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A review of production technologies and materials for manufacturing of cardiovascular stents

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ABSTRACT

The purpose of this article is to give a general overview of the production technologies of stents with consideration of their design and materials. Since the beginning of the use of stents in medicine for atherosclerosis treatment, their development has changed rapidly. Various stents have also been developed with the development of materials science, treatment techniques and new manufacturing processes. In this way the development has shifted from the initial bare-metal stents (BMS), to drug-eluting stents (DES) and bio-resorbable stents (BRS), which are made of biodegradable polymers or metals. Various studies agree that it will be necessary to further review the experimentally obtained material properties with analytical and numerical studies. Here, the computational modelling (Finite element analysis – FEA and Computational fluid dynamics – CFD) was found as a valuable tool when evaluating stent mechanics and optimizing stent design. The development of the stent manufacturing technologies has also changed and been supplemented over the years. Nowadays, 3D printing could be an exciting manufacturing method to produce polymeric bio-materials, suitable for the latest generation of bio-degradable stents applications.

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1. Introduction

A stent can be defined as an endovascular prosthesis. They are skeletal meshes made of metal, placed inside a clogged coronary artery. The stent is developed for the purpose of preventing complications which occur in atherosclerosis. The latter is a chronic disease caused by the accumulation of fatty deposits on the walls of blood vessels, which causes the blood vessels to constrict. In this case, the supply of tissues is insufficient, which may lead to a heart attack or stroke. The most important characteristics of a stent are corrosion resistance, low thrombosis rate, biocompatibility, radiopacity, easy positioning, flexibility, high radial strength, low elastic displacement, uniformity, minimum surface area, low pass profiles and low costs [1].

In 1977, the German physician Andreas Gruentzig performed the first coronary balloon angioplasty on a conscious man. Problems which occurred after such procedures were acute vascular closure, short-term elastic displacement and prolonged restenosis. Restenosis is the artery's response to severe damage, caused by balloon angioplasty. One of its characteristics is the increased proliferation of smooth muscle cells and deposition outside the cell matrix, leading to progressive luminal narrowing. This phenomenon was observed in 33 % of the patients [1].

In 1986, Siguart and Puel performed a technique with a self-expanding stainless-steel stent on a human. The technique involved the expansion and permanent installation of a mechanical support device. Since then, many improvements have been made in the fields of Design, Materials, Implementation technique, etc. All of this has helped to increase the use of stents. Furthermore, with the insertion of the stent, it was proven that the restenosis rate decreased compared with the balloon angioplasty. However, a new problem can arise, which is called in-stent restenosis (ISR). As a final product, a neointima formation appears, consisting of smooth muscle cells and components of the extracellular matrix. The process of neointima formation stabilises in the human body after about 3-6 months.

2. Basic characteristics of stents

2.1 Stent shape

The shape of a stent is usually cylindrical and has at least one structural element (Fig. 1). These elements are arranged so that the stent can be stretched and compressed radially. The structural elements can be splints, rods, fibres, wires, or threads. The platform of the stent must provide [2]:

- Mechanical characteristics which, in the process, means that it matches the curvature of the vessel easily after stretching and maintains sufficient radial strength to withstand the force of the load on the arterial wall.
- Radio impermeability, to prevent the transmission of X-rays or other ionising radiation due to any necessary interventions.
- An easily replaceable base, namely, the stent should have a narrow profile in a compressed state so that it can be placed easily and can pass through narrow veins, with stenoses, effortlessly.
- Biocompatibility, which means that the material of the stent should be compatible with the blood and the surrounding vascular wall.

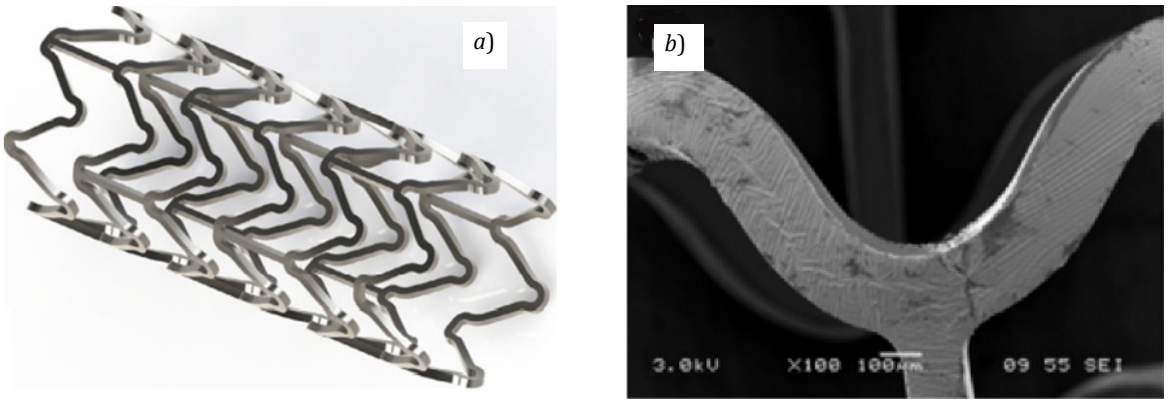


Fig. 1 a) Designed model of a cardiovascular stent, b) Scanning electron micrographs of a stent at 100× magnification with strut thickness of 150 µm [2]

2.2 Stent construction

The first stent implanted into humans was the Wallstent. It had a self-expanding platform that contained a stainless-steel metal structure. The Palmaz-Schatz stent introduced an alternative mechanism using an expandable balloon. Today, all stents are made from this principle. These stents have higher radial strength and better clinical outcome than the competing mesh and coil stent structures. Further platform developments have established a balance between coil flexibility and radial strength of stent models with mesh structures [3].

2.3 Stent geometry

The main attributes of a stent are its flexibility and radial strength. To achieve both, different geometric configurations must be made. Rogers and Edelman [4] showed that the geometry of the stent is an important factor in restenosis. If, at the same material and surface area, the number of junctions of the support struts increases, then the neointimal area increases proportionally. Other researches have proved that this condition is also necessary to reduce vascular damage [5, 6].

2.4 Stent strut thickness

Various clinical studies and researches have shown that the degree of restenosis depends on the thickness of the splint. The thinner the splint, the lower the rate of restenosis. Two stent brace thicknesses were compared in [7]. A 50 μm splint thickness caused 15 % restenosis, and a 140 μm caused 26 % restenosis. The thickness of the splint has more effect on restenosis than its geometry. Because of that, they started using metal splints with a minimum thickness (60-100 μm). The design and fabrication of the stent platform are two crucial factors in clinical success. Also, great attention is paid to the optimisation of materials and the design of the stent platform.

3. Materials for the stent's platform

The choice of materials for stents is very important (see Table 1). They must have several important characteristics, such as sufficient mechanical strength and ductility, they must be biocompatible and antibacterial. The material must also be flexible, and must have the ability to spread. Non-biocompatible material can trigger an immune response and lead to rapid cell proliferation via a stent, leading to a cytotoxic effect and chronic inflammation [8].

3.1 Bare-metal stents (BMS)

The first generation of stents were bare-metal stents (BMS), where 316L stainless steel was used as a base material. The main benefit characteristics of such stents were high durability, corrosion resistance and biocompatibility. However, these stents are poorly degradable, which may cause inflammation after some period of implementation.

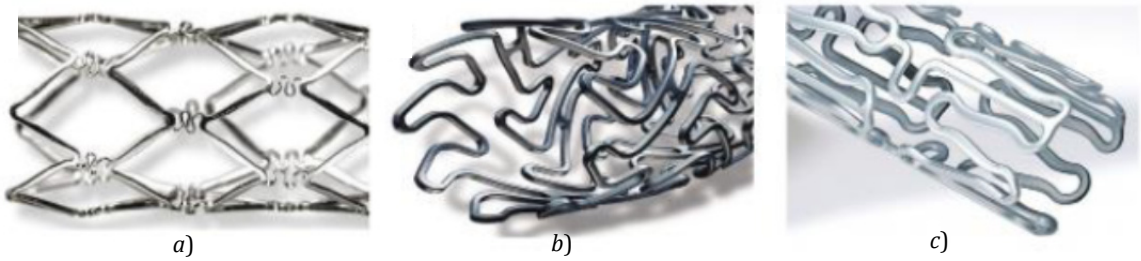
Improvements in stent design have been made possible due to the development in the science of materials. Significant progress in this area is seen in the use of metal alloys that have higher mechanical strength (compared to 316L stainless steel). Greater strength is crucial for the possibility of using thinner splints. Those are more effective and reduce further health problems, which can occur later [9]. In recent years, the emphasis has been placed on research on the types of materials for stents, where the emphasis has primarily been on observing the mechanical properties and biocompatibility of materials [10, 11]. The greatest progress has been made in the use of alloys and representative materials for bare metals, such as nickel-titanium, cobalt-chromium, magnesium, platinum-iridium, etc. The best mechanical strength was shown by the cobalt-chromium alloy; thus, it is used mostly for the stent platform. The use of metal alloys reduced the thickness of the struts, improved performance, and maintained radial strength. The disadvantage of these stents is the occurrence of late restenosis which may be avoided with the use of drug-eluting stents.

3.2 Drug-eluting stents (DES)

A drug-eluting Stent (DES) can load and deliver medicine that is inserted into polymer coatings on the surface of bare-metal stents. Drug-eluting stents began to develop because of restenosis problems after implantation of the previous stents. They have been shown to reduce the rate of restenosis development [12]. DES presents a revolution in stent development. The first generation was Cypher DES (Cordis Corp., Johnson & Johnson). Problems with these stents manifested as thrombosis (clogging of the veins). Therefore, the researchers focused their development on improving DES.

In general, three key components contribute to overall stent safety and efficacy, namely the stent platform, the remedy, and the medicine coating technology. Hence, it can be argued that the design of a DES stent is a multidisciplinary process. For the development of DES it is necessary to intervene in the science of materials, in the field of engineering, advanced technology, for the use of medicine areas such as physiology, pharmacology and chemistry. Delivery engineering, pharmaceutical science, and, again, chemistry, are once more important for delivering a medicament to the required location. The performance of the stent depends on the optimisation of each of these aspects [13, 14]. Different generations of stents have always used the most advanced stent platform during their development. The first generation, which includes Cypher (Cordis Corp.) in Fig. 2A and Taxus (Boston Science) in Fig. 2B, used a stainless-steel platform with a splint thickness of 130-140 μm. Later generations such as Driver (Medtronic), Multi-Link vision (Abbot Vascular) shown in Fig. 2C and Omega (Boston Scientific) have thinner splints (80-90 μm). Newer platforms are biodegradable. To ensure sufficient radial strength, these splints had to be made thicker [15]. The shape of the splint has changed, with development from rectangular to round shapes and with the latest DES with rounded edges.

The DES design included optimising drug release based on the proposed drug action mechanisms. The first generation contained drug coatings to ensure long-term release within 90 days [16]. Computer models show that there are opportunities to optimise drug release further for existing and new drugs. To achieve the desired release profile, it is necessary to attach a biological agent to the surface of the stent. The possibilities of polymer-based and non-polymer-based systems are being investigated [16].



a) *b*) *c*)

Fig. 2 a) Cypher by Johnson & Johnson, b) Taxus by Boston Scientific, c) XienceV by Abbott [44]

Release of drugs with permanent polymers

A wide range of polymers has been investigated as a possible solution for stent coating [17]. The first two generations used durable polymer coatings containing the drug (paclitaxel) and a copolymer of poly (styrene-B-isobutylene B-styrene). Research has led to improvements in drug efficacy and the development of improved approaches for stent drug administration [18].

The first-generation of DES reported hypersensitive responses to polymers. Therefore, research efforts have evolved towards greater biocompatibility. The biomimetic polymer Phosphorylcholine (ChoP) was used in the Endeavor stent (Medtronic) [19]. Because this stent released drugs too quickly, they began developing the Endeavor Resolute DES, which released the drug slowly over the time. The difference was in the new BioLinx polymer blend, which contains Polyvinyl Pirolipon as a carrier layer for the drug, which is mostly released over two months [20]. To improve biocompatibility, poly (vinylidene fluoride - co - hexafluoropropylene) (PVDF-HFP) was used as the outer carrier layer for the drug (Everolimus). This combination is used in DES at Abbot Vascular and Promus Element Boston Scientific. Research [21] has shown that prolonged exposure to durable polymer coatings prolongs the healing time of blood vessels. As a solution, further research has gone into the use of degradable polymer coatings and polymer-free coatings.

Release of drugs with degradable polymers

The latest generation of DES includes several biocompatible polymers to alleviate the inflammation and thrombosis risk. Degradable polymers are lactide and glycolide. Degradation produces lactic and glycolic acid, which is metabolised to non-toxic products in the body. Stents coated

with poly (lactide-co-glycolide) (PLGA) were considered in the study [22]. They produced different release profiles, and focused on changing the rate, duration of drug release by changing the number of layers, and the ratio of lactide and glycolide. In vivo, they discovered that the combination of paclitaxel and PLGA decelerates the formation of neointima in pigs. Similar results were obtained in vitro with the use of poly (d, 1,1-lactide - co - glycolide) when paclitaxel or sirolimus was released [23]. Poly (d, 1) lactide (PDLLA) is a polymer coating used in many stents, such as BioMatrix (Biosensors, International) and Nobori (Terumo) Biolimus A9. These stents were among the first to apply a polymer-drug coating only to the non-luminous side of the stent, which was an innovation. This resulted in better drug delivery to the artery tissue and faster endothelialisation. These stents have a relatively thick splint (120 μm). Stent Synergy (Boston Scientific), which uses a very thin layer of PLGA for the controlled release of Everolimus, has a platinum-chromium platform with a splint thickness of 74-81 μm. These splints have shown clinical benefits of use. Nevertheless, the second generation of DESs were fabricated on conventional bare-metal stent platforms and traditional coating application techniques. Some stents, however, have used alternative coating techniques (Cordis Corp.). Such platform designs allow precise loading of drug layers and polymer layers in specially designed tanks inside the splint [24]. Such a combined approach is used in the Yukon stent (Translumina GmbH). The stent is based on the application of a polymer layer of polylactide PLA (with drug application), on a microporous stainless-steel stent platform with Shellac resin coating. The analysis [25] found that the biodegradable DES polymer-coated stent improved safety and efficacy compared to the original generations of durable polymers in DES. Less well known is how much the biodegradable polymer in DES has improved the second generation of permanent DES.

Release of polymer-free drugs

DES polymer-free stents must include other mechanisms to control the release of drugs from the stent surface. The introduction of surface porosity on macro- and micro- or nano-structures has proven to be a popular approach to controlling drug release. It was proven clinically that the most useful structures were macro and microporous. The Jonus Tacrolimus-eluting carbostent (Sorin Group) have such stents, with pores or holes or grooves, with slots at the macro level, and a stent system filled with Medtronic [26].

The first stent in use with a microporous surface was the Yukon stent (Translumina GmbH) [27]. The usual stent plate was made of stainless steel, sandblasted, in order to create a rough surface treatment having microporous holes 1-2 μm in size, which were filled with spray-coated drugs to ensure the controlled release of the drug. The advantage of this stent was that it reduced the rate of restenosis and accelerated endothelialisation [28].

Newer microporous stents, DES BioFreedom (Biosensors International), create a rough surface using their micro-abrasion procedure. This gives a treated surface (like Yukon's). This stent allows for more targeted drug delivery to a lesion. The development of alternative approaches with the coating of polymer-free drugs continues, which is also reflected in the emergence of patents for various technologies [29]. An important role in further development will be played by the biocompatible surface and, thus, also by such stents, which inhibit neointima and accelerate the regeneration of a healthy endothelium.

3.3 Bio-resorbable stents (BRS)

The desire for ever better results and the reduction of problems, and, thus, the complete recovery of blood vessels, led to the concept of complete decomposition of the device, and thus developed bio-resorbable stents. BRS can be made of bio-resorbable polymers or metals. BRS made of polymers have emerged from materials such as PLLA (Poly-L-Lactic Acid). PLLA is a thermoplastic polymer, namely, aliphatic polyester. It consists of the L-enantiomer of lactic acid (2-hydroxy propionic acid). PLLA has a high solidity. At 55 °C, it has a reversible transition from a relatively hard state to a state like that of rubber. At 175 °C, it has a melting point, and the temperature required for processing is 185-190 °C. However, a problem arises, because, at 185 °C, it begins to lose molecular weight, due to chain reactions and thermal decomposition. PLLA is degraded by hydrolysis of the ester bond and metabolised to water and carbon dioxide. Decompo-

sition takes place in five steps. It begins with the absorption of water from the surrounding tissue and continues with depolymerisation, resulting in loss of molecular weight. The third step is the crushing of the polymer, which causes a loss of mass resulting in loss of radial solidity. This is where the chain breakage occurs, and the shorter chains are excised from the polymer stent. Cells process small polymer chains by phagocytosis (a process in which a cell devours and digests solid particles), then metabolises them to L-lactate and converts them to pyruvate. Pyruvate is eventually broken down into carbon dioxide and water. The first stent made from PLLA that could be absorbed in humans was the Igaki-Tamai stent (Igaki Medical Planning Co., Ltd.). It had a helical structure of a zigzag spiral coil. The length of the stent was 12 mm and the thickness of the splint was 0.17 mm [30]. The mentioned stent was a self-expanding, mounted on a standard balloon for angioplasty. The study showed that, after the expansion, the stent did not cause any significant inflammatory response in patients. Self-expansion occurred within 20 to 30 minutes after installation. The stent provided radial support for 6 months and was absorbed completely in 2-3 years. This stent required heat for the self-expanding process; therefore, it has not been used in the coronary arteries since. A more advanced form of a stent is the BRS, like a small mesh tube whose base is made of Poly-L-lactide (PLLA) covered with a surface layer of Poly-D-lactide (PDLLA) that releases an antiproliferative drug. They are comparable to DES. However, lower efficiency and a higher risk of thrombosis appeared. It provided mechanical support to the coronary artery, and its degradation time was two years [31-33] (Fig. 3).

The crucial advantage of a biodegradable polymer stent is in the slower and longer release of drugs. Their disadvantage is lower mechanical strength, and, consequently, the splint must be thicker. Biological problems, such as inflammatory reactions and increased neointima, are caused mainly by their decomposing products. Due to these problems, biodegradable metal stents with alloys based on iron (Fe) and magnesium (Mg), and later based on zinc (Zn), have started to develop in the last ten years [34]. In studies [35, 36], they were establishing characteristics and biocompatibility, and they determined that a biodegradable Fe-based stent is biocompatible and has proper mechanical properties. Their degradation is slow and causes poor regeneration with iron oxide residues [37, 38].

Another group of biodegradable stents are magnesium-based stents (Mg). Mg-alloys are well biocompatible and have good mechanical properties; on the other hand, their decomposition time is slightly too fast. Therefore, stents were made from a Mg-alloy with an optimised extrusion process and, they were treated with heat. This way a more even degradation and minimal inflammation in vivo was achieved. This is how the WE43 alloy was formed [39].

The newer generation of the bio-resorbable stents was based on zinc (Zn). It has a better in vivo degradation rate than its predecessor. Zinc-based BVS is a new generation that has many advantages over other materials: An ideal rate of in vivo degradation, overall biocompatibility and less proliferation of smooth muscle cells, and a good antibacterial effect. The response to inflammation is like that of BVS in Fe in vivo [40-44].

A review of the current state of BRS shows that the most commonly used biodegradable material is poly-1-lactic acid, followed by magnesium. Other investigated materials are tyrosine polycarbonate, polymer salicylic acid and iron. Fig. 4 shows BRSs also demonstrated by optical coherence tomography (OCT) [15].

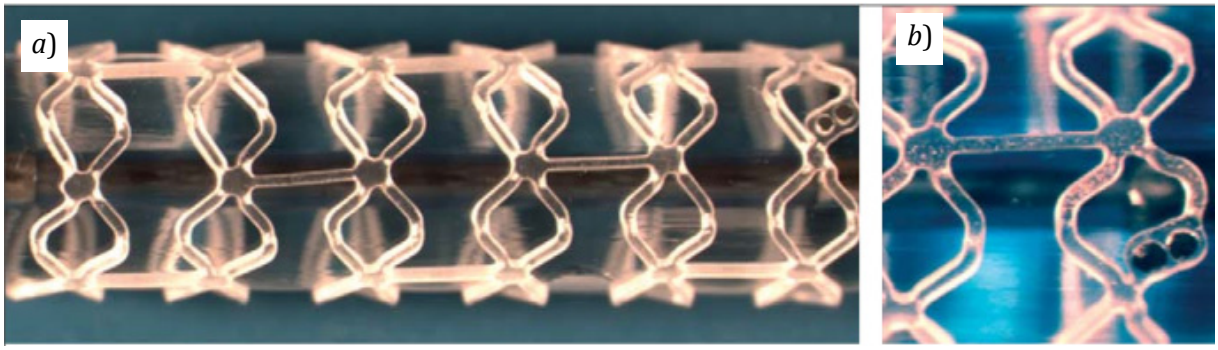


Fig. 3 a) PLLA bio-resorbable stent, b) Magnified image of the stent [31]

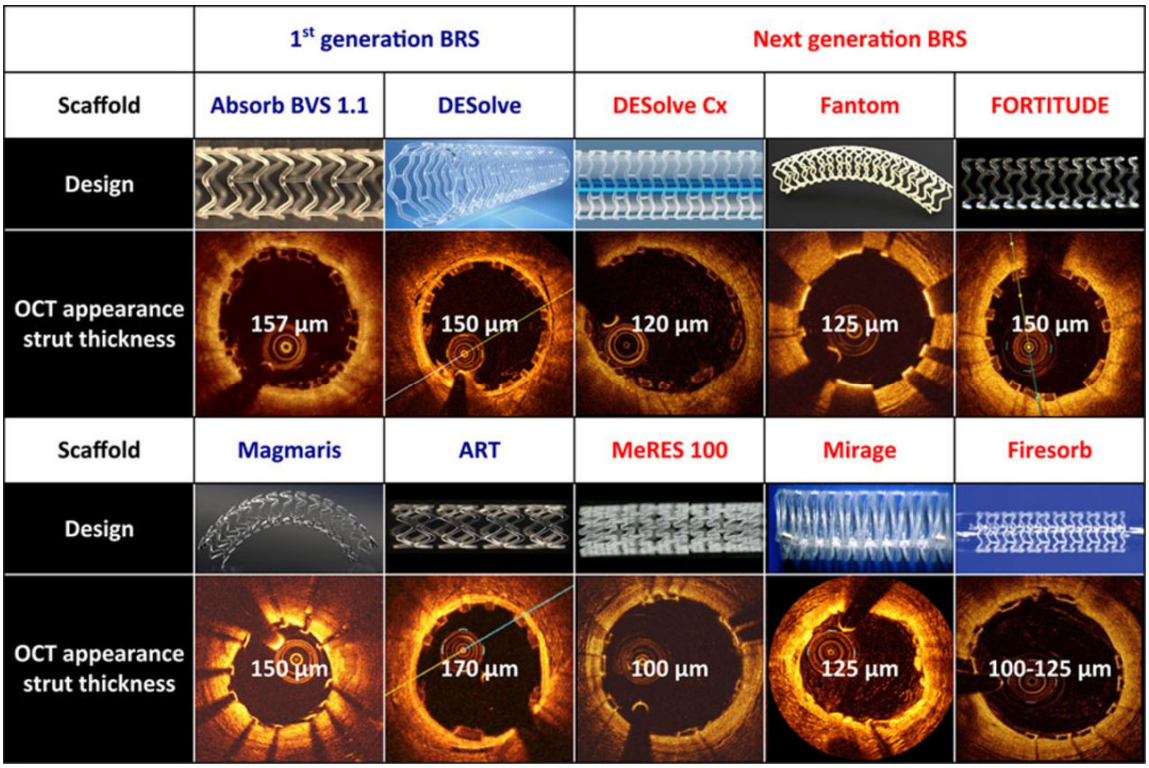


Fig. 4 Design and OCT appearance of BRSs [15]

Table 1 An overview of stent materials

	BMS	DES	BRS
Advantages	• Good mechanical properties, durability, good processing, biocompatibility, corrosion resistance	• Reduction of neointima due to drug release	• Slow and prolonged drug release • Reduction of adverse clinical events due to complete stent degradation • Possibility of restoring vascular function and performing MRI examination after stent degradation
Disadvantages	• Thick splints • Poor degradability	• Occurrence of late thrombosis	• Lower mechanical strength
Limitations	• Occurrence of late restenosis	• Design of DES is a multidisciplinary process	• The material must be a biodegradable polymer or metal • Thicker splints
Prospects	• Development stents from metal alloys, smart memory alloys and polymers • Development drug-eluting stents	• Development of several generations of DES • It leads to the development of BRS stents	• Development of BRS metal stent with Fe, Mg, and Zn based alloys • Good mechanical properties • Good degradation and biocompatibility

4. Production technologies for manufacturing of stents

A review through various literature shows that, in the manufacture of a stent, a distinction must be made between the manufacture of a stent and a stent-graft (see Table 2). This can be divided into nitinol stent and polymer film fabrication. Nitinol stents are made by laser cutting, weaving, or suturing processes, hence, the same as bare-metal stents. The stent-graft also contains a polymer film for which mouldings are used as for textiles. Looms are used, the material is extruded, an electrostatic base is used, and it has a micro to nano composition [46]. For the manufacture of stents, the following production processes are mentioned in the literature: The filament winding phase, micro-EDM using electro-erosion, stent injection, laser cutting and additive manufacturing technology, which also includes Selective laser melting.

4.1 The manufacture of a stent-graft

The existing methods for integrating metal and film moulds include sewing and application. The sewing method performs easy penetration of the film, which often results in tearing. Another bad attribute is that this method takes a lot of time to make. In the application method, the outer film is applied to the surface of the inner film of the stent-graft. When the solution evaporates, the inner and outer film wrap tightly around the metal stent. This method avoids possible tearing caused by hand sewing and has greater efficiency [45]. Therefore, the metal stent is combined with the film by the deposition method. However, it is difficult to use 3D printing for direct integration and to design composite materials containing a cover film and metal stent. To solve this problem, the Rapid Prototyping Sacrificial Core-Coating Technique (RPSC CF) can be used, first proposed by Huang *et al*. [47]. A vascular stent was designed using a patient's Computed Tomography (CT) scan. A water-soluble sacrificial core was fabricated using FDM (Fused Deposition Modelling). With the application process, biopolymer material was applied layer by layer. In the next step, a Nitinol alloy was woven into the stent and coated again with the biopolymer. This integrates the alloy and polymer film into the stent. The wall structure of the multilayer tube can also be formed layer by layer using coating, injection moulding or other material application procedures, and finally, the inner core is dissolved to obtain a stent.

4.2 Stent fabrication technologies

Wire winding with the help of laser local welding

This procedure was used mostly in the initial stages of stent fabrication when stents were made of stainless steel. Each unit related to the laser local welding. Difficulties in such stent manufacture arise in locating the weld, due to the small size and complexity of the vascular stent structure [46].

Micro-EDM

A micro-electrical discharge machining (micro-EDM) is a process where the material removal occurs by electro-erosion due to electric discharge generated between closely spaced electrodes in the presence of a dielectric medium. The shape of a stent's cells is the mirror image of the electrode [48].

Injection moulding

We distinguish between low-pressure reaction injection moulding (RIM) and high-speed injection (HSI). HSI is the injection into a mould with a significantly higher speed (more than 500 mm/s) at lower temperatures, which reduces polymer degradation. HSI was used for stents of arbitrary geometries with high radial length, small offset, and shape stability. This avoided the negative effects of laser cutting. RIM is a technical process for making polymer products. The molten polymer is injected at high pressure into a mould, which can be made of metal (steel or aluminium). Products are formed directly in the mould. The products can be solid or have a foam structure. Stents made in this way have low tolerance, the possibility of coating different materials, no visual defects, are durable, and offer flexibility. The additional advantage is that this kind of production offers low tool costs. However, the disadvantages of this process to produce stents are mainly in the uneven design, slow fabrication and high requirements for injection moulds, and the associated higher costs [45, 46].

Laser cutting

It is a commonly widely used manufacturing technique for industrial applications, mainly producing bare-metal and polymer stents. Laser cutting is a technology where a high energy density laser beam focuses on a raw tube surface. The stent is made of a nano or microtube by laser cutting to produce the desired structural elements. Different types of lasers have been used in stent manufacture, including CO2 lasers, Nd:YAG lasers, fiber lasers, excimer lasers, and ultra-short pulse lasers. The disadvantage of laser cutting is that this process can cause thermal damage such as heat-affected zone (HAZ), striation, recast layer, microcracks, tensile residual stress, and

dross. The splints may have sharp edges due to such construction, damaging the vessel or cause un-stable blood flow after implantation. However, the supporting component is rectangular, causing local eddy blood flows, followed by leukocyte aggregation leading to restenosis. Some post-processing techniques are used, like annealing and electropolishing to overcome the thermal da-mages. Due to introducing these post-processing techniques, the manufacturing cost are raised. Over the last decade, ultra-short pulse lasers (picosecond and femtosecond) have been available for high precision processing, which are an alternative to the longer pulse lasers for machining thin materials for stent applications. Although the thermal effect is reduced, debris and recast formation still have to be removed by other methods [47, 48].

Additive manufacturing technology

In the case of metal stents, this technology does not work due to oxidation problems. Additive production is suitable for biodegradable polymer stents. In 2013, Flege at al. [49] used PLLA and PCL material for the first time for processing selective laser melting (SLM). SLM is an additive technique in which a laser beam melts and joins the material layer by layer selectively [50]. The disadvantages of this process are reflected in poor surface accuracy and a long manufacturing process. Due to the poor properties of SLM, Park *et al*. [51] used bio cutting technology in 2015. The disadvantages of this technology have been demonstrated in the difficulty of stent personalisation and the lengthy stent fabrication process. The procedure takes more than 10 hours. Tumblestone *et al*. [52] developed the continuous liquid interface production (CLIP) technology. This is a process where UV projection hardens a photosensitive resin. The liquid resin maintains a stable area of the liquid, and ensures continuous solidification due to contact with oxygen. The good features of this process are the higher speed of 3D printing, namely by 25 to 100 times, and in the high precision of the product surface. In 2016, degradable citrate-based polymer material was synthesised using the micro CLIP process [53]. This process gave the stent very good properties, such as good elasticity, good strength, oxidation resistance and biodegradability. The manufacturing time is short, and, after 180 days, the stent degrades by 25%. The procedure also has negative properties which were shown during clinical tests. The mechanical properties of the stent do not match the BRS, the materials are not FDA approved and the biocompatibility is questionable. In 2017, Ware *et al*. [54] used photopolymerisable materials that can be embedded using the micro CLIP method to print flexible BRS, meeting the requirements for precision biomedical devices. According to research [56], the Micro CLIP process has quite a few advantages over SLM. The stent fabrication time is reduced (it is possible to fabricate a stent of length 2 cm, with 4,000 layers in 26.5 minutes), the surface treatment is of better quality, the mechanical properties are unified and match Ni stents. In 2017, Cabrera *et al*. [55] printed a stent with Fused Deposition Modelling (FDM) as shown in Fig. 5. The printing device used was the Baker Bot by Replicator, the material was Thermo-Plastic Copolyester (TPC). The stent made in this way fused with the vessel wall in 8-16 weeks. Guerra *et al*. [56, 57] used the same technology the following year and used PCL for the material. The disadvantage of this stent was in the poor resolution, and many experiments performed. With this procedure, the process of 3D stent printing was researched thoroughly. Lei *et al*. [44] mentioned a combination of bio 3D printing and electro-bonding technology to form a poly (p-dioxanone) sliding stent (PPDO) for the inner layer with 3D printing and prepared a mixture of chitosan and poly- (vinyl alcohol) (PVA) for the outer layer with electrospinning and in this way planted the cells on the stent. Due to the natural biological material on the outer layer, cell adhesion and proliferation were good. In [44] the authors also described the development of a 4-axis 3D printing platform with FDM technology. An additional axle is added to the platform, namely a rotating spindle structure, so that it is possible to avoid the supporting structure and develop a set of mini screw extrusion nozzles. This nozzle uses granular biological material, and the diameter of the extruded wire is 100 μm. PCL and PLLA material were used to study the effects of rapid rate quenching and centrifugation on the mechanical properties of the stent and to optimise them.

The lumen diameter of an organ and stent length are two parameters defined, among many others. The design optimization of a stent and using the 3D printing technique allows a patient-specific personalization of the device.

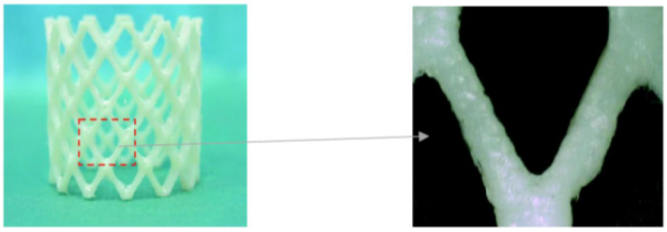


Fig. 5 3D printed FDM-stent [53]

Table 2 An overview of fabrication techniques for stent

	Wire winding	Injection and compression moulding process	Laser cutting	Additive manufacturing
Advantages	Widespread use of stents made in this way	• No visual defects, durable, offer flexibility • Fast production	• Fast processing • High accuracy	• Development of many different additive production techniques • High efficiency
Disadvantages	Difficulties in locating the weld	• Design restriction • Slow fabrication	• Thermal damage • Sharp edges • Incompatible for all material	• Poor surface accuracy • Long manufacturing process
Limitations	Only for stainless steel	• High requirements for moulds	• Heat load of the material	• Unsuitable for metal stent because of the oxidation problems • Nozzle diameter limitation
Prospects	For stainless steel	• Possibility of coating different material	• For all types of materials	• Possibility of individualization • Rapid prototyping
Economic aspect		• Low cost for tools	• High investment and operating costs	• Low cost

5. Conclusion

This research paper contains an overview of the development of the stents and the technology for their production. Different stent systems, new materials, metallic and polymeric, and bioresorbable stents can be traced in various studies. It will be challenging to discover an ideal stent suitable for all patients and their health problems. The lesion characteristics of individual patients, their age, their proneness to restenosis and thrombosis differ so much that it is difficult to produce a single device that would eliminate such a diverse spectrum of problems. The desire for the most qualified and useful stent, however, offers broad areas for further research.

Finding the stents' best manufacturing process has to be considered besides the stents' mechanical and medical properties. The stent industry needs to make continuous advances towards improving mechanical properties and reducing this medical device's costs by developing new production technologies. In this context, Additive Manufacturing techniques could be more economical than traditional laser micro-cutting used for manufacturing stents based on metallic materials. Nowadays, 3D printing could be an exciting manufacturing method to produce polymeric biomaterials, suitable for the latest generation of biodegradable stents applications. Further understanding and actualisation of those manufacturing methods are required in the field of Stent Technology.

Computational modelling is a valuable tool when evaluating stent mechanics and optimizing stent design. Finite element analysis (FEA) and computational fluid dynamics (CFD) are efficient methods to investigate and optimize a stent's mechanical behaviour virtually. FEA can help understand the role of the different geometrical and mechanical behaviour of the stents. Besides analysing stents' mechanical behaviour during the development process, these methods can be combined with special patient images to plan a surgery procedure.

The challenges associated with stents are numerous, like material, geometry, manufacturing process, biocompatibility, etc. Among the traditional design and manufacture, the most challenging is the development of a new generation of biodegradable materials, where medical devices function only during a specific period and then degrade.

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