Chapter 3

Microporous Titanium-Based Materials Coated by Biocompatible Thin Films

Ann D. Dobrzanska-Danikiewicz, Leszek A. Dobrzanski, Marek Szindler, Lech B. Dobrzanski, Anna Achtelik-Franczak and Eugeniusz Hajduczek

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.70491

Abstract

This chapter presents the outcomes of numerous own works concerning constructional solutions and fabrication technologies of a new generation of custom, original, hybrid, microporous high-strength engineering and biological materials with microporous rigid titanium and Ti6Al4V alloy skeletons manufactured by Selective Laser Sintering (SLS), whose pores are filled with living cells. The so constructed and fabricated implants, in the connection zone with bone stumps, contain a porous zone, with surface treatment inside pores, enabling the living tissues to grow into. As the adhesion and growth of living cells are dependent on the type and characteristic of the substrate it is necessary to create the most advantageous proliferation conditions of living cells inside the pores of a microporous skeleton made of titanium and Ti6Al4V alloy. In order to improve the proliferation conditions of cells ensured by a fully compatible substrate, internal coatings with TiO₂, Al₂O₃ oxides and Ca₁₀(PO₄)₆(OH)₂ hydroxyapatite of the surface of pores of a microporous skeleton made of titanium and Ti6Al4V alloy with SLS was used. Two technologies have been chosen for the deposition of thin coatings onto the internal surfaces of pores: Atomic Layer Deposition (ALD) and the sol-gel of deep coating from the liquid phase.

Keywords: implant-scaffold, scaffold, engineering biological composite, titanium, SLS, thin film, ALD, dip coating
1. The basis of biological interaction of living cells with a substrate made of metallic micro-skeletons manufactured by selective laser sintering and coated inside pores using atomic layer deposition or the sol-gel methods

The continuity of tissues requiring tissue regeneration in order to restore their normal condition is disrupted as a result of bodily injuries related to numerous accidents, most often work accidents, traffic accidents and sports accidents, as well as due to surgical interventions resulting from the employed therapeutic methods of treating numerous disorders, most often cancerous diseases or removal of inflammatory conditions [1]. One of the most significant and costly problems of modern medicine is the necessity to replace or supplement organs or tissues to prevent the biological and social degradation of patients and to restore their living functions, either normal functions or such acceptably similar to normal, resulting from a growing number of cases of organ or tissue loss or damage in the human population due to post-injury or post-resection losses as well as those originating from the operative treatment of cancerous tumours or inflammation processes and as a result of other disorders, and also work, traffic and sports accidents. The most widespread cases are caused by a strong development of civilisational diseases, including cancer, and the incidence rate of malignant cancers has been regularly rising. The number of traffic accident victims has been growing substantially, as well [2]. One of the fundamental tasks globally is to improve the society’s condition of health, medical care and health safety. The idea is to overcome problems which occur more and more often and to protect against serious health risks, especially such as civilisational diseases, pandemics and bioterrorism and to support research, particularly research into the development of modern technologies, serving to advance medicine and healthcare, most of all to replace the lost tissues and organs by technical means, to ensure more complete prophylactics of diseases and safe treatment of patients, which are one of the important indicators of economic welfare. Bone reconstruction, for example, of legs and hands and in the craniofacial area, as well as skin and other soft tissue reconstruction, and also the reconstruction of oesophagus and blood vessels, are often required due to the consequences of civilisational diseases and accidents, including malignant cancers. Patients’ healthcare expectations are also growing, and economic aspects at the global scale call for the efficient elimination of disabilities, in particular motoric disabilities, and the restoration of the previously handicapped persons to physical fitness and usually most often to full, or at least partial, professional activity, which considerably lessens pressure on the diminishing resources of social insurance funds. It is vital to reduce waiting times for treatment, to lower prices and to improve availability of medical products or services and therapy, to reduce the risk of treatment failure, in particular by tailor-made personalised medical products according to a patient’s individual anatomical features, and ultimately to reduce therapy discomfort for patients and their family.

The development of regenerative medicine started nearly a quarter of century ago along with the works [3], consisting of treatment by replacing old and sick cells with young cells using tissue engineering methods and cell-based therapies or gene therapy and creating numerous
new opportunities in counteracting diseases and their consequences [4–8]. On the other hand, tissue engineering – introduced somewhat earlier [9] – consists of the development of biological substitutes for restoration, maintenance or improvement of functions of tissues or entire organs [10, 11], involving the construction and fabrication of scaffolds maintaining the developing tissues and involving the production of a replacement tissue for clinical use [12] as a substitute of damaged tissues or entire organs [13, 14], capable of restoring, maintaining or improving the functions of particular tissues or organs [10]. It is obviously a continued endeavour to develop an engineering material with its properties corresponding to the tool being replaced, supplemented or aided, which does not cause an immunological response of the immunity system and expediting wound healing and not causing implant rejection. The advancement of tissue engineering methods poses further challenges for biomaterials which should not only be fully compatible, but when used for three-dimensional scaffolds, should ensure conditions for cellular cultures, taking into account the possibility of controlled growth, division and differentiation of different types of cells and the impact of various environmental factors on their living functions, and also for transporting medicines in a patient’s organism.

Among the biocompatible materials currently and widely used in many branches of industry are titanium and its alloys. These materials are characterised by excellent corrosion resistance in the majority of aggressive environments. Titanium has two allotrope types: Tiα and Tiβ. The α allotrope type endures to the temperature of 882°C and crystallises in a hexagonal structure with a compact lattice (A3). The β allotrope type endures to the temperature of 882–1068°C being a melting point and it crystallises in a regular structure with a centred spatial lattice (A2) [15]. Titanium alloys are classified as single-phase α and β, double-phase α + β and pseudo-α and pseudo-β. Double-phase α + β alloys are the most popular, widely used group of titanium alloys with good strength and plastic properties. This group includes the most popular Ti6Al4V titanium alloy. Titanium and titanium alloys, conventionally manufactured by casting and plastic treatment [16], are used in the arms, chemical, automotive, aviation, power and transport sector, as well as in architecture and sports [17–20]. Pristine titanium and its alloys, independent of the wide engineering application, are often used in medicine in order to replace damaged tissues. From many years, these materials have been used for endoprosthesis of hip-joints and knee-joints, bone plates, screws for fracture repair and heart valve prostheses [21–24]. Moreover, artificial heart is currently developed using these materials [25]. Recently, for medical applications, materials sintered from powders of pristine titanium, Ti6Al4V and Ti6Al7Nb are also applied [21–25]. Table 1 shows comparative analysis of these materials.

A structure of the extracellular matrix (ECM) occurring in living organisms, and acting as a natural scaffold of cells [26], can be imitated by biomaterials which, for this reason, can find their application as a substrate for the controlled breeding of living cells. Capable of growth, division and differentiation are such living cells only, which are attached to a substrate and have undergone adsorption on a substrate surface. In natural conditions, this is possible owing to the presence of the extracellular matrix. The coincidence of a metallic substrate with living cells is a very vital aspect. It is also vital to determine the potential favourable effect of indirect layers – in the form of thin coatings deposited onto the inner surfaces of pores of a metallic...
skeleton made of titanium and its alloys produced by SLS – on the potential adhesion and proliferation of living cells. Not all the factors are known, which are decisive for the influence of a substrate made of engineering materials on the attachment, division and growth of living cells, despite the fact that intensive research has been conducted in this field. A material’s specificity is one of the most essential factors crucial for the breeding or growth of cells on the surface of engineering materials [27, 28]. The domains ensuring the adhesion of cells to a substrate are very important in interactions between living organisms and engineering materials in cultures of living stem cells and in implantology. The one which is best recognised is arginyl glycyl aspartic acid (RGD), which is a tripeptide composed of L-arginine, glycine, and L-aspartic acid, as well as other proteins, including integrins, cadherins, selectins and immunoglobulin-like proteins [29–37]. After placing an implant in an organism, its surface is covered with a thin layer of water within a few seconds, and then, within a few seconds to several hours, with a layer of specific proteins [38] from those contained in physiological fluids [39]. A weakly vascularised, fibrous layer of cells [29, 40] is growing on such cells within several minutes to several days, and finally a cytoskeleton of cells is reorganised, leading notably to the flattening of cells [41]. Surface wettability influences the ability of adhesion proteins to attach to the substrate, and their affinity to the material surface has influence on the structure and composition of a layer of proteins [38]. The free enthalpy of surface and its wettability influence the growth of cells, but do not have an effect on their shape and orientation [42–44]. The adhesion domains placed on the surface of engineering biomaterials influence the behaviour of cells due to an effect on the functioning of integrins [29]. Cells’ material attachability depends on proteins’ substrate adhesion [29–35, 37–39, 42, 45]. An excessively hydrophilic and hydrophobic character of the surface with the wetting angle of over 80 or below 15° [46] is sometimes unfavourable for the growth of cells, although surface hydrophobicity may, in the initial phase, support cells’ adhesion, when hydrophilicity may support their division and multiplication [47]. In general, cells are preferentially attaching, dividing and growing on hydrophilic surfaces of a material, whilst their ability of adhesion to a substrate material is diminishing on hydrophobic surfaces [38, 39, 47–53].

As flexibility of different types of cells varies [54–66], their morphology and living functions depend on the stiffness of the substrate on which they are grown [54–69]. Usually cells’ differentiation ability increases due to increased material stiffness, although exceptions to this rule exist [55, 57, 58, 60–66]. Because cells are interacting with the substrate surface [55, 57, 58, 60–66, 70], the cells growing on a stiff substrate exhibit greater rigidity [64, 67, 71], a more organised cellular

| No. | Evaluation criteria                                                                 | Ti     | Ti6Al4V | Ti6Al7Nb |
|-----|-------------------------------------------------------------------------------------|--------|---------|----------|
| 1   | The current use of this material in medicine                                      | High   | Very high | Minor    |
| 2   | Powder granulation, μm                                                             | 10–45  | 15–45   | 0–100    |
| 3   | Density, g/cm³                                                                     | 4.51   | 4.43    | 4.52     |
| 4   | Melting point, °C                                                                  | 1600–1660 | 1660   | 1520–1580 |
| 5   | Price, €/kg (state for 2014 year)                                                   | 400    | 500     | 250      |
| 6   | Availability                                                                       | High   | High    | Low      |
| 7   | Powder application in SLS/SLM process                                               | Yes    | Yes     | No       |

Table 1. Comparative heuristic analysis of pristine titanium, Ti6Al4V and Ti6Al7N powders.
cytoskeleton [55, 59, 63–67] and greater flattening [55, 57, 60, 63–66, 70, 72] than those growing on a more elastic substrate. Cells, especially fibroblasts and cells of smooth muscles, exhibit mechanotaxis (durotaxis), moving towards a substrate with greater rigidity [57, 62, 64–66, 72, 73]. Increased substrate rigidity is decisive for the reduced ability of cells to migrate [65], and different types of cells react differently to differentiated rigidity of a substrate made of engineering materials [54]. A material’s surface topography influences cells’ adhesion ability [74, 75], and they show an ability of adaptation to a material’s surface specificity [53, 76–79]. Surface topography is dictating proteins’ adhesion and creation of bonds, which is essential for material biocompatibility, influencing also morphology, spatial orientation, division and differentiation of cells [38, 80]. Cells’ behaviour is also influenced by surface texture and smoothness [2, 38, 74, 76, 77, 81–84]. Cell adhesion is more difficult on less developed surfaces with higher smoothness [85], whereas the division of osteoblasts is faster on surfaces with smaller smoothness [86–88], opposite to fibroblasts which are proliferating fastest on smoother surfaces [56, 89–92]. The flattening of cells is decreasing as the smoothness of the substrate surface is deteriorating [86, 88, 91, 92].

Additive technologies [93–95] can be employed, in particular, for producing different implants, including dental implants and bridges, individualised implants of the upper jaw bone, hip joint and skull fragments using suitable biomaterials. An exceptional usefulness of additive technologies of producing solid and microporous materials in medicine and dentistry has been confirmed by comparing powder metallurgy technologies, casting technologies, metallic foam manufacturing technologies and additive manufacturing technologies with procedural benchmarking techniques [96, 97] using a universal scale of relative states for comparative evaluation [96–99]. Considering the additive technologies applied most widely in industry, only few have found their application in prosthetics, especially in prosthodontics, that is, electron beam melting (EBM) [100–105], and also 3D printing for production of indirect models, although selective laser sintering/selective laser melting offers broadest opportunities (SLS/SLM) [100, 106–125]. The sintering/melting of grains takes place by remelting the particles of a new powder on the surface with the existing piece of an item being constituted by a laser beam moving in a programmed fashion in line with the pre-defined geometrical characteristics of a metal element being produced. SLS/SLM technologies are so attractive due to the opportunities offered by 3D design with the use of CAD methods and due to the related overall control over the materials fabricated, both, in terms of the structure, sizes and repeatability of geometric features. Microskeletons with controlled sizes and shapes of pores can also be manufactured.

A microporous element manufactured by SLS can be further worked and combined with other materials, for example, by infiltration or internal treatment of pores’ surface in an appropriately chosen technological process [117–121, 126–128]. Titanium and titanium alloys from Al, Nb and Ta [1, 2, 15, 26, 127–138], well tolerated by a human organism, have been long used in medicine and dentistry for prosthetic and implantological purposes, also fabricated by SLS. Titanium matrix materials do not cause allergic reactions and are stainless, feature high strength and hardness and also thermal conductivity several times lower than traditional prosthetic materials [139]. Titanium is a very thrombogenic material [140], and biocompatibility, especially thrombocompatibility [141] of this material can be enhanced by introducing alloy elements. Pores are dimensionally adapted to be filled by the reconstructed cells and their migration and also neovascularisation [142] for preventing blood clots [143]. Their section cannot be too small to prevent their sealing [144]. A porous structure of scaffolds should secure the
diffusion of nutrients and metabolism products. Permanently fixated scaffolds do not ensure scaffold removal as is the case with scaffolds removable during regeneration in the natural condition [143–145]. Other metallic materials can also be utilised for this purpose, for example, polymer materials [40, 81, 146–153] or polymer matrix composite materials with a fraction of metals or ceramic particles [81, 150]. Unlike metals and their alloys, polymer materials can be not only biocompatible, but also biodegradable and bioresorbable [29, 46, 154, 155], and also in some cases osteoinductive [156] and can reduce thrombogenic properties of the material [40]. Another concept relates, however, to covering the surface of metallic materials with other materials, also as a result of working an internal surface of pores [125, 157]. Porous metallic materials, chiefly Ti and Ta [158] and Mg [159], are used for non-biodegradable scaffolds primarily due to relatively high compressive strength and fatigue strength [160, 161]. Coatings of internal surfaces of pores are used, however, because they meet the imposed requirements better than metals and their alloys [40, 162, 163]. The following is necessary, especially, not to cause disease-related changes: the lack of a toxic effect of the implant material, the lack of its mutagenic properties, the lack of its effect on the composition of body fluids, both by the material being implanted as well as in the case of polymer materials, also by its decomposition products [40, 81, 147].

Original own works [117–120, 126, 164–180] have been undertaken concerning constructional solutions and fabrication technologies of a new generation of custom, original, hybrid, microporous high-strength engineering and biological materials with microporous rigid titanium and titanium alloy skeletons manufactured by selective laser sintering, whose pores are filled with living cells (Figure 1). This will ensure the natural ingrowth of a living tissue, at least in the connection zone of prosthetic/implant elements, with bone or organ stumps, and will eliminate the need to apply for patients the mechanical elements which are positioning and fixating the implants. The so constructed and fabricated implants, in the

Figure 1. Chart of constructional assumptions (a) hybrid and multilayer biologically active microporous composite engineering materials consisting of biologically active cellular structures and of implant-scaffolds; (b) implant-scaffolds with microporous zones acting as scaffolds.
connection zone with bone stumps, contain a porous zone, with surface treatment inside pores, enabling the living tissues to grow and they remain in an organism permanently and do not require re-operation.

As the adhesion and growth of living cells are dependent on the type and characteristics of the substrate, in order to implement the planned concept of manufacturing engineering and biological materials and implant-scaffolds, it is required to seek the most advantageous proliferation conditions of living cells inside the pores of a microporous skeleton made of titanium and titanium alloys, which is the underlying scope of the research presented in this chapter. It appears that the improvement of proliferation conditions of cells is ensured by a substrate made of fully compatible materials, including TiO₂, Al₂O₃ oxides and a hydroxyapatite, Ca₁₀(PO₄)₆(OH)₂. For this reason, it was decided to employ these materials as coatings of internal surfaces of pores of a microporous skeleton fabricated by SLS. Two technologies have been chosen, respectively, for the deposition of thin coatings onto the internal surfaces of pores, ensuring the uniform thickness of coatings on all the walls and openings of a substrate being coated, even with highly complicated shapes, that is, the so-called atomic layer deposition (ALD) [96, 124, 126, 128, 181–184] (Figure 2) and the sol-gel technology of coating deposition from the liquid phase by the immersion method [96, 181, 185–194] (Figure 3).

Figure 2. Sequence of the phenomena associated with ALD technology [96].
2. Structure and properties of selectively laser sintered microskeletons made of titanium and Ti6Al4V alloy

The elements used for the research were produced by an additive method by powder sintering in an SLS process. Selective laser sintering can be grouped into a stage of designing a given element, the outcome of which is a 3D CAD model in the .stl format, then transferred into a machine’s software, and another stage, at which an item designed virtually in advance is produced for real, a layer by layer, until a final product is obtained (Figure 4).

The following was used for model designing: Solid Works 2015 Pro and 3D Marcaron Engineering AutoFab (Software for Manufacturing Applications) software, version Autofab MCS 2.0 and Autofab MTT 64 and the CAD/CAM tools available in, respectively, SLM 250H system by MTT Technologies Group and in AM 125 system by Renishaw for selective laser sintering. The software enables to select model dimensions, constructional features, the type of the model volume filling either as solid or porous and to choose the size of a cell unit making up the entire model. A set of “hexagon cross” unit cells was used, selected in a geometrical analysis, and as a result of preliminary studies, from the set available in the software. By duplicating them, the entire elements were designed, consisting of nodes and single lattice fibres, linking the particular skeleton node (Figure 5). Fabrication conditions were also selected, at the stage of virtual design of elements, achievable in, respectively, SLM 250H
system by MTT Technologies Group and AM 125 by Renishaw for selective laser sintering, including layer thickness, laser power, laser beam diameter, scanning rate, distance between particular remelting paths. A spatial orientation of unit cells of 45° relative to the x-axis of the system of coordinates was also chosen experimentally, because other orientations analysed initially turned out to be less advantageous due to the mechanical properties of the elements produced (Figure 5). The structures of microporous skeletons with appropriately differentiated average sizes of pores of ~450, ~350 and ~250 μm, with suitable sizes of a unit cell of 700, 600 and 500 μm, were defined by reproducing and assuming suitable values characterising the spatial lattice, such as height, depth and width. Solid specimens were also made for comparative purposes.

Figure 4. Selective laser sintering technology process diagram [195].

Figure 5. (a, b) Hexagon cross unit cell; (c) image of structure of computer models presenting the arrangement of unit cells in the space of the system of coordinates at the angle of 45° relative to the x-axis.
It was very important to establish the correct laser power value, ranging between 50 and 200 W, and the laser beam diameter, of 30–150 μm, and also the distance between laser beams and distance between laser remelting paths equal to or smaller than the laser beam diameter in case of solid elements, as opposite to the variant when it is larger than the laser beam diameter, which is decisive for the porosity of the produced element. Such conditions were selected as a result of preliminary studies.

When a model is designed and the selected fabrication conditions are taken into account, it is transferred to the software of the SLM 250H system machine by MTT Technologies Group or AM 125 by Renishaw, where selective laser sintering takes place. The YFL fibre laser, with an active material doped with Ytterbium and the maximum power of, respectively, 400 and 200 W, was used in the devices. The skeleton microporous materials, fabricated by SLS, exhibit porosity which depends on the manufacturing conditions, including mainly laser power and laser beam diameter and the distance between laser beams and the distance between laser remelting paths. Solid titanium with the density of 4.51 g/cm³, corresponding to the density of solid titanium given in literature, can be achieved if the laser power of 110 W is applied. The smallest porosity of 61–67% corresponds to the selectively laser sintered elements with the highest mass and the average pore size of ~250 μm, whereas the highest porosity of 75–80% corresponds to elements with the smallest mass and the average pore size of ~450 μm. The porosity of 70–75% was obtained for the average pore size of ~350 μm.

Two types of powders with a spherical shape were used, respectively, for selective laser sintering to produce solid specimens and microporous skeletons (Figure 6a,b) and with the composition shown in Table 2, also confirmed with spectral examinations with the energy dispersive spectrometry (EDS) method (Figure 6c,d):

- titanium powder with Grade 4 and grain size of up to 45 μm, oxygen concentration reduced to 0.14%, the aim of which is to ensure process safety,
- Ti6Al4V alloy powder with the grain diameter of 15–45 μm, for medical applications.

Figure 7a and b and shows a surface structure of pristine titanium and Ti6Al4V alloy manufactured by selective laser sintering with laser beam size of 50 μm and laser power of 110 W. Chemical composition, examined with an EDS spectrometer, shows that Ti only exists in the first case in the sample (Figure 7c), and Ti, Al and V (Figure 7d) were identified in the other case, which corresponds to the data given in Table 2 for chemical composition of powders used for selective laser sintering. It was revealed in both cases that, apart from the completely sintered materials with revealed paths of laser beam transition, fine powder particles exist, as well, which – after sintering – should be removed mechanically or by chemical etching. On the surface of porous titanium microskeletons (Figures 8–10), apart from sintered titanium, there are grains of powder loosely bonded with a skeleton, which were not fully melted with a titanium microskeleton; the results of local remelting also exist, as indicated by the surface topography of porous titanium skeletons for the different arrangement of cell units. In order to remove such unfavourable surface effects, porous titanium, after selective laser sintering, was subjected to preliminary cleaning in an isopropyl alcohol solution with an ultrasound
washer. After getting rid of excessive powder from the pores of the titanium skeleton, it was subjected to etching in an aqua regia solution with the fraction volume of 3:1 HCl:HNO₃, for 1 hour with an ultrasound washer, to etch the surface remelting not removed in preliminary cleaning and the fine powder particles not attached permanently to the previously constituted titanium microskeleton. The samples were subjected to etching in an aqua regia solution, as a result of which about 3% of the sintered material mass was removed (Figure 11). The roughness of skeletons before etching is much higher than after etching (Figure 11). A 14% aqueous hydrofluoric acid solution can also be used alternatively for etching.

| Powder       | Mass concentration of elements, % |
|--------------|-----------------------------------|
|              | Al   | V    | C    | Fe | O   | N   | H   | Others total | Others each | Ti            |
| Ti           | –    | –    | 0.01 | 0.03 | 0.14 | 0.01 | 0.004 | <0.4      | <0.01        | Remainder |
| Ti6Al4V      | 6.35 | 4.0  | 0.01 | 0.2  | 0.15 | 0.02 | 0.003 | ≤0.4       | ≤0.1         |              |

Table 2. Chemical composition of the powders used for selective laser sintering.

Figure 6. Powder of (a) Ti, (b) Ti6Al4V alloy (SEM), (c, d) relevant diagrams of EDS [119].
The structural examinations of selectively laser sintered titanium and Ti6Al4V alloy were carried out in a transmission electron microscope, TITAN 80–300, by FEI. Titanium and Ti6Al4V alloy have a crystalline structure, hence for the appropriately high microscope resolution, one can observe the rows of atoms arranged parallel to each other, both, when the microscope is in the TEM transmission mode and in the STEM scanning-transmission mode (Figure 12).

It is not possible to use standard normalised conditions of mechanical tests due to a porous structure of the analysed materials, which are not covered by the system of EN standards, and also due to the manufacturing costs and time of the samples for tests of mechanical properties and due to a limited size of a working chamber and manufacturing device efficiency. A custom, own method was therefore established for performing such examinations with a universal tensile testing machine, Zwick 020, in the conditions principally corresponding to static tensile tests, three-point bending and compression tests. Moreover, specially adapted miniaturised samples were also produced for examinations of strength properties (Figure 13), with the dimensions of measuring parts of, respectively, $3 \times 3 \times 15 \text{ mm}$, $3 \times 10 \times 35 \text{ mm}$ (for support spacing of $30 \text{ mm}$) and $10 \times 10 \times 10 \text{ mm}$.

The mechanical properties of solid and porous materials fabricated by SLS, that is, sintered titanium and sintered Ti6Al4V alloy, were compared each time. The results of examinations of, respectively, tensile strength, bending strength and comprehensive strength were presented in
such order. The impact of laser power ranging 70–110 W was investigated in the first place on tensile strength values of sintered titanium and sintered Ti6Al4V alloy. The results of examinations for five samples, for each treatment option of each of such materials, are presented in Figure 14.

Figure 15 presents the comparison of diagrams of dependency between tensile stress and elongation for solid and porous laser sintered Ti and Ti6Al4V alloy samples with the pore size of approx. 250 μm, subjected to static tensile tests. The results were obtained to compare the conditions of
Figure 10. Surface topography of microskeletons made of Ti6Al4V alloy manufactured as multiplication of different unit cells presented with different magnificence (a, b, c); SEM images.

Figure 11. Surface topography of porous titanium skeletons with the pore size of ~450 μm (a) after etching in aqua regia solution (SEM), (b) after ultrasound cleaning, (c) after etching in aqua regia solution; (b, c) laser confocal microscope.

Figure 12. Crystalline structure of: (a) pristine titanium, (b) Ti6Al4V alloy; HRTEM image.
selective laser sintering, that is, with the laser power of 60 W, which is favourable for porous materials. The examinations pinpoint, however, they are completely unacceptable for solid materials. Bending strength tests were performed the same as tensile strength tests. The geometrical characteristics of the samples given in Figure 13 were selected. The tests were carried out in relation to the investigated solid materials, that is, sintered titanium, sintered Ti6Al4V alloy as well as in relation to porous materials manufactured by SLS. The results concerning such tests were obtained as previously, for comparable conditions of selective laser sintering, that is, for the laser power of 60 W. The impact of laser power ranging 70–110 W on bending strength values of sintered titanium and sintered Ti6Al4V alloy for five samples for each treatment variant of each of the materials is shown in Figure 16. Figure 17 compares the diagrams of dependency between bending stress and deflection for solid and porous Ti and Ti6Al4V alloy samples with the pore size of approx. 250 μm, selectively laser sintered in the given conditions.
The results of compressive strength tests are also presented for solid and porous Ti and Ti6Al4V alloy samples with the pore size of approx. 250 μm, selectively laser sintered with the laser power of 60 W (Figure 18).

Figure 15. Comparison of diagrams of dependency between tensile stress and elongation for solid and porous laser sintered Ti and Ti6Al4V alloy samples with the pore size of approx. 250 μm [119].

Figure 16. Comparison of diagrams of dependency between bending stress and deflection for solid samples made of Ti6Al4V alloy and pristine titanium sintered at different laser powers [119].

The results of compressive strength tests are also presented for solid and porous Ti and Ti6Al4V alloy samples with the pore size of approx. 250 μm, selectively laser sintered with the laser power of 60 W (Figure 18).
3. Structure and properties of ALD coatings on the substrate from selectively laser sintered microskeletons made of titanium and Ti6Al4V alloy

The ALD technique enables to deposit a chosen TiO₂ coating very uniformly across the entire surface of a part being treated, also if this part has a porous structure, as is the case with scaffolds. Changes in the sample colour, depending on the number of the executed ALD cycles,
hence depending on the thickness of the deposited TiO$_2$ layer, is an interesting phenomenon observed with a bare eye (Figure 19) and in a light stereoscopic microscope, Discovery V12 Zeiss, allowing to view colourful magnified images. An uncoated element has silver-metallic colour, and when subjected to surface treatment by the ALD method, it becomes, respectively: brown-gold (500 cycles), navy blue (1000 cycles) and light blue with silver shade (1500 cycles) (Figure 19).

Scaffolds manufactured by the selective laser sintering method from powders of titanium and biocompatible Ti6Al4V titanium alloy, then coated with a thin layer of Al$_2$O$_3$ in the process of deposition of single atomic layers, ALD, were examined – analogously as TiO$_2$ layers – by means of a stereomicroscope, Discovery V12 Zeiss, allowing to identify that – along with the changing deposition thickness of an ALD layer – the colour of scaffolds is changing. The scaffolds, onto which Al$_2$O$_3$ layers were deposited in 500 cycles, are dark brown; such onto which Al$_2$O$_3$ layers were deposited in 1000 cycles are navy blue, and such onto which Al$_2$O$_3$ layers were deposited in 1500 cycles are dark blue (Figure 20). The differences in colours are also visible with a bare eye.

The measurements of layers’ thickness with a spectroscope ellipsometer for each sample with deposited TiO$_2$ layers were performed in 25 places and statistical calculations were carried out.
out, which has permitted to create a series of 2D maps of thickness distribution of the deposited atomic layers (Figure 21). The average thickness of TiO$_2$ layers deposited by ALD technique for the analysed cases of 500, 1000 and 1500 cycles is, respectively, 56, 99 and 149 nm. The difference in the thickness of the deposited TiO$_2$ layers on the studied area does not exceed 2 nm, which can be analysed in detail by studying layer thickness distribution maps. The best results were obtained for a layer deposited in 1000 cycles. A difference in the thickness of the deposited layer in this case does not exceed 1.1 nm across the entire area of the surface-treated item.

The topography of the scaffolds' surface coated with TiO$_2$ layers, deposited by the ALD method, was examined by means of an atomic force microscope, AFM XE-100 Park System, in two and three dimensions (Figure 22). There are irregularities with a nanometric scale on the scaffold surface, the number of which is rising proportionally to the number of the deposited layers. In particular, a layer deposited in 500 cycles has a rather uniform granular structure and the larger clusters of atoms are occurring on it only occasionally. In the case of a layer deposited in 1000 cycles, clusters of atoms with a diameter of about 1 μm occur every several microns. The biggest clusters of atoms, forming “islands” with the length of up to several micrometres, occur in the case of a layer deposited in 1500 cycles.

The detailed surface morphology examinations of the produced TiO$_2$ layers were performed with an electron scanning microscope, Supra 35, by Zeiss, with the accelerating voltage of
10–20 kV (Figure 22). Secondary Electrons detection with SE detectors by In Lens was used to obtain surface topography images. A nanometric thickness of TiO₂ layers deposited by ALD results in the fact that the layers can be observed in a scanning electron microscope only for very high magnifications of 150kx (Figure 22). A clear difference between a scaffold surface without surface treatment and scaffold surface covered with a TiO₂ layer in an ALD process can be observed only when such high magnifications are used. The scaffold surface, immediately following fabrication, is smooth with clear longitudinal bands arranged every several dozen/several hundreds of nanometres, corresponding to the laser activity direction.

Figure 21. Titanium scaffolds coated with TiO₂ layers deposited by ALD after: (a, b) 500 cycles, (c, d) 1000 cycles, (e, f) 1500 cycles; (a, c, e) thickness deposition maps; (b, d, f) AFM image of 3D surface topography.

Figure 22. Scaffold surface with TiO₂ layer deposited in 1500 cycles presented with different magnificence (a, b, c); SEM images.
The deposited atomic TiO$_2$ layer, when magnified by approx. 150kx, is visible as a “sheep”, that is, a set of numerous adjacent oval granules of which only a few have a larger diameter.

The detailed surface morphology examinations of thin Al$_2$O$_3$ layers produced in a process of deposition of single atomic ALD layers, the same as TiO$_2$ layers, was examined by means of a scanning electron microscope, Supra 35, by Zeiss, with the accelerating voltage of 2–10 kV (Figures 23 and 24) with different magnification of up to 100kx inclusive. The examinations performed with the highest magnification allow to spot a clear difference between the scaffold surface without surface treatment and the scaffold surface with a deposited layer of aluminium oxide, which is coated with convexities with the size of up to approx. 10 nm if 500 cycles are used, to approx. 200 nm if layers are deposited in 1500 cycles (Figures 23 and 24).

A TiO$_2$ layer deposited by ALD onto a surface of a scaffold made of pristine titanium is of an amorphous structure, opposite to a crystalline titanium structure clearly shown in TEM images (Figure 25), as confirmed by TiO$_2$ layer examinations with a transmission electron microscope, TITAN 80–300 by FEI. Depending on the number of cycles, the thickness of a TiO$_2$ layer deposited by ALD varies between several dozens to hundred and a few dozens of nanometres. The examinations of TiO$_2$ layers with a transmission electron microscope on samples in a form of thin foils prepared with a focused ion beam microscope (FIB) with the use of gallium arsenide with deposition of a thin layer of platinum show that the both chemical

![Figure 23. Surface topography of scaffolds manufactured from: (a–c) pristine titanium; (d–f) Ti6Al4V alloy and coated with Al$_2$O$_3$ layer in: (a, d) 500; (b, e) 1000; (c, f) 1500 cycles; SEM.](http://dx.doi.org/10.5772/intechopen.70491)
elements, apart from titanium and oxygen, are found on the EDS chart from an area situated on the periphery of the deposited layer, located in the direct neighbourhood of the protected layer of platinum (Figure 25). The EDS examinations of the deposited layers carried out in the region closer to the substrate reveal the presence of titanium and oxygen only (Figure 25), as is also confirmed by a prepared distribution map of chemical elements (Figure 26).

In order to confirm the presence of layers consisting of TiO$_2$ on the surface of a scaffold fabricated from TiAl6V4 powder, qualitative examinations of chemical composition were performed with the EDS scattered X-ray radiation spectroscopy method using an EDS (energy dispersive spectrometer), and a scaffold not containing a TiO$_2$ layer was considered a reference material. An analysis of the diagrams shown in Figure 27 indicates that a spectrum was recorded in both cases with reflexes distinctive for titanium, aluminium and vanadium, whereas a reflex coming from titanium and oxygen exists additionally in a material covered with a layer of ALD, which corresponds to the occurrence of a TiO$_2$ layer on the surface of this material. Examinations were also undertaken using the inVia Reflex device by Renishaw, being an automated Raman system. A Raman spectrum obtained with the wave dispersion method, after base line correction, within the spectral range of 150–3200 cm$^{-1}$, is coming from a material being a scaffold, while a Raman spectrum coming from a material coated with a thin layer of titanium dioxide is shown in Figure 27, which – just like an EDS analysis – confirms the presence of titanium, aluminium and vanadium in the reference material; moreover
oxygen, present in the surface layer, is found – apart from such chemical elements – in a material coated with a TiO$_2$ layer.

It was found, with special WiRETM 3.1 software, that a layer deposited by the ALD method is anatase, being a polymorphous type of titanium dioxide. **Figure 28** shows the images of

*Figure 25.* Amorphous TiO$_2$ layer deposited onto pristine titanium with a crystalline structure in a technological process lasting 1500 cycles; (a–c) HRTEM; (d, e) qualitative analysis of EDS chemical composition of TiO$_2$ layer: (d) from the peripheral region contiguous to the protective platinum layer; (c) near a titanium substrate.

*Figure 26.* Distribution map of chemical elements present in the TiO$_2$ layer situated near titanium substrate.

oxygen, present in the surface layer, is found – apart from such chemical elements – in a material coated with a TiO$_2$ layer.

It was found, with special WiRETM 3.1 software, that a layer deposited by the ALD method is anatase, being a polymorphous type of titanium dioxide. **Figure 28** shows the images of
points where spectra were recorded, originating from a reference Ti6Al4V scaffold and a scaffold covered with a layer of TiO2; the images were made with a confocal microscope.

Structural examinations were performed with the X-ray diffraction (XRD) method (Figure 29) with an X’Pert Pro X-ray diffractometer by Panalytical (CuKα radiation, $\lambda = 1.54050 \times 10^{-10}$ m) using filtered radiation of a copper lamp with the voltage of 45 kV and a filament current of 35 mA, and the deposited TiO2 layers were examined with the razing-incidence method due to the small thickness of not more than 150 nm, thus extinguishing
the peaks coming from the substrate. Reflexes coming from three polymorphous variants of 
titanium dioxide, that is, anatase, rutile and brookite, were identified in the examinations.  

In order to confirm that the observed ALD layers are fabricated from \( \text{Al}_2\text{O}_3 \) aluminium oxide, qualitative examinations were performed of chemical composition with the EDS scattered X-ray radiation spectroscopy method and were displayed as diagrams in Figure 30. For thin \( \text{Al}_2\text{O}_3 \) layers, deposited on a scaffold made of titanium, spectra were recorded with reflexes characteristic for aluminium and oxygen, coming from a layer and for titanium coming from the substrate (Figure 30a). A spectrum was recorded for a Ti6Al4V scaffold, with

---

**Figure 29.** X-ray diffraction pattern of \( \text{TiO}_2 \) layer applied by atomic layer deposition (ALD) performed with the razing-incidence X-ray diffraction method.

**Figure 30.** EDS spectrum made for scaffolds manufactured from: (a) pristine titanium; (b) Ti6Al4V titanium alloy; and coated with \( \text{Al}_2\text{O}_3 \) layers in 500 cycles.
reflexes characteristic for titanium and vanadium, coming from the substrate and oxygen from the layer. The reflex recorded from aluminium comes from the coating and substrate (Figure 30b). Distribution maps of chemical elements were additionally performed in the investigated materials. The presence of titanium, aluminium and oxygen was found in a titanium scaffold coated with aluminium oxide, and additionally vanadium is also found in a scaffold produced from Ti6Al4V. Supplementary X-ray examinations were also performed as a result of which no crystalline phase of aluminium oxide was found for ALD layers, which indicates their amorphous form. Such a result is expected due to the analogy with TiO$_2$ layers – deposited with the same method – subjected to examinations at a nanometric scale. An amorphous structure of the deposited layers is clearly seen in TEM images as opposed to crystalline titanium being the substrate.

4. Structure and properties of layers of hydroxyapatite deposited with the sol-gel immersion method on microporous selectively laser sintered skeletons made of titanium and Ti6Al4V alloy

Thin layers of hydroxyapatite were deposited with the immersion sol-gel technique (dip coating). The solution was prepared using hydroxyapatite nanopowder (HA), polyethylene glycol (PEG), glycerine and ethyl alcohol. The scaffolds manufactured from pristine titanium and Ti6Al4V alloy, coated with a layer of hydroxyapatite, manufactured by the sol-gel technique, were examined by means of a stereomicroscope microscope, Discovery V12 ZEISS. The detailed surface morphology examinations of the produced layers were undertaken with an electron scanning microscope Supra 35 by Zeiss. SEM images of thin layers were presented, on which hydroxyapatite particles are visible (Figures 31 and 32). The shape of the majority of hydroxyapatite particles is oval, however, a large content of particles with an elongated shape, with rounded, sometimes sharpened edges, is observed. The size of hydroxyapatite particles can be estimated at 20–80 nm. In case of sol-gel layers deposited on a scaffold made of titanium, spectra were recorded with reflexes characteristic for calcium, phosphorus and

![Figure 31. Scaffold made of Ti with the sol-gel layer of hydroxyapatite deposited after 10 immersions presented with different magnificence (a, b); SEM images.](image-url)
oxygen coming from a layer, and being the main hydroxyapatite components, and a reflex for titanium coming from the substrate (Figure 33). Similarly, for a scaffold made of Ti6Al4V alloy, spectra were recorded with reflexes characteristic for calcium, phosphorus and oxygen coming from the layer, and titanium, aluminium and vanadium, coming from the substrate. In addition, distribution maps of chemical elements were additionally performed in the investigated samples. Titanium was identified in a pure Ti scaffold, and also vanadium if Ti6Al4V alloy was also used. In the samples covered with a sol-gel layer, apart from the chemical elements coming from the substrate (e.g. titanium or titanium, aluminium and vanadium), calcium, phosphorus and oxygen were additionally identified, coming from a layer of hydroxyapatite (Figure 33). Structural examinations of sol-gel layers were performed by means of an X-ray structure analysis. Reflexes were identified coming from hydroxyapatite (Figure 34).
5. Final remarks

One of the many elements largely influencing the quality of the society’s life is the standard of healthcare. For this reason, all the activities in this sphere are considered as priorities in social policy in many countries and by international organisations. The life quality of patients after mechanical injuries, with tumorous and genetic diseases and with lost teeth greatly depends on the technical level, innovativeness and avant-garde solutions for medical and dental implants. It is obvious that the successfulness of the medical care provided depends on competencies of the doctors performing diagnostics, taking relevant decisions, applying appropriate therapies and related surgical procedures. The issue is a synergy of the actions jointly undertaken by medical doctors and engineers. The aspects of engineering-assisted medicine relate, both, to the constructional, material and technological design of, in particular, medical and dental implants. The development of medical implants is largely dependent upon advancements in biomaterials engineering, characterised by the required biological compatibility and harmonious interaction with living matter, without acute or chronic reactions, nor an inflammatory condition of the surrounding tissues after introduction into an organism. The advanced research efforts described in this chapter concern the engineering aspects of development of innovative implant-scaffolds, which enable the adhesion and proliferation of a patient’s living cells into an intentionally designed porous structure of an implant which, on one hand, acts as an element transferring high stresses existing in an organism, and on the other hand acts as a scaffold into which a patient’s cells are growing into. Metallic materials, despite their disadvantages, such as insufficient corrosive resistance and insufficient biotolerance in some areas of applications, are characterised by a pool of very advantageous mechanical properties. High fatigue corrosion resistance, brittle cracking resistance and tensile and bending strength should be considered especially significant. However, weak susceptibility of metallic materials as a substrate for cells’ development is undoubtedly an issue. An effect of a substrate on the proliferation of living cells has been described in detail based

Figure 34. X-ray diffraction pattern of hydroxyapatite layer made with the sol-gel method.
on comprehensive literature studies. This aspect is very complex. Porous metallic materials are an attractive implantation material due to better, as compared to traditional alloys, accommodation of the elasticity modulus to the bone and because bone tissue can grow on pores and by ensuring appropriate implant fixation to the bone. Dedicated technologies ensuring surface treatment inside pores with the size of 200–400 \( \mu m \) are fully innovative and require very advanced nanotechnological instrumentation. Titanium and titanium alloys belong to a group of metallic materials applied for many years in the fabrication of implants for bone surgery, maxillo-facial surgery and prosthetics. The principal reasons include relatively low density, a beneficial strength-to-yield stress limit ratio, good corrosive resistance and best biocompatibility in this group of biomaterials. Titanium and titanium alloys are considered as such allowing to eliminate the risk associated with a harmful effect of chemical elements occurring as alloy additives in metallic materials, and concerns and controversies around some of them have not been scientifically proven until now.

A porous scaffold, with its dimensions and shape perfectly suited to a patient’s tissue loss, made of a biocompatible material (Ti or Ti6AlV4), additionally coated with a nanometric layer of osteoconductive titanium oxide, aluminium oxide or hydroxyapatite inside pores, seems to be a breakthrough solution. It is a highly hybridised and composite engineering material, fabricated by a hybrid technology combining avant-garde and experimental additive technologies of selective laser sintering SLS, in conjunction with ALD and sol-gel technologies appropriate for nanotechnology. Modern CAD/CAMD software allows to convert the data acquired at a clinical stage into a 3D solid model of a patient’s lost tissues. The model is then converted into a porous model through the multiplication of a unit cell whose dimensions and shape may be designed according to a patient’s individual preferences. The pores existing in the material structure have the diameter of up to 500 \( \mu m \) and should be open, because a scaffold, in its intended conditions of use, is to grow through a patient’s living tissue.

This chapter presents the outcomes of numerous author’s complementary technological, structural and strength investigations which are a basis for optimised selection of engineering materials, adequate technologies and constructional assumptions for completely new and innovative products. Biomimetic, light, porous, rough and biocompatible materials with unique mechanical and functional properties finding their application for completely innovative scaffolds and implant-scaffolds can be manufactured owing to a custom combination of advanced methods of computer aided materials design and selective laser sintering (SLS) of titanium and Ti6AlV4 alloy powders with avant-garde deposition methods of single atomic ALD or sol-gel methods. A series of the investigations performed to date, in which technological conditions were established for the fabrication of this type of coatings inside pores, was completed successfully, which is presented thoroughly in this chapter. The role of the manufactured layers, with their thickness which can be programmed in advance, and not only controlled post factum, is to enhance osteoconduction of the materials which are to be ultimately placed in a human organism. The application of the technologies and materials described is of fundamental significance to ensure the synergy of clinical effects obtained by medical doctors and dentists by classical prosthetics and implantation and the natural nesting and proliferation of living tissues in a microporous bonding zone with scaffolds or implant-scaffolds created from the newly developed engineering materials. It is the authors’ intention to launch such new products soon for broad application in medicine and regenerative and
intervention dentistry. Scaffolds will be fabricated this way in the form of microporous skeletons, and, optionally, implant-scaffolds consisting of a solid core and a microporous, strongly developed surface layer, connected in a hybrid way into the solid whole. The results of the investigations conducted allow to perform the currently pursued author’s biological research pertaining to the nesting and proliferation of living tissues in the micropores of the created porous microskeletons and to assess the deposition of internal surfaces of micropores with layers supporting the growth of living tissues. Another report will be drafted following the completion of the research, concerning the details of the biological and clinical investigations performed, supplementary to the research and engineering works presented in this chapter.

Acknowledgements

The research presented in the chapter was realised in connection with the Project POIR. 01.01.01-00-0485/16-00 on “IMSKA-MAT Innovative dental and maxillofacial implants manufactured using the innovative additive technology supported by computer-aided materials design ADDMAT” realised by the Medical and Dental Engineering Centre for Research, Design and Production ASKLEPIOS in Gliwice, Poland and co-financed by the National Centre for Research and Development in Warsaw, Poland.

Author details

Anna D. Dobrzańska-Danikiewicz*, Leszek A. Dobrzański¹, Marek Szindler³, Lech B. Dobrzański¹, Anna Achtelik-Franczak¹ and Eugeniusz Hajduczek³#

*Address all correspondence to: anna.dobrzanska.danikiewicz@gmail.com

1 Medical and Dental Engineering Centre for Research, Design and Production Asklepios, Gliwice, Poland

2 University of Zielona Góra, Faculty of Mechanical Engineering, Zielona Góra, Poland

3 Faculty of Mechanical Engineering, Silesian University of Technology, Gliwice, Poland

# Deceased author

References

[1] Anselme K, Bigerelle H. Topography effects of pure titanium substrates on human osteoblast long-term adhesion. Acta Biomaterialia. 2005;1:211-222. DOI: 10.1016/j.actbio.2004.11.009
[2] Huang H-H, Ho C-T, Lee TH, Lee T-L, Liao KK, Chen FL. Effect of surface roughness of ground titanium on initial cell adhesion. Biomolecular Engineering. 2004;21:93-97. DOI: 10.1016/j.bioeng.2004.05.001

[3] Kaiser LR. The future of multihospital systems. Topics in Health Care Financing. 1992;18:32-45

[4] Cogle CR, Guthrie SM, Sanders RC, Allen WL, Scott EW, Petersen BE. An overview of stem cell research and regulatory issues. Mayo Clinic Proceedings. 2003;78:993-1003

[5] Metallo CM, Azarin SM, Ji L, De Pablo JJ, Palecek SP. Engineering tissue from human embryonic stem cells. Journal of Cellular and Molecular Medicine. 2008;12:709-729

[6] Atala A, Lanza R, Thomson JA, Nerem R, editors. Principles of Regenerative Medicine. Second ed. San Diego: Academic Press; 2011. p. 1202

[7] Regenerative Medicine 2006, Report. US National Institutes of Health. 2006. Available from: http://stemcells.nih.gov/staticresources/info/scireport/PDFs/Regenerative_Medicine_2006.pdf [Accessed: 2017-03-14]

[8] Placzek MR, Chung I-M, Macedo HM, Ismail S, Mortera Blanco T, Lim M, Cha JM, Fauzi I, Kang Y, Yeo DCL, Ma CYJ, Polak JM, Panoskaltsis N, Mantalaris A. Stem cell bioprocessing: Fundamentals and principles. Journal of The Royal Society Interface. 2009;6:209-232

[9] Fung YC. A Proposal to the National Science Foundation for an Engineering Research Center at UCSD. Center for the Engineering of Living Tissues. UCSD #865023; 2001

[10] Langer R, Vacanti JP. Tissue engineering. Science. 1993;260:920-926

[11] Viola J, Lal B, Grad O. The Emergence of Tissue Engineering as a Research Field. USA: The National Science Foundation; 2003. Available from: https://www.nsf.gov/pubs/2004/nsf0450/start.htm Accessed: 2017-03-17

[12] Mac Arthur BD, Oreffo ROC. Bridging the gap. Nature. 2005;433:19

[13] Atala A, Lanza RP, editors. Methods of Tissue Engineering. San Diego: Academic Press; 2002. p. 1285

[14] Lanza RP, Langer R, Vacanti J, editors. Principles of Tissue Engineering. San Diego: Academic Press; 2000. p. 995

[15] Dobrzańska-Danikiewicz AD, Gawel TG, Wolany W. Ti6Al4V titanium alloy used as a modern biomimetic material. Archives of Materials Science and Engineering. 2015;76:150-156

[16] Dobrzański LA, Basis of Material and Metal Science: Engineering materials with basis of materials design. WNT: Warszawa; 2002. 1500 p. ISBN 83-204-2793-2 (in Polish)

[17] Caiazzo F, Cardaropoli F, Alfieri V, et al. Disk-laser welding of Ti-6Al-4V titanium alloy plates in T-joint configuration. Procedia Engineering. 2017;183:219-226
[18] Donachie MJ, Donachie SJ. Superalloys: A Technical Guide. Materials Park, Ohio: ASM International; 2002

[19] Shin H, Jo S, Mikos AG. Biomimetic materials for tissue engineering. Biomaterials. 2003;24:4353-4364

[20] Farrell T. Superalloy materials now cost competitive in vacuum furnace hot-zone construction. Industrial Heating. 2005;72:129-133

[21] Ramakrishnaiah R, al Kheraif AA, Mohammad A, et al. Preliminary fabrication and characterization of electron beam melted Ti–6Al–4V customized dental implant. Saudi Journal of Biological Sciences. 2017;24:787-796

[22] Parthasarathy J, Starly B, Raman S, Christensen A. Mechanical evaluation of porous titanium (Ti6Al4V) structures with electron beam melting (EBM). Journal of the Mechanical Behavior of Biomedical Materials. 2010;3:249-259

[23] Toh WQ, Sun Z, Tan X, et al., Comparative study on tribological behavior of Ti-6Al-4V and Co-Cr-Mo samples additively manufactured with electron beam melting. Proceedings of the 2nd International Conference on Progress in Additive Manufacturing (Pro-AM 2016); 2016. pp. 342-348

[24] Ceretti E, Gay JDC, Rodriguez CA, JVL d S. Biomedical Devices: Design, Prototyping, and Manufacturing. John Wiley & Sons, Inc., Hoboken, New Jersey, USA; 2017

[25] Elias C, Lima J, Valiev R, Meyers M. Biomedical applications of titanium and its alloys. Journal of Metals. 2008;60:46-49

[26] Mrksich M. A surface chemistry approach to studying cell adhesion. Chemical Society Reviews. 2000;29:267-273. DOI: 10.1039/a705397e

[27] Ross AM, Jiang Z, Bastmeyer M, Lahann J. Physical aspects of cell culture substrates: Topography, roughness, and elasticity. Small. 2012;8:336-355. DOI: 10.1002/smm1.201100934

[28] Xu Y, Shi Y, Ding S. A chemical approach to stem-cell biology and regenerative medicine. Nature. 2008;453:338-344. DOI: 10.1038/nature07042

[29] Griffith LG. Polymeric biomaterials. Acta Materialia. 2000;48:263-277. DOI: 10.1016/S1359-6454(99)00299-2

[30] Dee KC, Andersen TT, Bizios R. Osteoblast population migration characteristics on substrates modified with immobilized adhesive peptides. Biomaterials. 1999;20:221-227

[31] Hynes RO. Cell adhesion: Old and new questions. Trends in Cell Biology. 1999;9:M33-M37

[32] Benoit DSW, Anseth KS. The effect on osteoblast function of colocalized RGD and PHSRN epitopes on PEG surfaces. Biomaterials. 2005;26:5209-5220. DOI: 10.1016/j.biomaterials.2005.01.045

[33] Garcia AJ, Vega MD, Boettiger D. Modulation of cell proliferation and differentiation through substrate-dependent changes in fibronectin conformation. Molecular Biology of the Cell. 1999;10:785-793
[34] Spargo BJ, Testoff MA, Nielsen TB, Stenger DA, Hickman JJ, Rudolph AS. Spatially controlled adhesion, spreading, and differentiation of endothelial cells on self-assembled molecular monolayers. Proceedings of the National Academy of Sciences of the USA. 1994;91:11070-11074

[35] Fuller G, Shields D. Molecular Basis of Cell Biology. Chapter 8. Warszawa: Wydawnictwo Lekarskie PZWL; 2005. 300 p. ISBN: 83-200-3259-8 (in Polish)

[36] Petersen S, Gattermayer M, Biesalski M. Hold on at the right spot: Bioactive surfaces for the design of live-cell micropatterns. Advances in Polymer Science. 2011;240:35-73. DOI: 10.1007/12_2010_77

[37] Lee MH, Ducheyne P, Lynch L, Boettiger D, Composto RJ. Effect of biomaterial surface properties on fibronectin-α5β1 integrin interaction and cellular attachment. Biomaterials. 2006;27:1907-1916. DOI: 10.1016/j.biomaterials.2005.11.003

[38] Roach P, Eglin D, Ronde K, Perry CC. Modern biomaterials: A review – Bulk properties and implications of surface modifications. Journal of Materials Science, Materials in Medicine. 2007;18:1263-1277. DOI: 10.1007/s10856-006-0064-3

[39] McClary KB, Ugarova T, Grainger DW. Modulating fibroblast adhesion, spreading, and proliferation using self-assembled monolayer films of alkylthiols on gold. Journal of Biomedical Materials Research. 2000;50:428-439

[40] Florjańczyk Z, Penczka S, editors. Chemistry of Polymers. Volume 3. Natural Polymers and Polymers with Special Properties. Warszawa: Oficyna Wydawnicza Politechniki Warszawskiej; 1999. 25 p. ISBN: 83-7207-029-6 (in Polish)

[41] Scotchford CA, Gilmore CP, Cooper E, Leggett GJ, Downes S. Protein adsorption and human osteoblast-like cell attachment and growth on alkylthiol on gold self-assembled monolayers. Journal of Biomedical Materials Research. 2002;59:84-99

[42] Comelles J, Estévez M, Martínez E, Samitier J. The role of surface energy of technical polymers in serum protein adsorption and MG-63 cells adhesion. Nanomedicine: Nanotechnology, Biology, and Medicine. 2010;6:44-51. DOI: 10.1016/j.nano.2009.05.006

[43] Yang L, Li Y, Sheldon BW, Webster TJ. Altering surface energy of nanocrystalline diamond to control osteoblast responses. Journal of Materials Chemistry. 2012;22:205-214. DOI: 10.1039/C1JM13593G

[44] Lai H-C, Zhuang L-F, Liu X, Wieland M, Zhang Z-Y, Zhang Z-Y. The influence of surface energy on early adherent events of osteoblast on titanium substrates. Journal of Biomedical Materials Research, Part A. 2009;93:289-296. DOI: 10.1002/jbm.a.32542

[45] Yap FL, Zhang Y. Protein and cell micropatterning and its integration with micro/nanoparticles assembly. Biosensors and Bioelectronics. 2007;22:775-788. DOI: 10.1016/j.bios.2006.03.016

[46] Fabianowski W, Polak B, Lewandowska-Szumiel M. Polymers used for bone reconstruction - evaluation of selected polymeric substrates in osteoblast culture in vitro. Polimery. 2004;49:522-529 (in Polish)
[47] Papenburg BJ, Rodrigues ED, Wessling M, Stamatialis D. Insights into the role of material surface topography and wettability on cell-material interactions. Soft Matter. 2010;6:4377-4388. DOI: 10.1039/B927207K

[48] Curran JM, Chen R, Hurt JA. Controlling the phenotype and function of mesenchymal stem cells in vitro by adhesion to silane-modified clean glass surfaces. Biomaterials. 2005;26:7057-7067. DOI: 10.1016/j.biomaterials.2005.05.008

[49] Keselowsky BG, Collard DM, Garcia AJ. Integrin binding specificity regulates biomaterial surface chemistry effects on cell differentiation. Proceedings of the National Academy of Sciences of the USA. 2005;102:5953-5957. DOI: 10.1073/pnas.0407356102

[50] Lan MA, Gersbach CA, Michael KE, Keselowsky BG, Garcia AJ. Myoblast proliferation and differentiation on fibronectin-coated self assembled monolayers presenting different surface chemistries. Biomaterials. 2005;26:4523-4531. DOI: 10.1016/j.biomaterials.2004.11.028

[51] Liu ZZ, Wong ML, Griffiths LG. Effect of bovine pericardial extracellular matrix scaffold niche on seeded human mesenchymal stem cell function. Scientific Reports. 2016;6(37089):1-12. DOI: 10.1038/srep37089

[52] Sakakibara K, Hill JP, Ariga K. Thin-film-based nanoarchitectures for soft matter: Controlled assemblies into two-dimensional worlds. Small. 2011;7:1288-1308. DOI: 10.1002/smll.201002350

[53] Faid K, Voicu R, Bani-Yaghoub M, Tremblay R, Mealing G, Py C, Barjovanu R. Rapid fabrication and chemical patterning of polymer microstructures and their applications as a platform for cell cultures. Biomedical Microdevices. 2005;7:179-184. DOI: 10.1007/s10544-005-3023-8

[54] Wells RG. The role of matrix stiffness in regulating cell behavior. Hepatology. 2008;47:1394-1400. DOI: 10.1002/hep.22193

[55] Rehfeldt F, Engler AJ, Eckhardt A, Ahmed F, Discher DE. Cell responses to the mechanochemical microenvironment – Implications for regenerative medicine and drug delivery. Advanced Drug Delivery Reviews. 2007;59:1329-1339. DOI: 10.1016/j.addr.2007.08.007

[56] Marklein RA, Burdick JA. Controlling stem cell fate with material design. Advanced Materials. 2010;22:175-189. DOI: 10.1002/adma.200901055

[57] Kim HD, Peyton SR. Bio-inspired materials for parsing matrix physicochemical control of cell migration: A review. Integrative Biology. 2012;4:37-52. DOI: 10.1039/c1ib00069a

[58] Ehrbar M, Sala A, Lienemann P, Ranga A, Mosiewicz K, Bittermann A, Rizzi CS, Weber FE, Lutolf MP. Elucidating the role of matrix stiffness in 3D cell migration and remodelling. Biophysical Journal. 2011;100:284-293. DOI: 10.1016/j.bpj.2010.11.082

[59] Engler AJ, Sen S, Sweeney HL, Discher DE. Matrix elasticity directs stem cell lineage specification. Cell. 2006;126:677-689. DOI: 10.1016/j.cell.2006.06.044
[60] Moore SW, Sheetz MP. Biophysics of substrate interaction: Influence on neural motility, differentiation, and repair. Developmental Neurobiology. 2011;71:1090-1101. DOI: 10.1002/dneu.20947

[61] Lutolf MP, Gilbert PM, Blau HM. Designing materials to direct stem-cell fate. Nature. 2009;462:433-441. DOI: 10.1038/nature08602

[62] Lo CM, Wang HB, Dembo M, Wang Y-L. Cell movement is guided by the rigidity of the substrate. Biophysical Journal. 2000;79:144-152. DOI: 10.1016/S0006-3495(00)76279-5

[63] Kollmannsberger P, Bidan CM, Dunlop JWC, Fratzl P. The physics of tissue patterning and extracellular matrix organisation: How cells join forces. Soft Matter. 2011;7:9549-9560. DOI: 10.1039/C1SM05588G

[64] Breuls RGM, Jiya TU, Smit TH. Scaffold stiffness influences cell behavior: Opportunities for skeletal tissue engineering. The Open Orthopaedics Journal. 2008;2:103-109. DOI: 10.2174/1874325000802010103

[65] Nemir S, West JL. Synthetic materials in the study of cell response to substrate rigidity. Annals of Biomedical Engineering. 2010;38:2-20. DOI: 10.1007/s10439-009-9811-1

[66] Bhatia SK. Engineering Biomaterials for Regenerative Medicine: Novel Technologies for Clinical Applications. New York, Dordrecht, Heidelberg, London: Springer Science+Business Media; 2012. p. 346. DOI: 10.1007/978-1-4614-1080-5

[67] Engler AJ, Griffin MA, Sen S, Bönne mann CG, Sweeney HL, Discher DE. Myotubes differentiate optimally on substrates with tissue-like stiffness: Pathological implications for soft or stiff microenvironments. The Journal of Cell Biology. 2004;166:877-887. DOI: 10.1083/jcb.200405004

[68] Miroshnikova YA, Jorgens DM, Spirio L, Auer M, Sarang-Sieminski AL, Weaver VM. Engineering strategies to recapitulate epithelial morphogenesis within synthetic 3 dimensional extracellular matrix with tunable mechanical properties. Physical Biology. 2011;8(026013). DOI: 10.1088/1478-3975/8/2/026013

[69] Zaman MH, Trapani LM, Sieminski AL, MacKellar D, Gong H, Kamm RD, Wells A, Lauffenburger DA, Matsuda ira P. Migration of tumor cells in 3D matrices is governed by matrix stiffness along with cell-matrix adhesion and proteolysis. Proceedings of the National Academy of Sciences of the USA. 2006;103:10889-10894. DOI: 10.1073/pnas.0604460103

[70] Guo W-H, Frey MT, Burnham NA, Wang Y-L. Substrate rigidity regulates the formation and maintenance of tissues. Biophysical Journal. 2006;90:2113-2130. DOI: 10.1529/biophysj.105.070144

[71] D’Andrea Markert L, Lovmand J, Duch M, Pedersen FS. Topographically and chemically modified surfaces for expansion or differentiation of embryonic stem cells. In: Atwood C, editor. Methodological Advances in the Culture, Manipulation and Utilization of Embryonic Stem Cells for Basic and Practical Applications. Rijeka: InTech; 2011. p. 139-158. DOI: 10.5772/15346
[72] Georges PC, Janmey PA. Cell type-specific response to growth on soft materials. Journal of Applied Physiology. 2005;98:1547-1553. DOI: 10.1152/japplphysiol.01121.2004

[73] Sochol RD, Higa AT, Janaiero RRR, Lib S, Lin L. Unidirectional mechanical cellular stimuli via micropost array gradients. Soft Matter. 2011;7:4606-4609. DOI: 10.1039/c1sm05163f

[74] Yang Y, Leong KW. Nanoscale surfacing for regenerative medicine. WIREs Nanomedicine and Nanobiotechnology. 2010;2:478-495. DOI: 10.1002/wnan.74

[75] Folch A, Toner M. Microengineering of cellular interactions. Annual Review of Biomedical Engineering. 2000;2:227-256. DOI: 10.1146/annurev.bioeng.2.1.227

[76] Zahor D, Radko A, Vago R, Gheber LA. Organization of mesenchymal stem cells is controlled by micropatterned silicon substrates. Materials Science and Engineering: C. 2007;27:117-121. DOI: 10.1016/j.msec.2006.03.005

[77] Poellmann MJ, Harrell PA, King WP, Wagoner Johnson AJ. Geometric microenvironment directs cell morphology on topographically patterned hydrogel substrates. Acta Biomaterialia. 2010;6:3514-3523. DOI: 10.1016/j.actbio.2010.03.041

[78] Owen GR, Jackson J, Chehroudi B, Burt H, Brunette DM. A PLGA membrane controlling cell behaviour for promoting tissue regeneration. Biomaterials. 2005;26:7447-7756. DOI: 10.1016/j.biomaterials.2005.05.055

[79] Eklblad T, Liedberg B. Protein adsorption and surface patterning. Current Opinion in Colloid & Interface Science. 2010;15:499-509. DOI: 10.1016/j.cocis.2010.07.008

[80] Roach P, Parker T, Gadegaard N, Alexander MR. Surface strategies for control of neuronal cell adhesion: A review. Surface Science Reports. 2010;65:145-173. DOI: 10.1016/j.surfrep.2010.07.001

[81] Olędzka E, Sobczak M, Kołodziejski WL. Polymers in medicine – Review of past achievements. Polimery. 2007;52:793-803 (in Polish)

[82] Tanaka M. Design of novel 2D and 3D biointerfaces using self-organization to control cell behaviour. Biochimica et Biophysica Acta. 1810;2011:251-258. DOI: 10.1016/j.bbagen.2010.10.002

[83] Diener A, Nebe B, Becker P, Bech U, Lüthen F, Neumann HG, Rychly J. Control of focal adhesion dynamics by material surface characteristics. Biomaterials. 2005;26:383-392. DOI: 10.1016/j.biomaterials.2004.02.038

[84] Fan YW, Cui FZ, Hou SP, Xu QY, Chen LN, Lee IS. Culture of neural cells on silicon wafers with nano-scale surface topography. Journal of Neuroscience Methods. 2002;120:17-23. DOI: 10.1016/S0165-0270(02)00181-4

[85] Ricci JL, Grew JC, Alexander H. Connective-tissue responses to defined biomaterial surfaces. I. Growth of rat fibroblast and bone marrow cell colonies on microgrooved substrates. Journal of biomedical materials research. Part A. 2007;85:313-325. DOI: 10.1002/jbm.a.31379
[86] Kieswetter K, Schwartz Z, Humrnert TW, Cochran DL, Simpson J, Dean SDD, Boyan BD. Surface roughness modulates the local production of growth factors and cytokines by osteoblast-like MG-63 cells. Journal of Biomedical Materials Research 1996;32:55-63. DOI: 10.1002/(SICI)1097-4636(199609)32:1<55::AID-JBM7>3.0.CO;2-O

[87] Washburn NR, Yamada KM, Simon CG Jr, Kennedy SB, Amis EJ. High-throughput investigation of osteoblast response to polymer crystallinity: Influence of nanometer-scale roughness on proliferation. Biomaterials. 2004;25:1215-1224. DOI: 10.1016/j.biomaterials.2003.08.043

[88] Kunzler TP, Drobek T, Schuler M, Spencer ND. Systematic study of osteoblast and fibroblast response to roughness by means of surface-morphology gradients. Biomaterials. 2007;28:2175-2182. DOI: 10.1016/j.biomaterials.2007.01.019

[89] Chung T-W, Wang S-S, Wang Y-Z, Hsieh C-H, Fu E. Enhancing growth and proliferation of human gingival fibroblasts on chitosan grafted poly (ε-caprolactone) films is influenced by nano-roughness chitosan surfaces. Journal of Materials Science: Materials in Medicine. 2009;20:397-404. DOI: 10.1007/s10856-008-3586-z

[90] Xu C, Yang F, Wang S, Ramakrishna S. In vitro study of human vascular endothelial cell function on materials with various surface roughness. Journal of Biomedical Materials Research, Part A. 2004;71:154-161. DOI: 10.1002/jbm.a.30143

[91] Takamori ER, Cruz R, Gonçalvez F, Zanetti RV, Zanetti A, Granjeiro JM. Effect of roughness of zirconia and titanium on fibroblast adhesion. Artificial Organs. 2008;32:305-309. DOI: 10.1111/j.1525-1594.2008.00547.x

[92] Łopacińska JM, Gradinaru C, Wierzbicki R, Köbler C, Schmidt MS, Madsen MT, Skolimowski M, Dufva M, Flyvbjerg H, Mølhvaen K. Cell motility, morphology, viability and proliferation in response to nanotopography on silicon black. Nanoscale. 2012;4:3739-3745. DOI: 10.1039/c2nr11455k

[93] Bandyopadhyay A, Espana F, Balla VK, Bose S, Ohgami Y, Davies NM. Influence of porosity on mechanical properties and in vivo response of Ti6Al4 implants. Acta Biomaterialia. 2010;6:1640-1648

[94] Nouri A, Hodgson PD, Wen C. Biomimetic porous titanium scaffolds for orthopedic and dental applications. In: Mukherjee A, editor. Biomimetics Learning from Nature. Rijeka: InTech; 2010. p. 415-450

[95] Yoshida K, Saiki Y, Ohkubo S. Improvement of drawability and fabrication possibility of dental implant screw made of pure titanium. Hutnik – Wiadomości Hutnicze. 2011;78:153-156

[96] Dobrzańska-Danikiewicz AD. The book of critical technologies of surface and properties formation of engineering materials. Open access. Library. 2012;6:1-823 (in Polish)

[97] Dobrzańska-Danikiewicz AD. Computer integrated development prediction methodology in materials surface engineering. Open access. Library. 2012;1:1-289 (in Polish)
[98] Dobrzańska-Danikiewicz AD. Foresight of material surface engineering as a tool building a knowledge based economy. Materials Science Forum. 2012;706-709:2511-2516. DOI: 10.4028/www.scientific.net/MSF.706-709.2511

[99] Dobrzański LA, Dobrzańska-Danikiewicz AD. Foresight of the surface Technology in Manufacturing. In: Nee AYC, editor. Handbook of Manufacturing Engineering and Technology. London: Springer-Verlag; 2015. p. 2587-2637 978-1-4471-4671-1

[100] Guo N, Leu MC. Additive manufacturing: Technology, applications and research needs. Frontiers of Mechanical Engineering. 2013;8:215-243. DOI: 10.1007/s11465-013-0248-8

[101] Cormier D, Harrysson O, West H. Characterization of H13 steel produced via electron beam melting. Rapid Prototyping Journal. 2004;10:35-41

[102] Rännar LE, Glad A, Gustafson CG. Efficient cooling with tool inserts manufactured by electron beam melting. Rapid Prototyping Journal. 2007;13:128-135

[103] Murr LE, Gaytan SM, Medina F, Martinez E, Martinez JL, Hernandez DH, Machado BI, Ramirez DA, Wicker RB. Characterization of Ti6Al4V open cellular foams fabricated by additive manufacturing using electron beam melting. Materials Science and Engineering A. 2010;527:1861-1868

[104] Han GW, Feng D, Yin M, Ye WJ. Ceramic/aluminum co-continuous composite synthesized by reaction accelerated melt infiltration. Materials Science and Engineering A. 1997;225:204-207

[105] Murr LE, Gaytan SM, Ceylan A, Martinez E, Martinez JL, Hernandez DH, Machado BI, Ramirez DA, Medina F, Collins S. Characterization of titanium aluminide alloy components fabricated by additive manufacturing using electron beam melting. Acta Materialia. 2010;58:1887-1894

[106] Kumar S. Selective laser sintering: A qualitative and objective approach. Modeling and Characterization. 2003;55:43-47

[107] Xue W, Vamsi KB, Bandyopadhyay A, Bose S. Processing and biocompatibility evaluation of laser processed porous titanium. Acta Biomaterialia. 2007;3:1007-1018

[108] Osakada K, Shiomí M. Flexible manufacturing of metallic products by selective laser melting of powder. International Journal of Machine Tools & Manufacture. 2006;46:1188-1193

[109] Kruth J-P, Mercelis P, Van Vaerenbergh J, Froyen L, Rombouts M. Binding mechanisms in selective laser sintering and selective laser melting. Rapid Prototyping Journal. 2005;11:26-36. DOI: 10.1108/13552540510573365

[110] Bertol LS, Júnior WK, da Silva FP, Kopp CA. Medical design: Direct metal laser sintering of Ti-6Al-4V. Materials and Design. 2010;31:3982-3988

[111] Pattanayak DK, Fukuda A, Matsushita T, Takemoto M, Fujibayashi S, Sasaki K, Nishida N, Nakamura T, Kokubo T. Bioactive Ti metal analogous to human cancellous bone: Fabrication by selective laser melting and medical treatments. Acta Biomaterialia. 2011;7:1398-1406
[112] Abe F, Osakada K, Shiomi M, Uematsu K, Matsumoto M. The manufacturing of hard tools from metallic powders by selective laser melting. Journal of Materials Processing Technology. 2001;111:210-213. DOI: 10.1016/S0924-0136(01)00522-2

[113] Darłak P, Dudek P. High porous materials - manufacturing methods and applications. Molding: Science and Practice. 2004;1:3-17 (in Polish)

[114] Kruth JP, Froyen L, Van Vaerenbergh J, Mercelis P, Rombouts M, Lauwers B. Selective laser melting of iron-based powder jet. Journal of Materials Processing Technology. 2004;149:616-622. DOI: 10.1016/j.jmatprotec.2003.11.051

[115] Lethaus B, Poort L, Böckmann R, Smeets R, Tolba R, Kessler P. Additive manufacturing for microvascular reconstruction of the mandiblein 20 patients. Journal of Cranio-Maxillo-Facial Surgery. 2012;40:43-46. DOI: 10.1016/j.jcms.2011.01.007

[116] Liao YS, Li HC, Chiu YY. Study of laminated object manufacturing with separately applied heating and pressing. International Journal of Advanced Manufacturing Technology. 2006;27:703-707. DOI: 10.1007/s00170-004-2201-9

[117] Dobrzański LA, Dobrzańska-Danikiewicz AD, Malara P, Gaweł TG, Dobrzański LB, Achtelik-Franczak A. Fabrication of scaffolds from Ti6Al4V powders using the computer aided laser method. Archives of Metallurgy and Materials. 2015;60:1065-1070. DOI: 10.1515/amm-2015-0260

[118] Dobrzański LA, Dobrzańska-Danikiewicz AD, Achtelik-Franczak A, Dobrzański LB, Szindler M, Gaweł TG. Porous selective laser melted Ti and Ti6Al4V materials for medical applications. In: Dobrzański LA, editor. Powder Metallurgy – Fundamentals and Case Studies. Rijeka: INTECH; 2017. pp. 161-181. DOI: 10.5772/65375

[119] Dobrzański LB. Structure and Properties of Engineering Materials for Prosthetic Restorations of Stomatognitve System Manufactured by Additive and Defective Methods. [Ph.D. Thesis in Progress]. Kraków: AGH University of Science and Technology; 2017

[120] Dobrzański LA, Dobrzańska-Danikiewicz AD, Achtelik-Franczak A, Dobrzański LB. Comparative analysis of mechanical properties of scaffolds sintered from Ti and Ti6Al4V powders. Archives of Materials Science and Engineering. 2015;73:69-81

[121] Dobrzański LA. Overview and general ideas of the development of constructions, materials, technologies and clinical applications of scaffolds engineering for regenerative medicine. Archives of Materials Science and Engineering. 2014;69:53-80

[122] Dobrzański LA, Dobrzańska-Danikiewicz AD, Gaweł TG, Achtelik-Franczak A. Selective laser sintering and melting of pristine titanium and titanium Ti6Al4V alloy powders and selection of chemical environment for etching of such materials. Archives of Metallurgy and Materials. 2015;60:2039-2045. DOI: 10.1515/amm-2015-0346

[123] Karoluk M, Pawlak A, Chlebus E. Using of SLM additive technology in Ti-6Al-7Nb titanium alloy processing for biomedical applications. XI Scientific Conference named after Prof. Dagmara Tejszerska “May-Picnic of Young Biomechanics”. Ustroń, Poland; 2014. pp. 53-54 (in Polish)
[124] Dobrzański LA, Dobrzańska-Danikiewicz AD, Achtelik-Franczak A, Szindler M. Structure and properties of the skeleton microporous materials with coatings inside the pores for medical and dental applications. International Conference on Frontiers in Materials Processing, Applications, Research, & Technology, FiMPART’2015; 12-15 Juni 2015; Hyderabad, India. Singapore: Springer; 2017 (in press)

[125] Dobrzański LA & Dobrzańska-Danikiewicz AD (eds.), Microporous and solid metallic materials for medical and dental application, Open Access Library, Annal VII(1) 2017. pp. 1-580 (in Polish)

[126] Achtelik-Franczak A. Composite engineering materials with matrix made from selective laser sintered microporous titanium [Ph.D. thesis]. Gliwice, Poland: Silesian university of Technology; 2016 (in Polish)

[127] Dobrzański LA, Dobrzańska-Danikiewicz AD, Gaweł TG. Ti6Al4V porous elements coated by polymeric surface layer for biomedical applications. Journal of Achievements in Materials and Manufacturing Engineering. 2015;71:53-59

[128] Dobrzański LA, Dobrzańska-Danikiewicz AD, Szindler M, Achtelik-Franczak A, Pakiela W. Atomic layer deposition of TiO₂ onto porous biomaterials. Archives of Materials Science and Engineering. 2015;75:5-11

[129] Klimas J, Łukaszewicz A, Szota M, Laskowski K. Work on the modification of the structure and properties of Ti6Al4V titanium alloy for biomedical applications. Archives of Materials Science and Engineering. 2016;78:10-16. DOI: 10.5604/18972764.1226308

[130] Kirmanidou Y, Sidira M, Drosou M-E, Bennani V, Bakopoulou A, Tsouknidas A, Michailidis N, Michalakis K. New Ti-alloys and surface modifications to improve the mechanical properties and the biological response to orthopedic and dental implants: A review. BioMed Research International. 2016. Art no. 2908570. DOI: 10.1155/2016/2908570

[131] Parchańska-Kowalik M, Klimek L. Wpływ obróbki chemicznej na stan powierzchni tytanu. Inżynieria Materialowa. 2013;34:526-529

[132] Dobrzański LA. Applications of newly developed nanostructural and microporous materials in biomedical, tissue and mechanical engineering. Archives of Materials Science and Engineering. 2015;76:53-114

[133] Burnat B, Parchańska-Kowalik M, Klimek L. The influence of chemical surface treatment on the corrosion resistance of titanium castings used in dental prosthetics. Archives of Foundry Engineering. 2014;14:11-16. DOI: 10.2478/afe-2014-0052

[134] Majkowska B, Jażdżewska M, Wołowiec E, Piekoszewski W, Klimek L, Zieliński A. The possibility of use of laser-modified Ti6Al4V alloy in friction pairs in endoprostheses. Archives of Metallurgy and Materials. 2015;60:755-758. DOI: 10.1515/amm-2015-0202

[135] Klimas J, Łukaszewicz A, Szota M, Szota K. Characteristics of titanium grade 2 and evaluation of corrosion resistance. Archives of Materials Science and Engineering. 2016;77:65-71. DOI: 10.5604/18972764.1225596
[136] Jedynak B, Mierzwińska-Nastalska E. Titanium - properties and use in dental prosthodontics. Dental. Forum. 2013;41:75-78 (in Polish)

[137] Emsley J. Nature's Building Blocks: An A-Z Guide to the Elements. Oxford: Oxford University Press; 2001. 538 p 978-0198503408

[138] Hong J, Andersson J, Ekdahl KN, Elgue G, Axen N, Larsson R, Nilsson B. Titanium is a highly thrombogenic biomaterial: Possible implications for osteogenesis. Thrombosis and Haemostasis. 1999;82:58-64

[139] PN-EN ISO 10993-4:2017. Biological Evaluation of Medical Devices. Part 4: Selection of Tests for Interaction with Blood, Technical Committee ISO/TC 194, ICS: 11.100.20, Available from: https://www.iso.org/standard/63448.html Accessed: 2017-08-23

[140] Street J, Winter D, Wang JH, Wakai A, McGuinness A, Redmond HP. Is human fracture hematoma inherently angiogenic? Clinical Orthopaedics and Related Research. 2000;378:224-237

[141] Karp JM, Sarraf F, Shoichet MS, Davies JE. Fibrin-filled scaffolds for bone-tissue engineering: An in vivo study. Journal of Biomedical Materials Research, Part A. 2004;71:162-171

[142] Yang F, Neeley WL, Moore MJ, Karp JM, Shukla A, Langer R. Tissue engineering: The Therapeutic Strategy of the Twenty-First Century. In: Laurencin CT, Nair LS, editors. Nanotechnology and Tissue Engineering: The Scaffold. Boca Raton, FL: CRC Press Taylor & Francis Group; 2008. p. 3-32

[143] Leong KF, Cheah CM, Chua CK. Solid freeform fabrication of three-dimensional scaffolds for engineering replacement tissues and organs. Biomaterials. 2003;24:2363-2378

[144] Nair LS, Laurencin CT. Polymers as biomaterials for tissue engineering and controlled drug delivery. Advances in Biochemical Engineering, Biotechnology. 2006;102:47-90

[145] Velema J, Kaplan D. Biopolymer-based biomaterials as scaffolds for tissue engineering. Advances in Biochemical Engineering, Biotechnology. 2006;102:187-238

[146] Kannan RY, Salacinski HJ, Sales KM, Butler PE, Seifalian AM. The endothelialization of polyhedral oligomeric silsesquioxane nanocomposites: An in vitro study. Cell Biochemistry and Biophysics. 2006;45:129-136

[147] Nowacka M. Biomaterials used in cellular engineering and regenerative medicine. Wiadomości Chemiczne. 2012;66:909-933 (in Polish)

[148] Ulery BD, Nair LS, Laurencin CT. Biomedical applications of biodegradable polymers. Journal of Polymer Science, Part B, Polymer Physics. 2011;49:832-864. DOI: 10.1002/polb.22259

[149] Ghanbari H, Kidane AG, Buriesci G, Ramesh B, Darbyshire A, Seifalian AM. The anti-calcification potential of a silsesquioxane nanocomposite polymer under in vitro conditions: Potential material for synthetic leaflet heart valve. Acta Biomaterialia. 2010;6:4249-4260. DOI: 10.1016/j.actbio.2010.06.015
Motwani MS, Rafiei Y, Tzifa A, Seifalian AM. In situ endothelialization of intravascular stents from progenitor stem cells coated with nanocomposite and functionalized biomolecules. Biotechnology and Applied Biochemistry. 2011;58:2-13. DOI: 10.1002/bab.10

Kidane AG, Burriesci G, Edirisinghe M, Ghanbari H, Bonhoeffer P, Seifalian AM. A novel nanocomposite polymer for development of synthetic heart valve leaflets. Acta Biomaterialia. 2009;5:2409-2417. DOI: 10.1016/j.actbio.2009.02.025

Słomkowski S. Hybrid polymeric materials for medical applications. Polimery. 2006;51:87-94

Kidane AG, Burriesci G, Cornejo P, Dooley A, Sarkar S, Bonhoeffer P, Edirisinghe M, Seifalian AM. Current developments and future prospects for heart valve replacement therapy. Journal of biomedical materials research, part B, applied. Biomaterials. 2008;88:290-303. DOI: 10.1002/jbm.b.31151

Middleton JC, Tipton AJ. Synthetic biodegradable polymers as orthopedic devices. Biomaterials. 2000;21:2335-2346

An YH, Woolf SK, Friedman RJ. Pre-clinical in vivo evaluation of orthopaedic bioabsorbable devices. Biomaterials. 2000;21:2635-2652

Robinson BP, Hollinger JO, Szachowicz EH, Brekke J. Calvarial bone repair with porous D,L-polylactide. Otolaryngology - Head and Neck Surgery. 1995;112:707-713. DOI: 10.1016/S0194-5998(95)70180-X

Das K, Balla VK, Bandyopadhyay A, Bose S. Surface modification of laser-processed porous titanium for load-bearing implants. Scripta Materialia. 2008;59:822-825

Balla VK, Bodhak S, Bose S, Bandyopadhyay A. Porous tantalum structures for bone implants: Fabrication, mechanical and in vitro biological properties. Acta Biomaterialia. 2010;6:3349-3359

Witte F, Ulrich H, Palm C, Willbold E. Biodegradable magnesium scaffolds: Part II: Periimplant bone remodelling. Journal of Biomedical Materials Research, Part A. 2007;81:757-765

Bose S, Roy M, Bandyopadhyay A. Recent advances in bone tissue engineering scaffolds. Trends in Biotechnology. 2012;30:546-554

Yun Y, Dong Z, Lee N, Liu Y, Xue D, Guo X, Kuhlmann J, Doepke A, Halsall HB, Heineman W, Sundaramurthy S, Schulz MJ, Yin Z, Shanov V, Hurd D, Nagy P, Li W, Fox C. Revolutionizing biodegradable metals. Materials Today. 2009;12:22-32. DOI: 10.1016/S1369-7021(09)70273-1

Vert M. Not any new functional polymer can be for medicine: What about artificial biopolymers? Macromolecular Bioscience. 2011;11:1653-1661. DOI: 10.1002/mabi.201100224

Li B, Ma Y, Wang S, Moran PM. Influence of carboxyl group density on neuron cell attachment and differentiation behavior: Gradient-guided neurite outgrowth. Biomaterials. 2005;26:4956-4963. DOI: 10.1016/j.biomaterials.2005.01.018
[164] Gawel TG. Manufacturing technology obtaining and research of innovative porous biomimetic materials. Ph.D. Thesis (in progress). Gliwice, Poland: Silesian University of Technology; 2017 in Polish

[165] Dobrzański LA, Dobrzańska-Danikiewicz AD, Achtelik-Franczak A, Dobrzański LB, Hajduczek E, Matula G. Fabrication technologies of the sintered materials including materials for medical and dental application. In: Dobrzański LA, editor. Powder Metallurgy – Fundamentals and Case Studies. Rijeka: INTECH; 2017. p. 17-52. DOI: 10.5772/65376

[166] Dobrzański LA, Dobrzańska-Danikiewicz AD, Malara P, Dobrzański LB, Achtelik-Franczak A. Biological and engineering composites for regenerative medicine. Patent Application P. 2015;414723(9):11

[167] Dobrzański LA, Dobrzańska-Danikiewicz AD, Malara P, Gawel TG, Dobrzański LB, Achtelik-Franczak A. Bone implant scaffold. Patent Application P. 2015;414424(19):10

[168] Dobrzański LA, Dobrzańska-Danikiewicz AD, Malara P, Gawel TG, Dobrzański LB, Achtelik-Franczak A. Implant scaffold and a prosthesis of anatomical elements of a dental system and craniofacial bone. Patent Application P. 2015;414423(19):10

[169] Dobrzański LA, Dobrzańska-Danikiewicz AD, Malara P, Gawel TG, Dobrzański LB, Achtelik A. Composite fabricated by computer-aided laser methods for craniofacial implants and its manufacturing method. Patent Application P. 2015;411689(23):03

[170] Dobrzański LA, Dobrzańska-Danikiewicz AD, Malara P, Achtelik-Franczak A, Dobrzański LB, Kremzer M. Sposób wytwarzania materiałowych kompozytów o mikro-porowatej szkieletowej strukturze wzmocnienia. Patent Application P. 2016;417552(13):06

[171] Dobrzański LA, Dobrzańska-Danikiewicz AD, Malara P, Dobrzański LB, Achtelik-Franczak A, Gawel TG. Implant-scaffold or prosthesis anatomical structures of the Stomatognathic system and the craniofacial. Gold medal on international exhibition of technical innovations, patents and inventions, INVENT ARENA 2016; Třinec, Czech Republic. 2016;6:16-18

[172] Dobrzański LA, Dobrzańska-Danikiewicz AD, Malara P, Dobrzański LB, Achtelik-Franczak A, Gawel TG. Implant-scaffold or prosthesis anatomical structures of the Stomatognathic system and the craniofacial. Gold Medal and International Intellectual Property Network Forum (IIPNF) Leading Innovation Award on International Intellectual Property, Invention, Innovation and Technology Exposition, IPITEX 2016. Bangkok, Thailand. 2016;2:2-6

[173] Dobrzański LA, Dobrzańska-Danikiewicz AD, Malara P, Gawel TG, Dobrzański LB, Achtelik-Franczak A. The novel composite consisting of a metallic scaffold, manufactured using a computer aided laser method, coated with thin polymeric surface layer for medical applications. Gold Medal on 9th International Warsaw Invention Show IWIS 2015. Warsaw, Poland; 12-14.10.2015
[174] Dobrzański LA, Dobrzańska-Danikiewicz AD, Malara P, Gawel TG, Dobrzański LB, Achtelik-Franczak A. The novel composite consisting of a metallic scaffold, manufactured using a computer aided laser method, coated with thin polymeric surface layer for medical applications. Semi grand prize on global inventions and innovations exhibitions Innova cities Latino-America, ICLA 2015. Foz do Iguaçu, Brazil; 2015;12:10-12

[175] Dobrzański LA. Fabrication, structure and mechanical properties of laser sintered materials for medical applications. Invited lecture on XXV International Materials Research Congress. Cancun, Mexico; 14-19 August 2016

[176] Dobrzański LA. Application of the additive manufacturing by selective laser sintering for constituting implants scaffolds and hybrid multilayer biological and engineering composite materials. Keynote lecture on international conference on Processing & Manufacturing of advanced materials THERMEC’2016, processing, fabrication, properties, applications. Graz, Austria; 29 May – 3 June 2016

[177] Dobrzański LA. Metallic implants-scaffolds for dental and orthopaedic application. Invited lecture on 9° COLAOB - Congresso Latino-Americano de Orgãos Artificiais e Biomateriais; Foz do Iguaçu, Brazil; 24-27 August 2016

[178] Dobrzański LA et al. Investigations of Structure and Properties of Newly Created Porous Biomimetic Materials Fabricated by Selective Laser Sintering, BIOLASIN. Project UMO-2013/08/M/ST8/00818. Gliwice: Silesian University of Technology; 2013-2016

[179] Kremzer M, Dobrzański LA, Dziekońska M, Macek M. Atomic layer deposition of TiO₂ onto porous biomaterials. Archives of Materials Science and Engineering. 2015;75:63-69

[180] Project POIR.01.01.01-00-0485/16-00 IMSKA-MAT Innovative dental and maxillo-facial implant-scaffolds manufactured using the innovative technology of additive computer-aided materials design ADD-MAT. Design, Research and production Centre of Medical and Dental Engineering ASKLEPIOS in Gliwice; 2017-2021. In progress

[181] Dobrzański LA, Dobrzańska-Danikiewicz AD. Forming of Structure and Properties of Engineering Materials Surface. Gliwice: Wydawnictwo Politechniki Śląskiej; 2013. 492 p (in Polish)978-83-7880-077-7

[182] Kim TH, Lee KM, Hwang J, Hong WS. Nanocrystalline silicon films deposited with a modulated hydrogen dilution ratio by catalytic CVD at 200°C. Current Applied Physics. 2009;9:e108-e110

[183] Kim TH, Lee KM, Hwang J, Hong WS. Nanocrystalline silicon films deposited with a modulated hydrogen dilution ratio by catalytic CVD at 200°C. Current Applied Physics. 2009;9:e108-e110

[184] Bala H. Introduction into Materials Chemistry. Warszawa: WNT; 2003. 445 p (in Polish)8320427991
[186] Pajdowski L. General Chemistry. 11th ed. Wydawnictwo Naukowe PWN: Warszawa; 2002. 616 p (in Polish)

[187] Jasińska B. General Chemistry. Kraków: Wydawnictwa AGH; 1998. 315 p (in Polish)

[188] Głuśzek J. Oxidative Protective Coatings Obtained by sol-gel Method. Oficyna Wydawnicza Politechniki Wrocławskiej: Wrocław; 1998. 154 p (in Polish)

[189] Wrigth JD, Sommerdijk NAJM. Sol-gel Materials, Chemistry and Applications. Amsterdam: Gordon and Breach Science Publishers; 2001. 125 p 90-5699-326-7

[190] Hwang K, Song J, Kang B, Park Y. Sol-gel derived hydroxyapatite films on alumina substrates. Surface and Coatings Technology. 2000;123:252-255

[191] Dong Y, Zhao Q, Wu S, Lu X. Ultraviolet-shielding and conductive double-functional films coated on glass substrates by sol-gel process. Journal of Rare Earths. 2010;28:446-450

[192] Langlet M, Kim A, Audier M, Guillard C, Herrmann JM. Transparent photocatalytic films deposited on polymer substrates from sol-gel processed titania sols. Thin Solid Films. 2003;429:13-21

[193] Seo M, Akutsu Y, Kagemoto H. Preparation and properties of Sb-doped SnO₂/metal substrates by sol-gel and dip coating. Ceramics International. 2007;33:625-629

[194] Łączka M, Terczyńska A, Cholewa-Kowalska K. Gel coatings on the glass, part 1. Świat Szkła. 2008;9:52-55 (in Polish)

[195] Dobrzański LA, editor. Powder Metallurgy – Fundamentals and Case Studies. Rijeka: InTech; 2017. 392 p. DOI: 10.5772/61469
