Update on Interventional Cardiology – Bioabsorbable Stents

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Faculty Disclosure

• Robert C. Welsh

• Relationships with commercial interests:
  – Grants/Research Support: Abbott Vascular, Astra Zeneca, Bayer, Boehringer Ingelheim, Bristol Myers-Squibb, Eli Lilly, Jansen, Johnson and Johnson, Pfizer, Portola, Regado, Roche, Sanofi Aventis
  – Honoraria: Abbott Vascular, Astra Zeneca, Bayer, Bristol Myers-Squibb, Edwards Lifesciences, Eli Lilly, Medtronic, Roche, Sanofi-Aventis
  – Consulting Fees: Abbott Vascular, Astra Zeneca, Bayer, Edwards Lifesciences, Eli Lilly, Medtronic, Roche, Sanofi-Aventis
  – Other: Employee of Alberta Health Services and University of Alberta and President of The Canadian Centre for Clinicians and Scientists
## Trends in PCI: Improvement in Patient Outcomes with the Opportunity for Further Advances

<table>
<thead>
<tr>
<th>Plain Old Balloon Angioplasty – POBA</th>
<th>Bare Metal Stent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Decade</strong></td>
<td><strong>Decade</strong></td>
</tr>
<tr>
<td>1980s</td>
<td>1990s</td>
</tr>
<tr>
<td><strong>Acute Success rate</strong></td>
<td><strong>Acute Success rate</strong></td>
</tr>
<tr>
<td>70-85%</td>
<td>&gt;95%</td>
</tr>
<tr>
<td><strong>Restenosis</strong></td>
<td><strong>Restenosis</strong></td>
</tr>
<tr>
<td>40-45%</td>
<td>20-30%</td>
</tr>
<tr>
<td><strong>Early Thrombosis &lt;30 days</strong></td>
<td><strong>Early Thrombosis &lt;30 days</strong></td>
</tr>
<tr>
<td>3-5%</td>
<td>1-2%</td>
</tr>
<tr>
<td><strong>Late Thrombosis &gt;30 days</strong></td>
<td><strong>Late Thrombosis &gt;30 days</strong></td>
</tr>
<tr>
<td>NA</td>
<td>&lt;0.5%</td>
</tr>
<tr>
<td><strong>Very Late Thrombosis (&gt;1y)</strong></td>
<td><strong>Very Late Thrombosis (&gt;1y)</strong></td>
</tr>
<tr>
<td>NA</td>
<td>≈0%</td>
</tr>
</tbody>
</table>

**Note:**
- **Early Thrombosis** refers to thrombosis occurring within 30 days of the procedure.
- **Late Thrombosis** refers to thrombosis occurring after 30 days but within a year of the procedure.
- **Very Late Thrombosis** refers to thrombosis occurring more than a year after the procedure.
Trends in PCI: Improvement in Patient Outcomes with the Opportunity for Further Advances

**First Generation Drug Eluting Stents - DES**

<table>
<thead>
<tr>
<th>Drug Eluting Stent</th>
<th>Decade</th>
<th>Acute Success rate</th>
<th>Restenosis</th>
<th>Early Thrombosis &lt;30 days</th>
<th>Late Thrombosis &gt;30 days</th>
<th>Very Late Thrombosis (&gt;1y)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2000s</td>
<td>&gt;95%</td>
<td>&lt;10%</td>
<td>1-2%</td>
<td>1-2%</td>
<td>1-2%</td>
</tr>
</tbody>
</table>
Cumulative rate of restenosis (A) and definite stent thrombosis (B) up to 2 years in bare-metal stents (BMS), old-generation drug-eluting stents (o-DES), and new-generation drug-eluting stents (n-DES).

<table>
<thead>
<tr>
<th>N at risk</th>
<th>0 months</th>
<th>6 months</th>
<th>12 months</th>
<th>18 months</th>
<th>24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMS</td>
<td>64631</td>
<td>56070</td>
<td>47968</td>
<td>40539</td>
<td>32698</td>
</tr>
<tr>
<td>o-DES</td>
<td>19202</td>
<td>17862</td>
<td>16014</td>
<td>13517</td>
<td>10533</td>
</tr>
<tr>
<td>n-DES</td>
<td>10551</td>
<td>8092</td>
<td>4188</td>
<td>2005</td>
<td>847</td>
</tr>
</tbody>
</table>

Sarno G et al. Eur Heart J 2012;33:606-613

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Reflection on the potential role of bioabsorbable stents

- leave behind only the healed natural vessel
- Leave vessel ‘free’ for future revascularization
- allowing restoration of vasoreactivity
- potential of positive vessel remodeling
- late stent thrombosis is unlikely
- are compatible with MRI and MSCT imaging
- suitable for complex anatomy where stents impede on vessel geometry and morphology
  - potential in peripheral arterial disease
- could be used as a delivery device for agents such as drugs and genes
- perhaps play a role in the treatment of vulnerable plaque
Are bioabsorbable stents a disruptive Innovation?

A disruptive innovation is an innovation that helps create a new market and value network, and eventually disrupts an existing market and value network (over a few years or decades), displacing an earlier technology.
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XIENCE V versus ABSORB BVS

- **XIENCE V** –
cobalt chromium with fluoropolymer with controlled release of everolimus

- **Absorb** – original version:
poly-L-lactide (PLLA) covered with poly-D,L-lactide (PDLLA), containing and controlling release of everolimus

- **Absorb** – Clinical version:
uniform strut distribution, even support, higher radial strength, storage at room temperature
Initial clinical data support the concept of Vascular Reparative Therapy (VRT).
BVS Works in 3 Phases to Deliver VRT

Data and images on file at Abbott Vascular. Histology images are from porcine animal models. *Small platinum markers at scaffold edges remain for fluoroscopic landmarking.
Late lumen enlargement/gain and ‘characteristic ‘final golden tube’ on OCT illustrating functional reparation of the vessel.

Images courtesy of Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands
Very late lumen enlargement noted from 6 months to 2 years

*Serruys, PW., TCT 2011
Similar Rates of MACE Compared to Historical XIENCE Data

Case presentation – Mr MPL

- 55 yo. Male with recurrent retrosternal chest pressure with prior PCI/stent in 1st diagonal – 3 years ago
- Clinical impression of Non ST-ACS
  - No dynamic ECG changes and negative troponin
- Type 2 Diabetes – oral hypoglycemics and long acting insulin
- Treated hypertension
- Echocardiogram – Normal LVEF – no wall motion abnormalities
Comments: NSTEMI. Tight RCA long lesion. Suggest PCI of RCA.
BVS positioning – Distal RCA

2.5mm X 28mm BVS
‘proximal’ BVS positioning – distal RCA

2.5mm X 18mm BVS
Limitations of Current Polymer Technology

**Acute Delivery**

**BVS:**

*Significant vessel prep often required, non-uniform deployments*

**Over-Expansion**

**BVS:**

*Over-expansion by 0.75 mm*

*Porcine animal study, MicroCT*

**Side Branch Access**

**BVS:**

*Side Branch Access*

*Bench testing with stent deployment per IFU*
Unique Continuous Sinusoid Technology Enables New Stent Constructions

<table>
<thead>
<tr>
<th>Uniform Cross-Section Wire</th>
<th>Core Wire</th>
<th>Core Wire, Decore, and Hole Drilling</th>
<th>New Alloys</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resolute Integrity™</td>
<td>Resolute Onyx™</td>
<td>Drug Filled Stent</td>
<td>Metal Bioabsorbable</td>
</tr>
</tbody>
</table>
Material Selection – A Balancing Act

Challenge Is to Balance the Trade-offs

**Mechanical Properties**

Polymer properties that enable radial strength and deliverability

- **CoCr**
  - 50%

- **Mg**
  - 240%

- **PLLA**

**Surface Treatment**

- **Day 0**
- **Day 66**
- **Day 126**

Strut cross-section after degradation

- Feasibility proven, currently optimizing
- Design target:
  - 6 months structural integrity
  - ~12 months full degradation

**Biocompatibility and Safety**

Must not cause significant inflammatory response as it degrades

1. Internal Medtronic calculation based on material properties
2. ‘Biodegradable systems in tissue engineering and regenerative medicine’, Reis and Roman, CRC PRESS, 2005
Metallic Bioabsorbable – Acute Performance

Radial Strength

![Graph showing stiffness (N/mm) for Integrity, Mg Spiral, and Vision.]

- Integrity
- Mg Spiral
- Vision

2D Tracking

![Graph showing average peak force (gf) for Integrity*, Mg Spiral, and Vision*.]

- Integrity*
- Mg Spiral
- Vision*

* Integrity and Vision are 2.5 x 18 mm
* Mg spiral is 3.0 x 18 mm

No stepped inflation to nominal

CAUTION: Design concepts not approved for sale or clinical use
Metallic Bioabsorbable Stent: Developing a Workhorse Technology

**Deliverability**

Results of blinded randomized pairwise deliverability comparisons*

*1 physician running each design 3 times

**Porcine Carotid Pin Model**

*Animal deliverability test*

Repeatable tortuous vascular path created by placing carotid between pre-set pins

*Higher is better*
Conclusion

The potential of BVS and Vascular Reparative Therapy

- DES
- VRT: Improved long-term outcomes
- Native CAD
- PCI
- Revascularizes
- Resorbs
- Restores
- Vasomotion
- Functional endothelium
- Mechanical conditioning
- Scaffold degradation
- Late lumen gain
- Delayed disease progression

Native Vessel Function vs. Time
Conclusion

ABSORB supports Vascular Reparative Therapy by

• With available data - Revascularizing like currently available DES

• Restoring mechanical freedom to the vessel, unconstrained by a permanent metal implant

• Resorbing benignly leaving no permanent implant behind

Images courtesy of Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands, ABSORB A 5 yr
*Small platinum markers at scaffold edges remain for fluoroscopic landmarking.