The Role of Lithotripsy in Solving the Challenges of Vascular Calcium

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Disclosure

Speaker name: Thomas Zeller

I have the following potential conflicts of interest to report:

- [x] Consulting
- [ ] Employment in industry
- [x] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)
- [ ] I do not have any potential conflict of interest
Localized Lithotripsy to Treat Vascular Calcium

**Lithotripsy**

30 years of safety data in kidney stone treatment

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

**Lithoplasty Technology**

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

Optimized for the treatment of vascular calcium
Shockwave Peripheral Intravascular Lithotripsy (IVL) System

Generator

Connector Cable

Lithoplasty Catheter
IVL: Hard on Hard Calcium, Soft on Soft Tissue
IVL: Primary & Adjunctive Therapy

EVAR deployment in Calcium

DES wall apposition

DCB drug uptake in Calcium

TAVI delivery through Calcium

BVS deployment in Calcium

BVS = bioabsorbable vascular stents; DCB = drug coated balloons; DES = drug eluting stents; EVAR = endovascular aneurysm repair; TAVI = transcatheter aortic valve insertion
Peripheral IVL

Iliac
- Pre IVL
- Post IVL

SFA/POP
- Pre IVL
- Post IVL

CFA
- Pre IVL
- Post IVL

BTK
- Pre IVL
- Post IVL
Peripheral Lithoplasty System: Clinical Programs

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

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

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

DISRUPT PAD III
- Post Market
- Randomized
- N = 334

Study Completed

Enrolling
**Objective:** To study the safety and effectiveness of the Shockwave Medical Intravascular Lithotripsy System in the treatment of calcified, stenotic infrainguinal peripheral arteries.

- Two-phase, prospective, non-randomized, multi-center study
- Monitoring with 100% source document verification
- Independent angiographic and duplex ultrasound core labs
- Independent clinical events committee
DISRUPT PAD Study Design and Endpoints

**Design**

**Key eligibility criteria**
- Intermittent claudication: Rutherford Classification 2–4
- Ankle-brachial index ≤0.9
- SFA/Popliteal lesions ≥70% stenosis
- RVD 3.5–7.0 mm, ≤150 mm length
- Moderate and severe calcification by angiography

**Study device**
- Shockwave Medical Peripheral Lithoplasty Catheter
- Diameters: 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 6.5, 7.0 mm
- Length: 60 mm

**Endpoints**

**Procedural**
- Procedural success: <50% residual stenosis
- Exploratory endpoint: ≤30% residual stenosis

**Follow up: 30 days, 6 Mo, & 12 Mo**
- Major adverse events
- Target lesion patency by DUS (stenosis <50%)
- Target lesion revascularization (TLR)
- Functional outcomes
# DISRUPT PAD I/II: Patient Demographics and Angiographic Findings

<table>
<thead>
<tr>
<th>DISRUPT PAD I/II</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 95</td>
</tr>
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</table>

## Patients Included

<table>
<thead>
<tr>
<th>Rutherford</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>33.7% (32)</td>
</tr>
<tr>
<td>3</td>
<td>65.3% (62)</td>
</tr>
<tr>
<td>4</td>
<td>1.1% (1)</td>
</tr>
<tr>
<td>5</td>
<td>-</td>
</tr>
</tbody>
</table>

## Calcification

<table>
<thead>
<tr>
<th>Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>44.2% (42)</td>
</tr>
<tr>
<td>Severe</td>
<td>54.7% (52)</td>
</tr>
</tbody>
</table>

## Angiographic Findings

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVD (mm)</td>
<td>5.3</td>
</tr>
<tr>
<td>Lesion length</td>
<td>71.9</td>
</tr>
<tr>
<td>Calcified length</td>
<td>92.5</td>
</tr>
<tr>
<td>CTO</td>
<td>18.9% (18)</td>
</tr>
</tbody>
</table>

DISRUPT PAD & DISRUPT BTK categorized calcified lesions as per PARC definitions. Both studies utilized independent core labs and clinical events committees. DISRUPT BTK data based on European studies.
| Safety                      | Dissections | 1% (1) Grade D or greater
|                            |             | 1% (1) stent placed          |
| Embolization               |             | 0 Embolic Events             |
| Perforations, abrupt       |             | 8% EPD Usage                 |
| closure, slow/no reflow or |             |                              |
| thrombosis                 |             | 0 Complications              |
| Effectiveness              | Residual Stenosis | 23.8%                     |
| Acute Gain                 |             | 2.9mm                        |
| Follow-Up                  | 30 days     | 100% Freedom from TLR       |
|                            | 6 months    | 96.8% Freedom from TLR      |

DISRUPT PAD & DISRUPT BTK categorized calcified lesions as per PARC definitions. Both studies utilized independent core labs and clinical events committees. DISRUPT BTK data based on European studies.
DISRUPT PAD Effectiveness*

- 100% procedural success with a 24% residual stenosis
- Compelling 6 month results in a challenging lesion cohort

*By angiographic and DUS core labs
DISRUPT PAD Functional Outcomes

Sustained hemodynamic and Rutherford Category improvement

ABI Shift

Baseline | Discharge | 6 months

| 0.2 | 1 | 1.6 |

p < 0.0001

Rutherford Category Shift (%)

Baseline | Discharge | 30 Days | 6 Months

| RC0 | RC1 | RC2 | RC3 | RC4 |

N | Baseline | Discharge | 30 Days | 6 Months

| N | 91 | 88 | 89 | 95 | 81 | 93 | 89 |
DISRUPT PAD Procedural Success by Subgroups

Pre and Post % Diameter Stenosis

Achieves consistent successful procedural outcomes in calcified lesions regardless of lesion complexity or location.

![Bar chart showing pre and post % diameter stenosis by subgroups]

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Pre</th>
<th>Post</th>
<th>50% Primary Performance</th>
<th>30% Exploratory Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Subjects</td>
<td>78</td>
<td>76</td>
<td>81</td>
<td>73</td>
</tr>
<tr>
<td>SFA</td>
<td>81</td>
<td>73</td>
<td>81</td>
<td>22</td>
</tr>
<tr>
<td>Popliteal</td>
<td>73</td>
<td>22</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Moderate Ca</td>
<td>81</td>
<td>22</td>
<td>25</td>
<td>28</td>
</tr>
<tr>
<td>Severe Ca</td>
<td>75</td>
<td>23</td>
<td>28</td>
<td>70</td>
</tr>
<tr>
<td>Lesion &lt;5 cm</td>
<td>77</td>
<td>28</td>
<td>79</td>
<td>79</td>
</tr>
<tr>
<td>Lesion 5–10 cm</td>
<td>82</td>
<td>70</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>Lesion &gt;10 cm</td>
<td>78</td>
<td>24</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>Concentric</td>
<td>17</td>
<td>17</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Eccentric</td>
<td>17</td>
<td>17</td>
<td>17</td>
<td>17</td>
</tr>
</tbody>
</table>

| N              | 95  | 70   | 24  | 42  | 52  | 33  | 39  | 23  | 78  | 17  |

N = Number of subjects
IVL Case Example: Severely Calcified SFA Lesion

Heavily calcified sub-total SFA occlusion

5.5 x 60mm IVL Catheter, 120 pulses

Post IVL

Post 6.0mm DCB treatment
Disrupt PAD III Study Design

**Study Design:** Randomized study of the Shockwave Medical Peripheral Intravascular Lithotripsy 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.
Objective: To study the safety and performance of the Shockwave Medical Lithoplasty® System in the treatment of calcified, stenotic infrapopliteal peripheral arteries.

Design

Key eligibility criteria
- Rutherford category 1-5 infrapopliteal disease
- Infrapopliteal lesions ≥50% stenosis
- RVD 2.5–3.5 mm, ≤150 mm length
- Moderate and severe calcification by angiography

Endpoints

Procedural
- Primary Effectiveness: Acute reduction in % diameter stenosis

Follow up: 30 days
- Major adverse events (Death, MI, TLR, amputation)

DISRUPT BTK categorized calcified lesions as per PARC definitions. Study utilized independent core labs and clinical events committees. DISRUPT BTK data based on European studies.
DISRUPT BTK:  
**Safety & Effectiveness**

<table>
<thead>
<tr>
<th>Safety</th>
<th>Dissections</th>
<th>0 Grade D or greater</th>
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<tr>
<td></td>
<td>Embolization</td>
<td>0 Embolic Events</td>
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<td>0 Complications</td>
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</table>

<table>
<thead>
<tr>
<th>Effectiveness</th>
<th>Residual Stenosis</th>
<th>26.2%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Acute Gain</td>
<td>1.5mm</td>
</tr>
</tbody>
</table>

**Follow-Up**

- 30 days
- 100% Freedom from TLR
- 0% MAE (death, amp. or MI)

*DISRUPT BTK data based on European studies. Brodmann, M. Presentation, CIRSE, 2017*

DISRUPT PAD & DISRUPT BTK categorized calcified lesions as per PARC definitions. Both studies utilized independent core labs and clinical events committees.
IVL Case Example: Anterior Tibial Lesion

Diagnostic Angiogram

Calculated

IVL Catheter Image

3.5 mm IVL @ 4 atm

Final Angiogram

21% Residual
1.6mm Acute Gain

Case courtesy of: Prof Andrew Holden

65% Stenosis
Summary: IVL is Uniquely Capable of Treating Vascular Calcium

• The Disrupt PAD trials have demonstrated that heavily calcified SFA/popliteal lesions can be treated safely with compelling acute gain and without the need for adjunctive tools like filters and specialty balloons.

• The DISRUPT BTK study demonstrated excellent safety with consistent acute gain, minimal stent utilization, along with low reported rates of recoil.

• IVL is proving safe and effective in treatment of heavily calcified common femoral and iliac lesions without the need for stenting.

• Ongoing and future trials are targeting even broader clinical applications for this platform technology for vascular therapy.
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