Is Lithoplasty followed by DCB the answer in case of calcified vessels?

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Disclosure

Speaker name: William A. Gray

I have the following potential conflicts of interest to report:

- [x] 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
Calcification is a Frequent Problem

Above 70 years, all have calcium in at least one vascular bed and 2/3 in all arterial beds

Calcification Risk Factors and Prevalence

Occurs in 30-50% of asymptomatic US patients

**Problem:**  Rigid fibrotic, calcified tissue

Today’s endovascular therapies fail

**Current Cycle of Therapy**
Severe Calcium May Act as a Barrier to DCB

Calcium distribution evaluation by CTA (circumferential) and DSA (longitudinal)


Zeller T. ViVa 2014
Calcified Lesions Are Challenging to Treat

• Calcified lesions respond poorly to balloon angioplasty and require high use of stents ¹

• Calcified lesions are associated with high incidence of angiographic complications ², ³

• Calcified lesions limit effectiveness of drug-coated balloons ⁴

• Calcium is not well studied – excluded or limited follow-up

# Insights from Prior Studies

## IN.PACT Global Long Lesion Imaging Cohort: Lesion/Procedural Characteristics

<table>
<thead>
<tr>
<th>Lesions (N)</th>
<th>164</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lesion Type:</strong></td>
<td></td>
</tr>
<tr>
<td>de novo</td>
<td>83.2% (134/161)</td>
</tr>
<tr>
<td>restenotic (no ISR)</td>
<td>16.8% (27/161)</td>
</tr>
<tr>
<td>ISR</td>
<td>0.0% (0/161)</td>
</tr>
<tr>
<td><strong>Lesion Length</strong></td>
<td>26.40 ± 8.61 cm</td>
</tr>
<tr>
<td>Total Occlusions</td>
<td>60.4% (99/164)</td>
</tr>
<tr>
<td>Calcification</td>
<td>71.8% (117/163)</td>
</tr>
<tr>
<td>Severe</td>
<td>19.6% (32/163)</td>
</tr>
<tr>
<td>RVD (mm)</td>
<td>4.594 ± 0.819</td>
</tr>
<tr>
<td>Diameter Stenosis (pretreatment)</td>
<td>90.9% ± 14.2</td>
</tr>
<tr>
<td>Dissections: 0</td>
<td>37.9% (61/161)</td>
</tr>
<tr>
<td>A-C</td>
<td>47.2% (76/161)</td>
</tr>
<tr>
<td>D-F</td>
<td>14.9% (24/161)</td>
</tr>
</tbody>
</table>

### Device Success [1]
99.5% (442/444)

### Procedure Success [2]
99.4% (155/156)

### Clinical Success [3]
99.4% (155/156)

### Pre-dilatation
89.8% (141/157)

### Post-dilatation
39.1% (61/156)

### Provisional Stent
- LL 15-25 cm: 40.4% (63/156)
- LL > 25 cm: 33.3% (33/99)
- LL > 25 cm: 52.6% (30/57)

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1. Device success: successful delivery, inflation, deflation and retrieval of the intact study balloon device without burst below the RBP
2. Procedure success: residual stenosis of ≤ 50% (non-stented subjects) or ≤ 30% (stented subjects) by core lab (if core lab was not available then the site reported estimate was used)
3. Clinical success: procedural success without procedural complications (death, major target limb amputation, thrombosis of the target lesion, or TVR) prior to discharge
Lithoplasty®

Lesion modification using localized lithotripsy in a balloon

Tissue-selective: Hard on hard tissue, Soft on soft tissue

Lithotripsy waves travel outside balloon

- Designed to normalize vessel wall compliance prior to controlled, low pressure dilatation
- Effective lesion expansion with minimized impact to healthy tissue
- Familiar Balloon-based endovascular technique
- “Front-line” balloon strategy (.014”compatible)
Mechanism of Action and Possible DCB enabling

Lithoplasty

DCB

Drug coating transfer

Calcium

Diffusion

Tissue Binding

Retention

Clinical Development Phases

Lithoplasty as primary therapy

Results:
• Low rate of vascular complications
  • provisional stenting (1.1%)
• Consistent effectiveness
  • high acute gain (3.0 mm)
  • low residuals stenosis (23.8%)
• Sustained 6 month results

Combination therapy

Goal is to create level one evidence on the benefit of combination therapy
DISRUPT PAD Acute Effectiveness

By angiographic core lab

% Stenosis

Pre-Proc

Post-Proc

% Residual Stenosis = 23.8%

Acute Gain

Minimal Adjunctive Therapy

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-dilatation</td>
<td>11.6% (11)</td>
</tr>
<tr>
<td>Post-dilatation</td>
<td>7.4 % (7)</td>
</tr>
<tr>
<td>Provisional stenting</td>
<td>1.1% (1)</td>
</tr>
</tbody>
</table>

N=95

Acute Gain = 3.0 mm
**Study Design:** Randomized study of the Shockwave Medical Peripheral Lithoplasty® System used in combination with DCB versus standard balloon angioplasty used in combination with DCB to treat moderate and severely calcified femoropopliteal arteries (Disrupt PAD III).

**Objective:** The objective of the study is to assess the safety and effectiveness of Lithoplasty treatment used in combination with DCB versus standard balloon angioplasty used in combination with DCB to treat moderate and severely calcified femoropopliteal arteries.
DISRUPT PAD III : Key Inclusions

- Rutherford Clinical Category 2, 3, or 4 of the target limb.
- Target lesion in de novo superficial femoral artery (SFA) or popliteal artery.
- Target lesion reference diameter is 4.0mm to 7.0mm.
- Target lesion is ≥70% stenosis.
- Target lesion length is 50-180mm for occlusive disease.
- Chronic total occlusion lesion length is ≤100mm.
- One patent tibial vessel with runoff to the foot, defined as no stenosis >50%.
- Calcification is at least moderate defined as presence of calcification: 1) on parallel sides of the vessel and 2) extending > 50% the length of the lesion.
DISRUPT PAD III: Key Exclusion

- MI or stroke within 60 days.
- Renal disease (serum creatinine of >2.5 mg/dL or >220 umol/L), or on dialysis.
- In-stent restenosis within the target zone.
- Lesions extending into common femoral or within 10 mm of the anterior tibial.
- Evidence of aneurysm or thrombus in target vessel.
- No calcium or mild calcium in the target lesion.
- Target lesion within native or synthetic vessel grafts.
- Stenosis (>50% stenosis) or occlusion of inflow tract not successfully treated.
- Requires treatment of a peripheral lesion distal to target site at the same time.
- Unable to pass the guidewire across the target lesion.
Primary Effectiveness Endpoint

Procedural Success defined as:

- Residual stenosis $\leq 30\%$ prior to DCB or stenting by angiographic core lab quantitative assessment

Powered Secondary Effectiveness Endpoint

Primary Patency defined as freedom from:

- Clinically-driven target lesion revascularization (TLR)
- Restenosis determined by duplex ultrasound or angiogram $>50\%$ stenosis
Summary

• Calcium has not been well studied in existing clinical studies
• Existing 6 month DISRUPT PAD data has demonstrated safety and performance of Lithoplasty as a primary therapy for calcified lesions
• DISRUPT PAD III is the largest, randomized study in a difficult to treat, calcified patient population.
• The goal is to provide level one evidence on the best treatment strategy for calcified lesions in a leave nothing behind strategy
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