Just remove it: calcium and arterial compliance

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# Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
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<tbody>
<tr>
<td>Grant/Research Support</td>
<td>Abbott, Covidien/Medtronic</td>
</tr>
<tr>
<td>Consulting (non-compensated)</td>
<td>Covidien/Medtronic, Boston Scientific, Abbott</td>
</tr>
<tr>
<td>Major Stock Shareholder/Equity</td>
<td>Arsenal, Primacea, TissueGen, CV Ingenuity, Spirox, Scion Cardiovascular, Syntervention, Essential Medical</td>
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<tr>
<td>Royalty Income</td>
<td>None</td>
</tr>
<tr>
<td>Ownership/Founder</td>
<td>Innovative Vascular Partners</td>
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<tr>
<td>Intellectual Property Rights</td>
<td>None</td>
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<tr>
<td>Other Financial Benefit</td>
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</table>
Shortcoming of SFA-Stents

Insufficient radial strength in calcified lesions
<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>Device</th>
<th>Lesion length (cm)</th>
<th>1 year primary patency (%) (PSVR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIMIC</td>
<td>81</td>
<td>PTA</td>
<td>NA</td>
</tr>
<tr>
<td>ABSOLUTE</td>
<td>104</td>
<td>Stent</td>
<td>10.2</td>
</tr>
<tr>
<td>RESILIENT</td>
<td>137</td>
<td>Stent</td>
<td>9.3</td>
</tr>
<tr>
<td>DURABILITY</td>
<td>287</td>
<td>Stent</td>
<td>8.9</td>
</tr>
<tr>
<td>STROLL</td>
<td>250</td>
<td>Stent</td>
<td>7.7</td>
</tr>
<tr>
<td>ZilverPTX</td>
<td>240</td>
<td>DES-SES</td>
<td>5.4</td>
</tr>
<tr>
<td>THUNDER</td>
<td>54</td>
<td>DCB</td>
<td>7.4</td>
</tr>
<tr>
<td>LEVANT</td>
<td>476</td>
<td>DCB</td>
<td>6.3</td>
</tr>
<tr>
<td>IN-PACT</td>
<td>301/220</td>
<td>DCB</td>
<td>8.9</td>
</tr>
<tr>
<td>DEFINITIVE LE</td>
<td>598/201</td>
<td>DA</td>
<td>7.8</td>
</tr>
</tbody>
</table>
Clinical Limitations & Unmet Needs

Calcium as a Barrier

**Calcium Limits Vessel Expansion**

Significant difference in vessel compliance leads to overstretch in non-diseased tissue causing dissections, recoil, excessive injury, and poor outcomes.

![Diagram of Calcium Limits Vessel Expansion](image)

**Calcium May Limit Drug Effect**

Increased lesion length is an independent predictor of decreased patency.

![Graph showing Calcium May Limit Drug Effect](image)

Longer Lesion Length

![Graph showing 12, 24, and 36-Month Primary Patency Summary](image)

Increased lesion length is an independent predictor of decreased patency.

1. Freed MS, Manual of Interventional Cardiology.
4. SMART Control IFU.
Why atherectomy?

• Calcification is the norm not the exception
• No trial to date included heavy calcification in their inclusion criteria except for one trial
• Arterial compliance allows final therapy
  – Debulking
  – Stenting
  – DCB
  – DES
• Opportunity for dedicated combination therapy equally available
Atheroablative

LASER
The LACI Studies

The LACI Trial: 6 Month Results

- Laird et al
- 145 pt, 155 critical ischemic limbs
- 423 lesions
- 41% SFA, 15% Popliteal, 41% Infrapop
- 70% of Pts had combo occlusion and stenosis
- 29% Rutherford Class 4
- 71% Rutherford Class 5 or 6
- Limb salvage 92% at 6 months
LASER

Laser – Spectronetics

• Ultraviolet 308 nm excimer laser
• The “step-by-step” technique can be used to cross chronic total occlusion
  – Lead with laser not wire
    • Probe lesion as you advance
• Perforation ~ 2%
• Embolization ~ 4%
• Excellent debulking thrombus, atheroma and emboli
• Questionable with heavy calcium
• Off label ISRS
Atheroablative data

- **ExCITE**
  - Indication for ISRS
  - 6 month patency 48%

- **PATENT**
  - European ExCITE
    - 90 patients freedom from TLR at 6 months 76%

- **Illuminate**
  - Initial evaluation of laser with DCB
  - US IDE trial
    - Builds on PHOTOPAC European experience
Rotational devices

Pathway (rotational debulking)

- Rotates, Aspirates, Adjunctive RX
- Early data - 4.9 cm
- JET registry began 2012 discontinued

CSI (sanding debulking)

- Centrifugal force
  - Sands atheroma
  - Debris relatively small
    - <1-7 µm
- Offset burr determines diameter
- Oasis trial used for approval - 3.1 cm
- CONFIRM registry 3000 patients device safety, efficacy study
Pathway PV™ Atherectomy System

- **Differential and Circumferential Excision**
- **Accommodation** (size adaptation)
- **Evacuation** (debris removal)
Pre Treatment
Heavy calcific burden

Post Jetstream G3™ NXT
2 passes BD, 2 pass BU

Jetstream G3™ NXT
Final post adjunctive PTA

30 cm calcific artery serial lesions

Case of Dr. Garcia
Aspiration rotablation

- Effective to over 4mm with larger Gen 3 device
- Standard sizing in Gen 2 device is to 3.1 mm with blades up
- Tibial device available for vessels under 1.6mm
- European/US JetStream 2012
  - Assess JetStream in denovo lesions at 12 months primary patency endpoint—on hold to resume
- Combination therapy with DCB under investigation
Unique Mechanism of Action
Preferential Sanding

- Elastic healthy tissue “gives” and is not affected by diamond grit
- Diseased tissue provides resistance and allows grit to “sand” the plaque

Effective plaque removal

Diamond Grit
Diseased Tissue
Compliant Tissue

No detrimental effect
• 6 month data
• 124 patients for infrapopliteal revascularization (201 lesions)
• Claudicants 55%
• CLI 45%
• Treatment OA either stand alone or with adjuctive Rx
Orbital data

• CONIRM 3000 patient registry to be released 2012
• Treatment 3000 patients 4700 lesions with no exclusion criteria, outcomes at 12 months
• COMPLIANCE 360 and Calcium 360 evaluated OA with PTA compared with PTA alone. OA had much lower balloon inflation pressure compared with PTA alone
Vessel preparation through compliance change with Orbital Atherectomy enables lower-pressure adjunctive balloon angioplasty leading to low procedural events.

Less medial damage $\rightarrow$ Better long term durability

Orbital Atherectomy procedural efficacy with lower bail-out stents PRESERVES TREATMENT OPTIONS in future

**Dr. Das presentation VIVA 2012/CCI 2015**
Directional atherectomy

SilverHawk
DEFINITIVE CA

Key Eligibility Criteria

• Inclusion
  – ≥ 75% stenosis
  – Moderate to severe calcification
  – Rutherford 2-4
  – Each discrete target lesion ≤ 10cm (If multiple lesions qualify, cumulative length of target lesions ≤ 15 cm)

• Exclusion
  – In-stent restenosis
  – Guidewire cannot cross target lesion and/or a subintimal approach is required
  – Presence of aneurysm or thrombus in target vessel
### Procedural Characteristics

<table>
<thead>
<tr>
<th>Procedure Characteristic</th>
<th>N=133</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total procedure time (min)</td>
<td>74.2 ± 28.4</td>
</tr>
<tr>
<td>Total fluoroscopy time (min)</td>
<td>21.1 ± 9.7</td>
</tr>
<tr>
<td>Total amount of contrast administered (cc)</td>
<td>182.3 ± 72.4</td>
</tr>
<tr>
<td>Visible debris in SpiderFx</td>
<td>88.4%</td>
</tr>
<tr>
<td>Adjunct (post-dil) PTA</td>
<td>53.3%</td>
</tr>
<tr>
<td>Adjunct / bail-out stenting</td>
<td>4.1%</td>
</tr>
<tr>
<td>Preservation of run-off (per angio core lab)</td>
<td>98.3%</td>
</tr>
</tbody>
</table>
# DEF LE outcomes

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Claudicants (n=743)</th>
<th>CLI (n=279)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patency (PSVR ≤ 2.4)</td>
<td>Lesion Length (cm)</td>
</tr>
<tr>
<td>All (n=1022)</td>
<td>78%</td>
<td>7.5</td>
</tr>
<tr>
<td><strong>Lesion type</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stenoses (n=806)</td>
<td>81%</td>
<td>6.7</td>
</tr>
<tr>
<td>Occlusions (n=211)</td>
<td>64%</td>
<td>11.1</td>
</tr>
<tr>
<td><strong>Lesion Location</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SFA (n=671)</td>
<td>75%</td>
<td>8.1</td>
</tr>
<tr>
<td>Popliteal (n=162)</td>
<td>77%</td>
<td>6.0</td>
</tr>
<tr>
<td>Infrapopliteal (n=189)</td>
<td>90%</td>
<td>5.5</td>
</tr>
</tbody>
</table>
Effective in calcium

12 Month Primary Patency in Calcified Lesions from DEFINITIVE LE

- **All Calcified Lesions**: 76%
- **Fempop Lesions**: 76%
- **Infrapopliteal Lesions**: 92%

- **Mean lesion length (cm)**:
  - All Calcified Lesions: 8.3
  - Fempop Lesions: 8.4
  - Infrapopliteal Lesions: 5.6

- **Num. of lesions**:
  - All Calcified Lesions: 274
  - Fempop Lesions: 262
  - Infrapopliteal Lesions: 12
## DEFINITIVE AR

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>DAART (N= 48)</th>
<th>DCB (N = 54)</th>
<th>p-Value*</th>
<th>DAART Severe Ca++ Arm (N=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion Length (cm)</td>
<td>11.2</td>
<td>9.7</td>
<td>0.05</td>
<td>11.9</td>
</tr>
<tr>
<td>Diameter Stenosis</td>
<td>82%</td>
<td>85%</td>
<td>0.35</td>
<td>88%</td>
</tr>
<tr>
<td>Reference vessel diameter (mm)</td>
<td>4.9</td>
<td>4.9</td>
<td>0.48</td>
<td>5.1</td>
</tr>
<tr>
<td>Minimum lumen diameter (mm)</td>
<td>1.0</td>
<td>0.8</td>
<td>0.34</td>
<td>0.7</td>
</tr>
<tr>
<td>Calcification</td>
<td>70.8%</td>
<td>74.1%</td>
<td>0.82</td>
<td>94.7%</td>
</tr>
<tr>
<td>Severe calcification</td>
<td>25.0%</td>
<td>18.5%</td>
<td>0.48</td>
<td>89.5%</td>
</tr>
</tbody>
</table>

* *p-value for DAART and DCB groups*
Key Study Outcome at 12 Months

Angiographic Patency shows similar pattern

Results for all patients who returned for angiographic follow-up
Summary

• Calcium remains a predominant impediment for revascularization both intervention and durability.
• You need to modify or remove plaque from large and small vessels either “all the time” or in “specific instances”.
• DEFINITIVE CA confirms debulking with directional atherectomy if feasible and safe.
• A “change arterial compliance” strategy has shown benefit for lower limb intervention through CONFIRM360—long term benefit pending.
• Critically calcific lesions require treatment and rotational or directional devices seem best suited to treat these difficult lesions.
Just remove it: calcium and arterial compliance

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