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(54) Title: A TECHNIQUE FOR OBTAINING BIOACTIVE COATINGS ON MEDICAL IMPLANTS AND BIOACTIVE COATINGS PRODUCED USING THIS METHOD

(57) Abstract: The technique in this invention depends on the fact that a target-plate made of a heterogeneous mixture of carbon powder, iridium, and platinum, with a composition of 80-95% carbon, 3-8% iridium and 3-8% platinum, is placed in a high vacuum chamber at not less than 10^{-6} mbar and bombarded with a beam of ions of noble gas, with a target-plate bombardment angle in a range from 60° to 80°, for which the sputtering rates of carbon, platinum, and iridium characterizing the spraying process are calculated individually for each of the proposed coatings, preferably using Monte Carlo methods for a binary collision model, using programs created on the basis of a TRIM program, e.g. SRIM or SDTrimSP.

A technique for obtaining bioactive coatings on medical implants and bioactive coatings produced using this method

The present invention is a process for the preparation of biologically active coatings on medical implants, as well as bioactive coatings obtained by this method applicable to joint prostheses, aural implants, or implants used incardiac surgery, made of polyethylene, UHMWPE (ultra-high-molecular-weight polyethylene) or other biocompatible plastics or metals and their alloys approved for medical applications.

Two techniques for the formation of protective layers using ions are known from the literature and from patent descriptions: IBSD (ion beam sputtering deposition) and DB IBAD (dual-beam ion beam assisted deposition).

The publication "Formation of carbon coatings by dual beam IBAD method" informs us of the use of wear-resistant carbon coatings to improve the tribological properties of head-cup hip joint replacement, which can greatly extend the working life of the endoprosthesis. Techniques using ions (IBSD, IBAD) enable the formation of composite coatings with excellent adherence to the substrate, and, given the appropriate layered structure, coatings formed using ion techniques can significantly reduce the mechanical stress of the coating/substrate. The biochemical and mechanical properties of coatings formed by ionic technique are strongly dependent on insufficiently investigated physical processes occurring during the formation of the coating. Multilayer coatings are formed using IBAD techniques on flat pieces of steel or an alloy of Ti-Al-V.

From the Polish patent application P-386899, we learn of a process for producing an active protective coating on medical implants, based on its application to surfaces subject to friction and adjacent surfaces, i.e. the external surfaces of the implant or orthopedic joint prosthesis, using high-vacuum (10^{-6} mbar) adhesion methods and an wear-resistant carbon

coating with a diamond-like (DLC) structure whose source is a carbon target-plate bombarded by ion beams of noble gases or laser-beam ablation. Then, for selected portions of the surface coated with a carbon layer, ions of at least two metals selected from the galvanic series are applied by bombarding the surface with diamond-like beams of ions or metal atoms to form metal-doped regions, which act as mini-electrodes. Initially, in order to ensure proper adhesion, the optimal energy of the bombarding particles should be less than 100 eV, and subsequently, for the purpose of forming a metal coating, should be reduced below the potential barrier of carbon, i.e. to about 50 eV.

We also know, from the Polish patent application P-388281, of a technique for the production of immunologically resistant protective coating on medical implants, consisting of the following stages: In the first stage, a nanolayer of a carbon, preferably diamond-like (DLC), is formed in a high vacuum (preferably 10^{-6} mbar or higher) to those surfaces of the implant in contact with the living tissue of the patient. This is followed by a second stage in which this nanolayer is locally doped by bombarding the surface with a mixture of ions and atoms of at least two metals, M_1 and M_2, preferably silver (Ag) and titanium (Ti), obtained by sputtering a target made of a mixture of Ag and Ti,, in which the bombarding energy of the particles must be below the potential barrier of carbon, i.e., about 50 eV, and the ratio of the concentration of noble metal M_1 to another metal from the galvanic series M_2 on the surface of the implant should be $0.5 \leq \frac{N_{M_1}}{N_{M_2}} \leq 1.0$, where N_{M1} and N_{M2} are concentrations of, preferably, silver and titanium, in which the ratio M_1: M_2 is optimal for a given implant in terms of nanoelectrolytic effect and ranges from 50:50 to 20:80, with a deposition time between 60 to 120 min.

From the U.S. patent application US2011272276 we learn of an implant whose coating has an antibacterial effect. This coating releases silver ions within the human body. One of the components of the coating is formed from anode material. The second component is formed from cathode

material which is higher in the galvanic series than the anode material. The cathode and anode are connected in an electrically conductive manner. Together with the electrolytes in the human body surrounded by the implant, the anode and the cathode form a multitude of galvanic elements.

In the British patent application GB2362892 we find an implant made of plastic at least one of whose coatings contains iridium. Such coatings can be made with iridium or iridium oxide and may contain the iridium isotope Ir-192. This iridium coating is formed by CVD (chemical vapor deposition) using a radio frequency of 13.56 MHz. A layer containing Ti, Ta, Nb, Zr or Hf can be formed between the plastic substrate and the coating containing iridium. The implant may be, for example, a vascular prosthesis. The plastic product can be made of polypropylene, polyethylene terephthalate, polyurethane or PTFE, may contain pores, and may be made of textile fibers.

In the U.S. patent application US5980974 we learn of a coating that enhances the properties of an orthopedic implant. The implant may be coated with platinum, iridium or other metals with properties that enhance the implant surface. This also applies to orthopedic parts coated with a layer containing zirconium ions through the use of ionic methods. Parts of the implants may also be immersed in a medium containing oxygen. The layer thus formed is further enriched by the removal of impurities using the technique of bombardment with a stream of ions and the deposition of a layer of platinum, a similar metal or silicon between the metal from which the part of the orthopedic implant is made and the layer of zirconium oxide. Annealing in a furnace causes atomic diffusion and increases the adhesion between coatings. Zirconium oxide ensures minimal friction and reduces wear on the contact surfaces.

The international patent application WO2011129754 presents an implant whose coating contains an amorphous layer of the oxide of Me, which may also be Ti, Si, Cr, Hf, Zr, Ta or Nb. The coating is produced by PVD

(plasma vapor deposition, a method of vacuum deposition). A layer of hydroxyapatite may be formed on such a coating.

The aim of the invention is to obtain layers with special properties, ensuring physicochemical activity and bioactivity of the coating when in contact with pathogens.

In this invention, the technique depends on the fact that a plate made of a heterogeneous mixture of carbon powder, iridium, and platinum, with a composition of 80-95% carbon, 3-8% iridium and 3-8% platinum, is placed in a high- vacuum chamber at a pressure of no less than 10^{-6} mbar and is bombarded by an ion beam of noble gases, with the angle of bombardment of the material plate ranging from 60° to 80°, while the sputtering rates for carbon, platinum, and iridium characterizing the sputtering process are calculated individually for each of the proposed coatings, preferably by Monte Carlo methods for the binary collision model using programs created on the basis of a TRIM program such as SRIM or SDTrimSP.

The bioactive coating obtained via the technique of this invention, formed from a beam of atoms and ions, is amorphous, consisting of carbon in an atomic amount of 83% to 95%, while the atomic concentration of iridium is between 2.5% to 9.0% and platinum from 2.5% to 9.0%, and is characterized by random distribution of carbon, iridium and platinum throughout the volume of the coating.

This carbon-doped bioactive coating is hydrophobic because it is acted upon by electrical effects on a nanoscopic scale; therefore, bacterial-viral biofilms cannot moisten them and thus cause inflammation in the vicinity of the implant. On the implant coating appear nanoelectrode matrices that are activated in the environment of the patient's physiological fluid with a pH of 7.2 and enable the occurrence of local potential differences on the surface of the implant in any physiological fluid of the patient so as to allow a very weak flow of electric charge and thus a Maxwell-Lorentz force on a nanoscopic scale.

Example 1

A carbon-iridium-platinum (C (Ir, Pt) coating on the surface of a knee pad made of ultra-high-molecular-weight polyethylene (UHMWPE), formed by IBAD dual beam. Sputter deposition was carried out using plates made from a compressed heterogeneous mixture of three elements with a chemical composition as follows: $C[94\%] + Ir[3\%] + Pt[3\%]$. For this process, the sputtering rates for coal, platinum and iridium are as follows: $C : Ir : Pt = [9.3800 : 0.2742 : 0.2978]$ atom/ion, which ensures a suitably uniform concentration throughout the volume of the elements in the coating: $C : Ir : Pt = [94.25\% : 2.76\% : 2.99\%]$.

In a high-vacuum chamber with a pressure of 10^{-6} mbars, a target-plate is bombarded by an Ar^+ ion beam with an energy of 15 keV at an angle of 70° to the normal in order to obtain the energy flux of atoms and ions of carbon, iridium and platinum, which then bombard the surface of a knee pad made of UHMWPE. The coating thus formed is characterized by excellent adhesion to coated ultra-high-molecular-weight polyethylene and especially bioactivity.

Example 2

A coating of carbon-platinum-iridium (C(Ir, Pt), on the surface of an acetabular surface made of ultra-high-molecular-weight polyethylene (UHMWPE), formed by the dual beam IBAD method. Flat target-plates made by compressing a mixture of graphite, iridium and platinum with the chemical composition $C[84\%] + Ir[8\%] + Pt[8\%]$ were used for sputtering. For this process, the sputtering rates of carbon, platinum, and iridium are as follows: $C : Ir : Pt = [7.9900 : 0.7779 : 0.8601]$ atom/ion, which ensure a suitably uniform concentration of elements throughout the coating: $C : Ir : Pt = [83.00\% : 8.90\% : 8.10\%]$.

In a high-vacuum chamber with a pressure of 10^{-6} mbars, a target-plate is bombarded with an ion beam Ar + with an energy of 15 keV at an angle of

70° to the normal in order to obtain the energy flux of atoms and ions of carbon, iridium and platinum, which then bombard the surface of the acetabular component made of UHMWPE. The coating thus formed is characterized by excellent adhesion to coated ultra-high-molecular-weight polyethylene and especially bioactivity.

Patent Claims

1. The technique of obtaining biologically active coatings on implants and medical grafts using the ion method is characterized by the fact that the target-plate is made of a heterogeneous mixture of carbon powder, iridium and platinum, with a composition of 80-95% carbon, 3-8% iridium and 3-8% platinum, bombarded by a beam of ions of noble gas, with the bombardment angle of the material plate in the range of 60° to 80°, in which the sputtering rates of carbon, platinum, and iridium characterizing the spraying process are calculated individually for each of the proposed coatings, and the process of applying the coating is carried out in a high-vacuum chamber at a pressure not less than 10^{-6} mbar.
2. The bioactive layer, formed from a stream of atoms and ions, is amorphous, consisting of carbon in an atomic amount of 83% to 95%, iridium 2.5%-9% and platinum 2.5%-9%, and is further characterized by the fact that carbon, iridium and platinum are randomly distributed throughout the layer on a substrate.
3. The technique, according to claim 1, is characterized by the fact that for a target-plate made of a compressed mixture of three heterogeneous elements with a chemical composition as follows: $C[94\%] + Ir[3\%] + Pt[3\%]$, the sputtering coefficients of carbon, platinum and iridium are as follows: $C : Ir : Pt = [9.3800 : 0.2742 : 0.2978]$ atom/ion.
4. The technique, according to claim 1, is characterized by the fact that for a target-plate made by compressing a mixture of graphite, iridium and platinum with the chemical composition: $C[84\%] + Ir[8\%] + Pt[8\%]$, the sputtering coefficients of carbon, platinum and iridium are as follows: $C : Ir : Pt = [7.9900 : 0.7779 : 0.8601]$ atom/ion.

5. The technique, according to claim 1, is characterized by the fact that the sputtering rates of carbon, platinum, and iridium are calculated using the Monte Carlo method for a binary collision model, using programs based on a TRIM program, e.g. SRIM or SDTrimSP.

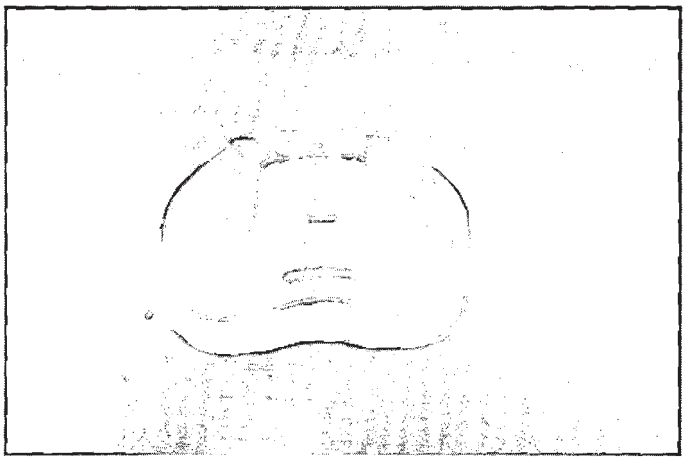

Figure 1

Insert for knee endoprosthesis made of ultra-high-molecular-weight polyethylene, covered with an amorphous layer of C (Ir, Pt).

Figure 2

Hip replacement acetabular cup made of polyethylene, covered with a high-molecular-weight amorphous coating C (Ir, Pt).

INTERNATIONAL SEARCH REPORT

International application No
PCT/PL2013/000004

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61L27/30 A61L27/54
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	J. GRABARCZYK, D. BATORY, P. LOUDA, P. COUVRAT, I. KOTELA, K. BAKOWICZ-MITURA: "carbon coatings for medical implants", JOURNAL OF ACHIEVEMENTS IN MATERIALS AND MANUFACTURING ENGINEERING, no. 1-2, 2007, pages 107-110, XP002699124,	1-5
Y	abstract page 107, left-hand column, paragraph 1 - page 108, right-hand column, paragraph 2.3 page 109, left-hand column, paragraph 4.1 - page 110, left-hand column, paragraph 5 -----	1-5
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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 June 2013	04/07/2013

Name and mailing address of the ISA/	Authorized officer
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INTERNATIONAL SEARCH REPORT

International application No
PCT/PL2013/000004

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2010/233227 A1 (WEBER JAN [NL]) 16 September 2010 (2010-09-16) page 2, paragraph 30 page 3, paragraph 42 - paragraph 44 page 6, paragraph 85 - page 7, paragraph 86 claims 1-21	1-5
A	WO 2007/022174 A2 (BOSTON SCIENT SCIMED INC [US]; KONDYURIN ALEXEY [DE]; MAITZ MANFRED FR) 22 February 2007 (2007-02-22) page 9, line 30 - page 10, line 27 page 13, line 13 - line 16 page 17, line 10 - line 25 example 1	1-5
A	US 5 980 974 A (ARMINI ANTHONY J [US] ET AL) 9 November 1999 (1999-11-09) cited in the application column 2, line 5 - line 34 column 3, line 31 - line 50 page 5, line 45 - line 58 claims 1-6	1-5

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/PL2013/000004

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