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DEVELOPMENT OF CORONARY STENTS USING ADVANCED RESULTS OF MATERIALS SCIENCE AND TECHNOOGY

L. Major
Managing director, Cardio-Vascular Intervention Public Company
H-1137 Budapest, Újpest rkp. 8. Tel: (20) 934 4371, e-mail:kandminc@mail.datanet.hu

J. Dobránszky
Senior researcher, Research Group for Metals Technology of HAS–BUTE
H-1111 Budapest, Goldmann tér 3. Tel: (1) 463 1934, e-mail: dobi@eik.bme.hu

Zs. Nyitrai
Researcher, K&M Tentaur Ltd., Department of Electronics Technology
H-1111. Budapest, Goldmann tér 3. Tel: (1) 463 2740, e-mail: nyitrai@ett.bme.hu

Zs. Puskás
Managing director, K&M Tentaur Ltd.
H-1212. Budapest, POB. 123. Tel: (1) 123 456, e-mail: tentaur@vodafone.hu

Summary

Stents are high tech endovascular implants. K&M Inc. is the single Eastern European stent producer company. The market needs more biocompatible devices as the trend of the stent development all the producers have to react. The other members of a R&D consortium is research institutions deals with diamond-like and drug-eluting coatings for decade. These biocompatible coatings can avoid the metallic stent surface to directly contact to the living tissues. This way a biologically active drug connected to the surface can be delivered directly to the diseased vessel wall. The Cardiovascular Institution has the clinical facility to test the new products. This group of applicants is obliged to develop, test and put on the market the new generation biocompatible coated stents.

1 INTRODUCTION

Stent endoprotheses have been used by cardiovascular therapy for ten years to substitute serious "by-pass" operations in case of coronary-artery disease with cheaper, quicker operations that do not wear the patients down. The stent shown in Fig. 1 is placed to the site of stenosis in compressed form on a balloon catheter then with the inflation of the balloon catheter it is dilated. In the vessel treated by this method, the circulation of the blood is restored. Stents are being used more and more frequently to treat the obstruction of urinary, biliary, respiratory tracts and the oesophagus besides the stenosis of arteries and other vessels.

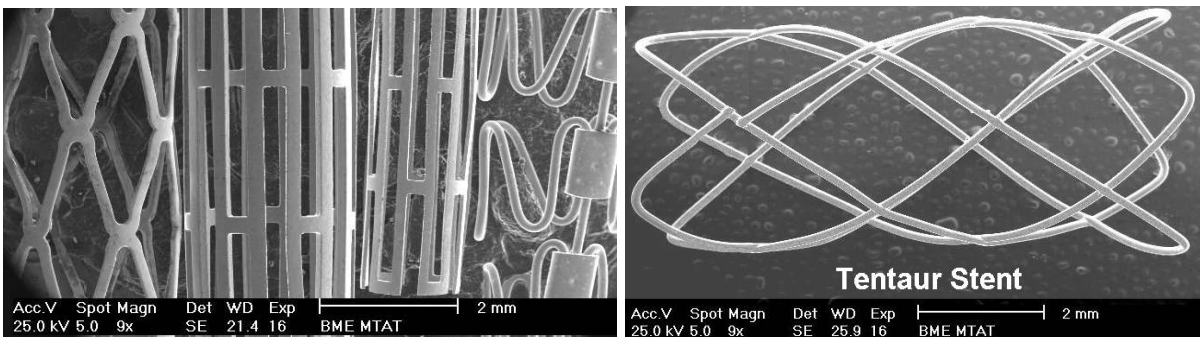

Fig. 1. SEM-image of different coronary stents.

Stents are high-technology industrial products that are the creation of the knowledge of health sciences, surface physics and chemistry, material study, engineering and technology. Its further development can be efficiently carried out only by the involvement of these areas of knowledge. Since there are one million stents implanted in the world every year, the first stent of the world, called Schatz-Palmaz, produced by the Johnson & Johnson Company has already gone through several generation changes. The original wire-mesh cut for those replaced size made of wire, welded or with laser cut from tubes. This was the second large step forward in the development of production technology, following the first one, the appearance of balloon catheters.

The third significant step forward is the improvement of the surface and material of the stents. There have been several projects seeming to be world sensations and proved to be inappropriate by clinical application. However the most important question of the quickly growing stent industry is how the surface of stents should look like. Even if only the stents implanted into vessels are considered, it is visible that the medical science is more and more careful at stating what type of surface is ideal for a stent. It is because there are opposing opinions concerning the short- and long-term reactions of the human body or even concerning the characteristics of the patients' blood. The most important development trend in the last three or four years, the special surface treatment of stents can be divided into the following main groups:

- Treatment or modification of surface (e.g.: electropolishing, passivation),
- Golden or other neutralising coating,
- Coatings that increase the hydrophobic or hydrophilic characteristic of the surface,
- Active coatings (antithrombotic materials),
- Diamond-like coatings carrying simple or active materials,
- Special coatings for non-vascular stents.

Clinical applications show that there is demand for such type of stents that can be implanted to those areas where the non-flexible tube-like wire-meshes cannot be. The nowadays dominant 8-20 mm long stent types mounted on balloon catheters are not flexible enough. To increase the flexibility new production technology is necessary. Producers continuously concentrate on the development of these. The competing producers influence the opinion and choice of the experts working in haemodynamic laboratories by the fact that they sell stents mounted on balloon catheters. This type of packaging, originally promoting more comfortable application has become the norm of selection (at least on the Hungarian market where higher price is advantage for those making decisions about buying).

2 THE BASIC CHARACTERISTICS OF STENTS

Stents are biocompatible implants that have webbed structure and are able to sustain vessel walls. The destination of stents is the prevention of restenosis. In case of stents made of metal corrosion characteristics determine biocompatibility. In case of materials being in direct contact with blood, haemocompatibility is demanded which means that the surface has to be hydrophobic, the electrical charge of the surface has to be the most negative and the surface roughness has to be the lowest.

The form of the stents is the same all around the world. This webbed structure was formed due to medical experiences and due to the effect of the continuous development (flexibility, radial stability) of basic requirements. The Tentaur stent is made of wire where the junction points are sutured by welding. As a product it is the result of authentic research, protected by patent and successfully applied in the Hungarian health care.

During the development vessel prostheses, different materials were tested as structural material or coating. The most widespread according to American patent is 316L that proved to be the most reliable based on ten-year-long clinical experiences. Besides this, stents made of nitinol, tantalum and previously gold are known.

The material of the continuously developed Tentaur and the goal of this project, the TentaFlex stent is AISI 316LVM austenitic steel. The diameter of the wire is 150 micrometers, its dilatation is 34% and its limit of fluidity is 510 MPa. The chemical composition of the stent (its amount being given as a percentage of its mass) is shown in the following table:

C	Si	Mn	P	S	Cr	Ni	Mo	N	Cu	Co
0,016	0,40	1,8	0,015	0,004	17,5	14,7	2,78	0,05	0,04	0,03

Table 1. Chemical composition of Tentaur stent's base material

Concerning the bio- and haemocompatibility of 316L austenitic steel clinical experiences prove that the human body accepts these materials and they do not cause irritation, which would lead to restenosis in the affected vessel section. The metalosis occurring in the neighbouring tissues most probably hinders the abnormal growth of neighbouring tissues. The disadvantage of the 316L type steel is that a stent made of this material cannot be implanted into patients suffering from Ni or Cr allergy. In contrast to the above mentioned, we have the opinion that the issue the material of the stents is not yet to be abandoned. Like all researchers, planning for long-term results, we intend to examine the appropriateness of materials like nitinol, super austenitic steel and duplex steel.

3 SURFACE TREATMENT AND COATINGS OF STENTS

The Tentaur and TentaFlex stents are actually under development. These made of biocompatible stainless steel. It is known that metal surfaces irritate the wall of the vessels but experiences show that metalosis occurring this way have favourable effects as well. The first goal of our development is to increase the biocompatibility of the stents with coatings. We intend to carry out the following coating types and surface modification technologies:

- Coating with diamond-like carbon, more precisely, a carbon cover that adheres to the stent and forms a multilayer on whose surface area a polymer-like layer can be formed.
- Chemical modification of surfaces for biochemical and immunological characteristics.
- Development of stents coated with Teflon. On one type of stents it would carry out the modification of moisturising characteristics and the isolation of the metal surface. The other type (stents for the air tract) of stents would be completely covered by it.
- Development of silicon-coated stents in hydrophilic and hydrophobic variation (Fig. 2).
- Creation of stents of specially modified surface in order to change the characteristics of free metal surface and to be able to form surface for special coatings.

The surface quality of stents is determined by the surface quality of their material. Welded junction points and cutting edges where change can occur due to heat and pressure can make the stent different. This is very important in case of coating the stents because at these sites the adherence of the coating material could worsen and its continuity can break.

In case of the Tentaur stents the colour change (caused by the stiffening of the surface due to the change of the shape of different particles) occurring at the welded joints has to be treated. The most appropriate treatment to achieve this is electrochemical polishing. This

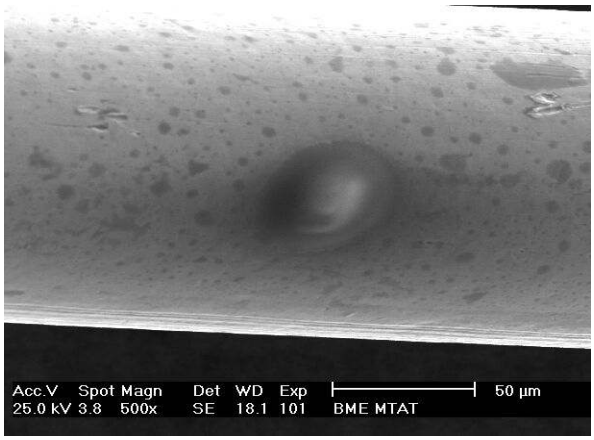

Fig. 2. Silicon coated of Tentaur stent.

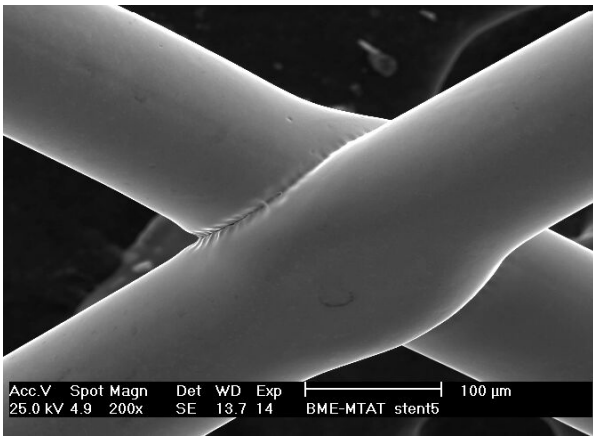

Fig. 3. Electropolished joint of Tentaur stent.

surface treatment modifies the characteristics of the stent's surface. We consider the clarification of the effects of the structure of the metal surface on the formational characteristics of the coating important (Fig. 3).

The diamond-like amorphous carbon is tissue friendly. This characteristic is complemented by the fact that the webbed structure consisting of small carbon atoms is able to prevent the entering heavy metal ions (Cr, Ni) to the bloodstream. The coating is such a diamond-like multilayer on whose surface a polymer-like or teflon layer is formed either in massive or in porous form. The aim with porosity is to make the pores able to take in and to ration medicines.

When the Tentaur stent is coated with silicon the dust free drying of the stent has to be provided. To achieve this Laminar Air Flow equipment, which provides dust free, drying has to be inserted into the production technology. Drying is necessary in order to make the solvent evaporate from the silicon. The solvent makes the even distribution of the thin film layer on the stent's surface possible. Heat treatment is necessary for polymerisation. This operation has to be inserted as well into the production technology. In all phases of production avoiding contamination is the basic requirement.

The hydrophobic characteristic of the stent's surface increases significantly due to silicon coating. This characteristic can be described by measuring of the wettability in case of plain surfaces. The angle of a blood drop on a surface coated with silicon is much less than on a metal surface without coating (Fig. 4).

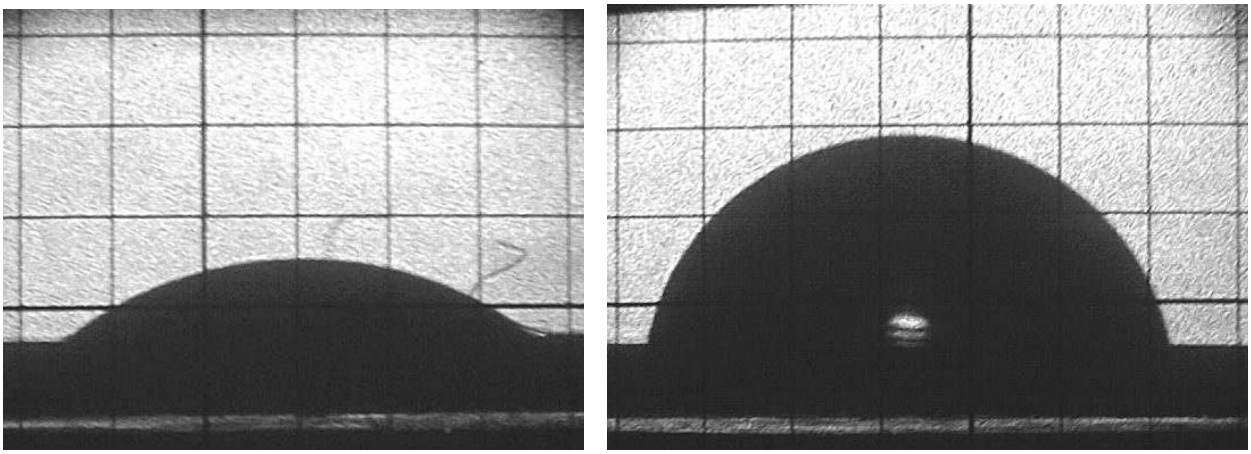

Fig. 4. Human blood drop on the surface of stainless steel: uncoated in left, silicon-coated in right.

4 ADVANCED TECHNOLOGIES OF STENT FABRICATION

Preparing stents with mask technology and etching is very similar to those used in electronic technology to prepare printed wiring boards. The differences are, firstly, that the basic material is not copper, but a stainless steel tube, and, secondly, that the pattern of the mask will be projected on a cylindrical surface and not on a flat surface. These differences cause many problems since the conventional etching cannot be used and so we have to use electro-chemical etching. The steps of the technology:

- Cleaning and degreasing of the surface,
- Coating of the tube surface with resist,
- Dehydration,
- Projection of the mask on the surface with laser beam,
- Chemical or electrochemical etching of sample.

After etching the stent has to be removed from the little bar. The stent produced this way can we see on Fig. 5. In the enlarged picture (right) more abnormalities of the stent can be noticed. It is sharp as a razor in some places. When the stent is expanded with a little silicon-balloon on 6-12 bar pressure (during the implantation), the sharp edges of the stent can cause the bursting of the balloon. This problem can be solved using a low current polishing after removing the stent from the bar and the resist from the surface.

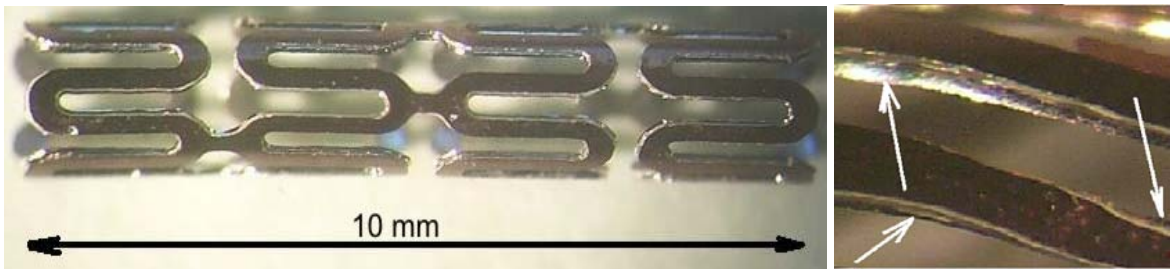

Fig. 5. Stent after etching (left) and sharp edges of the stent (right)

REFERENCES

[1] Puskás Zs, Major L: Ausztenites acélból készült stent érprotézisek felületi jellemzőinek és bevonatainak vizsgálata, BKL Kohászat, 134:5 (2001), p. 191-195.
[2] Wang Kai: Biocompatibilisation of Coronary Artery Stents (Acta Biomedica Lovaniensia , No 162), Coronet Books, 1998.
[3] Kuehne T, Saeed M, Higgins CB, Gleason K, Krombach GA, Weber OM, Martin AJ, Turner D, Teitel D, Moore P. Endovascular Stents in Pulmonary Valve and Artery in Swine: Feasibility Study of MR Imaging–guided Deployment and Postinterventional Assessment, Radiology 2003;226:475-481.
[4] Serruys PW: Handbook of Coronary Stents, Blackwell Science Inc. 2002.
[5] Nyitrai Zs, Illyefalvi-Vitéz Zs, Pinkola: Preparing Stents with Masking & Etching Technology, Procedings of the 26th International Spring Seminar on Electronics Technology, May 8-11, 2003, Stará Lesná, Slovak Republic