

# DISRUPT CAD

**A multicenter, prospective, single-arm study of  
percutaneous Lithoplasty prior to stent implantation  
in heavily calcified coronary lesions**

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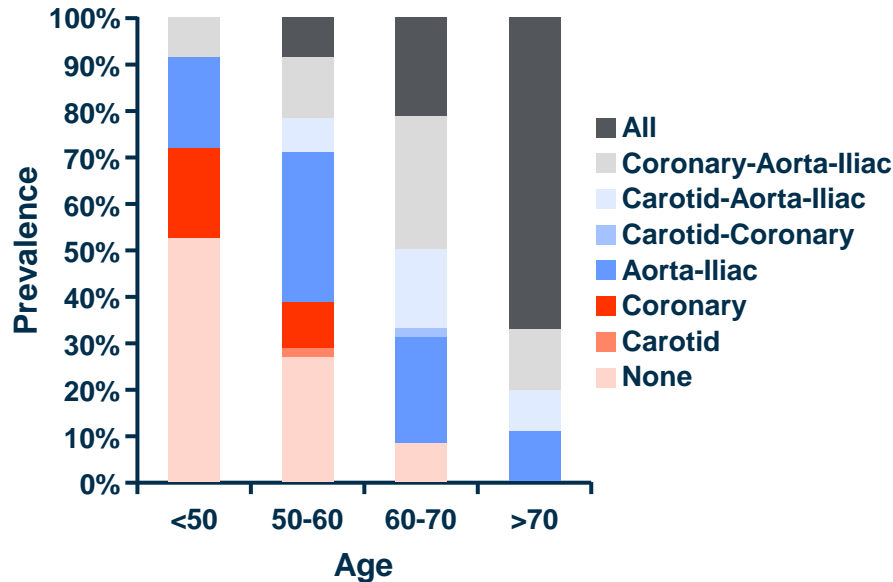
# Disclosure Statement of Financial Interest

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	None
Consulting Fees/Honoraria	Shockwave Medical, Inc., Kona Medical, Inc., Qool Therapeutics
Major Stock Shareholder/Equity	Kona Medical, Inc., Qool Therapeutics, ELS
Royalty Income	None
Ownership/Founder	Shockwave Medical, Inc., BioParadox, Inc.
Intellectual Property Rights	None
Other Financial Benefit	None

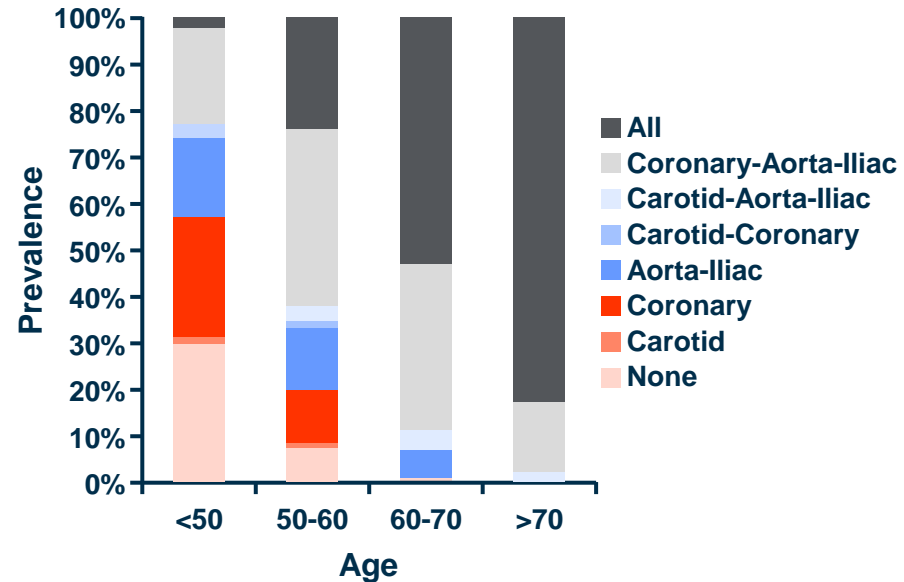
# Impact of Age on Vascular Calcification

A



Prevalence of calcium per vascular pattern in women

B



Prevalence of calcium per vascular pattern in men

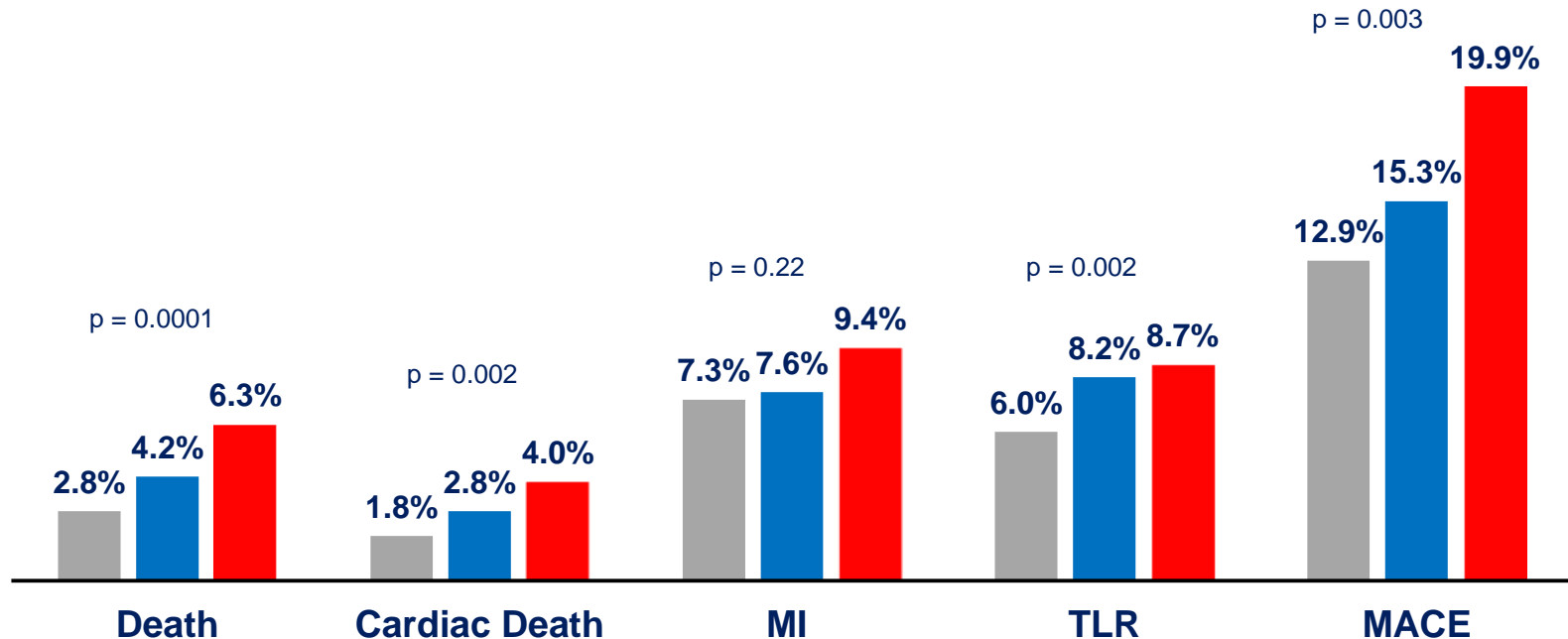
**>70 years, all have calcium in at least 1 vascular bed and 2/3 in all arterial beds**

Allison et. al Arterioscler Thromb Vasc Biol. 2004;24:331-336

# Challenges of Treating Calcified Coronary Lesions

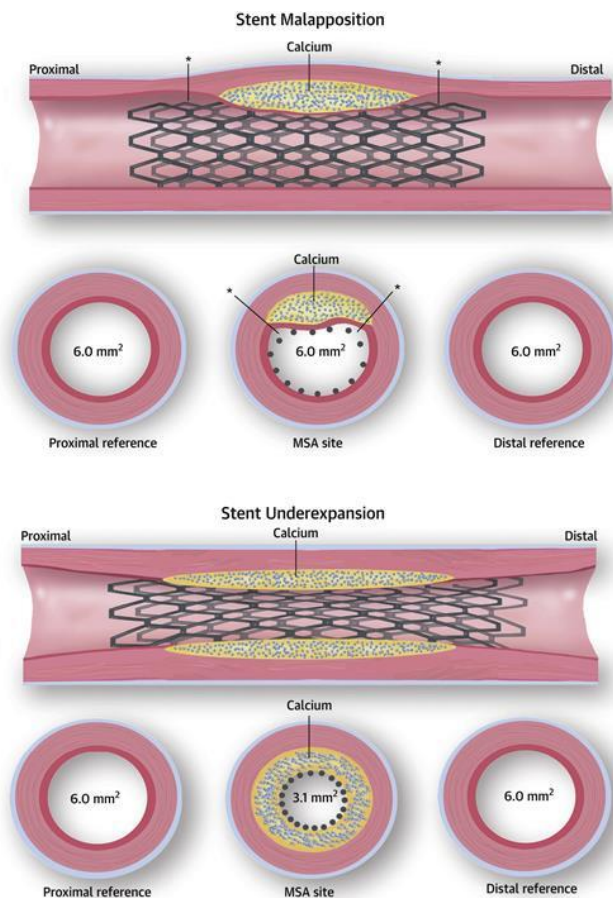
**HORIZONS-AMI and ACUITY CORONARY CALCIUM: 1 Yr Outcomes**  
**6855 Patients Enrolled**

■ None/Mild ■ Moderate ■ Severe



Généreux P; Ischemic outcomes after coronary intervention of calcified vessels. J Am Coll Cardiol 2014;63:1845–54.

# Challenges of Treating Calcified Coronary Lesions



Mintz et al. J Am Coll Cardiol 2014;64(2):207-222

Increased Coronary Calcification



Higher pressure to dilate effectively  
Higher number of dissections  
Decreased stent expansion  
More complications  
Poor outcomes

1. Fitzgerald et al. Circulation 1992;86:64-70
2. Potkin et al. J Am Coll Cardiol 1992;20:942-51
3. Kovach et al. J Am Coll Cardiol 1993;22:1024-32
4. Mintz et al. Circulation 1995;92:3408-14
5. Von Birgelen et al. Am J Cardiol 2003;92:5-10

# Currently Approved Devices

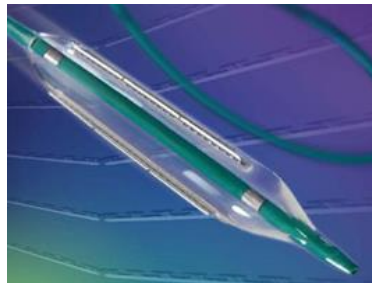
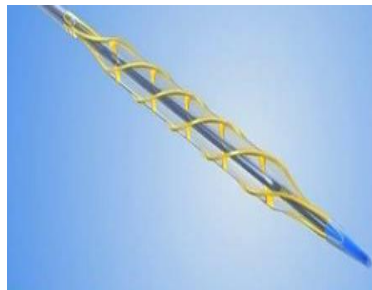
## Traditional Balloons

Compliant  
Non-Compliant



## Specialty Balloons

AngioSculpt  
Scoring Balloon



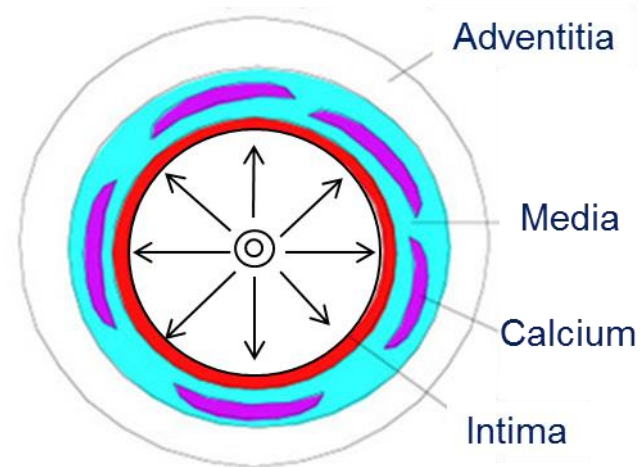
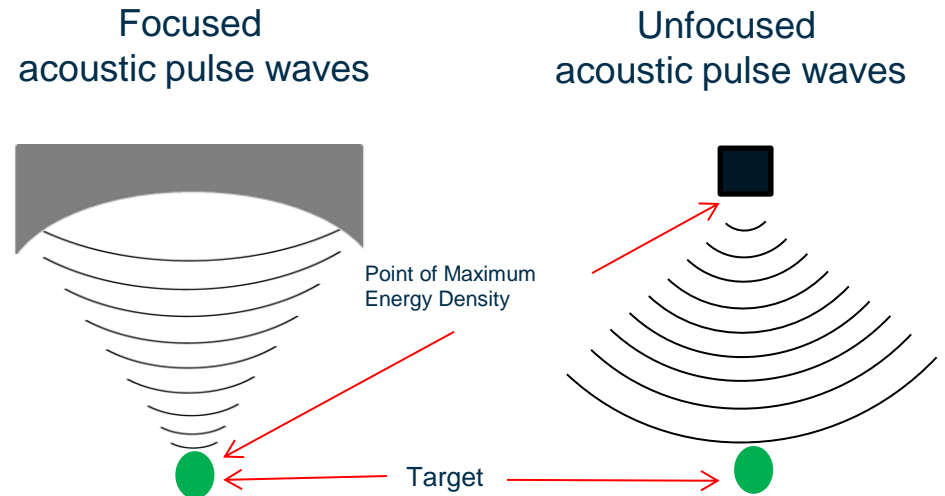
## Atherectomy

Rotational : Rotoblator  
Orbital : CSI



# Insight: Lithotripsy → Lithoplasty

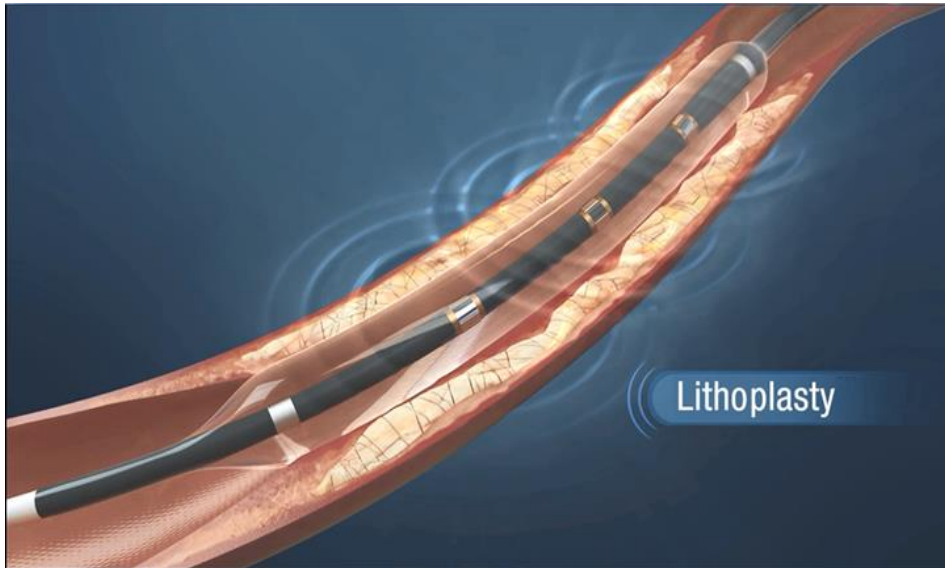
- Dispersive, non focused lithotripsy
- Dose dependent result
- Circumferential mechanical energy distribution
- 25 years of safety data in kidney stone treatment





# Lithoplasty

*Lesion modification using lithotripsy in a balloon*



## **Tissue-selective:**

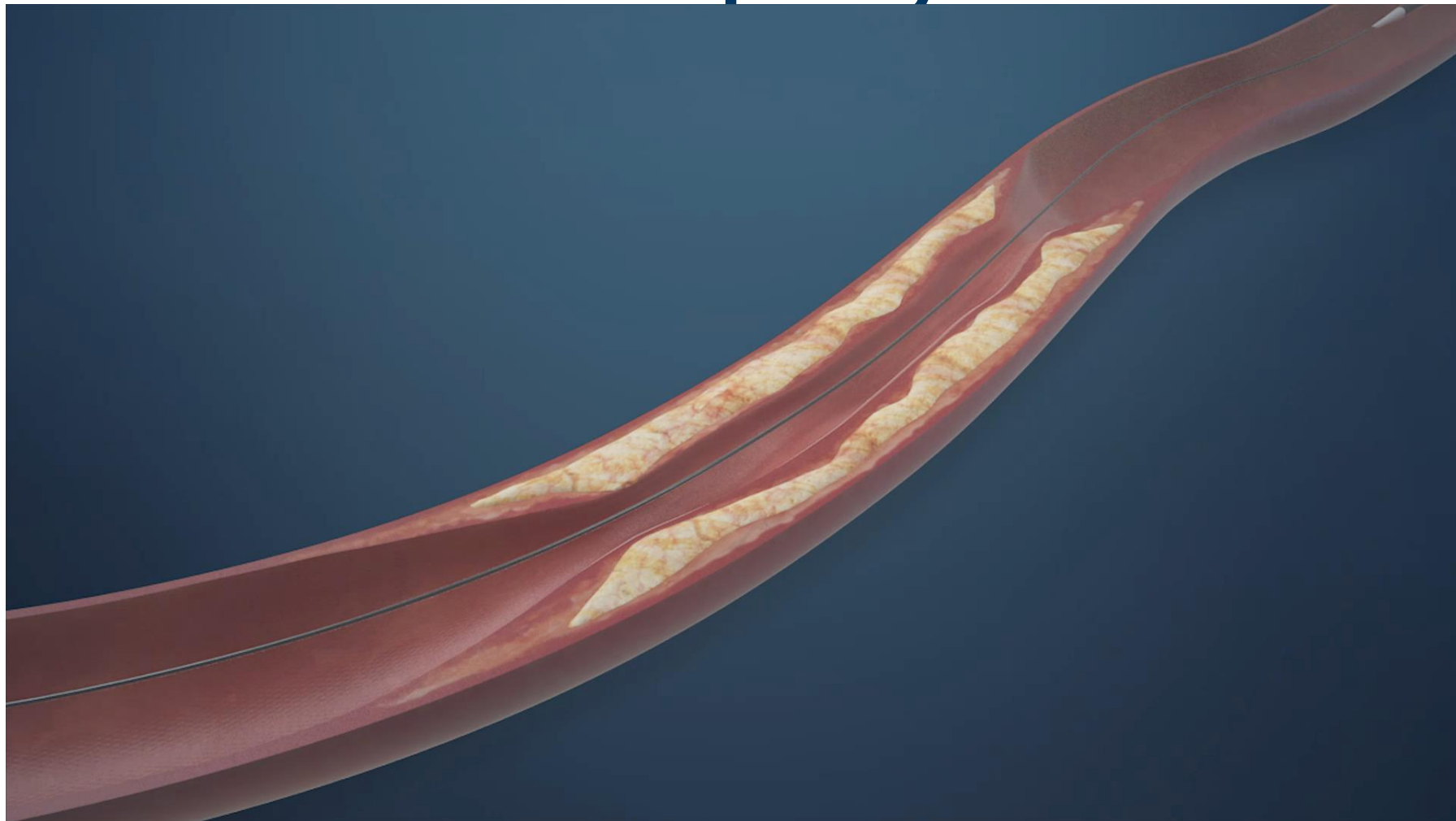
- **Hard on hard tissue,  
Soft on soft tissue**
- **Lithotripsy waves travel  
outside balloon**
- **Designed to disrupt both  
superficial, deep calcium**

- **Designed to normalize vessel wall compliance prior to controlled,  
low pressure dilatation**
- **Effective lesion expansion with minimized impact to healthy tissue**
- **“Front-line” balloon-based Rapid Exchange .014 platform**

The Shockwave Medical Coronary Lithoplasty System is investigational and is not available for sale.



# Lithoplasty



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# Active Lithoplasty

Baseline



Lithoplasty



Final



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# Investigational device



Lithotripsy delivery	4 atm
Nominal pressure	6 atm
Rated burst pressure	10 atm

0.014" guidewire compatible  
138 cm working length  
6F sheath compatibility

## Balloon Sizes

Diameter	Length
2.5 mm	12 mm
2.75 mm	12 mm
3.0 mm	12 mm
3.25 mm	12 mm
3.5 mm	12 mm
3.75 mm	12 mm
4.0 mm	12 mm

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# Disrupt CAD Study Design

Stable angina, unstable angina or silent ischemia









Moderate and severely calcified, *de novo* coronary lesions  
RVD 2.5 – 4.0 mm, stenosis  $\geq 50\%$ ,  
Lesion length  $\leq 32$  mm

60 patients enrolled  
31 subject OCT sub-study  
30 day & 6 months follow-up  
Core Angiographic & OCT Labs  
(Yale University & CRF)

- **Objective:** To assess the safety and performance of the Shockwave Medical Coronary Rx Lithoplasty® System
- **Primary Safety Endpoint:** MACE within 30 days defined as: Cardiac death, MI or TVR
- **Primary Performance Endpoint:** Clinical Success defined as residual stenosis ( $< 50\%$ ) after stenting with no evidence of in-hospital MACE.

# Investigational Sites

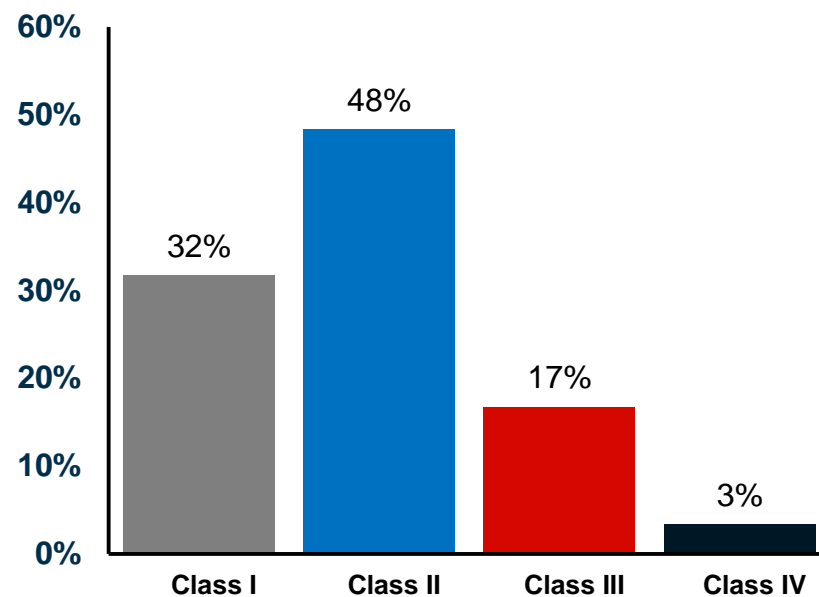
60 patients enrollment completed in Sep 2016

Investigator	Site	Enrollment
Jean Fajadet, MD (PI)	Clinic Pasteur, France	 10
Carlo Di Mario, MD (Co-PI)	Royal Brompton, England	 15
Ian Meredith, MD	Monash Health, Australia	 13
Jonathan Hill, MD	King's College, England	 14
Nicolas Van Mieghem, MD	Erasmus, Netherlands	 4
Robert Whitbourn, MD	St Vincent's, Australia	 3
Matthias Götberg, MD	Skane University Hospital, Sweden	 1

# DISRUPT CAD

## Baseline Characteristics

	Medical History N= 60
Age	72.1 (9.6)
Male gender	80.0%(48)
Diabetes	30.0% (18)
Hypertension	80.0% (48)
Hyperlipidemia	80.0% (48)
Myocardial Infarction	40.0% (24)
Prior CABG	23.3% (14)
Stroke/TIA	13.3% (8)
Current Smoker	15.0% (9)
Renal insufficiency	10.0% (6)



# Pre-procedure Angiographic Findings

*core lab adjudicated*

	Pre-Procedure N=60
RVD (mm)	3.0 ± 0.5
MLD (mm)	0.9 ± 0.4
% Diameter stenosis	68.1 ± 13.1
Lesion length (mm)	20.3 ± 10.5
Calcified length (mm)	22.3 ± 12.5
Calcification	
Moderate	13.3% (8)
Severe	80.0% (48)
Lesion Assessment	
Concentric	78.3% (47)
Eccentric	21.7% (13)
Side branch involvement	28.3% (17)



# Procedural Characteristics

	Procedural Time N= 60
Lithoplasty Time (min)	6.4
Fluoroscopy time (min)	32.3
Total procedure time (min)	92.9

	Procedural Details N= 60
Pre-dilatation > 1.5mm PTCA *	15% (9)
Number of Lithoplasty balloons	2.0
Number of pulses	88
Mean Lithoplasty pressure (atm)	6.0
Avg. Number of stents	1.4
Post-dilatation	86.7% (52)

\*1.5mm PTCA balloon was allowed to facilitate OCT imaging catheter

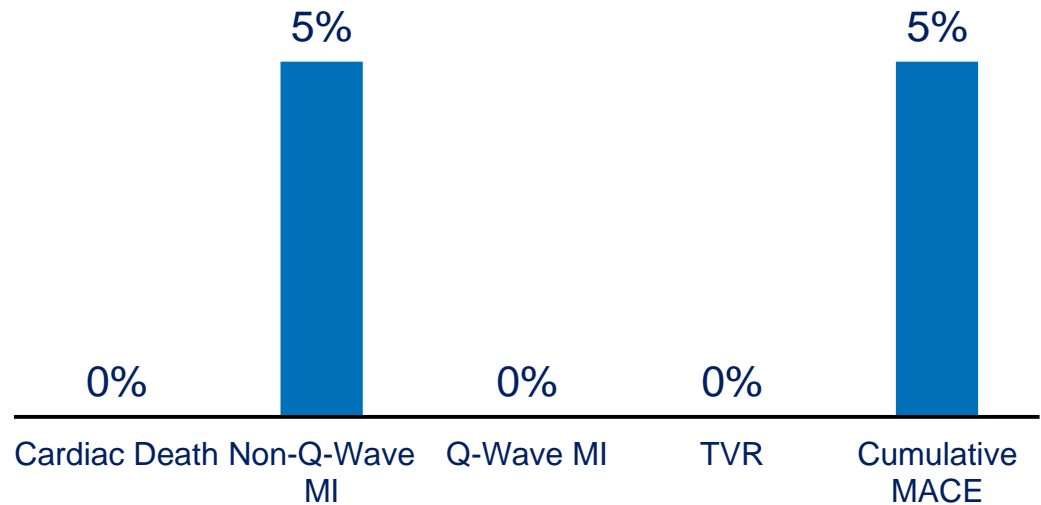
# Safety Outcomes

## Procedural Angiographic Complications

	Final N = 60
Dissection	
None	100% (60)
A to C	0.0%
D to F	0.0%
Perforation	0.0%
Abrupt Closure	0.0%
Slow flow	0.0%
No reflow	0.0%

Angiographic core lab adjudicated

## Freedom from 30-day MACE: 95%



CEC adjudicated

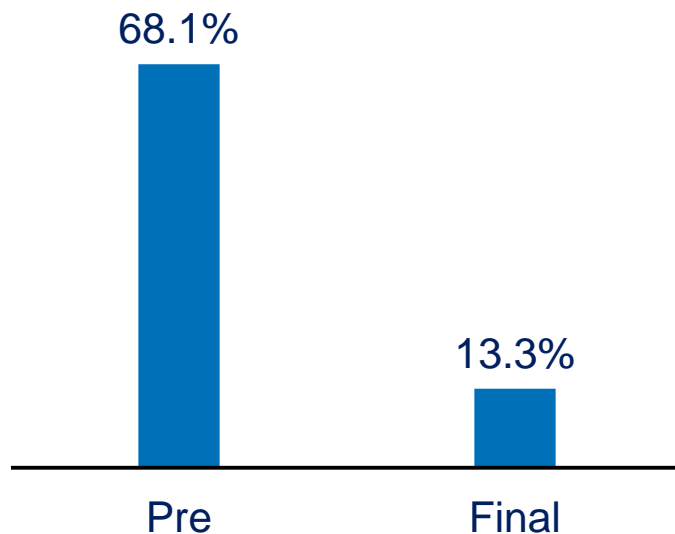
# Primary Performance Outcomes

	N= 60
Clinical Success	95.0% (57)
Device Success	98.3% (59)
Facilitated Stent Delivery	100% (60)

- Clinical success defined as residual stenosis <50% after stenting with no evidence of in-hospital MACE.
- Device success defined as successful device delivery and Lithoplasty treatment at the target lesion.

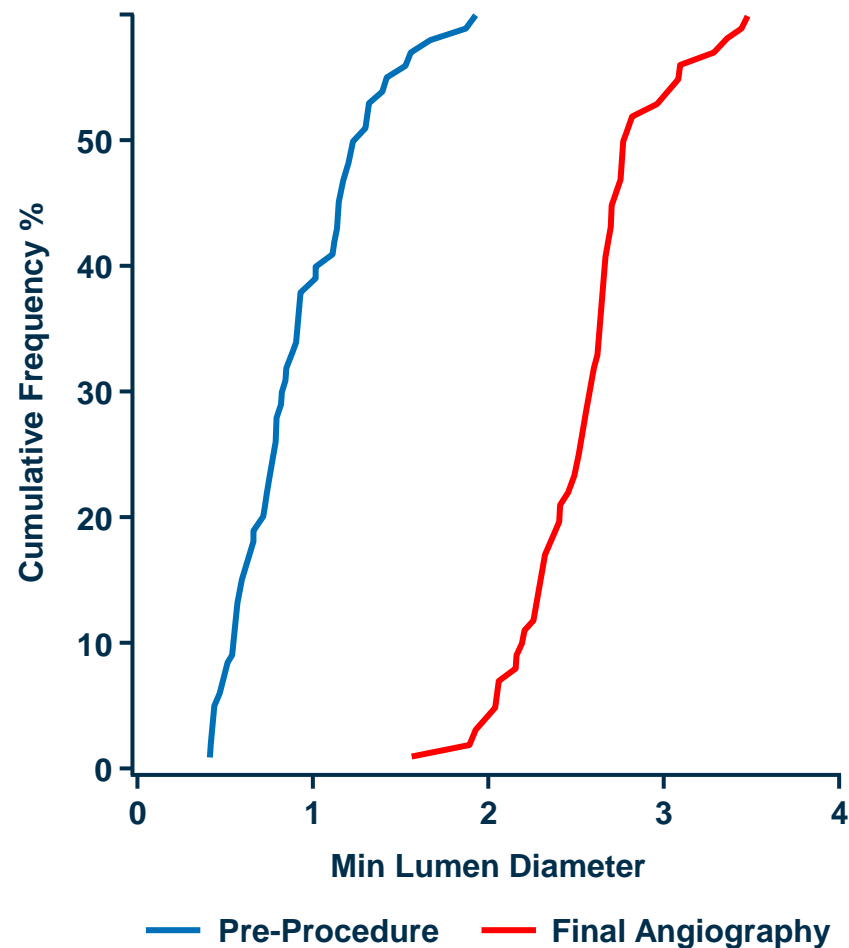
# Performance Outcomes

## % Diameter Stenosis



	Pre	Final
MLD (mm)	0.9 ± 0.4	2.6 ± 0.5
Acute Gain (mm)	NA	1.7 ± 0.6

## Cumulative Frequency Distribution



# Case 1

Baseline



2.4mm RVD  
80.3% stenosis  
7.6mm length

Post Lithoplasty



2.75 and 3.0mm  
Lithoplasty

Final



4.7% stenosis  
Acute gain 2.1  
Stent length 18.3mm

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# Case 2

Baseline



3.6mm RVD  
87.6% stenosis  
37.5mm length

Post Lithoplasty



4.0mm  
Lithoplasty

Final

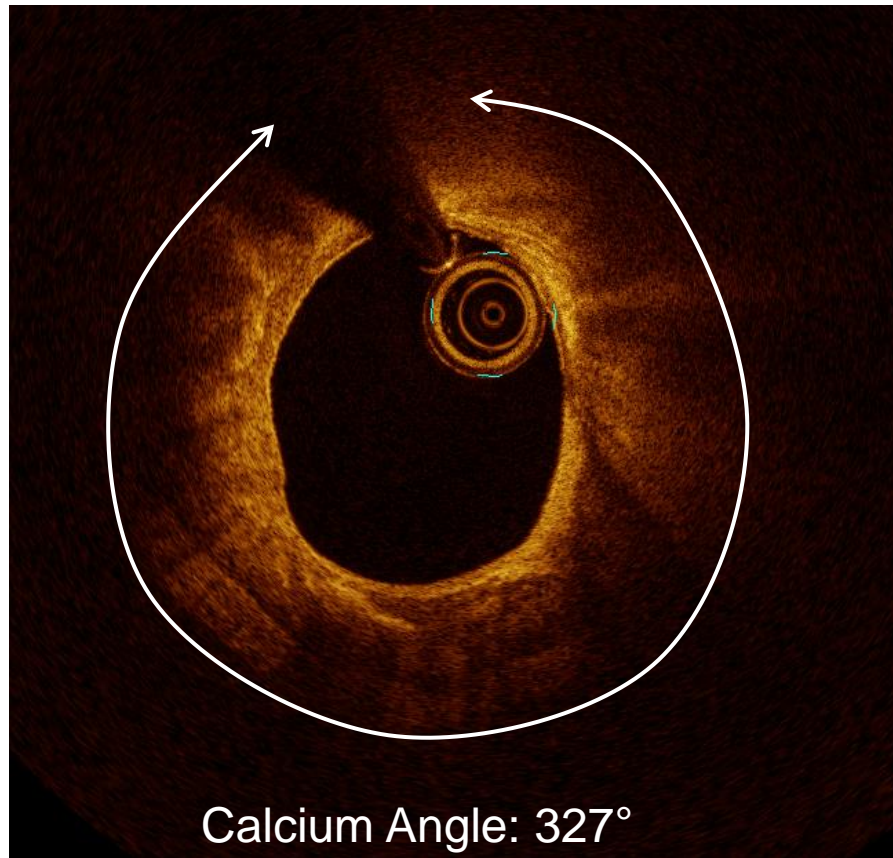


4.0% stenosis  
Acute gain 3.1  
Stent length 40.5mm

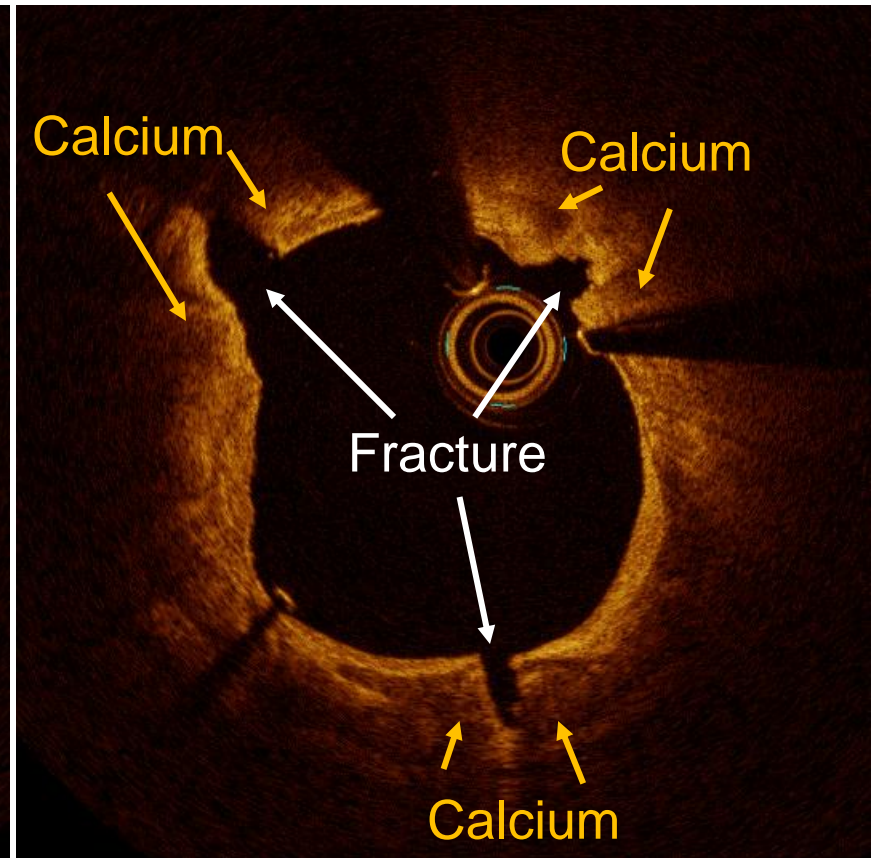
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# Mechanism of Lithoplasty



**Pre-Procedure**



**Final**

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# OCT Case Review

**Pre-  
procedure**

**Example 1**

Lumen Area: 6.00mm<sup>2</sup>

**Example 2**

Lumen Area: 2.98mm<sup>2</sup>

**Example 3**

Lumen Area: 4.12mm<sup>2</sup>

**Post-  
Lithoplasty**

Lumen Area: 7.69mm<sup>2</sup>

Lumen Area: 6.34mm<sup>2</sup>

Lumen Area: 6.40mm<sup>2</sup>

**Post Stent  
Final**

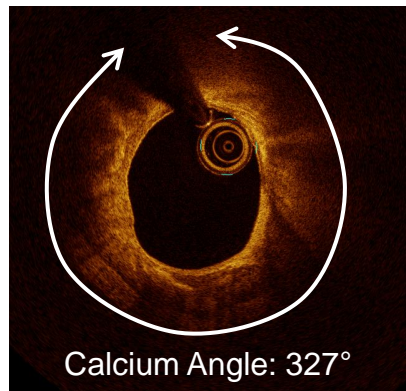
Lumen Area: 9.79mm<sup>2</sup>  
Stent Area: 8.55mm<sup>2</sup>

Lumen Area: 8.15mm<sup>2</sup>  
Stent Area: 7.44mm<sup>2</sup>

Lumen Area: 8.99mm<sup>2</sup>  
Stent Area: 8.16mm<sup>2</sup>

# OCT Summary

	Pre	Final
Minimum lumen area (mm <sup>2</sup> )	2.2 ±1.1	6.0 ± 2.0
Area stenosis (%)	66 ± 11	20 ± 20
Acute gain (mm <sup>2</sup> )		3.7±1.5



Calcium Measurements	
Maximum Ca angle (degree)	229 ± 93
Maximum Ca thickness (mm)	0.97 ± 0.25
Quadrants of Ca Fracture / Lesion	34

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# OCT Tertile Analysis

## By Calcium Burden

	Lowest Tertile	Middle Tertile	Highest Tertile	P-value
<b>Pre Procedure</b>				
Minimum lumen area (mm <sup>2</sup> )	1.4	2.0	2.4	0.12
Area stenosis (%)	69	69	64	0.67
Maximum Ca angle (°)	130	233	323	<0.001
Ca length (mm)	11.7	16.3	30.2	<0.001
<b>Final</b>				
Stent area (mm <sup>2</sup> )	4.5	5.0	6.3	0.32
Complete Ca fracture, %	22%	55%	78%	0.059
Acute gain (mm <sup>2</sup> )	1.8	1.6	2.5	0.38

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# Conclusions

- The Disrupt CAD Study successfully enrolled a population with complex, calcified, obstructive coronary disease.
- The Lithoplasty balloon-based therapy resulted in 98% device success and facilitated 100% stent delivery.
- The study demonstrated a low MACE rate of 5.0% with minimal vascular complications.
- Core lab angiographic analysis demonstrated high acute gain and low residual stenosis.
- OCT sub-study showed clear evidence of circumferential calcium fracture as the mechanism for vessel dilatation prior to stent placement.
- OCT sub-study demonstrated high luminal acute gain independent of the degree of calcification in this hard to treat population.

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