INTRODUCTION

Drug-eluting bioresorbable scaffolds were developed as an alternative to metallic stents for the treatment of coronary artery disease. Scaffolds are designed to support the artery during healing following balloon angioplasty and then disappear (or “resorb”) from the body over a period of time. This resorption is intended to avoid the long-term complications of a permanent implant including adverse events and limitations on retreatment and non-invasive diagnostic imaging.

BIORESORBABLE SCAFFOLDS

First Generation

The first bioresorbable scaffold, called Absorb from Abbott, became commercially available in Europe in 2012. Absorb, made from high-molecular weight PLA, or polylactic acid, was quickly followed by a second PLA BRS (P-BRS) called DESolve from Elixir Medical and by a magnesium BRS (M-BRS) called Magmaris from Biotronik. Both P-BRS and M-BRS are designed with a PLA-based coating that incorporates an anti-proliferative drug. First generation BRS received an enthusiastic response but their limitations resulted in a decline in interest and utilization. Assessment of first generation BRS identified areas of improvement for future generations: strut thickness, radiopacity, and deliverability.

Second Generation

A second generation BRS, called Fantom from REVA Medical, was designed to overcome the limitations of first generation BRS. Fantom, made from Tyrocore (T-BRS), became commercially available in Europe in 2017. T-BRS are designed with an integrated Tyrocore coating that contains an anti-proliferative drug. T-BRS offer improvements needed to achieve broader adoption: thinner struts, full radiopacity, and ease-of-use.

Third Generation

The third generation BRS, Fantom Encore from REVA Medical, is the most advanced BRS. Like Fantom, it is made from Tyrocore with an integrated coating. Fantom Encore offers the thinnest struts of any commercially available BRS with 95 µm in the 2.5 mm diameter. The 3.0 and 3.5 mm diameter scaffolds have strut thicknesses of 105 µm and 115 µm, respectively.

TYROCORE PROPERTIES

Tyrocore is a unique, proprietary polymer developed and manufactured by REVA Medical. It is designed to meet the requirements for vascular scaffold applications including radiopacity, strength, ductility, benign degradation with low lactic acid release, and storage stability. It is comprised of analogs of the amino acid tyrosine (desaminitotyrosine) and biocompatible hydroxy-esters. Tyrocore consists of an iodinated diphenol and a low molecular weight oligomer of polylactic acid diol (Figure 1), with a significantly higher molar ratio of the iodinated diphenol.

The properties of Tyrocore and PLLA, as previously published, are shown in Table 2. The phenyl-ring of the iodinated diphenol is an inherently strong molecular structure, which contributes to Tyrocore’s high tensile strength. The capability to retain ductility, while maintaining strength, is directly associated with Tyrocore’s composition and high molecular weight. Tyrocore’s radiopacity results from the iodine, which is covalently bound to the tyrosine analog to create the iodinated diphenol.

Radiopacity

Fantom gets its radiopacity from the iodinated diphenol in Tyrocore. Iodine atoms scatter x-rays and impart radiopacity due to their high mass, allowing Fantom to be visualized using standard angiographic techniques (Figure 2). The amount of iodine in a Fantom scaffold is less than 1% of the iodine found in 1 mL of contrast media.

Radial Strength and Recoil

Tyrocore’s high tensile strength enables Fantom to have thin struts (125 µm) while improving strength and reducing recoil compared to P-BRS and M-BRS with strut thickness ≥ 150 µm (Table 3).

Table 1: Improvements of 2nd and 3rd Generation Compared to 1st Generation BRS

<table>
<thead>
<tr>
<th>Attribute</th>
<th>1st Generation P-BRS, M-BRS</th>
<th>2nd Generation T-BRS</th>
<th>3rd Generation T-BRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strut thickness (µm)</td>
<td>≥ 150</td>
<td>125</td>
<td>95-115</td>
</tr>
<tr>
<td>Lack of radiopacity requiring metal markers</td>
<td></td>
<td>Full radiopacity without metal markers</td>
<td>Full radiopacity without metal markers</td>
</tr>
<tr>
<td>Distinct drug coating</td>
<td></td>
<td>Integrated drug coating</td>
<td>Integrated drug coating</td>
</tr>
<tr>
<td>Ease-of-use challenges</td>
<td></td>
<td>Ease-of-use features</td>
<td>Ease-of-use features</td>
</tr>
</tbody>
</table>

Table 2: Properties of Tyrocore and PLLA

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Tyrocore $^3$</th>
<th>PLLA $^4$</th>
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</thead>
<tbody>
<tr>
<td>Ultimate Tensile Strength</td>
<td>100-110 MPa</td>
<td>50-70 MPa</td>
</tr>
<tr>
<td>Elongation at Break (Ductility)</td>
<td>150-200%</td>
<td>2-10%</td>
</tr>
<tr>
<td>X-Ray Visible</td>
<td>Yes</td>
<td>No</td>
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</table>

Table 3: BRS Performance Characteristics $^{2,3}$

<table>
<thead>
<tr>
<th></th>
<th>Fantom</th>
<th>Absorb</th>
<th>Magmaris</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strut Thickness (µm)</td>
<td>125</td>
<td>157</td>
<td>166</td>
</tr>
<tr>
<td>Radial Strength (N/mm)</td>
<td>0.22</td>
<td>0.14</td>
<td>0.17</td>
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<tr>
<td>Recoil</td>
<td>2.0%</td>
<td>2.3%</td>
<td>7.7%</td>
</tr>
</tbody>
</table>

Figure 1: Iodinated diphenol (left) and polylactic acid diol (right)

Figure 2: X-ray image demonstrating radiopacity of Fantom and Absorb $^5$

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*OH

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**OH

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CONCLUSION

T-BRS is differentiated from P-BRS and M-BRS based on improvements achieved through the development of the novel Tyrocore polymer: strut thickness ≤ 125 μm, full scaffold radiopacity without metal markers, an integrated coating, and ease-of-use features. These attributes contribute to improved ease-of-use during the implant procedure and better vessel healing. Complete scaffold healing into the vessel wall ensures that the scaffold is secure during the degradation and resorption process. The long-term goal is complete resorption and absence of a permanent implant in order to reduce long term adverse events and improve options for retreatment and non-invasive diagnostic imaging.

References
3. Tests performed by and data on file at REVAmidical.

www.revamedical.com

Fantom, Fantom Encore, and Tyrocore are trademarks of REVAmidical. Absorb is a trademark of Abbott. DESolve is a trademark of Eliilor Medical. Magmaris is a trademark of Biotronik. CE Mark only. Fantom is not available in the U.S. or countries that do not accept CE Mark.

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