Best Strategy is Still Out There: Bioresorbable Vascular Scaffold (BVS) and New Technology?

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DISCLOSURES

Consultant/Medical/Scientific Boards
- Abbott
- Boston Scientific
- Cardiva
- Cook Medical
- CR Bard
- Lake Regional Medical
- Medtronic
- Spectranetics

PVD Training
- Abbott
- Bard
- Boston Scientific
- Spectranetics
- TriReme Medical

Stockholders
- CardioProlific
- Cardiva
- Spectranetics
- Vasamed

Speaker’s Bureau
- Abbott
- Bard
- Boehringer-Ingelheim
- Bristol-Myers-Squibb/Sanofi
- Cardiva
- Cook Medical
- Cordis
- DSI/Lilly
- Spectranetics
• The SFA is the most commonly diseased artery in the body and is subjected to external compression, bending, elongation, and shortening.

• SFA disease is the most common cause of claudication but is also important in CLI which is often the product of multilevel disease.
The Goal of Endovascular Therapy of SFA Lesions in Claudicants

- Claudication results in a limitation of quality of life, only 5% of those patients will progress to CLI
- Thus, revascularization procedures are only justified if they are
  - Safe
  - Effective
- Potential redo-procedures
  - Expose the patient to a risk of complications
  - Result in incremental costs (Device cost minimal when compared to overall procedural costs)
SFA disease is Heterogenous

- Length of disease
- Vessel size and disease location (vessel mobility)
- Stenosis or Occlusion
- DeNovo or restenosis
- Associated thrombus (new or old)
- Coagulability status
- Ability to take antiplatelet drugs (bleeding issues, need for full anticoagulation with AF and valves.
- Degree of calcification
History of Interventional Therapy


Angioplasty Mechanism

Plaque Fracture

Stretching of Vessel Wall

Lumen Expansion


Blood Flow = \( f \ (r^4) \)

Small increase in lumen results in significant increase in blood flow
Andreas Grüntzig:

“Angioplasty is a **controlled** injury”

Too little → Elastic recoil → Restenosis

Too much → Neo-intimal hyperplasia → Restenosis
Must Look at Interventional Success Definitions

- Time frame (Procedural, 1 month, 6 mos, 1 yr, 5 yr)
- Limb Salvage or claudication
- Symptom Alleviation and Functional Capacity
- Lack of complications
- Ability to re-intervene if disease progresses (stents limit positive remodeling therefore potentially having a negative impact on re-intervention)
- Cost effectiveness
Therapy is Rapidly Evolving

• Balloons (Very high restenosis rate particularly long lesions, CTO’s)
  – DEB’s developed to address this

• Stents (Better initial patency than balloons but restenosis difficult to treat), stent fractures particularly with first generation stents, need for longer-term antiplatelet therapy)
  – High radial force fracture-resistant stents developed (Supera)
  – Covered stents (Viabahn)-long lesions and in-stent restenosis
    • Must have good outflow
      – Drug-eluting stents (Zilver PTX)

• Atherectomy devices to remove plaque and thrombus
• Atherectomy coupled with DEB
Long Term Problems: Which stents should we use?

Type I

Type II

Type III

Type IV
Impact of Stent Fracture on Patency: The Festo Study

Scheinert et al, JACC 2005, 45: 312-315
Multiple DEB’s have demonstrated a significant impact on SFA stenosis
No head-head comparisons so we can’t determine which is best
Two presently FDA approved
  – Bard Lutonix (Paclitaxol/Polysorbitol excipient)
  – Medtronic Impact DES (Paclitaxol/Urea excipient)
Delivers drug evenly to vessel wall
Not enough data in dense calcium, poor initial PTA results
No very long lesions in most studies
No present compensation to offset cath lab costs (Just Changed)
Drug Eluting Balloon

6 Months Binary Restenosis

<table>
<thead>
<tr>
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<th>DEB</th>
<th>PTA</th>
<th>DEB</th>
<th>PTA</th>
<th>DEB</th>
<th>PTA</th>
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<tr>
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</table>
THUNDER
5-Year Outcomes – Freedom from TLR

Logrank p=0.0003

Tepe, Zeller TCT 2011
Drug-Eluting SFA Stents (ZILVER PTX)

- Paclitaxol applied directly to stent with no polymer
- Delivers drug only to area of stent tines
- Initial studies in relatively short lesions
- No incremental revenue to offset increased cath lab costs
DES

3-Year Freedom from TLR Zilver PTX vs. Standard Care

<table>
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<th>Group</th>
<th>3-year TLR Rate</th>
<th>Reduction</th>
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<tr>
<td>Zilver PTX</td>
<td>16.3%</td>
<td></td>
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<tr>
<td>Optimal PTA + Provisional Bare Zilver</td>
<td>29.8%</td>
<td>45%</td>
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</tbody>
</table>

- Zilver PTX: 83.7% for 240 patients (p < 0.01 log-rank)
- Optimal PTA + Bare Zilver: 70.2% for 139 patients

- 3-Year TLR Rate Reduction: 45%
It requires 18.5 lbs. of force to compress the Supera™ stent 0.20 inches at its nominal length.
Correction of Ca++ Induced Stent Deformation

Baseline | Post BMS | Supera restores max stent lumen CSA

Courtesy of D. Cohen
Approved in June 2005, the GORE® VIABAHN® Endoprosthesis is the only stent-graft available in the US with an *SFA, Iliac and AV Access indication.*

Contoured proximal edge

CARMEDA® Bioactive Surface (CBAS® Surface)

Ultra-thin wall ePTFE tube

Unique, durable bonding film

Polished nitinol support

Lengths: 2.5, 5, 10, 15, 25 cm

Diameters: 5 mm – 13 mm

*Consult IFU for full indications, contraindications, and warnings*
Gore VIPER Clinical Study Data: 73% primary patency and 92% secondary patency at 1-year

- Prospective, multi-center
- 119 limbs at 12 sites
- Primary patency by duplex (peak systolic velocity ratio (PSVR) < 2.5)
- Independent Core Lab vessel sizing
- Average lesion length 19 cm
- 56% Chronic Total Occlusions
Recent Clinical Studies: Gore VIPER Clinical Study

Gore VIPER Clinical Study Data:\(^\text{11}\)

**Device Sizing**
Patency improved when device not oversized > 20% proximally

**Device Diameter**
Patency independent of device diameter (5, 6, 7 mm devices utilized, \(p = 0.22\))

**Lesion Length**
Patency independent of lesion length (lesions > 20 cm versus \(\leq 20\) cm, \(p = 0.51\))

Patency advantage with GORE® VIABAHN® Endoprosthesis amplified in lesions ≥ 20 cm.

When treating lesions at the same TASC II level, BMS were 2.71 times more likely to lose patency.

* Kaplan-Meier patency calculated at the end of the follow-up window
12-Month Primary Patency (K-M) for SFA Endovascular Therapies

See appendix for sources

Data differences depicted between these trials may not be statistically significant or clinically meaningful and different clinical trials may include differences in the demographics of the patient populations.
Rationale for the Development of Bioresorbable Vascular Scaffolds

• Limitations of metallic stents

  – restenosis
  – stent thrombosis
  – chronic inflammation
  – imaging artifacts
  – jailed side branches
  – inhibition of positive remodeling (shear stress adaptation)
  – prevention of normal physiologic function such as vasomotion
  – need for prolonged anti-platelet therapy
  – permanent implant complicating repeat intervention

Adapted from Waksman R. Update on bioabsorbable stents: From bench to bedside. J Interven Cardiol 2006;19:414-421.
Igaki-Tamai PLA Stent

Tamai et al, CCI 2001

Hideo Tamai
<table>
<thead>
<tr>
<th>Device</th>
<th>Study</th>
<th>Drug</th>
<th>Lesions</th>
<th>n</th>
<th>Outcome</th>
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<td>Igaki-Tamai</td>
<td>Igaki-Tamai FIM</td>
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<td>coronary</td>
<td>50</td>
<td>18% restenosis @ 12-months 28% TLR @ 10-years</td>
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<td>AMS (Biotronik)</td>
<td>PROGRESS AMS</td>
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<td>24</td>
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<td>REVA</td>
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<td>RESTORE I</td>
<td>none</td>
<td>coronary</td>
<td>22</td>
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<td>2 MACE @ 6-months</td>
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<tr>
<td>ABSORB (Abbott)</td>
<td>ABSORB Cohort A</td>
<td>everolimus</td>
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<td>30</td>
<td>12% restenosis @ 6-months</td>
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<td></td>
<td>ABSORB Cohort B</td>
<td>everolimus</td>
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<td>45</td>
<td>2.4% restenosis @ 6-months</td>
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<td>56</td>
<td>3.5% restenosis @ 12-months</td>
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<td>ABSORB Extend</td>
<td>everolimus</td>
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<td>200</td>
<td>0.5% TLR @ 6-months</td>
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<tr>
<td>DESolve (Elixir)</td>
<td>DESolve I</td>
<td>novolimus</td>
<td>coronary</td>
<td>15</td>
<td>0% restenosis @ 6-months</td>
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## Abbott Vascular Everolimus Eluting Bioresorbable Vascular Scaffold Components

<table>
<thead>
<tr>
<th>Scaffold</th>
<th>Coating</th>
<th>Drug</th>
<th>Delivery system</th>
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<tbody>
<tr>
<td>Bioresorbable</td>
<td>Bioresorbable</td>
<td>Everolimus</td>
<td>XIENCE V</td>
</tr>
</tbody>
</table>
| • Poly(L-lactide) (PLLA)  
• Naturally resorbed, fully metabolized | • Poly(D,L-lactide) (PDLLA) coating  
• Naturally resorbed, fully metabolized | • Similar dose density and release rate to XIENCE V | • World-class deliverability |

Photos taken by and on file at Abbott Vascular.
Absorb™ v. Cypher®

Absorb™

Representative photomicrographs of porcine coronary arteries, 2x

1 month 6 months 1 year 2 years 3 years 4 years

Cypher®

Photos taken by and on file at Abbott Vascular.

Tests performed by and data on file at Abbott Vascular.
• Lower MCUSA (maximum unsupported scaffold area)
• More even support of arterial wall
• More uniform strut distribution
• Lower late stent area loss
• Improved stent retention
• Unchanged material and strut thickness


Radial Strength

Figure 5. Acute radial strength data for ABSORB Cohort B (3.0 x 18 mm), XIENCE V (3.0 x 18 mm), Cypher Select (3.0 x 18 mm), and Taxus Liberté (3.0 x 20 mm) ($n = 5$ for each set) obtained using the MSI RX550 radial expansion force gauge. Tests were performed by and data are on file at Abbott Vascular.

A comparative assessment by optical coherence tomography of the performance of the first and second generation of the everolimus-eluting bioresorbable vascular scaffolds.

ABSORB Cohort B – two-year results

Pre-Absorb  | Immediately Post Absorb  | 6 Months  | 2 Years
--- | --- | --- | ---

Ormiston J, Serruys PW. ABSORB Cohort B Trial – Two year clinical and angiographic results of the ABSORB everolimus eluting bioresorbable vascular scaffold (poster). Transcatheter Cardiovascular Therapeutics; 2011 November 8; San Francisco, CA.


Ormiston J, Serruys PW. ABSORB Cohort B Trial – Two year clinical and angiographic results of the ABSORB everolimus eluting bioresorbable vascular scaffold (poster). Transcatheter Cardiovascular Therapeutics; 2011 November 8; San Francisco, CA.

Absorb™ v. XIENCE V® at 2-years

ABSORB™ BVS(B1+B2)
XV®(3.0 x 18mm subgroup, SPI+SPII+SPIII RCT)

758-day HR
0.97 [0.42,2.21]
p=0.9379

MACE (C-Death, MI, ID-TLR)

Time Post Index Procedure (Months)

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<th>Days</th>
<th>0</th>
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<th>194</th>
<th>284</th>
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<tr>
<td>XIENCE V®</td>
<td>227</td>
<td>224</td>
<td>219</td>
<td>211</td>
<td>204</td>
<td>202</td>
<td>191</td>
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Rapoza R. Absorb BVS Program: Long-term experimental data angiography, IVUS, OCT, histology and micro CT. Local Drug Delivery and Cardiovascular Course on Revascularisation; 2012 February 4; Geneva, Switzerland. ABSORB and XIENCE V are trademarks of the Abbott Group of Companies.
Recovery of Vasoreactivity after Absorb Implantation

• I don’t know what best therapy is. I try to tailor Rx to individual circumstances but we need randomized controlled trials rather than guesswork.
• Newer therapies show great promise but most come at substantial increased cost with no incremental coverage for cath lab expense. (Just changed)
• BVS with drug-elution promising but will need more flexible compression resistant iterations.
• A great start would be a registry on all devices to determine how we should treat patients.
Closing Remarks