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Advancement and Development in Stent Engineering

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MASTER THESIS OF:

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ABSTRACT

Coronary artery disease is major health care and economic burden worldwide. A stent implantation is major advanced since the introduction of coronary angioplasty. Coronary stents have been proven as an effective treatment device for heart diseases such as acute myocardial infarction. There are numerous studies on the design of coronary stents and many significant manufacturing methods have been reported in the past two decades. However, there is no comprehensive methodology for the product development of coronary stents in terms of design, simulation, and manufacturing. One of the major enduring challenges to the use of vascular stent includes a selection of stent size. Critical oversizing or under-sizing of stent often results in incomplete stent apposition or under expansion. Geometric constraints within the patient's vessel, such as a significant curvature causing disturbance blood flow which leads to the failure of traditional stent. Final stent expansion often fails fulfil exact stent dimensions after drug-eluting stent implantation, and suboptimal stent expansion will results in adverse clinical events.

Advancement in 3D printing materials, equipment, methods, and techniques are currently empowering on-demand, highly customized patient treatments. This study aims to highlight the importance of customized stent with 3d printing technique based on fused deposition modelling that has an exact geometric of the patient blood vessels to minimize the probability of irregular stent size and rejection. The exact dimensions of a patient's vessel are obtained using standard imaging techniques available at hospitals and a stent is then printed on-site to precisely fit the vessel's dimensions. The inspiration for this novel 3D-printing technique was to develop a way to realize not “one size fits all”. This project emphasizes the importance of Additive manufacturing along with design and material characteristics.

Keywords

Coronary stent, Geometric constraints,3D printing, customized patient treatments, imaging techniques

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CHAPTER 1

1. INTRODUCTION

Cardiovascular Disease (CVD) is highly prevalent, affecting an estimated 17 million global death annually. CVD is a class of diseases that involves the heart and blood vessels. CVD includes coronary artery disease (CAD) such as angina, myocardial infarction (commonly known as a heart attack), peripheral artery disease, hypertensive heart disease, abnormal heart rhythms, aortic aneurysms, cardiomyopathy, rheumatic heart disease, thromboembolic disease, venous disease. Coronary artery disease arises from the build-up of plaque on the inner surface of the arteries. The blockage of the arteries by plague accumulation is called atherosclerosis. Vascular intervention as a clinical alternative to bypass graft surgery for the treatment of coronary and peripheral artery disease caused by arteriosclerosis was introduced with the concept of balloon angioplasty. Nowadays, angioplasty, also known as percutaneous coronary intervention (PCI), or peripheral artery balloon dilation and stenting are frequently used interventional therapeutic methods, in which a tiny tube called a stent is used in an artery or duct to keep it open and restore the flow of bodily fluids in the area. From the introduction of PCI, nobody was able to predict the advances that will occur in stent technology over the upcoming decades.

Since 1986 stent technology has rapidly evolved from a mechanical solution to abrupt vessel closure and elastic recoil following plain balloon angioplasty, to become a vector for local drug delivery and modification of coronary plaque pathophysiology [1]. Metallic characteristics, bulk and surface properties, design, and chemistry are all important factors to consider in the conception of an optimal stent. The first generation of stents, the bare metal stent (BMS), usually fabricated from stainless steel (316L), cobalt-chromium(Co–Cr) and platinum-iridium (Pt–Ir) alloys, tantalum (Ta), or nitinol (Ni-Ti) have shown numerous problems leading to tissue hyperplasia, in-stent restenosis and the necessity to explant them or to keep them as a foreign body during the whole life. While effective in preventing abrupt closure, early recoil, and reducing the risk of restenosis when compared with balloon angioplasty alone, BMS had unacceptably high rates of restenosis [2]. Re-stenosis is related to patient-specific factors such as genetic predisposition or diabetes mellitus, lesion-specific factors such as vessel calibres, lesion length or plaque burden, and procedure-specific factors such as the extent of vessel damage, residual dissections[3]. Most studies have consistently

shown that patients who undergo PCI are more likely to have recurrent angina and to require a repeat procedure. These considerations emerge the development of drug-eluting stent (DES), coated stent, and biodegradable stent. The development and advancement of DES have been critical to the success of PCI. The three important components of DES are platform, antiproliferative agent, and polymer coating [4]. Although BMS and DES are effective, in most cases, the role of a stent is temporary and is limited to the intervention. As time has progressed, there have been many continued technological advancements, including several new-generation DES with thinner stent struts, wider cell design, biodegradable polymer coating, and new antiproliferative agents for better clinical outcomes. Bioresorbable stents (BRS) were introduced to overcome the limitations with the important advantages of complete bio resorption, mechanical flexibility, etc. An ideal biodegradable stent should be able to compromise its degradation and mechanical integrity during implantation. The duration and process of stent resorption also require careful attention. The optimal duration for the presence of a stent scaffold following balloon dilation of a coronary artery is 6 months [5].

Biodegradable stents offer the potential to improve long-term patency rates by providing support just long enough for the artery to heal. However, design a biodegradable structure for an intended period of support is rather difficult. An ideal stent should possess the properties such as the ability to be crimped on the balloon catheter, good expandability ration, sufficient flexibility, high thrombo resistivity, absence of restenosis after implantation, non-toxicity, drug delivery capacity, sufficient radial hoop strength, and negligible recoil, adequate radiopacity/magnetic resonance imaging (MRI) compatibility [6].

Several studies with percutaneous coronary interventions have focused on the influence of vessel size on angiographic restenosis after coronary stent placement. (8) It is well recognized that vessel size is one of the strongest determinants of long-term outcomes after coronary stenting. Specifically, smaller target vessel dimensions have been reported as an independent predictor of restenosis and repeat revascularization even after DES implantation. Furthermore, there is compelling clinical evidence that significant stent under-sizing of DES often ends up with suboptimal results, particularly stent under expansion, which can lead to adverse clinical events, such as restenosis and stent thrombosis.

Therefore, the Selection of stent size relative to the target vessel is considered as important as a post-deployment optimization strategy. The traditional manufacturing process in the stent industry is laser micro-cutting. Recently, three-dimensional (3D) printing, a specific technique in the biomedical field, has emerged as an alternative system for producing biomaterials. The 3D printing system, applied to rapid prototyping in structural fabrication can easily manufacture biomaterials, such as BRS, better than other devices.3-dimensional printing biodegradable vascular stent technology has obvious advantages over traditional processing technology. 3-dimensional printing technology is an additive manufacturing technology that can control the distribution of materials, reduce product development costs, and shorten product development cycles. Therefore, relying on 3D printing technology based on fused deposition modeling (FDM) is of great significance to carry out digital design and manufacturing research on biodegradable polymer stents. The objective of this paper is to develop a methodology for coronary stents product development that focuses on design, simulation, and manufacturing. The methodology brings together insights from numerous engineering design disciplines to make coronary stent development more flexible and more cost-efficient.

1.1 CORONARY STENT

Heart disease involves one of the problems with valves, muscles, or coronary arteries all of which cause the heart not to function well. Atherosclerosis is a heart disease treated by interventional cardiology. In atherosclerosis, a plaque which is a composition of fat, cholesterol, fibrin, and calcium develops on the inner walls of the arteries. (Fig.1)

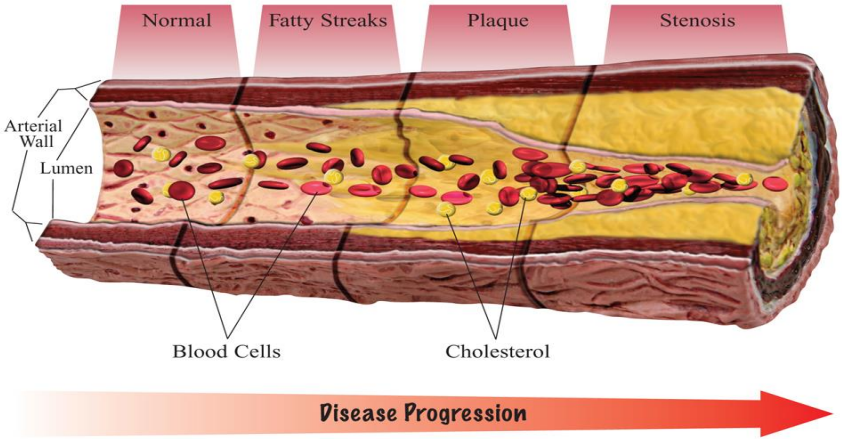


Figure 1 Artery with atherosclerosis

This is a virtually widespread disease in industrialized countries, where modifiable risk factors such as hyperlipidaemia, smoking, hypertension and diabetes mellitus, stressful lifestyle, sedentary lifestyle and a poor, high-fat diet. This blockage is usually treated by expanding a balloon or inserting a stent or combination of both procedures at the clogged site. Based on medical device stent of these scaffolds that go into arteries to open the blocked arteries. Stents are deployed by being laid over the balloon.(Fig.2) The stent and the balloon are passed into the narrowing and then the balloon is inflated [7].The stent stays in place as the balloon is deflated and then removed from the artery leaving the scaffold in place which holds the artery opening.

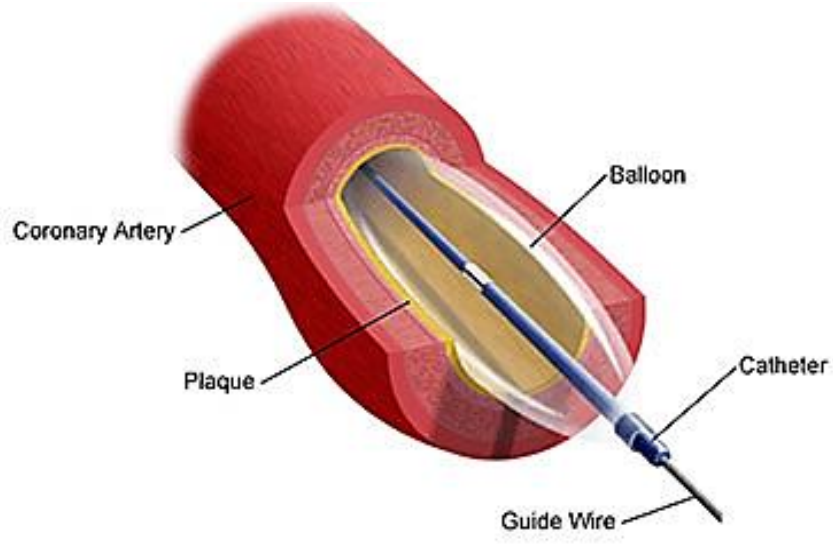


Figure 2 Inflation of balloon inside a coronary artery

Contemporary coronary stent technology continues to seek to improve on the outcomes of the preceding generation of devices by refining their design, structure, and component materials. These technologies include new generations of drug-eluting stents, non-polymeric stents, bioresorbable polymer-coated stents, and fully bioresorbable scaffolds.

Desirable stent characteristics

- Low crossing profile
- High flexibility
- Radio-opaque
- Thromboresistant

- High stent/host compatibility
- High radial strength
- Low metallic surface
- Favourable radiographic properties
- Circumferential coverage
- Good trackability
- Easy deployment.

1.2 CORONARY STENT MARKET SIZE AND MARKET SHARE

Rising predominance of cardiovascular infections (CVDs, for example, stroke and respiratory failure, along with the developing geriatric populace at higher danger of these heart illnesses is expected to impel the interest for coronary stents over the forecast period.

The study estimates approximately 17.7 million (i.e. 31% of global death) were affected due to cardiovascular disease (CVD). (Fig.3). Total of 55 million deaths occurred across the world in 2017. While cardiovascular disease was the most common cause of deaths among middle-aged adults globally, accounting for 40% of all deaths, but that ranged from only 23% in high income countries (HIC) to 41% in middle income countries (MIC) and 43% in It accounted for nearly 836,546 deaths in U.S. in 2018. i.e. about 1 out of 3 deaths [8]. Consequently, remarkable development in the quantity of CAD prevalence is foreseen to expand the interest for an effective coronary stent for the treatment. This factor is required to support interest over the estimate years**.**

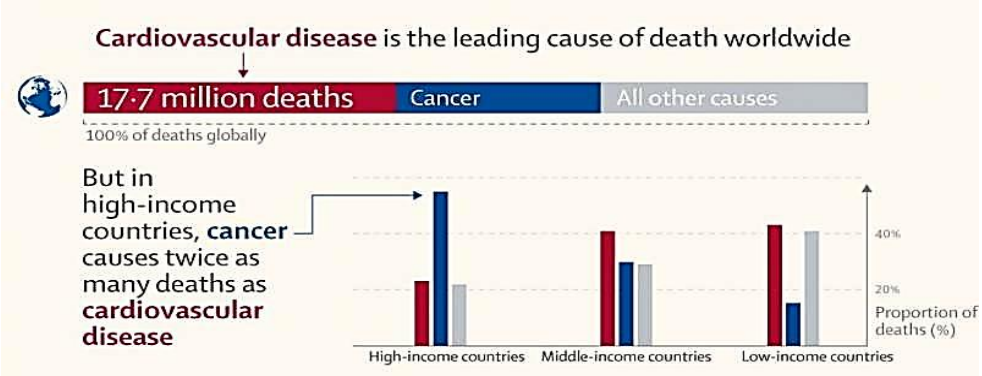


Figure 3 CVD leading cause of death

The global coronary stents market size was estimated at USD 7.7 billion in 2019 and is expected to witness a CAGR of 4.7% during the forecast period.

Every year about 2 million people are treated with coronary stent. According to global stent market, Stent market size surpassed $ 9.5 billion in 2018 and is forecast to register more than 5.3% CAGR up to 2025. The cost of CAD-related healthcare in the USA is expected to increase by approximately $51.3 billion by 2040 because of the aging population.

1.3 STENT TECHNOLOGY FOR DIFFERENT APPLICATIONS

Stents vary in size and material based on their purpose. Cardiac stents implanted into arteries through wire mesh are the most common technology that comes to mind, the basic concept of stenting can be used in several other organ systems. Stents are simply tubing that keep a passageway open, and the human body contains several non-cardiac passageways.

Biliary (Bile duct) Stents

Endoscopic biliary stenting is a procedure done to open your blocked bile duct (tube). Stent is placed into your impeded bile duct during the procedure. A bile duct is kept open with the help of metal or plastic tube called stent (Fig.4). It ranges of diameters from 5 to 12 and in a range in lengths from 1 cm to >15 cm [9].

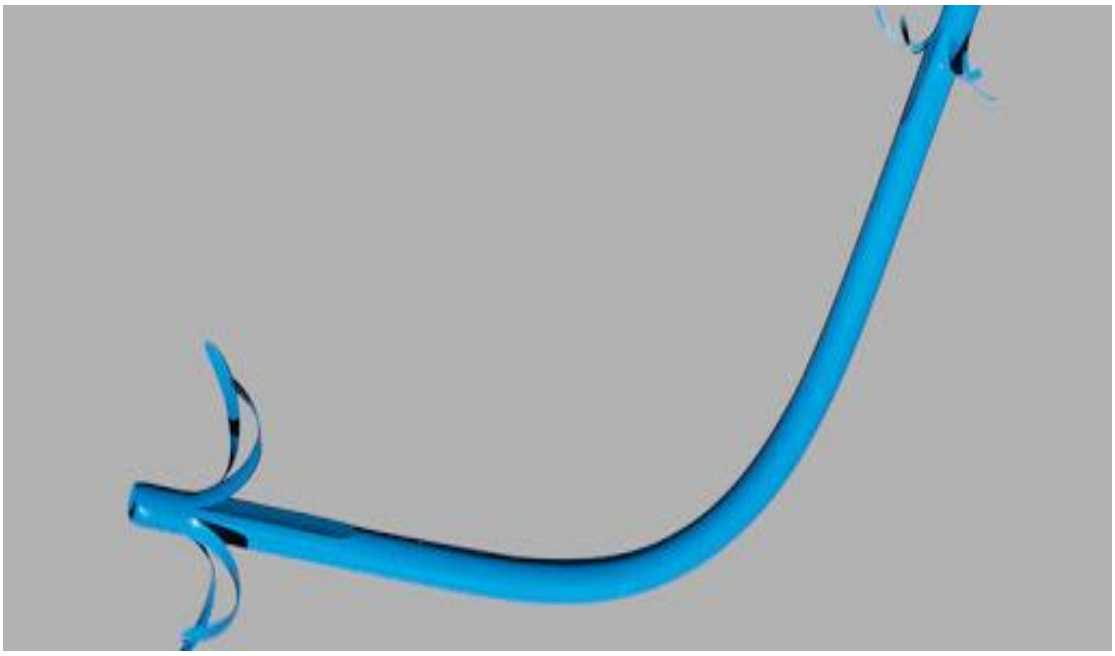


Figure 4: Representation of Biliary stent

Ureter Stents

Ureter stents help open the ureters, the pipes between the kidneys and bladder. Ureteral stents are adaptable and made of polymers (plastic). A stent is a thin plastic cylinder used to hold your ureter open and permit urine to pass.(Fig.5) Stenting might be utilized for the present moment or long term (if 3 months) depending upon the patient's necessities. The length of the stents utilized in grown-up patients shifts somewhere in the range of 24 and 30 cm. Also, stents come in contrasting breadths or measures, to fit distinctive size ureters. The stent is generally embedded with the guide of a cystoscope.

Figure 5: Ureteral Stent

Oesophageal Stents

Oesophageal stents are a widely used treatment method for various oesophageal pathologies such as malign and benign obstruction and contained perforations of the oesophagus. In an oesophageal stent technique, a cylinder is set in your (throat) to keep open a hindered zone. The solids and liquids swallowed by stent tube. Stent sizing options including a 60mm length and 14mm diameter designed to meet a variety of clinical needs.

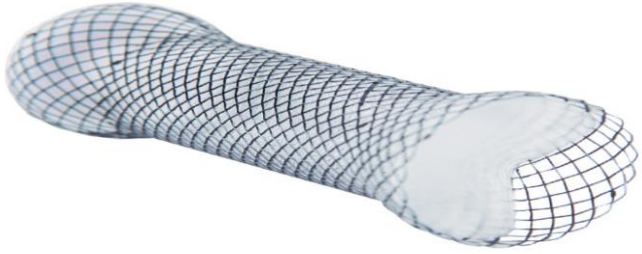


Figure 6: Stents Oesophageal

Colorectal Stents

Colorectal stents are designed to treat malignant luminal obstruction of the large bowel. Over the last few years use of colonic stents has significantly evolved. Emergency surgery for colonic obstructions is typically connected with significant mortality, morbidity and often stoma formation. Colonic stents provide an elective way to relieve colonic obstruction.

Cerebral stent

A cerebral stent opens a clogged or blocked artery in the brain to promote the circulation of blood. The principle behind is the prevention of strokes by ensuring the brain's blood supply is not compromised.

Figure 7: Cerebral stent

1.4 TECHNICAL TRENDS AND CHALLENGES

Despite many advancements in stent development, numerous studies are continued to show high efficacy, long-term safety, and clinical outcomes in medical studies Stents are classified by their mechanism of expansion, construction, and coatings. The key segmentation of the stent market is by stent type, deployment, manufacturing process, end-user, and other aspects.

The Major challenges are the influence of vessel size on long-term clinical and angiographic outcome after coronary stent placement. Failure of stent occurs when unfit stent moves in the artery. In these cases, physicians must somehow re-open the blocked stent or bypass it with a vascular graft. It is a costly and risky process. There are cases where a physician tries to stent a patient, and the fit is not good. Traditional stents fail when there is a geometric

constraint in the vessel, such as a significant curvature disturbs blood flow. It is especially a problem for patients whose conditions to prevent the use of blood thinners, which are commonly given to patients who have stents. Hence to minimize the probability of these complications, printing a stent that has the exact geometric and biologic requirements of the patient's blood vessel is necessary.

Apart from the design aspects, manufacturing methods also play a vital role as they face stent efficacy challenges. Precision manufacturing techniques such as laser machining, photochemical etching, electro-discharge machining, water jet, braiding, vapor deposition, etc., are considered necessary to manufacture the stents. Proper surface treatment techniques must be carried out to remove burrs and oxidation layers.

1.5 RESEARCH SCOPE

The aspects of stent behaviour that are studied in research involve elastic recoil, foreshortening, longitudinal recoil, radial stiffness, coverage area, fracture mechanics, bending, and flexibility. Materials of the stents also have a great effect on the stent performance. The materials are selected based on mechanical properties, biocompatibility, and bio functionality. Another important material aspect considered in current studies is the biodegradability of stents. Stents are expected to stay in the body for a period of 12-24 months and biodegrades after the artery is back to its normal position. The method of manufacturing matters in the proper functioning of stents. Surface finishing is a machining operation which is an important process after manufacturing stents. Material, design, manufacturing, clinical outcomes are some characteristics, the researchers investigate in the field of coronary stents. The study reviews an overview of the current stent types, their functionality, materials, and manufacturing conditions demonstrating the still tremendous potential for the advancement of promising stent solutions.

CHAPTER 2

2. EVOLUTION OF STENT

London dentist Charles stent derives the word stent from dental prosthesis (1807-1885), for fixing in an expanded state. The first stent was implanted in human coronary arteries in 1986 by Ulrich Siegwart, Jacques puel, and colleagues, who placed the Walls stent sheathed self-expanding metallic mesh scaffold in the peripheral and coronary arteries of eight patients. It was a self-expanding mesh design arranged in 20 strands of 0.06 to 0.09 mm diameter. Its length ranging from 15 to 30 mm; and its diameter between 3.0 to 6.0 mm made flexible. The bare metal, self-expanding stent, known as the "Wall" stent was able to provide a scaffold that prevented acute vessel closure and late constrictive recoil. Cesare Gianturco and gray roubin developed a balloon-expandable coil stent-made with stainless-steel wire which resembles clamshell [10].

A phase 2 study evaluating the gianturco roubin stent to reverse plain old balloon angioplasty (POBA) in acute or threatened vessel closure was started in 1988,which ultimately leading to united states food and drug administration FDA approval for this indication in June 1993.

A rectangular diamond-shaped balloon-expandable slotted stainless stent is devised by Julio Palmaz stent. The Gianturco Roubin stent10 (approved in the United States in 1993) had a poor radial strength, which was responsible for an increased rate of restenosis and stent thrombosis. Later, Medtronic proposed a coil stent or Wiktor stent. The field has continually evolved, since the first coronary angioplasty was performed to relieve angina in a human.

various BMS designs of self- or balloon expandable were made of 316 L stainless steel, nitinol wire coils, or nitinol coils. Unfortunately, like POBA, bare-metal stents (BMS) were associated with excessive neointimal formation as a response to procedure-related wound healing in up to 30–40% of cases [11]. The evolution of stent : brief view is shown in Fig.8.

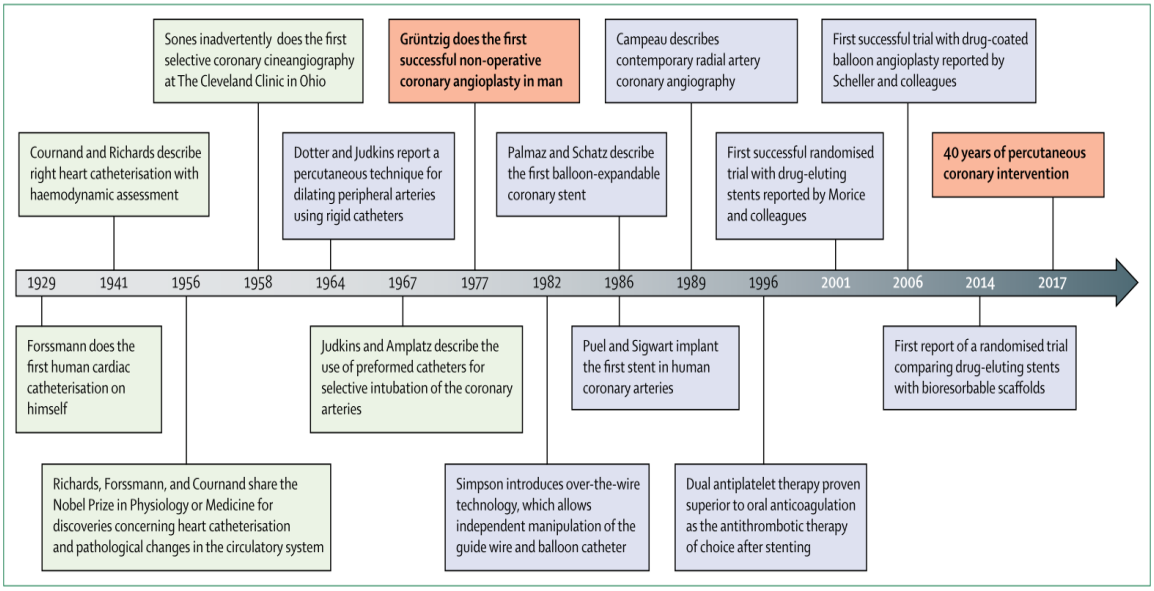


Figure 8: Timeline of diagnostic cardiac catheterisation, coronary balloon angioplasty, stent, and scaffold implantation

In flowchart Developments in diagnostic catheterisation are shown in green, coronary angioplasty in red, and catheter therapeutics in blue. References to support milestones are provided in the appendix.

The stent design was one of the first to employ to achieve a successful balance of strength and flexibility. The primary types: The Wall stent, fabricated from braided wire of a cobalt alloy called elgiloy; The Wiktor stent, fabricated from tantalum wire formed into a helical ring structure; the Gianturco-Roubin Flex-Stent, fabricated from stainless steel wire in a clamshell design; and finally the Palmaz and Palmaz-Schatz stents, fabricated from slotted stainless steel tubes (Table.1).

The three of the above designs were not successful in combating restenosis. But the Palmaz-Schatz stent proved to be different than the rest.

	Wallstent	**Wiktor**	**GR Flex-Stent**	**Palmaz/Palmaz-Schatz**
Material	elgiloy	tantalum	stainless steel	stainless steel
Form	wire	wire	wire	tube
Fabrication	braid	bend	bend	EDM
Geometry	braid	helical rings	clamshell	slotted tube

Table 1 Evolution of stent design

The development of a coronary stent with a drug coating, the DES has been developed to overcome the failure of oral administration and local delivery. The first human Drug eluting stent implant was developed by J. Eduardo Sousa in Sao Paulo in December 1999 at the start of the 2 first-in-man studies that recruited a total of 45 patients and reported minimal in-stent neointimal proliferation through to 12-month [12]. In 2000 DES were introduced. They are composed of 2 elements the compound coating the strut one or many layers and therefore the drug delivered into the vessel wall. The drugs act on the cell cycle and can suppress smooth muscle cell proliferation without toxicity and with a low inflammatory risk. Sirolimus (sirolimus, everolimus, zotarolimus, biolimus, the sirolimus metabolite novolimus, and myolimus, a macrocyclic lactone close to the rapamycin family) were used in most of the DES.The first-generation DESs were another leap forward compared with BMS; however, there was still concern about late stent thrombosis (LST) and reduced deliverability with the 140 μm strut/polymer.

Thinner cobalt chromium alloys, new cell-cycle inhibitors (everolimus/zotarolimus), and more biocompatible polymers are used to overcome the flaws, which in turn called as second generation DESs. while being typically thought-about biocompatible the compound coating of the primary and second generation des prevents prevents them from truly behaving like BMS, after time, even after all the drug is eluted. BMS and DES of chronic inflammation, angiogenesis, neo-atherosclerosis, restenosis, obstruction of side branches, and LST via stent fracture have implicated alloyed stents themselves. Therefore, late stent/polymer-vessel interactions remain appealing by the concept of a biodegradable polymer coating or fully biodegradable vascular scaffolds [13]. Therefore, the thought of a perishable chemical compound coating or biodegradable vascular scaffolds remains appealing as a method of mitigating these late tubing chemical compound vessel interactions.

Fully bioresorbable vascular scaffolds (BVS), including: (Igaki-Tamai (Igaki Medical Planning), BVS 1.0 (Abbott Vascular), DESolve (Elxir Medical Corporation), REVA (Reva Medical), ART 18AZ (Arterial Remodelling Technologies), and Amaranth stents are considered as third generation drug eluting stents. Igaki and Tamai pioneered the development of a completely biodegradable polymeric stent (poly-L-lactic acid [PLLA] polymer) (Igaki–Tamai stent, Kyoto Medical Planning Co. Ltd, Kyoto, Japan) with 170 μm strut thickness and 24% stent strut surface/vessel coverage that is both self-expanding and balloon expandable.(18) Several important features such as optimal polymer composition,

gradation, drug release kinetics, impact of neo atherosclerosis, and stent fracture are the focus of current investigations

Though the current generation DESs have improved the rates of adverse events in clinical practice, the quest to minimize late stent thrombotic events while maintaining maximal lumen diameters and retuning normal vessel physiology is ongoing.

2.1 TYPES OF STENT

Bioengineered stent- Bioengineered stent is also called antibody-coated stent. Antibody coated stents promote the natural healing of the artery by attracting the Endothelial Progenitor Cells (EPCs). This will speed up the formation of the healthy epithelium cell lining and reduces the chance of additional blood clots. Thus, it helps for speeding up the cell lining of the artery (endothelialisation), which promote natural healing.

Bare metal stent(BMS)-Bare metal stent are the first generation stents are better suited to treat bleeding disorders and for the surgeries not related to your heart, such as hernia and stomach operation .BMS is a stent without a coating or covering (as used in covered stents drug-eluting stents). BMS act as self-expanding scaffolding and are used extensively in cardiology to maintain coronary artery patency.

Drug eluting stent (the second revolution in coronary stenting)

DES is a semi rigid tube-like device made of metal and coated with drug. The drug is slowly discharged to assist the hindrance of restenosis or reoccurrence of blood vessel blockage. The rapid technology advancement in the stent design and stent delivery system are anticipated to reduce the cases of restenosis, even for the most complex lesions.

Bioresorbable stent

Bioresorbable stents are very promising as they offer the vascular scaffold for a certain amount of time and then the implanted materials are progressively resorbed. This offers several advantages, including the elimination of foreign bodies inside the wall, restoration of endothelial coverage, and possibly restoration of vasomotion. These biodegradable stents can be divided into two categories: metallic stents that are magnesium based and those that are polymeric resorbable— more than 10 stents of this type have been studied, made of poly-L-lactic acid (PLLA) and poly-D,L-lactic acid.

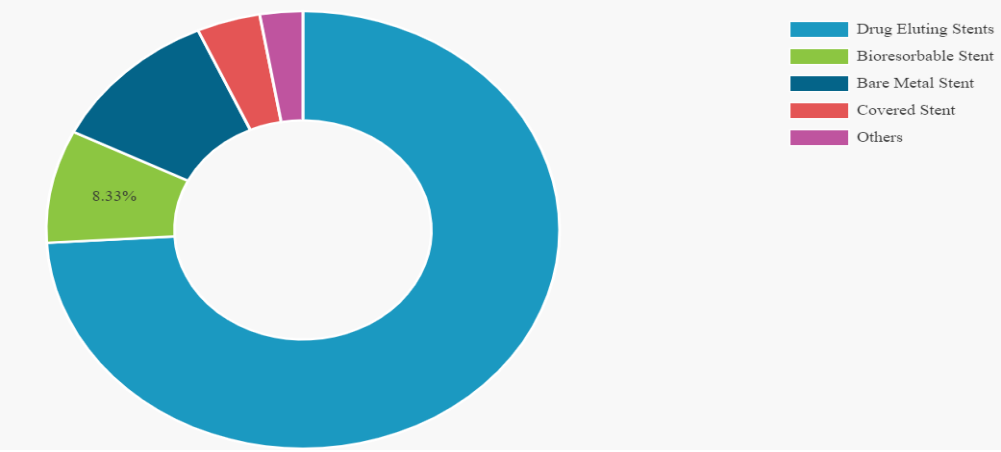


Figure 9: Global coronary stent market share, by stent type,2019

2.2 MECHANISM OF EXPANSION

Balloon- Expanding

The BE stent was pre-mounted on a balloon catheter and expanded and deployed by inflation of the balloon. The nominal stent diameter had to match the reference vessel diameter (RVD) of the target lesion. Post-dilation was permitted. Balloon expandable stents should have the ability to undergo plastic deformation and then maintain the required size once deployed.

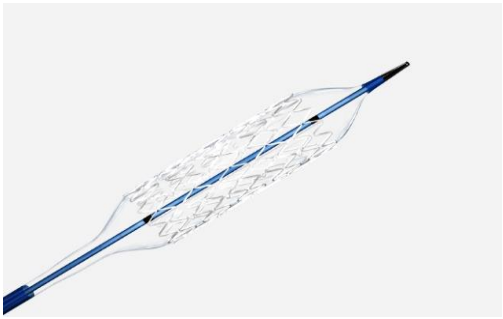


Figure 10: Balloon expandable sequential ring design

Self- Expanding

Self-expanding stents are affected among a delivery tube till positioned and deployed. Within a delivery catheter until positioned and deployed. Due to smaller delivery devices than balloon-expandable stent systems no balloon is required to deploy the stent. SE stents are manufactured at the vessel diameter (or slightly higher) and are crimped and strained to the smaller diameter until the intended delivery site is reached, where the constraint is removed, and the stent deployed.

Accordingly, Balloon expanding stents resist the balloon expansion process, whereas Self expanding stents assist vessel expansion. During deployment, balloon expandable stents exhibits plasticity and self-expandable stents exhibits elasticity.

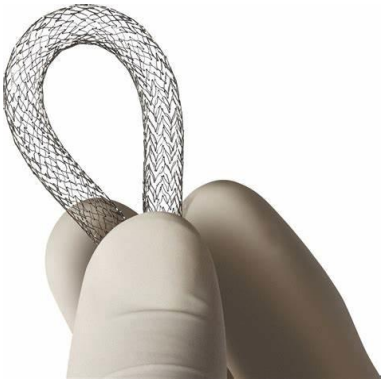


Figure 11: Smart -self-expanding peripheral stent

Final optimization of stent expansion usually requires additional dilatation within the stent using a high-pressure, noncompliant angioplasty balloon.

2.3 STENT CONFIGURATION AND DESIGN

Cardiovascular stent material engages in an important role in the clinical performance because of the mechanical support offered to the artery and compatibility of the material to the artery. Thus, material, configuration, design, and manufacturing method play an important role in proper functioning of the stent.

2.3.1 MATERIAL SELECTION

The materials of stents are selected based on mechanical properties, bio functionality, biocompatibility (i.e., corrosion resistant, less toxic, non-inflammatory anthromboresistant), and biological inertness. Materials for metallic balloon-expandable or self-expanding stents must exhibit excellent corrosion resistance and biocompatibility(Fig.13).These materials are classified into metals metal alloys polymers and ceramics.Fig.12 shows the stress-strain curve of metals, ceramics, and polymers.

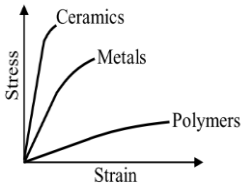


Figure 12: Properties of ceramics, metals, and polymers

Metals

Stents are also applied to vessels of the bile duct, oesophagus, and other passages for dilation. Therefore, elasticity or plasticity for expansion, and rigidity for the maintenance of dilatation and resistance to elastic recoil are required. Metals are the main materials utilized for stents because of their mechanical properties and visibility on X-ray imaging passages for dilation.[14]. Therefore, elasticity or plasticity for Metals have a high elastic modulus due to high tensile strength, leading to low stresses in the material Thus, metals such as iron, titanium, tantalum, cobalt, chromium, magnesium, nickel, iron, zinc, stainless steels 304L, 304V, 316LV; mild steels, Ni-Cr-Fe alloys, platinum enriched stainless steels, and tungsten alloys are biocompatible and are considered as biomaterials. Table 2 details the properties of metals. The materials such as stainless steel, nitinol (Ni-Ti), cobalt-chromium (Co-Cr) are corrosion resistant metal alloys. Iron and magnesium are considered as fewer toxic metals and little amounts of calcium, zinc, and manganese alloys show beneficial properties.

METALS	PROPERTIES	ALLOYS
Stainless steel	Passivative, Corrosion resistance	316 L
Nitinol	Self-expanding, Super elastic, Good MRI	
Titanium	Passivative, Less ductile, corrosion	
Tantalum	Passivative, Highly ductile, Corrosion resistance	
Nickel	Highly toxic, Inflammatory	
Chromium	Highly toxic, Inflammatory	Co-Cr
Magnesium	Biodegradable, less toxic, immediate degradation, less ductile	MgLi
Gold	Radio opaque	
Niobium	Passivative	
Zirconium	Passivative	

Table 2: Stent metals and their properties

New techniques for treatments using metallic stents are continuously being developed, and such development will continue into the foreseeable future.

Polymers

Polymers are used as stent materials as they have viscoelastic properties. Synthetic polymers, such as poly(ethylene) (PE), polyurethanes (PUR), poly(glycolide) (PGA), and polylactides (PLA), have been the choice for implants and alternative medical devices. While PURs are well established as scaffold materials for vascular grafts due to their excellent hemocompatibility, PGA is used as suture material for various surgical applications [15]. Further, PGA-containing scaffolds blended with poly(ϵ-caprolactone) (PCL) are used for PGA-based drug delivery systems. Overall, PLA has been intensely tested as temporary material in cardiology because of its long track records of in vivo biocompatibility.

The application of medical devices related to bioresorbable polymers is of increasing importance within the medical and pharmaceutical field. Typical representatives of polymers are polyhydroxy carboxylic chemical acids, such as PGA, PLA, poly(three-hydroxybutyrate) (P(3HB)), poly(4-hydroxybutyrate) (P(4HB)), and PCL. while P(4HB) is applicable for vascular grafts and heart valves [16]. Owing to extensive inflammatory responses in porcine models P(3HB) has not been accepted for vascular applications. The biocompatibility of these polymers, specifically in vascular stenting, depends to a huge extent on degradation kinetics. Polymers, such as phosphorylcholine (PC), poly(vinylidene fluoride)hexafluoropropylene (PVDF-HFP), or the BioLinx polymer, do not interfere with stent reendothelialization and are currently in use in second- and third-generation DES[17].

Besides biodegradable polymers, such as PLA and poly(lactide-co-glycolide) (PLGA), were extensively studied to optimize their properties and biocompatibility.

To improve the functionality of stents, drugs are used as anti-thrombogenic, anti-proliferative, anti-inflammatory, anti-coagulants, or cholesterol-lowering agents. A few drugs used on the DES's are heparin, paclitaxel, sirolimus, zotarolimus and everolimus.

Polymer coatings help in reducing the rates of thrombosis and neointimal hyperplasia. The concern with polymer coatings is the loss of adhesion coating while crimping and unsheathing of stents.

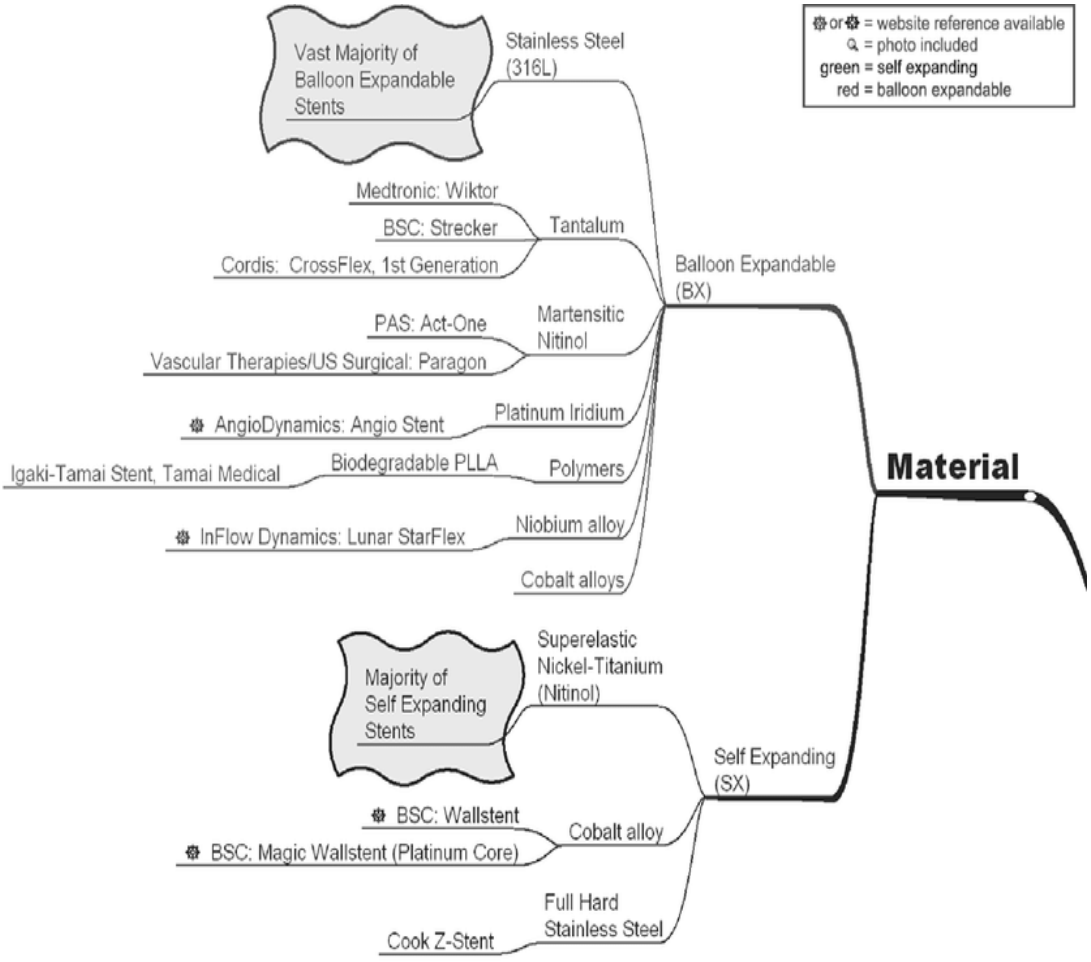


Figure 13: Overview of materials used in stent

2.3.2 CONFIGURATION

Struts, rings, cells, crowns, and connectors form the backbone of a stent (Fig.14).

- Strut: larger structural entities are formed by single element (cells, rings, and crowns).
- Cell: delimited by 2 layers of rings small but regularly repetitive structure of a stent, and the connectors and might be open or closed.
- Connectors: attach the adjacent rings can be straight or curved or can be direct welds that link the rings directly.
- Rings and crowns: involve a cluster of cells held together by connectors i.e. 1 crown is equal to 2 struts

- Orientation of the stent (in-phase or out-of-phase) and connectors (offset peak-to-peak; mid-shaft; peak-to-peak–out-of-phase; peak-to-valley–in-phase).

The mechanical performance of a stents defined by design and geometry of these components. crowns and rings determine radial support and expansion capacity; the number of connectors is responsible for the longitudinal stability, flexibility, deliverability, side branch access and longitudinal integrity. Reduced number of connectors by open cell designs provide greater stent flexibility along with reduced arterial injury and low neointimal response.

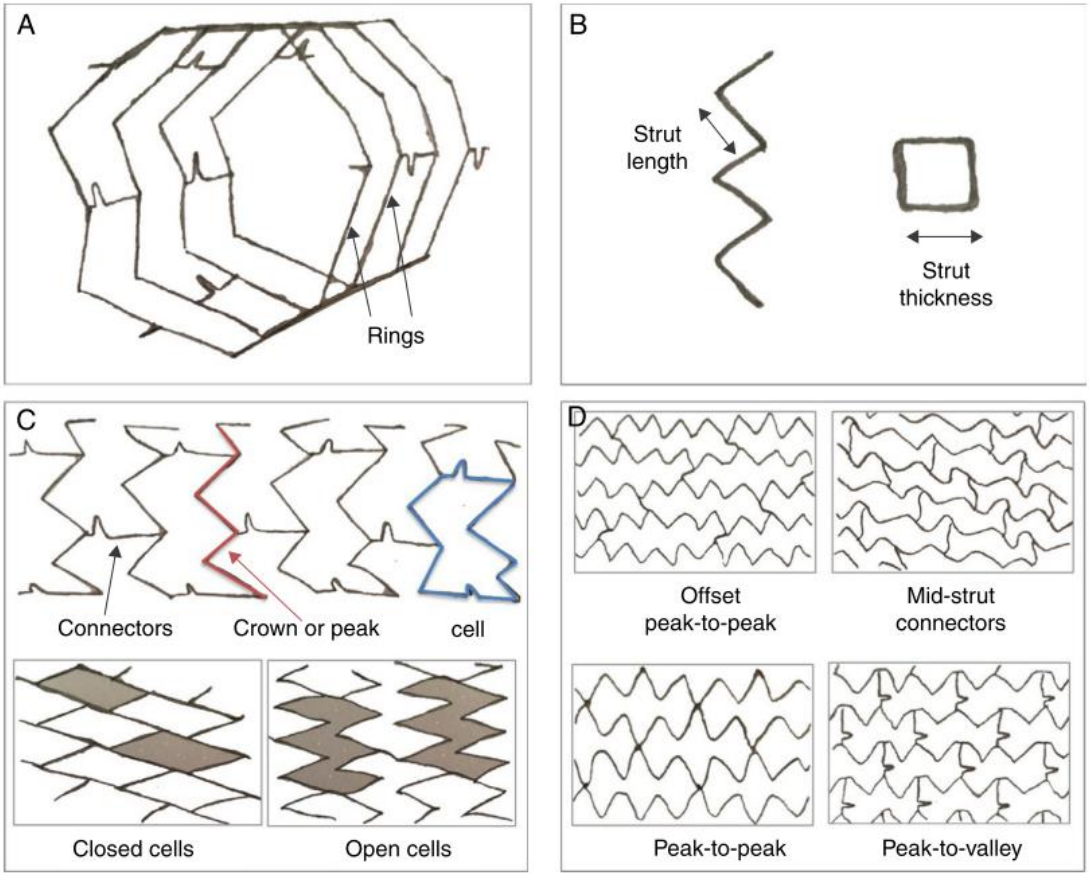


Figure 14: Structure and orientation of stent

2.3.2.1 OPEN CELL

- Bridging elements are not connected in some internal inflection points of the structure.

- Periodic peak-to-peak connections, peak-to-valley connections, and middle strut to middle strut connections. The unconnected structural elements contribute to longitudinal flexibility.
- Stents with larger or open cells were designed to reduce the meta surface area and to improve access to side branches.

2.3.2.2 CLOSED CELL

- Sequential ring construction
- All Internal inflection points of the structural members are connected by bridging elements.
- Regular peak-to-peak connections.
- Optimal scaffolding and a uniform surface, regardless of the degree of bending.
- Less flexible than a similar open-cell design

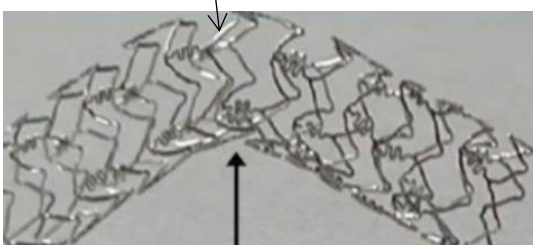
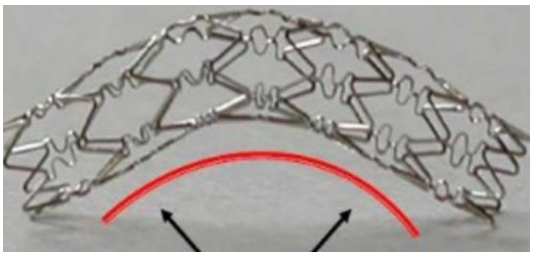
Open cell (Support segments are connected at 3 place)	Closed cell (support segment are fully connected)
Gap-Low drug concentration  Pinch-High drug concentration	 More uniform drug concentration

Table 3: Stent design impacts drug delivery

Properties	OPEN CELL	CLOSED CELL
Radial strength	Low	High
Plague Prolapse	High	Low
Metal: Artery ratio	Low	High
Conformability	High	Low
Side branch access	High	Low

Table 4: Properties of open and closed cell

2.4 DESIGN REQUIREMENTS OF CORONARY STENTS

Design plays a major role in stent performance. The design considerations for stents are high radial strength, low elastic radial recoil, good flexibility, low stent profile, good trackability, minimal foreshortening, minimal elastic longitudinal recoil, and optimal scaffolding.

Stents are manufactured with a nominal diameter and then compressed to smaller diameter (crimped) to actuate through the passage to the lesion site and expanded to the size of nominal diameter (deployment) [18].

Some characteristics of stents that have to be considered while designing and simulation include outer diameter, inner diameter, strut thickness, strut width, strut length, number of struts, length, metal to artery ratio, foreshortening, recoiling and dogboning.

- Flexibility-The ability of the stent to pass inside the artery through the lesion area
- Radial stiffness-The support provided by the stent to the artery wall after the
- deployment of stent
- Longitudinal recoil- The ability of the stent to shorten after deployment and
- removal of balloon catheter
- Foreshortening-The ability of the stent to deform longitudinally after deployment.
- Radial recoil-The ability of stent to contract after the balloon catheter is removed.
- Dogboning- The design characteristic to prevent restenosis caused my mechanical
- stress.
- Coverage area-The area between the arterial wall and stent
- Target life-The fatigue durability to undergo cycling loads.

Some other of stent performance that are not readily obtained during PCI, but which can have a very significant influence on PCI outcome

These metrics include:

a) Radial (and longitudinal) strength.

b) Fatigue resistance.

c) Stent malposition.

d) Tissue damage.

e) Drug distribution (for DESs) and

f) Flow metrics, particularly related to flow disturbance and the wall shear stress

environment.

Considering all the above characteristics, the design plays a significant role in stent's performance.

2.5. PROPERTIES AND CHARACTERISTICS OF STENT

2.5.1. Geometric aspects

Stents have various patterns and are classified according to diameter of stents, shape of struts, width, length, and thickness of struts. Coronary stents usually have a length of 8-60 mm, diameter of 2.25-5 mm, strut width of 0.08-0.1 mm and thickness of 0.07-0.14 mm [19]. The geometry depends on stent design and varies along the length of a single stent.

Geometrical configurations/design (mesh structure, coil, slotted tube, ring, multi-design)

Based on design, stents divided into three groups:

- Coil, tubular mesh, and slotted tube
- Tubular mesh stents encompass of wires wound along in a mesh material, forming a tube. In tubular, there are 2 type of forms, a slotted tube and modular tube.
- Slotted tube stents made of laser cut stent design. This type of stents has the members disposed predominantly along the longitudinal axis and are inherently rigid along this axis.

Coil

Coil stents are characterised by metallic wires or strips formed into a circular coil shape. Coiled stents are more flexible due to its members disposed substantially perpendicular to long axis. Greater strut width with gaps and fewer connections between struts. The width of strut is greater, which make gap between struts, and no connections between struts gives it more flexibility.

But still, the design lacks radial strength, and the wide gap gets tissues to dangle. As a result, by superior in radial strength coil design has become obsolete, the tube design [20]. Fig.15 shows the coil shaped stent fabricated from nitinol ribbon.

Figure 15: coil stent fabricated from nitinol ribbon

Helical spiral

Helical spiral designs have an advantage of flexibility. They lack longitudinal support even with minimal internal connection points. Hence, they subject to irregular cell size due to its elongation or compression during delivery and deployment. Flexibility is sacrificed in exchange for longitudinal stability and extra control over cell size with internal connection.

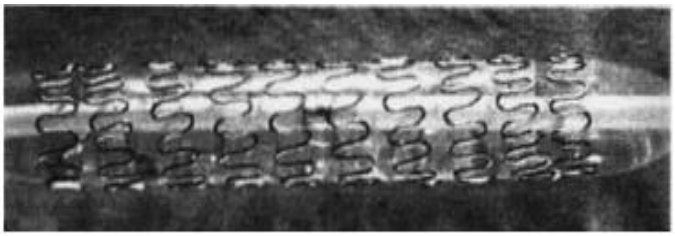


Figure 16: Minimally connected helical spiral geometry.

Woven

Variety of structures are designed from one or more strands of wire. Axial fixation at its ends is extremely attached to the radial strength of braided structure. Excellent coverage has been reported. And typically shorten during expansion.

Individual rings

Single ‘Z’-shaped structure is used to support grafts or regular prostheses; Rings are individually sutured or attached to the graft material during manufacturing. Like vascular stents they are not typically used.

Sequential rings

Z-shaped expandable series structural elements (known as ‘struts’) joined by connecting elements (known as ‘bridges’, ‘hinges’, or ‘nodes’). Most commercially available stents are of this type.

This category can be further refined by describing the way the structural elements are connected, and the nature of the resulting cells are:

- Regular connection details bridging elements of connections to every inflection point around the circumference of a design.
- Periodic connection details bridging components of connections to a set of the inflection points round the circumference of a structural member. In some outlined pattern, connected inflection points alternate with unconnected inflection points.
- ‘Peak–peak connection’ or ‘peak–valley connection’ are terms used to detail the locations of place where adjacent structural members join. ‘Peak–peak’ elements join the outer radii, and ‘peak–valley’ elements join outer radii to inner radii of the inflection points of adjacent structural members.

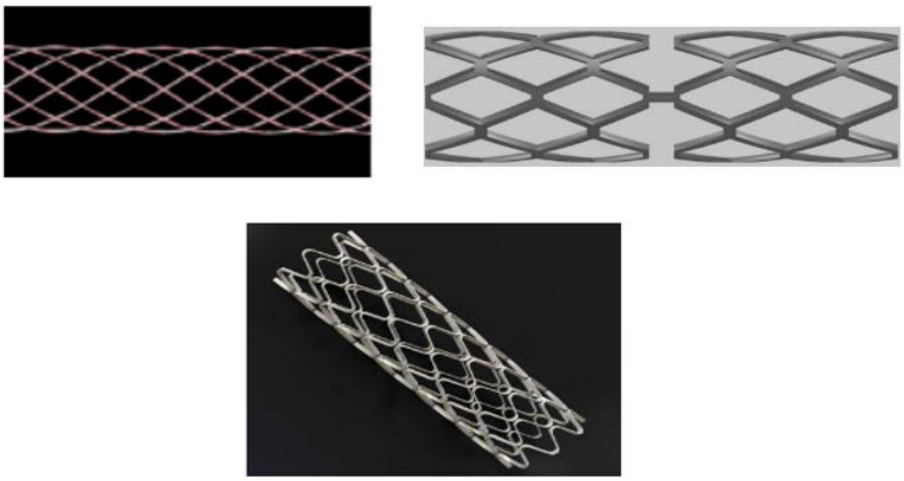


Figure 17: Woven, Sequential, Individual ring structure

2.5.2. MATERIAL ASPECTS

A huge majority of the balloon expandable and self-expanding stents are created up of wire or tubing. After the pattern created, stent made of sheet metal must rolled to tubular configuration. The ability of mechanical support offered to the artery, depends upon material properties, which include considerations such as Young's modulus and tensile strength which are important in material selection process. Some of the mechanical properties of materials consist of ductility, good elongation, high tensile strength, etc.

Stent material, geometry, and medical aspect of the stent are the important mechanical concerns: Mechanical properties=f (material, geometry, application)

The main materials currently used, or which are being investigated are briefly presented in Table 5.

Type	Material	Description
Nondegradable	316 stainless steels (SS316)	It is also referred to as marine-grade stainless steel; is a chromium, nickel, and molybdenum alloy of steel that exhibits relatively good strength and corrosion resistance; and is a common choice for biomedical implants, such as stents
	Nitinol (NiTi)	Nitinol is a metal alloy of nickel and titanium, where the two elements are present in roughly equal atomic percentages. Nitinol alloys exhibit two closely related and unique properties—shape memory (SME) and superelasticity (SE)— perfect to self-expandable stents
Fully degradable	Magnesium (Mg)	Magnesium is the third most commonly used structural metal. Magnesium is used in super strong, lightweight materials and alloys. Magnesium alloys have been historically used by the magnesium tendency to corrode, creep at high temperature, and combust
	Poly-l-lactide acid (PLLA)	PLLA is a biodegradable thermoplastic aliphatic polyester derived from renewable resources, such as corn starch. Degradation is produced by hydrolysis of its ester linkages in physiological conditions
	Polycaprolactone (PCL)	PCL is a biodegradable polyester with a low melting point (60°C) and a glass transition of about -60°C. Degradation is produced by hydrolysis of its ester linkages in physiological conditions and has therefore received a great deal of attention

Table 5: Stent materials

To understand the mechanical behavior of the new polymeric BRS many efforts are being taken in simulating polymeric materials [21].

One of the main factors of stent re-occlusion in the clinic is bacterial adherence and biofilm formation on the surface of the material.

Most importantly, it is not solely necessary to understand the characteristics of the material at its initial non-degraded stage, conjointly however do these evolve with degradation. Most studies of polymer degradation were performed without mechanical loading.

Despite the advances, many concerns remain; one of the most important is the investigation of the cell proliferation of the material that helps to induce a rapid endothelialisation.

CHAPTER 3

3. MANUFACTURING PROCESS OF STENT

Stents are manufactured from several forms of materials such as machining from tubular Laser cut with water jet forms, machining on the sheet, and later, the ends are attached by welding, rolling, etc., to form into a tubular form. Stents are manufactured in several methods and they are classified according to traditional and modern manufacturing methods.

The manufacturing process mainly depends on the materials and stent type are chosen:

Manufacturing process=f (material, stent type).

3.1 LASER MACHINING

Laser cutting is most widely used manufacturing method in medical device industry because of its precision machining process. A high energy density laser is concentrated on piece of work surface the thermal energy is absorbed that heats and transforms the workpiece volume into a molten, vaporized, or chemically modified state which will be simply removed by flow of high pressure assist gas jet [22].

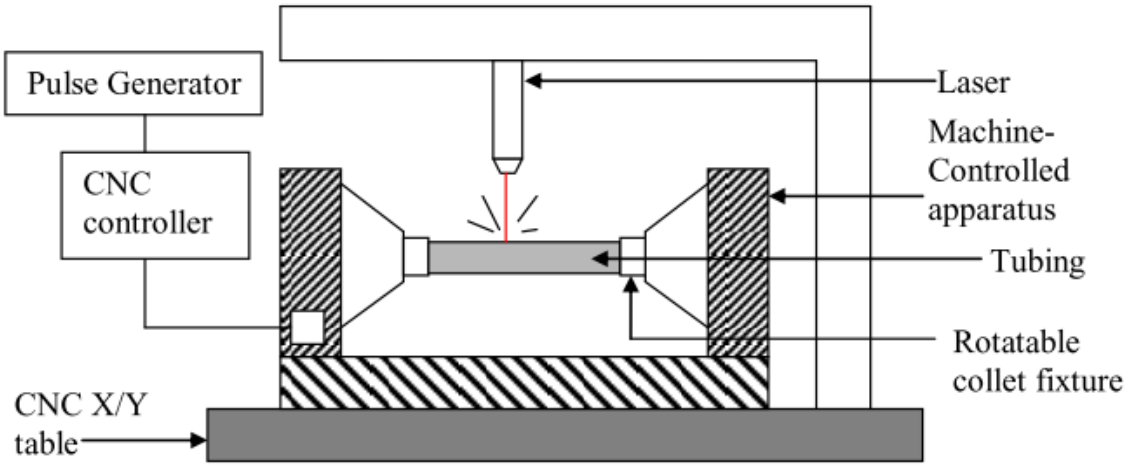


Figure 18: Laser beam cutting machine

This method results in thermal damage such as heat-affected zone (HAZ), striation, recast layer, microcracks, tensile residual stress, and dross. some of the post-processing techniques are applied to avoid thermal damages are pickling techniques, soft etching, annealing, and

electropolishing. But these post-processing techniques has enhanced the manufacture price and probably have effect on the mechanical properties of stents.

Various works, which study how the process parameters affect the quality, trying to diminish the thermal problems and the cost of the stent manufacturing process also to be reduced.

Laser cutting with computer numerical control (CNC) machine and pulse generator

For linear motion in x and y directions the machine-controlled apparatus aligns on a CNC X/Y table and this table further acts as a base to support the equipment. A pulse generator connects the CNC controller and laser simultaneously as shown in Fig.18. Laser beam with no pulse generators causes high heat and melts the work piece material. Therefore, ultrashort pulse lasers that produces short pulses of less than 10-11 seconds are introduced. This makes a good surface finish and after machining surface treatments are insignificant.

Laser cutting with linear and rotary motors

This method as stent cutting device with linear and rotary motions to manufacture the stent. A common base on the bottom surface attaches the linear motor. On the top surface of this common base aligns the laser machine that remains stationary.

Laser cutting with water jet

This method as water with high intensity of force and pressure is rendered for cooling as well as for internal reflection. The main advantage of this method is that the work piece is free from heat, chemicals, flame charring, burrs, and contamination [23].

Despite the advances, the applicability of the current laser-cutting manufacturing process for making BRS of polymers are made wonder by the concept of inclusion of BRS.

3.2 ELECTRIC DISCHARGE MACINING

It is a process in which electrical energy is used to generate the Spark between the tool and workpiece submerged under the dielectric medium so removal of material takes place from the surface of the workpiece by melting or Vaporization called as Electric Discharge.

Micro electric discharging machining stent manufacturing method with a metal foil method consists of 50 µm thick stainless steel 304 foil, µEDM, design pattern. The µEDM stent manufacturing method with metal coil as represented in Fig.19.

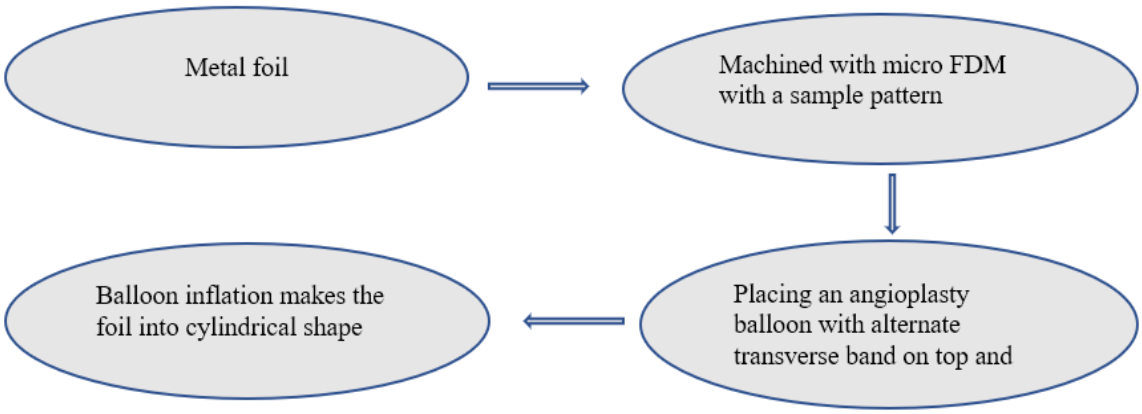


Figure 19: Process flow of the Micro EDM on metal foil to make a stent

The Micro EDM process machines the metal foil in involutes pattern. An angioplasty balloon inserts into alternate transverse bands of the foil and the inflation of the balloon expands the foil into cylindrical shape or tubular stent.

3.3 HYDRO CUTTING

The method introduces a jet stream with high intensity of water on the surface of the material to cut the material into slots. In hydro cutting, the material exposes to jet stream with abrasives such as garnet to form the slots. Apart from abrasives, hot water with chemical applications also promotes the cutting process.

3.4 PHOTOSENSITIVE CHEMICAL ETCHING

Etching is based on the photolithography process. To developed and etched for the desired pattern the desired mask pattern is first projected on plain sheet coated with photoresist and later to be exposed. The UV rays from the light source exposes the work piece and this endows photo sensitive resistance coat on the material to react and change the properties of exposed areas on the work piece. The work piece withstands electrochemical etching treatment to form the stent structure.

3.5 CASTING

Stents are produced by casting the metal directly in stent like form or cast into sheet or tubes. There are several methods of casting and they are centrifugal casting, Pouring the stent material in the indentations/ grooves.

3.6 VAPOUR DEPOSITION

Vapor deposition or evaporation involves the heating of precursor powders beneath the high vacuum until the vapor pressure is sufficient to coat a substrate suspended higher than the evaporation sources. The evaporation process as a chamber with rotary motor, mandrel, source material and vacuum represents in Fig.20.

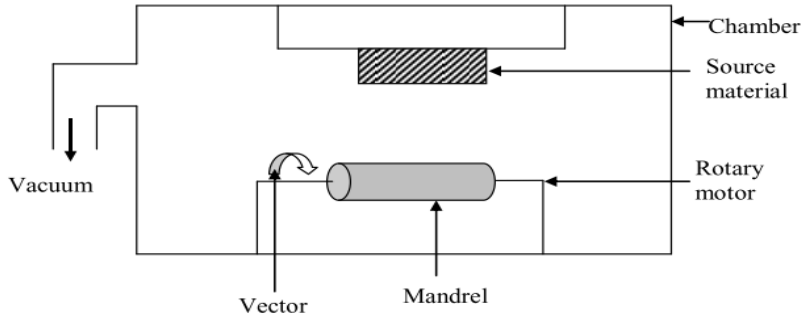


Figure 20: Vacuum deposition by evaporation

The set up allocates the mandrel on the rotary motor and it rotates in the direction of vector with a speed of 1-60 rev/min. Vacuum fills the chamber and develops appropriate vacuum pressure. The source material flows from top of the chamber towards the mandrel. The termination of the process takes place when a desired thickness of material deposits on the mandrel.

3.7 WIRE BRAIDING

The spools provide yarn and reinforced wire to the knitting machine as shown in the Fig.21. The break mechanism connects the spool of wire and inactivates whenever the wire is inessential. The supply speed of the yarn and wire to weave is in the ratio of 4:1. The materials employed for yarns are natural fabric, polyester, polypropylene, polyethylene and for wire are metal alloys. And final Single braided wire is shown in Fig.22.

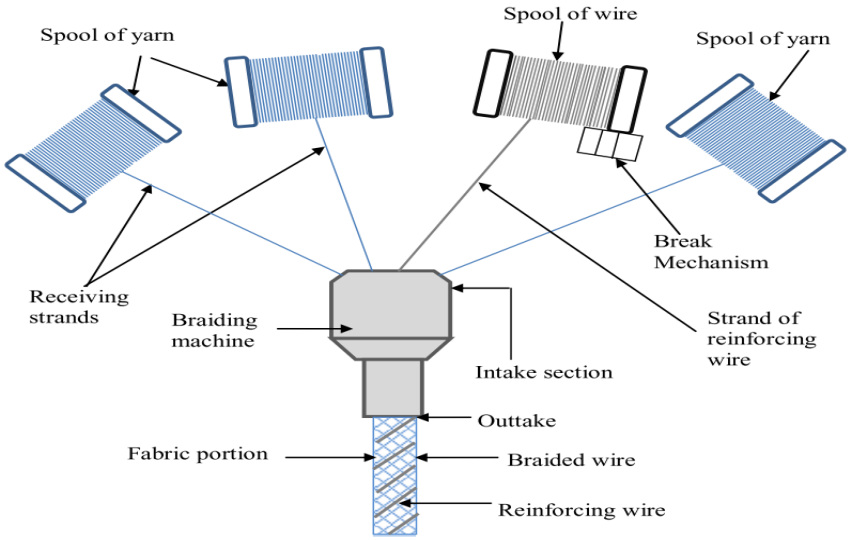


Figure 21 Braiding machine with yarn and wire to form tubular stent

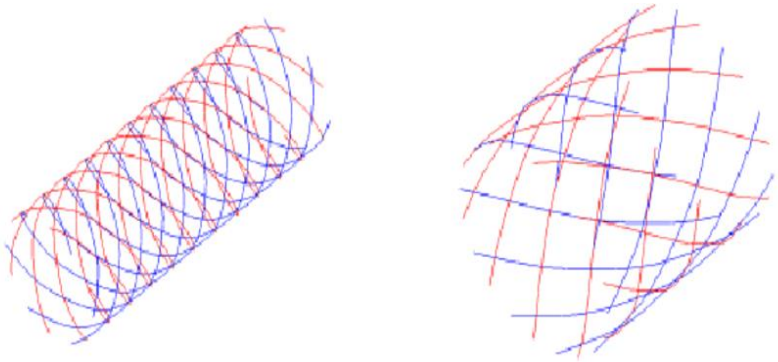


Figure 22 Single wire braided wire stent

3.8 ELECTROMAGNETIC FOAMING

The apparatus consists of a forming coil (electromagnetic generators), energy storage capacitors, power supply, conductive metal object (workpiece), and field shape mandrel. The energy storage capacitor connects the power supply and forming coils. The work piece and field shape mandrel are positioned between forming coils and the apparatus is shown in Fig.23.The forming coil generates electromagnetic pulses from the capacitors and the workpiece (conductive material) thus induces eddy currents. The magnetic field from the forming coil and eddy currents from the work piece interacts with each other and leads to the formation of repulsions between them. These repulsions simultaneously lead to stress

formation and deform the metal permanently. The field shape mandrel helps to cut the metal with the magnetic field at precise points, thus forming the desired shape.

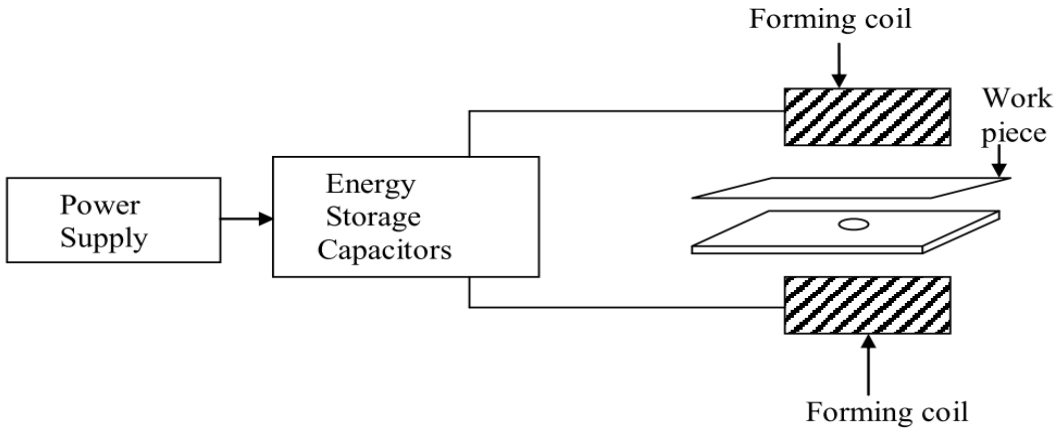


Figure 23 Electromagnetic forming: apparatus manufacturing medical stents

CHAPTER 4

4. TECHNOLOGICAL ADVANCEMENT IN STENT MANUFACTURING

For the safe and effective treatment for patients with angina due to coronary artery disease, field of PCI has witnessed numerous advances over last decades.

4.1 ADVANCED COATINGS FOR IMPROVED BIOCOMPATIBILITY

Although there is no strong scientific evidence exists, it is found that surface optimization could help in reducing restenosis rates for bare-metal stents below the typical range of 20% - 30%. To achieve stability of surface oxide-layer to reduce metal-ion release, reduced surface thrombogenicity, and surface texturing to promote endothelialisation wide variety of surface modifications and inorganic coatings were explored. To improve biocompatibility by minimizing metal-ion release, corrosion resistant oxide surface such as titanium oxide or chromium oxide can be used. In Coating fabrication three types of material used: inorganic compounds, polymers, and endothelial cells. Inorganic materials and polymers can be used for creation of porous coatings.

The process of preparing a nitric oxide-generating adherent coating, comprising of polyphenol compounds, organic selenium or sulphur compounds and soluble copper salts is disclosed in the invention[25].The nitric oxide-generating material has the capability of scavenging free radicals and catalysing S-nitroso thiols to produce nitrogen monoxide, which leads to reduce the risks of thrombosis, inflammation, and restenosis related to the stent applications.

Inorganic Coating

Prospective inorganic materials for producing of stent coatings are oxides, nitrides, compounds, silicide and carbide, noble metals, hydroxyapatite-based materials, diamond, and diamond-like carbon.

DLC

Carbon coatings were explored earlier as another means of surface modification, with several different methods examined including “diamond-like carbon (DLC)”. Few DLC-coated

stents are available on market and development stage, due to their ability to reduce metal ion release. And probably still has a marketable advantage over bare-metal stents. Mostly inorganic coatings of stent provide either ineffective or inconclusive results in terms of reducing restenosis, which was the primary goal behind their development.

Bio-Based Coatings

Primarily, endothelial cells placed on the stent surface before its implantation with the aim of cell proliferation, differentiation, release of growth, and, finally, inhibit thrombosis and neointimal hyperplasia. The effect of coated stent with antibodies to endoglin (ENDs) on coronary neointima formation is the aim of the study [26]. The results demonstrated there is a reduction in restenosis in the porcine model of endoglin antibody-coated stents and considered as a new approach to prevent restenosis.

4.2 NANOMATERIAL-BASED HYDROGELS FOR CORONARY STENT

Several materials have been utilized as a PCI tool in the treatment of Myocardial infraction. Soft material-based hydrogels are being used in various forms in cardiac tissue engineering (CTE). The stiffness of materials, bioactivity, and biodegradability are the key factors that play an important role in the selection of hydrogels for PCI. Use of chitosan as a hydrogel for cardiac disease, especially as a stent, have been performed due its tunable stiffness, wettability, and swelling properties. The bioactivity of the material can be enhanced due to sulfated chitosan. In a recent study, designed a 3D-printed bioresorbable stent using polycaprolactone (PCL), surface modified with sulfated chitosan [27].

Chitosan coating has been reported to improve compression resistance. It was found that the chitosan coated PVA stents were suitable for use in PCI because of their higher bioactivity and cytocompatibility (80% cell viability).

Various other studies have been conducted using chitosan as hydrogel material for PCI. Chitosan because of its highly bioactive, biocompatible, and moderately biodegradable property, used as a coating material on various stents for the treatment of MI.

Recent findings suggested that chitosan-containing stents are very effective for use in stents for PCI.

4.3 DRUG, NANOPARTICLE, AND GENE-ELUTING STENTS

Stents can be improved by using DNA, siRNA, and miRNA as well as nanoparticles instead of drugs. For example,[28] developed a novel coating method using sirolimus-loaded PDLLA (Poly DL Lactide) nanoparticles applied on a 3D-printed biodegradable PLLA stent with the result of good inhibition effect on smooth muscle cell (SMC) proliferation than on endothelial cell proliferation.

Currently, there is a tendency to fabricate polymer-free drug-coated stents (PF-DES). Examples of this are the stainless steel sirolimus-containing stent, the stainless-steel Bio Freedom stent (Biosensors) coated with Biolimus A9, and the polymer-free cobalt-chromium Amazonia Pax stent with paclitaxel [29]. Stent surface modification is the first step aiming to creating the sites of drug localization and drug deposition. The drug localization sites may be a drug reservoir—a system of nano, micropores, nanoparticles in a matrix compound on a stent surface.

4.4 IMPROVEMENTS INTO THE DESIGN ASPECTS AND MECHANICAL ASPECTS OF STENTS

There are significant numbers of improvements in achieving the ideal stent design Standard lengths is the problem of currently available stents. As mentioned, the longer the stent, the more prone it is to fracture. Therefore, having a stent of a customized length would reduce this problem. Thus, one of the most innovative stent designs is the NX Co-Cr stent designed by Xtent Custom is shown in Fig.24.

Figure 24 Interdigitating NX stent design by Xtent Custom

Stents of multiple 6 mm inter-digitating segments is the unique feature, which indicates that the length of the stent is “infinitely” variable, and hence, system allows for lesion

determination of stent length instead of relying on fixed length stents. Therefore, small, or long lesions of variable lengths and diameters can be treated with a single device.

Overlapping of stent design studied the interaction types and location of overlapping stents. It was found that all the overlapping contact patterns between struts are edge-to-edge or edge-to-surface with no surface-to-surface contact pattern [30]. This phenomenon is mainly due to its non-uniform deformation of the stents in the radial direction during the implantation and their tubular structure. The contact pressure is primarily concentrated on its edges after the expansion of second stent, which results in the failure of an overlapping stent. It is often occurring along the edges. Later created a nitinol overlapping open ring with asymmetrical, intermeshed saw-tooth design—called recoil-resilient ring (RRR)—to potentially integrated with currently developed stents for reducing the mechanical failure due to recoil.

Coating integrity plays a major role in reliability and protection of the stent device. Distribution of small coating parts by the blood flow can lead to various health risk due to effects of cracking, delamination and peeling off stent surface. Therefore, there is a high need to tailor a stent design to reduce the probability of mechanical damage of the coating and the whole stent itself. It is important to consider the areas of the largest plastic deformation due to high mechanical stresses, i.e., the strut crowns.

Coated stents were investigated the coating which retained its original integrity after being crimped to ~Φ1.4 mm and then followed by expansion to ~Φ3.1mm of no peeling-off or delamination detected [31].

CHAPTER 5

5. 3D PRINTING – A PROMISING MANUFACTURING PROCESS FOR STENT

Recently, three-dimensional (3D) printing, a particular technique in the medical field, has emerged as an alternative system for manufacturing biomaterials. 3-dimensional printing technology (3D printing) is an additive manufacturing technology which reduce product development costs, control the distribution of materials and short cycles in development of products. Therefore, relying on 3D printing technology, it is of great significance to carry out digital design and manufacturing research on biodegradable polymer stents [32]. Compared with other devices, 3D printing system applied to rapid prototyping in structural fabrication can easily manufacture biomaterials, such as BRS.

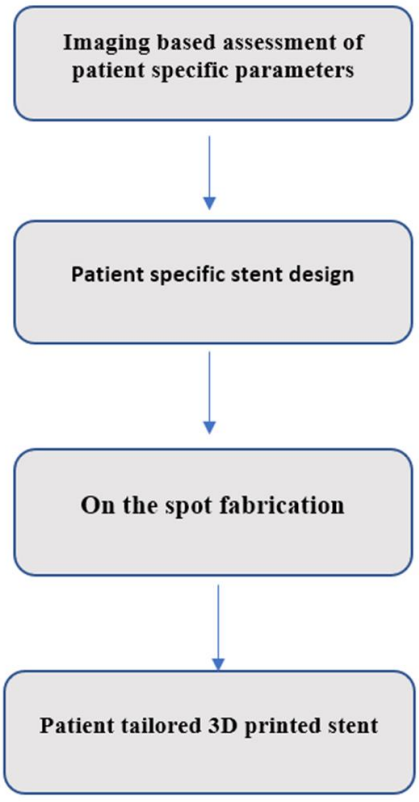


Figure 25 flow of stent design

Clinicians use Computed Tomography technology to obtain 3D images for a complete and deep view of the anatomical region of interest to better understand any associated medical condition. However, Computer tomography is not the only technique working in the 3D domain. However, several other approaches are possible , including 3D magnetic resonance (MRI), positron emission tomography (PET), 3D Ultrasound and 3D laser scanning (for external imaging) [32].Exploring Additive Manufacturing solutions for productions based on the medical data obtained from specific patients allows to fabricate unique devices, customized to answer individual needs. The strategy of on spot fabrication is tailored in Fig.25.

5.1 3D PRINTING METHODOLOGY

Equipment

By using a 3D-printing process in a 3D tubular printer, stents are manufactured. This 3D additive manufacturing machine is based on the FDM method (Fig.27).

FDM technology is easy to be used and capable to produce complex geometries. Though there is several advantages, the layer-by-layer fabrication strategy strongly affects this process and causes an important limitation in terms of achievable surface finishing. Therefore, the possible solution is a post-processing phase to be performed on the components produced by FDM. These treatments can be mechanical and chemical.

In the extruder nozzle the filament gets melted, which later deposits the melted material onto a controlled rotatory cartesian platform (Fig.26). The machine provides 0.9375 µm precision on the X-axis, 0.028125° on the W axis, 0.3125 µm on the Z-axis, 0.028125° in the extruder that has a 0.4 mm diameter.

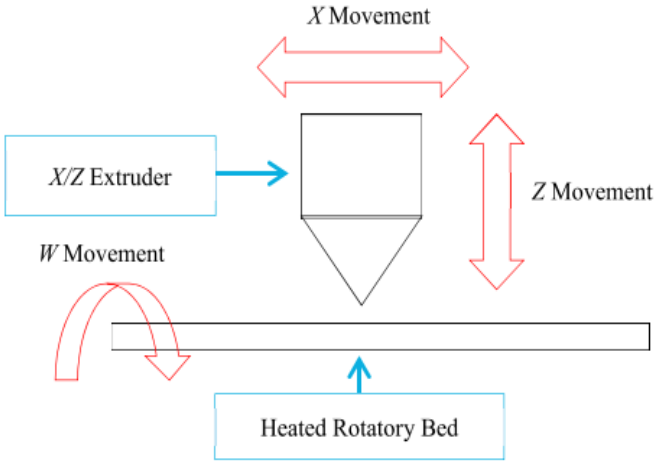


Figure 26 Machine methodology

Figure 27 3D Printer (creality ender 3 plus)

Recently, there is an intense research effort ongoing focused on the application of 3D printing research to a range of health applications.

Advantages of 3d printing

3D printing has been applied mainly to low volume production, the products available are far superior (lighter, stronger, and customizable) and cheaper than if created with traditional

manufacturing processes. 3D printing can control exactly deposition of materials which makes it possible to create structures that cannot be produced using conventional methods.

It can create vastly different products from ceramics to human tissue with high manufacture speeds, a low footprint and cost, and the flexibility to build a wide range of products.

3D printing also done at far near the point of application and consumption. All these features make it a serious change to manufacturing, medicine, warehousing, and retail methods and practices.

5.2 CUSTOMIZED 3D PRINTING PROCESS

The stent model used for the experiments was a hexagon and diamond-cells stent. The stent parameters were the following: inner diameter, stent thickness (ST), number of circumferential cells (NC), width and length of the cell (WC, LC), strut width (SW). These parameters determine the behaviour of the stent, the correct adjustment of them is crucial for calibrating the stent to the needs of each patient [33]. The preparation of the stent size and setting parameters was shown in Table 6.

Rhinoceros (generally called as rhino or rhino 3d) is a commercially developed 3d computer graphics and CAD software. Based on the NURBS mathematical model, rhinoceros geometry focuses on producing mathematically representation of curves and freeform surfaces in computer graphics.

- Through the 3D modelling software Rhino 3d to establish the two-dimensional plane of the stent to expand the 3D graphics, save the file as STL format.
- The saved STL file is imported into the slicing software called ultimaker_cura 4.7.1, the path is generated, and then the generated path is exported from the slicing software and stored as the identifiable G-code of the coronary stent forming device.Fig.28 and 29 respectively established to define the model.
- Based on the influence of different 3D printing process parameters on the fabricating quality of the vascular stent, the optimum parameters of the 3D printing molding were determined, and the biodegradable polymer material PLA was used for printing.

- The filamentous Poly Lactic Acid (PLA) was selected as the scaffold molding material, and the outlet diameter of the printing nozzle d was 0.4 mm. The printing speed of 200 mm/minute printing speed and temperature was 220 ◦C for nozzle, 25 ◦C for bed is set for PLA stent.

Structure	Geometry of nozzle (mm)	d(mm)	Strut thickness(mm)	L(mm)
Hexagon	0.4	3.0	0.3	19.86
Diamond	0.4	4.0	0.3	21.43

Table 6: Geometry of stent

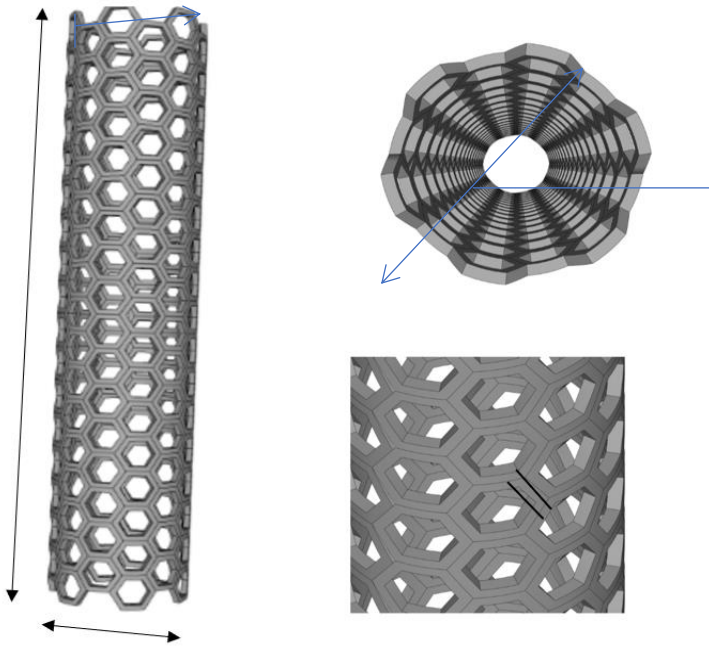


Figure 28 Design 1 - View of CAD Stent design displayed in perspective view and top view

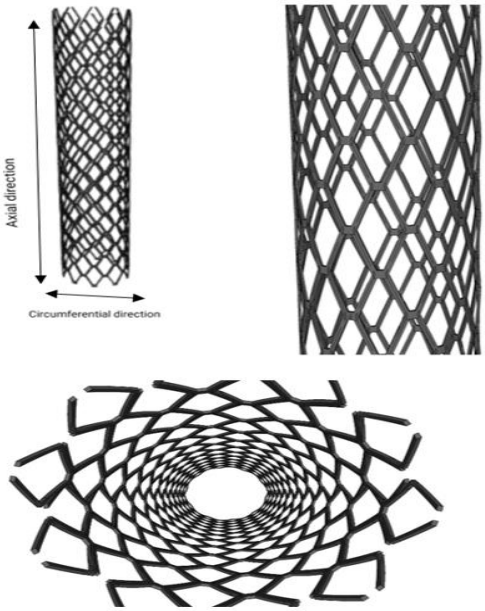


Figure 29 Design 2- Diamond shaped cell -perspective view

Stents with a longer connector and a smaller width of stent strut (t) have advantages of bending flexibility of stents with same diameter; therefore, stents with a loose geometric tend to show better flexibility in structure. Stents with a larger connector (h) and a moderate strut width are more conducive for a balance between bending flexibility and radial strength.

CHAPTER 6

6. CONCLUSIONS

Due to a very high mortality rate caused by cardiovascular diseases worldwide, and a promising approach of stent technology, researchers and clinicians are paying great attention to develop new materials, methods, and solutions in order to improve the clinical outcome of currently existing stent types, aiming at more safety for patients, and a higher success rate of cardiovascular treatments. In the frame of this review paper, different technologies of stent fabrication, especially related to coated, bioresorbable, as well as drug-eluting stents, have been considered.

3D Printing is distinguished from traditional manufacturing technologies by its ability to handle complex shapes with great design flexibility. This feature makes the 3d printing techniques particularly suitable to produce customized components. In fact, the production of custom made devices concerns the realization of products suitable to the specific needs of the customer, and Additive Manufacturing allows to achieve in a simple and cheap way complex geometries to produce even a single piece (notoriously a critical aspect for traditional technology).

The idealized geometry used for the study makes it possible to have a good approximation of the mechanical interaction between the stent and the vessel, but a patient specific geometry would enable a much better understanding of the behaviour in stent–artery interaction conditions.

This Project highlights the importance of additive manufacturing using 3d printing technology which makes the stent platform quite easy to fabricate. Stents are complicated support structure/Bridges which should meet basic design and size of every individual to avoid rejection and to increase the quality of life. Numerous amounts of Stent models can be designed out of CAD and can be simulated to identify the proper proportion of stent with the given materials provided that the materials are changed with change of designs. My internship at MedCuore Medical Solutions Pvt. Ltd, India focuses only on the review, characterisation, and design of coronary stent.

6.1 FUTURE PERESPECTIVE

Despite the revolutionary role of vascular stents in terms of clinical outcomes in interventional cardiology, complications associated with stent implantation have remained a major problem. To overcome the limitations, there have been many reports for the treatment option of choice for stent design. Stent design with multiple materials as well as in combination of materials needed to be simulated to understand the most viable element that can be used for synthesis and to identify the best possible design which are highly stable. These reported treatments can be categorized into the main list which includes the following attempts: Surface modification with polymer coating materials, nanocomposite materials, and tissue engineering-contributed strategy to improve surface properties. To improve the stent properties like brand new covered stents, polymer-free stents, brand new bioresorbable, and biodegradable materials. New technologies are under development to take advantage of biodegradable polymer-based stents. Biomolecule-decorated polymeric surfaces in association with nano-devised techniques would be the most common strategy for future. Unleashing the potential of additive manufacturing will surely open the door to new era of stent technology.

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