Bioabsorbable Stents Made by Rapid Fabrication System

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Statement of Purpose: Peripheral artery disease (PAD) causes the narrowing of peripheral arteries which reduces the blood flow to legs or other peripheral parts of human body. For PAD treatment, stenting has become the first-line intervention option. The current stent market is dominated by nitinol, stainless steel, and drug-eluting metal stents. However, problems associated with these large and long permanent metal stents have been known to be the cause of neointimal hyperplasia, thrombosis and inflammation; the increased chance of stent fracture and migration due to the frequent movements of the limbs; the re-narrowing of the treated peripheral arteries in the long run. Recent studies have shown that the stent is only required for a limited time in the arteries as the stented vessel remodels itself [1]. Bioabsorbable polymer stents have created an attractive alternative approach to permanent metallic stents. Once absorbed, they may leave behind only the healed natural arteries. It could eliminate the concerns some patients have at the thought of having a foreign implant remained in their body for the rest of their lives. Our group in 3D Biotek, LLC has recently invented a rapid polymer stent fabrication system. The purpose of this research is to demonstrate the feasibility to develop a bioabsorbable drug-eluting stent (DES) using our innovative polymer stent fabrication technology.

Methods: Poly(L-lactide) (PLLA) stents were manufactured using a Rapid Stent Fabrication (RSF) method which was developed from our 3D precision micro-fabrication (3DMF) system (Fig. 1).

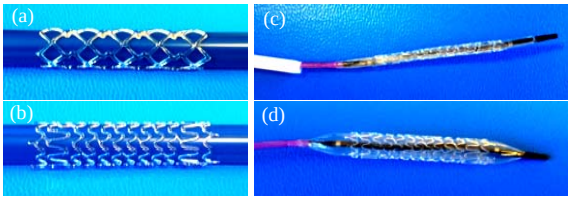

Figure 1. Images of PLLA stents of different patterns fabricated using the 3D RSF system. (a) a closed-cell design, ID=6 mm, length=33 mm; (b) an open-cell helical design, ID=6 mm, length=36 mm; (c) helical stent crimped onto a balloon catheter passing through an 8-French guiding catheter; (d) balloon-expanded helical stent.

The PLLA drug-eluting stents (DES) were fabricated using a dip-coating method with rapamycin/poly-D,L-lactide (PDLLA) as drug/polymer coating. The DESs were crimped on a 6-mm balloon and sterilized by E-beam. After expansion with balloon, the stents were assayed by performing radial force test (Model TTR2 by Blockwise Engineering LLC) at 37°C. The drug release behavior of DES was studied in PBS with 5% of DMSO (for enhancing the drug solubility) at 37°C. The release medium was collected and refreshed daily for 30 days. The released drugs in sample media were quantified by a HPLC with a UV detector. The *in vitro* biodegradation of stents was performed in PBS at 37°C and characterized by both the physical and chemical property changes over time, including molecular weight, stent mass, crystallinity, and radial stiffness, at different time intervals for up to 6 months.

Results: PLLA stents with various patterns were successfully fabricated directly from polymer powders using our RSF system (Fig. 1a and 1b). Compared with the laser-cutting method which takes multiple steps and wastes up to 90% of the material, the RSF technology is a single-step stent fabrication process with high efficiency and low consumption of medical grade materials. The RSF-fabricated PLLA stents with strut thickness of 0.3-0.4 mm showed a radial strength (radial force per stent length) of 6.0 N/cm at a 2 mm oversize. The crimped PLLA stent on balloon displayed high flexibility and could be easily delivered through an 8-French guiding catheter (Fig. 1c). Upon expansion, the acute recoil of PLLA stents is <5% and the foreshortening is <2% (Fig. 1d).

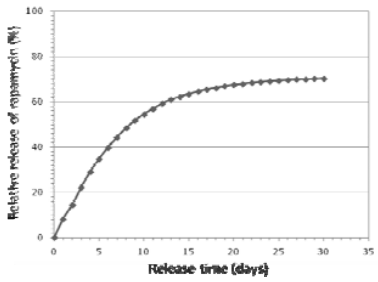

Figure 2. The accumulated release profile of rapamycin from PLLA DES into aqueous media.

The drug-releasing results showed that 70% of the drug was released from PLLA DES within 30 days (Fig. 2). The release rate of PLLA DES appears to be comparable to the reported release rate of Cypher® stent (75% of drugs released within 25 days) [2].

Conclusions: The study demonstrates that our innovative Rapid Stent Fabrication (RSF) technology is highly efficient in manufacturing polymer stents with one-step processing. With the RSF, we have developed bioabsorbable drug-eluting stents which display similar drug-releasing behavior compared with commercial metal stents. Our incoming work is to do the animal study with the RSF-fabricated PLLA stents.

References: (1) Adlakha S. J Interv Cardiol. 2010;23:411-419. (2) Granada JF. Circ Cardiovasc Interv. 2010;3:257-266.

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