Yes

ANGIOGRAM



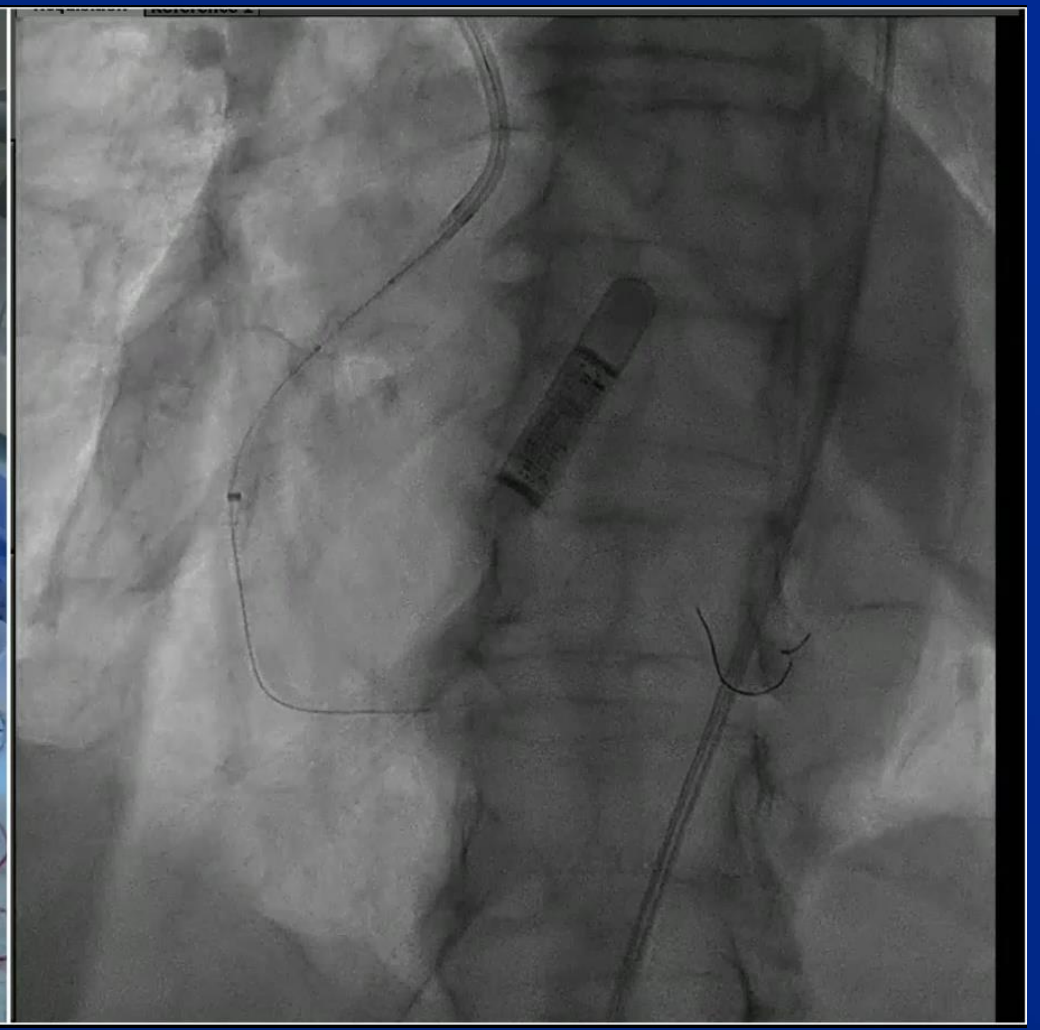


Guide Extension Assisted IVL Delivery

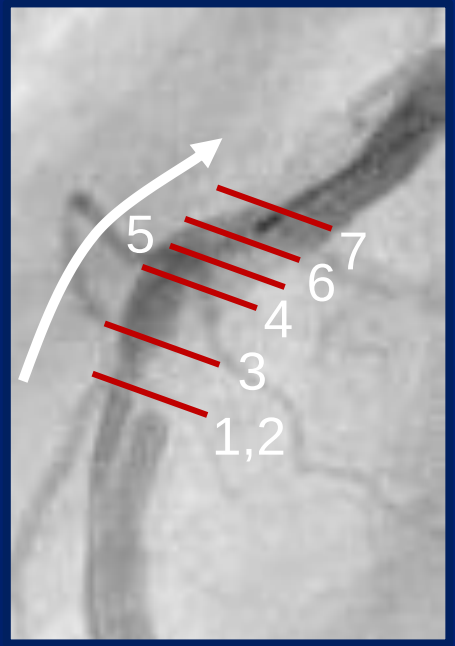


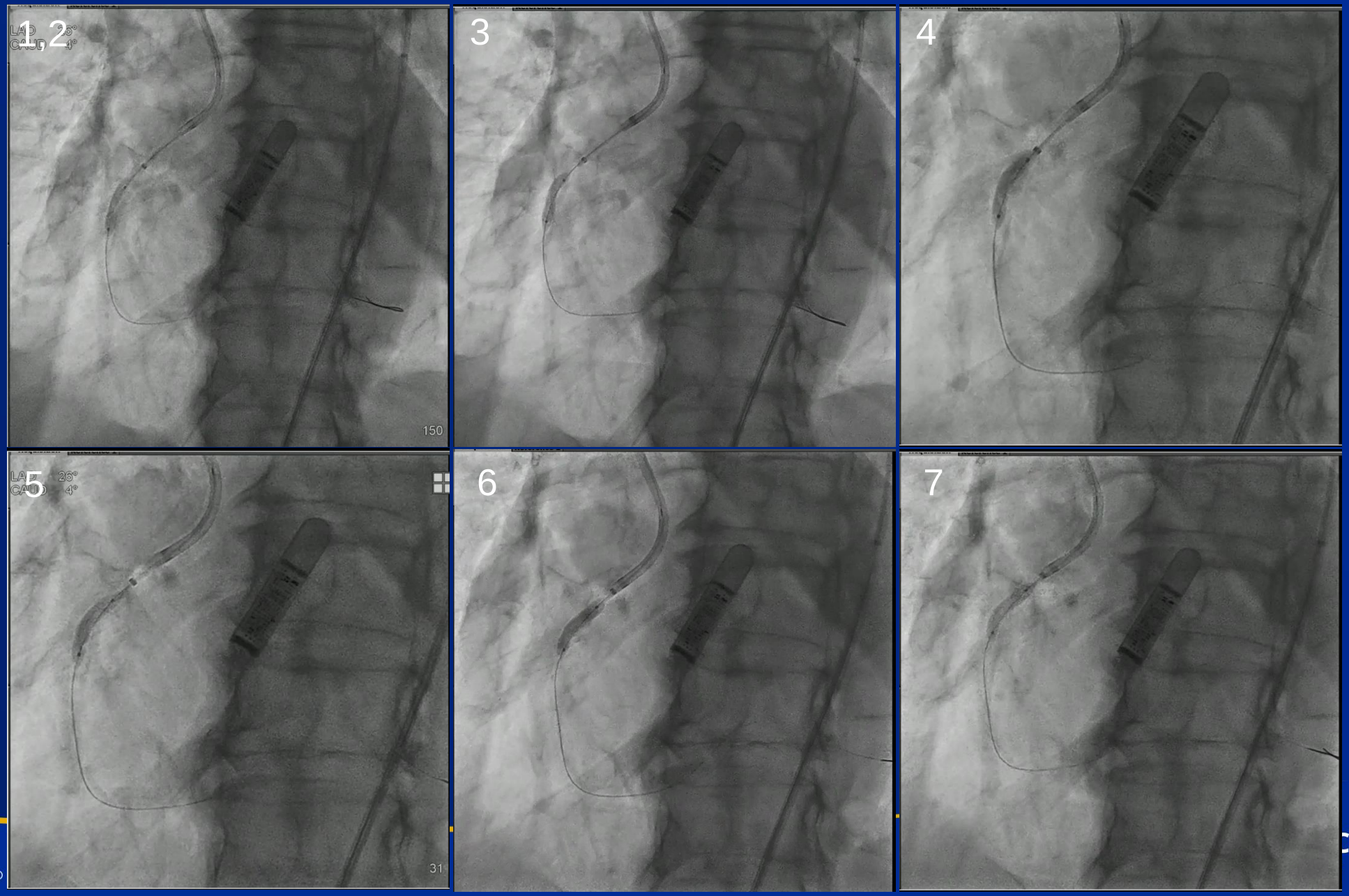
SCB + Guide Extension Tracking

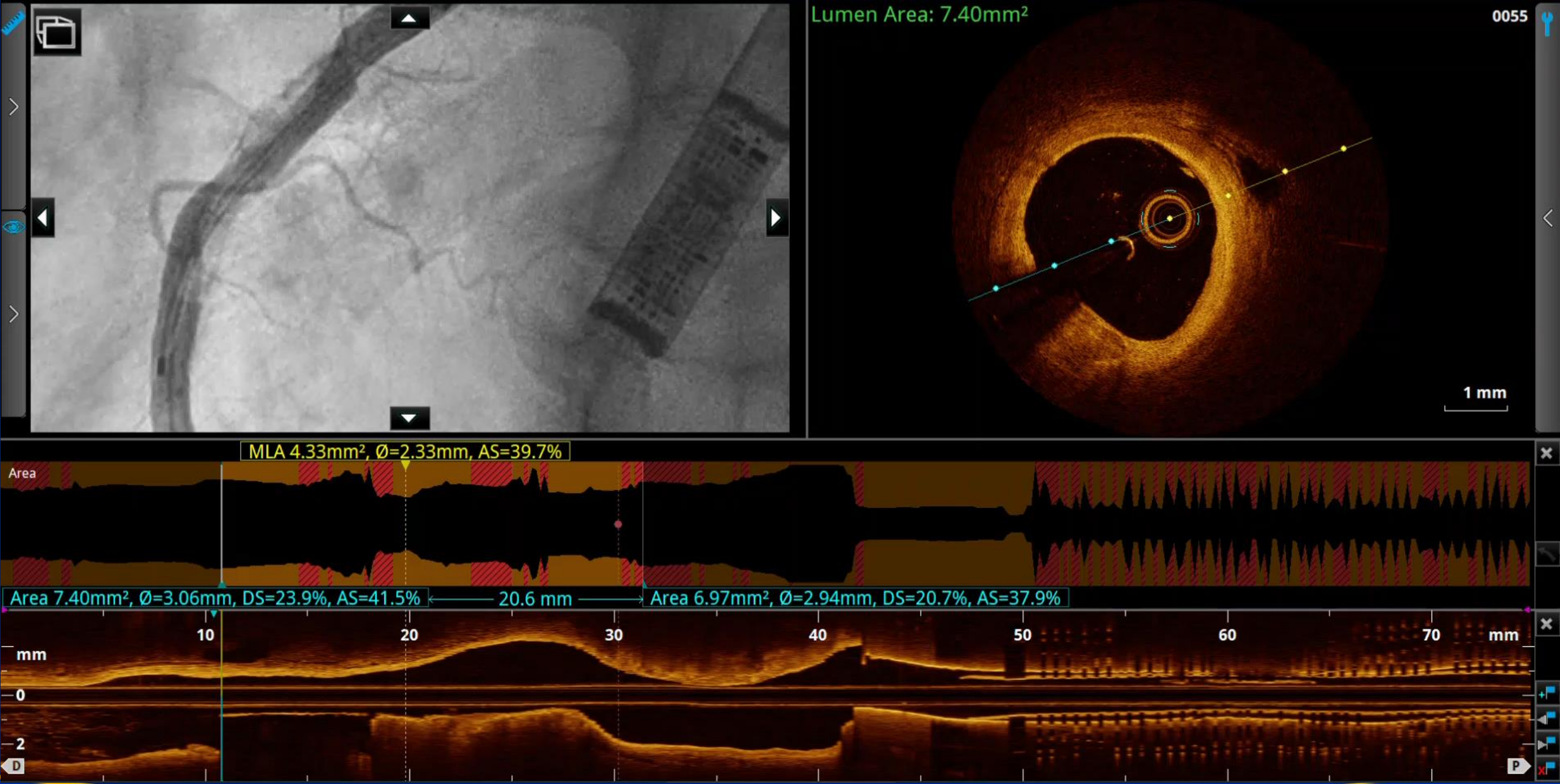
IVL Balloon Unsheathing and Activation



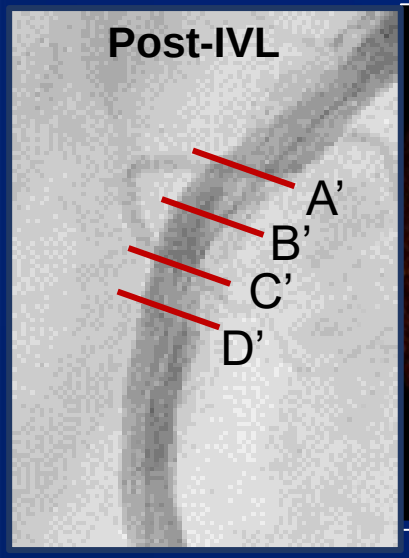
Pulse Management

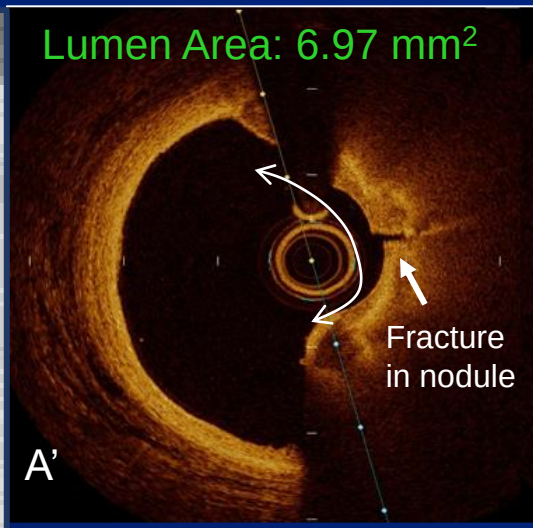


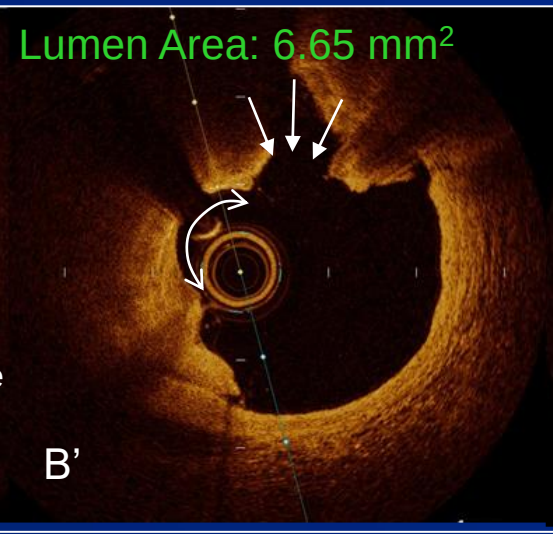


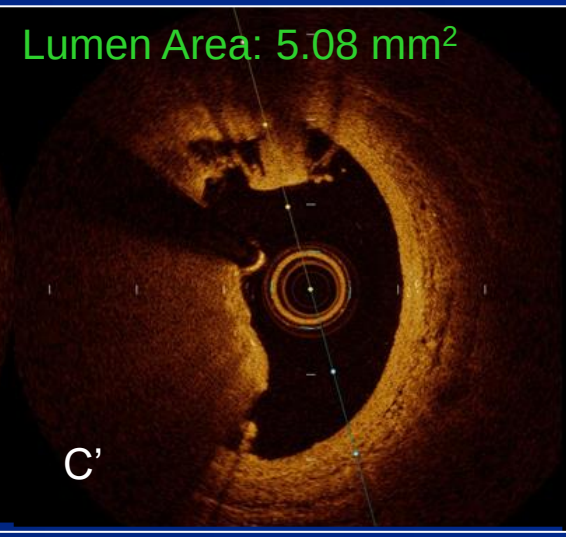

Lumen Area: 7.40mm²
0055
1 mm
MLA 4.33mm², Ø=2.33mm, AS=39.7%
Area
Area 7.40mm², Ø=3.06mm, DS=23.9%, AS=41.5%
20.6 mm
Area 6.97mm², Ø=2.94mm, DS=20.7%, AS=37.9%
10
20
30
40
50
60
70
mm
mm
0
2
D
P

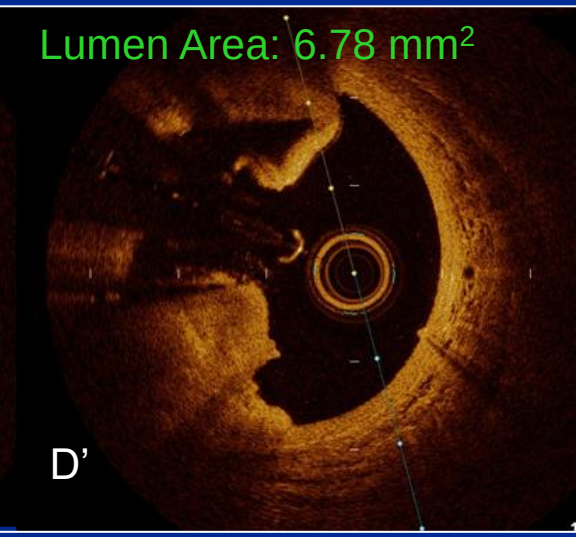
Ca+ Fractures



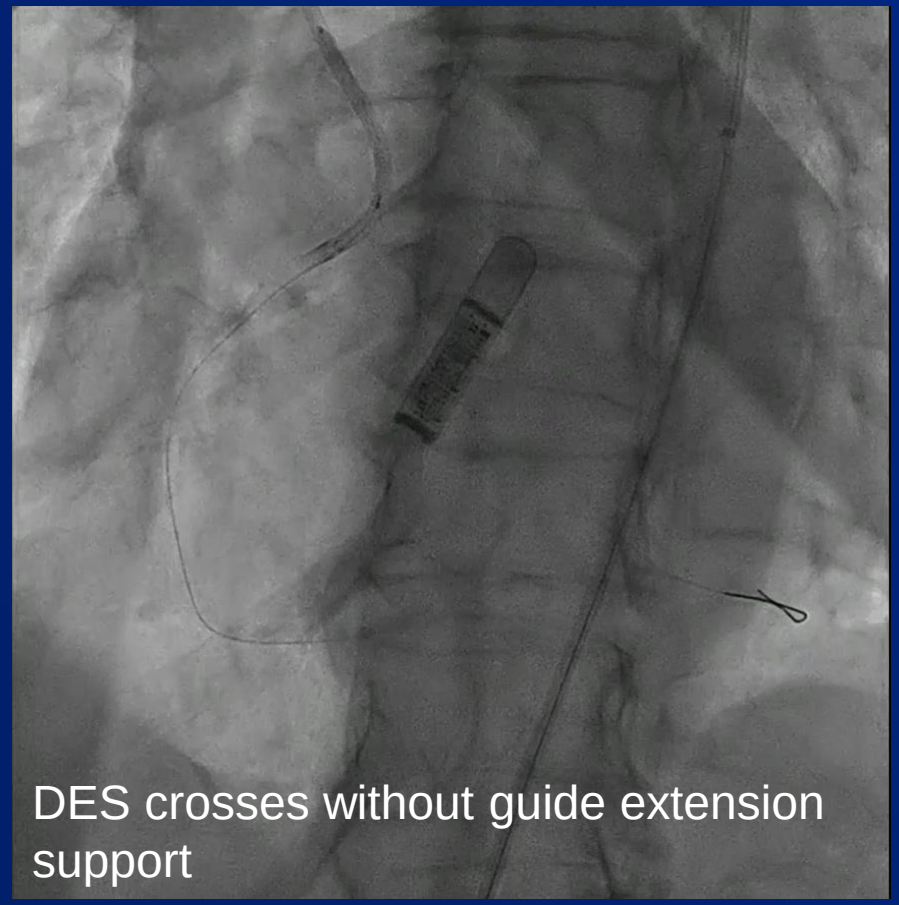




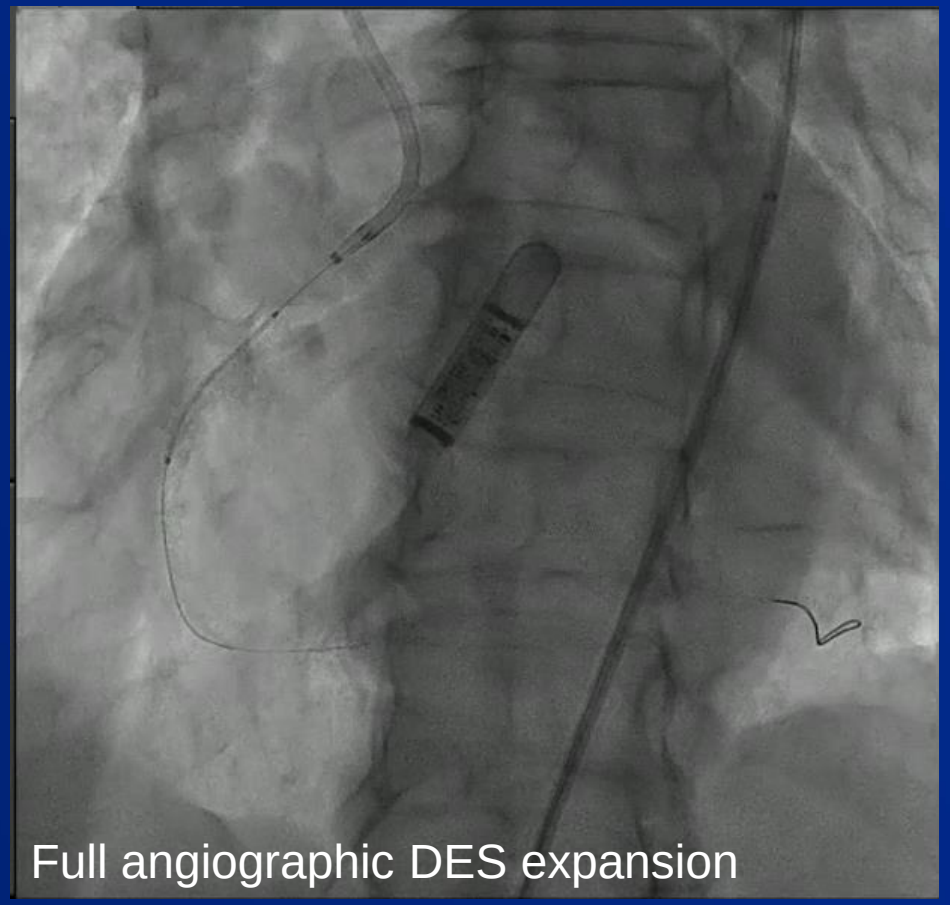




Post IVL

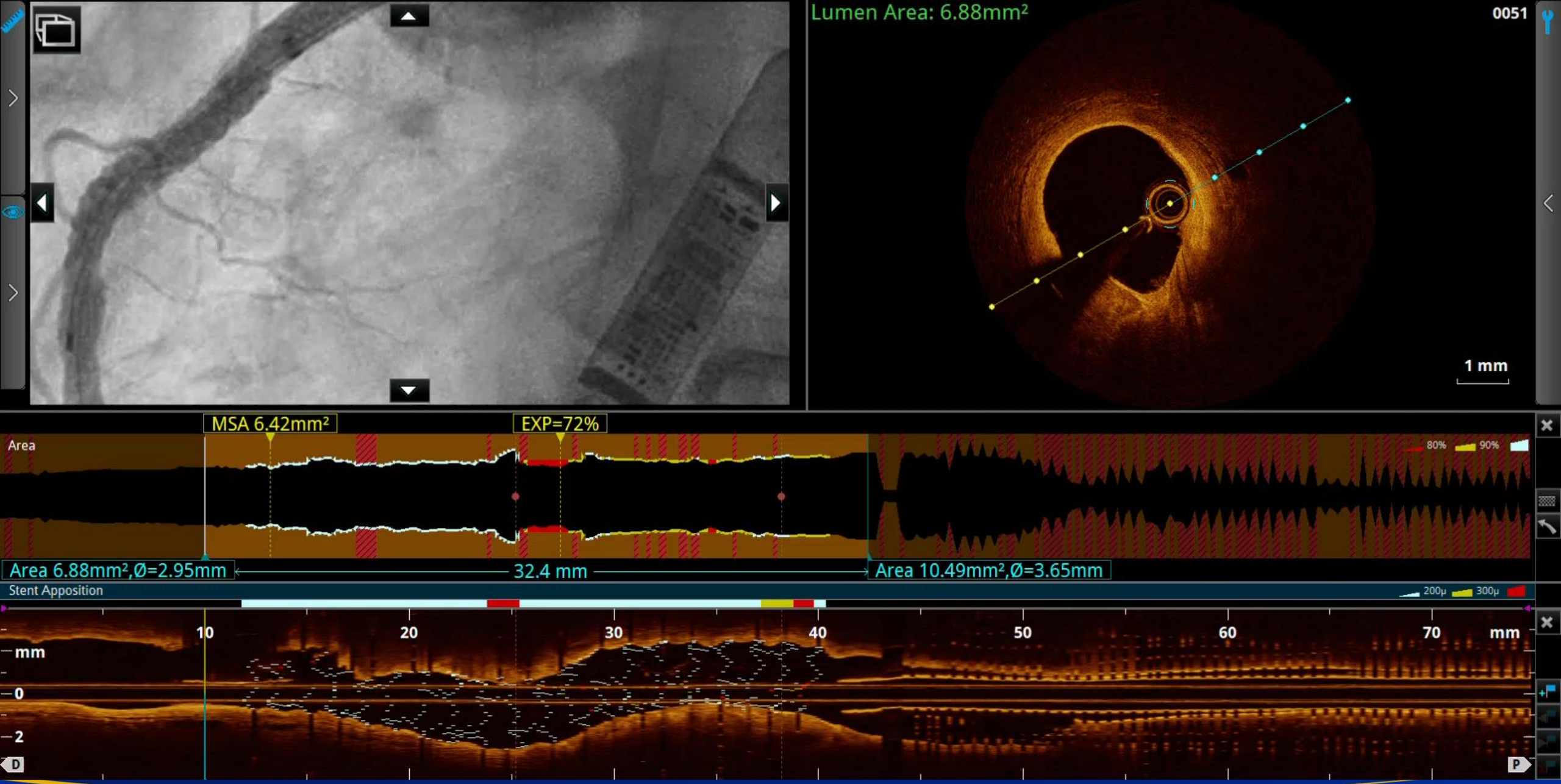


DES crosses without guide extension support

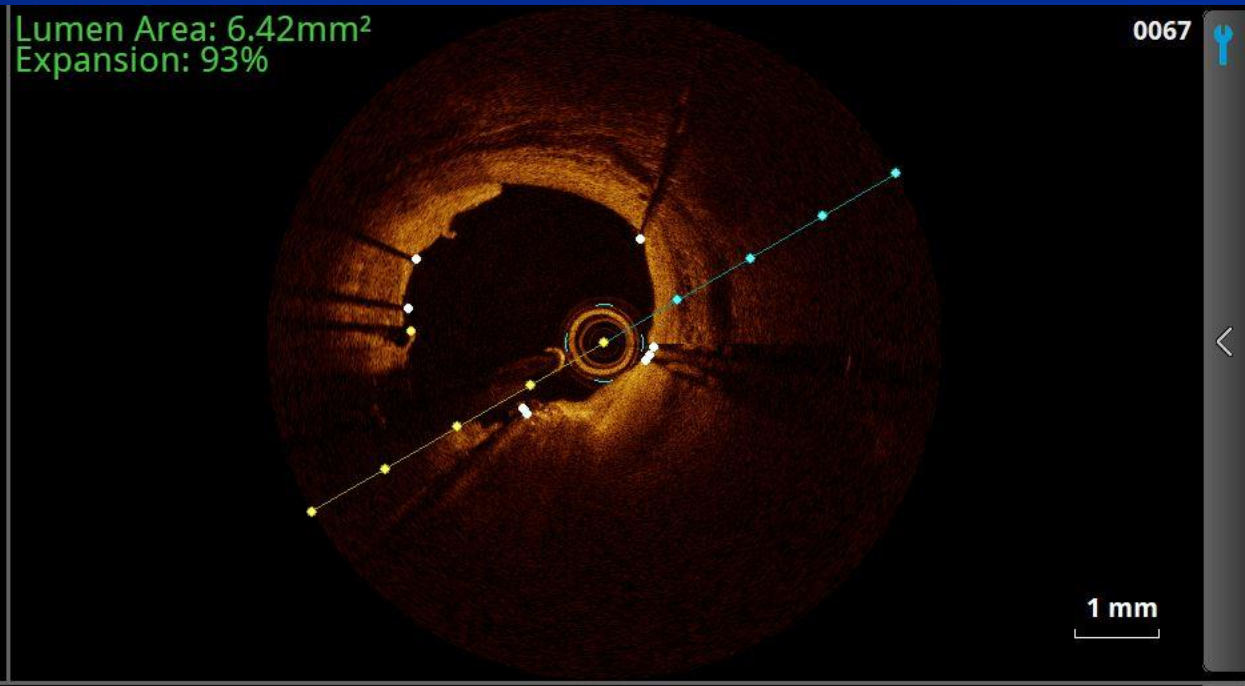


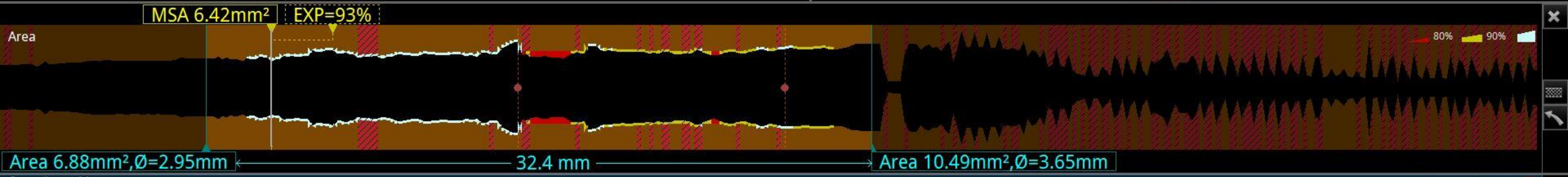
Full angiographic DES expansion

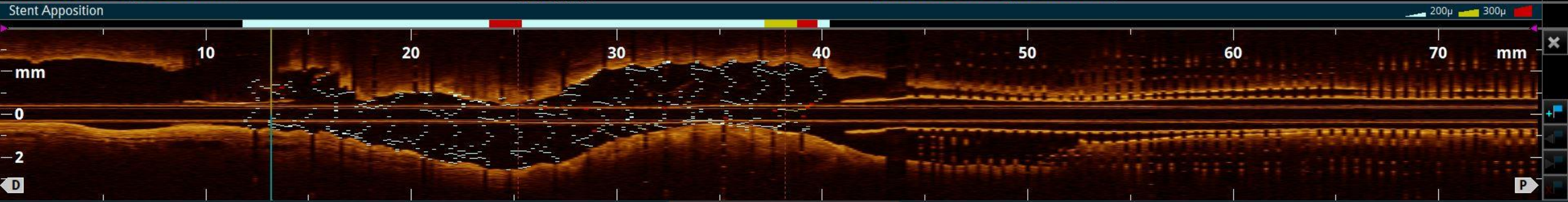
Full NC expansion


Lumen Area: 6.88mm²
0051
1 mm
MSA 6.42mm²
EXP=72%
Area
80%
90%
Area 6.88mm²,Ø=2.95mm
32.4 mm
Area 10.49mm²,Ø=3.65mm
Stent Apposition
200µ
300µ
10
20
30
40
50
60
70
mm
mm
0
2
D
P

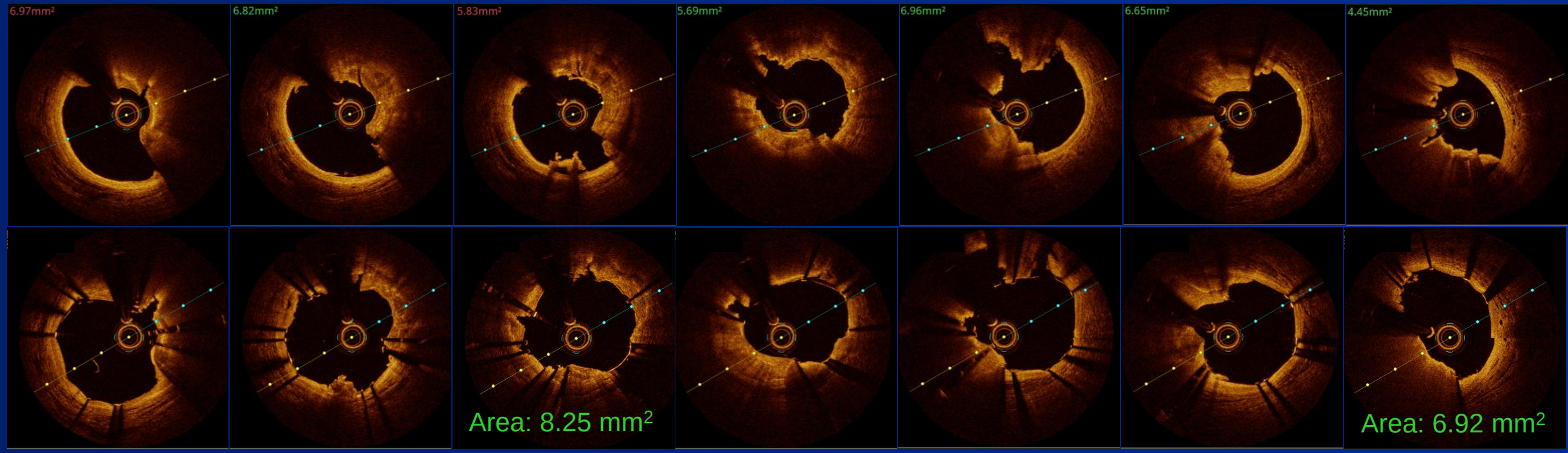
Final Expansion





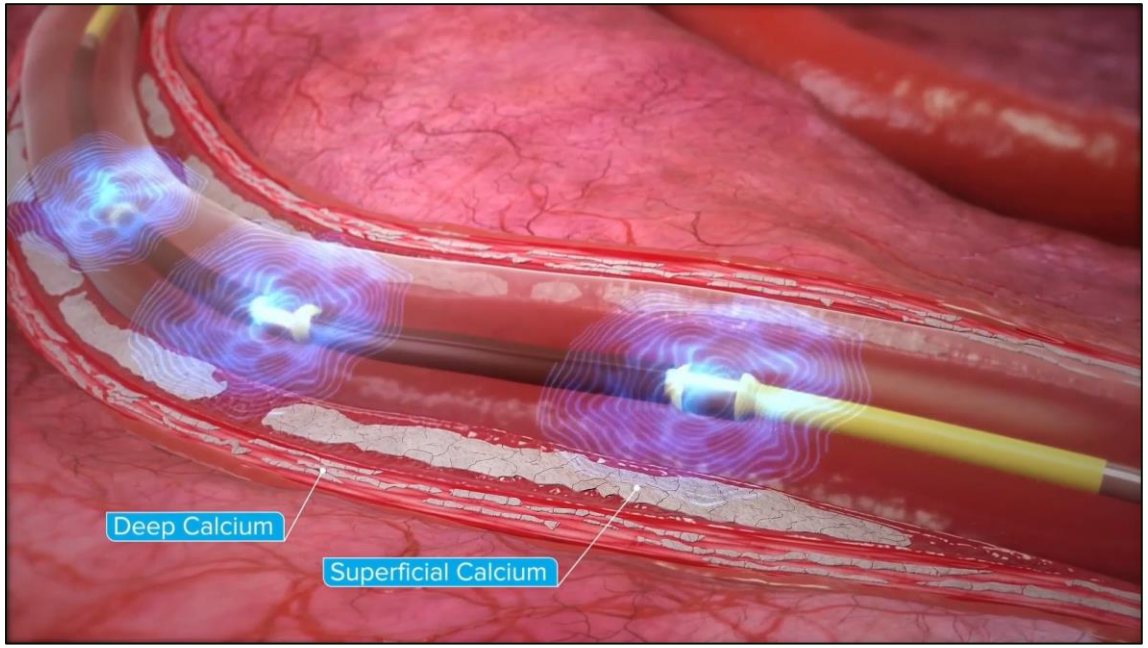


IVL Impact


IVL
Post
6.97mm²
6.82mm²
5.83mm²
5.69mm²
6.96mm²
6.65mm²
4.45mm²
Area: 8.25 mm²
Area: 6.92 mm²

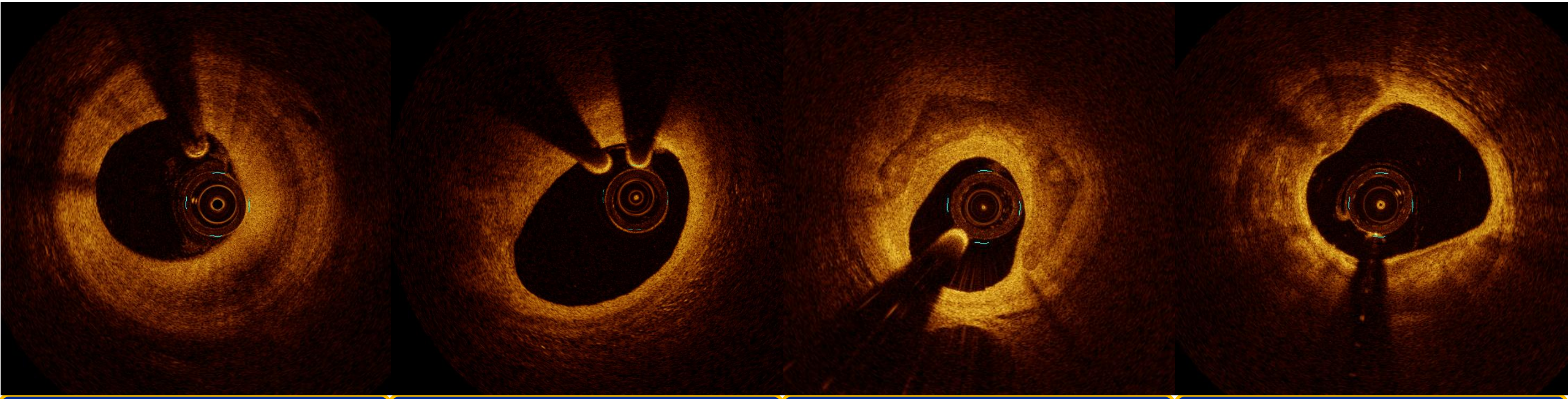
Intravascular Lithotripsy

- Acoustic pressure waves fracture calcium



Acoustic pressure waves travel through tissue with an effective pressure of ~50 atm and fractures both superficial and deep calcium

Morphology Guided Lesion Preparation



FIBROTIC	LIPIDIC	MILD/MODERATE Ca^{2+}	SEVERE Ca^{2+}

DIRECT STENTING

COMPLIANT BALLOON

NON-COMPLIANT BALLOON

ATHERECTOMY OR IVL

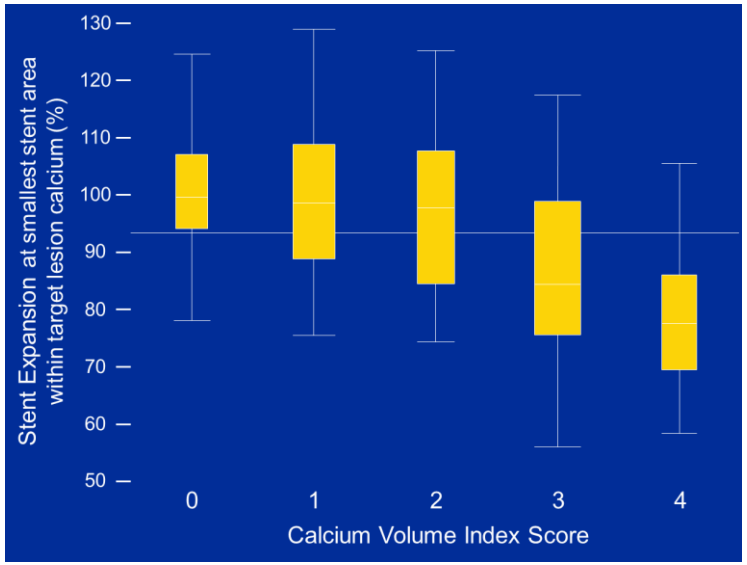
Influence of Ca^{2+} on stent Expansion by OCT

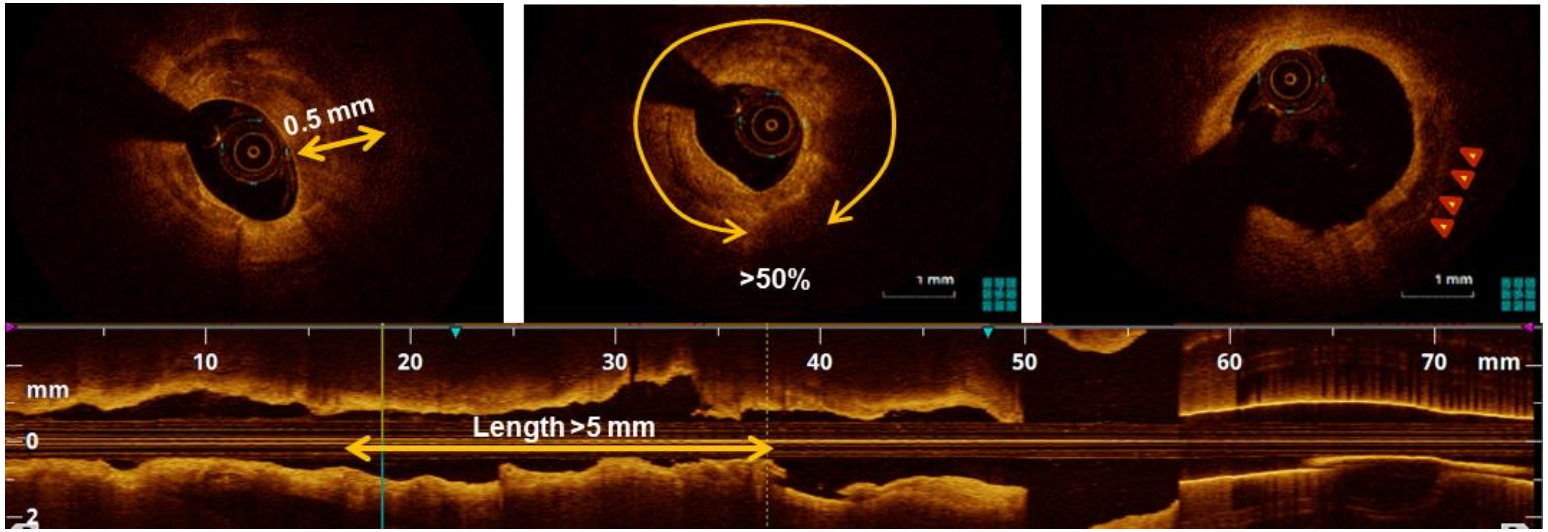
OCT-based Calcium Volume Index Score	
1. Maximum Calcium Angle (°)	≤ 90 ° ➡ 0 point 90° < Angle ≤180° ➡ 1 point > 180 ° ➡ 2 points
2. Maximum Calcium Thickness (mm)	≤ 0.5 mm ➡ 0 point > 0.5 mm ➡ 1 point
3. Calcium Length (mm)	≤ 5.0 mm ➡ 0 point > 5.0 mm ➡ 1 point
Total score	**0 to 4 points**

Rule of 5's

- **0.5mm thickness**
- **5mm long**
- **50% vessel arc**

Consider advanced lesion preparation ≥3

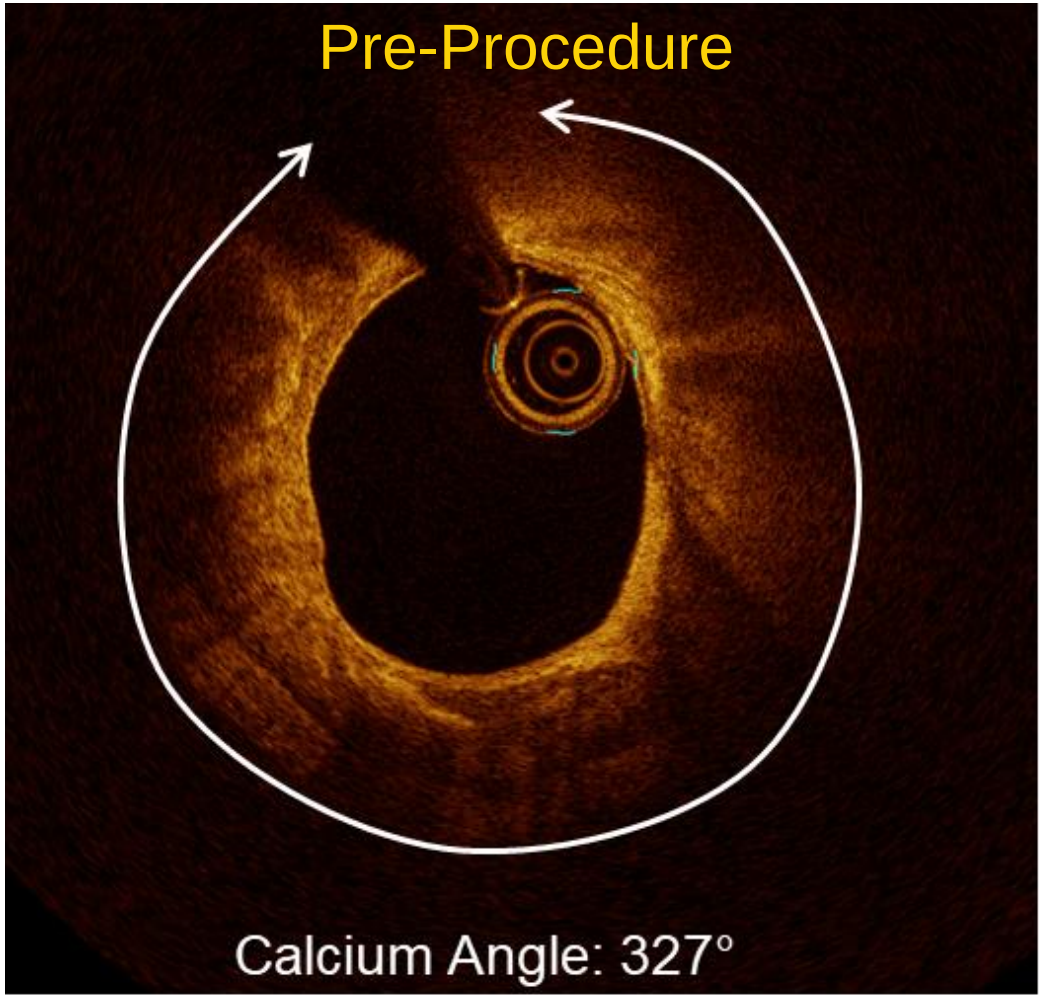


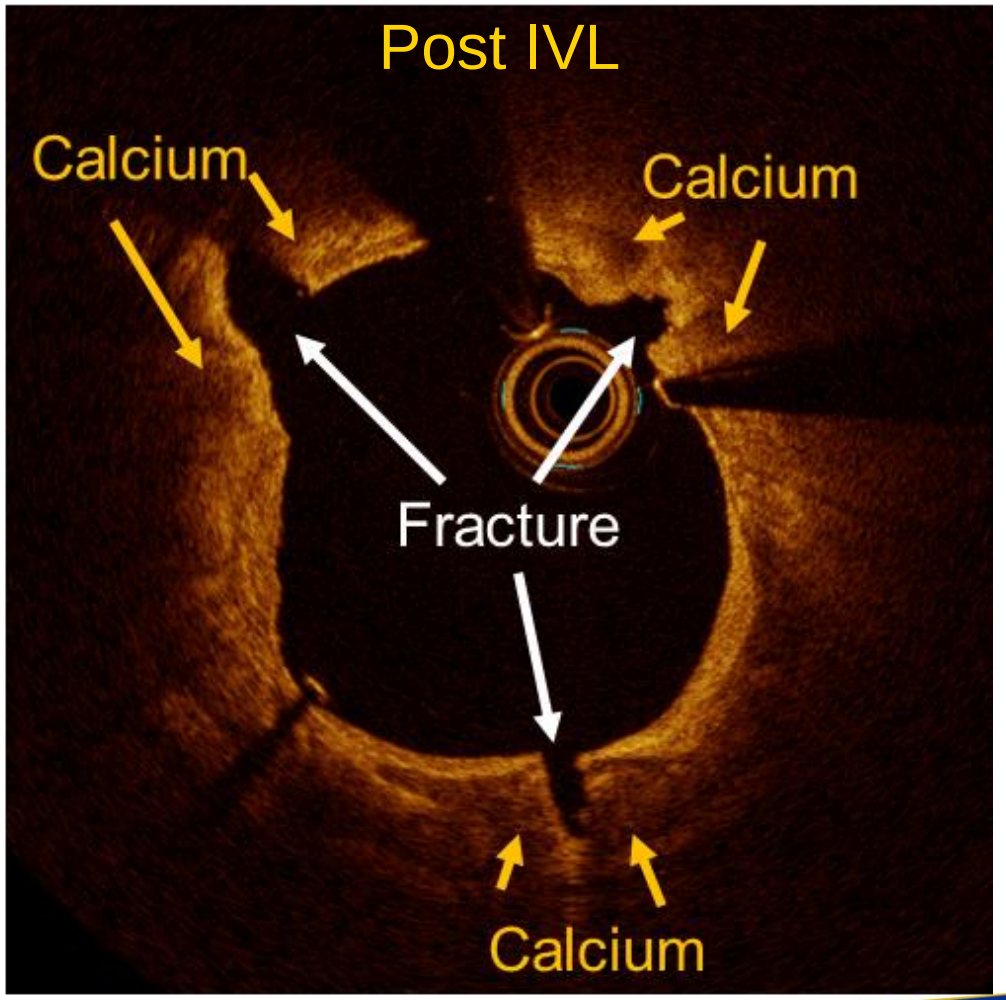


Fujino & Maehara. EuroIntervention. 2018 Apr 6;13(18):e2182-e2189.

Mechanism of Action

Circumferential Calcium Fracture





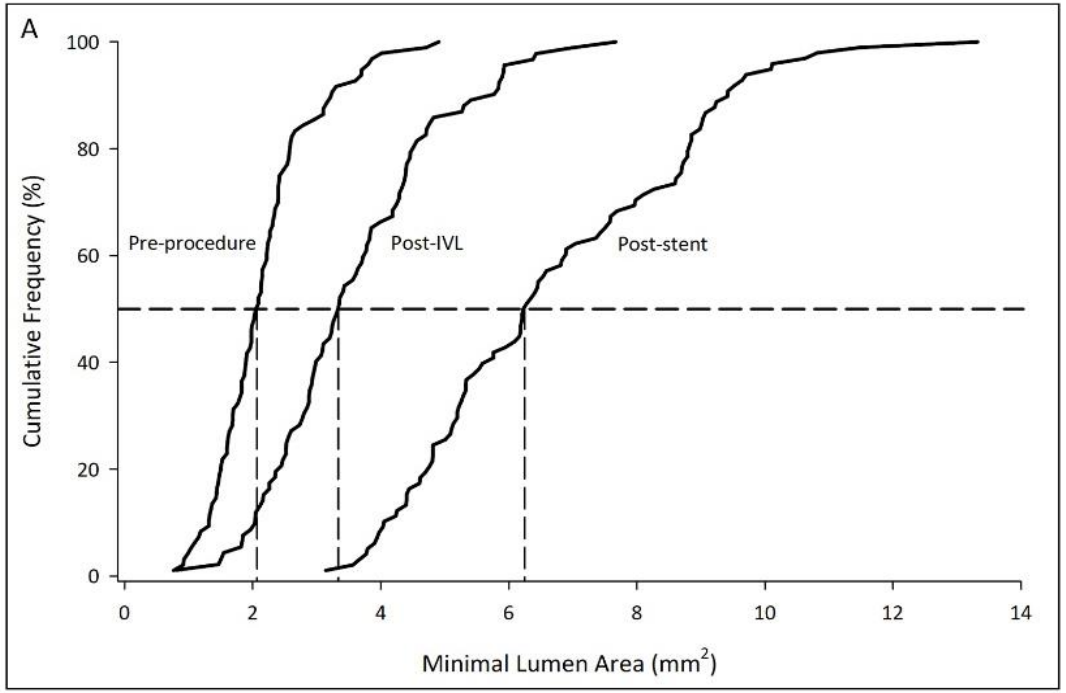
Ali and Fajadet et al. iJACC.2017;10(8):897-906.

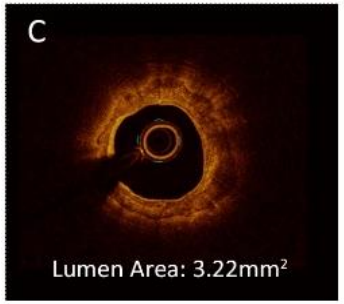
Serial OCT

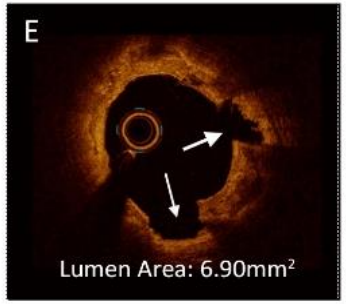
	Pre-IVL N=97	Post-IVL N=92	Post-stent N=98
At MLA site			
Minimum Lumen area, mm^2	2.2 ± 0.8*	3.6 ± 1.4*	6.5 ± 2.0*
Maximum Area stenosis	72 ± 12%*	56 ± 16%*	22 ± 19%*
At Maximum Ca^{++} site			
Maximum calcium angle, °	293 ± 77		
Maximum calcium thickness, mm	0.96 ± 0.25		
Stent expansion			102 ± 29%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

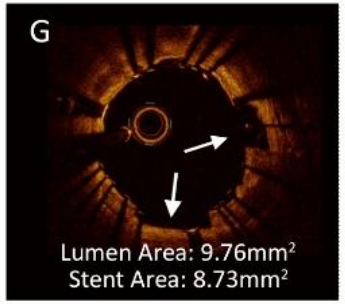
*P<0.01 for all comparisons between pre-IVL, post-IVL, post-stent

Mechanism of Action

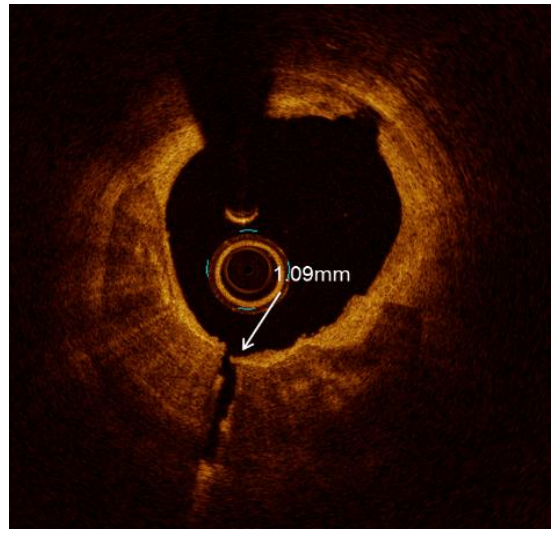




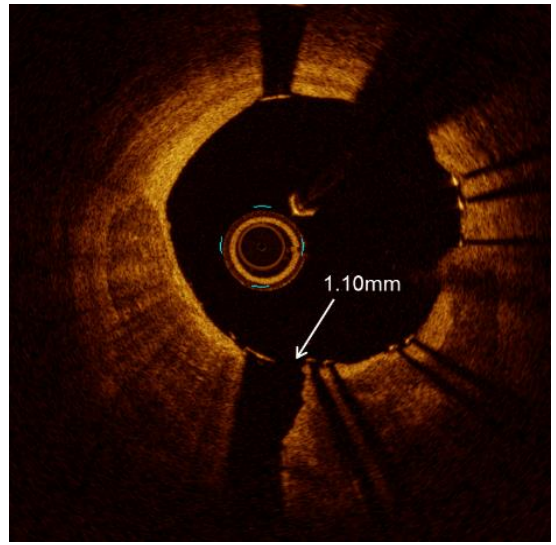




Post-IVL



Post-DES



Kereiakes and Ali et al. JACC Interv. 2021 28;14(12):1275-1292

Disrupt CAD: OCT Sub-studies

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

First Description

Ziad A. Ali, MD, DPhil,[a,b] Todd J. Brinton, MD,[c] Jonathan M. Hill, MD,[d] Akiko Maehara, MD,[a,b] Mitsuaki Matsumura, BS,[a,b] Keyvan Karimi Galougahi, MD, PhD,[a] Uday Illindala, MS,[e] Matthias Götberg, MD, PhD,[f] Robert Whitbourn, MD,[g] Nicolas Van Mieghem, MD,[h] Ian T. Meredith, MBBS, PhD,[i] Carlo Di Mario, MD, PhD,[j] Jean Fajadet, MD[k]

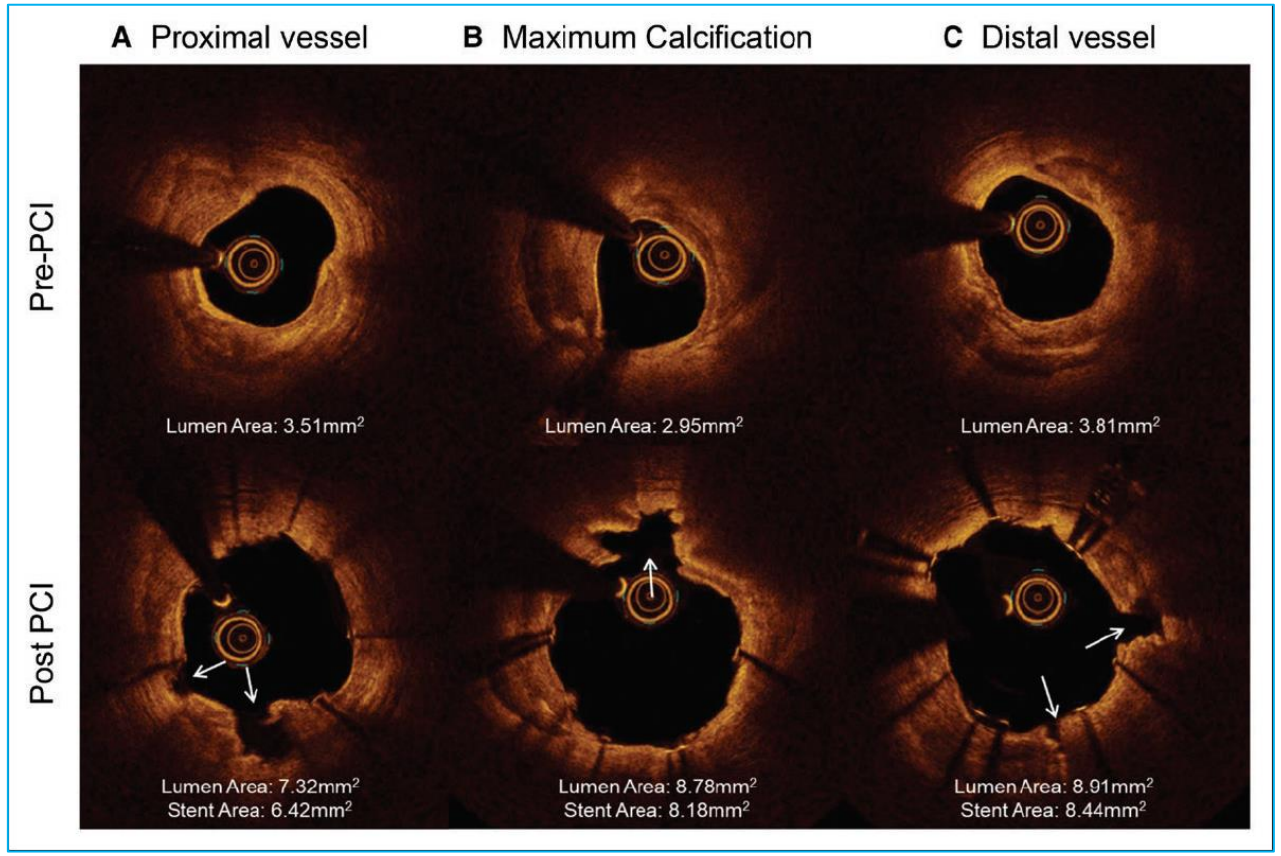
Circulation: Cardiovascular Interventions
Volume 12, Issue 10, October 2019
https://doi.org/10.1161/CIRCINTERVENTIONS.119.008434

CORONARY INTERVENTIONS

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

The Disrupt CAD II Study

Ziad A. Ali, MD, DPhil, Holger Nef, MD, PhD, Javier Escaned, MD, PhD, Nikos Werner, MD, PhD, Adrian P. Banning, MD, Jonathan M. Hill, MD, Bernard De Bruyne, MD, PhD, Matteo Montorfano, MD, Thierry Lefevre, MD, Gregg W. Stone, MD, Aaron Crowley, MA, Mitsuaki Matsumura, BS, Akiko Maehara, MD, Alexandra J. Lansky, MD, Jean Fajadet, MD, and Carlo Di Mario, MD, PhD



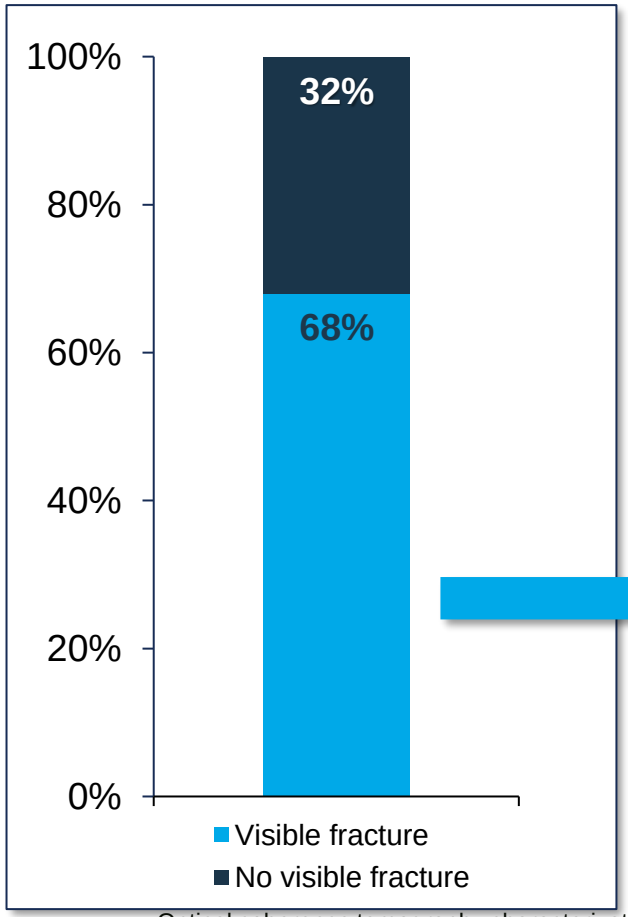
Ali et al. iJACC. 2017
Ali et al. Circ Cardiovasc Interv. 2019

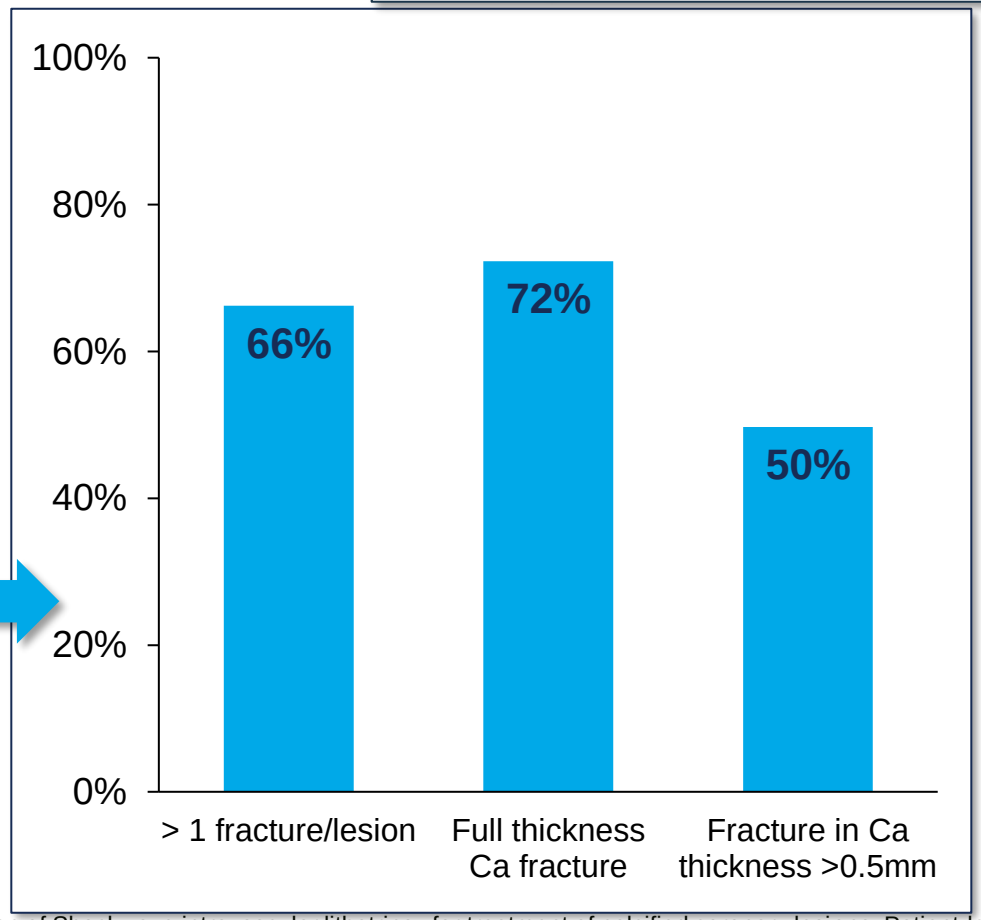
DISRUPT CAD : OCT demonstrated multiple circumferential calcium fractures and excellent stent expansion

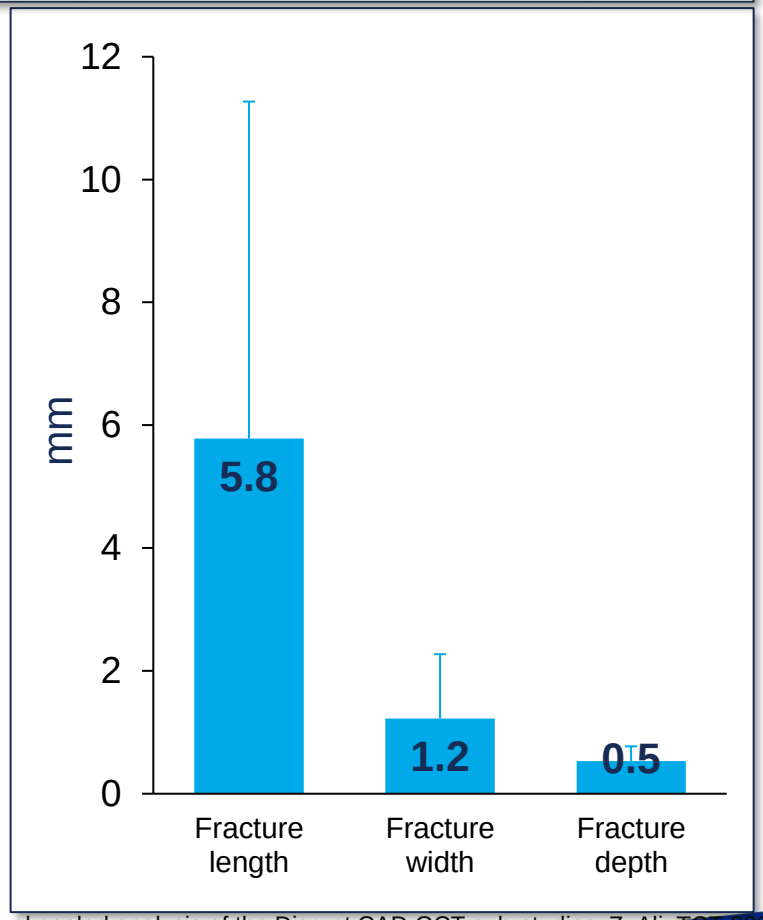
Visible Calcium Fracture by OCT

- Disrupt CAD I-IV pooled OCT sub-study patient-level analysis (N = 245)

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

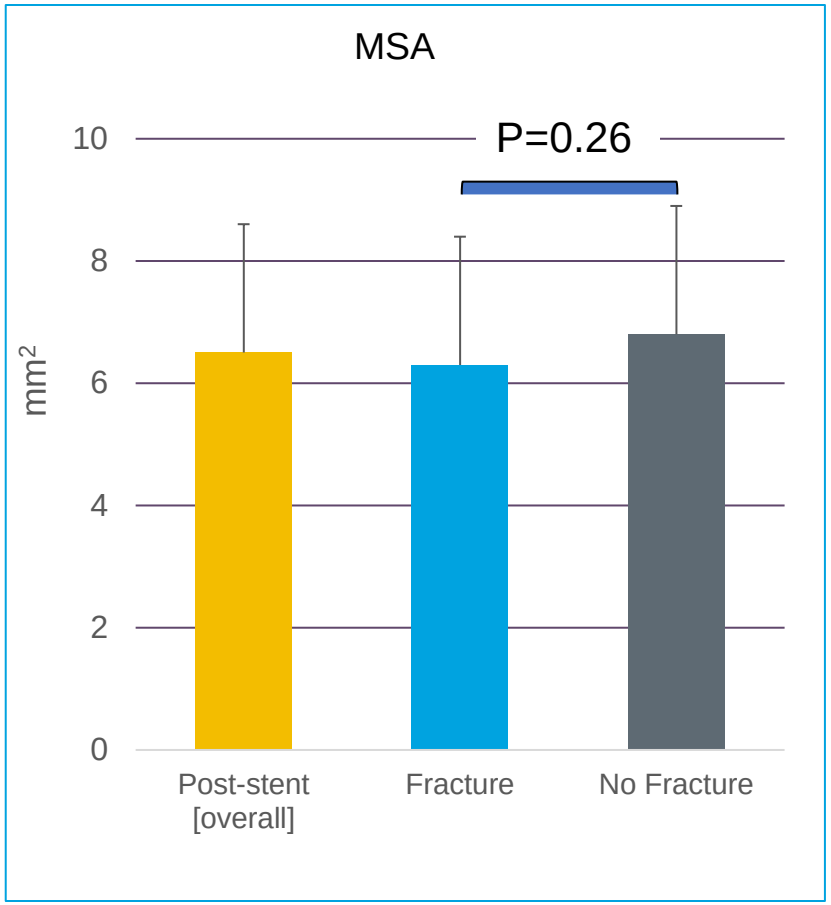


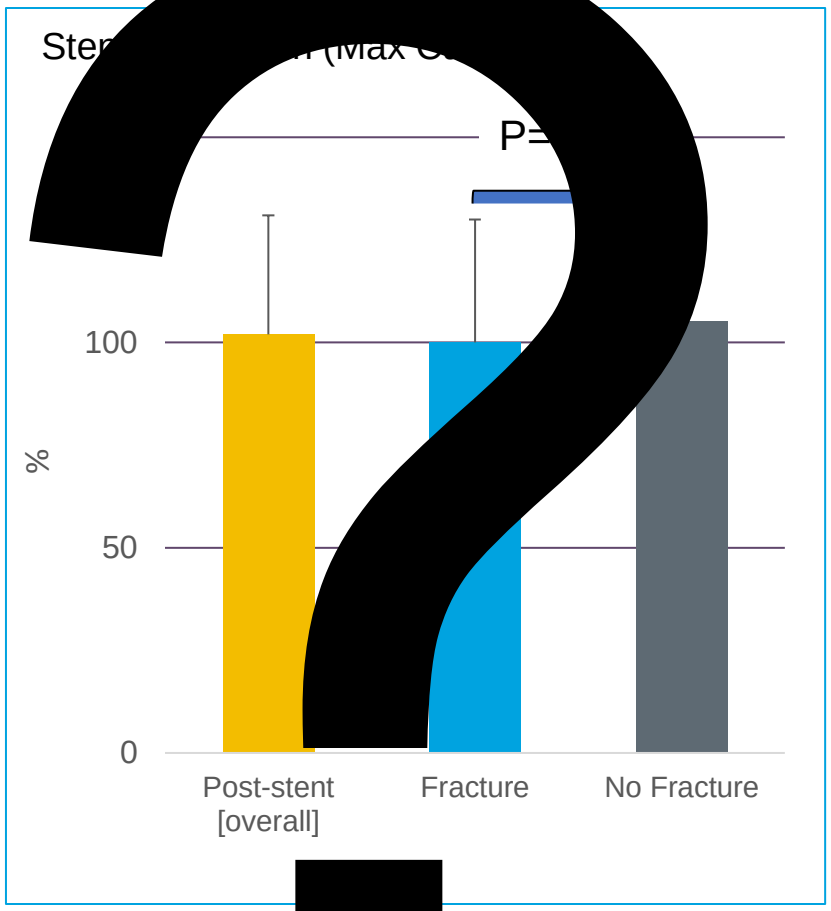


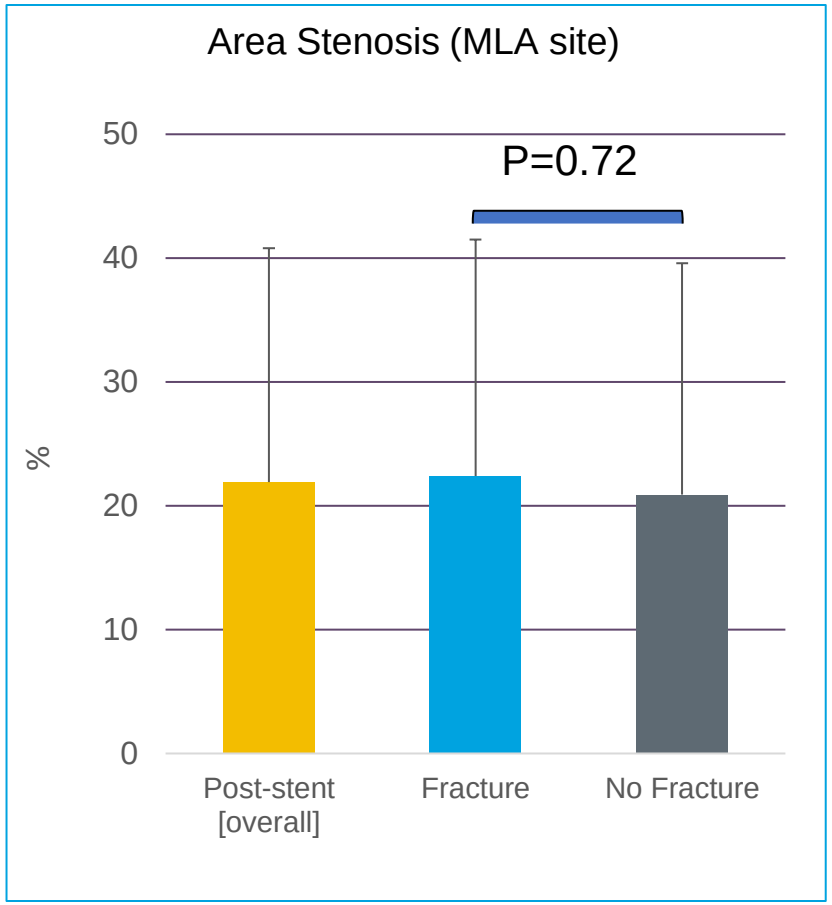


- Optical coherence tomography characterization of Shockwave intravascular lithotripsy for treatment of calcified coronary lesions: Patient-level pooled analysis of the Disrupt CAD OCT sub-studies. Z. Ali, TCT 2021

Outcomes by Fracture Characteristics



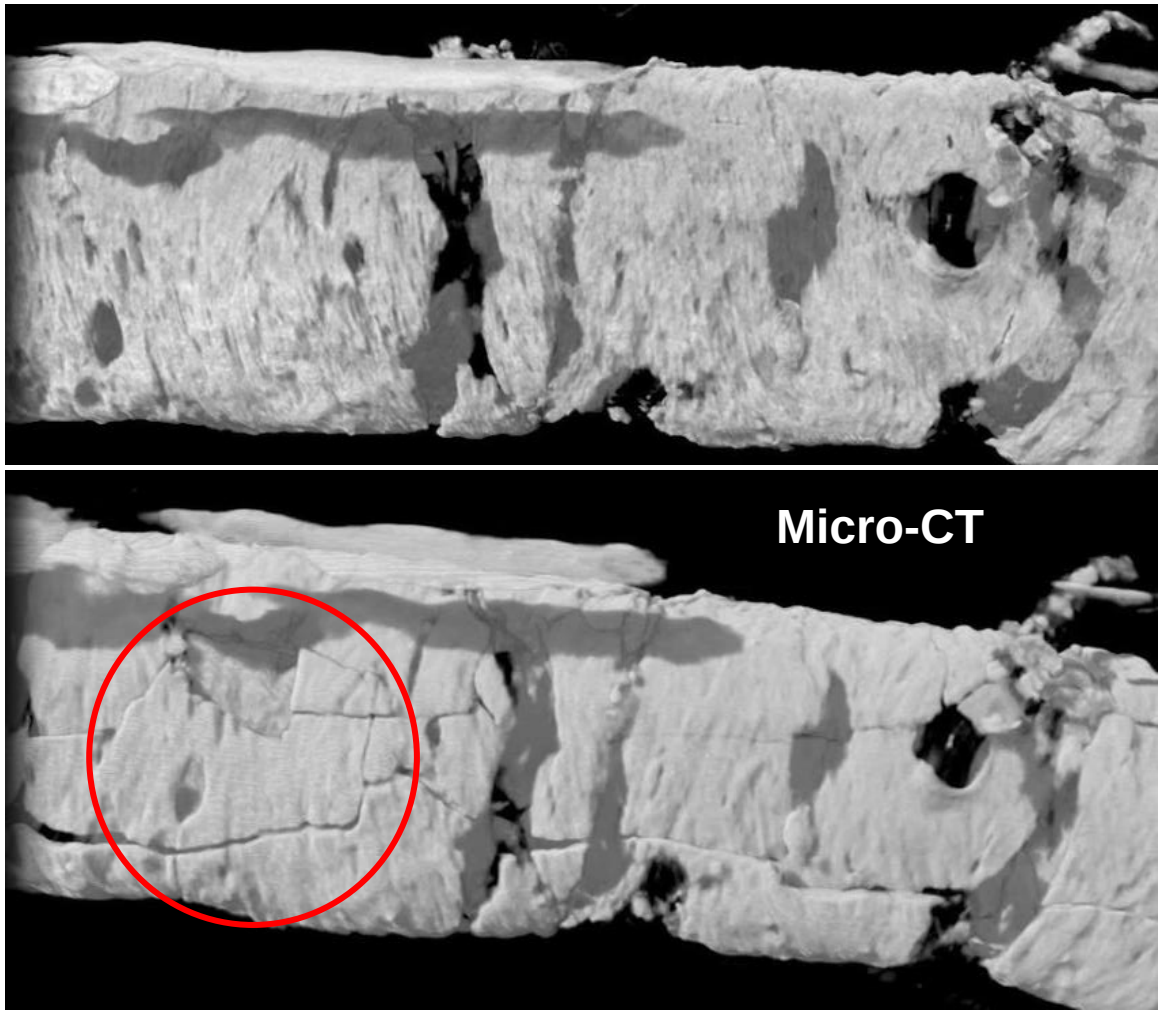




Consistent outcomes regard[redacted]f fracture visualization by OCT

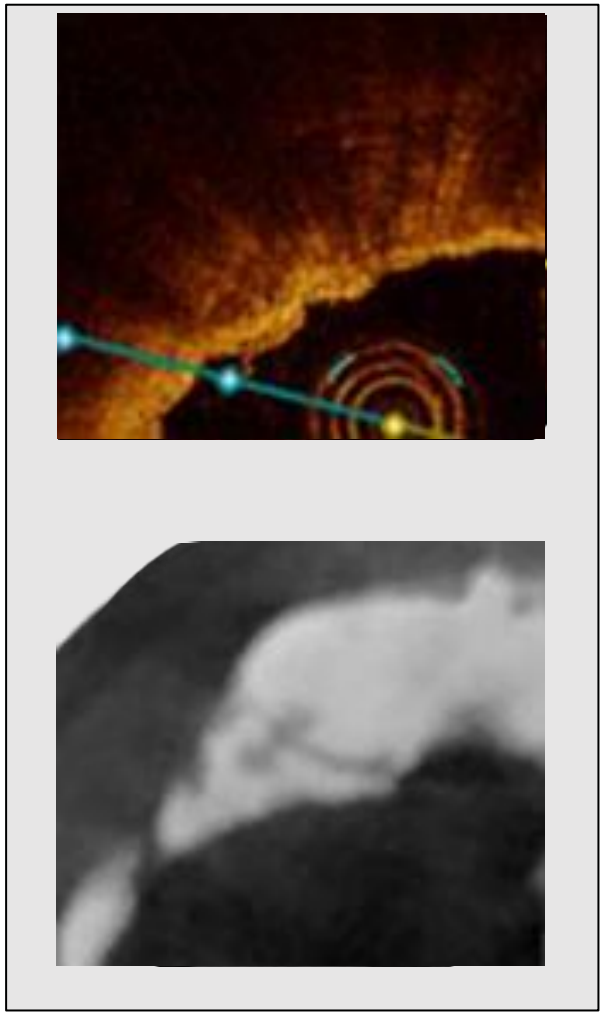
Pre-IVL

Post-IVL



OCT

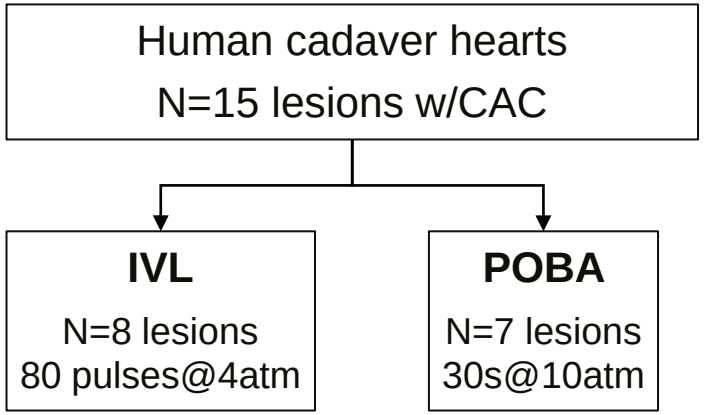
Micro-CT



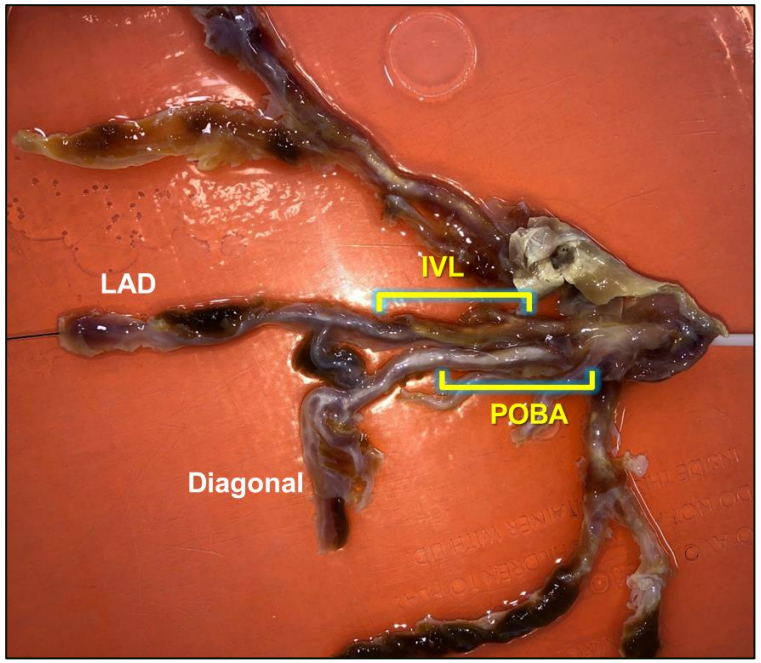
Kereiakes and Ali et al. JACC Interv. 2021 28;14(12):1275-1292

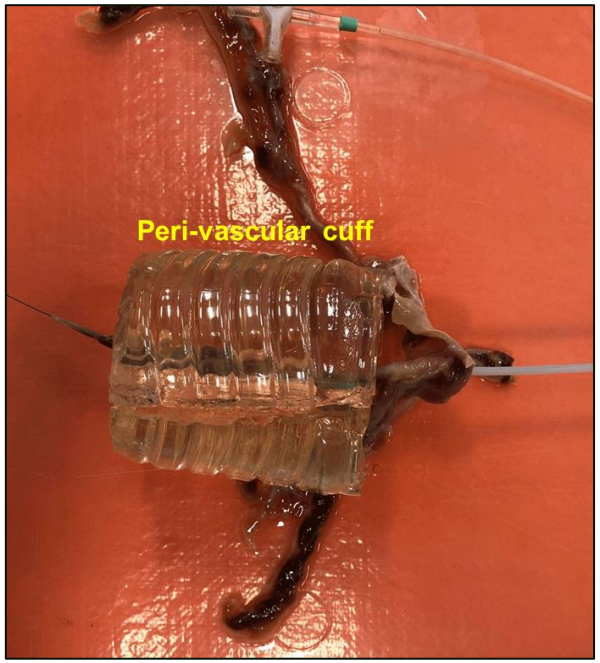
Study design and methods

Objective: Compare the sensitivity of OCT, micro-CT, and histology for calcium fracture detection



- OCT and micro-CT imaging performed before and after treatment with IVL or POBA only (no stent placement).
- Presence and characterization of calcium fracture assessed with OCT and micro-CT; compared against co-registered histological sections.





Coronary arteries were dissected free from each heart

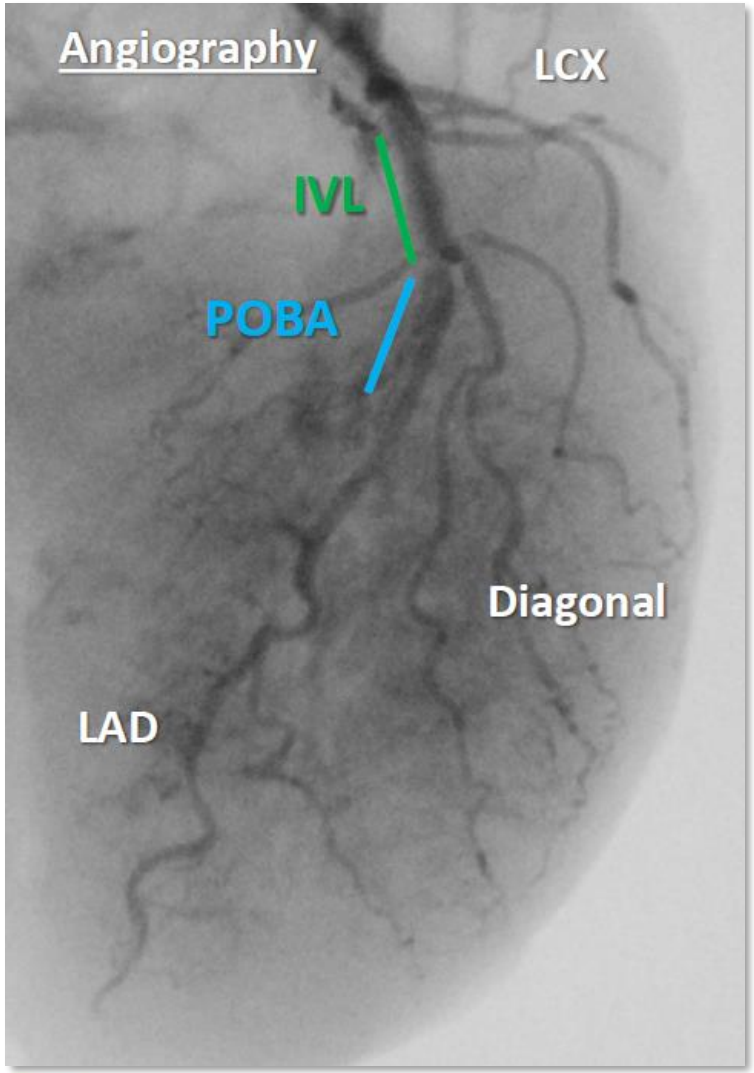
Perivascular cuff placement for immobilization and application of back pressure to simulate *in situ* environment

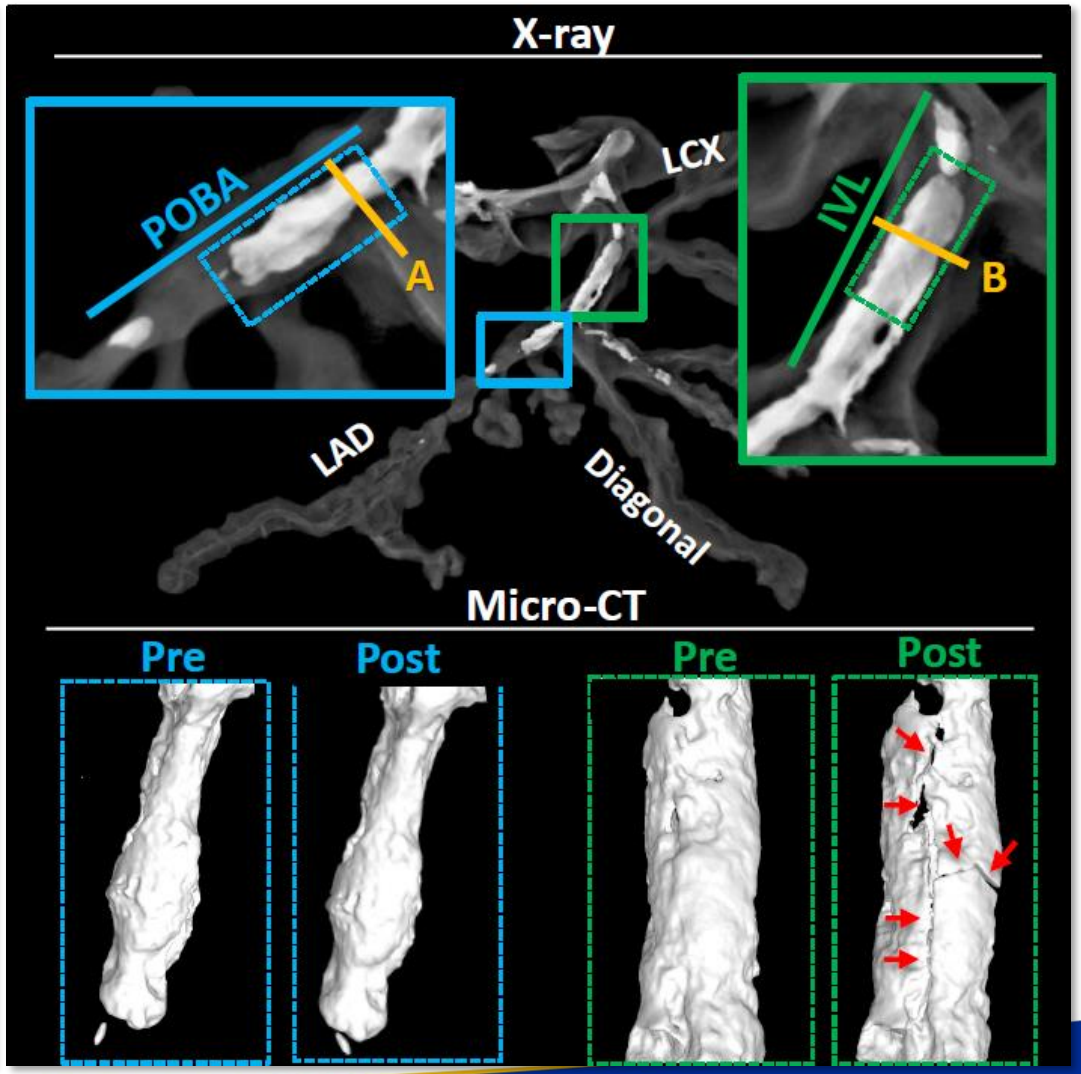
Lesion characteristics

	IVL (N = 8 lesions)	POBA (N = 7 lesions)	P-value
Target vessel			
LAD	6 (75.0)	5 (71.4)	0.51
LCX	1 (12.5)	2 (28.6)	
RCA	1 (12.5)	0 (0.0)	
Location			
Proximal	6 (75.0)	6 (85.7)	0.63
Mid	1 (12.5)	1 (14.3)	
Distal	1 (12.5)	0 (0.0)	
DS, %	57.8 (46-59.1)	50.7 (46.7-55.3)	0.56
Max arc, degree	145.2 (83.4-270.6)	121.0 (91.3-123.9)	0.31
Min thickness, mm	0.5 (0.4-0.6)	0.6 (0.6-1.0)	0.19
Max thickness, mm	1.1 (1.1-1.3)	1.1 (1.1-1.6)	0.46

IVL and POBA treatment of calcified lesions

Pre-treatment angiography and x-ray visualization





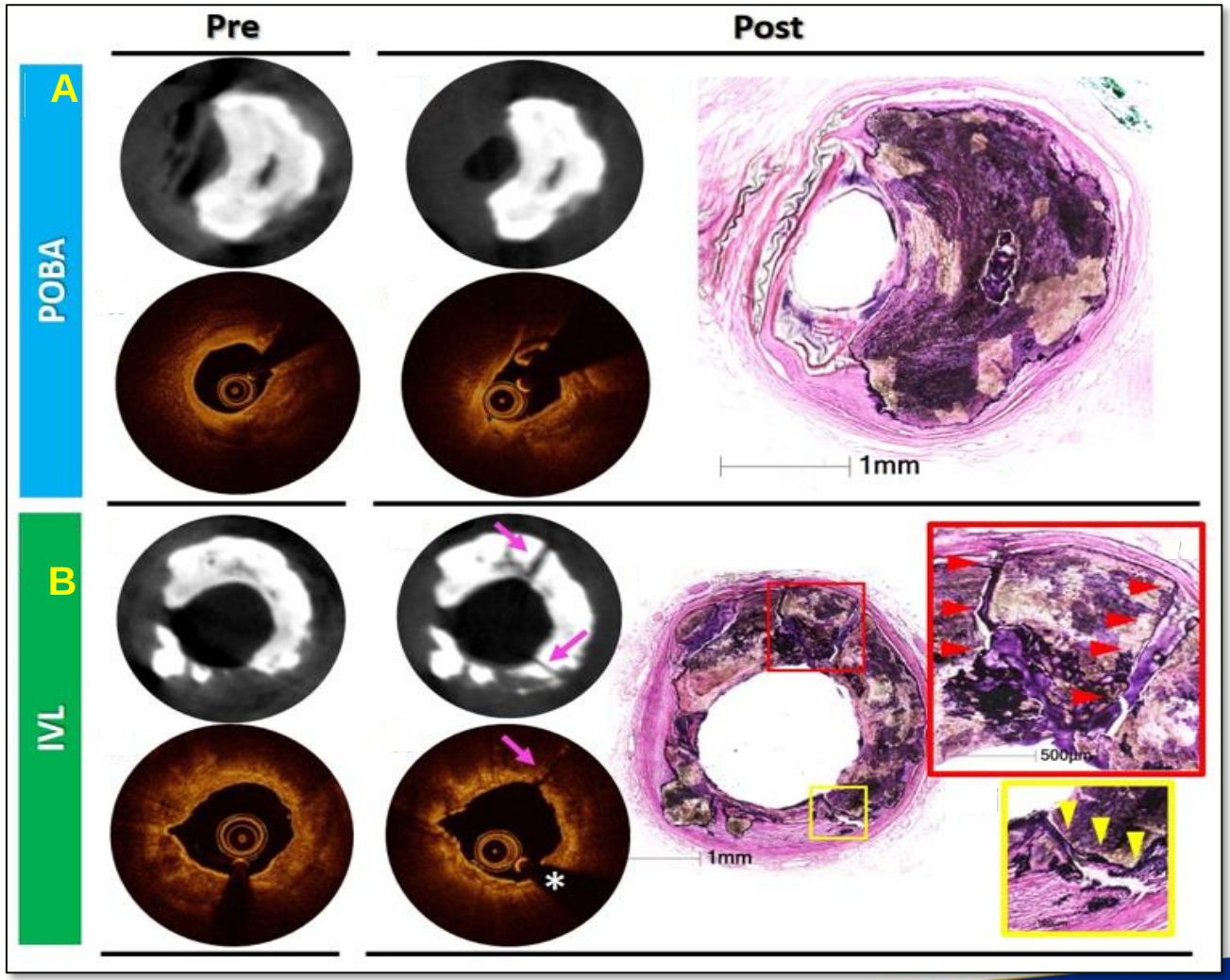
Fracture visualization:

- POBA: 0 fractures
- IVL: 14 fractures

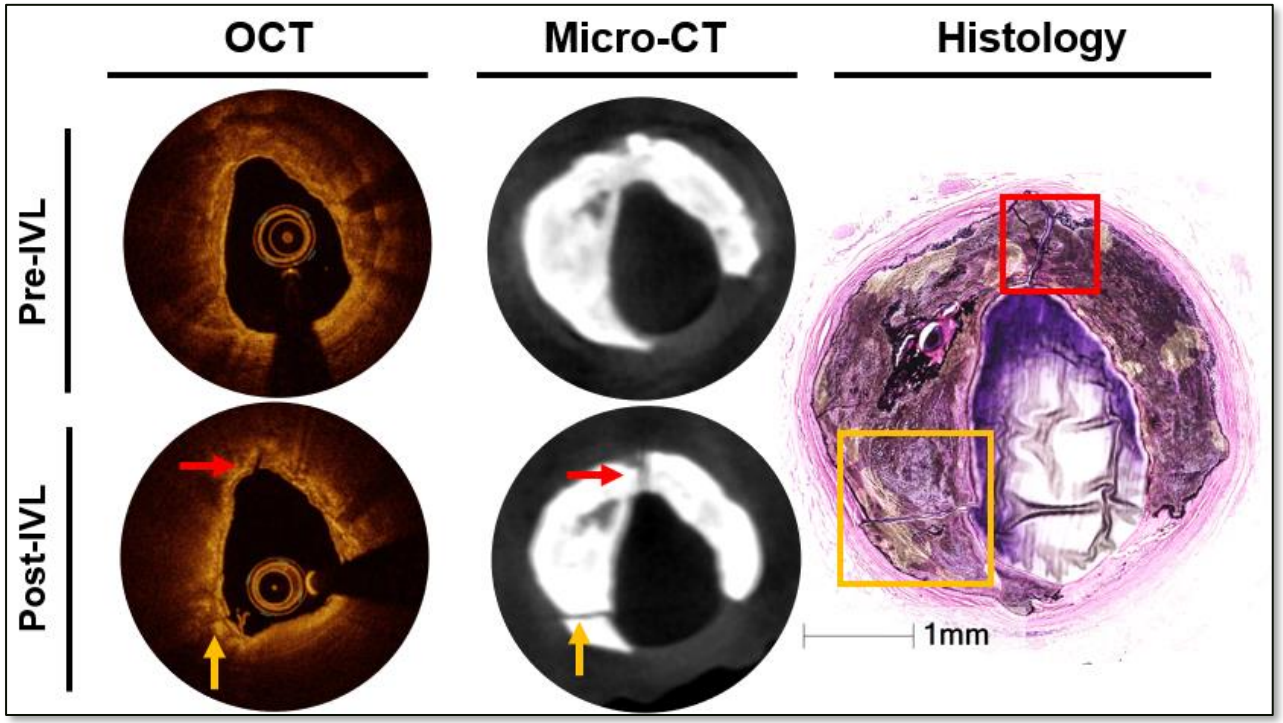
3D micro-CT: longitudinal and transverse calcium fracture following IVL treatment

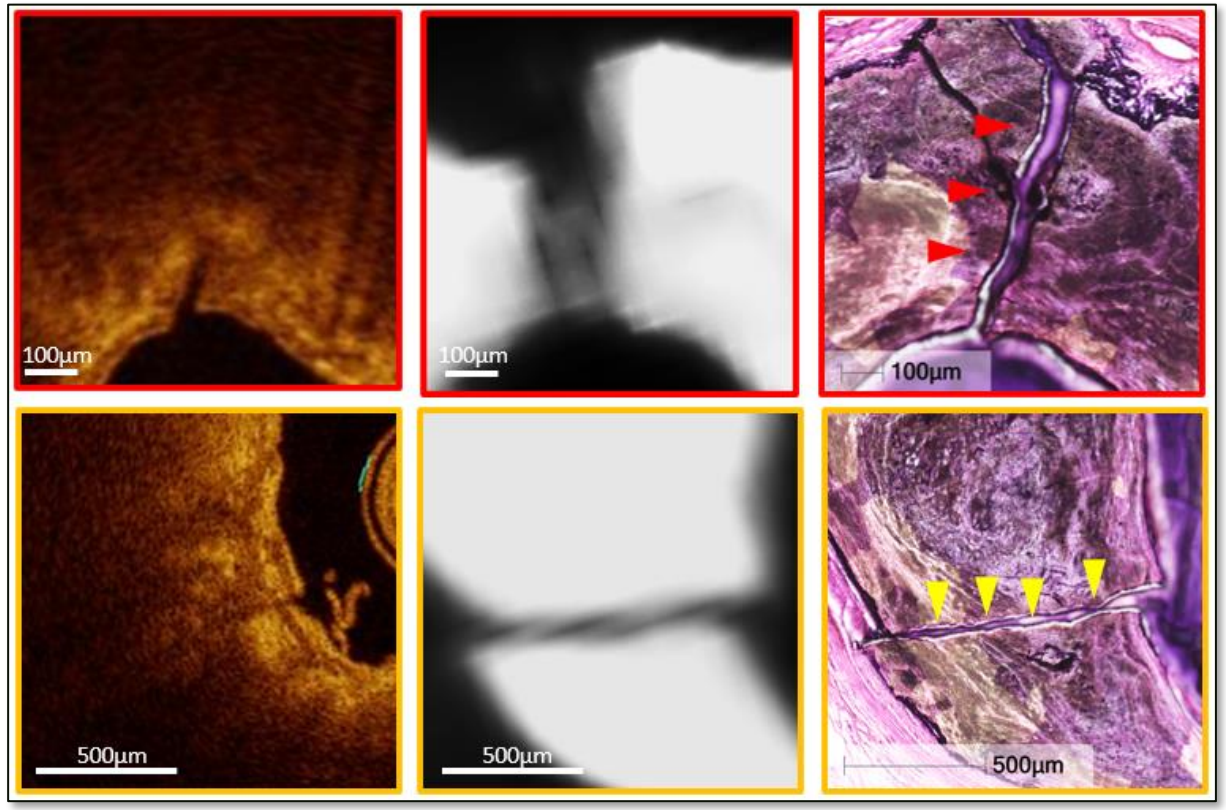
Calcium fracture visualization

Co-registered pre- and post-treatment cross-sections of micro-CT, OCT, and histology in POBA and IVL groups

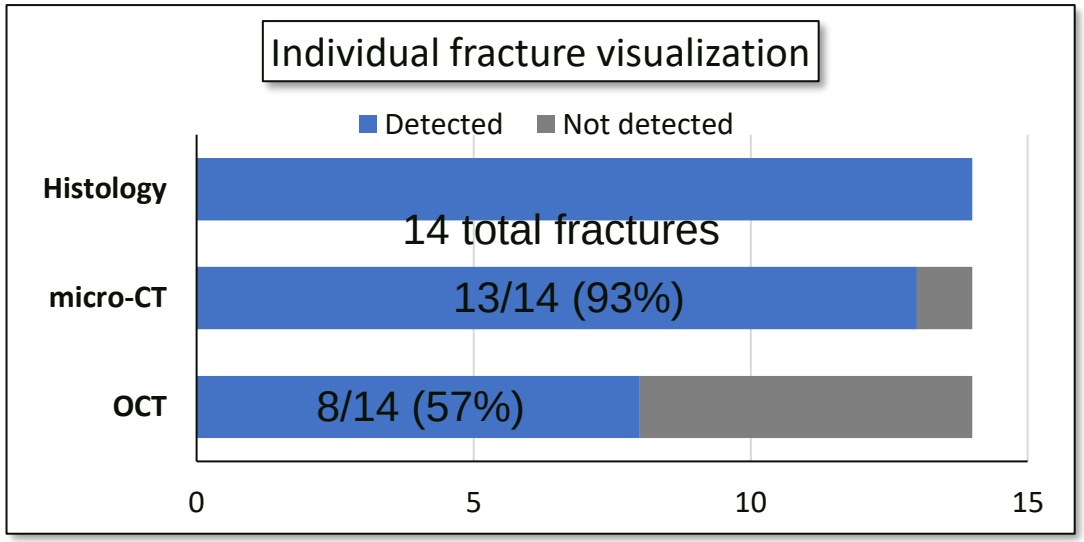


OCT Imaging May Underestimate Calcium Fracture Depth



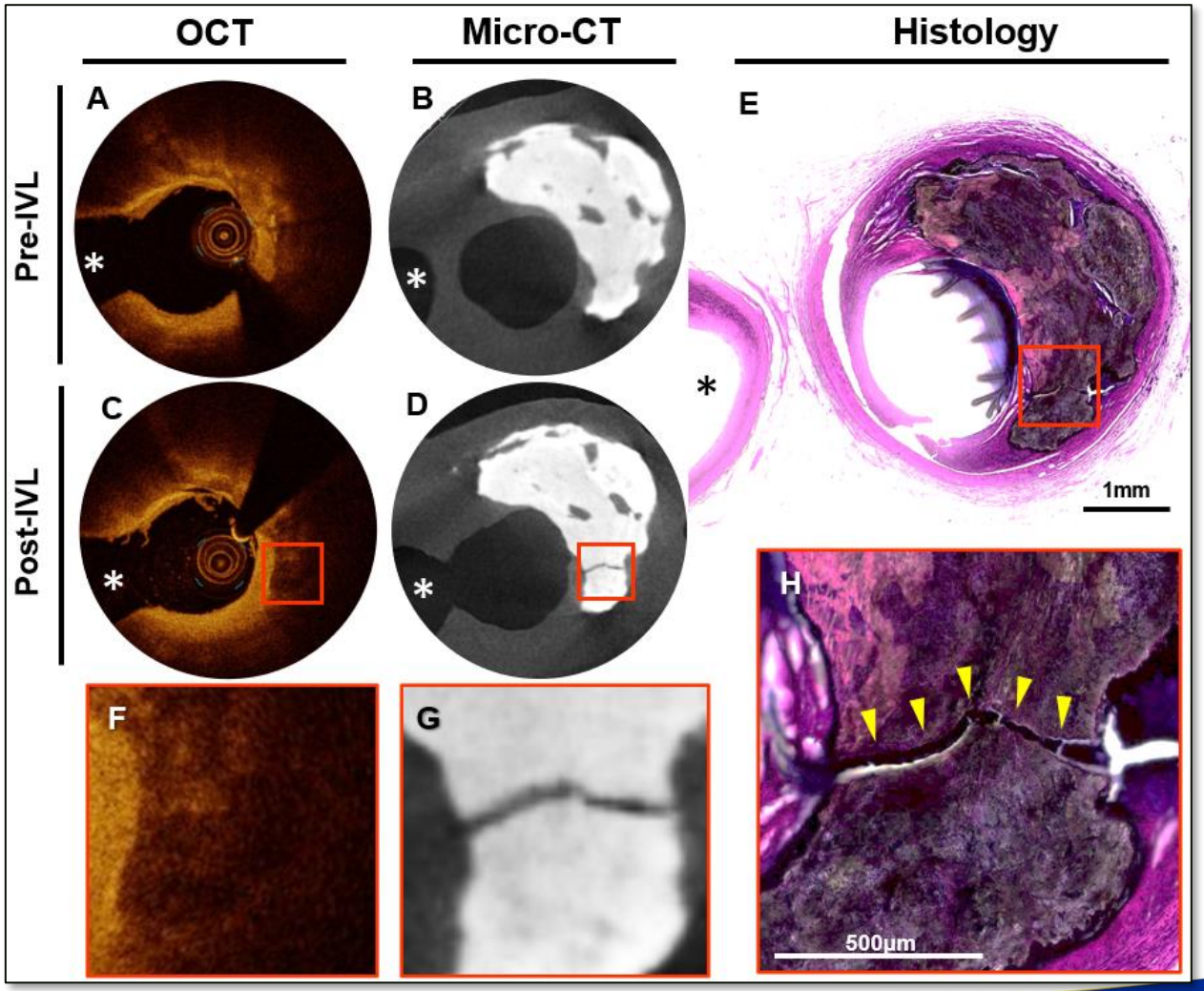


Calcium Fracture Visualization Following IVL Treatment



- 14 fractures visualized by histology
- Micro-CT detected **93%** of fractures
- OCT detected **57%** of fractures

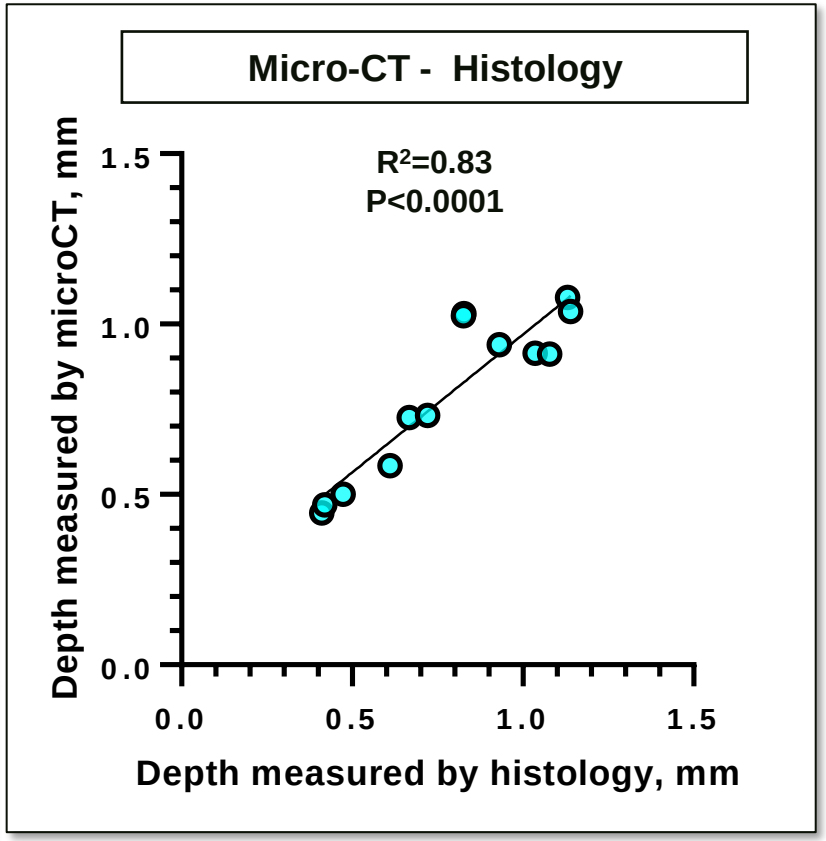
OCT may underestimate the presence of calcium fracture

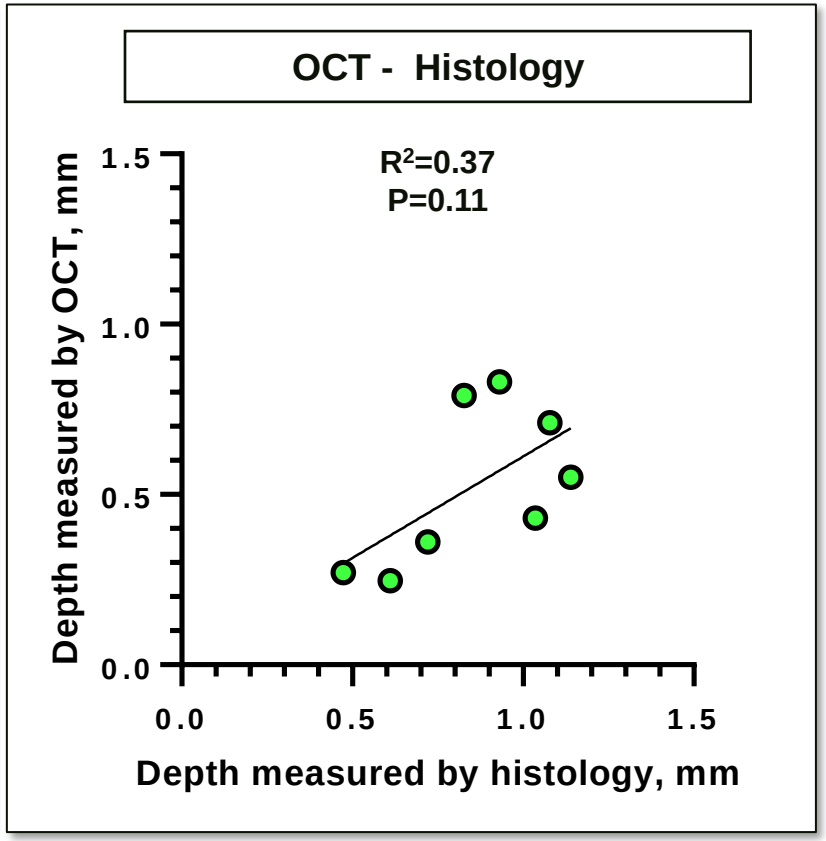


*Side branch

OCT Imaging May Underestimate Calcium Fracture Depth

N = 13 Co-localized fractures	Micro-CT	Histology
Fracture depth, mm	**0.91** (0.54 – 1.0)	**0.83** (0.54 – 1.1)
N = 8 Co-localized fractures	**OCT**	**Histology**
Fracture depth, mm	**0.49** (0.29 – 0.77)	**0.88** (0.64 – 1.1)





Conclusions

- This *ex-vivo* study represents the first histological examination and comparison of OCT and micro-CT imaging modalities to evaluate calcium fracture following IVL treatment.
- IVL treatment demonstrated histologically more calcium fracture compared to POBA treatment.
- OCT may underestimate the **presence of calcium fracture** and calcium **fracture depth** compared to micro-CT.