Chapter 4

Stent's Manufacturing Field: Past, Present, and Future Prospects

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Additional information is available at the end of the chapter

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Abstract

From the introduction of stents, nobody was able to predict the advances that will occur in stent technology over the upcoming decades. Since their appearances, it became evident that this device had significant limitations, such as vessel occlusion and/or restenosis. Despite that, this medical device is the best clinical solution for cardiovascular vessel occlusions. Stents require a deep analysis, in terms of thrombogenicity, manufacturing process, geometrical aspects, and mechanical performance, among many other characteristics. The surface quality obtained in their manufacture process is crucial to blood compatibility, prevents the activation process of thrombosis, and improves the healing efficiency. The forecast stent market makes necessary continuous studies on this field, which help to solve the medical and engineering problems of this device, which are in constant development. Stents have been the center of many research lines over the last decades. The present chapter aims to summarize the state of the art of this medical device in the last years in the fields of design, manufacturing, and materials.

Keywords: stent, BMS, DES, BRS, ETS, permanent, fully absorbable, design, FEA, manufacturing, processes, material

1. Introduction

In medicine, atherosclerotic vascular diseases are common and life-threatening diseases that narrows the vessels and reduces the blood flow in the arteries. 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 special tubing (stent) is usually placed to open the narrowed arterial vessel.

From the introduction of PCI, nobody was able to predict the advances that will occur in stent technology over the upcoming decades [1]. Since PCI appearances, it became evident that this approach has significant limitations, such as vessel occlusion and/or restenosis [2]. To overcome these problems, bare metal stents (BMS) were introduced, and despite reducing the vessel occlusion, however, high rates of restenosis constituted their major limitation [3]. To surmount this hurdle, the metallic stent coated with antiproliferative drug was conceived, the drug-eluting stents (DES). With the introduction of DES, the antiproliferative drug over the struts prolonged vessel wall healing, reduced neointima hyperplasia, and consequently decreased the target lesion revascularization (TLR). The most important limitation of the first generation of DES was related to the lack of biocompatibility of the drug-eluting polymer leading to a persistent inflammatory response after the drug-eluting period. Although permanent stents (BMS and DES) are effective, in most cases, the role of stent is temporary and is limited to the intervention, and shortly thereafter, until healing and re-endothelialization are obtained [4]. Bioresorbable stents (BRS) were introduced to overcome these limitations with important advantages: complete bioresorption, mechanical flexibility, etc. The BRS concept introduced the use of polymers in stenting procedures for the first time. With the inclusion of polymeric materials in the field of stents, a new and promising idea makes its way, electrospun tubular scaffolds (ETS) for stenting process. Unlike current stents, ETS theoretically could present some advances such as (I) better longitudinal flexibility to help the placement of the stent and (II) their surface mimics body tissue to help to obtain a best proliferation rates [5] and thus a rapid endothelialization. Nevertheless, ETS could have some disadvantages such as their radial flexibility. The radial expansion of ETS will occur by elongation of its fibers, in contrast to current stents in which it occurs by elongation of its radial cells. This fact could make correct vessel support difficult, which would restrict the use of ETS for only peripheral applications. With the author's best knowledge, this new idea has been overlooked, but it presents a promising approach to solve cardiovascular problems.

Stents can be used for a wide range of indication: de novo lesions, small vessel disease (SVD), bifurcation lesions, and tortuous and narrows lesions. Stents can improve the clinical outcomes for all of these indications as well as quality of life for patients suffering from this debilitating disease. In 2013, sales of DES and BMS in the 10 major markets were $ 4.89 billion. Global data [6] estimates that by 2020, sales of stents will grow to $ 5.65 billion.

2. Stent manufacturing process design

Regardless of the stent choice, BMS, DES, BRS, or ETS, the challenges associated to this medical device remain similar. **Figure 1** shows the *pyramid of stent manufacturing process design*. It represents the main issues to consider at the time to design and manufacture this medical device.

The mechanical properties of the stent govern the decision process. This important property will be in charge of providing the correct longitudinal and radial behavior. The mechanical properties of the stents mainly depend on the material, geometry, and medical application of the stent:

$$\text{Mechanical properties} = f(\text{material, geometry, application}) \quad (1)$$

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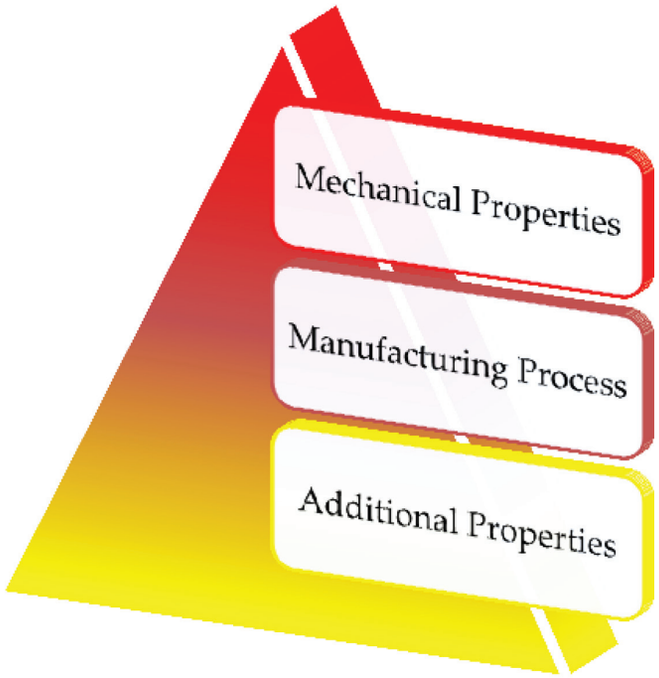


Figure 1. Pyramid of stent manufacturing process design.

Once we have decided the mechanical properties, we give way to the manufacturing process step. The manufacturing process mainly depends on the materials and stent type chosen:

$$\text{Manufacturing process} = f(\text{material, stent type}) \tag{2}$$

Finally, the additional properties step. Although it constitutes the final layer of the stent pyramid, additional properties cover a range of modifications to stent designs. This last step indirectly relates to the stent type and its medical application:

$$\text{Additional properties} = f(\text{stent type, application}) \tag{3}$$

The next sections present the main issues to consider in the abovementioned decision pyramid steps with special attention to the manufacturing process step.

3. Stent mechanical properties

Stent's mechanical properties are interrelated and sometimes contradictory, requiring careful compromise between geometrical and material aspects.

3.1. Geometrical aspects

Following the classification done by Stoeckel et al. in their manuscript "A survey of stent designs," stents can be classified into five categories [7].

3.1.1. Coil

Most common in nonvascular applications, the coil design allows for retrievability after implantation (**Figure 2a**). These designs are extremely flexible, but their strength is limited, and their low expansion ratio results in high-profile devices.

3.1.2. Helical spiral

These designs are generally promoted for their flexibility. With no or minimal internal connection points, they are very flexible but also lack longitudinal support. As such, they can be subject to elongation or compression during delivery and deployment and, consequently, irregular cell size. With internal connection points, some flexibility is sacrificed in exchange for longitudinal stability and additional control over cell size.

3.1.3. Woven

Woven designs are often used for self-expanding structures. While these designs offer excellent coverage, they typically shorten substantially during expansion. The radial strength of such a woven structure is also highly dependent on axial fixation of its ends.

3.1.4. Individual rings

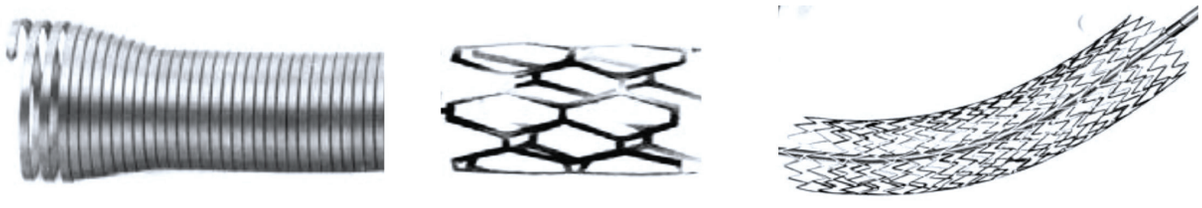
These are commonly used to support grafts or similar prostheses. This design is not typically used as vascular stents by itself.

3.1.5. Sequential rings

This design is the most common in the market and includes two different categories: (I) closed cell, made of sequential ring construction wherein all internal inflection points of the structural members are connected (**Figure 2b**) and (II) open cells, a stent wherein some or all the internal inflection points of the structural member are not connected by bridging elements (**Figure 2c**).

3.2. Material aspects

Since the introduction of the first stainless steel devices, the materials used for stents have evolved and diversified rapidly. In the drive to obtain a share of what was becoming a vast and growing market, manufacturers invested heavily in research and development to gain continuous.



(a) **(b)** **(c)**

Figure 2. Designs: (a) coil EsophaCoil, (b) closed cell Palmaz-Schatz, and (c) open cell SMART.

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The main materials currently used or which are being investigated are briefly presented in **Table 1**.

In the field of mechanical properties of stents, many authors have focused their investigations in the study of the effects of the geometry and the material that this medical device have. Due to the high cost of these medical devices, much of the works have been performed by finite element analysis (FEA).

In 2007, Kiousis et al. [8] proposed a methodology to identify optimal stents for specific clinical criteria. They presented a numerical study to understand the interaction between the stent and a patient-specific atherosclerotic human lesion of type V. Mortier et al. [9] compared three different second-generation drug-eluting stents (DES) using a parametric modeling approach, when being implanted in the curved main branch of a coronary bifurcation with the aim of providing better insights into the related changes of the mechanical environment. Hopkins et al. [10] carried out a study which provided insight into the critical factors governing coating delamination during stent deployment and offered a predictive framework that can be used to improve the design of coated stents. They concluded that delamination initiation is governed by coating thickness and stiffness, interface strength, and hinge curvature. Augsburger et al. [11] proposed an alternative strategy, which is based on the modeling of the device as porous medium. Results predicted by the porous medium approach compare well with the real stent

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 1. Stent materials.

geometry model and allow predicting the main effects of the device on intra-aneurismal flow, facilitating thus the analysis. Hsiao et al. [12] proposed to apply the parametric design concept onto the stent design and integrate it with the developed FEA and CFD models to evaluate these key clinical attributes as a function of the stent design parameters. They concluded that the most critical parameter for the equivalent plastic strain and the expansion recoil was the crown radius. Grujicic et al. [13] investigated the fatigue-controlled service life of the self-expanding nitinol vascular stents. Praveen Kumar et al. [14] provided a simple, fast, and cost-effective tool to quantitatively determine the fatigue resistance of stent components. Their results showed that the stent model passed the fatigue test under the aforementioned loading conditions. Nowadays the main efforts are being done in simulating polymeric materials in order to understand the mechanical behavior of the new polymeric BRS [15, 16].

Stent materials have been investigated in-depth in the last decades. Understand how the manufacturing processes affect the material properties; develop new materials, analyses for new coating and its effect on the biological aspects, etc.; and have been the main research lines.

In 2010, Liu et al. [17] analyzed the inhibition of bacterial adherence on the surface of biliary stent made of 316L SS modified with chitosan. Bacterial infection plays an important role in the initiation of biliary sludge formation. Bacterial adherence and biofilm formation on the surface of a material have been considered as one of the main factors of stent re-occlusion in clinic. Results suggested that that chitosan could be applied to biliary stent in clinical setting because of its antimicrobial activities. In 2011, Man et al. [18] used a Nd:YAG laser to cut NiTi alloy employing air and argon environment, respectively. The corrosion resistance improved for samples treated in air.

In 2012, Ye [19] coated WE43 magnesium alloy with phytic acid (PA) by immersion. Authors aim to study the effect of PA's pH on the microstructure. Results showed that PA can enhance the corrosion resistance of WE43 magnesium especially when the pH value of the modified solution is 5 and the cytotoxicity of the PA-coated WE43 magnesium alloy is much better than that of the bare WE43 magnesium alloy. Moreover, all the hemolysis rates of the PA-coated WE43 Mg alloy were lower than 5%, indicating that the modified Mg alloy met the hemolysis standard of biomaterials. Therefore, PA coating is a good candidate to improve the biocompatibility of WE43 magnesium alloy.

The inclusion of BRS concepts was made that many author started to study bioresorbable materials. In the design of biodegradable stent, it is advantageous to consider materials that have received regulatory approval for other applications such as PLA. Other synthetic biodegradable polymers with regulatory approval have been attempted as stent materials, such as PCL, PGA, and P4HB. Regardless of polymer choice, the challenges associated with material formulation, polymerization process, material processing, and material property characterization remain similar. Most importantly, it is not only necessary to know the characteristics of the material at its initial non-degraded stage but also how do these evolve with degradation. The vast majority of studies of polymer degradation were performed without mechanical loading. The few studies that have included mechanical loading indicate that degradation is accelerated, depending on the specific type of loading. Wiggins et al. [20] found that the degradation rate of polyurethane increased with cyclic strain rate, whereas strain magnitude has essentially no effect. In a separate study, the same group demonstrated that polymer from

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the cyclic uniaxial strain region degraded at the same rate as unstressed and constant stress controls. In 2000, Tamai et al. [21] evaluated the feasibility, safety, and efficacy of the PLLA stent in humans. Fifteen patients electively underwent PLLA Igaki-Tamai stent implantation for coronary artery stenosis. The results were promising. Zilberman et al. [22] focused their studies on the mechanical properties of bioresorbable fibers. PLLA, PDS, and PGACL were studied in vitro. The three fibers combined a relatively high initial strength and modulus together with sufficient ductility. Venkatraman et al. [23] reported, for the first time, the development of a fully biodegradable polymeric stent that can self-expand at body temperatures. Ajili et al. [24] reported new self-expanding polymer made from polyurethane/polycaprolactone (PU/PCL). The results showed that the blend supported cell adhesion and proliferation, which indicated good biocompatibility. Their results suggested that this blend might be a potential material as a stent implant. Xue et al. [25] designed a biodegradable shape-memory block copolymer (PCTBV-25) for fast self-expandable stents. The stent made from PCTBV-25 film showed nearly complete self-expansion at 37°C within only 25 s, which is much better and faster than the best-known self-expandable stents. Vieira et al. [26] studied the evolution of mechanical properties during degradation based on experimental data. The decrease of tensile strength followed the same trend as the decrease of molecular weight. Weinandy et al. [27] designed a new viable stent structure (BioStent) to overcome in-stent restenosis. Despite the advances, many concerns still remain; one of the most important is the investigation on the cell proliferation of the material that helps to induce a rapid endothelialization.

4. Traditional stent manufacturing processes

Five technique has been used to manufacture stents: etching, micro-electro discharge machining, electroforming, die-casting, and, nowadays, laser cutting [28].

4.1. Etching

Etching method is based upon the photolithography process (**Figure 3a**). In this process, the desired mask pattern is first projected on the plain sheet coated with photoresist, which after exposure can be developed and etched for the desired pattern [29, 30].

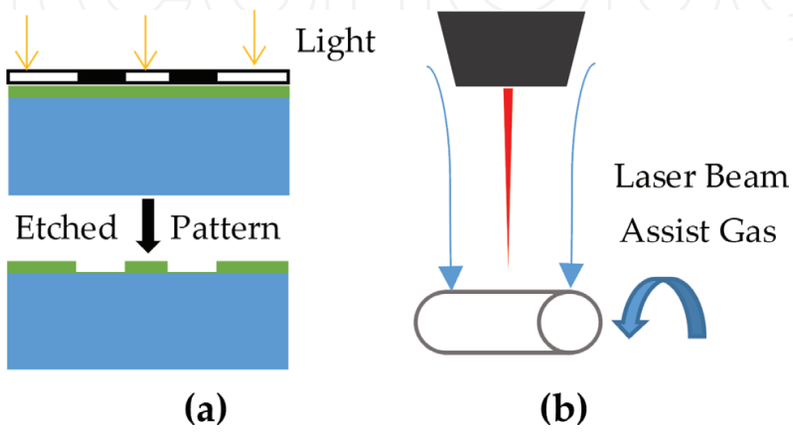

Figure 3. Stent manufacturing processes: (a) etching and (b) laser cutting.

4.2. Micro-EDM

In micro-EDM, the material removal takes place by electro-erosion due to electric discharge generated between closely spaced electrodes in the presence of a dielectric medium. The shape of the machined feature is the mirror image of electrode [31].

4.3. Electroforming

In this process, electroplating is performed on a mandrel in a given pattern. When the desired thickness has been reached, the mandrel is etched away from the electroformed stent, leaving a free standing structure, a fully functional stent [32, 33].

4.4. Die-casting

This is another technique in which the stent can also be formed by subjecting one or more. The metal may be cast directly in a stent-like form or cast into sheet or tubes from which the inventive stents are produced by using any of the method mentioned here.

4.5. Laser cutting

A high energy density laser beam is focused on workpiece surface; the thermal energy is absorbed which heats and transforms the workpiece volume into a molten, vaporized, or chemically changed state that can easily be removed by flow of high pressure assist gas jet [34, 35] (**Figure 3b**). Currently, this is the technology in the market.

Different types of lasers have been used in stent manufacture including CO_2 lasers, Nd:YAG lasers, fiber lasers, excimer lasers, and ultra-short pulse lasers. Fiber lasers have advantages compared to other laser technologies such as better beam quality, reliability, and process efficiency with lower acquisition cost and maintenance. Laser cutting is a thermal process which results in thermal damage such as heat-affected zone (HAZ), striation, recast layer, microcracks, tensile residual stress, and dross. To overcome the thermal damages, basically the following post-processing techniques are applied: pickling techniques, soft etching, annealing, and electropolishing. All these post-processing techniques raise the manufacture cost and could affect the mechanical properties of stents.

There are several works, which study how the process parameters affect the quality, trying to reduce the thermal problems and thus reduce the cost of the stent manufacturing process. Kathuria [36] described the precision fabrication of metallic stent from stainless steel by using short pulse Nd:YAG laser. They conclude that the processing of stent with desired taper and quality shall still be preferred by the short pulse and higher pulse repetition rate of the laser. Meng et al. [35] analyzed the cut parameters with a fiber laser system. They concluded that the high-quality coronary stent has been cut with the power of 7 W, pulse length of 0.15 ms, frequency of 1500 Hz, scanning speed of 8 mm/s, and oxygen gas at 0.3 MPa as assistance gas. Muhammad et al. [37] studied the capability of picosecond laser micromachining of nitinol and platinum-iridium alloy in improving the cut quality. Process parameters used in the process have achieved dross-free cut and minimum extent of HAZ. Scintilla and Tricarico [38] analyzed the influence of processing parameters and laser source type on cutting edge quality

of AZ31 magnesium alloy sheet, and differences in cutting efficiency between fiber and CO_2 laser were studied. They investigate the effect of processing parameters in a laser cutting of 1 and 3.3-mm-thick sheets on the cutting quality. Their results showed that productivity, process efficiency, and cutting edge quality obtained using fiber lasers outperform CO_2 laser performances. Teixidor et al. [39] carried out an experimental study of fiber laser cutting of 316L stainless steel thin sheets. They analyzed the effect of laser parameters on the cutting quality for fixed nitrogen assistance gas. Besides that, they presented a mathematical model based on energy balance for the dross dimensions.

Notwithstanding, avoiding the thermal damages in laser processing is impossible by itself. Another alternative would be to solve it during the laser ablation process itself. This can be accomplished by laser machining under liquid. Laser processing in the presence of liquid has been studied for more than 40 years for various applications [40, 41]. Nevertheless underwater laser micromachining for tubes specifically for coronary stent applications received less attention. Work by Muhammad et al. [42] directed a water flow through the tubes during the fiber laser micromachining to reduce HAZ, as well as protecting the opposite surface of the tube. Yang et al. [43] reported underwater machining of deep cavities in alumina ceramic. They found that underwater machining has the capability of preventing crack initiation, reducing heat damage, and giving an insignificant recast layer. In other works, Muhammad and Li [44] studied the underwater femtosecond laser micromachining of thin nitinol tubes.

Despite the advances, the inclusion of the BRS concept should make us wonder about the applicability of the current laser-cutting manufacturing process for making BRS due to the new materials that have to be used, mostly polymers. There are several works about laser processing of biodegradable materials, both polymers and metals, trying to answer this question. Lootz et al. [45] analyzed the influence of laser-cutting process (CO_2 laser) in morphological and physicochemical properties of polyhydroxybutyrate. The result showed that cells preferred laser-machined areas. They concluded that not only were the material properties altered as a result of processing but also the biological response was affected. Grabow et al. [46] studied the effect of laser cutting on poly-L-lactide (PLLA). The results showed the dramatic influence of the plasticizer content and sterilization procedure on the mechanical properties of the material. Laser cutting had a lesser effect. Hence the effects of processing and sterilization must not be overlooked in the material selection and design phases of the development process leading to clinical use. Tiaw et al. [47] studied the effect of Nd:YAG laser on microdrilling and microcutting of thin PCL films. Melting and tearing of the thin polymer film were not much of an issue for the thin spin-cast film, but a slight extent of melting was observed in the thicker biaxial drawn film.

Baer et al. [48] described the fabrication of a laser-activated shape memory polymer (SMP) stent and demonstrated photothermal expansion of the stent in an in vitro artery model. In 2008, Davim et al. [49] realized some experimental studies on CO_2 laser cutting of polymeric materials. Their results showed that HAZ increases with the laser power and decreases with the cutting velocity. Yeong et al. [50] analyzed the effect of femtosecond laser micromachining on poly-E-caprolactone (PCL). Ortiz et al. [51] examined the picosecond laser ablation of PLLA as a function of laser fluence and degree of crystallinity. High-quality microgrooves were produced in amorphous PLLA, revealing the potential of ultra-fast laser processing technique. Demir et al. [52] demonstrated the feasibility of laser micro-cutting to produced magnesium BRS. By Q-switched fiber laser authors cut AZ31 magnesium alloy. The cutting process was

followed by a subsequent chemical etching to clean the kerf and surface finish. Stepak et al. [53] presented the impact of the KrF excimer laser irradiation above the ablation threshold on physicochemical properties of biodegradable PLLA. It could be concluded that the usage of the 248 nm wavelength resulted in simultaneous ablation at the surface and photodegradation within the entire irradiated volume due to high penetration depth. Furthermore, the thermal activation originating from relaxation of excited chromophores to vibrationally excited ground states enhances the degradation process. Stepak et al. [54] fabricated a polymer-based biodegradable stent using a CO_2 laser. They noted that the high-temperature gradient during the process altered the properties of the material within the heat-affected zone (HAZ). Guerra et al. [55, 56] demonstrated the feasibility of fiber lasers of 1.8 μm of wavelength to cut polycaprolactone sheet with higher precisions. The process is barely affected by the material properties. Nowadays there are many authors that carry on this field trying to give an answer to the current problems. Nevertheless, the inclusion of BRS concept has motivated most of the researchers to move to new technologies. The next section presents the most promising manufacturing techniques under investigation nowadays for producing BRS.

5. Promising stent manufacturing processes

Despite the proved feasibility of laser cutting to produce BRS, both metallic and polymeric, there is a need to develop new technologies to produce these medical devices. In this context, additive manufacturing (AM) could be a more economical solution. AM refers to processes used to create a 3D object in which layers of material are formed under computer control. The use of this technology for stent manufacture is recent [57–64] and could be a really interesting method to produce stent. Mainly, there are four different AM technologies in the stent field.

5.1. Stereolithography (SL) processes

Stereolithography (SL) (**Figure 4b**) works by focusing an ultraviolet (UV) light or visible light onto a vat of photopolymerizable resin. It can differentiate three types of SL technologies, laser-based stereolithography (SLA), digital light processing (DLP), and very recently liquid crystal display (LCD).

5.2. Selective laser sintering (SLS)

Selective laser sintering (SLS) uses a laser as the power source to sinter powdered material (metals, polymers, etc.), aiming the laser automatically at points in space defined by a 3D model, binding the material together to create a solid structure.

5.3. Fused filament fabrication (FFF)

Also known as fused deposition modeling (FDM), here a hot thermoplastic is extruded from a temperature-controlled print head to produce fairly robust objects to a high degree of accuracy. The filament is melted into the extruder, which deposited the material onto a

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computer-controlled platform (**Figure 4a**). It can differentiate two FFF processes for stent manufacturing, (I) traditional Cartesian FFF or (II) novel tubular FFF.

5.4. Electrospinning (SE)

Electrospinning (SE) is a fiber production method which uses electric force to draw charged threads of polymer solution or polymer melts up to fiber diameter in the order of some hundred nanometers (**Figure 4c**). Traditionally, this technique has been used for coating permanent stents to produce DES.

In this new context, in the AM processes, some authors have focused their efforts to produce stents mainly focused on the new BRS. The novel use of polymeric materials joined with these new manufacturing methods opens a window to a novel concept, electrospun tubular bioabsorbable scaffold for stenting application. This new idea could reduce the problems derived from the current stents, such as its placements or rapid endothelialization.

Regarding the traditional BRS, the first document that presented a stent produced by AM was reported in 2015 when Park et al. [57] evaluated the properties of a 3D-printed BRS drug-coated stent in animals. Their results were promising in animals (20.7% restenosis). van Lith et al. [58] built a novel μCLIP setup capable of speed ranging from 2.5 to 100 μm s^{-1}. Employing a Cipher BMS design, they analyzed the effect of UV intensity, UV absorber, and wall thickness. Although results were promising, there are some limitations since the best-performing stent had a fabrication of 70 min. Misra et al. [61] performed an in silico analysis to optimize the stent design for printing and its prediction of sustainability under force exerted by the coronary artery or blood flow. Ware et al. [63] reported the process development in manufacturing high-resolution bioresorbable stents using the μCLIP system. They employed 26.5 min to manufacture a 2 cm stent. Cabrera et al. [62] manufactured a BRS stent employing a traditional 3D printer. Although the results were promising, the traditional 3D printer presents some limitations to manufacture tubular devices such as stent. Guerra et al. [59, 64] design and implement a novel 3D tubular printer to BRS manufacture, the first full research paper that applies 3D-printing process based on FFF to manufacture a BRS stent with nontraditional printer. Their approach presented a new and interesting method to produce stents based on polymers in less than 2 min (**Figure 5**).

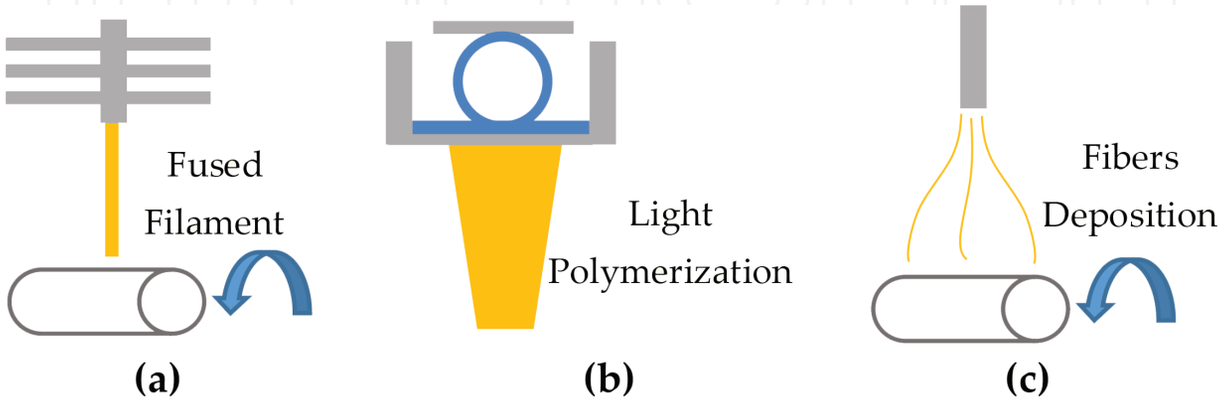

Figure 4. Promising manufacturing processes: (a) FFF, (b) SL, and (c) electrospinning.

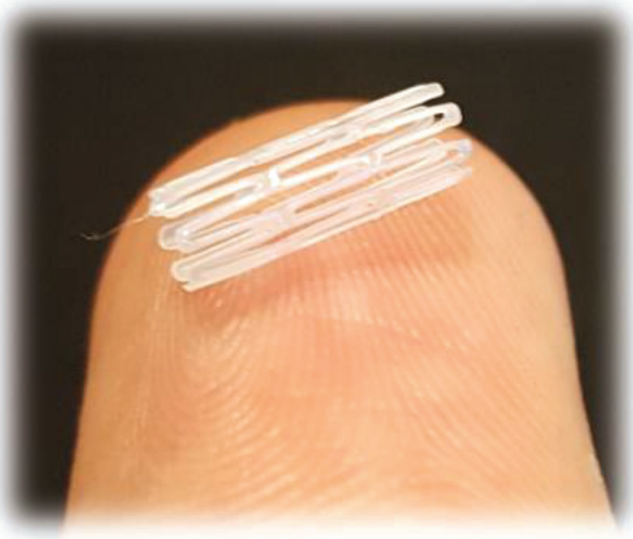

Figure 5. 3D-printed PCL stent [65].

Demir and Previtali [60] produced CoCr stent through SLM as an alternative method to the conventional manufacturing cycle. Results showed that SLM can be considered as a substitute operation to laser micro-cutting. Prototype stents with acceptable geometrical accuracy were achieved, and surface quality could be improved through electrochemical polishing. The chemical composition remained unvaried, with a marginal increase in the oxide content.

In recent studies, Guerra et al. [66] manufactured a PCL/PLA composite stent by FFF. They suggested that composite stents could improve the mechanical behavior of polymeric materials. Also, their results suggested that composite stents could improve the biological requirements, namely, high proliferation external surface, to help the endothelialization with low proliferation internal surface to avoid the adhesion and proliferation of the cell in charge of restenosis.

Regarding the novel electrospun tubular scaffolds (ETS) for stenting applications, some authors have been trying to produce them by electrospinning. Scaffold for stenting applications presents some advances as regards the traditional closed-cell stents. The longitudinal flexibility of scaffolds is higher than traditional stents, making their placement easy and reducing the risk during the stenting protocol. Also, scaffolds, produced by electrospinning, mimic the human tissue being able to increase the cell proliferation and helping a better and faster endothelialization of the vessel. However, scaffolds, due to their geometrical aspects can have worse radial behavior making it difficult for the vessel support. As a new idea, scaffold for stenting application has been barely studied. Bakola et al. [67] manufactured a drug-eluting bioabsorbable stent with PCL and PLA by electrospinning process. Authors focus their work in its application as coating to produce DES; nevertheless, results showed good morphology and topography. Nevertheless authors did not perform radial tests to check the feasibility of scaffold for stenting purposes. ETS present a new research field into the stent world. Further works that get into the manufacturing process and mechanical behavior of this new concept are completely necessary.

AM process	Manufacturing issues			Final stent properties		
	Costs	Speeds	Precisions	Radial	Longitudinal	Biological
SL	■	■	■	■	■	■
SLS	■	■	■	■	■	■
Traditional FFF	■	■	■	■	■	■
Tubular FFF	■	■	■	■	■	■
ES	■	■	■	■	■	■

■, poor property; ■, good property; ■, medium property

Table 2. Additive manufacturing (AM) process advantages and disadvantages.

AM processes have proved their effectiveness, and clearly they present a novel method to produce stents that could replace the current laser-cutting process. Depending on the AM process use, the manufacturer will have some advantages and disadvantages. **Table 2** summarized some on them.

Despite the few works about AM of stents, results have proved that these techniques could be promising. Further studies with new materials and technologies become crucial to understand the effect the process parameters has on stent properties and enclose the best material and process.

6. Additional properties

Although it constitutes the final layer of the stent manufacturing pyramid, additional properties cover a range of modifications to stent designs that sometimes become crucial. This section presents briefly the most common additional properties that are added to the stents.

6.1. Radiopacity markers

Stents made from stainless steel, nitinol, or polymers are sometimes hard to see fluoroscopically, particularly if they are small and/or have thin and narrow struts. To improve X-ray visibility, markers are often attached to the stents. These additions are typically made from gold, platinum, or tantalum and can be sleeves crimped around a strut [7].

6.2. Drug release

It is the main additional property usually added to stents in the current clinic practice. The main stent currently used in clinic is DES. There are a variety of coating techniques to incorporate drugs to the stent [68]. **Table 3** briefly presents the most common techniques.

Multiple variables can be adjusted to optimize drug release for cardiovascular stent applications, including biocompatible polymers and antirestenotic drugs. While the presence of a

Technique	Brief description
Dip coating	Coating by submerging the stent in a solution of drug and/or polymer in a solvent. The stent is then left to dry, allowing for evaporation, in the air/oven. In this technique the drug/polymer can vary their concentration and/or their homogeneity
Electro-treated coating	The drug/polymer particles are suspended in a liquid medium migrate under the influence of an electric field and are deposited onto an electrode (stent)
Plasma-treated coating	Plasma coating (plasma activation) is a method of surface modification which improves surface adhesion properties. Plasma produce a reduction of metal oxides, surface cleaning from organic contaminants, and modification of the topography
Spray coating	These techniques use apparatuses that spray polymer and drug solutions (using various solvents) onto a stent, enabling consistent deposit of a uniform drug release layer(s) onto the stent surface

Table 3. Most common coating techniques in stent manufacturing industry.

polymer coating on a DES is not required, the process to choose one can be difficult because it has been previously shown that most polymers listed as biocompatible and used in medicine can cause vascular inflammation.

7. Summary

Stents have been the center of many research lines in the last decades. The challenges associated with this medical device are numerous: geometry, material, manufacturing process, biocompatibility, etc. Finite element analysis (FEA) studies have been trying to understand the role of the different geometrical and material aspects in the mechanical behavior of stents. Material studies have been developing new material that accomplishes with the stent requirements in terms of mechanical and medical properties, both in the permanent field and in the biodegradable field. Finally, in the manufacturing research field, authors have been focused in improving the process by analyzing the parameters to obtain a stent with the higher precision and the minimal costs. In this research line, there are noteworthy lines: laser micro-cutting and, more recently, additive manufacturing. Additive manufacturing studies are showing their huge potential in the field of polymeric BRS.

There is a need to develop techniques for evaluating the ability of biodegradable stents to provide not only acute support but also reliable structural integrity for an appropriate period of time. In all these properties, the material and manufacturing process plays an important role. To achieve this, the previously mentioned research fields should be converged. The FEA field is developing new geometries with bioabsorbable polymer such as polycaprolactone that accomplishes with the stent mechanical requirements. The material field is developing new materials that accomplish the strict stent requirements. In the case of metallic alloys, develop material degraded with an appropriate rate. In the case of polymers, develop material accomplish with the mechanical and manufacturing properties of metallic ones. Lastly, the

manufacturing process field should work to increase the knowledge about the process parameters to obtain a more accurate result in the case of tubular FFF process and faster production in the case of SL processes that nowadays are presented as the most promising technique under investigation. Also, further works about ETS are necessary. ETS present a new research field into the stent world that could solve some current medical problems. Finally, the sterilization process should be noted. This last but mandatory manufacturing step could be critical for the final properties of stents. As Grabow et al. [46], or more recently Guerra et al. [65], have demonstrated, sterilization processes can change the final properties. Further works that get into the effect the sterilization processes has on stent properties are completely necessary.

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Conflict of interest

The authors declare no conflict of interest.

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