

# Ink-Jet Technology Applied to Drug-Eluting Stents

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This paper addresses a new technology used to coat drug-eluting stents (DES). It also reviews the background of different stent types and problems faced by current DES. A stent is metal wire mesh-like tube used to prop open an artery during angioplasty (widening of a narrowed or totally obstructed blood vessel). The stent is collapsed to a small diameter and placed over a balloon catheter. Once the blockage is reached the balloon is inflated and the stent forms a scaffold to support and hold open the artery. After a few weeks the endothelium of the artery grows over the metal surface of the stent

## *Drug-Eluting Stents*

Drug-eluting stents have evolved from bare metal stents. The physical difference however is that they are coated with a pharmacological agent that interferes with biological process of remodeling and over aggressive healing. The idea being that the drug will prevent restenosis (the re-narrowing of an artery or vein after stenting). DES has helped reduce incidence of restenosis from 20-30% to single digits. However DES does not have any different effect on late stent thrombosis than BMS. Thrombosis is the formation of a clot or obstruction of blood flow in the circulatory system.

## *Ink-Jet Technology*

Tiny medical devices such as a coronary stent have cylindrical dimensions of 1mm diameter x 15 mm length. Finer control in coating is desirable to avoid overspray and drug wastage during manufacturing. During the Jetting Process a glass tube fills with the reagent solution and voltage is applied to a piezoelectric crystal causing the walls of the tube to be bowed outward. This distortion drops the pressure in the tube and draws in more of the reagent, when the voltage is released the walls go back to normal and a droplet is expelled out of the nozzle orifice. There are two Ink-Jet Modes: Continuous Mode – pressurized fluid is forced through the nozzle producing spheres of diameter 15-200um at rates of 1 MHz; and Drop-on-Demand Mode – the fluid is maintained at ambient pressure, the transducer creates volumetric change in the fluid which in turn creates pressure waves that result in a drop being ejected from the orifice. This produces spheres of diameter 15-200um at rates of 1 Hz to 25 KHz.

## *Problems with Application of Coating*

The fact that the stents are 3D structures complicates the coating process exponentially. The stent could be moved and rotated in front of the jet nozzle to jet reagent onto every surface of the stent. This would require high level software programs to coordinate the movement of the stent with the ink-jet. The solution to this problem is called off-axis jetting. During this process the stent is positioned so that the jet of reagents is tangent to the cylindrical surface of the stent. The stent is rotated about its longitudinal axis and the coating is applied.

The benefits of off-axis jetting are that it requires timing similar to 2D jetting rather than 3D jetting. It maximizes the probability of hitting one of the struts on the stent. And also removes the need for complex optical or

imaging feedback to ensure droplets are hitting the stent without excessive loss of efficiency.

## *Testing*

Four different applications of the off-axis jetting were tested to check the efficiency of the coating. The first dosage was jetted into vials. A concentration of 40mg/mL and 15k droplets of 170pL were jetted into the vials and all were recovered. Next three different stent tubes were tested. All of the stent tubes and stents were pre-coated with a PC Polymer to form an adhesion base. The recovered values are a mean value of all trials and the reagents were in a solution of isobutanol.

- Uncut Stent Tubes – Five 1.5x15mm tubes, 20mg/mL, target dosage of 150ug = 21,900 droplets, 140ug was recovered
- Nine 1.5x15mm Coronary Stents, 40mg/mL, target dosage of 150ug, 134ug was recovered
- Eight 8x40mm Femoral Artery Stents, 40mg/mL, target dosage of 600ug, 598ug was recovered

The jet coated stents were compared to Spray

Atomization coated stents for drug release comparison. The test was done over a 24 hour period and proved that jetting allows for proper drug release.

The time required to jet one stent including mounting and dismounting times was on average 6.5 – 7 min per stent. The actual drug dispensing time was less than 2 min. and it is hoped that by the addition of robotic mounting and dismounting the overall time could be improved.

## *Conclusion*

It is still unclear if drug-eluting stents are better or worse than bare metal stents. But, the off-axis jetting technique greatly reduces the complexity of the jetting system, and it also allows for the coating of several different scaffold patterns with out reprogramming. The efficiency of this method decreases as the open space percentage of the stents increase. The programmability of this method of coating could allow for stents with custom drug concentrations. It will also allow for the application of multiple drugs over various areas of the stent. With this technology there are even possibilities for the use of over coats to control the release of the drugs.

## *References*

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