Hertz Contact Intravascular Lithotripsy (HC-IVL) for Treating Complex Calcific Coronary Lesions

PINNACLE I Clinical Trial
Six-Month and OCT Procedural Imaging Outcomes

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On behalf of the PINNACLE I Investigators

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Disclosure of Relevant Financial Relationships

Within the prior 24 months, I have had a relevant financial relationship with a company producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:

Nature of Financial Relationship	Ineligible Company
Consultant Fees/Honoraria	Elixir Medical Corporation; Boston Scientific Corporation; Terumo Medical Corporation; Medtronic; Biotronik
Grant/Research Support	Shockwave Medical

PINNACLE I Study Organization

Principal Investigators and Study Centers by Country

Belgium

- Johan Bennett, MD, PhD, Universitaire Ziekenhuizen Leuven (Study Co-PI)
- Stefan Verheye, MD, PhD, ZNA Middelheim (Study Co-PI)
- Bert Ferdinande, MD, Ziekenhuis Oost-Limburg, Campus Sint Jan
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- B.J.B. Hamer, MD, Meander Medical Centre
- Valeria Paradies, MD, Maasstad Ziekenhuis
- Pim A.I. Tonino, MD, PhD, Catharina Ziekenhuis

Imaging Core Lab QCA and OCT

CERC Cardiovascular European Research Center

Clinical Events Committee

RARAS CRO

Lithotripsy - From Greek “Breaking (or pulverizing) Stones”

(litho- + τρίψω [tripso])

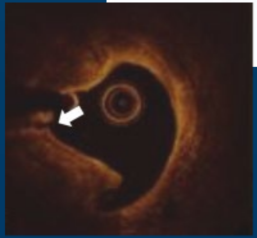
Lithotripsy

1832- first kidney stone removal procedure by Jean Civiale

- Mechanical
- Extracorporeal
- Laser

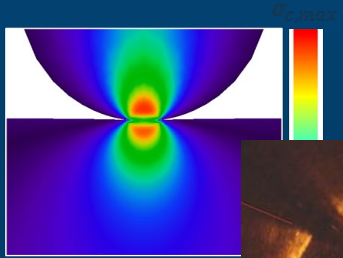
Shockwave Intravascular Lithotripsy

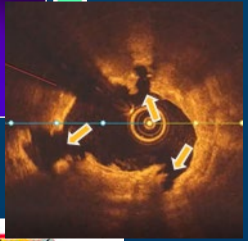
Pressure waves generated inside the balloon to create fractures in adjacent calcium

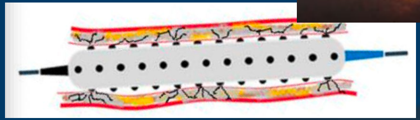


Hertz Contact Intravascular Lithotripsy

Calcium fractures resulting from **amplified discrete focal stresses** via Hertz Contact Stress principle







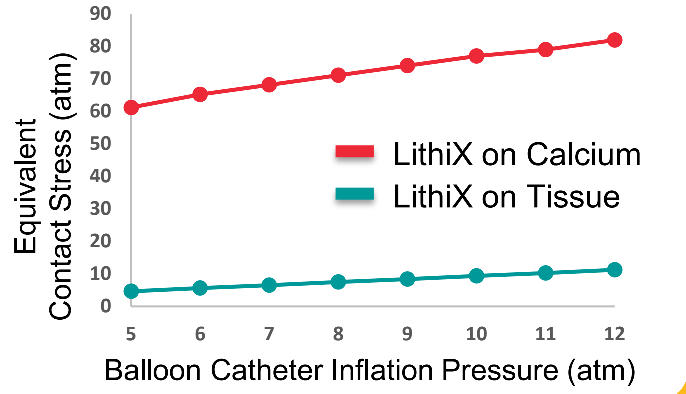
Hertz Contact Stress Mechanism

- ***Focal localized stresses develop*** when a curved sphere contacts a plane and deforms it under the imposed loads

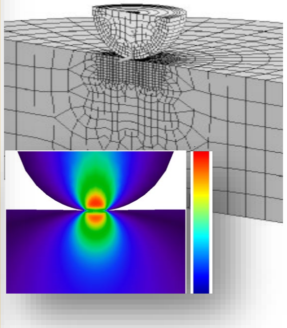
Parameters

- Contact force
- Modulus of elasticity
- Discrete area of contact

Discrete and High Stress for Calcium Fragmentation



Hard on Calcium



Soft on Tissue

Data on file.

PINNACLE I Trial Design

Study Objective

To assess safety and performance of the LithiX Coronary Hertz Contact Intravascular Lithotripsy (HC-IVL) Catheter to treat moderate to severely calcified coronary artery lesions by calcium fragmentation.

60 patients enrolled† in 7 clinical sites in Belgium and The Netherlands (ITT)

Up to two de novo coronary artery lesions
with moderate to severe calcification
RVD 2.25 to 3.5 mm, lesion length ≤34 mm

↓

Imaging subgroup (n=32‡)

OCT at pre-procedure, post-LithiX HC-IVL and final post-stent

↓

Primary effectiveness and safety endpoint (clinical success)

Residual stenosis <50% with no in-hospital MACE through hospital discharge

Primary safety endpoint

MACE through 30 days

↓

6-month clinical follow-up

Follow-up Completion: 98% (n=59/60)

†, Included 8 roll-in patients that met the study eligibility criteria.

‡, Subjects with OCT images analyzable by the imaging core lab.

Baseline Demographics

Patient characteristics	N=60
Age, years	72.1 ± 6.8
Male	39 (65.0%)
Hypertension	46 (76.7%)
Dyslipidemia	45 (75.0%)
Diabetes mellitus	18 (30.0%)
Prior MI	12 (20.0%)
Prior PCI	17 (28.3%)
Prior CABG	4 (6.7%)
Prior stroke	5 (8.3%)
Current smoker	13 (21.7%)
Renal insufficiency	9 (15.0%)

Clinical presentation	N=60
Acute coronary syndrome§	11 (18.3%)
Chronic/Stable coronary syndrome‡	49 (81.7%)

§, Unstable angina, STEMI or NSTEMI.
‡, Stable angina or silent ischemia.

Baseline Lesion Characteristics

Angiographic measurements	N=60, L=63
Target lesion vessel	
LAD	33 (52.4%)
LCx	5 (7.9%)
Protected LM	1 (1.6%)
RCA	23 (36.5%)
Ramus	1 (1.6%)
ACC/AHA lesion classification (B2/C)	50 (79.4%)

Angiographic measurements	N=60, L=63
RVD, mm	2.79 ± 0.47
MLD, mm	1.09 ± 0.34
DS, %	60.66 ± 10.87
Lesion length, mm	14.38 ± 6.80
Calcified length, mm	25.11 ± 11.90
Bifurcation lesion with side branch involvement	9 (14.3%)

N: Total number of subjects.
L: Total number of lesions. Three subjects had 2 lesions treated.

Procedure Characteristics

	N=60
Procedural duration, min	59.5 (40.5, 76.0)
Fluoroscopic time, min	13.1 (9.9, 20.4)
Number of LithiX HC-IVL used	2.0 (1.0, 2.0)

	L=63
Pre-dilatation	60 (95.2%)
PTCA balloon	48 (80.0%)
1.5mm LithiX*	12 (20.0%)
Number of stents implanted	1.0 (1.0, 1.0)
Post-stent dilatation	57 (90.5%)

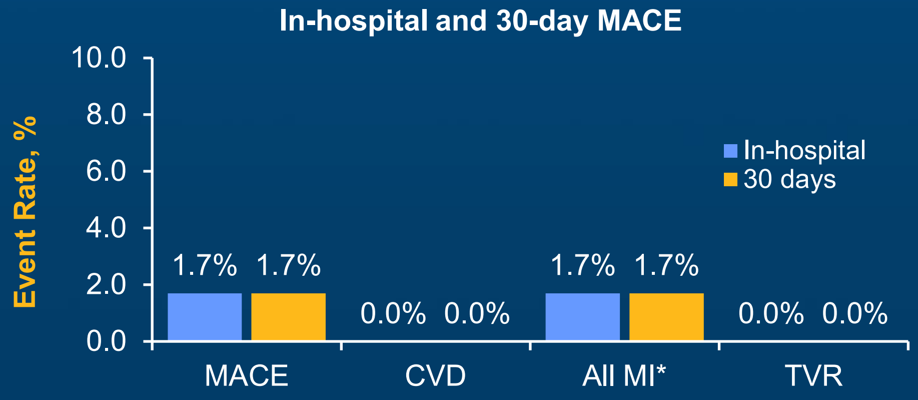
Values are n (%) or median (interquartile range).
*, 1.5mm LithiX was an option for pre-dilatation.

Excellent Safety and Performance Outcomes

Consistent with IVL Mechanism of Action

Final post-stent	N=60, L=63
Angiographic success (main branch, in-lesion)†	63 (100.0%)
Angiographic complications (main branch)	
Any severe dissection (Type D-F)	0 (0.0%)
Any perforation	0 (0.0%)
Any abrupt closure	0 (0.0%)
Any no-reflow	0 (0.0%)
Any thrombus	0 (0.0%)
Any spasm	0 (0.0%)
Any distal embolism	0 (0.0%)
Angiographic outcomes	
Minimum lumen diameter, mm	2.69 ± 0.47
In-lesion DS, %	12.5 ± 4.5
Acute gain, mm	1.60 ± 0.48
In-lesion DS <50%	63 (100.0%)
In-lesion DS <30%	63 (100.0%)

	N=60, L=63
Clinical success (primary effectiveness and safety endpoint)*	98.3% (91.1% to 100.0%)



Performance goal was met

Clinical success (primary effectiveness and safety endpoint) rate >80%

*, One subject with TVMI (peri-procedural, non Q-wave).
†, Stent delivery success, with residual stenosis <50% and no serious angiographic complications.

Six-month Clinical Outcomes

Only three (3) subjects had clinical events through 6-month follow-up

	N=60
Target lesion failure*, %	1/59 (1.7%)
TV-MI*, %	1/59 (1.7%)
CV Death, %	0/59 (0.0%)
CI-TLR, %	0/59 (0.0%)
TVR†, %	1/59 (1.7%)
Non-TVR†, %	1/59 (1.7%)
Non-TVMI†, %	1/59 (1.7%)
Non-CV Death‡, %	1/60 (1.7%)
Stent Thrombosis (definite/probable), %	0/59 (0.0%)

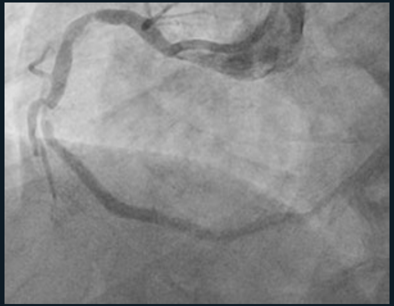
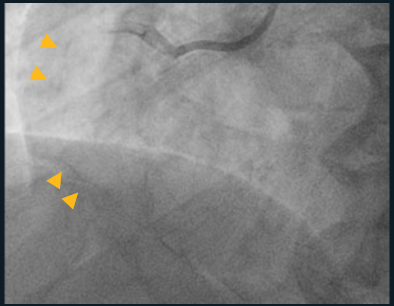
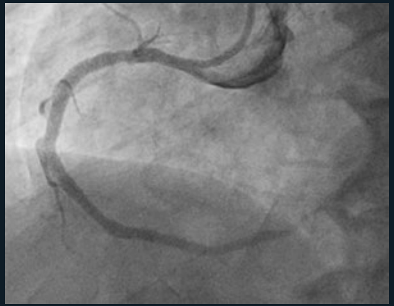
*, One subject had TVMI (peri-procedural, non Q-wave)

†, One subject had non-TVR, Non-TVMI (spontaneous, non Q-wave) and TVR for non-TLR

‡, One subject had non-CV death due to acute myeloid leukemia

Eccentric Calcified Lesions

Hertz Contact IVL

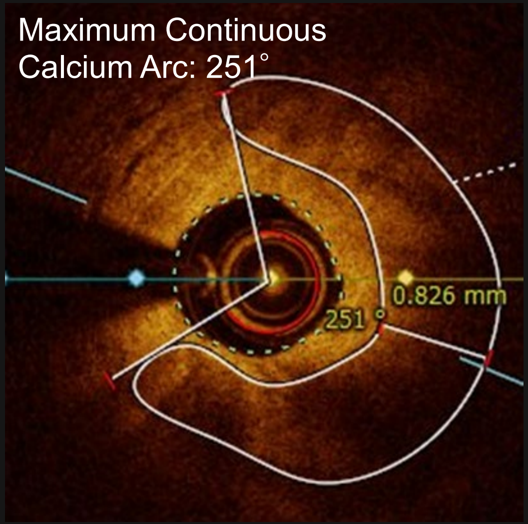
Pre-procedure	Calcium	Post-LithiX HC-IVL	Final Post-stent
			
Mid-RCA ACC/AHA lesion classification: B2 % DS: 75%	Calcification: Severe	LithiX HC-IVL size: 3.5 mm	%DS: 0%

Site reported measurements.

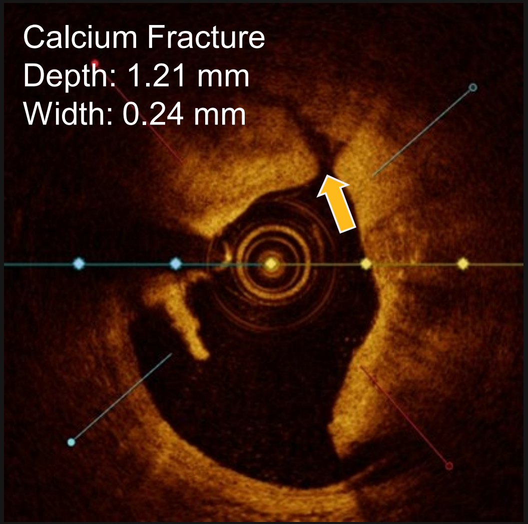
Eccentric Calcified Lesions

Patterns of Stent Expansion

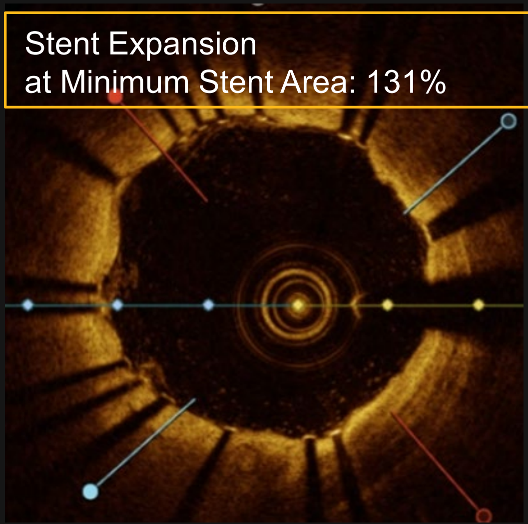
Pre-procedure



Post-LithiX HC-IVL



Final Post-stent



Expert Consensus Document of EAPCI*

Previous studies showed that achieving >90% stent expansion was very challenging.

Optimal stent expansion target in imaging-guided PCI of >80% is recommended for clinical practice.

*Räber L, et al. Eur Heart J. 2018;39(35):3281-3300

Eccentric Calcified Lesions

Deep Calcium Fractures Confirm Mechanism of Action of HC-IVL

Pre-procedure Measurements	Eccentric Calcium# L=13
Minimal lumen area†, mm^2	2.45 ± 1.00
Area stenosis†, %	67.78 ± 11.72
Calcium length, mm	23.15 ± 6.93
Maximum continuous calcium arc, °	184.38 ± 56.42
Maximum calcium thickness, mm	1.32 ± 0.36
Presence of calcified nodule†	4 (33.3%)

Post LithiX HC-IVL Measurements	Eccentric Calcium# L=13
Calcium fracture, any	**11 (84.6%)**
1 fracture	3 (23.1%)
2 fractures	4 (30.8%)
≥3 fractures	4 (30.8%)
Fracture depth, mm	**0.76 ± 0.28**
Fracture width, mm	**0.51 ± 0.23**
Maximum calcium arc at calcium fractures, °	144.18 ± 64.11
Minimum calcium angle at calcium fractures, °	125.55 ± 56.27

#, Maximum continuous calcium arc ≤270°.
†, L=12.

Eccentric Calcified Lesions

Optimal Stent Expansion at MLA, MCS and MSA

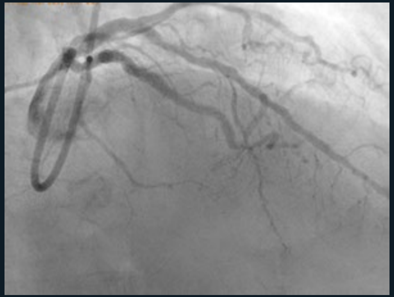
Eccentric Calcium#	At Minimum Lumen Area (MLA)		At Maximum Calcium Site (MCS) †		At Minimum Stent Area (MSA)‡	
	Pre-procedure L=12	Final Post-stent L=10	Pre-procedure L=12	Final Post-stent L=11	Pre-procedure L=10	Final Post-stent L=11
Calcium angle, °	122.75 ± 50.04		133.36 ± 63.09		60.30 ± 45.74	
Maximum calcium thickness, mm	0.85 ± 0.36		1.16 ± 0.45		0.74 ± 0.60	
Area stenosis, %	67.78 ± 11.72	12.19 ± 17.28	34.29 ± 26.15	1.53 ± 4.22	49.91 ± 16.53	15.37 ± 15.49
Lumen area, mm^2 and Stent Area, mm^2	2.45 ± 1.00	7.14 ± 2.16	5.02 ± 2.79	8.64 ± 1.73	3.60 ± 1.31	6.30 ± 2.07
Acute area gain, mm^2		3.98 ± 1.74		3.57 ± 2.05		3.14 ± 1.68
Stent expansion*, %		**100.97 ± 19.64**		**97.86 ± 19.28**		**101.38 ± 23.70**

#, Maximum continuous calcium arc ≤270°.
*, Stent area at MLA, MCS or MSA / Average reference lumen area x 100.
†, L=11 in lumen area; L=9 in acute area gain.
‡, L=10 in acute area gain.

Concentric Calcified Lesions

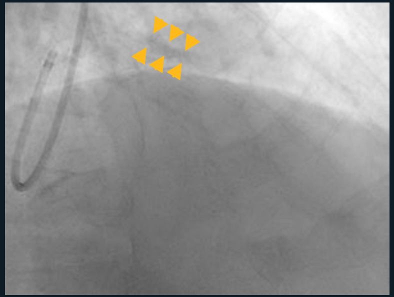
Hertz Contact IVL

Pre-procedure



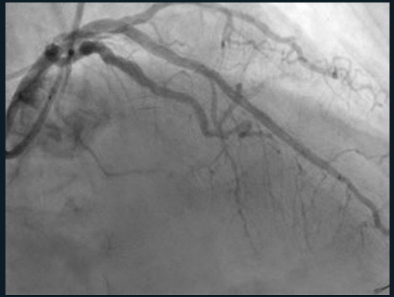
Mid-LAD
ACC/AHA lesion classification: B2
% DS: 80%

Calcium



Calcification: Severe

Post-LithiX HC-IVL



LithiX HC-IVL size*: 1.5 mm and 3.0mm

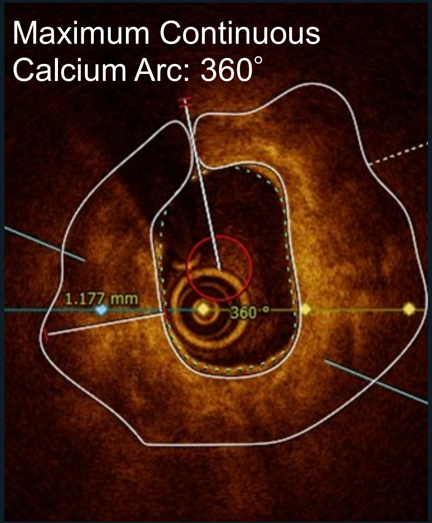
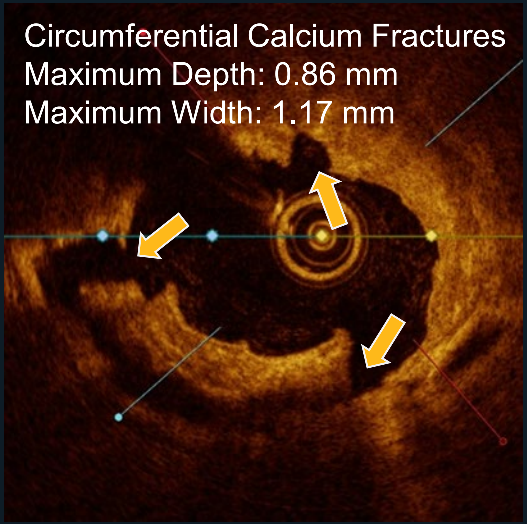
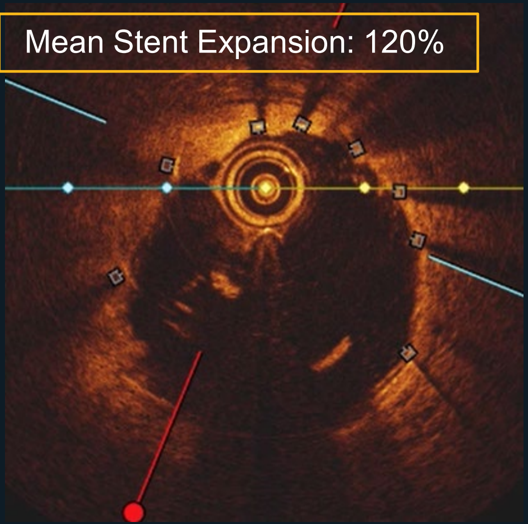
Final Post-stent

%DS: 0%

Site reported measurements. *, 1.5mm LithiX was an option for pre-dilatation per the earlier versions of the PINNACLE I protocol.

Concentric Calcified Lesions

Patterns of Stent Expansion

Pre-procedure	Post-LithiX HC-IVL	Final Post-stent
		

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*Räber L, et al. Eur Heart J. 2018;39(35):3281-3300

Concentric Calcified Lesions

Deep Calcium Fractures Confirm Mechanism of Action of HC-IVL

Pre-procedure Measurements	Concentric Calcium‡, * L=19
Minimal lumen area†, mm^2	2.12 ± 0.94
Area stenosis†, %	75.76 ± 7.38
Calcium length, mm	24.45 ± 6.56
Maximum continuous calcium arc, °	317.47 ± 22.51
Maximum calcium thickness, mm	1.24 ± 0.21
Presence of calcified nodule§	5 (29.4%)

Post LithiX HC-IVL Measurements	Concentric Calcium‡, * L=19
Calcium fracture, any	**18 (94.7%)**
1 fracture	2 (10.5%)
2 fractures	8 (42.1%)
≥3 fractures	8 (42.1%)
Fracture depth, mm	**0.85 ± 0.36**
Fracture width, mm	**0.75 ± 0.29**
Maximum calcium arc at calcium fractures, °	219.11 ± 90.81
Minimum calcium angle at calcium fractures, °	196.94 ± 88.40

‡, Maximum continuous calcium arc >270°.
*, One subject has two target lesions with OCT analysis on one target lesion only.
†, L=18; §, L=17.

Concentric Calcified Lesions

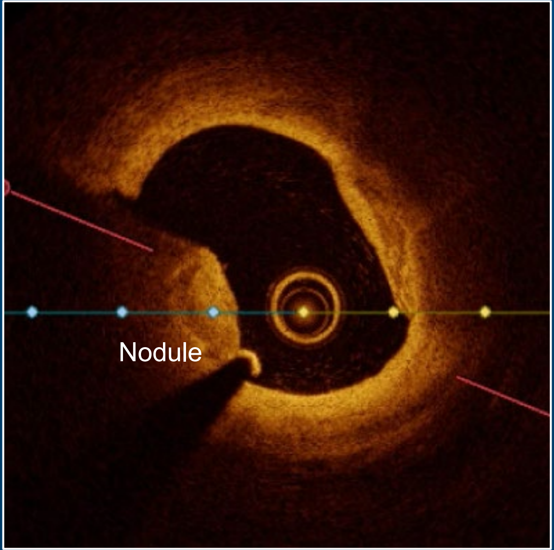
Optimal Stent Expansion at MLA, MCS and MSA

Concentric Calcium[#]	At Minimum Lumen Area (MLA) †		At Maximum Calcium Site (MCS) †		At Minimum Stent Area (MSA) †	
	Pre-procedure L=18	Final Post-stent L=19	Pre-procedure L=18	Final Post-stent L=19	Pre-procedure L=18	Final Post-stent L=19
Calcium angle, °	202.39 ± 90.69		261.33 ± 78.96		162.22 ± 91.53	
Maximum calcium thickness, mm	0.72 ± 0.24		0.97 ± 0.23		0.71 ± 0.32	
Area stenosis, %	75.76 ± 7.38	10.75 ± 12.85	40.81 ± 28.21	4.66 ± 6.15	52.61 ± 25.37	13.51 ± 11.11
Lumen area, mm^2 and Stent Area, mm^2	2.12 ± 0.94	7.72 ± 2.51	4.76 ± 2.32	8.17 ± 2.58	3.94 ± 2.01	6.73 ± 2.22
Acute area gain, mm^2		5.09 ± 1.81		4.03 ± 2.70		3.51 ± 2.04
Stent expansion*, %		**100.84 ± 26.93**		**106.58 ± 28.69**		**93.95 ± 26.67**

#, Maximum continuous calcium arc >270°.
*, Stent area at MLA, MCS or MSA / Average reference lumen area x 100.
†, L=18 in acute area gain.

Optimal Stent Expansion in Lesions with *Calcified Nodules* at MCS

At Maximum Calcium Site (MCS)	Pre-procedure L=9	Final Post-stent L=9
Calcium angle, °	202.56 ± 96.4	
Maximum calcium thickness, mm	1.22 ± 0.34	
Area stenosis, %	35.32 ± 21.34	3.68 ± 5.60
Lumen area#, mm^2 and Stent Area, mm^2	4.73 ± 1.50	8.02 ± 2.19
Acute area gain#, mm^2		3.32 ± 1.54
Stent expansion*, %		**102.81 ± 15.99**



*, Stent area at MCS / Average reference lumen Area x 100.
#, L=8.

Conclusion

- PINNACLE I trial demonstrated the safety and effectiveness of LithiX™ Hertz Contact IVL for calcium fragmentation in a broad complex range of calcium morphologies:
  - 98.3% met primary safety and effectiveness endpoint (clinical success) and 100% main branch, in-lesion, post-stent angiographic success
  - No stent thrombosis (definite/probable), low target lesion failure rate through 6 months
- OCT analysis demonstrated effectiveness of the novel mechanism of action:
  - *Deep calcium fractures in eccentric and concentric calcified lesions* post HC-IVL, confirming the mechanism of action of HC-IVL.
  - *Optimal stent expansion (>90% average) achieved at MLA, MCS, MSA* in eccentric and concentric calcified lesions including those with calcium nodules
- LithiX™ HC-IVL offers a safe, effective approach for calcium fragmentation to optimize stent implantation, without a need for external energy source and a simplified IVL workflow and learning curve.