New and Emerging Stent Designs

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Disclosures

Speaker’s Bureau:
• Boston Scientific
• Medtronic

Consultant:
• Boston Scientific

Medical/Scientific Boards:
• Boston Scientific
Current SFA stent technology

- Limitations are present though each generation appears to be improving
- Risk/reward in delivery vs patency vs cost
- Question of atherectomy/DCB as adjunct vs alternate therapy
- Operator use/ease of deployment
- Drug or nor drug?
- Are we following the coronary trail??
Previously approved stent technology

<table>
<thead>
<tr>
<th>Standard Nitinol Stents (SNS)</th>
<th>Wire Interwoven Stents</th>
<th>Covered/Stent Grafts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smart (Cordis)</td>
<td>SUPERA (IDEV)</td>
<td>Viabahn (Gore)</td>
</tr>
<tr>
<td>Protégé Everflex (eV3)</td>
<td></td>
<td>Fluency (Bard)</td>
</tr>
<tr>
<td>LifeStent (Bard)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Luminexx (Bard)</td>
<td></td>
<td></td>
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<tr>
<td>Absolute (Abbott)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xpert (Abbott)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zilver / PTX (Cook)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete SE (Medtronic)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Misago (Terumo)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FlexStent (Flexible Stent Tech)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Basic stent features

<table>
<thead>
<tr>
<th>Bare Metal Stents (BMS)</th>
<th>Drug-Eluting Stents</th>
<th>Covered Stents</th>
<th>Bioabsorbable Stents (BAS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncoated stents composed of bare metal that are permanently placed inside the affected artery</td>
<td>BMS that are coated with a polymeric material and release drugs locally</td>
<td>Metal stent structures with coverings composed of fabric or graft material such as polytetrafluoroethylene (PTFE)</td>
<td>Composed of biodegradable materials that can be absorbed or resorbed by the body</td>
</tr>
<tr>
<td>Constructed from a range of metals, including nitinol, stainless steel, cobalt chromium, platinum chromium</td>
<td>Stent releases the anti-proliferative or immunosuppressive drug over time, leaving behind the metallic stent in the artery</td>
<td>Graft material covering provides a direct barrier to tissue ingrowth and reduces the risk of chronic inflammation and restenosis</td>
<td>Bioabsorbable DES deliver anti-proliferative agents to prevent restenosis and degrade over time, eliminating concerns regarding late-stent thrombosis, chronic inflammation, acute vessel closure, and biocompatibility</td>
</tr>
<tr>
<td>Either self-expanding or balloon-expandable</td>
<td>Either self-expanding or balloon-expandable</td>
<td>Either self-expanding or balloon-expandable</td>
<td>Represent the future of stent technology</td>
</tr>
</tbody>
</table>

Biomimetic

• “Relating to or denoting synthetic methods that mimic biochemical processes”
• IDEV Supera
• Veryan medical- Biomimics 3D stent system
• Stents to adjust/conform to anatomy, rather than having anatomy adjust (i.e. “straighten out”) to technology
• Current investigational
BioMimics 3D

Contemporary nitinol stents use various connector configurations:

- **Complete SE:** *short co-linear*
- **Zilver PTX:** *longer co-linear*
- **EverFlex:** *spiral*

Veryan’s design utilizes:
SHORT + LONG connectors in SPIRAL configuration ...

... and also adds 3D helical geometry to nitinol shape memory

- Promotes swirling flow + increase wall shear stress
- Enhances biomechanical performance

1. Caro et al., 2013
2. Data held on file at Veryan Medical
BioMimics 3D Stent Design

- Longer connectors enable more movement between stent crowns
- Use of 3 longer connectors ensures
  - stent fully supports a patent lumen during flexion
  - stent moves more freely with the vessel during leg bending
- Shorter connectors between subsequent crowns provide the support to the 3D helical centreline geometry
Stent Flexibility

- 3-point bend test is a measure of stent flexibility.
- Lower resistance exerted equates to better flexibility.

Data held on file at Veryan Medical
Stent Platform

Unique 3D Stent Geometry

Size Matrix

<table>
<thead>
<tr>
<th>Stent Length (mm)</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>80</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>100</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>125</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>150</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

- Highly flexible pattern
- Tapered radial stiffness at ends
- Stent ends formed to be collinear with vessel

CAUTION: Investigational Device. Limited by Federal (or United States) Law to Investigational Use
Improved Biomechanical Performance

- 3D helical geometry in BioMimics 3D stent is designed to manage vessel slack and reduce risk of buckling / kinking during knee flexion/extension

Increased curvature in stented segment as leg bends
Swirling Flow in Stented Segment

- High wall shear protects against atherosclerosis and restenosis
- 3D helical geometry promotes swirling flow to elevate wall shear

3. Malek et al., JAMA, 1999
4. Caro et al., 2013
Drug eluting stents

• Zilver PTX already in the arena
• New and emerging methods of elution/stent make-up
• Which drug? Which stent?
• Polymer or no polymer?
• Suspect this will be a very large growth field but cost has to be a consideration
## Drug Eluting Stents - Peripheral

<table>
<thead>
<tr>
<th>Product Image</th>
<th>SFA</th>
<th>BTK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zilver PTX</td>
<td>Eluvia DES</td>
<td>Promus Element Plus BTK</td>
</tr>
<tr>
<td>Cook Medical</td>
<td>Boston Scientific</td>
<td>Boston Scientific</td>
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</table>

### CE Mark/US Approval

<table>
<thead>
<tr>
<th>CE</th>
<th>US</th>
<th>CE</th>
<th>US</th>
<th>CE</th>
<th>US</th>
<th>CE</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td>✓</td>
<td>No</td>
<td>No</td>
<td>✓</td>
<td>No</td>
<td>✓</td>
<td>No</td>
</tr>
</tbody>
</table>

### Stent Platform

<table>
<thead>
<tr>
<th>Zilver Flex</th>
<th>Innova</th>
<th>Promus Premier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitinol</td>
<td>Nitinol</td>
<td>Platinum Chromium Alloy</td>
</tr>
<tr>
<td>None</td>
<td>Biostable Fluorinated Polymer Matrix</td>
<td>Biostable Fluorinated Polymer Matrix</td>
</tr>
</tbody>
</table>

### Material

<table>
<thead>
<tr>
<th>Nitinol</th>
<th>Nitinol</th>
<th>Cobalt Chromium</th>
</tr>
</thead>
</table>

### Polymer

<table>
<thead>
<tr>
<th>None</th>
<th>Biostable Fluorinated Polymer Matrix</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel</td>
<td>Paclitaxel</td>
<td>Everolimus</td>
</tr>
</tbody>
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### Drug

<table>
<thead>
<tr>
<th>Paclitaxel</th>
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<th>Everolimus</th>
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</table>

### Deployment

<table>
<thead>
<tr>
<th>Self-expandable</th>
<th>Self-expandable</th>
<th>Balloon Expandable</th>
<th>Balloon Expandable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter</td>
<td>Length</td>
<td>Diameter</td>
<td>Length</td>
</tr>
<tr>
<td>6-8mm</td>
<td>40-120mm</td>
<td>6-7mm</td>
<td>40-150mm</td>
</tr>
<tr>
<td>Diameter</td>
<td>Length</td>
<td>Diameter</td>
<td>Length</td>
</tr>
<tr>
<td>2.25-4mm</td>
<td>12-38mm</td>
<td>2.5-4mm</td>
<td>28-38mm</td>
</tr>
</tbody>
</table>

www.abbottvascular.com/int/products/peripheral-intervention/xience-prime-btk.html#ordering-information
www.medicalexpo.com/prod/abbott-vascular/peripheral-stents-drug-eluting-90137-572891.html
Cook Medical (2014). Zilver PTX Drug-Eluting Peripheral Stent Instructions for Use
http://zilverptx.cookmedical.com/us/index.html#

Eluvia is an investigational device. Limited under U.S. law for investigational use only. Not available for sale.
Eluvia Drug-Eluting Vascular Stent System

- CE Mark February 2016
- Innova stent platform
  - Self-expanding nitinol
- Biostable polymer matrix
- Paclitaxel

- 6F Tri-axial SDS, 0.035” guidewire compatible
- Blue Tri-Ax shaft fixed as the clear middle shaft is retracted releasing stent during deployment

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Eluvia Drug Eluting Stent:

Stent Architecture

Balanced geometry designed for even stress distribution and optimal radial strength

Spacing of interconnects provides balanced stress distribution for all deformation modes

Width, Length and angles optimized for maximum strength

Radial Force and Flexibility must be matched by excellent Fracture Resistance

Stent Fracture rates in studies using the INNOVA Stent platform:

- SuperNOVA Study (Innova): 2.2 at 24M
- The MAJESTIC Study (Eluvia): 0.0% at 12M

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Eluvia Coating Design

- Dual Layer System
- Conformal Coating for Both Layers
- Primer Layer (PBMA): Promotes Adhesion of Active Layer to Stent
- Active Layer (PTx, PVDF-HFP) – Controls Release of Paclitaxel
  - 0.167µg PTx/mm² stent surface area
## Coating Design Specifications

<table>
<thead>
<tr>
<th></th>
<th>Zilver PTX</th>
<th>Eluvia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medicinal Substance</strong></td>
<td>Paclitaxel</td>
<td>Paclitaxel</td>
</tr>
<tr>
<td><strong>Coating Design</strong></td>
<td>No carrier</td>
<td>Proven PROMUS Polymer</td>
</tr>
<tr>
<td><strong>Drug/Total Dose</strong></td>
<td>3µg/mm², 8 x 120mm = 1112 µg</td>
<td>0.167µg/mm², 7 x 150mm = 517 µg</td>
</tr>
<tr>
<td><strong>Size Matrix</strong></td>
<td>6-8mm, 40-120mm</td>
<td>6 &amp; 7mm, 40-150 mm</td>
</tr>
<tr>
<td><strong>SEM Image 100x</strong></td>
<td><img src="image1.png" alt="SEM Image" /></td>
<td><img src="image2.png" alt="SEM Image" /></td>
</tr>
</tbody>
</table>

Boston Scientific Data on File.
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# Eluvi Drug-Eluting Vascular Stent System for SFA: MAJESTIC Clinical Study

## MAJESTIC Clinical Study

<table>
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<tr>
<th>Study Overview: MAJESTIC</th>
</tr>
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<tbody>
<tr>
<td><strong>Device</strong></td>
</tr>
<tr>
<td><strong>Objective</strong></td>
</tr>
<tr>
<td><strong>Study Design</strong></td>
</tr>
<tr>
<td><strong>Subjects</strong></td>
</tr>
</tbody>
</table>
| **Investigational Centers** | 14 sites (Europe, Australia, New Zealand)  
No center to enroll > 20% (11 subjects) of the total study population |
| **Follow-up**            | Baseline, Procedure 1 month, 9 months, 1 year, 2 years, 3years |
| **Primary Endpoint**     | Primary patency of target lesion at 9 months  
• Primary endpoint met: 9M patency of 94.4% |
Patency at 12 Months: DES vs BMS

- Kaplan-Meier estimate for Eluvia DES: 96.4%
- Paclitaxel effect suggested by divergence from bare metal platform

Primary patency defined as duplex ultrasound peak systolic velocity ratio ≤2.5 (MAJESTIC) or ≤2.4 (SuperNOVA) and absence of TLR or bypass.

*Patients who received 20-120 mm length Innova stents (n=202).
Bioabsorbable stents

PLLA Igaki--Tamai (Remedy) Scaffold
Patency of the Igaki---TamaiR scaffold in the SFA

- High re-stenosis rates
STANZA Bioresorbable Scaffold
Esprit Bioresorbable Vascular Scaffold (BVS)
Structure/design

- Bioresorbable scaffold: Poly (L-lactide) (PLLA)
- Naturally resorbed, fully metabolized
- Designed for SFA and Iliac Arteries
- Poly (D,L-lactide) (PDLLA) coating
- Everolimus
- Balloon-Expandable delivery system
- 035” OTW platform
- ESPRIT I: 13% restenosis @ 12-months
Conclusions

• Very exciting time for peripheral arterial stent technology
• The truth may not lie with one specific technology but rather a possible “cocktail” of technologies
• DCB, atherectomy, DES in conjunction rather than one tool
• Difficulty in performing studies given the myriad of combinations
• Cost will also be a factor as well as patency
Thank You!!
New and Emerging Stent Designs

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18th Annual Conference
May 31 - June 02
THE PERIPHERAL EVENT OF THE YEAR