Yunbing Wang
Nadine Ding, James Oberhauser
Thierry Glauser, Xiao Ma, Derek Mortisen

Bioabsorbable Vascular Solutions (BVS)
Abbott Vascular
Santa Clara, CA
Evolution of Intravascular Technology

- **1929**: Human Cardiac Catheterization by Dr. Werner Forssman
- **1960**: Bypass Surgery by Dr. Robert Goetz
- **1977**: Balloon Angioplasty by Dr. Andreas Gruentzig
- **1994**: Metallic Stents
- **2003**: Drug Eluting Stent

Source: PTCA.org
Key challenges:
- Vessel recoil / closure
- Cellular proliferation / restenosis
Metallic Stent

Key challenge:
- In-stent stenosis
- Intimal proliferation
# DES with durable polymeric coating layer

## First Generation DES

<table>
<thead>
<tr>
<th>Product name</th>
<th>Company</th>
<th>Structure thickness</th>
<th>Drug</th>
<th>Drug carrier</th>
<th>Coating thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYPHER</td>
<td>Cordis</td>
<td>140 µm</td>
<td>Sirolimus</td>
<td>PBMA/EVA</td>
<td>12.6 µm</td>
</tr>
<tr>
<td>TAXUS</td>
<td>Boston Scientific</td>
<td>132 µm</td>
<td>Paclitaxel</td>
<td>PS-PIB copolymer</td>
<td>16 µm</td>
</tr>
</tbody>
</table>

## Second Generation DES

<table>
<thead>
<tr>
<th>Drug</th>
<th>Drug carrier</th>
<th>Coating thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zotarolimus</td>
<td>PC copolymer</td>
<td>5.3 µm</td>
</tr>
<tr>
<td>Everolimus</td>
<td>PVD-HFP</td>
<td>7.8 µm</td>
</tr>
<tr>
<td>ENDEAVOR</td>
<td>Medtronic Vascular</td>
<td>91 µm</td>
</tr>
<tr>
<td>XIENCE V</td>
<td>Abbott Vascular</td>
<td>81 µm</td>
</tr>
</tbody>
</table>

Carlos Calderas, et al. TCT2008
Evolution of DES Technology

➢ **First Generation of DES:** Cypher and Taxus

➢ **Second Generation:** Endeavor and Xience

➢ **New Generation:**
  • Biodegradable drug carrier
  • Non-polymeric based drug carrier
  • Direct deposition of drug on the device surface (w/o drug carrier)
  • Direct “burst” delivery of drug into the vessel wall (w/o using stent)
  • Fully bioabsorbable implant
Criteria for Future Generation Drug Eluting Implants

- Reduce long-term dual antiplatelet therapy

- Long-term biocompatibility and safety
  - promote stable intimal formation/healing
  - fully functional endothelium
  - optimized drug release kinetics

- Efficacy in inhibiting re-stenosis
  - inhibition of excessive SMC growth and matrix deposition
  - promotion of re-endothelialization

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# DES with bioabsorbable coating

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>NEVO™ stent</th>
<th>JACTAX stent</th>
<th>BioMatrix Stent</th>
<th>Supralimus Stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug carrier</td>
<td>PLGA</td>
<td>DLPLA</td>
<td>PLA</td>
<td>PLLA/PLGA/PVP</td>
</tr>
<tr>
<td>Drug</td>
<td>Sirolimus</td>
<td>Paclitaxel</td>
<td>Biolimus A9</td>
<td>Sirolimus</td>
</tr>
<tr>
<td></td>
<td>abluminal surface only</td>
<td>abluminal surface only</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
DES with bioabsorbable coating – NEVO™

Cordis NEVO™ Sirolimus eluting Coronary Stent

- Fully bioresorbable PLGA polymer (exclusively housed in reservoirs)
- Complete resorption in 3-4 months
- Highly biocompatible and hemocompatible
- Controlled Sirolimus release without a surface coating
- Drug delivered over period of ~3 months (in vivo)
DES with bioabsorbable coating – JACTax

JACTax Stent – Ultrathin Abluminal coating of microdots on precrimped stent

Polymer thickness ≤1 µm

Designed to fully release drug in 60 days and resorb in 4 month
Polymer-Free DES System

Potential Advantage:

• Possible shorter need of dual antiplatelet therapy

• Prevent access clot formation that might be attribute to the polymeric coating

• Improved integrity since no coating layer would be sheared or peeled away from the stent struts

• Less inflammation

• Greater healing
Polymer-Free DES System

Design Types

• Drug in “pure” form is impregnated into nano/micro porous surface

• Non-polymeric drug carrier

• Drug is attached to the stent surface through chemical bonding or physical bonding
## Polymer-Free DES System

<table>
<thead>
<tr>
<th></th>
<th>Medtronic Setagon stent</th>
<th>Biosensor BioFreedom Stent</th>
<th>MIV Therapeutics stent</th>
<th>Minvasys Nile PAX</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
<td><img src="image5.png" alt="Image" /></td>
</tr>
<tr>
<td><strong>Drug</strong></td>
<td>Zotarolimus</td>
<td>Biolimus A9</td>
<td>Sirolimus</td>
<td>Paclitaxel</td>
</tr>
<tr>
<td><strong>Drug carrier</strong></td>
<td>No</td>
<td>No</td>
<td>Hydroxyapatite</td>
<td>No</td>
</tr>
<tr>
<td><strong>Drug in nano-porous metal surface</strong></td>
<td>Drug in nano-structured surface holds drug in abluminal surface structures</td>
<td>Drug in thin hydroxyapatite coating</td>
<td>Microdrop spray crystallization process. Abluminal drug release</td>
<td></td>
</tr>
</tbody>
</table>

Juan F. Granada, Alexandre Abizaid, J.N. Wilcox, TCT 2008
SETAGON Nano-Porous Polymer Free DES

- Nanoporous, non-polymeric stent surface with the ability to deliver a therapeutic agent

- The nanoporous surface to provide rapid, healthy endothelialization and vascular healing - potential to be a pro-healing surface

- Ability to inhibit restenosis and cell proliferation

- Potential to reduce long-term DAPT
Drugs Eluting Balloon (DEB)

- No residue polymer or other implant left
- Deliver drugs to vessel areas not directly covered by the stent (edges, small vessels, tortuous vessels)
- Homogenously drug distribution to the arterial wall (~80% of the stented vessel wall area is not covered by the stent struts).
- Additional flexibility and efficacy
- No sustained drug release from stent struts to allow for potential early healing and re-endothelialization

[Images of uncoated, coated, and expanded DEB balloons]
Potential Advantages of a Bioabsorbable implant

➢ Perform the functions of a DES, then be naturally absorbed and metabolized by the body.

➢ Leave no permanent metallic implant.
  – No stimulus for chronic inflammation – potentially reducing the need for long-term dual antiplatelet therapy.
  – No permanent scaffold – Likely permitting return of normal vasomotion and late expansive remodeling.
  – Facilitate re-intervention

➢ Provide compatibility with non-invasive diagnostic imaging (MR/CT), allowing non-invasive follow-up.
Principles of Bioabsorbable Implant Design: Three Phases of Device Performance

History of Bioabsorbable Implant Development

1980s  Duke Implant

REVA implant

BTI implant

1990s  Igaki-Tamai implant

Cordis implant

OrbusNeich implant

2000s

Medtronic prototype

Biotronik Magnesium implant

Abbott BVS implant
REVA Bioabsorbable Implant: Slide & Lock Design

“Steel like” performance in a tyrosine-derived polycarbonate implant

• High radial strength
• Flexible and conformable
• Standard balloon deployment
• MRI/CT compatible
• Expansion based on sliding, locking parts rather than material deformation
Structure of the Abbott BVS Bioabsorbable Implant

- **Everolimus/PLA Matrix Coating**
  - Thin coating layer
  - Amorphous (non-crystalline)
  - Everolimus/PLA matrix
  - Conformal Coating
  - Controlled drug release

- **PLLA Stent Backbone**
  - Highly crystalline
  - Provides stent integrity
  - Processed for increased radial strength and toughness
Radial Strength

Flat Plate Compression Testing (3.0 x 18mm)

Radial strength comparable to metal stent at T=0

Data on file at Abbott Vascular.
Radial Strength Over Time

In Vitro Degradation Testing (Cohort B BVS)

Data on file at Abbott Vascular.
Stent/SDS Flexibility

VISION
n=5

Cohort B BVS
n=5

Force (gf)

LESS Flexible

MORE Flexible

Data on file at Abbott Vascular.
ABSORB 24-Month OCT Images

Case Example
24-Month Results – A Glimpse at One Patient

Vasomotor Function Study

<table>
<thead>
<tr>
<th></th>
<th>Pre-Methergine</th>
<th>Post Methergine (5 min)</th>
<th>Change N (%)</th>
<th>Post Nitroglycerine</th>
<th>Change N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-Stent Mean Diameter</td>
<td>2.62 mm</td>
<td>1.98 mm</td>
<td>-0.64mm (-24.4%)</td>
<td>2.58 mm</td>
<td>+0.60mm (+30.3%)</td>
</tr>
<tr>
<td>Mean Diameter 2-17mm Distal to Stent</td>
<td>2.70 mm</td>
<td>2.08 mm</td>
<td>-0.62mm (-23.0%)</td>
<td>2.62 mm</td>
<td>+0.54mm (+26.0%)</td>
</tr>
</tbody>
</table>

Adapted from P. Serruys presentation, ESC, Munich, Sept. 2008

Product currently in development at Abbott Vascular. Not available for sale.
Questions