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# Use of coronary stents - material and biophysical conditions

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**Materials**

## ABSTRACT

**Purpose:** The paper discusses application issues of using the metallic implants for treatment of the cardiovascular diseases. The analysis of the biophysical conditions of the heart – coronary vessels system has been used to distinguish the tissue environment properties which should be compatible with properties of the metal biomaterial and stent's surface. On this basis the author presented results of experiments concerning the usefulness of the passive-carbon layer for surface treatment of vascular stents made of stainless steel.
**Design/methodology/approach:** In order to determine the usefulness of the layer for implants in cardiology the following tests were carried out on the layer: structure, thickness, corrosion resistance, electrical properties and biocompatibility in experimental animals. The structure and thickness of the layer were tested in high resolution transmission electron microscope. Corrosion resistance was carried out by recording anodic polarization curves. Methodology of measurements took into consideration both implantation conditions and application of vascular stents. In tests concerning electrical properties of the layer, current-potential as well as capacity-potential characteristics were determined.
**Findings:** The passive-carbon layer of nanocrystlline structure and high smoothness created on coronary stents' surface fully ensures pitting corrosion resistance in both implantation and application conditions.
**Research limitations/implications:** Deposition of the dielectric carbon layer on coronary stents' made of stainless steel is effective method of reducing reactivity of their surface in blood environment and blood clotting in consequence.
**Originality/value:** The need to determine the correct quality and properties of coronary stents was indicated. The properties refer to stents' design, physio-chemical properties of the metallic biomaterial and its surface.
**Keywords:** Biomaterials; Cr-Ni-Mo steel; Corrosion resistance; Electrical properties; Coronary stents

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## 1. Introduction

Employment of the intravascular implants called stents has become one of the most important achievements of the nineties of the last century in the area of surgical cardiology in the ischaemic heart disease treatment. These implants feature a sort of a metal, small sized, springy scaffolding with the spatial cylindrical design grafted into the critically stenosed coronary vessel to support and simultaneously dilate its active section. The Percutaneous Transluminal Coronary Angioplasty (PTCA) was one of the main coronary heart disease treatment methods used to dilate the

vascular lumen in the period before the stents were introduced, apart from the pharmacological therapy and Coronary Artery Bypass Graft (CABG). The idea of such operation was presented first by Dotter and Judkins in 1964. This method was effective mainly for peripheral arteries. Potsmann modified this operation using the catheter ending with delivery baloon for the first time. To dilate the coronary arteries this operation was improved and introduced for the first time by Gruentzig in 1977 at the University in Zurich [1-3].

In spite of many advantages resulting from introducing the PTCA operation in the ischaemic heart disease treatment it has also some limitations. They include the risk of restenosis (about 30-50% patients) and of the rapid occlusion of the coronary artery (about 7% patients) [1,4-6]. Introduction of the coronary stents into the clinical practice has been the effect of many years of attempts to overcome these problems. A significant interest in this treatment method has followed the simultaneous publication of two, classic as of today, scientific contributions resulting from the Belgian-Dutch cooperation: BENESTENT (Belgium Netherlands Stent) and STRESS (Stent Restenosis Study) [7]. The authors of these works proved that grafting a stent into the proper location of the coronary system reduces significantly the angiographic restenosis frequency (by about 50%) with patients at risk of the new lesions.

It follows from studies of most works pertaining to use of the coronary stents that their effectiveness is decided mostly by the physical and chemical properties of the implants surfaces. Therefore, the current research is focused mostly on development of a method for deposition of coatings on the metal stents surfaces, which reduce significantly the blood clotting process and ensure their good biotolerance in the cardiovascular system tissues environment. Numerous publications in the world literature confirm these activities. However, they present most often the partial research results only (mostly biological ones in the in vitro and in vivo conditions) which do not make full assessment possible of the fabricated coatings usefulness, e.g., their corrosion resistance or adhesion to the stent surface. Moreover, differentiation of methodologies of the research carried out does not always make it possible to compare results obtained by different authors. The issue of the relevant metal biomaterial selection is also left out in the presented works (chemical composition, microstructure, and mechanical properties) deciding the service properties of the investigated stent. Therefore, fabricating the atrombogeneous coatings on stents surfaces should be preceded by selection of the biomaterial with a structure and physical properties taking into account specific features of stents (their miniaturisation, implantation technique) conditioned by the cardiovascular system (mainly by the biochemical, bioelectronic and biomagnetic factors). The quality criteria for the metal biomaterials presented so far do not specify recommendations for this form of implants - stents.

## 2. Materials conditions of implants used in interventional cardiology

Analysis of stents used in clinical practice makes it possible to specify the following material groups used for their fabrication: Cr-Ni-Mo austenitic steel, alloys of Ni-Ti and platinum, Co-Cr-Ni-W, and tantalum [1,8-10]. The Cr-Ni-Mo austenitic steel grades are used most often for the coronary stents - Table 1 [11]. This group of biomaterials is known and commonly used since many years, mostly for the short-term implants in the injury-orthopaedic-, maxillofacial-, and thoracosurgery.

Coronary stents, albeit made from the Cr-Ni-Mo steel belong to the long-term implants. Therefore, lastly the interest has grown in this metal materials group because of its applications for implants contacting blood. This interest is focused mostly on development of various coatings technologies with the atrombogeneous properties, i.e., counteracting the blood clotting process on their surface. However, a few works only are dedicated to the problem of forming the structure and physical properties of the Cr-Ni-Mo steel. Quality criteria pertaining their use for various implants are included in the relevant legislative acts [1,11-13]. However, the presented recommendations do not take into account the specific problems connected with using this steel for the coronary stents and do not refer to their geometrical features and discussed above conditions of the cardiovascular system. Therefore, there is a need to specify clearly the qualitative criteria for this group of the implant materials.

### 2.1. Structural factors in metal biomaterials

The qualification base for the metal biomaterials is, first of all, determining their chemical composition and structure. Based on the many years long investigation of their biotolerance in the environment of tissues and body fluids, the ranges were determined for the particular chemical elements ensuring the paramagnetic austenitic structure and good pitting corrosion resistance of the steel - Table 1. High requirements connected with service properties of the Cr-Ni-Mo steel grades intended for implants force using smelting methods ensuring their relevant metallurgical purity. However, the non-metallic inclusions remaining after these processes have a significant effect on the service properties of products. This effect depends on the shape, geometrical features, and homogeneity of their distribution. Moreover, during the plastic treatment some of these inclusions are subject to deformation, which is the cause for the mechanical properties anisotrophy.

This issue assumes the particular importance when referred to the coronary stents because of the miniature sizes of this type of implants. This forces the need to use steel with the good metallurgical quality characteristic of the minimum amount of the non-metallic inclusions with big dispersion and fine austenite grains. Such structure ensures also a good corrosion resistance, especially in the environment of tissues and body fluids. The methods (mostly comparative ones) recommended in the standard [11] and criteria for the structure quality assessment are useless for determining the quality of steel for coronary stents. Therefore, it seems necessary to specify the exact quantitative relations using the automatic image analysis methods for this type of medical products connected with high risk for the user. Applications of such techniques make measurement possible of the commonly used stereological parameters of a single particle, e.g., its volume, transverse section area, maximum and minimum chord length.

Table 1.
Chemical composition of the Cr-Ni-Mo steel used on implants

| Standard | Steel grade | Concentration of elements, % | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | C | Si | Mn | P | S | $N_2$ | Cr | Mo | Ni | Cu | Fe |
| ISO 5832-1 | D | max 0.030 | max 1.0 | max 2.0 | max 0.025 | max 0.01 | max 0.10 | 17.0~19.0 | 2.25~3.50 | 13.0~15.0 | max 0.50 | rest |
| | E | max 0.030 | max 1.0 | max 2.0 | max 0.025 | max 0.01 | 0.10~0.20 | 17.0~19.0 | 2.25~3.50 | 14.0~16.0 | max 0.50 | rest |
| ASTM F-139-96 | AISI 316L | max 0.030 | max 0.75 | max 2.0 | max 0.025 | max 0.01 | max 0.10 | 17.0~19.0 | 2.0~3.0 | 12.0~4.0 | max 0.50 | rest |

Moreover, features like number of particles in a unit volume (area) and range of their sizes are connected with the notion of distribution of dimensions of the non-metallic inclusions. The effect of such analysis may be, therefore, elimination of the template scale used so far according to standards, or assigning them the particular geometrical parameters of the non-metallic inclusions.

The issue of Cr-Ni-Mo steel quality and its application in coronary stents using quantitative metallography has been studied by the author [1]. The studies were based on a Cr-Ni-Mo steel in a bar form with a diameter d = 0.12 mm used for the production of a coronary coil stent. To assess the level of steel pollution with non-metallic inclusions, the author has proposed the following parameters: the area of non-metallic inclusions (S), the relative area of their cross-sections ($S_{rel}$) and the maximum chord length ($L_{max}$). Such stereological parameters of inclusions are in close correlation with resistance to pitting corrosion in biomaterials. The mean values of the analysed parameters were S = 1.51 $\mu m^2$, $S_{rel.}$ = 0.04 % and $L_{max}$ = 1.73 μm. The author has shown that steel having this type of stereological features of non-metallic inclusions may be used in the formation of the discussed stent, which may be freely expanded and used safely.

The austenite grain size is an important issue pertaining to the metal biomaterials for stents. It is the main structural parameter affecting strongly the mechanical properties of metal materials. Hall-Petch equation is the most known relationship determining the effect of the average grain diameter on the lower yield point $\sigma_y$ [1].The grain size affects significantly also the fatigue strength $\sigma_f$ of the constructional materials. Results of many investigations confirm that the fatigue strength grows as the grain size gets smaller. Therefore, the analysis above - taking into account the service conditions of the coronary stents (cyclic loading) and their miniaturisation - indicates to the need to use biomaterials with the fine-grained structure. According to requirements posed by the standard it is assumed for the Cr-Ni-Mo steel that the grain size should not exceed the one corresponding to template G = 4 [11]. Assuming this value as the grain size criterion the average grain size is $d_m$ = 0.088 mm. Analysis of the geometrical features of stents manufactured nowadays shows that stent thickness is in the g = 0.06~0.14 mm range. This means that a single grain is contained on the transverse section of the stent wall with the thickness of g = 0.09 mm. In this situation the undoubtedly low ductility of the implant material renders it useless as early as at its implanting stage. This may also be the cause of the unsatisfactory stent life, which is of the utmost importance when the long-term implants are concerned. Therefore, one can state that dispersion of the metal biomaterials structure features the key issue for this form of implants and is not fully determined by the standard recommendations used nowadays.

## 2.2. Selection of mechanical properties

Selection of the mechanical properties of the metal biomaterial is an important problem in the process of forming the service properties of implants. This problem has been discussed rather widely in literature referring to implants used in the orthopaedic- and maxillofacial surgery, as well as in alloplastics of joints [14-18].

The optimisation process of the mechanical properties for implants used in the interventional cardiology should be carried out taking into account loads resulting from the implanting technique, which do not occur in their service. This is connected with the necessity to deform the stent permanently to the required diameter to place it in the blood vessel whose patency is being restored. Results of the model testing carried out using the finite elements method are presented in the literature, as there is no possibility to determine the mutual interactions of stents and blood vessels in the investigations in vivo. Having the 3-D model of the stent implanted into the blood vessel and its mechanical properties one can evaluate interactions between these objects. The numerical calculations carried out refer most often to the stress and strain distributions of the particular elements of the assumed system and the blood flow [19-22]. This makes optimisation possible of the implant's geometrical features and of its biomechanical properties. The degree of strain hardening of the proposed metal biomaterial should be selected so that the determined values of the reduced stress in the stent elements after it expands to the required diameter would exceed its yield point $Rp_{0.2}$. The numerical simulations carried out make it also possible to determine many parameters essential for evaluation of the

clinical usefulness of the particular stent forms, e.g., expanded metal surface area and shortening of the stent after its expansion.

In recent studies, the author has dealt with the issue of selection of mechanical properties of metal biomaterials for vascular stents with the use of the finite element method. For the assumed implant form, i.e. coil stent, the author has conducted a numerical analysis of the stent-coronary vessel system [1,9]. The assumed border conditions of the conducted analysis reflected the phenomena taking place in the real object during the extension and unloading phase. The calculations have particularly allowed determination of equivalent stress distribution in coronary stent elements for the two analysed bar diameters ($d_1$ = 0.12 mm and $d_2$ = 0.16 mm) - Fig. 1. This way, the areas of highest stent tension have been determined. The obtained stress values were higher than the assumed border value of Cr-Ni-Mo steel plasticity ($R_{p0.2}$ = 190 MPa). This ensures permanent deformation of the analysed stent form during implantation, which is necessary for correct implant embedding in vascular walls. The results of the numerical analysis form the basis for selection of optimal geometric features of the analysed stent form and proper mechanical properties of the metal biomaterial.

Another important issue is the interaction between stent and coronary vessel resulting from load variability induced by cyclic changes in blood pressure. Therefore, the stent-coronary vessel interaction has also been determined by the author [1,9]. The author analysed the quantitative relations of radial displacement of vascular wall elements resulting from stent expansion to internal diameter d = 3 mm and flow of blood with varied pressure values ($p_1$ = 10 kPa, $p_2$ = 16 kPa) due to physiological factors - Table 2. The numerical model of a coronary vessel reflects real geometrical features and mechanical properties of vessels with regard to the influence of pathological changes in the vessel [1]. The numerical analysis results may be a foundation for studies of phenomena taking place on the stent-coronary vessel border.

Table 2.
Radial displacement of coronary vessel wall elements for varied blood pressure values [1,9]

| Diameter of stent bar d, mm | Maximum radial displacement $u_{rmax}$, μm | |
|---|---|---|
| | $p_1$ = 10 kPa | $p_2$ = 16 kPa |
| 0.12 | 51.61 | 53.14 |
| 0.16 | 98.96 | 99.98 |

The issue of selection of metal biomaterial mechanical properties for the coronary stent has also been studied by Walke [9,23,24]. He studied the slotted tube form of stent for two types of biomaterial - Cr-Ni-Mo steel and Co-Cr-W-Ni alloy. For the assumed implant geometrical features, he has determined the state of displacement, deformation and stress for different expansion pressure values used in clinical practice - Fig. 2. This method of analysis also allowed determining the biomechanical profile of the studied vascular implant showing the correlation of stent external diameter $d_{zs}$ as a function of expanding pressure p - $d_s$ = f (p). This type of implant reveals a high level of usefulness in clinical practice. For the assumed implant form, it allows selection of an appropriate expanding pressure value p, assuring the proper course of the angioplasty procedure.

a)

b)

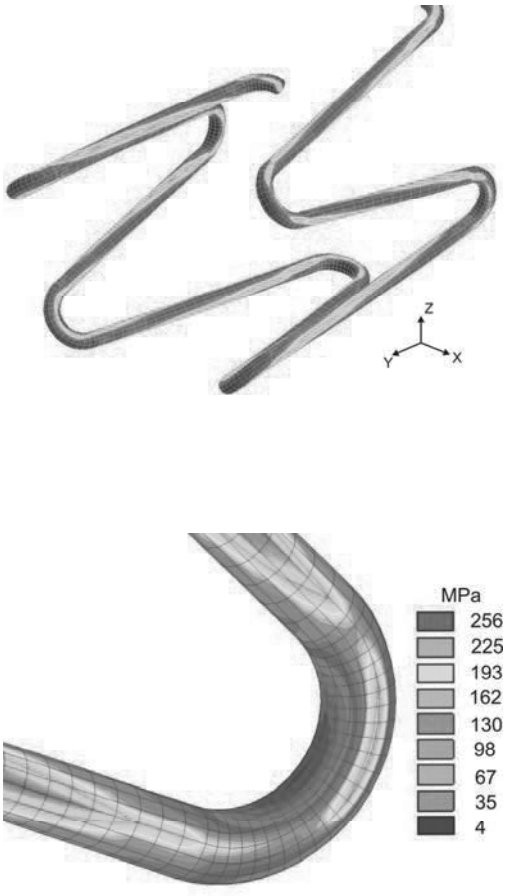


Fig. 1. Stress distribution in the coronary bar stent of 0.12 mm diameter after expansion to 3 mm [1,9]: a) in a single coil, b) in a single segment

The usefulness and correctness of the assumptions and analyses employing computer mechanics should be verified in experimental conditions. In addition, in vitro studies allow verification of mechanical properties of metal biomaterial chosen for a particular implant form. Walke [9,24,25] conducted such tests for the vascular stent form also analysed with using FEM. In order to perform experimental studies, he prepared a research workstation suitable for performing a controlled implant expansion. The experiment involved measurement of stent outer diameter $d_{zs}$ as a function of an expanding pressure p. Implant expansion was performed with the instrument set used in clinical procedures of coronary angioplasty. The obtained results confirmed the correctness of the assumptions he had made for the numerical analysis. This is indicated by a large correlation between displacement values obtained in the computer analysis and experimental studies.

a)

b)

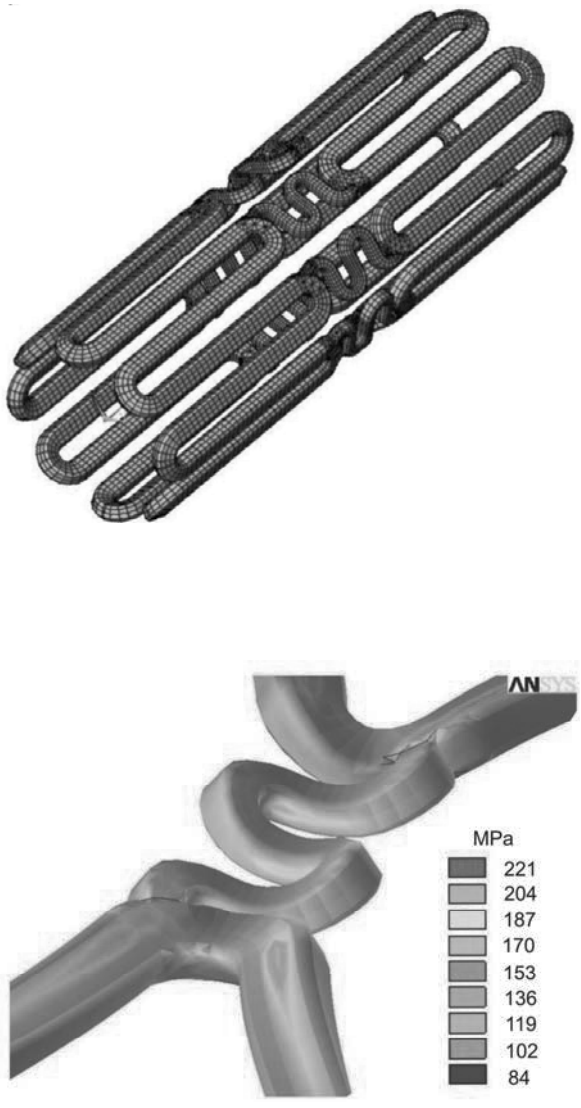


Fig. 2. Results of numerical analysis of a Cr-Ni-Mo steel coronary stent: a) geometrical model of implant, b) stress distribution in expanded coronary stent elements (p = 3 atm)

## 3. Biophysical conditions of the heart - coronary vessel system

Biophysical conditions of the cardiovascular system result from the possibility of generating the action potentials by the cardiac muscle cells and from the specific features of the coronary vessels system. Mechanisms of generating the action potentials are based on ion- and electric charges transport through its cell membranes. The effect is the flow of the ion electric current (action current) with the varying intensity. Therefore, these currents are responsible for generating the alternating electrical field in the living organism. So, the beating heart may be considered to be an electric dipole changing in time. This macroscopic dipole is a resultant of many microscopic dipoles, as the activated cardiac muscle fibres are assumed to be. The activated part of the muscle fibre is the negative-, and the inactive part - the positive pole of such dipole. The resultant of these dipoles at a given moment features the main electrical vector of the heart [1].

Electrical excitations in the cardiac muscle cells are also the main source of the organism's magnetic field. The magnetic field, in the simplified mathematical description, is considered to be generated by the current dipole or a set of dipoles placed in the isotropic conducting material with the constant conductance. The density values of the ion currents passing during the heart work are small. Therefore, the real values of the generated magnetic field induction measured outside of the organism are also small and are several picoteslas only [1].

Changes of the electrical- and magnetic fields are orthogonal to each other. They are considered separately at low frequencies of the emitted electromagnetic waves. Emission of the electromagnetic waves with low frequency from the ELF (Extremely Low Frequency) range takes place during heart action. Therefore, to evaluate its action, separate analysis methods for its electrical- (electrocardiography - ECG) and magnetic (magnetocardiography - MCG) fields changes were proposed.

The need results from the analysis carried out to adjust the physical properties (electrical and magnetic) of the metal implants to the specific features of the cardiovascular system. Interference with such system by grafting a metal implant should not affect processes connected with generation and propagation of the action potentials in the tissues. Moreover, appearance of an implant with the ferromagnetic properties would not leave the electromagnetical processes unaffected. The effect of such implant might turn out to be even more harmful if the effect of the external electromagnetic field, to which its user may be subjected, is taken into account.

The biophysical properties of the coronary vessels affect strongly the coronary blood flow process. The fundamental role in ensuring the relevant properties of the vessels is played by their internal layer - endothelium. That is just the endothelium cells that produce many substances (mostly NO) affecting, among others, the active tension state of the vascular muscles and their atrombogeneous properties of their internal walls. Therefore, the development of the disease process and in consequence the faulty oxygen delivery to the cardiac muscle cells are eventually dependant on the proper flow of processes of synthesis and releasing the biologically important elements, as well as on phenomena on the endothelium surface - flowing blood interface. Therefore, the grafted intravascular implant should be characteristic of such physical and chemical properties of its surface that it would not initiate development of the disadvantageous reactions disturbing additionally functioning of the endothelium (apart from the originated already disease process).

Haemostasia induced by presence of the metal implant is one of the negative phenomena occurring in the cardiovascular system environment [1]. The process of blood interaction with the

implant materials is still not fully understood. It is generally assumed that due to blood contact with the "artificial" implant surface adsorption of proteins (mostly of fibrinogen) occurs first. In case when the adsorbed fibrinogen undergoes the denaturisation process, the next platelet and plasma blood clotting factors get activated in a cascading way. This in consequence leads to development of a clot.

One of the mechanisms explaining the nature of the clotting process initiation is based on the energy band diagram [26,27]. It was found out based on investigations of Gutmann and his associates that fibrinogen has the electron structure characteristic of the semiconductor materials. The width of its forbidden band is 1.8 eV. Its valence- and conduction bands are at 0.9 eV below or above Fermi level respectively. Therefore, the protein transformation process from its inactive form (fibrinogen) into the active one (fibrin) may be connected with the electrochemical reaction occurring between the protein and the material surface being in contact with blood. Electrons from the fibrinogen valence band transferred, e.g., to implant material cause disintegration of protein. The consequence is transformation of the protein into a monomer and fibrin peptide. Next the process of their networking occurs leading to the irreversible form of a thrombus. Therefore, it seems purposeful to carry out modification of the physical properties of implant materials by their surface treatment. Fabrication of a layer on implant surface with the high corrosion resistance and semiconductor or dielectric properties may effectively impede transferring electrons from the fibrinogen valence band. This may, in consequence, feature the effective method to limit the blood clotting process due to contact with the grafted implant's surface.

## 4. The issue of vascular stent biotolerance

Metal stent implantation into the vascular system initiates a complex reaction between blood components and the surface of the stent [28]. Endotelialisation of the implanted stents (covering the stent with endothelium) is a slow process lasting 2-3 months. The greatest danger during this period, determining the implantation success, is the process of blood clotting on the implant surface. Its effect is a decrease in active cross-section of the blood vessel just at the beginning of implant adaptation in the organism. A traumatic effect of PTCA, which restricts the long-term effect of coronary interventions, is restenosis [1]. The process involves reoccurrence of stenosis in the affected vessel. This results from numerous cellular and molecular mechanisms occurring in the lumen and wall of the vessel. This effect appears in about 30% of cases or even more often in certain types of complex atherosclerotic changes. Angiographic restenosis is defined as a 50% or greater reduction of the previously treated vessel.

### 4.1. Modification of physicochemical properties of vascular stents

In recent years, a growing interest in polymer application in implants used for cardio logical procedures can be observed. It's not a new issue to use polymers for implants in the circulatory system. Their benefits include good biotolerance in blood environment, and especially atrombogenity related to wetability, value and type of surface electrostatic charge and the value of surface conduction of these biomaterials. They are used for artificial blood vessels, heart valves, construction elements of an artificial heart and implanted pumps supporting the heart, and as isolation for pacemaker wires [1,28].

There are a large number of polymer types used for protective layers on the surface of coronary metal stents and it is constantly increasing. A large group comprises synthetic non-biodegradable polymers. Their role is to create a neutral barrier on the stent surface between the metal stent and tissues of the circulatory system. These layers are usually formed with polyurethane, polysiloxane, ethylene polyteraftalan or phosphorylcholine [5,6,10]. Their efficiency was evaluated mainly on the basis of in vivo tests (in swine coronary vessels). Studies conducted by van der Giessen, de Scheerder and Fontain revealed their role in inhibiting the process of early blood clotting on implant surfaces. However, this solution was not successful in restricting the process of restenosis in comparison with stents without the additional layer.

Results of these studies have aroused interest in another group of polymers. These are biodegradable polymers (e.g. lactic polyacids, polyglycolide) [29,30]. The best results were obtained with dilactide (L-lactide) used for the stent surface. Studies conducted by Lincoff employing Wiktor stents in swine coronary vessels demonstrated this type of layer is efficient both in restricting blood clotting and restenosis [30].

Holmes and Baker were among a few researchers who introduced a natural polymer as coating for stents, which does not initiate the inflammatory process [31,32]. They evaluated the usefulness of stents made of tantalum and Cr-Ni-Mo steel (Palmaz-Schatz) coated with a polyurethane layer, into which fibrin was introduced. Results of their in vitro and in vivo studies (swine coronary vessels, canine iliac vessels) shows that the layer restricts the process of platelet adhesion and prevents blood clotting. Faster stent endothelialisation was also observed.

Another method of stent modification is heparinization of the outer layer [33-38]. It allows refraining from administering anti-thrombotic drugs to patients during the postoperative period. Heparin contains several anion groups (e.g. carboxylic, sulphane, sulphamide), which negatively charge the outer surface of vessels. This phenomenon was first used by Bonan [33]. He used the zigzag type stents with a deposited heparin coating in his investigations. The results of the tests did not reveal a positive effect of these coatings on limiting the clotting process. Similar results were obtained by Zidar using the tantalum stents coated with a heparin layer [34]. However, Hardhammar, Serruys, Chronos and de Scheerder, in their tests carried mostly under in vivo conditions, have observed an efficiency of such coating in limiting activation of blood platelets and originating of clots [35-38].

Investigations are also ongoing on using the amorphous silicon carbide (a-SiC:H) as a coating for the coronary stents. They are connected with the effort to limit the fibrinogen into fibrin conversion occurring on the implant's surface. This type of coating material for stents with dielectric properties effectively reduces the reactivity of its surface in the blood environment. The

investigations carried out indicate a high atrombogenity of stents with a SiC layer. Moreover, the implants show good elasticity, which is an important quality in this type of implantation. The layer thickness was within the range of 0.07 – 0.09 μm. This type of layer is mainly introduced in steel stents. Ongoing clinical trials confirm the efficiency of stents coated with silicon carbide in the treatment of vascular stenosis [1,39].

## 4.2. Drug eluting stents

Significant progress in the treatment of early and late thrombosis and restenosis of coronary vessels was achieved thanks to the use of drug eluting stents. In this group of drugs, rapamycin (sirolimus) and paclitaxel appeared to be most effective in preventing restenosis. Both these drugs inhibit cell proliferation, although by means of different mechanisms [40,41]. Positive results obtained for stents coated with sirolimus (FIM, RAVEL and SIROLIMUS studies), paclitaxel (TAXUS I-VI study) and rapamycin analogues (ABT578 - ENDEAVOR I-II study, everolimus - SPIRIT I, II study) enabled them to be approved for clinical usage.

Results of clinical studies comparing stents with sirolimus and paclitaxel coatings (REALITY study) did not reveal significant differences in treatment efficacy. The only conclusion was that the sirolimus stent has a lower value of late lumen loss. SPIRIT II study comparing stents with paclitaxel and everolimus showed a higher value of late lumen loss in implantation of the stent with paclitaxel.

The high efficiency of DES stents resulted in undertakings by numerous manufacturers. The most extensive clinical experiments related to the number of implantations are related to four of them: implants releasing rapamycin (Cypher stents), paclitaxel (TAXUS stents) and releasing rapamycin analogues (ENDEAVOR and XIENCE stents).

The next step towards higher efficiency in the treatment of ischemic heart disease was the introduction of the second generation XIENCE V stent by Abbot Vascular. This implant is produced from a Co-Cr alloy. The stent is coated with a non-biodegradable polymer soaked with everolimus. This coating is only 5.3 μm thick. In contrast, the thickness of the polymer layer on the Texus stent surface is about 15.6 μm, and on the Cypher stent about 7.2 μm. Such stent structure lowers the risk of restenosis. The stent efficiency was confirmed in the clinical study SPIRIT FIRST [42,43].

After the initial period of delight with DES stents, there came the time for deeper reflection. In the BASKET-LATE study, announced in 2006, researchers pointed to a very high proportion of subjects with the episode of late thrombosis in DES stent in relation to patients with stents without a polymer coating (BMS stents) [44]. The results of the Swedish register of coronary angioplasty interventions published in 2007, including almost 19 000 patients, revealed an increase in the risk of death after six months of observation of subjects with DES stents [45].

During the Congress of Cardiology held in Barcelona in September 2006, researchers presented studies revealing the occurrence of thrombosis in different periods following implantation. Moreover, there was a problem with prolonged endothelial healing, incomplete endothelialisation and the presence of fibrin observed 30 days after the intervention. This is of great significance for later thrombosis. The day of presentation of these results was called the "black Tuesday" of interventional cardiology.

Cumulative analysis of clinical studies published in March 2007 did not reveal statistically significant differences in the risk of thrombosis episodes between groups with DES and BMS stents. The American Food and Drug Administration Agency also confirmed the lack of convincing data that would fully explain mechanisms, risk and prevalence of thrombosis in drug eluting stents. It was also claimed that it is impossible to avoid adverse reactions and that further long-term studies are necessary [46].

## 4.3. Coronary stents with passive-carbon coating

Following analysis of the use of metal biomaterials for coronary stents and biophysical conditioning of the heart-coronary vessels system, the author of this work has developed his own methodology of forming and monitoring their functional properties. This methodology is based on the statement that the required stent properties may be achieved only through appropriate formation of their structure, mechanical properties of implant biomaterial and physicochemical properties of their surfaces with regard to specifics of low-invasive implantation technique and biophysical conditionings of the heart-coronary vessels system. On the basis of the author's own research and positive experience with implants of Cr-Ni-Mo steel and Co-Cr-Mo with a passive-carbon coating, he has proposed such a coating also on the surface of the coil type stent - Fig. 1 [47-50].

Formation of the passive-carbon coating involves several phases. These include the process of electrolytic polishing, chemical passivation and application of the carbon layer (rf PACVD) [1]. To assess the use of this kind of layer for processing of stent layers, in vivo studies on its structure, corrosion resistance, electric properties and biotolerance were carried out.

The thickness of the passive-carbon coating, measured by high-resolution transmission electron microscopy, was 40-60 nm. The structure of the layer revealed varying levels of cross-section crystallinity - Fig. 3. The layer was in fact fully crystalline on the area of the metallic stent base. 20-40 nm nanocrystals formed clusters separated by small areas of amorphous structure [1].

The analysis of phase composition with Raman spectroscopy revealed, with regard to carbon atoms, the presence of bindings typical of diamond (type $sp^3$) and graphite (type $sp^2$). Studies with using atomic force microscopy revealed that the obtained passive-carbon coating on stent surfaces assures high surface smoothness ($R_a$ = 16.5-20.3 nm) - Fig. 4 [28].

Studies on electric properties of the passive-carbon coating involved determining electricity-voltage and capacity-voltage characteristics [28]. The measurements allowed determination of resistivity ρ and electric permittivity $\varepsilon_r$ of the carbon layer formed on the silicon plate surface. Carbon layer resistivity was ρ = 1-5 x $10^8$ Ωcm, while electric permittivity was $\varepsilon_r$ = 8.2-11.1. The obtained results show that the process of application of a carbon layer revealing dielectric properties on the Cr-Ni-Mo steel stentsρ = 0.7x$10^{-4}$ Ωcm) may be an effective method limiting their surface

reactivity in the blood environment, and in consequence the clotting process.

The usefulness of such a formed surface for processing coronary stents was confirmed under in vitro studies (on corrosion resistance) accounting for implantation and usage conditions [51]. The assessment of corrosion resistance was performed with the potentiodynamic method recording anodic polarization curves. Measurements were taken in Tyrode's physiological solution.

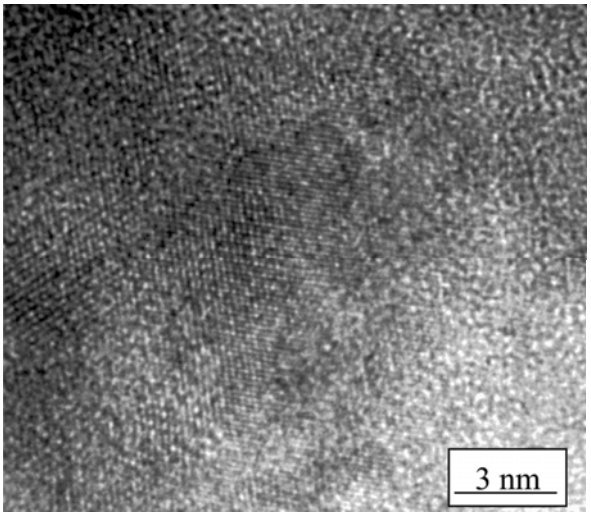


Fig. 3. Nanocrystalline structure of the passive-carbon coating - cross-section [1]

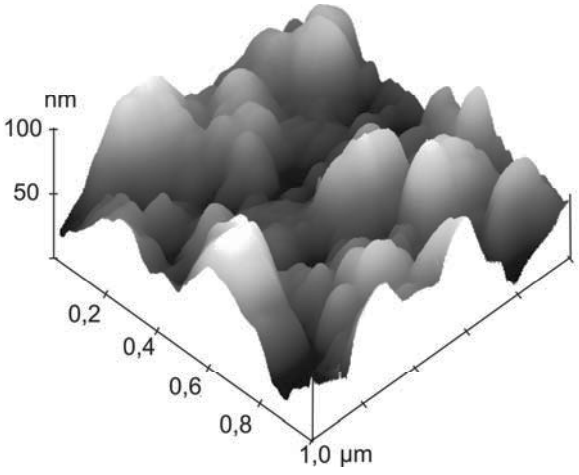


Fig. 4. Surface topography of passive-carbon coating [1]

The studies revealed that formation of the passive-carbon coating on stent surfaces made them resistant to pitting corrosion - Table 3. During this phase, layer susceptibility to deformation in conditions simulating coronary angioplasty was also determined. For this reason, stents were expanded with a kit used in angioplasty to diameter d = 3 mm, using pressure p = 0.8 MPa. The obtained results indicated that the process of implant expansion did not initiate pitting corrosion. This was confirmed by monitoring stent surfaces in a scanning electron microscope. Observation of implant surfaces did not reveal the presence of pits - Fig. 5.

The subsequent phase of studies involved assessment of stent corrosion resistance after fatigue tests. For this reason, a special workstation was designed and prepared in order to perform simulation of stent usage following their implantation into blood vessels - Fig. 6 [51]. Studies conducted on stents, after 3-month fatigue tests, did not reveal significant changes in corrosion resistance - Table 3.

Table 3.
Results of studies on corrosion resistance of vascular stents with passive-carbon coating

| Tested stents | Corrosion potential, $E_{corr}$, mV | Transpassivation potential $E_{tr}$, mV |
|---|---|---|
| Unexpanded stents | 0 – +20 | +1030 – +1080 |
| Expanded stents | -30 – -5 | +980 – +1020 |
| Expanded stents after fatigue tests | -40 – -25 | +950 – +990 |

Results of pre-clinical in vivo tests on tissues of experimental animals were an important factor determining the functional quality of the proposed stent form. The experiments were conducted on rabbits with a weight of about 3.000 g. Stents with the passive-carbon coating were symmetrically implanted into both iliac arteries of rabbits. No peri-implant reactions or histopathological changes in the studied blood vessels were observed during a 5-week control period. This indicates good biotolerance of the suggested coating on the coronary coil type stent of Cr-Ni-Mo steel [1].

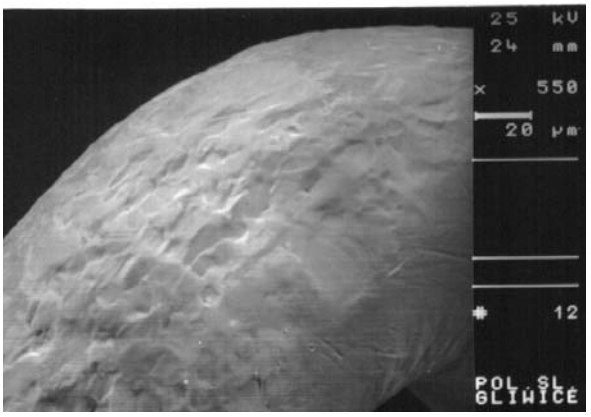


Fig. 5. Surface of the expanded stent with the passive-carbon coating after corrosion tests

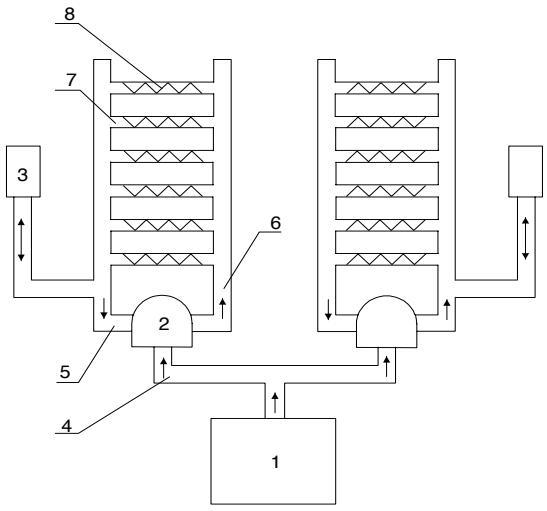


Fig. 6. Block scheme of the stand for fatigue tests of coronary stents [51]: 1- pneumatic programmer, 2 - heart supporting chambers, 3 - flexibility tanks, 4 - tubes supplying air to heart chambers, 5 - inflow tubes with physiologic solution, 6 - outflow tubes with Tyrode's solution, 7 - elastic tubes simulating coronary vessels, 8 - tested stents

## 5. Conclusions

Coronary stents have changed fundamentally during the last dozen years or so the methods and effectiveness of the ischaemic heart disease treatment. However, the clinical practice, indicates certain limitations connected mostly with introducing the metal material into the human blood stream.

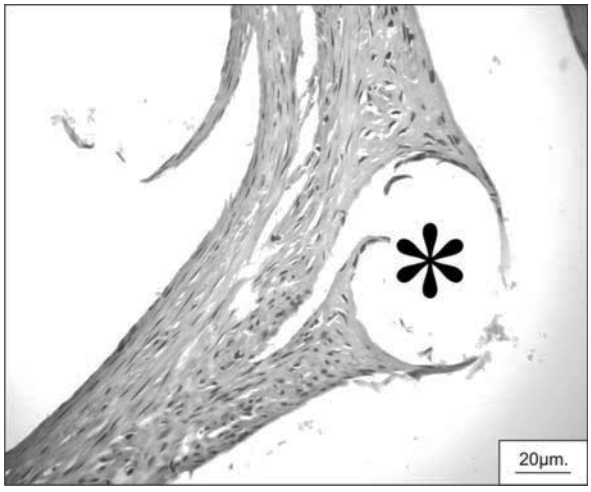


Fig. 6. Microscopic image of the histopathological specimen after the stent removal - insignificant change of the neointima, no inflammatory reaction

Analysis of the literature data carried out makes it possible to state that these issues are mainly connected with blood clotting on stents surfaces and with restenosis. Much less attention is paid to the problem of selection of the form and geometrical features of stents, as well as to forming the structure and mechanical properties of the metal biomaterial. After all these issues are of the deciding significance during the stent implanting operation and its capability to carry the loads. Also miniaturisation of this form of implants enforces the need to use the biomaterial with the fine-grained structure with the strictly limited content of the dispersive non-metallic inclusions.

On the basis of literature data and results of studies conducted by the author it may be stated that further studies are required in order to improve functional properties of vascular stents. They should primarily focus on:

- determination of quantitative features of metal biomaterial structure and their influence on ductility and corrosion resistance of such implants,
- determination of the influence of technological conditions on the structure, corrosion resistance and susceptibility to deformation of layers formed on stent surfaces,
- determination of the influence of surface layers' structure on their physiochemical properties in the blood environment (e.g. hydrophilicity, platelet adhesion, electric properties).

## References

[1] Z. Paszenda, Forming of physicochemical properties of coronary stents made of Cr-Ni-Mo steel applied in interventional cardiology. Printing House of the Silesian University of Technology, Gliwice 2005 (in Polish).
[2] Z. Paszenda, Issues of metal materials used for implants in interventional cardiology, Engineering of Biomaterials 21 (2002) 3-9.
[3] H. Zhao, J. van Humbeeck, Electrochemical polishing of 316L stainless steel slotted tube coronary stents, Journal of Materials Science: Materials in Medicine, 13 (2002) 911-916.
[4] T. Peng, P. Gibula, K. Yao, M. Goosen, Role of polymers in improving the results of stenting in coronary arteries, Biomaterials 17 (1996) 685-694.
[5] J. Lahann, D. Klee, Improvement of hemocompatibility of metallic stents by polymer coating, Journal of Materials Science: Materials in Medicine 10 (1999) 443-448.
[6] I. Verweire, E. Schacht, B. Qiang, K. Wang, Evaluation of fluorinated polymers as coronary stent coating, Journal of Materials Science: Materials in Medicine 11 (2000) 207-212.
[7] P. Serruys, M. Kutryk M, Handbook of coronary stens. Martin Dunitz Ltd. 1998.
[8] A. Colombo, G. Stankovic, J. Moses, Selection of coronary stent. Journal of the American College of Cardiology 6 (2002) 1021-1033.
[9] J. Marciniak, Z. Paszenda, W. Walke, J. Tyrlik-Held, W. Kajzer, Stents in minimally invasive surgery, Printing House of the Silesian University of Technology, Gliwice 2006 (in Polish).
[10] P. Serruys, B. Rensing, Handbook of coronary stents. Martin Dunitz Ltd. 2002.

[11] ISO 5832/1:2007 Implants of surgery - metallic materials - Part 1: Wrought stainless steel.
[12] EN 12006/3:1998 Non-active surgical implants - Part 3: Intravascular devices.
[13] EN ISO 14630:1997 Non-active surgical implants - General requirements.
[14] W. Walke, J. Marciniak, M. Kaczmarek, Biomechanical analysis of tibia - double threaded screw fixation, Archives of Materials Science and Engineering 30 (2008) 41-44.
[15] A. Krauze, J. Marciniak, Numerical method in biomechanical analysisi of intramedullary ostheosynthesis in children, Journal of Achievements in Materials and Manufacturing Engineering 15 (2006) 120-126.
[16] J. Marciniak, M. Kaczmarek, Biomechanical usefulness of Polfix stabilizers in multi level fractures, Proceedings of the 10th International Scientific Conference "Achievements in Mechanics and Materials Engineering", Gliwice-Kraków-Zakopane, 2001, 347-350 (in Polish).
[17] A. Ziebowicz, The use of miniplates in mandibular fractures - biomechanical analysis, Journal of Materials Processing Technology 175 (2006) 452-456.
[18] A. Krauze, W. Kajzer, J. Marciniak, Biomechanical characteristic of intramedullary nails - femoral bone, Proceedings of the 11th International Scientific Conference "Achievements in Mechanics and Materials Engineering 2003", Gliwice-Zakopane, 2003, 533-558 (in Polish).
[19] F. Migliavacca, L. Petrini, Mechanical behaviour of coronary stents investigated through the finite element method, Journal of Biomechanics 35 (2002) 803-811.
[20] N. Benard, D. Coisne, R. Perrault, Experimental study of laminar blood flow through an artery treated by a stent implantation, Journal of Biomechanics 36 (2003) 991-99.
[21] W. Walke, Z. Paszenda, W. Jurkiewicz, Biomechanical behaviour of coronary stent design with OCC technology, Journal of Achievements in Materials and Manufacturing Engineering 20 (2007) 199-202.
[22] W. Walke, Z. Paszenda, W. Jurkiewicz, Numerical analysis of three-layer vessel stent made from Cr-Ni-Mo steel and tantalum, International Journal of Computational Materials Science and Surface Engineering 1 (2007) 129-139.
[23] J. Marciniak, W. Walke, Numerical analysis of stent - coronary vessel system, Engineering of Biomaterials 38-42 (2004) 86-88.
[24] W. Walke, J. Filipiak, Experimental and numerical biomechanical analysis of vascular stent, Journal of Materials Processing Technology 164-165 (2005) 1263-1268.
[25] W. Walke, J. Filipiak, Experimental and numerical analysis of vascular stent, Proceedings of the 13th International Scientific Conference "Achievements in Mechanical and Materials Engineering 2005", Gliwice-Wisła, 2005, 699-702.
[26] J. Chen, Y. Leng, X. Tian, L. Wang, N. Huang, P. Chu, P. Yang, Antithrombotic investigation of surface energy and optical bandgap and haemocompatibility mechanism of $Ti(Ta^{+5})O_2$ thin films, Biomaterials 23 (2002) 2545-2552.
[27] N. Huang, P. Yang, Y. Leng, J. Chen, H. Sun, J. Wang, Haemocompatibility of titanium oxide films, Biomaterials 24 (2003) 2177-2187.
[28] Z. Paszenda, J. Tyrlik-Held, W. Jurkiewicz, Investigations of antithrombogenic properties of passive-carbon layer, Journal of Achievements in Materials and Manufacturing Engineering 17 (2006) 197-200.
[29] W. Van der Giessen, A. Lincoff, R. Schwartz, Marked inflammatory sequelae to implantation of biodegradable and nonbiodegradable polymers in porcine coronary arteries, Circulation 94 (1996) 1690-1697.
[30] A. Lincoff, J. Furst, S. Ellis, E. Topol, Sustained local delivery of dexamethasone by a novel intravascular eluting stent to prevent restenosis in the porcine coronary injury model, Journal of American College of Cardiology 29 (1997) 808-816.
[31] D. Holmes, A. Camrud, M. Jorgenson, W. Edwards, R. Schwartz, Polymeric stenting in the porcine coronary artery model: differential outcome of exogenous fibrin sleeves versus polyurethane-coated stents, Journal of American College of Cardiology 24 (1994) 525-531.
[32] J. Baker, J. Horn, V. Nikolaychik, N. Kipshidze, Fibrin stent coatings in: Sigwart U. (ed): Endoluminal stenting. W.B. Saunders Company Ltd., London, Philadelphia, Toronto, Sydney, Tokio, 1996.
[33] R. Bonan, K. Bhat, T. Lefevre, Coronary artery stenting after angioplasty with self-expanding parallel wire metallic stents, American Heart Journal 121 (1991) 1522-1530.
[34] J. Zidar, J. Jackman, R. Gammon, Serial assessment of heparin coating on vascular responses to a new tantalum stent, Circulation 89 (1992) I-185.
[35] P. Hardhammar, H. Van Beusekom, H. Emanuelsson, Reduction in thrombic events with heparin-coated Palmaz-Schatz stents in normal coronary arteries, Circulation 93 (1996) 423-430.
[36] P. Serruys, H. Emanuelsson, W. Van der Giessen, Heparin-coated Palmaz-Schatz stents in human coronary arteries, Circulation 93 (1996) 412÷422.
[37] N. Chronos, K. Robinson, A. Kelly, Thrombogenicity of tantalum stents is decreased by surface heparin bonding, Circulation 92 (1995) I-490.
[38] I. De Scheerder, K. Wang, K. Wilczek, Experimental study of thrombogenicity and foreign body reaction induced by heparin-coated coronary stents, Circulation 95 (1997) 1549-1553.
[39] P. Serruys, J. Kutryk, Handbook of the coronary stents, Martin Dunitz Ltd., London, 2000.
[40] I. Buhaescu, H. Izzedine, A. Covic, Sirolimus-challenging current perspectives, Therapeutic Drug Monitoring 28 (2006) 577-584.
[41] S. Park, W. Shim, D. Ho, A paclitaxel-eluting stent for the prevention of coronary restenosis, The New England Journal of Medicine 348 (2003) 1537-1545.
[42] M. Beijk, J. Piek, XIENCE V everolimus-eluting coronary stent system - a novel secondo generation drug-eluting stent, Expert Reviews of Medical Devices 4 (2007) 11-21.
[43] K. Tsuchida, H. Garcia-Garcia, A. Ong, Revisiting late loss and neointimal volumetric measurements in a drug-eluting stent trial: analysis from the SPIRIT FIRST trial, Catheterization and Cardiovascular Interventions 67 (2006) 188-197.
[44] M. Pfisterer, H. Brunner-la Rocca, P. Buser, Late clinical events after clopidogrel discontinuation may limit the benefit of drug-eluting stents, Journal of the American College of Cardiology 19 (2006) 2584-2591.

[45] B. Lagerqvist, S. James, U. Stenestrand, Long-term outcomes with drug-eluting stents versus bare-metal stents in Sweden, The New England Journal of Medicine 356 (2007) 1009-1019.
[46] A. Farb, A. Boam, Stent thrombosis redux - The FDA perspective, The New England Journal of Medicine, 356 (2007) 984-987.
[47] Z. Paszenda, J. Marciniak, The influence of the base structure and carbon coating on the corrosion resistance of the Co-Cr-Mo alloy, Proceedings of the 5th International Scientific Conference „Achievements in Mechanical and Material Engineering 1996", Wisła, 1996, 211 - 214.
[48] P. Niedzielski, S. Mitura, Z. Paszenda, J. Marciniak, Diamond coated implants for medicine, Proceedings of the 8th International Scientific Conference „Achievements in Mechanical and Materials Engineering 1999", Rydzyna, 1999, 423-428.
[49] Z. Paszenda, J. Marciniak, The influence of the base structure and carbon coating on the corrosion resistance of the Co-Cr-Mo alloy, Journal of Materials Processing Technology 78 (1998) 143-149.
[50] J. Szewczenko, J. Marciniak, W. Chrzanowski, Corrosion of Cr-Ni-Mo steel implants in conditions of sinusoidal current electrostimulation, Proceedings of the 9th International Scientific Conference „Achievements in Mechanical and Material Engineering 2000", Gliwice-Sopot-Gdańsk, 2000, 511-514.
[51] Z. Paszenda, J. Tyrlik-Held, Z. Nawrat, J. Wilczek, Usefulness of passive-carbon layer for implants applied in interventional cardiology, Journal of Materials Processing Technology 157-158C (2004) 399-404.