

Coating of Vascular Stents with Antithrombogenic Amorphous Silicon Carbide

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Summary

Coronary stenting became a fast growing field in interventional cardiology in the last few years. At the beginning of stent development significant improvements have been achieved by focussing just on the mechanical properties of the design. Optimization with regard to both the mechanical properties as well as biocompatibility is possible by using a hybrid concept. While the mechanical requirements can be fulfilled by using 316L stainless steel as a material for the stent body, biocompatibility can be improved by an α -SiC:H-coating. The thin film of silicon carbide is deposited by Plasma Enhanced Chemical Vapor Deposition (PECVD) using techniques to optimize the adhesion on the stent.

Key Words

Coronary stent, hybrid stent design, surface coating, stent thrombosis, hemocompatibility

Introduction

Coronary artery disease remains the most common cause of death in industrialized countries despite the steady progress in treatment and prevention. Beside drug therapy, a first significant advance in the treatment of coronary artery disease has been the introduction of coronary artery bypass grafting [1,2]. However, the need for less invasive and potentially less expensive procedures has stimulated the development of percutaneous transluminal coronary angioplasty (PTCA) as a non-surgical revascularization technique. Nevertheless, the safety and efficacy of PTCA are limited by the risk of acute and subacute closure (occurring during or immediately after the intervention) and chronic luminal re-narrowing or restenosis [3]. Today, the most promising technique to improve the immediate and long-term results of PTCA is coronary stenting. However, even for coronary stenting the reduction of the rate of acute and subacute closure as well as restenosis is the major challenge for today's stent development. Even if the mechanical properties of metal stents could be improved by optimization of the geometrical design, significant success in avoiding unwanted interactions between the implanted stent and the surrounding blood and tissue could not be achieved.

This article presents the hybrid design concept consisting of the combination of two different materials as a new approach to reduce the complication rate due to short- and long-term re-narrowing of the vessel after stent implantation. The aim of the hybrid concept is to fulfil the mechanical and biocompatibility requirements on the stent independently:

- On the one hand the mechanical properties like radial strength, longitudinal flexibility, recoil and foreshortening have to be optimized for suitable delivery of the stent and for restoring the lumen of the narrowed vessel. Thus, proper functionality of the stent depends on the combination of an optimized geometrical design and a suitable bulk material.
- On the other hand it is well known that different mechanisms finally resulting in restenosis of the vessel are induced by interactions of the body with the implant's surface. For example, via the surface the clotting system may be triggered, the proliferation of smooth muscle cells can be activated and metallic corrosion products may diffuse into the vascular system. The idea behind the approach of the hybrid concept is to provide the stent with a coating that works like a "magic hat" in order to minimize these unwanted interactions.

Amorphous silicon carbide as hemocompatible surface coating

Today, about 90% of all stents commercially available consist of uncoated 316L medical grade stainless steel. However, metals have well described effects on blood [4]. Blood proteins adsorb at the stent surface and change their conformation. These degraded proteins induce reactions of the body such as inflammation. In particular, fibrinogen is decomposed into fibrin monomers directly by the metal. Thus, a metal induced thrombosis occurs immediately after implantation. In addition, platelets adsorb at the stent's surface. Platelets are activated and may initiate smooth muscle cell proliferation through the release of growth factors. Platelet involvement leads to complex thrombus formation, containing fibrin, thrombin, and other blood components. The generated thrombin stimulates smooth muscle cell hyperplasia.

One of the basic reaction mechanisms is the interaction of fibrinogen with an alloplastic material, for which a physical model could be found explaining the observed degeneration of fibrinogen [4,5]. According to this model, thrombogenesis at surfaces of alloplastic materials can be described by means of an electron transfer process, in which electrons are transferred from the adsorbed fibrinogen molecule to the solid (Figure 1). This process instigates the cleavage of the fibrinogen molecule into the activated fibrin monomer and the fibrinopeptides resulting in polymerization of fibrin and thrombus formation.

The physical model of the system fibrinogen/implant is described in terms of the electronic structure of fibrinogen and the implant's surface. The starting point of

thrombus formation is assumed as an electron transfer from the fibrinogen molecules to the solid. Since the electronic structure of fibrinogen is well known, one also knows "where the electrons are sitting" in terms of energy (Figure 2). In other words, the electrons of the protein are at 0.9 eV below Fermi's level (the reference potential for electronic calculations) or lower. According to the "preservation of energy"-theorem the transfer of electrons can only happen at this level. However, according to Pauli's theorem there must be an empty electronic state in the solid to allow the transfer. In conclusion, the degeneration of the protein can be prevented if the electron transfer is prevented. This can be achieved when the alloplastic material has no empty electronic states lower than 0.9 eV below Fermi's level. A detailed discussion of this rationale [4] leads to the following physical requirements for good hemocompatibility:

1. To prevent the electron transfer the solid must have no empty electronic states at the transfer level, i.e., deeper than 0.9 eV below Fermi's level. This requirement is met by a semiconductor with a sufficiently large band gap (precisely: its valence band edge must be deeper than 1.4 eV below Fermi's level) and a low density of states inside the band gap.
2. To prevent electrostatic charging of the interface (which may interfere with requirement 1) the electric conductivity must be higher than 10^{-3} S/cm.

A material that meets these electronic requirements is silicon carbide in an amorphous, heavily n-doped, hydrogen-rich modification (a-SiC:H). The amorphous

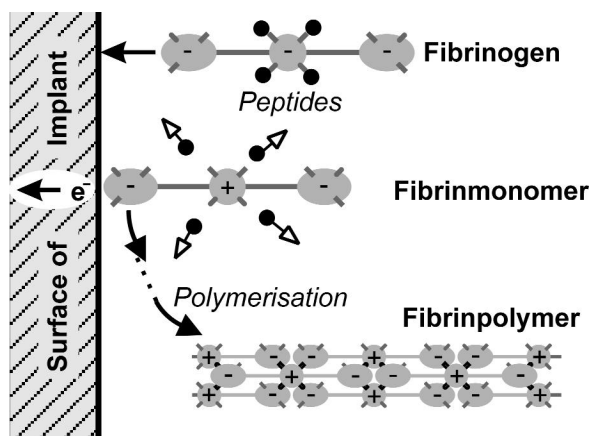


Figure 1. Electron transfer from fibrinogen to the solid's surface induces the release of fibrinopeptides.

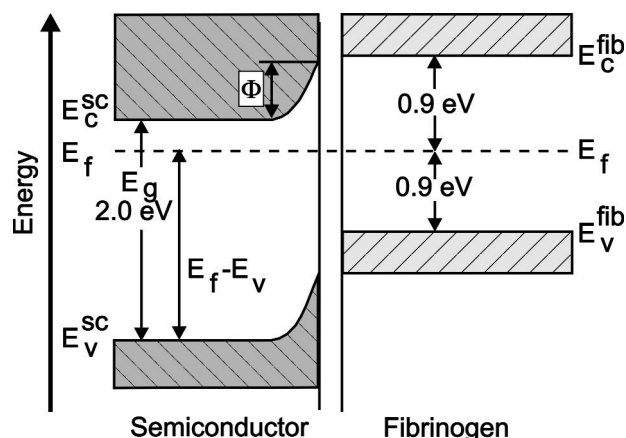


Figure 2. Potential distribution at the fibrinogen / semiconductor phase boundary (with a band gap of 2.0 eV).

structure is required in order to avoid any point of increased density of electronic states, especially at grain boundaries.

The Coating Process

The deposition of this particular modification of amorphous silicon carbide is performed by means of the plasma-enhanced chemical vapor deposition technique (PECVD). The idea behind this technique is to use gaseous agents of the elements that have to be deposited and to crack these agents in a plasma. Due to the cracking the components are chemically activated and bound to the substrate. In case of depositing n-doped a-SiC:H, silane (SiH_4), methane (CH_4) and phosphine (PH_3) are used. To combine deposition as well as plasma pretreatment of the substrates, an apparatus is used as shown in Figure 3. Details of the process and the technology behind it are summarized in [4].

Since amorphous silicon carbide is a ceramic material, its mechanical properties are significantly different to the metallic substrate. Especially during the dilatation of the stent, enormous mechanical stresses are created

at the interface between coating and substrate, while deformations up to 30% are taking place. Therefore, the coating must have strong adhesion to the substrate. There are four steps in the coating process which have to be optimized in sequence to fit both the required electronic properties as well as strong adhesion: the cleaning process, surface activation, deposition of a thin intermediate film and finally coating the surface with a-SiC:H.

Cleaning process

Since stents are submitted to several processes (tube production, laser cutting, thermal annealing) before being coated, there is a need of specific cleaning processes to remove any residues. First, grease and lubricates from the laser cutting process and handling have to be removed by an ultrasonic treatment with tensidic agents at 50 °C. A mordant containing nitric acid and sulphuric acid cleans the substrates from residues of the electrochemical polishing. Remains of the cleaning agents have to be purged by several rinses with distilled water and alcohol. Just before introducing the substrates into the PECVD reactor, careful removal of dust particles takes place in an alcohol vapour bath.

Surface activation

Remaining residues as well as the native oxide at the surface of 316L-substrates prevent optimal adhesion of the coating. Therefore a plasma etching process is applied right before the deposition processes. The positive effect of this treatment is shown in Figure 4 where

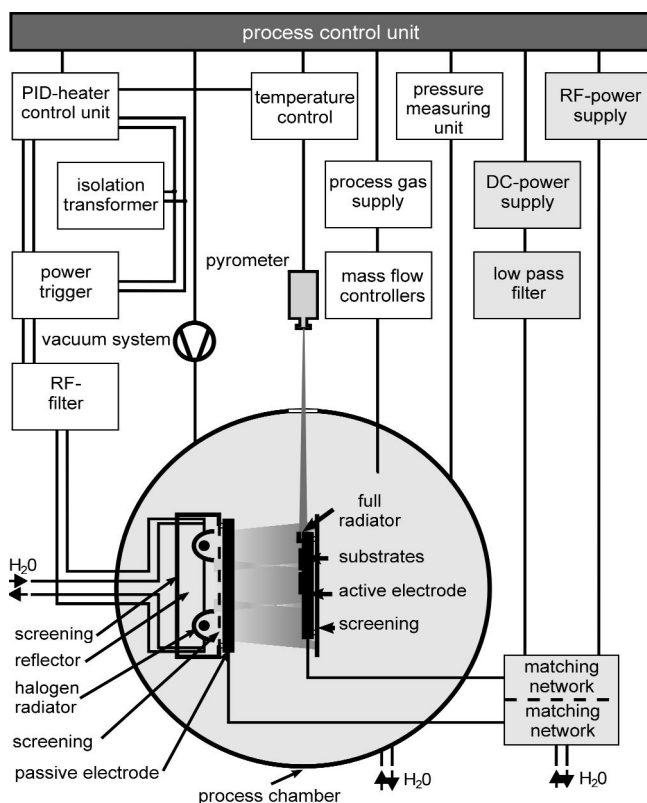


Figure 3. PECVD equipment for deposition of a-SiC:H.

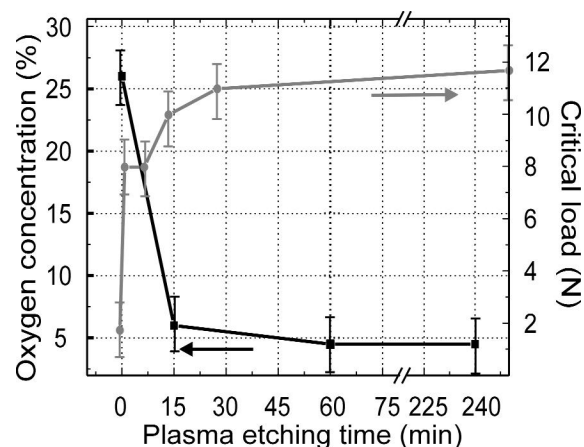


Figure 4. Critical load and oxygen concentration (measured by AES at the interface) as a function of plasma etching time.

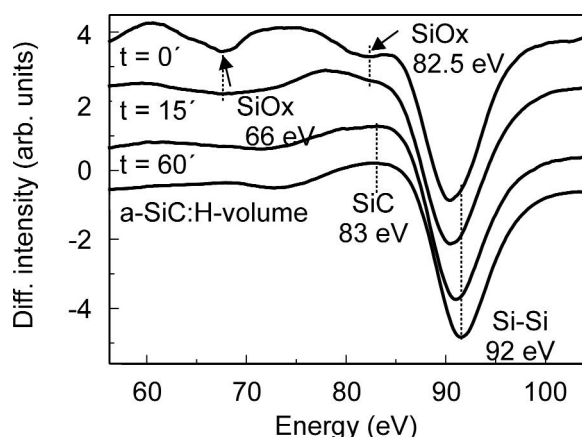


Figure 5. Comparison of the Auger electron spectra of silicon and silicon-oxygen bonds at the interface, taken after different plasma etching times.

the adhesion of a-SiC:H is shown in terms of the critical load as result of a scratch test.

In addition, Auger electron spectroscopy (AES) measurements have been carried out at the interface between coating and substrate. AES is a sensitive method to determine the type of atoms at the surface as well as their chemical bonding to neighbors. Thus, it allows examination on a ppm scale of the atomic structure of the interface between a-SiC:H coating and the stent body.

The AES results show a significant decrease in oxygen concentration at the substrate-coating interface during plasma etching. The longer the etching, the lower the oxygen concentration is. Further investigations with AES showed changes of the chemical bonds formed at the interface. With increasing plasma etching time the density of silicon-oxygen bonds decreases (the peaks at 67 eV and 82.5 eV in Figure 5 are reduced and the peak at 90 eV is shifted towards 92 eV). In conclusion, plasma etching helps to remove adsorbed oxygen (and certainly other pollutions of the interface) that deteriorate the adhesion of the coating.

Intermediate film

Although plasma etching results in acceptable critical loads, the adhesion of the coating can still be further improved by an intermediate coating. The idea of this approach is to relieve the intrinsic mechanical stress of the a-SiC:H coating due to a "soft" layer. The "softness" is achieved by a hydrogen rich pure silicon layer.

a-SiC:H - coating

The specific requirements for the electronic properties of the surface need a careful selection of process parameters. The electronic band gap is mainly influenced by two physical effects: On the one hand the band gap of all semiconductors is a property of the material's chemical composition. On the other hand the band gap of amorphous semiconductors is affected by the density of unsaturated bonds ("dangling bonds"). To achieve a large band gap as well as a low density of states within the gap the dangling bonds have to be saturated by hydrogen atoms (Figure 6).

By using pure silane as process gas, band gaps not greater than 1.6 eV can be achieved. Even if silane is highly diluted in hydrogen the band gap is not significantly increased. However, hydrogen enrichment leads to a band gap density of states of well below $10^{17} \text{ cm}^{-3} \text{ eV}^{-1}$. Only when a second component is added (like carbon or nitrogen) the band gap can be adjusted to the required value. Thus, varying the methane concentration of the process gas leads to the deposition of a-Si_xC_{1-x}:H with a band gap adjustable, via "x," between approximately 1.6 eV and 2.2 eV. An optimum x is achieved when the silane to methane ratio in the plasma is 1:2.

Besides the composition of the process gas, temperature is another parameter which affects the electronic properties of a-SiC:H. Temperatures above 300 °C

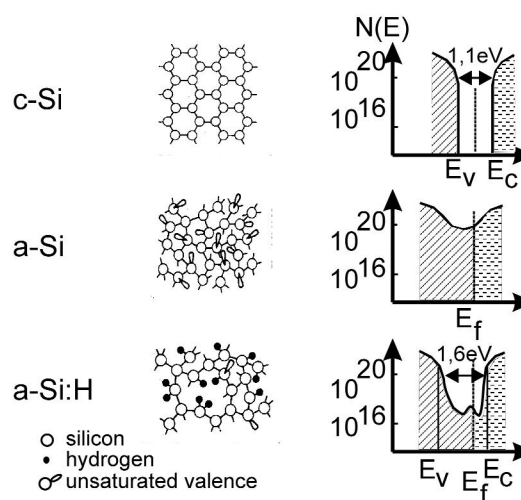


Figure 6. Microstructure and electronic density of states of crystalline silicon (c-Si), amorphous silicon with dangling bonds (a-Si), and amorphous silicon with hydrogen-saturation of dangling bonds (a-Si:H).

result in diffusion processes leading to the loss of hydrogen atoms and therefore to a high density of states within the band gap. Temperatures below 200 °C lead to poor corrosion behavior and surface structure. Thus, the process temperature should be approximately 250 °C.

The conductivity of intrinsic (i.e., not doped) a-SiC:H is of the order of 10^{-7} S/cm or even less. Adding 1% of phosphine to the process gas leads to an acceptable increase in conductivity to 10^{-5} S/cm. In conclusion, PECVD deposited amorphous silicon carbide meets the electronic requirements for good hemocompatibility.

Evaluation of the a-SiC:H-coating

The above described optimization of the coating process led to a further enhancement of the coatings adhesion compared to earlier applications of a-SiC:H, like the Tensum® (BIOTRONIK, Germany) coronary stent [6,7]. It has to be emphasized, that an enlarged coverage of the coating is of special interest whenever substrates are used which contain toxic elements like chromium or nickel (in contrast to coronary stents like the Tensum® with a stent body out of tantalum). a-SiC:H coated Tenax® (BIOTRONIK, Germany) coronary stents were used to examine the coatings mechanical performance. After dilatation the surface was inspected by means of optical microscopy and scanning electron microscopy (SEM). Results are shown in Figures 7 and 8. Images were taken at me-



Figure 7. SEM micrograph of a dilated S-shaped region with high mechanical stress (magnification: 350).

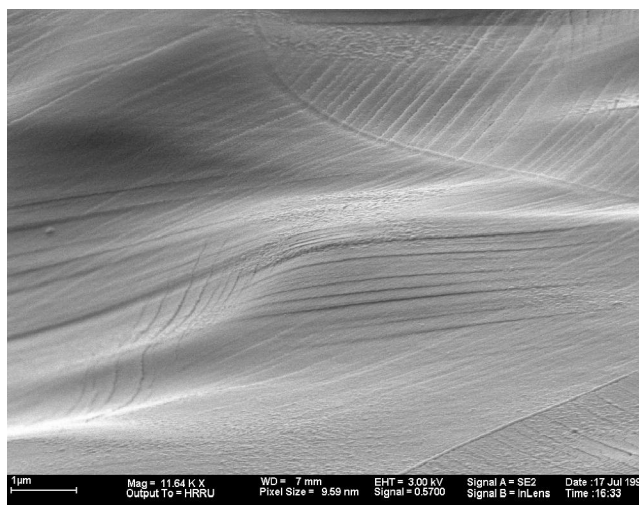
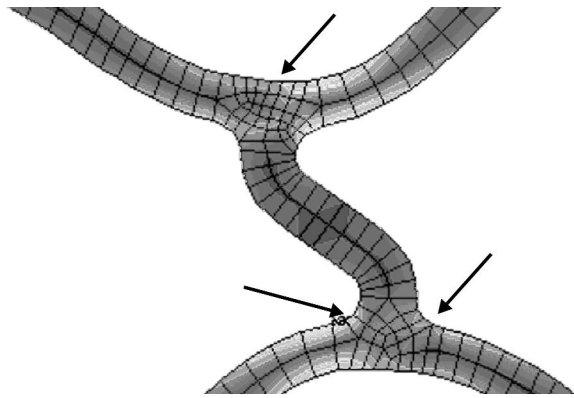


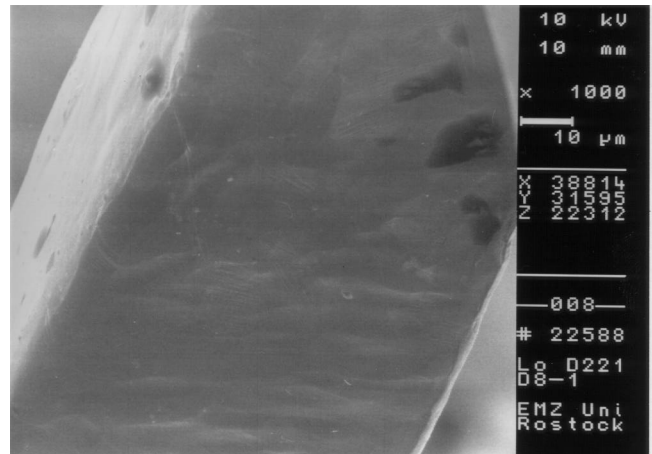
Figure 8. SEM micrograph of a highly stressed a-SiC:H coating (magnification: 12000). No defects can be found.

chanically highly stressed regions of the stent (dilated to 4 mm). There are no defects of the coating besides micro cracks much smaller than 1 μ m. These cracks are due to the limited tensile strength of the ceramic like a-SiC:H-coating. The fine lines in Figure 8 are due to the gliding planes of the substrate material that become visible during plastic deformation. In conclusion, these results show that the adhesion of the coating is excellent, although some cracks cannot be avoided. As a further confirmation of these results at the "Institute for Implant Technology and Biomaterials (IIB)" (Warnemünde, Germany) further investigations were carried out. Again the surface of the Tenax® stents was inspected after dilatation by means of scanning electron microscopy (SEM; ZEISS DSM-960A). To avoid image distortions a reduced acceleration power of 10 kV was applied and no sputtered gold coating or conductive glue was added. The stents were dilated by a Meator SFX 4.5 (BIOTRONIK, Germany) balloon catheter using an ACS pump after manual crimping. The maximum pressure of 8 bar was reached within 30 seconds. The nominal diameter of the balloon at this pressure is 4.5 mm. Results are shown in Figure 9.

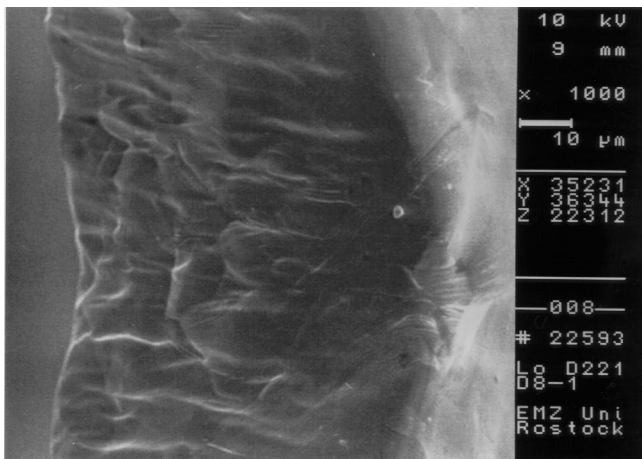
The images of the highly stressed a-SiC:H-coating show the occasional occurrence of small microcracks at the surface. These are mostly situated at the S-shaped links between two elements of the stents structure (Figure 7). Mechanically these cracks are inevitable whenever high tension is applied to a hybrid



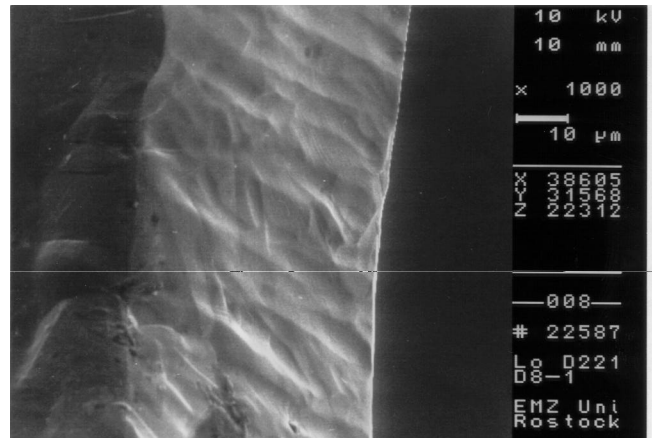
(a) Maximal stressed regions of the TENAX stent.



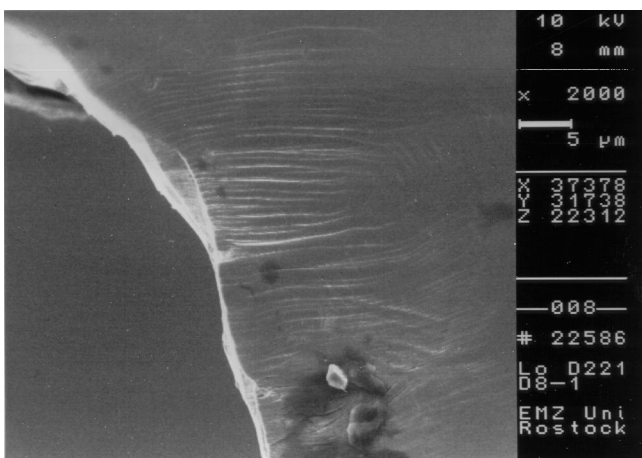
(b) Magnification 1000. Homogeneous surface of the coating in a region of maximum mechanical stress.



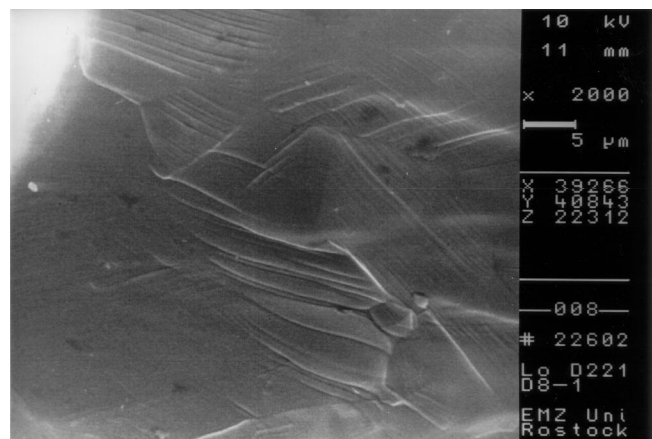
(c) Magnification 1000. Folds due to high mechanical pressure without any detachments of the coating.



(d) Magnification 1000. The edge shows a wavy structure orthogonal to the direction of lasercutting.



(e) Magnification 2000. Microcracks due to the high tension without detachment of the coating.



(f) Magnification 2000. Small microcracks and microfolds on the outer side of the stent.

Figure 9. SEM micrographs of a-SiC:H coated TENAX stent after maximum dilatation.

system consisting of a material with high elasticity, like the annealed stainless steel, and a brittle material, like the ceramic a-SiC:H. The observed improvements of the coatings adhesion are founded in the optimization of the coating process as well as in the reduction of the coatings thickness. As a consequence no detached particles were observed. Furthermore the SEM pictures show an improvement in the morphology of the a-SiC:H coating. In comparison to the Tensum® stent [7], the surface of the Tenax® stent is rather smooth with minimal roughness and without burs at the edges. Due to the optimized laser cutting and electrochemical polishing processes the risk of thrombogenesis and arterial trauma is further reduced.

Crystalline silicon carbide is well known as a chemically inert material that is suitable for worst chemical environments even under high temperatures. The same is true for the amorphous modification although the thermal stability is limited to 250 °C. Corrosion resistance under normal biological conditions (neutral pH, body temperature) is excellent. The dissolution rate is well below 30 nm per year [4].

However, the most important benefit of the coating with regard to corrosion is that it acts as a diffusion barrier. Ions from the underlying substrate (especially chromium or nickel ions) may induce toxic or allergic reactions. In an uncoated design the slow dissolution of 316L leads to a small chromium and nickel release. Thus, uncoated stents may cause cell reactions or reactions of the immune system. However, when coated the ions must diffuse through the coating before they can get into the patient. Due to the internal structure of amorphous silicon carbide this diffusion is so slow that the ion release is negligible.

Conclusion

During the last years coronary stenting became a well established therapy of coronary artery disease.

However, in up to 30% of all stent implantations the process of restenosis leads to a re-narrowing of the vessel within several months. Since optimization of the stent design with regard to mechanical properties only resulted in limited success in reduction of the restenosis rate, a hybrid concept for stent design is proposed: On the one hand the mechanical requirements for an optimized geometrical design are met by using 316L stainless steel as bulk material. On the other hand unwanted interactions of the implant's metal surface with surrounding tissue and blood diminishing biocompatibility and inducing the process of restenosis are reduced by a suitable coating working as a "magic hat". This article presented the deposition technique as well as thin-film-properties of a semiconducting a-SiC:H coating.

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