Bench-testing evaluation of a novel fully drug-eluting BRS

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19th May Thursday, 16:30-16:38, ROOM 351
Potential conflicts of interest

Speaker's name: Patrick W. Serruys, MD, PhD

- I do not have any potential conflict of interest
If a bioresorbable scaffold is ultimately expected to have the same range of applicability as a durable metal stent, the gap in mechanical properties must be reduced.

Currently, three primary limitations exist:

- **Low tensile strength and stiffness** which require thick struts to prevent acute recoil
- **Insufficient ductility** which impacts scaffold crimping and retention on balloon catheter and limits the range of scaffold expansion during deployment
- **Instability of mechanical properties** during vessel remodeling if bioresorption is too fast
Let’s take a “crash course” of material science

- Tensile strength (Mpa)
- Tensile modulus of elasticity (GPa)
- Elongation at break (%)
- Plastic elongation
- Yield
- Ultimate Strength
- Fracture

Graph showing stress (MPa) vs elongation (%), with sections for strain hardening, necking, and fracture.
**DUCTILITY** is a solid material's ability to deform under tensile stress; Insufficient ductility impacts scaffold retention on balloon delivery system catheter and limits the range of scaffold expansion during deployment.

- **Minimal ductility - Brittle fracture**
- **Medium ductility**
- **Ductile but with low ultimate stress**
- **Necking+**
- **Necking+++**
Performance goal and mechanical dilemma

Current generation BRS

Greater Tensile strength

More ductility

Greater % elongation at break

Performance goal for NEW generation BRS
# Mechanical properties of metal vs. PLLA

<table>
<thead>
<tr>
<th>Polymer/ metal</th>
<th>Tensile modulus of elasticity (Gpa)</th>
<th>Tensile strength (Mpa)</th>
<th>Elongation at break (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poly(L-lactide)</td>
<td>3.1-3.7</td>
<td>60-70</td>
<td>2-6</td>
</tr>
<tr>
<td>Poly (DL-lactide)</td>
<td>3.1-3.7</td>
<td>45-55</td>
<td>2-6</td>
</tr>
<tr>
<td>Magnesium alloy</td>
<td>40-45</td>
<td>220-330</td>
<td>2-20</td>
</tr>
<tr>
<td>Cobalt chromium</td>
<td>210-235</td>
<td>1449</td>
<td>~40</td>
</tr>
</tbody>
</table>

Onuma and Serruys Circulation 2011
Polymer composition

Poly(L-lactide)
Poly (DL-lactide)
Poly (glycolide)
50/50 DL-lactide/glycolide
82/18 L-lactide/glycolide
70/30 L-Lactide/ε-caprolactone etc...

Onuma and Serruys Circulation 2011
#1 “Playing” with composition of polymers

Acute Radial Strength Comparison

In-vitro @ 37 °C

Radial Strength (psi)

Formulation 01: 4.4
Formulation 02: 5.8
Formulation 03: 6.3
Formulation 04: 5.5
Formulation 05: 6.8
Formulation 06: 6.6
Formulation 07: 10.2
Formulation 08: 10.5
Formulation 09: 7.7
Formulation 10: 7.3
Formulation 11: 13.3

Absorb: 157μ
Tube wall thickness of < 95 µm can be achieved
Scaffold tube thickness comparable to metallic DES
Oriented material properties significantly higher than un-oriented PLLA

Favourable comparison to strength of metallic materials used in stent production

<table>
<thead>
<tr>
<th>Material</th>
<th>PLLA</th>
<th>Oriented PLLA</th>
<th>Stainless Steel</th>
<th>Cobalt Chrome</th>
<th>Magnesium Alloy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultimate tensile strength (MPa)</td>
<td>~30-50</td>
<td>220-260</td>
<td>670</td>
<td>820-1200</td>
<td>280</td>
</tr>
<tr>
<td>Tensile Modulus (Gpa)</td>
<td>1.2-3.0</td>
<td>5-7</td>
<td>193</td>
<td>243</td>
<td>45</td>
</tr>
<tr>
<td>Elongation (%)</td>
<td>2-6</td>
<td>40-70</td>
<td>48</td>
<td>35-55</td>
<td>23</td>
</tr>
</tbody>
</table>
Radial force at inflexion point

Platform 1: 9.5 N
Platform 2: 11.2 N
ABSORB: 14.35 N
Metallic stent: 15.8 N

Crush resistance test

Impact of platform and polymer on radial force compared to metallic stents

Metallic stent

15.8 N
- Crush resistance with radially applied load
- ISO 25539-2 test performed by ProtomedLabs
- ArterioSorb™ has comparable radial strength to ABSORB despite a 95 µm wall thickness

<table>
<thead>
<tr>
<th>Scaffold</th>
<th>Wall Thickness (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ArterioSorb™ 95 µm-3.5mm</td>
<td>95</td>
</tr>
<tr>
<td>ArterioSorb™ 120 µm-3.5mm</td>
<td>120</td>
</tr>
<tr>
<td>ABSORB 3.5mm</td>
<td>157</td>
</tr>
<tr>
<td>Xience 3.0 mm</td>
<td>81</td>
</tr>
</tbody>
</table>

Crush resistance data on file at Arterius
- Second design iterations are ArterioSorb™ 95 µm and ArterioSorb™ 120 µm strut thickness design leading to lower disruption of arterial flow and less likelihood of thrombosis
- 8 crowns, Smaller cells at the centre provide increased structural support where the stenosis is most severe and a larger dose of drug
- Wider crowns redistributes stresses during expansion
- Dual Platinum markers
- Sirolimus eluting scaffold with different size (PDLA coating)
- Spiral connectors, design provides high radial strength and yet appropriate flexibility for ease of implantation
- Design provides high radial strength and yet appropriate flexibility for ease of implantation
Bench Testing – Scaffold Crimping and Expansion

- Low crimp profiles for ArterioSorb™ compared to other bioresorbable scaffolds

![Diagram showing crimped OD (mm) for ArterioSorb™ 95 µm, ArterioSorb™ 120 µm, BVS, and DESolve.]

BVS and DESolve crossing profiles from Ormiston; EuroIntervention February 2015
Bench Testing – Scaffold Crimping and Expansion
Bench Testing – Scaffold Crimping and Expansion

 Expansion and post-dilatation

ArterioSorb™ -95µm

BVS -157µm

Crimped

3.5mm (nominal)

4.0mm (post-dilatation)

4.5mm (post-dilatation)

BVS images from Foin; EuroIntervention July 2015
Bench Testing – Drug Release

- Sirolimus / PDLA coating
- 1 µg / mm² drug loading

ArterioSorb™ and Orsiro: Data on file at Arterius
Amaranth, Xience V, BVS, DESolve: Data from literature sources
Future Directions

Future directions

Thinner strut thickness samples
  • Extensive bench-testing of a 95-120 µm strut thickness scaffold has been undertaken
  • Further pre-clinical trials of this thinner strut thickness scaffold

Clinical Trials
  • FIM: 30 patients - 6 months follow-up
        Start Q2-2017
  • CE Mark: 100 patients - 6 months and 1 year follow up
         Start Q2-2018
Thank you for your attention

Acknowledgements...

- Southampton University (UK) – Stent Design
- Nottingham University (UK) – Stent Characterization
- Bradford University (UK) – Polymer Processing
- AccelLab (Canada) – Pre-clinical trials
- Cardialysis, Erasmus University (The Netherlands) – First-in-man and CE mark clinical trials
- Innovate UK for financial support