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PROSPECTS FOR THE USE OF PLASMA SPRAYING IN MEDICINE

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Мета статті – проаналізувати досвід і перспективи використання плазмового напилення для вирішення завдань, пов'язаних з медициною.

Основні напрямки використання плазмового напилення для медичних цілей – виготовлення імплантатів для стоматологічної практики, а також протезів для протезування кісток і суглобів в ортопедії.

Система «металевий імплантат – кісткова тканина» є найбільш складним варіантом композиційного матеріалу, формування якого відбувається в живому організмі. У статті проаналізовано чинники, які треба враховувати для успішного виготовлення імплантатів, призначених для тривалого використання в організмі пацієнта. Для біотехнологій їх виготовлення в даний час застосовують переважно титан і його сплави (наносяться на металеві частини протезів, збільшуючи їх зносостійкість), гідроксиапатит і флюорит (мають близьку до кісткової тканини структуру, в результаті чого протези не відторгаються і вростають в кістки).

Представлено практичні результати використання плазмового напилення для виготовлення протезів, а також особливості формування поверхонь імплантатів. Обговорюються аспекти «остеоз'єднання» пористої структури – здатності матеріалу сприяти проростанню кісткової тканини вглиб і вздовж імплантату, «остеоуведення» – додаткової здатності структури і поведінки нової кісткової тканини на локальному рівні. Викладено уявлення про структуру поверхні імплантатів, яка найбільшою мірою сприяє інтеграції їх з кістковою тканиною.

Наведено результати діагностичних методів, які в даний час використовуються в медико-біологічних дослідженнях з метою контролю якості протезів, виготовлених із застосуванням методів плазмового напилення.

Загальним висновком аналізу досягнень у галузі використання плазмового напилення при виготовленні протезів є таке: щільність заповнення пористого шару на поверхні імплантату новою кістковою тканиною і міцність цієї кісткової тканини визначають ефективність передачі навантаження з імплантату на кісткову тканину, механічну міцність такого композиційного матеріалу, довговічність роботи імплантату. Дане положення є критерієм контролю результатів під час подальшого вдосконалення технології плазмового напилення при використанні її для медичних цілей.

Ключові слова: *плазмове напилення, виготовлення протезів, виготовлення зубних імплантів, дослідження структури матеріалів, методи контролю міцності, біосумісність, методи дослідження біологічних тканин.*

Цель статьи – проанализировать опыт и перспективы использования плазменного напыления для решения задач, связанных с медициной.

Основные направления использования плазменного напыления для медицинских целей – изготовление имплантатов для стоматологической практики, а также протезов для протезирования костей и суставов в ортопедии.

Система «металлический имплантат – костная ткань» является наиболее сложным вариантом композиционного материала, формирование которого происходит в живом организме. В статье проанализированы факторы, которые надо учитывать для успешного изготовления имплантатов, предназначенных для длительного использования в организме пациента. Для биотехнологий их изготовления в настоящее время применяют преимущественно титан и его сплавы (наносятся на металлические части протезов, увеличивая их износостойкость), гидроксиапатит и флюорит (имеют близкую к костной ткани структуру, в результате чего протезы не отторгаются и врастают в кости).

Представлены практические результаты использования плазменного напыления для изготовления протезов, а также особенности формирования поверхностей имплантатов. Обсуждаются аспекты «остеосоединения» пористой структуры – способности материала содействовать прорастанию костной ткани вглубь и вдоль имплантата, «остеовведения» – дополнительной способности структуры и поведения новой костной ткани на локальном уровне. Изложены представления о структуре поверхности имплантатов, которая в наибольшей степени благоприятствует интеграции их с костной тканью.

Приведены результаты диагностических методов, которые в настоящее время используются в медико-биологических исследованиях с целью контроля качества протезов, изготовленных с применением методов плазменного напыления.

Общим выводом анализа достижений в области использования плазменного напыления при изготовлении протезов является следующее: плотность заполнения пористого слоя на поверхности имплантата новой костной тканью и прочность этой костной ткани определяют эффективность передачи нагрузки с имплантата на костную ткань, механическую прочность такого композиционного материала, долговечность работы имплантата. Данное положение является критерием контроля результатов в ходе дальнейше-

го совершенствования технологии плазменного напыления при использовании её для медицинских целей.

***Ключевые слова**: плазменное напыление, изготовление протезов, изготовление зубных имплантов, исследование структуры материалов, методы контроля прочности, биосовместимость, методы исследования биологических тканей.*

The aim of this paper is to analyze the experience in and the prospects for using plasma spraying in the solution of medicine-related problems.

The main lines in the medical use of plasma spraying are dental implant making and bone and joint prosthesis making.

The metal implant – bone tissue system is the most complex composite material formed in the human body. The paper analyzes the factors that must be considered for the successful making of implants intended for a long-term use in the patient's body. The main materials that are currently used in their making are titanium and its alloys (they are applied to the metal parts of prostheses to increase their wear resistance), hydroxyapatite (HA), and fluorite (they have a structure similar to the bone tissue, as a result of which the prostheses are not rejected and grow into the bone).

The paper presents practical results of the use of plasma spraying in prosthesis making and the features of implant surface formation. The aspects of porous structure "osteojunction" (the ability of the material to promote the growth of the bone tissue deep into and along the implant) and osteointroduction (an additional capability of the structure and the behavior of the newly formed bone tissue at the local level) are discussed. Ideas of the surface structure of implants best suited to their integration with the bone tissue are outlined.

The results of the diagnostic methods currently used in biomedical research to control the quality of prostheses made using plasma spraying are presented.

The general conclusion of the analysis of the achievements in the use of plasma spraying in prosthesis making is as follows: the density of filling of the porous layer on the implant surface with the newly formed bone tissue and the strength of that bone tissue determine the efficiency of implant-to-bone load transfer, the mechanical strength of the resulting composite material, and the implant durability. This statement is a result assessment criterion in the course of further improvement of plasma spraying for medical purposes.

***Keywords:** plasma spraying, prosthesis making, dental implant making, material structure study, strength control methods, biocompatibility, biological tissue study methods.*

Introduction. The bone system of a living organism is formed and maintained as a result of complex biochemical reactions. One of the main elements in these reactions are: calcium, phosphorus, oxygen, hydrogen. In case of failure of a part of the skeletal system, it becomes necessary to replace the lost part with an implant. At the present stage of prosthetics, large volumes of lost bones to the human bone system are not regenerated. Lost areas of bone tissue are replaced by implants, which are usually made of metallic materials based on titanium, cobalt or tantalum.

The system «metal implant - bone tissue» is the most complex version of a composite material, the formation of which occurs in a living organism. The complexity of such a composite material has several components:

– the «building material» of the new bone tissue should be easily delivered to the implant surface,

– the implant surface must have a certain physicochemical affinity for this «building material»,

– the interface must have a developed geometric surface and have an intermediate modulus of elasticity to reduce the stress concentration resulting from a tenfold difference in the elastic moduli of the metal and bone,

– after bone tissue has grown into the implant surface, the boundary of the case should have a strength not lower than the bone tissue strength,

– the implant surface structure should ensure the functioning of the new bone tissue (delivery of nutrients and oxygen). There are three main factors that must be considered for the successful use of implants for a long time in the patient's body [1]:

– bone quality in patients deteriorates after 60 years;

– the majority of high–strength materials for prostheses have high elastic moduli in comparison with bone and, therefore, there is a «stress field» in the original bone;

– micro–mobility at the «implant – bone» border leads to instability of this border and deterioration of the implant, which further leads to damage to the original bone tissue.

The last two factors are associated with a significant difference in the physicochemical and mechanical properties of the implant and bone tissue. To reduce the influence of these factors, it is necessary to create a transition zone between the bone and the implant, which, along with a strong chemical bond, must have optimal macro- and microstructures. Apparently, such a zone should have a composite structure. It is assumed that the outer layer of this zone should coincide as much as possible with the chemical composition of natural bone or be able to form bone tissue on its surface. Plasma evaporation has become widespread to form the interface between the implant and bone tissue.

1. Features of the use of plasma evaporation for solving problems related to medicine. For biotechnology, the following materials are used: titanium and its alloys (applied to the metal parts of the prostheses, increasing their wear resistance), hydroxyapatite (HA) and fluorite (have a structure close to the bone tissue, as a result of which the prostheses do not reject and grow into the bones). When choosing materials that will be in contact with body tissues, the prevention of the further formation of a large mass of non-functional connective tissue plays an important role. Most often, HA - $Ca_{10}(PO_4)_6(OH)_2$ is used as a starting material for bioactive coatings. During plasma evaporation of coatings, there is the problem of preserving its initial chemical composition when creating a specific coating structure. Therefore, for evaporation, HA-related compounds are used: tetracalcium phosphate — $Ca_4P_2O_4$, three-calcium phosphate — $Ca_3(PO4)_2$, fluorideapatite. For the formation of coatings, bioactive glasses are used, both independently and as additives (up to 50%) to HA [2]. To obtain bioactive glass, the following materials are used [3]: (CaO) (SiO_2), Na_2CO_3, $CaCO_3$, H_2PO_4, and CaF_2.

For evaporation HA or similar material for its intended purpose, mainly arc plasma torches are used. For evaporation, the conventional evaporation scheme is used when the substrate is located from the plasma torch at a distance of 80 mm - 120 mm [4]. When evaporation oxides and materials with thermic-physical properties close to them, mixtures of plasma gases are used. This is due to the relatively high melting point and the relatively low heat capacity of the material of the HA particles. Therefore, in order to preserve the particle in the molten state before the impact with the substrate, a sufficiently effective heating of the particles is necessary.

A dense coating structure consisting of disc-shaped amorphous particles is formed from completely melted HA evaporated particles. The decrease in the efficiency of heating the particles leads to the retention of their unmelted core and an increase in the porosity of the coating. The increase in the content of crystalline phases in the coating during the formation of it is not fully molten particles [5], has two aspects:

– improving the stability of crystalline HA during implant operation (a lower degree of dissolution of HA);

– increasing the probability of destruction of a porous coating formed by weakly deformed, not completely molten particles.

Bioactive continuous glass coatings with a thickness of 25–150 μm can be successfully obtained by enameling [6], the technology takes into account most of the physic-chemical phenomena associated with enameling of titanium implants.

The optimal structure of the surface of the prosthesis should have a composite structure. The sublayer used titanium coating. During the deposition of HA coatings, ZrO_2, Zr-Ti, and Ti sublayers were used. ZrO_2 sublayers make it possible to reduce the cooling rate of HA evaporated particles when they solidify on the substrate. Zr-Ti and Ti sublayers can increase the adhesion of HA coatings by 50% and 100%, respectively [7]. In this case, a titanium oxide layer is formed on the surface of the titanium alloy.

At present, as a rule, the micro-rough surface of the implant (after abrasive treatment) is used for the deposition of coatings, and the macro roughness is used less frequently. A significant effect of the size of cavities and ridges on the growth of fibroblasts has been established [8]. The influence of the implant surface relief and the application of cyclic load on the behavior of fibroblasts are analyzed. Thus, increasing the depth of the grooves improves the orientation of fibroblasts [8].

Significant differences in the shear strength of implants with coatings [9] indicate the need for additional studies on the general (standard) test method. At the same time, quite definite conclusions can already be drawn from these data — HA-coated implants have 6-60 times higher shear strength than uncoated implants. Even when processing them with an abrasive, which creates a roughness, commensurate with the roughness of the coating. High shear strength in the case of HA coating seems to be related to the ingrowth of bone into the HA coating. However, it can be assumed that the bone tissue grows into the porous titanium substrate as well as in the HA coating.

H. Harris [10] conducted a large-scale study of coatings of titanium and HA. Two types of titanium coatings are formed by particles with a size of 22 - 90 microns and 75 - 180 microns. On top of these coatings evaporated coatings from HA with a particle size of 90 microns. A titanium coating with a rougher surface is deposited from a wire with a diameter of 1.6 mm. This coating on top was also dusty HA. Photographs of the surface and transverse thin sections indicated that the porous structure of the titanium coatings was filled with a HA coated coating. It has been suggested that HA after implantation dissolves, and then a new HA is formed, firmly connected to the surface of the titanium implant.

The high temperature of the plasma jet causes changes in the chemical composition of the evaporated material, and the high cooling rate of the evaporated particles when they harden on the substrate leads to changes in the phase composition of the evaporated material [11]. Thus, when evaporation HA coatings, there is a contradiction between obtaining a dense HA coating structure consisting of amorphous (completely melted during sputtering) particles and more rapid dissolution of these amorphous particles in the human body. This contradiction can be eliminated by subsequent heat treatment of the HA of the amorphous coating in order to transfer it to the crystalline state [11]. This treatment achieves three goals:

– to increase in the content of the crystalline phase from 26% to 88%;

– to increase in the content of OH groups in HA;

– reducing the content of decomposition products of HA.

The positive result of this treatment is a reduction of almost three times the dissolution rate of the coating in distilled water for 200 hours. There are options for hydrothermal treatment, which allows to increase the content of HA phase in the coating from 76% to 96% [12].

Bioactive materials based on crystalline calcium phosphates, calcium phosphate ceramics and glasses containing oxides of calcium and phosphorus, have the

unique ability to connect with bone tissue without a connective tissue layer and form a single fragment «implant – bone» [13]. The bond strength between the bone and the implant of bioactive material is much higher than with an implant of bioinert material. A significant drawback of bioactive materials, limiting their widespread use in bone arthroplasty, is their low mechanical strength. The combination of the bioactive properties of glasses and glass-ceramic materials with the mechanical properties of titanium opens up great prospects for increasing the service life of implants [13].

«Osteoconnection» of a porous structure is defined as the ability of a material to promote the growth of bone tissue deep into and along the implant, while «osteoversion» is an additional ability of the structure and behavior of new bone tissue at the local level [14]. The stoichiometry of HA and its mechanical properties affect the ingrowth and fixation of bone tissue (its ultimate compressive strength ranges from 1 to 11 MPa).

The use of implants with strictly deterministic surface properties has limitations, since it is not possible to find the key surface characteristics that determine the optimal biocompatible and functional properties of the implantable product [15]. There is another area of research where «self-regulating» materials are developed that change their properties due to relatively small changes in the physical or chemical effects of the environment. When contacting with blood, hem-compatible materials should have a minimum value of interfacial free energy and the same distribution pattern of polar and dispersive components of free energy of the surface of the material and blood (plasma proteins).

Plasma technologies for producing materials are widely used to form porous coatings on intraosseous implants. At the same time, the need for further improvement of coatings, which provides for ensuring high mechanical strength, and at the same time - the creation of an adjustable porous structure with bioactive properties, has become urgent. In studies, special attention is paid to the possibility of bone tissue to grow freely into the porous structure of implants [14]. Currently, the following ideas about the structure of the surface of implants, which is most favorable for their integration with bone tissue, have been formed in the scientific literature:

– the pore size should be 50 – 500 microns;

– the porous structure should maximally promote the supply of nutrients and oxygen involved in the construction of new bone tissue;

– the porous layer should have an intermediate modulus of elasticity between the moduli of elasticity of the bone and the metal implant;

– high strength of the porous structure itself;

– bioactivity of the coating.

2. Methods for monitoring the results of the application of plasma evaporation for solving problems related to medicine. A number of works published in scientific literature demonstrate the level of research methods that are used to control the results obtained. This applies to both in vivo and in vitro experiments. In particular, the bone cells of an adult, isolated from the jaw bone by biopsy, were grown in culture on cover glasses, on polished surfaces, and also on plasma-coated surfaces of titanium, HA [16]. The content of various metabolic fractions was compared after 2 and 5 days of culture. Both types of titanium surfaces significantly increased the size of the populations of the caudate and caudate precursors in vitro. But, the plasma-evaporated titanium surface showed between 2 and 5 days a

greater increase in the number of bone cells, markedly increasing their proliferative activity and alkaline phosphatase activity.

The structure and phase composition of hydroxyl-apatite coatings and their changes occurring during plasma evaporation on titanium substrates with an increase in coating thickness and outflow regimes of plasma jets were studied [17]. Data on the fine structure of plasma-evaporated hydroxyapatite coatings were obtained by electron microscopy on the lumen and X-ray structural analysis. Research results indicate the complexity of the evaporated coatings and the possibility of obtaining coatings with a given crystal structure, which should be considered when predicting the performance of coatings on implants in orthopedics and dentistry.

The presence and distribution of the amorphous phase is a key factor in ensuring the functioning and good bone adhesion of plasma-evaporated HA coatings [18]. The microanalysis of the coatings was carried out using a scanning cathode-fluorescent microscope. It was confirmed that the darker areas of polished transverse cuts correspond to the amorphous phase. To detect two structurally different sites in the sample, stronger cathode-luminescent emission from the amorphous phase was used during the electron beam irradiation (compared to the crystalline phase). Thanks to the choice of the emission peak corresponding to 450 nm, it became possible to conduct raster scanning of the surface with an electron beam and obtain a map of the amorphous phase of polished sections, the fracture surface and the freshly obtained surface of the plasma-evaporated coating. Cathode-luminescent microscopy, using the phenomenon of unequal light emission from the amorphous phase of HA, allows to identify and map the component, which is the amorphous phase in plasma-evaporated coatings.

The crystallinity and residual stresses at the interface between HA and titanium were investigated [19]. The traditional method used in laboratories is based on the x-ray diffraction of HA samples with standard crystallinity of aluminum oxide. Four methods were studied to determine the crystallinity of HA samples. Two of them are based on X-ray diffraction, one on neutron diffraction, and one on infrared adsorption spectrometry. All four methods give results that are very different from each other. The greatest accuracy was at x-ray and infrared methods.

The influence of thermochemical reactions on interactive processes in the biosystem of a living organism's tissue — a bioactive coating — a bio-inert metal implant is analyzed [20]. Body fluids contribute to increased adhesion of the bone with a bioactive coating. However, corrosion may form on the interfaces. It was experimentally shown that corrosion processes can prevent and simultaneously increase the adhesion force between the bioactive HA coating applied by the plasma evaporation method and the surface of the titanium alloy using an intermediate glass coating. A biocompatible phosphate glass coating is applied to the titanium substrate in vacuum at 9000°C. Then ceramic glass with HA content, powder, in argon plasma is evaporated onto the glass. The adhesive force between the bone and the implant was tested 4 months after the implant was placed in the rabbit's thigh.

The chemical composition of the outermost layer of phosphorus-silicate glass, which was applied to a titanium alloy substrate by plasma evaporation, was studied [21]. In this case, X-ray photoelectron spectroscopy was used. Samples were immersed in a potassium phosphate buffer solution, or in a solution of human albumin with phosphate buffer. The characteristics of phosphate-silicate glass were

compared with the characteristics of soda-calcium glass treated in the same way. After keeping in buffer solution, the enriched Ca and P layer was formed only on the surface of phosphorus-silicate glass. Human serum albumin is bonded to the glasses of both species, while maintaining its native state. However, the protein completely covered the surface of phosphate-silicate glass for 24 hours, with the formation of a layer of a mixture of albumin, Ca and P. It took 4 days to fully cover the surface of the sodium-calcium glass. Mouse fibroblasts, sown on phosphorus-silicate glass, were characterized by almost the same pattern of proliferation as the control cells were grown. The growth of cells sown on soda-calcium glass was less intense.

3. Trends for the development of plasma evaporation for solving problems related to medicine. Currently, third generation materials (polymers, artificial plastics) are most commonly used for plasma evaporation [22]. Nevertheless, innovative research is trying to initiate development for fourth generation biomaterials [23]. The fourth generation of biomaterials is based on the integration of electronic systems with the human body, with the aim of providing diagnostics and mastering therapeutic tools for basic research and their clinical use. The functionality of such biomaterial systems significantly expands the capabilities of this area of medicine and technology. They include the use of radio channels, the study of bioelectric reactions of tissue regeneration, as well as the monitoring of cellular responses in order to establish a response by feedback from the patient's tissues through bioelectric signals [24]. This will open up a number of opportunities for plasma evaporation.

Conclusions. During plasma evaporation of prostheses, a composite coating consisting of a bioactive ceramic coating and a capillary-porous titanium coating has the most favorable macro- and microstructure and bioactive properties. This has a positive effect on the fixation of bone tissue on the implant surface [12]. The presence of bioactive properties of these coatings, named «osteoinductive» and «osteoconductive», determines the stability and strength of the «implant-bone tissue» interface.

The system «implant - bone tissue» is a complex version of a composite material, the structure of which and, above all, the interface «implant - bone system» is finally formed in a living organism. The volume limit allows to reduce the stress concentration resulting from a significant difference in the elastic moduli of titanium and bone tissue. The joint boundary of the «implant-bone tissue» section of the composite is formed after the implant is installed in the bone system.

The percentage of filling the porous layer on the implant surface with new bone tissue and the strength of this bone tissue almost completely determine the efficiency of transferring the load from the implant to the bone tissue, the mechanical strength of such a composite material, and the durability of the implant. This provision is a criterion for monitoring the results in the further improvement of plasma evaporation technology when using it for medical purposes.

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