CORONARY INTRAVASCULAR LITHOTRIPSY

NO PRESSURE, IT’S JUST CALCIUM. LET’S GET CRACKING.
Impact of Coronary Calcium & Unmet Need for IVL
Severely Calcified Coronary Lesions: An Unmet Clinical Need

Coronary Artery Calcium (CAC) Prevents Safe & Predictable PCI

Greater risk of procedural complications, including major dissection and artery perforation\(^1\)-\(^5\)

Severe calcium is an independent predictor of not being able to implant DES\(^6\)

The more severe the calcium the greater the likelihood of stent under-expansion, which is associated with an increase in ischemic events\(^7\),\(^8\)


PCI of heavily calcified lesions is associated with procedural complications and/or late adverse events
Limitations & Risks Posed by Current Technologies

High Pressure Balloons & Atherectomy Can Result in Serious Complications

High pressure balloons preferentially expand away from calcium, having limited effect on eccentric calcium.\(^1\)

High pressure inflations are often required to modify calcified plaque, predisposing them to major dissection and perforation - often at the interface between calcium and healthy tissue.\(^1\)

Balloons are typically unable to modify deep or very thick calcium.\(^1\)

Atherectomy has a steep learning curve compared to balloon-based therapies. Ablation is contact dependent. May struggle in larger caliber lumens and is unable to modify deep calcium.\(^2-3\)

It causes thermal injury that leads to increased risk of clotting.\(^4\)

Unable to protect side branch with a second guide wire.\(^2-3\)

Potential to transect wire and for large dissection and/or perforation, especially in tortuous anatomy.\(^2-3\)

Distal embolization is associated with slow flow / no reflow and peri-procedural MI.\(^2-3\)

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2 Tomey et al, J Am Coll Cardiol Intv. 2014
Opportunities for Shockwave IVL

Potential Advantages of Lithotripsy

No requirement for a specialized wire.\(^1\)

Shockwaves are selective for disrupting calcium.\(^1\)

Shockwaves pass through the plaque/vessel wall enabling modification of deeper lying calcium.\(^1\)

Disrupted calcium remains within vessel wall thereby reducing the risk of distal embolization.\(^1\)

Lithotripsy allows calcium modification at low balloon pressure to avoid the risk associated with high pressure inflations.\(^1\)

Able to protect side branch with second wire.\(^1\)

As with balloon-based therapies, the Shockwave IVL system is easy to learn compared to other forms of calcium modification.\(^1\)

Coronary IVL System & Mechanism of Action
Lithotripsy for Cardiovascular Applications

**Extracorporeal Lithotripsy**

30 years of safety data in kidney stone treatment

*Sonic Pressure Waves* preferentially impact hard tissue, disrupt calcium, leave soft tissue undisturbed

**Intravascular Lithotripsy (IVL)**

Miniaturized and arrayed lithotripsy emitters for localized lithotripsy at the site of the vascular calcium

Optimized for the treatment of coronary arterial calcium
Shockwave Coronary IVL System Components

Integrated 12mm SC balloon facilitates energy transfer; IVL=4 atm; Nominal=6 atm; RBP=10 atm

Distal and proximal marker bands

2 emitters that pulse once per second (80 pulses/catheter)

Generator
Portable, IV-pole Mountable
Battery-Powered
No External Connections

Connector Cable
Smart Magnetic Connection
Push-Button Activated

Catheter
RX System
Any .014” Guidewire
Standard PCI Technique
80 Lithotripsy Pulses

<table>
<thead>
<tr>
<th>Diameter</th>
<th>Length</th>
<th>Pulses</th>
<th>Guidewire</th>
<th>Guide Cath</th>
<th>Length</th>
<th>Tip Profile</th>
<th>Crossing Profile</th>
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<tbody>
<tr>
<td>2.5-3.0-3.5-4.0mm</td>
<td>12mm</td>
<td>80</td>
<td>0.014in</td>
<td>6F</td>
<td>138cm</td>
<td>0.023in</td>
<td>0.044-0.047in</td>
</tr>
</tbody>
</table>
How IVL Cracks Calcium In Situ

After inflating the integrated balloon to 4-atm, a small spark at the emitters vaporizes the saline-contrast solution and creates a bubble which rapidly expands and collapses within the balloon; creating a short burst of sonic pressure waves.

The sonic pressure waves travel through the coronary tissue, while reflecting off and cracking calcium with an effective pressure of ~50 atm.\(^1\) The emitters along the length of the device create a localized field effect within the vessel to fracture both superficial and deep calcium.

The integrated balloon plays a unique role; its apposition to the vessel wall facilitates efficient energy transfer during IVL, after which, it is used to dilate the lesion to maximize lumen gain.

\(^1\) Data on File
IVL’s Unique Mechanism of Action
High Speed Sonic Pressure Wave Created Safely Inside Integrated Balloon

1. Unfocused lithotripsy energy is created at the emitters which are contained in a fluid filled coupler.

2. Electrical energy is delivered to the emitter, initiating the steam bubble, which expands & collapses – creating sonic pressure waves.

Video: Actuation of Single Pulse (20µs/frame)
At the calcium interface, the relatively large difference in density, coupled with the concentration of multiple sonic pressure waves in a small area, produces a large dissipation of energy.

The sonic pressure waves propagate through the body with negligible dissipation of energy (and therefore damage) owing to the minimal difference in density of the soft tissues.
OCT Images Show Large Multi-plane & Longitudinal Calcium Fractures

1 DISRUPT CAD III Case Example
Microfractures Occur Beyond Resolution of IVUS & OCT

Cadaveric Superficial Femoral Artery (Micro CT)  

Histologic & Micro CT after IVL Treatment (SFA)  

Pre-IVL  

Post-IVL  

A  

B  

C  

D  

Histology (A,B)  

Micro CT (C,D)  

Courtesy: Renu Virmani, MD, CV Path Institute
Coronary IVL Clinical Program
## Coronary IVL Clinical Program

### Excellent Outcomes in Core Lab Adjudicated Studies

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<tr>
<th>Status</th>
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<th>DISRUPT CAD II</th>
<th>DISRUPT CAD III</th>
<th>DISRUPT CAD IV</th>
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<td>Circ</td>
<td>Circ Intrv</td>
<td>JACC</td>
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<td>Single arm, post-market, safety and effectiveness</td>
<td>Single arm, IDE, safety and effectiveness</td>
<td>Single arm, pre-market safety and effectiveness</td>
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<th>DISRUPT CAD III</th>
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<td>384</td>
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<td></td>
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<tr>
<td>U.S., EU</td>
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<tr>
<td>Japan</td>
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>60 Peer-reviewed Journal Publications

>1,200 Published Patient Outcomes
## Consistent Outcomes Across Disrupt CAD I, II & III

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<th>DISRUPT CAD III</th>
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<td>Calcium Severity</td>
<td>100%</td>
<td>94%</td>
<td>100%</td>
<td>TBD</td>
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<tr>
<td>Procedural Success</td>
<td>95%</td>
<td>94%</td>
<td>92%</td>
<td>TBD</td>
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<tr>
<td>Stent Delivery</td>
<td>100%</td>
<td>100%</td>
<td>99%</td>
<td>TBD</td>
</tr>
<tr>
<td>Final Severe Dissections</td>
<td>0%</td>
<td>0%</td>
<td>0.3%</td>
<td>TBD</td>
</tr>
<tr>
<td>Final Perforations</td>
<td>0%</td>
<td>0%</td>
<td>0.3%</td>
<td>TBD</td>
</tr>
<tr>
<td>Final Abrupt Closure</td>
<td>0%</td>
<td>0%</td>
<td>0.4%</td>
<td>TBD</td>
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<tr>
<td>Final Slow Flow/No Reflow</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>TBD</td>
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<tr>
<td>Acute Lumen Gain (mm)</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td>TBD</td>
</tr>
<tr>
<td>Final Residual Stenosis</td>
<td>12%</td>
<td>7.8%</td>
<td>11.9%</td>
<td>TBD</td>
</tr>
<tr>
<td>In-Hospital MACE</td>
<td>5.0%</td>
<td>5.8%</td>
<td>7.0%</td>
<td>TBD</td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>0%</td>
<td>0%</td>
<td>0.3%</td>
<td>TBD</td>
</tr>
<tr>
<td>Q-Wave MI</td>
<td>0%</td>
<td>0%</td>
<td>1.0%</td>
<td>TBD</td>
</tr>
<tr>
<td>Non-Q-Wave MI</td>
<td>5.0%</td>
<td>5.8%</td>
<td>5.7%</td>
<td>TBD</td>
</tr>
<tr>
<td>30d Target Vessel Revascularization</td>
<td>0%</td>
<td>0.8%</td>
<td>1.6%</td>
<td>TBD</td>
</tr>
<tr>
<td>30d MACE</td>
<td>5.0%</td>
<td>7.6%</td>
<td>7.8%</td>
<td>TBD</td>
</tr>
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</table>

1. https://www.ahajournals.org/doi/full/10.1161/CIRCULATIONAHA.118.036531
2. https://www.ahajournals.org/doi/full/10.1161/CIRCINTERVENTIONS.119.008434
Disrupt CAD III: Study Design
Prospective, multicenter, single-arm global IDE

- **Objective:** Designed to assess safety and effectiveness of the Shockwave Medical Coronary Intravascular Lithotripsy (IVL) System
- **Performance Goal:** Based on ORBIT II
  - Primary safety endpoint: 30d MACE rate
  - Primary effectiveness endpoint: <50% residual and no in-hospital MACE
- **Enrollment:** 384 subjects, across 47 sites
- **Sub-Studies:** OCT, PPM/ICD and Hemodynamics
- **Follow Up:** Procedural, 30d, 6, 12 & 24mo

†Radio-opacities both sides of vessel ≥15 mm length by angiography or calcium angle ≥270° by OCT or IVUS

Roll-in Population
N = 47

ITT Population
N = 384

30-day Follow-up

1-year Follow-up

2-year Follow-up

OCT Sub-study
N= 100
(Shlomfmitz TCT 2020)
## Angiographic & Procedural Characteristics

Severely Calcified Lesions with Long Length of Calcium

### Core Lab Analysis

<table>
<thead>
<tr>
<th>Target vessel</th>
<th>N=384</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>56.5%</td>
</tr>
<tr>
<td>LCx</td>
<td>12.8%</td>
</tr>
<tr>
<td>RCA</td>
<td>29.2%</td>
</tr>
<tr>
<td>LM</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

| Reference vessel diameter, mm | 3.0 ± 0.5 |
| Minimum lumen diameter, mm    | 1.1 ± 0.4 |
| Diameter stenosis             | 65.1 ± 10.8% |
| Lesion length, mm             | 26.0 ± 11.7 |
| Calcified length, mm          | 47.9 ± 18.8 |
| Severe calcification          | 100%     |

### Characteristic

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=384</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total procedure time, min</td>
<td>59.0 ± 29.6</td>
</tr>
<tr>
<td>Pre-dilatation</td>
<td>55.2%</td>
</tr>
<tr>
<td>IVL catheters</td>
<td>1.2 ± 0.5</td>
</tr>
<tr>
<td>IVL pulses</td>
<td>68.8 ± 31.9</td>
</tr>
<tr>
<td>Max IVL inflation pressure, atm</td>
<td>6.0 ± 0.3</td>
</tr>
<tr>
<td>Post-IVL dilatation</td>
<td>20.7%</td>
</tr>
<tr>
<td>Number of stents</td>
<td>1.3 ± 0.5</td>
</tr>
<tr>
<td>Stent delivery</td>
<td>99.2%</td>
</tr>
<tr>
<td>Post-stent dilatation</td>
<td>99.0%</td>
</tr>
</tbody>
</table>

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Primary Safety & Effectiveness Endpoints Exceeded

30-day freedom from MACE: 92.2% (353/383)

1-sided lower 95% CI: 89.9%
P value: <0.0001*

Safety Performance Goal: 84.4%

Primary Safety Endpoint Met
Freedom from 30-day MACE: Cardiac death, MI, TVR
One-sided lower 95% CI of 89.9% > pre-specified performance goal of 84.4%

Procedural success: 92.4% (355/384)

1-sided lower 95% CI: 90.2%
P value: <0.0001*

Effectiveness Performance Goal: 83.4%

Primary Effectiveness Endpoint Met
Procedural success: Stent delivery with residual stenosis <50% without in-hospital MACE
One-sided lower 95% CI of 90.2% > pre-specified performance goal of 83.4%

*One-sided asymptotic Wald test for binomial proportion
Angiographic Outcomes & Complications
Luminal Gains Post-IVL & Post-Stent with Minimal Complications

Core Lab Analysis

<table>
<thead>
<tr>
<th></th>
<th>Immediately Post-IVL</th>
<th>Final</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any serious angiographic complication</td>
<td>2.6%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Severe dissection (Type D-F)</td>
<td>2.1%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Perforation</td>
<td>0.0%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Abrupt closure</td>
<td>0.0%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Slow flow</td>
<td>0.6%</td>
<td>0.0%</td>
</tr>
<tr>
<td>No-reflow</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

In-Hospital and 30-Day MACE

*Per protocol: CK-MB level >3x ULN at discharge (peri-procedural MI) and using the 4\textsuperscript{th} Universal Definition of MI beyond discharge

No Evidence of Learning Curve with IVL

- Roll-in patients represent the first case for each site in the study
- Baseline clinical and angiographic characteristics were similar between the two groups
- Key study outcomes were similar between roll-in and pivotal patients

Outcomes by Fracture Visualization

Consistent outcomes regardless of fracture visualization by OCT

U.S. Pivotal Study Conclusions

- Disrupt CAD III trial success was achieved as both primary safety and effectiveness endpoints were met following treatment with coronary IVL in severely calcified lesions.

- Coronary IVL prior to DES implantation was well tolerated with a low rate of major peri-procedural clinical and angiographic complications.

- Although this study represents the initial coronary IVL experience for U.S. operators, high procedural success and low angiographic complications were achieved, reflecting the relative ease of use of IVL technology.

- OCT demonstrated longitudinal and circumferential calcium fractures in heavily calcified lesions resulting in 1) Increased vessel compliance, 2) Large post-procedural MSA, 3) 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.
Real World Coronary IVL Utilization
Key Learnings from over 3 Years of International Experience
IVL is Effective Across Many Different Types of Calcium

- >45 Countries offer IVL to their patients
- >25,000 Patients treated since 2018
- >60 Publications in peer-reviewed journals
- >1,200 Patient outcomes in publications

Eccentric & Concentric

Superficial & Deep
High Value IVL Applications
Treat Complex Calcium With Ease & Predictability

Left Main* & Large Vessels
Bifurcations
Tortuous & Ostial Disease

*Protected Left Main
How Coronary IVL is Typically Integrated Into Clinical Practice

Shockwave Physician Training Algorithm

IF CALCIUM SEEN ON...

ANGIOGRAPHY +

AND THERE IS...

DOG-BONED NC BALLOON

CORONARY IVL

First Line Therapy

NC Balloons

Utilization Insights Gleaned From Real-World Use of 25K+ Coronary IVL Catheters Globally

IVL

Dog-boned Balloon High Risk Patients Thick/Deep Ca++ LM/Ostial/Bifur

Atherectomy

Uncrossable Lesions Nodular Ca++ Thin/Intimal Ca++

Scoring/Cutting Balloons

Dog-boned Balloon Focal Ca++ Thin/Intimal Ca++
Sample Calcium Algorithm Using OCT
Courtesy of Margaret McEntegart (UK) & James Spratt (UK)

IVL Use Summary
- >180° Ca²⁺
- Thick Ca²⁺
- Deep Ca²⁺
- Large Lumens
- LMS/Ostial RCA
- Bifurcations
- Tortuous Anatomy
- Atherectomy failure
Case: Bifurcation in LAD

Summary: Severely calcified mid-LAD involving septal branch; patient was high-bleeding risk and IABP used for hemodynamic support; operators wanted to avoid distal embolization for this patient and chose IVL; 3.0mm IVL catheter used across diffuse calcified disease; significant fractures seen under OCT in multiple planes; circumferential and well-apposed 3.0x32mm DES.
Case: Multi-Lesion RCA

Summary: Multi-lesion RCA; Couldn’t advance guideliner to distal lesion despite predilation; advanced 3.5mm IVL catheter as far as possible (1); delivered one cycle (10 pulses) and vessel opened; pulled back to the ostium (2) and vessel opened after one cycle (10 pulses); advanced to distal lesion (3) and vessel opened after one cycle (10 pulses); easily delivered 80mm of DES.

Baseline

IVL 0-10 Pulses (4atms)

IVL 10-20 Pulses (4atms)

Post-Stent

IVL 20-30 Pulses (4atms)
Summary: Nearly occluded RCA that was a planned rotablation case; however guidewire went through and 3.0 IVL catheter followed and opened up nicely after 40 pulses; once the RCA was open, we realized we undersized and used a 3.5 IVL – all 80 pulses in the two ostial segments; implanted a 3.5 x18 DES.
Case: Angulated LCX

Summary: Highly angulated LCX with lesions proximal and distal; OCT wouldn’t cross either lesion; guideliner-assisted IVL catheter delivery followed by successful IVL therapy; the case was completed with easy deployment of two long DES.
Case: IVL After Unsuccessful Rota

Summary: ACS patient with calcified LAD & RCA; heart team deemed to be high surgical risk & recommended staged PCI in prox LAD first. Pre-dil semi-compliant balloon failed to dilate; rota ensued with 1.75mm burr, however there was persistent balloon under-expansion; 3.0 IVL pulled with immediate waist resolution; Pre-dil expanded and 3x48 DES used.
IVL in Eccentric Calcium: Achieving Optimal Outcomes
Different Challenges With Different Types of Calcium

Concentric
*Napkin rings typically resistant to high pressure balloons*

Eccentric
*Non-calcified vessel wall susceptible to dissections*

**IVL Performs Differently But Enables Optimal Outcomes Across All Types**

OCT images shown to represent calcium morphology, not IVL cases.
Why IVL Performs Differently in Concentric and Eccentric Calcium
Eccentric Ca++: Fewer Fractures But Similar Stent Expansion

Concentric Ca++ Lesions Correlate to More Fractures than Eccentric Lesions
• Greater the calcium arc = more calcium fractures per lesion (p=0.009)

Similar Outcomes Across Eccentric & Concentric
• Stent expansion similar across all lesions, despite arc of calcium (p=0.21)
### Consistent Clinical Outcomes in Eccentric & Concentric Ca++

#### Inclusion:
- **Stable angina, unstable angina or silent ischemia**
- **Moderate and severely calcified, de novo coronary lesions**
  - RVD: 2.5 – 4.0 mm, stenosis ≥50%, Lesion length ≤ 32 mm

#### Table: Eccentric vs Concentric Lesions

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<tr>
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<th>Eccentric Lesions (N=34)</th>
<th>Concentric Lesions (N=86)</th>
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<tr>
<td><strong>Min Stent Diameter (mm)</strong></td>
<td>3.0</td>
<td>2.8</td>
</tr>
<tr>
<td><strong>%DS</strong></td>
<td>8.6%</td>
<td>7.5%</td>
</tr>
<tr>
<td><strong>Acute Gain (mm)</strong></td>
<td>1.7</td>
<td>1.7</td>
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Important Safety Information

Rx only

Indications for Use— The Shockwave Intravascular Lithotripsy (IVL) System with the Shockwave C² Coronary IVL Catheter is indicated for lithotripsy-enabled, low-pressure balloon dilatation of severely calcified, stenotic de novo coronary arteries prior to stenting.

Contraindications—The Shockwave C² Coronary IVL System is contraindicated for the following: This device is not intended for stent delivery. This device is not intended for use in carotid or cerebrovascular arteries.

Warnings—Use the IVL Generator in accordance with recommended settings as stated in the Operator’s Manual. The risk of a dissection or perforation is increased in severely calcified lesions undergoing percutaneous treatment, including IVL. Appropriate provisional interventions should be readily available. Balloon loss of pressure was associated with a numerical increase in dissection which was not statistically significant and was not associated with MACE. Analysis indicates calcium length is a predictor of dissection and balloon loss of pressure. IVL generates mechanical pulses which may cause atrial or ventricular capture in bradyarrhythmic patients. In patients with implantable pacemakers and defibrillators, the asynchronous capture may interact with the sensing capabilities. Monitoring of the electrocardiographic rhythm and continuous arterial pressure during IVL treatment is required. In the event of clinically significant hemodynamic effects, temporarily cease delivery of IVL therapy.

Precautions— Only to be used by physicians trained in angiography and intravascular coronary procedures. Use only the recommended balloon inflation medium. Hydrophilic coating to be wet only with normal saline or water and care must be taken with sharp objects to avoid damage to the hydrophilic coating. Appropriate anticoagulant therapy should be administered by the physician. Precaution should be taken when treating patients with previous stenting within 5mm of target lesion.

Potential adverse effects consistent with standard based cardiac interventions include— Abrupt vessel closure - Allergic reaction to contrast medium, anticoagulant and/or antithrombotic therapy-Anusm-Arhythmia-Arteriovenous fistula-Bleeding complications-Cardiac tamponade or pericardial effusion-Cardiopulmonary arrest-Cerebrovascular accident (CVA)-Coronary artery/vessel occlusion, perforation, rupture or dissection-Coronary artery spasm-Death-Embolii (air, tissue, thrombus or atherosclerotic emboli)-Emergency or non-emergency coronary artery bypass surgery-Emergency or non-emergency percutaneous coronary intervention-Entry site complications-Fracture of the guide wire or failure/malfunction of any component of the device that may or may not lead to device embolism, dissection, serious injury or surgical intervention-Hematoma at the vascular access site(s)-Hemorrhage-Hypertension/Hypotension-Infection/sepsis/fever-Myocardial Infarction-Myocardial Ischemia or unstable angina-Pain-Peripheral Ischemia-Pseudoaneurysm-Renal failure/insufficiency-Restenosis of the treated coronary artery leading to revascularization-Shock/pulmonary edema-Slow flow, no reflow, or abrupt closure of coronary artery-Stroke-Thrombus-Vessel closure, abrupt-Vessel injury requiring surgical repair-Vessel dissection, perforation, rupture, or spasm

Risks identified as related to the device and its use: Allergic/immunologic reaction to the catheter material(s) or coating-Device malfunction, failure, or balloon loss of pressure leading to device embolism, dissection, serious injury or surgical intervention-Atrial or ventricular extrasystole-Atrial or ventricular capture

Prior to use, please reference the Instructions for Use for more information on warnings, precautions and adverse events. www.shockwavemedical.com/IFU
Back-Up Slides
Use of IVL in Under-expanded Stents

- Our current indication is for de novo severely calcified lesions (prior to stenting) and our labeling includes the following precaution statement: “Precaution should be taken when treating patients with previous stenting within 5mm of target lesion”

- There are potential impacts on stent integrity as a result of the electrohydraulic lithotripsy discharge occurring in close proximity to the stent:
  - Bench testing has been performed on DES to mimic the acute setting (newly implanted, under-expanded stent that is not endothelialized)
  - RESULT*: Damage to the polymer was observed (polymer spalling and peeling off the stent removing patches of coating, see below)
  - RESULT*: Pitting damage to the coating and potentially to the stent (metal) was observed (in metals, pitting can increase the propensity of the metal to corrode)

For additional info/discussion, contact Shockwave Medical Affairs: medicalaffairs@shockwavemedical.com

*Data on file
Potential IVL Impacts on Heart Rate, Rhythm and Implantable Devices

If a patient’s heart rate is < 60 bpm, IVL may become the fastest pacer (for 10 seconds during delivery of pulses)

This stretch activated response from the acoustic pressure waves, produce extremely low amounts of energy (8-10µJ), lower than is required to induce ventricular fibrillation (>500µJ) or cause damage to implantable devices.
IVL-Induced Ventricular Capture

IVL-induced capture results from the mechano-electric coupling of the acoustic pressure waves with the cardiac conduction system mediated by the cardiac stretch-activated channels used for conduction.
### IVL-Induced Ventricular Capture*

<table>
<thead>
<tr>
<th></th>
<th>NO IVL-INDUCED CAPTURE (N=245)</th>
<th>IVL-INDUCED CAPTURE (N=171)</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-procedure heart rate, bpm</td>
<td>69.0 ± 11.9</td>
<td>65.9 ± 11.4</td>
<td>0.009</td>
</tr>
<tr>
<td>Drop in systolic BP during procedure</td>
<td>24.5%</td>
<td>40.5%</td>
<td>0.0007</td>
</tr>
<tr>
<td>Magnitude of systolic BP decrease, mmHg</td>
<td>23.5 ± 15.0</td>
<td>18.9 ± 14.2</td>
<td>0.07</td>
</tr>
<tr>
<td>Sustained ventricular arrhythmia during or immediately after IVL procedure</td>
<td>0.4%</td>
<td>0.0%</td>
<td>1.0</td>
</tr>
</tbody>
</table>

*41% of patients with no sustained ventricular arrhythmias or clinical sequelae

# Safety in CAD III Among Other Calcium Studies

## DISRUPT CAD III - ORBIT II - PREPARE CALC - ROTAXUS

<table>
<thead>
<tr>
<th>Device</th>
<th>Intravascular Lithotripsy</th>
<th>Orbital Atherectomy</th>
<th>Rotational atherectomy</th>
<th>Rotational Atherectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study (N)</td>
<td>Disrupt CAD III (N=384)(^a)</td>
<td>ORBIT II (N=443)(^b)</td>
<td>PREPARE CALC (N=100)(^c)</td>
<td>ROTAXUS (N=120)(^d)</td>
</tr>
<tr>
<td>Severe dissections</td>
<td>0.3%</td>
<td>3.4%</td>
<td>3.0%(^1)</td>
<td>3.3%</td>
</tr>
<tr>
<td>Perforations</td>
<td>0.3%</td>
<td>1.8%</td>
<td>4.0%</td>
<td>1.7%</td>
</tr>
<tr>
<td>Abrupt closure</td>
<td>0.3%</td>
<td>1.8%</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Slow flow</td>
<td>0.0%</td>
<td>0.9%</td>
<td>2.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>No reflow</td>
<td>0.0%</td>
<td>0.0%</td>
<td>12.6%</td>
<td>10.8%</td>
</tr>
<tr>
<td>Final diameter stenosis</td>
<td>11.9%</td>
<td>4.7%</td>
<td>12.6%</td>
<td>10.8%</td>
</tr>
</tbody>
</table>

### Clinical outcomes

| In-hospital cardiac death   | 0.6%                      | 0.2%                | 0.0%                   | 0.8%                   |
| Q-Wave MI                   | 1.0%\(^4\)               | 0.7%\(^4\)          | NR\(^2\)               | NR\(^3\)               |
| Non-Q-Wave MI               | 5.7%                      | 8.6%                |                         |                        |

**References:**
- \(^c\)Abdel-Wahab et al. PREPARE-CALC. *Circ Cardiovasc Interv*. 2018;11:e007415. DOI: 10.1161/CIRCINTERVENTIONS.118.007415
CAD III & ORBIT II In Context

Baseline Lesion Characteristics

- Lesion Length (mm)
- Calcified Length (mm)

<table>
<thead>
<tr>
<th>Lesion Length (mm)</th>
<th>Calcified Length (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAD III</td>
<td>26.0</td>
</tr>
<tr>
<td>CAD III Long</td>
<td>47.9</td>
</tr>
<tr>
<td>ORBIT II</td>
<td>18.9</td>
</tr>
<tr>
<td>ORBIT II Long</td>
<td>31.2</td>
</tr>
<tr>
<td>ORBIT II Long</td>
<td>34.1</td>
</tr>
</tbody>
</table>

Primary Outcomes

- FF 30-day MACE
- Procedural Success

<table>
<thead>
<tr>
<th>FF 30-day MACE</th>
<th>Procedural Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAD III</td>
<td>92.2%</td>
</tr>
<tr>
<td>CAD III Long</td>
<td>90.0%</td>
</tr>
<tr>
<td>ORBIT II</td>
<td>89.6%</td>
</tr>
<tr>
<td>ORBIT II Long</td>
<td>85.9%</td>
</tr>
</tbody>
</table>

1 Lesion length ≥ 25 mm
2 Chambers et al., JACC Cardiovas Interv 2014;7(5):510-518
3 Kumar et al., Cardiovasc Revasc Med 2020;21(2):164-170s

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