What is Intravascular Lithotripsy and When to Use It

Pr Marianne Brodmann, MD
Univ. Klinik für Innere Medizin
Medizinische Universität Graz
Disclosure

Speaker name: Marianne Brodmann, MD

I have the following potential conflicts of interest to report:

- ☐ Consulting
- ☐ Employment in industry
- ☐ Stockholder of a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)

☐ I do not have any potential conflict of interest
Intravascular Lithotripsy (IVL): Localized Lithotripsy to Treat Cardiovascular Calcium

Inspired by urological applications, but designed for cardiovascular system

**Lithotripsy**

- 30 years of safety data in kidney stone treatment
- *Sonic Pressure Waves* preferentially impact hard tissue, disrupt calcium, leave soft tissue undisturbed

**Cardiovascular Lithotripsy**

- Miniaturized and arrayed Lithotripsy Emitters for localized lithotripsy at the site of the vascular calcium
- Optimized for the Treatment of Cardiovascular Calcium

Peripheral IVL Catheters
The Shockwave IVL System consists of an IV pole-mountable generator, a connector cable, and a catheter that houses an array of lithotripsy emitters enclosed in an integrated balloon.
How IVL Cracks Calcium In Situ

Expanding and collapsing vapor bubble creates a short burst of sonic pressure waves.

Sonic pressure waves travel through the vessel tissue with an effective pressure of ~50 atm.

A localized field effect within the vessel fractures both intimal and medial calcium.
How Shockwave Creates Localized Lithotripsy

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.

   - **Emitter**
   - **Fluid filled Balloon**

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

   - **Bubble expands-collapses**
   - **Sonic Pressure Waves**

*Video: Actuation of Single Pulse (20µs/frame)*
IVL Impact on Cardiovascular Calcium

OCT demonstrated calcium disruption leading to **acute luminal gain and alteration in vessel compliance** in both peripheral and coronary arteries.

Micro CT demonstrated calcium fractures leading to an **acute reduction in mean gradient** and improved coaptation of Aortic Valve leaflet.

**Coronary Arteries**

Pre

Post

**Peripheral Arteries**

Pre

Post

**Excised Aortic Leaflet**

Arrows denote fractures in calcium

*The Coronary and Aortic Valve Lithotripsy Systems are not approved or available for sale in the United States.*
IVL Fractures Calcium While Minimizing Soft Tissue Damage

Sonic Pressure waves **crack calcium**, softening vessel compliance. Fractured calcium remains inside the vessel wall.

Sonic Pressure Waves transmit ~50 atm of instantaneous pressure to the site of calcium, but pass through soft tissue.
Broad Application: Got Calcium?

IVL as Primary or Adjunctive Therapy in Calcified Lesions

- Stand-alone or Vessel preparation (DCB or Stent)
- Claudicant or CLI
- Intimal or Medial Calcium
- Concentric or Eccentric Calcium
- Symptomatic disease or access for large bore procedure (TAVI, Impella, TEVAR, EVAR)
- CFA as alternative to surgery in a select group of patients
Peripheral IVL System: Clinical Programs

**DISRUPT PAD I**
- Pre Market
- Single Arm
- N = 35
- 2014

**DISRUPT PAD II**
- Post Market
- Single Arm
- N = 60
- 2015

**DISRUPT BTK**
- Post Market
- Single Arm
- N = 20
- 2017

**DISRUPT PAD III**
- Post Market
- Randomized
- N = 400
- 2017

**Observational Registry**
- Post Market
- Single Arm
- N = 1000
- 2017

Objective: To study the safety and effectiveness of the IVL System in the treatment of *calcified*, stenotic femoropopliteal or infrapopliteal peripheral arteries.
IVL in Calcified, Occlusive Lower Extremity Disease

Consistently shows: High Acute Gain, Low Residual Stenoses with Minimal Complications

- **Iliac**
  - Pre IVL
  - Post IVL

- **CFA**
  - Pre IVL
  - Post IVL

- **SFA/POP**
  - Pre IVL
  - Post IVL

- **BTK**
  - Pre IVL
  - Post IVL
IVL in Calcium: Unique Mechanism of Action

IVL works in both eccentric and concentric calcified lesions, however due its MOA, it may take more pulses for similar results in eccentric lesions.

Sonic pressure waves from IVL impact both intimal and medial calcium leading to improved vessel compliance and acute gain.

Holden, LINC 2018
IVL to Enable Transfemoral Access

1. Prohibitive calcified iliac disease
2. IVL Tx
3. Successful TAVI with Evolut Pro

Case Courtesy, Brian Kolski

1. Prohibitive calcified iliac disease
2. IVL Tx
3. Successful AAA endograft placement
IVL in Claudicant and CLI Patients

- Disrupt PAD I/II – heavily calcified, Claudicant Population
- Disrupt BTK – heavily calcified, CLI population

Consistent Results:
- Low residual stenosis
- High acute gain
- Minimal complications

<table>
<thead>
<tr>
<th>Patients Included</th>
<th>DISRUPT PAD I/II N = 95</th>
<th>DISRUPT BTK N = 20 (21 lesions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rutherford 2</td>
<td>33.7% (32)</td>
<td>-</td>
</tr>
<tr>
<td>Rutherford 3</td>
<td>65.3% (62)</td>
<td>20.0% (4)</td>
</tr>
<tr>
<td>Rutherford 4</td>
<td>1.1% (1)</td>
<td>5.0% (1)</td>
</tr>
<tr>
<td>Rutherford 5</td>
<td>-</td>
<td>75.0% (15)</td>
</tr>
</tbody>
</table>

Calcification:
- Moderate: 44.2% (42)
- Severe: 54.7% (52)

Angiographic Findings:
- RVD (mm): 5.3, 3.2
- Lesion length: 71.9, 52.2
- Calcified length: 92.5, 72.1
- CTO: 18.9% (18), 9.5% (2)

<table>
<thead>
<tr>
<th>Safety</th>
<th>DISRUPT PAD I/II N = 95</th>
<th>DISRUPT BTK N = 20 (21 lesions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dissections</td>
<td>1% (1) Grade D or greater</td>
<td>0 Grade D or greater</td>
</tr>
<tr>
<td>Embolization</td>
<td>0 Embolic Events 8% EPD Usage</td>
<td>0 Embolic Events</td>
</tr>
<tr>
<td>Perforations, abrupt closure, slow/no reflow or thrombosis</td>
<td>0 Complications</td>
<td>0 Complications</td>
</tr>
</tbody>
</table>

Effectiveness:
- Residual Stenosis: 24%, 26%
- Acute Gain: 3 mm, 1.5 mm

Brodmann, et al, JEVT 2018
Brodmann, et al, CCI 2018

Core lab adjudicated
Results from the early common femoral experience have similar results in both acute performance and safety as was seen in Disrupt PAD I/II and Disrupt BTK.

- 100% of patients had moderate or severe calcifications
- No vascular complications including flow-limiting dissections, perforation, distal embolization or stenting

<table>
<thead>
<tr>
<th>Final Procedure</th>
<th>N=21</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean luminal diameter, mm, mean ± SD (range)</td>
<td>4.8±1.1 (2.8-6.5)</td>
</tr>
<tr>
<td>Diameter stenosis, % mean ± SD (range)</td>
<td>21.3% ± 10.7 (5.1-40.0)</td>
</tr>
<tr>
<td>Acute gain, mm, mean ± SD (range)</td>
<td>3.1±1.3 (0.7-5.5)</td>
</tr>
<tr>
<td>Dissection</td>
<td></td>
</tr>
<tr>
<td>Flow-limiting (Grade D-F)</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Stents</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Perforation</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Distal embolization</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Thrombus</td>
<td>0% (0)</td>
</tr>
<tr>
<td>No reflow</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Abrupt closure</td>
<td>0% (0)</td>
</tr>
</tbody>
</table>

Core lab adjudicated

Brodmann, et al, manuscript submitted
Disrupt PAD III Study: Combination Therapy

Next Steps in Clinical Development

**Study Design:** Randomized study of the Shockwave Medical Peripheral Intravascular Lithotripsy (IVL) System with DCB versus standard balloon angioplasty with DCB to treat moderate and severely calcified femoropopliteal arteries (Disrupt PAD III).

**Objective:** The objective is to assess the optimal therapy to dilate heavily calcified lesions with IVL versus traditional angioplasty, in achieving less than 30% stenosis without the need for a stent. In addition, all patients who do not receive a stent will be treated with a drug-coated balloon.
Summary

- IVL is based on years of safety and effectiveness data of lithotripsy used in urologic applications, but has miniaturized for vascular calcium
- Due to its unique mechanism of action, IVL impacts both intimal and medial calcification
- IVL is being utilized in a broad range of applications including
  - IVL enabled Transfemoral access for TAVI, T/EVAR, Impella, etc
  - Calcified, occlusive disease iliac, Fem-pop and infrapopliteal arteries
  - Endovascular option for calcified CFA disease as alternative for surgical intervention
- Outcomes across the applications show consistent outcomes
  - Low residual stenosis, high acute gain
  - Minimal complications
- Disrupt PAD III RCT and Observational Study is the next step in clinical evaluation
  - RCT: IVL + DCB in Fem-pop calcified disease
  - OS: IVL real-world use in LE calcified disease
What is Intravascular Lithotripsy and When to Use It

Pr Marianne Brodmann, MD
Univ. Klinik für Innere Medizin
Medizinische Universität Graz