Intravascular Lithotripsy: Results of the DISRUPT Studies and Value of Combination with DCBs: Single Center Experience

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Disclosures

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Challenges with Calcium in Lower Limb Revascularization

Unpredictable Outcomes

Barrier to Drug Uptake with DCB/DES

Shockwave IVL System Components

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 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.

Peripheral IVL System: Clinical Programs

Objective: To study the safety and effectiveness of the IVL System in the treatment of calcified, stenotic femoropopliteal peripheral arteries.
Disrupt PAD II

Only study to enroll this significant of calcium burden with severe calcification 85% (PARC) as determined by the core lab and an average length of calcium of 98.1 mm

- Multi-center study, prospectively enrolling heavily calcified, stenotic fem-pop lesions
- Initial experience using IVL as a stand-alone treatment
- 6 centers in Europe and New Zealand
- 60 patients enrolled in 2015

**Pre-Procedure**

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Diameter Stenosis</td>
<td>78.1 ± 13.6</td>
</tr>
<tr>
<td>Diameter (mm)</td>
<td>5.7 ± 0.7</td>
</tr>
<tr>
<td>CTO</td>
<td>16.7% (10)</td>
</tr>
<tr>
<td>Lesion Length (mm)</td>
<td>78.6 ± 38.6</td>
</tr>
<tr>
<td>Calcified Length (mm)</td>
<td>58.4 ± 42.7</td>
</tr>
<tr>
<td>Maximum by PARC</td>
<td>7.9% (5)</td>
</tr>
<tr>
<td>Minimal</td>
<td>0% (0)</td>
</tr>
</tbody>
</table>

Safety Results*

A sustained low rate of safety events occurred following treatment with IVL

<table>
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<tr>
<th>Event Description</th>
<th>30 Days</th>
<th>12 Months</th>
</tr>
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<tbody>
<tr>
<td>Major Adverse Events (MAE*)</td>
<td>17.2%</td>
<td>18.3%</td>
</tr>
<tr>
<td>Emergency surgical revascularization of target limb</td>
<td>0% (0)</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Target limb amputation</td>
<td>0% (0)</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Symptomatic thrombus or emboli</td>
<td>0% (0)</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Perforation or Gr D dissections w/ interventions</td>
<td>1.7% (1)</td>
<td>1.8% (1)</td>
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</table>

Safety Results (Core CEAd Adjudicated)

12-Month Patency*: Optimal Technique

Optimal IVL technique was associated with significant improvement in clinical patency

Primary patency: 54.5% for intent-to-treat versus 62.9% for those with optimal technique.

Clinically-driven TLR: 20.7% for intent-to-treat versus 8.6% for those with optimal technique.

**Acute Angiographic Findings**

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<th>Acute Gain</th>
<th>High Acute Gain, Low Residual Stenosis, and Minimal Complications</th>
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<td>Pre-Pro</td>
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<td>24% Residual Stenosis</td>
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**Functional Outcomes**

A significant and sustained improvement in functional outcomes across all time intervals

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**Optimal Technique Optimizes Therapeutic Energy**

Oversize Device 10% vs RVD

Well-appled facilitates efficient energy transfer. Optimal balloon sizing leads to improved patency

Overlap Segments by 1 cm

The sonic pressure waves create a spherical field effect that drops as the longitudinal distance from the emitters increases.
Summary Disrupt PAD II: 12-Month Follow-up

- Disrupt PAD II is the first and only core lab adjudicated study to exclusively enroll and follow out to 12-months, heavily calcified lesions.
- Acute results with IVL were strong with high acute gain following low pressure inflation resulting in low dissections and minimal use of stents.
- Low rate of clinically-driven TLR in a stand alone technique, and revascularizations were completed with simple endovascular procedures.
- We learned 12-month primary patency outcomes improve by optimizing procedural technique.
- Disrupt PAD III will investigate the optimal energy based therapy vs. PTA to address plaque modification in heavily calcified arteries. Those without a stent will be treated with DCB.

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.

Treatment arm (N=200)
IVL + IN.PACT DCB

Control arm (N=200)
PTA + IN.PACT DCB

400 subjects
60 global sites
Randomization 1:1
24 months follow-up

Case from my lab

Case Example

- Pre Intervention Images
- After Treatment with Turbohawk
- Hawk Reocclusion treated with Viabahn
• New restenosis treated with IVL

Lessons Learned
Atherectomy failed after 6 months
IVL + DCB with sustained benefit after 6 and 12 months in severe calcification

• Plus DCB