

Features of the cardiovascular stent coatings

[Health & Medicine](#), [Disease](#)



Today, cardiovascular diseases (CDs) are one of the major concerns in the research community. They play a huge role in increasing the mortality rate all over the world. For example, Atherosclerosis is a kind of CDs in which the inner wall of the artery gets narrow due to the deposition of plaque. Plaques are generally lipid molecules, calcium, cholesterol, macrophage cells and some fibrous tissues which forms layers inside the artery disrupting the flow of the blood. Since the reasons are not precisely known, obesity, unhealthy food, smoking, diabetes, genetic abnormalities and advancing age could be some of the possible risk factors for CDs. Many people have died in the past years due to CDs. According to the statistics, China alone has approximately 20 million CD patients which is increasing with an alarming increase rate of 1 million patients per year. In a survey by World Health Organisation (WHO), there will be approximately 23.6 million deaths due to CDs by 2030. However, the main way to treat this disease is to perform Percutaneous Coronary Intervention (PCI).

PCI is used to treat the narrowing of the vessels (Stenosis). The procedure includes an initial imaging step which is followed later by angioplasty. In order to find the narrowing or blockings, a catheter is passed through the femoral or radial artery in the blood stream till the target position. Then a special dye is inserted in the area through the catheter to find size and shape of the blockings via X-ray imaging. Once the size and shape are determined, the process called angioplasty is carried on. This includes insertion of a narrow wire initially in the position. A balloon is then passed over the wire along with a cylindrical metal mesh (stent). When the balloon is

inflated, it clears the blockade and opens the stent. After the stent is permanently opened, the balloon and the wire can be removed.

About 30 years ago, the introduction of Bare Metal Stents (BMS) was a revolution in PCI. Soon it was realised that the BMS was not the ultimate solution since it gave rise to In-Stent Restenosis (ISR) which needed repeated angioplasty. At present, the research to improve the stent technology is going on. The BMS is very vulnerable to the adhesion of blood platelets. This activates the coagulation cascade. The arterial injury caused by the BMS implantation activates the inflammatory and vascular repair responses further inducing the migration and growth of vascular smooth cells. This results in re-narrowing of the vessel. Meanwhile, one more challenge that has always been for any implants is biocompatibility. The material that is implanted in the human body must be biocompatible. Otherwise, the contact between the layer and the body fluids, enzymes, proteins, lipids or electrolytes can result in chemical reactions that can harm the health of the human being. A second probability can be the formation of a tissue capsule or film by the human cells on the implant. In both the cases, the efficacy of the implant will be altered providing a challenge for the therapy. Since the material for the stent is usually a metal, coatings will be the best approach to make it biocompatible. The coating material and process needs to be chosen so that the geometry and the performance of the stent will not be compromised.

The problem was however solved by Drug Eluting Stents (DES). Basically, it is the stent that is coated with some polymers that is embedded with drugs

capable of degrading in the human body by hydrolysis. These drugs reduce the inflammatory response and thrombosis activated by the arterial injury during implantation. However, the study has showed that the drugs used to reduce the thrombosis also impairs the normal healing response and slows down the re-endothelialisation in the stent region. This is relatively less effective than the BMS in the patients in terms of local endothelial regeneration. Due to this controlled drug release, the poor re-endothelialisation and tenacity of polymer coatings after the release of drugs caused slow wound healing which was determined to be a potential risk factor. The first generation DES used poly(styrene-b-isobutylene-b-styrene) (SIBS), poly(ethylene-covinyl acetate) (PEVA) and poly(n-butyl methacrylate) (PBMA) block polymers which reported many cases of myocardial infraction and even deaths after implantation. So, there is need of novel material that can be used for the stent coatings which is biocompatible, non-toxic and shows a controlled release of drugs without altering the endothelial cell generation. Rapid endothelial regeneration after the stent implantation has proven to be helpful in the treatment of ISR. Many researchers have successfully altered the material surface for the cell adhesions by immobilising Extracellular Matrix (ECM) or synthetic cell adhesive peptides.

Processes and materials

Coating of cardiovascular stents is itself a very complicated process since it lies in the very delicate part of the body. Selection of right material for coating and right process is very important. Similarly, the functionality of the material, in this case polymers is one of the key factors for the success of the system. The size and the structure of the stent creates many challenges for

the researchers. The polymers for the coatings need to be biocompatible, biodegradable, non-toxic and must possess good adhesion properties.

Coating techniques for DES

Dip coating

Dip coating is one of the effective coating techniques used for the cardiovascular stent coatings. The stent is dip coated in a solution of polymers and drugs in a proper concentration in organic miscible solvent. The polymers can be non-degradable or degradable depending upon the system being designed. It should adhere on the metal surface very well and possess rate controlling properties.

Spray coating

Drug/polymer coating can be done also by spray coating on the strut surface. Microdroplets of drug/polymer is sprayed on the DES through the nozzle. The stent device is mounted on a rotating mandrel where it is sprayed on with the polymer solution. For uniform thickness, the nozzle moves along the stent till the desired coating is achieved. Finally, the stent is cured at 65-70°C for three hours in a preheated oven.

Plasma coating

Plasma coatings have been reported in DES where solution cannot be used. In case of both organic polymers and inorganic materials, this process has proved to be an alternative for stent coatings. The material is deposited on the stent via Chemical Vapour Deposition (CVD) process. A novel plasma coating technique called Plasma Enhanced Chemical Vapor Deposition

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(PECVD) has been revealed as very applicable for stent coating. Parylene and its derivatives has been reported to be biocompatible and have negligible toxicity which is coated on stents by PECVD.

Polymers used for DES coatings

Currently, DES is undergoing a lot of research and many polymers are used for coating and drug carriers. Bioderived and resorbable polymers are the first choice for the stent coatings today. Polyglycolic acid (PGA), polylactic acid (PLA) and polyurethane (PU) have been used in the human body for implants. PGA has been used for suture in surgeries. PU has very high hemocompatibility so, it has been used as a scaffold material for vascular grafts. PLA is biocompatible and therefore it has been actively researched on for stent material. The polymers that are naturally acquired are capable of degrading through hydrolysis making them very compatible for in vivo use. However, the degradation kinetics of these polymers are major challenges in their use. The late degradation of PLA causes late stent-thrombosis.

The degradable polymers release carbon dioxide during the degradation which is excreted by the body. The drug release is controlled by the degradation behaviour of the polymers. Since pH, dispersity, crystallinity, etc. plays a very important role in altering the drug release mechanism, the degradation of polymers might also increase the pH of the localised area increasing the chance of inflammation and restenosis. However, the first generation of DES used nondegradable polymers for coatings which resulted in causing deaths in some time after implantation. The second generation of

DES also used nondegradable polymers but with drugs which proved to be safe in long term use. Many other materials are also being developed which do not use the polymer system.

Table 1: Components and performances of clinically approved DES2

Type	DES	Coating	Drug	Clinical performance
Durable	Taxus Express	SIBS	Paclitaxel	Superior to BMS in reducing ISR and TLR
Promus	Element	PBMA/PVDF-HFP	Everolimus	Comparable to Xience-V
Endeavour	PC	Zotarolimus		Similar safety and efficacy as Taxus with higher ST; impaired polymer integrity
Xience-V		PMBA/PVDF-HFP	Everolimus	Prevents ISR and restores vasomotion, low ST
Biodegradable	Symbio	PLGA	Pimecrolimus/Paclitaxel	No beneficial effect compared to Taxus
Endeavour	Resolute	BioLinx	Zotarolimus	Non-inferior in safety and efficacy trials compared to durable DES
BioMatrix		PLA	Biolimus A9	reduced risk of CE compared to durable DES

glycolide), BioLinx: hydrophobic C10-polymer/hydrophilic C19-polymer/poly(vinyl-pyrrolidone) (PVP), and PLA: polylactide; DES: drug-eluting stent, BMS: bare metal stent, ISR: in-stent restenosis, TLR: target lesion revascularization, ST: stent thrombosis, and CE: cardiac events.