Development and Examination of Coated Coronary Stents

Eszter Bognár[1,a], György Ring[1,b], Hilda Zsanett Marton[1,c]
János Dobránszky[2,d]

[1]Budapest University of Technology and Economics, Department of Materials Science and Engineering. 1111 Budapest, Goldmann tér 3. Hungary

[2]Research Group for Metals Technology of HAS and BUTE. 1111 Budapest, Goldmann tér 3. Hungary

[a]eszter@eik.bme.hu, [b]gyring@eik.bme.hu, [c]martonhi@gmail.com, [d]dobi@eik.bme.hu

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Abstract. The aim of this study is to show the developments carried out by us with coated stents, expansion properties, furthermore the failures of the coatings. The coating was examined before and after expansion, paying special attention to the curves. The quality and the changing of the coatings were examined by different methods: optical microscopy, atomic force microscopy, scanning electron microscopy and EDS analysis. The results show that the expansion to a higher pressure did not change the coating.

Polyurethane coating was given to TentAur stents. The coatings were produced by a method of dipping. The sterile and dust free environment is crucial to produce a suitable coating. Electro-polished and non-electro-polished sheets and stents were used for these experiments. The quality and the changing of the coatings were examined by different methods after drying. The fatigue tests showed that the polyurethane coating had suitable adherence.

Introduction

The stents used in the cardiology are cylindrical metal meshes made from wires by welding or from tubes by laser cutting. The ideal stents are to resist thrombus formation, be stainless, bio-compatible and solid enough. At the same time it is also important that the stent can get to the constriction easily, the blood can get to the sides through it and it has to adjust itself to the anatomy of the coronary. Most of the stents are made of metal most often 316L stainless steel. Metal ions may dissolve from the stents after implantation and it may cause allergic reactions for the ones sensible to it. There are polymer stents as well which do not contain any metal; however, they are not used for the time being because they may produce biological reactions in themselves. Besides the material of the stent clinical efficiency depends on other factors such as the thickness of the struts or the closeness of the construction [1, 2].

In angioplasty high pressure is put on the plaque and the wall of the artery. Therefore the material of plaque is compressed and pressed into the membranes of the artery. The endothelia and lamina elastica crack, the media, lamina elastica externa and lamina elastica interna stretch and also get injured. Hereby neointima hyperplasia starts whose role is to reconstruct the integrity of the artery. At best the regeneration of the wall of the artery will be complete, however, usually this process does not stop at this point, the proliferation of the non-striated muscles continues. Therefore the lumen of the artery becomes narrower again. This stricture is called restenosis [3].

There is no effective, systematic medicinal treatment to prevent restenosis. However, there are two main methods to prevent the proliferation of the non-striated muscles. The first method called brachytherapy is an intravascular solution which consists of the implantation of emitter stents. Therefore the cells are not able to proliferate. The quantity of approximately 14-20 Gray is used. Nevertheless, a big problem called edge effect occurs when using this method. The reason for this is probably the fact that the dose of emitting at the end of the stents intensifies the intimal hyperplasia and does not inhibit it. Therefore the so-called “cold”, not radioactive stent-edge and the so-called "warm", radioactive stent-edge were tested but they did not work [4, 5]. The other method is based on the delivery of the cytostaticum by a stent so that it can generate local inhibition. Controlled drug eluted stents were developed for the local inhibition of cell proliferation. The result depends on the material of the coating, the coating technology, the dose and efficiency of the applied drug. The main groups of coatings are precious metals, oxide, nitride, carbide coatings, polymers and human polymers. Numerous types of polymer coatings of stents have been tested: polyurethane, polyethylene terephthalate, polidimethylsiloxane (silicone). These coatings caused both inflammation and thrombosis in experiments on animals. Therefore it is necessary to mix the coatings with drugs. The five main groups of the drugs by their effect on the human system:

- anti-proliferative (Colhicine, Paclitaxel);
- anti-thrombins (Hirudin);
- immunomodulators (Sirolimus, Tacrolimus);
- anti-migration (Probucol);
- promote healing endothelization (NO donors) [6, 7].

The inhibition of cell proliferation is necessary for a few months, so it is practical to plan the liberation of the cytostaticum at least for this period of time [3].

Investigation of coated coronary stents

Tecnic Carbostent™ (3,5×25). Mid-air expansion method was used for this stent. The balloon was expanded above the nominal pressure (to 20 bars), which simulated clinical use. Before, during and after expansion the coating was examined and analyzed by different methods using scanning electron microscopy, EDS-analysis, atomic force microscopy and optical microscopy. Fatigue methods were used for the examination of the coating.

The material of this stent is stainless steel, 316LVM, coated with permanent turbostratic carbon. The struts have rectangle shape and they are rounded. The nominal diameter of this stent is 3,5 mm and the nominal length is 25 mm. The coating was intact before expansion. After expansion slip lines and grain boundaries were outlined, but the coating did not change significantly, it remained uniform. Its surface remained smooth (Fig. 1). The foreshortening (0,4 %) and recoil (2,1 %) were measured and had correct values.

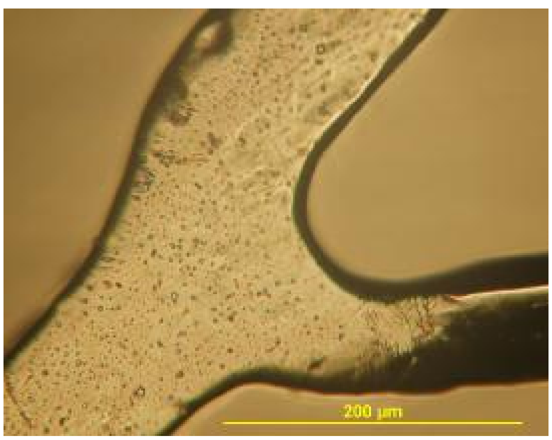

Fig. 1 Smooth surface of Tecnic Carbostent™, after expansion at 200 times magnification

Fig. 2 Strain-lines of Tecnic Carbostent™, after expansion at 200 times magnification

Fig. 2 shows an arc of the stent and grain boundaries are visible. The electro-polishing resulted in the round shape of the inner arc. The surface of the stent remained clean and the coating was uniform, but several fragments were found (Fig. 3). Reliable and precise positioning and proper visualization can be realized due to the platinum markers (Fig. 4).

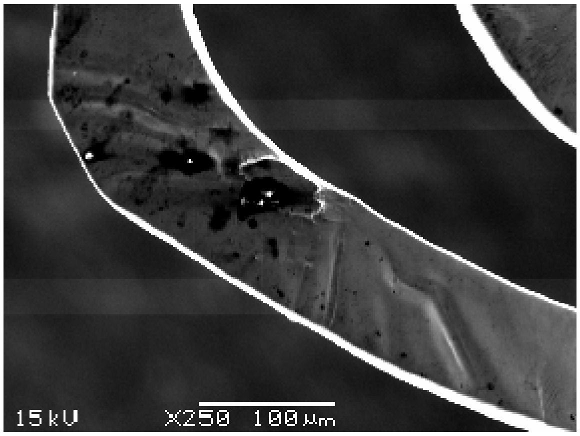

Fig. 3 Fragment resulting from cutting after expansion of Tecnic Carbostent™ at 250 times magnification

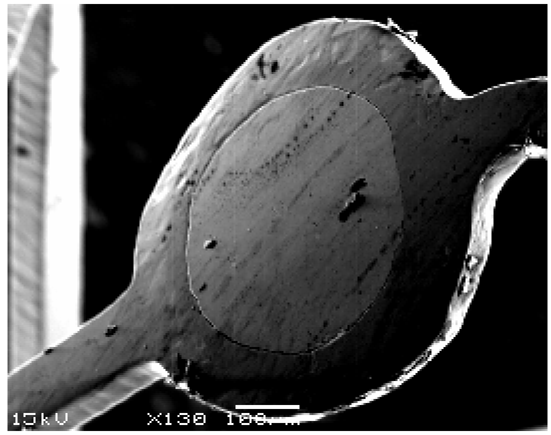

Fig. 4 Radiopaque platinum marker of Tecnic Carbostent™ at 130 times magnification

After expansion the stent was examined on air by contact method with an atomic force microscope. In AFM, a sip attached to a cantilever is scanned across a surface. Changes in surface topography that are encountered as the tip moves over the material's surface change the interatomic attractive or repulsive forces between the surface and tip [8]. The surface was examined in a contact way and was found homogeneous (Fig. 5). The left side of Figure 5 shows the height image with colour codes and the right side is the deflection image. The average roughness was 2,202 nm.

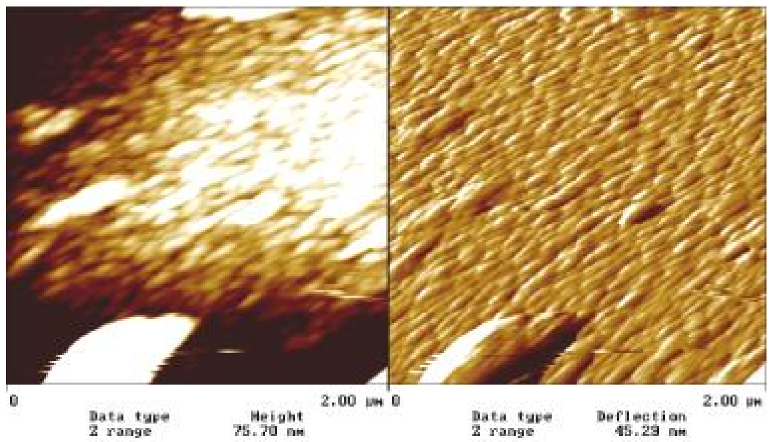

Fig. 5 Atomic force microscopy image of Tecnic Carbostent™

Coating experiments

The surface modifications and coating experiments were done on sheets first because the TentAur stents are made of thin wires so it is difficult to examine the surface features on stents, for example, contact angle measurement. Therefore 316L sheets were used to start the experiments of the surface modifications. It was important to start with a clean surface, therefore the sheets and the stents were cleaned with isopropyl alcohol in an ultrasonic resonator. It is a very effective method of cleaning. The sheets were electro-polished by different parameters. The most common method was used, which is the dipping method. Polyurethane coating was applied to the sheets [9].

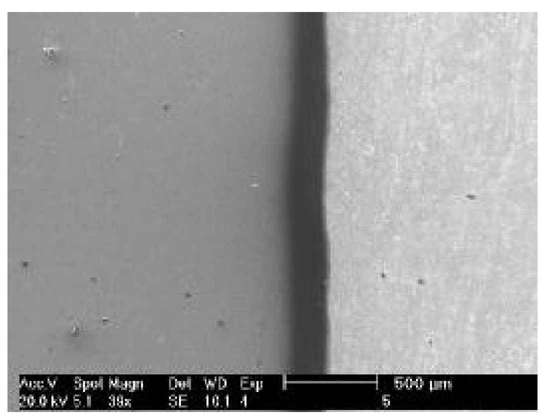

Fig. 6 Smooth polyurethane coating on sheet at 39 times magnification

The coatings were made by mixing the polyurethane with tetrahydrofuran solvent to produce different solutions. Fig. 6 shows an electro-polished, coated sheet with 10 w/w% tetrahydrofuran solution. The coating was scratched in order to examine the adhesion to the steel. Fig. 7 shows that the coating has suitable adhesion.

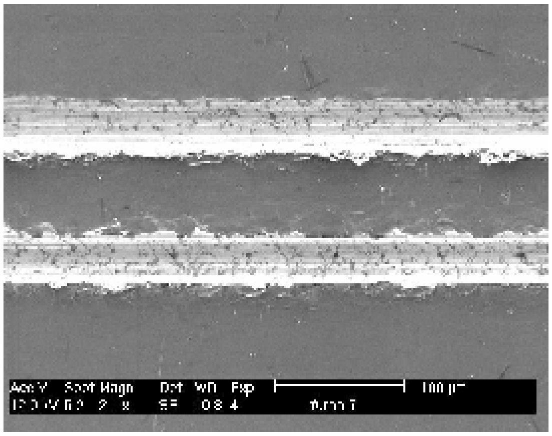

Fig. 7 The scratched 10 w/w% tetrahydrofuran solution polyurethane coating at 211 times magnification

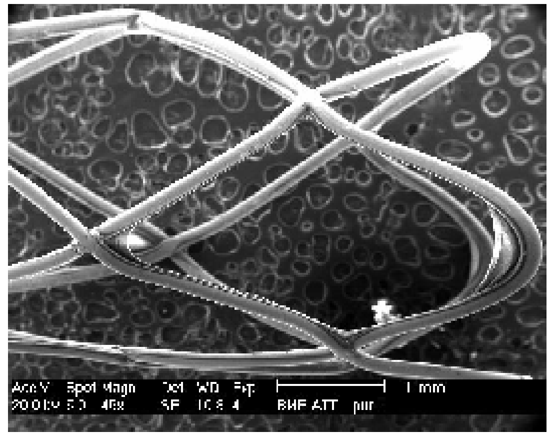

Fig. 8 Polyurethane film (10 w/w% tetrahydrofuran solution) between the struts of the stent at 39 times magnification

The same method was used for the stents, however, the stents were rotated during the drying process. Fig. 8 shows the results of the experiments with TentAur stents. The fact that the solution was too concentrated resulted in the formation of film between the struts.

1 w/w% tetrahydrofuran solution was prepared to eliminate the formation of polyurethane film and the sheets were dipped into it five times (Fig. 9). The experiment was carried out on electro-polished sheets. The coating became smooth and uniform (Fig. 10).

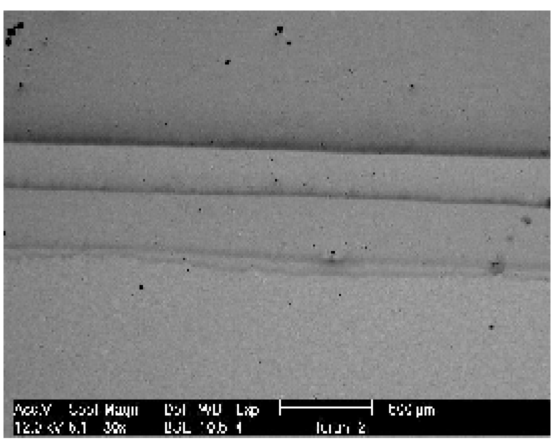

Fig. 9 Surface of the sheet after having been dipped five times into 1w/w% tetrahydrofuran solution at 30 times magnification

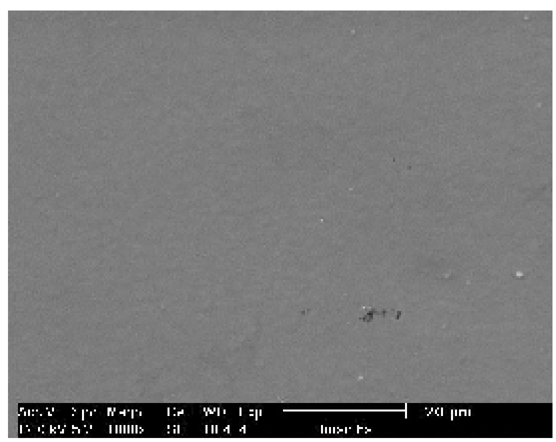

Fig. 10 Smooth texture of the sheet after having been dipped five times into 1w/w% tetrahydrofuran solution at 1000 times magnification

The stents were also dipped into this solution. A bending machine was used for the test of fatigue features and adhesion properties of the polyurethane coated stent. The bending machine simulates the bending stress in the coronary arteries (Fig. 11). A plastic tube is attached to the equipment. One end of the tube is steadily fixed and the other end is connected to an excenter disc. Turning round of the disc results in bending of the plastic tube and therefore the stents placed into the tube are also bent.

The movement of the tube simulates the movement of the coronary arteries in systolic phase. Two TentAur stents coated with polyurethane were tested with this equipment. The testing time was 12 600 000 cycles. After the test the stents were examined by different methods. Electron microscopy showed slip lines and the surface of the stents become coarse. The coating remained on the surface, the adherence was suitable, even though the coating deformed a bit (Fig. 12).

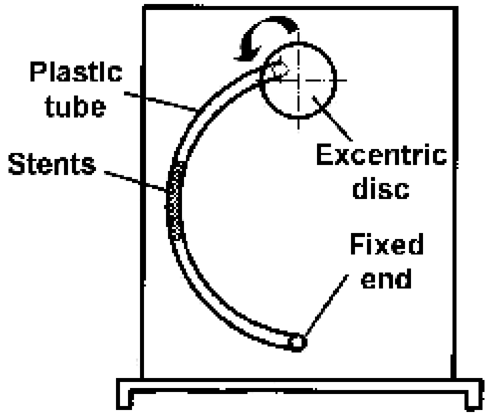

Fig. 11 The equipment of the fatigue test to simulate bending stress

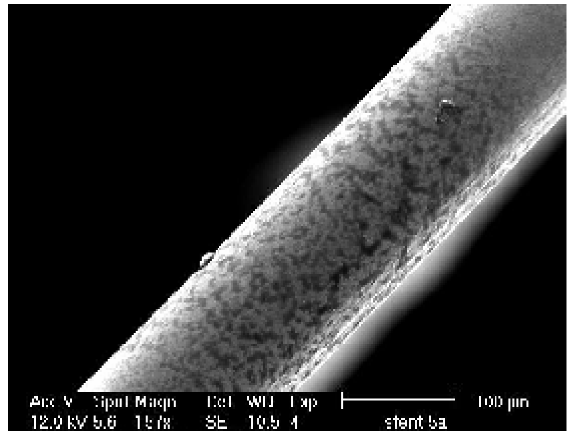

Fig. 12 Surface of the stent after fatigue test at 157 times magnification

Comparative contact angle measurements were made on the coated and uncoated metallic sheets. These measurements were made on non-electro-polished, electro-polished and polyurethane coated non-electro-polished and electro-polished metallic sheets. The maximum progressive and the minimum receding contact angles were measured with a method of drop conformation and drop taking method. The results of the contact angle measurements of different metallic sheets were compared (Table 1).

Metallic sheet type	Tetrahydrofuran solution concentration [w/w%]	Drop size [µl]	Progressive contact angles [°]	Receding contact angles [°]
Non-electro-polished	Uncoated	10	56	37
Non-electro-polished	Uncoated	20	60	41
Non-electro-polished	Uncoated	30	65	44
Electro-polished	10	10	76	54
Electro-polished	10	20	74	55
Electro-polished	10	30	74	55
Non-electro-polished	1	10	76	59
Non-electro-polished	1	20	79	56
Non-electro-polished	1	30	73	57
Electro-polished	1	10	80	57
Electro-polished	1	20	80	56
Electro-polished	1	30	73	59

Table 1 The results of the contact angle measurements

Electro-polished sheets have better hydrophilic properties than non-electro-polished sheets. Water drops spread on the electro-polished sheets better than on the non-electro-polished surface. Water drops spread on the electro-polished surface better, the reason for this is the dissimilarity of the layers covering the surface. The oxide layer was thicker on the non-electro-polished sheets and the surface of these sheets was rougher. There were no significant differences between the coatings of electro-polished and non-electro-polished sheets concerning wettability (Fig. 13-14). A hydrophilic surface is given by the polyurethane coating.

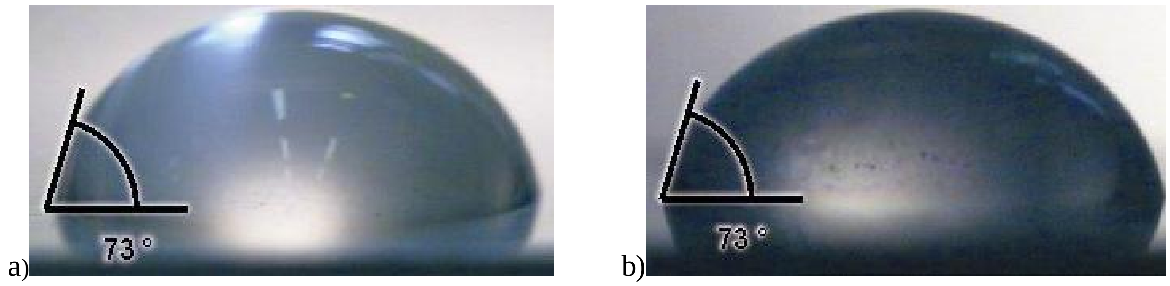

Fig. 13 Photos of the progressive contact angles: a) Polyurethane coated non-electro-polished sheet with a 30 µl drop, b) Polyurethane coated electro-polished sheet with a 30 µl drop

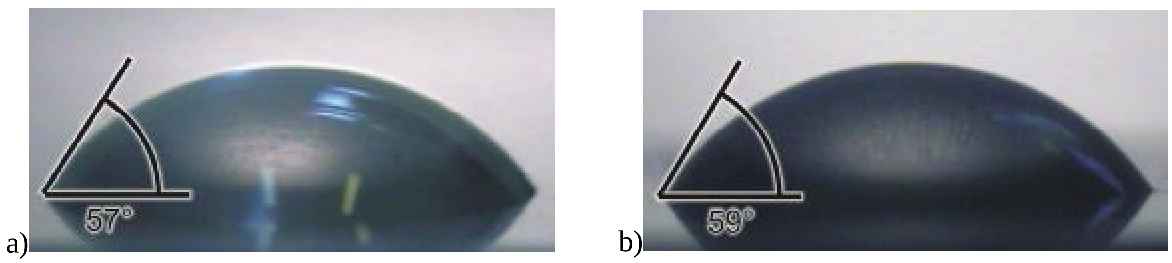

Fig. 14 Photos of the receding contact angles: a) Polyurethane coated non-electro-polished sheet with a 30 µl drop, b) Polyurethane coated electro-polished sheet with a 30 µl drop

Conclusions

In the present paper the properties of the coatings were studied using different methods: scanning electron microscopy, atomic force microscopy and optical microscopy and a fatigue method was shown for the examination of the adherence of the coatings. Before expansion the most frequent surface failures of Tecnic Carbostent™ were scratches and small shrinkage of materials originating from the manufacturing and finishing processes, therefore the coating was not totally smooth. The foreshortening (0.4 %) and recoil (2.1 %) were measured and had correct values. After expansion the carbon coating was examined. Slip lines occurred, grain boundaries were outlined, so the roughness was grown locally because of the anisotropic plastic deformation but the coating did not change significantly.

Our first coatings became too thick as a result of the concentration of the solution. Therefore the dilution of the solution was necessary. Polyurethane coating had suitable adhesion to the steel and it was also proved by fatigue tests. In the future drugs will be added to the polyurethane coating. Altogether the coatings examined had only minor injuries and failures as a result of expansion and fatigue tests.

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