No Metal Left Behind: Improving POBA and Biodegradable Stents

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Disclosure
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Potential conflicts of interest to report:
Consultant to start-ups: Silk Road, Altura, Revascular,
Intact Vascular, Pro-med
Enter patients in studies: Abbott, Gore, Medtronic, Cordis
Modest royalty from Cook

Location and Severity of Disease Determines Type of Reconstruction

TASC
Currently “implant based”

Rutherford class
Angiosomal anatomy
Runoff
Currently “balloon based”

Performance Goals and Endpoint Assessments for Clinical Trials of Femoropopliteal Bare Nitinol Stents in Patients With Symptomatic Peripheral Arterial Disease

- PTA control arm from 3 randomized, industry-sponsored device trials
  - Lesion length = 8.7 cm
  - 12-month duplex patency = 28%
- Results combined with a survey of medical literature from 1990 – 2006
  - Lesion length = 8.9 cm
  - 12-month duplex patency = 38%

Catheter Cardiovasc Interv 2007
How Does Balloon Angioplasty Work?

- Equal pressure in all directions around the circumference of the irregular lumen.
- Pressure increases until it overwhelms the lesion through compression and plaque fracture.
- When the lesion gives way, the pressure propagates along the artery and there is usually uncontrolled damage.

Problems with balloon angioplasty

Achilles heal of balloon angioplasty = dissection

Recanalizing Atherosclerotic Vessels

- Balloon Angioplasty – Uncontrolled Dissection
  - Minimally invasive
  - Technique “dissects” plaque from wall allowing adventitia to expand to maximum diameter
  - New larger lumen accommodates pre-existing plaque and increased cross-section for blood flow
  - Problems:
    - Plaque is not “molded” but dissected and fractured in uncontrolled (random) manner
    - Plaque often “falls into” lumen → obstruction
    - Irregularity of “injury” and plaque conformation can initiate restenosis → reaction to injury

RESILIENT: Primary Patency

12 Months*
LifeStent: 80%
PTA: 38%

> 40% immediate failure of PTA requiring bailout stents
SFA Treatment

Stent Results

<table>
<thead>
<tr>
<th>Trial</th>
<th>Patency 12 months</th>
<th>Lesion Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fast</td>
<td>68%</td>
<td>4.4 cm</td>
</tr>
<tr>
<td>Resilient</td>
<td>80%</td>
<td>6.2 cm</td>
</tr>
<tr>
<td>Durability</td>
<td>72%</td>
<td>9.3 cm</td>
</tr>
<tr>
<td>Astron</td>
<td>65%</td>
<td>9.9 cm</td>
</tr>
<tr>
<td>Vienna</td>
<td>68%</td>
<td>10.9 cm</td>
</tr>
</tbody>
</table>

35-50% stent bailout rate in current SFA trials

Femoral-popliteal Disease

TASC C and D

- Type C lesions
  - Multiple stenoses or occlusions totaling >15 cm with or without heavy calcification
  - Recurrent stenoses or occlusions that need treatment after two endovascular interventions

- Type D lesions
  - Chronic total occlusions of CFA or SFA (>20 cm, involving the popliteal artery)
  - Chronic total occlusion of popliteal artery and proximal trifurcation vessels

C lesions: Surgery preferred unless high risk
D lesions: Surgery treatment of choice

SFA Treatment

Our Challenge

Surowiec et al. JVS, 2005

Poor results in more complex lesions.

SFA Treatment

139 limbs

<table>
<thead>
<tr>
<th></th>
<th>Patency at 12 months</th>
<th>Patency at 24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>TASC C stent</td>
<td>83%</td>
<td>80%</td>
</tr>
<tr>
<td>TASC D stent</td>
<td>54%</td>
<td>28%</td>
</tr>
<tr>
<td>Above knee PTFE fem-pop</td>
<td>81%</td>
<td>75%</td>
</tr>
</tbody>
</table>

Baril et al. J Vasc Surg 2010

**TASC D:** Diminished patency at 12 and 24 months.

Is it possible: The poor results of long lesions are due as much to stent length as they are to lesion length?

<table>
<thead>
<tr>
<th></th>
<th>No. of patients</th>
<th>12 months</th>
<th>24 months</th>
<th>36 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>TASC A/B</td>
<td>46/82</td>
<td>79%</td>
<td>67%</td>
<td>57%</td>
</tr>
<tr>
<td>TASC C/D</td>
<td>38/35</td>
<td>53%</td>
<td>36%</td>
<td>19%</td>
</tr>
</tbody>
</table>


210 patients

Primary Patency

**Failed SFA Intervention**

After primary stent, TASC C and D lesions are more likely to fail with occlusion rather than stenosis, lose run-off vessels, and extend the length of contiguous diseased arterial segments than their TASC A and B counterparts.


**SFA Treatment**

Conformational Forces

Dramatic changes in configuration with movement.

Recanalizing Atherosclerotic Vessels

- **Stents**
  - Effective apposition of dissected plaque to expanded lumen wall
  - Problems
    - Large amount of foreign body
    - Rigidity of stent / fracture / micro-trauma
    - Restenosis
    - Poor options for reintervention

Our Challenge

- Too much metal to artery interaction
- Too much outward force
- Tissue apposition rather than scaffolding
  - PTA technique
  - Balloon angioplasty
  - Bioabsorbables
  - Stents

We need a new paradigm

Lower Extremity Stents
Too Much Scaffolding

Factors Associated with Stent Failure
- Stent overlap
- Chronic outward force
- Stent material
- Strut thickness
- Stent length
- Design/Fracture

No one volunteers for a full metal jacket!
**No Metal Left Behind: Improving POBA and Bioresorbable Stents**

**Improve Balloon Angioplasty Technique**

- Use a balloon that covers the entire length of the lesion.
- Increase pressure gradually so that it is only as high as it needs to be to dilate the lesion.
- Leave balloon inflated for 2-3 minutes.
- Repeat if necessary.

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**Bioresorbable Vascular Scaffold**

*CAUTION: Investigational use only. Not available for sale in or outside the U.S.*

- Provide acceptable lumen after treatment, then resorb naturally into the body, leaving the vessel in its native state.
- No implant left behind
- No permanent implant – restore natural vascular response to physiological stimuli and potentially late expansive remodeling
- No stimulus for chronic inflammation
- Future re-intervention is facilitated
- Compatible with non-invasive diagnostic imaging

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**Bioresorbable Stent Technology Overview**

- Product(s) / Technology overview:
- Polymer (PLLA) vs metal alloy (magnesium)
- Challenges: degradation rate, control of radial force, diameter sizing, brittleness, cost
1st Gen Porcine Coronary Safety Study: Representative Photomicrographs (2x)

Porcine Coronary Artery Model

BVS

Representative photomicrographs 2X.

CYPHER

Bioresorbable Scaffolds in the Peripheral Vasculature

<table>
<thead>
<tr>
<th>Study</th>
<th>Device</th>
<th>Lesions</th>
<th>n</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>PERSEUS</td>
<td>BE Poly-l-lactic acid</td>
<td>SFA</td>
<td>45</td>
<td>50% restenosis @ 6-mos.</td>
</tr>
<tr>
<td>BEST BTK</td>
<td>BE Magnesium alloy</td>
<td>infrapopliteal</td>
<td>20</td>
<td>90% clinical patency @ 3-mos.</td>
</tr>
<tr>
<td>AMS INSIGHT</td>
<td></td>
<td>infrapopliteal</td>
<td>37</td>
<td>68% restenosis @ 6-mos.</td>
</tr>
</tbody>
</table>


Igaki-Tamai bioabsorbable stent in the SFA

AMS INSIGHT – 6-mos. patency results

Fig. 4 Kaplan-Meier estimation (life-table method) of patency measured by quantitative vascular angiography. Lesion-based ITT analysis.

AMS INSIGHT – 6-mos. patency results

New Studies of Lower Extremity Bioabsorbable Stent

- **ESPIRIT I**
  - SFA and iliac, 30 patients, December 2011
  - Bioabsorbable Drug Eluting Vascular Scaffolds
  - Everolimus, same polymer as ABSORB
  - New scaffold design, larger diameter, longer length

- **ABSORB BTK in CLI**
  - CLI, infrapopliteal, September 2011
  - ABSORB device, CE mark for coronary artery disease

**Tack: Key Components**

- **Anchor Fixation:** Therapeutic component; 6 pair of anchors tack down focal irregularities
- **Pressure delivered at Focal Points**
- **Radiopaque Markers:** 6 RO markers aid in visualization

**Supporting Frame**
- Self expanding Nitinol, supports Inner Circle of 6 Anchor Fixation components
- **Short length** (6.0mm), effective implant: less metal, less friction
- **Hinged design prevents watermelon seeding during delivery**

**Outward Force**
- Substantially lower outward force than commercially available stents
- High outward force
- Always changing with artery diameter
Above-the-knee SFA stenosis

Tack: Above the Knee

Post-PTA dissection
Completion Arteriogram After Tack
1 yr angio follow-up After Tack

Tack: IVUS

Dissection Flap Seen Using Intravascular Ultrasound
Post Treatment Tack Permits Tissue Apposition

Goal is tissue apposition with positive remodeling

Popliteal artery occlusion
After wire loop subintimal recanalization and balloon angioplasty

Entry site

Re-entry site

Tack placement at dissection sites
After PTA

Completion arteriogram

Tack: Minimally Invasive to Minimal Injury

• Minimal Injury
  – Acute stent-like result without a stent.
  – Address major disadvantages of stents, without burning bridges.
  – Provide a new option, between PTA and stents.

• Incredibly versatile
  – Treat multiple lesions, a broad range of vessels, with a single catheter.
  – ‘Touch-up’ strategy that complements other therapies.
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Conclusion

- Current treatment paradigms with angioplasty and stents have limited success.
- No metal or less metal through bioresorbable stents or focal treatment with less metal implant may provide a more successful option.