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# The potential of biocompatible metallic stents and preventing restenosis☆

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**Abstract**

Metallic stents have now become an indispensable integral part in cardiovascular treatment of patients in the public hospital. Both bare metallic stents and drug eluting stents have been used in practise. Fine structures with slit width of 0.1 mm and pitch better than 0.2 mm created with sharpness and low roughness in the cut surface of such stents have now become a life saving structural part implanted in the body. This paper reviews and describes the current status on various fabrication techniques for metallic stents of length 20 mm and diameter 2.1 mm with an annular tube thickness of 0.1 mm, by classifying the use of short pulse Nd-YAG laser. Some features on improving the surface characteristics of the cut surfaces of the stent, as well as a few techniques on preventing restenosis are also discussed.


*Keywords:* Laser cutting; Stent; Restenosis; Etching; Electric discharge machining; Surface modification

## 1. Introduction

In medicine, cardiovascular disease, which results in heart failure is a life threatening disease. This is mainly caused by too much cholesterol in the bloodstream, which can build up plaques inside the blood vessel walls and can restrict the blood flow to the heart. Basically the immune cells which adhere to the vessel walls, scavenge cholesterol from blood due to inflammatory signals and then it develop a new type of cell called foam cells thus causing formation of plaques [1]. These results in coronary artery obstruction, which leads to complicate problem of haemorrhage eventually leading to bypass surgery. In order to treat this coronary artery obstruction, usually a standard angioplasty technique is applied. But its clinical efficacy is limited by acute vessel occlusion and restenosis problems in the first 6 months. To reduce these deficiencies a new clinical therapy has been introduced with the implantation of metallic cardiovascular stent with adequate radio opacity. Metallic stent is typically a hollow cylindrical tube [$d$ = 2–4 mm; $l$ = 15–20 mm] with a patterned slit structure in two or three segments. It controls the flow of blood in the damaged vessel, thus avoiding it from being ruptured. The study shows [2] that stent geometry, i.e. diameter and mesh density produced with different porosities, defined as a percentage of metal free unit area per total unit area of the stent are most important for long term successful results. It actually offers regulatory resistance to the blood flow in the vessel. The metal coverage area of the stents range from 8% (Victor stents) to 24%, but the majority of stents are between 11 and 18% metal area when fully expanded. These mesh/fine slit structures are usually created with the electric discharge machine, which takes considerable processing time, but recently with the application of laser technology, the process has become relatively much faster. Various biomaterials such as stainless steel, nitinol, platinum, titanium and tantalum alloys and gold or polymer coated stents have been used for such applications. Improving the surface as well as the cut roughness of the stent is crucial to blood compatibility, because the first-layer cell formation on the surface is essential to minimize the blood clotting [3]. Besides that plastic deformation and heating during laser machining can also affect the material properties. Furthermore, melting also can result in the formation of precipitates and alter the material characteristics. On the other hand better surface and cut quality can prevent the activation process of thrombosis and show a decrease in neointimal hyperplasma as well as improve the

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healing efficiency [4,5]. Additionally, nuclear irradiation and fluorinated polymer coating as post processing techniques can also be found much beneficial for the increased life and the biocompatibility of the in vitro stent. Based upon these techniques, the present paper aims to review the current status and the future aspects of laser processed stent, highlighting its advantages and limitations in actual application. It describes various steps involved, i.e. material choice/selection, CAD design and FEM analysis, processing and surface modification properties so as to produce a biocompatible stent. A few suggestions for preventing restenosis are also discussed.

## 2. Background and status

Stent is a device made of inert materials and designed to maintain or to increase the lumen of a vessel [6]. It is usually made of a mesh type structure patterned in a metallic or polymer tube. It was introduced as early as 1960s but got its importance after the introduction of a tubular spring in 1969 to treat the arterial shrinkage [7]. Later in the year 1977, the balloon angioplasty technique was developed for the heart cardiovascular surgery [8]. In some cases to overcome the re-collapse of vessel, stent therapy was introduced [9,10] during 1980s. For insertion it is crimped onto a plastic balloon, which is transported to the lesion site by the catheter. Thereby after the expansion of the balloon with high pressure, the stent is unfolded and pressed against the wall. The balloon is deflated, the catheter is withdrawn and stent remains placed in the opening in order to prevent it from further collapse, so that the functioning of the blood vessel becomes normal again.

As such stents are fabricated from a number of biocompatible materials both from polymer as well as metal. Typically polypropylene, acetol homopolymer or copolymer, elgiloy wire, nitinol, platinum, tantalum, stainless steel and more recently iridium are in use for stent fabrication. However, due to radiopacity metallic stents are preferable. Currently there are more that 50 different configuration of stents available, but only 12 have been justified [11]. Depending upon the deployment, these stents can be further classified mainly into two categories: Balloon expandable (Bx) and Self-expanding (Sx). Table 1 summarizes a few of its comparative features [12,13].

For proper placement of the stent, radiopacity is an important factor. Therefore, metallic stents are always preferred and their selection depends upon the degree of radiopacity, biocompatibility and plasticity. It is realized that the noble metals platinum and gold bears better radiopacity than bare stainless steel and may be a better choice for the stent material. However, in a recent study platinum mesh cylinder made from thin platinum wire has been tried as coronary stent, but the initial results are still at preliminary stages. On the other hand, gold stent when fabricated through electroforming processs and surface treated with a monolayer of thiol group organic molecules can give acceptable results for optimal biocompatibility [15], but a study on the use of gold-coated stainless steel (SS316L) stents have shown some mixed results [16,17]. Although the gold coating of stainless steel stent improves the radiopacity but it elicited greater restenosis than similar uncoated stainless steel stent. In fact the compatibility of the gold-coated stent is negated by the post plating and heating. Though the post heating can give better surface roughness and remove adverse material-tissue interaction, including smoothening of the stent surface. Irregular spaces or pores in porous material within the coating are sealed or cover over and thus reduced. However, gold-coated stent produce greater neointima than bare stainless steel stent. Some gold plating techniques endow stents with an excessive inflammatory or proliferative reaction resulting increased risk of restenosis [16]. Process has also been developed to directly plate gold on nitinol stents to improve the radiopacity. Adhesion to the surfaces of nitinol as well as to the stainless steel has been excellent, but problem arises from hydrogen embrittlement during the plating process (Table 2).

In order to improve the biocompatibility, the bare metallic stents are further treated externally with an appropriate coating. For example, the amorphous oxide or silicon carbide coating provides better corrosion resistance and prevents damage as well as adversary effects to the cells thus presumed to be superior not only in strength safety but also in biocompatibility. An optimized adhesion of amorphous silicon carbide coating on metallic

Table 1
Comparative features of Balloon expandable (Bx) and Self-expanding (Sx) stent [12,13]

| Balloon expandable (Bx) | Self-expanding (Sx) |
|---|---|
| 1. Usually manufactured in the crimped state and then expanded to the vessel diameter by inflating a balloon, thus plastically deforming the stent. | 1. Usually manufactured at the vessel diameter or slightly above. Prior to deployment, constrained to the smaller crimped diameter, which is released during the deployment. |
| 2. Resist the balloon expansion process. | 2. Assist the vessel expansion. |
| 3. Recoil after balloon deflation. | 3. Assist balloon inflation and thus there is no recoil of the stent alone. |
| 4. After the placement, they can only become smaller in diameter over time and termed chronic recoil. | 4. Usually oversized and continue to open over time, thus undergo a negative chronic recoil. |
| 5. The delivery profile is governed by the profile of the balloon upon which they are mounted. | 5. Their profile is governed by the strut dimension. |
| 6. They exhibits predefined strength to the radial force, but if exceeded, can collapse. | 6. Almost do not depend upon the radial strength and can recover their shape elastically. |
| 7. They are stiffer. | 7. They are less stiff. |
| 8. No temperature dependence, especially in the body range temperature. | 8. Malleability at low temperature, stress increases with the temperature. |
| 9. Typically fabricated from SS316L material (Table 2) [14]. | 9. Typically fabricated from Ni-Ti shape memory alloy with Ni = 50.8%; Ti = 49.2%. |