Chapter 3

Microporous Titanium-Based Materials Coated by Biocompatible Thin Films

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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 TiO_2, Al_2O_3 oxides and $Ca_{10}(PO_4)_6(OH)_2$ 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

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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 $\alpha + \beta$ and pseudo-α and pseudo-β. Double-phase $\alpha + \beta$ 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

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/cm^3	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.

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 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

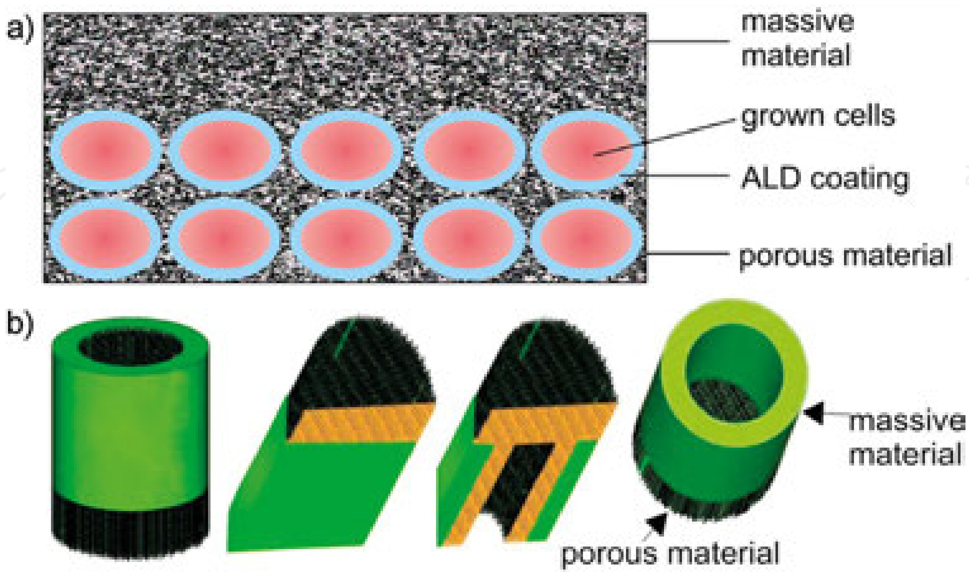

Figure 1. Chart of constructional assumptions (a) hybrid and multilayer biologically active microporous composite engineering materials consisting of biologically active cellular structures and of implant-scaffolds; (b) implant-scaffolds with microporous zones acting as scaffolds.

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 TiO_2, Al_2O_3 oxides and a hydroxyapatite, $Ca_{10}(PO_4)_6(OH)_2$. 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**).

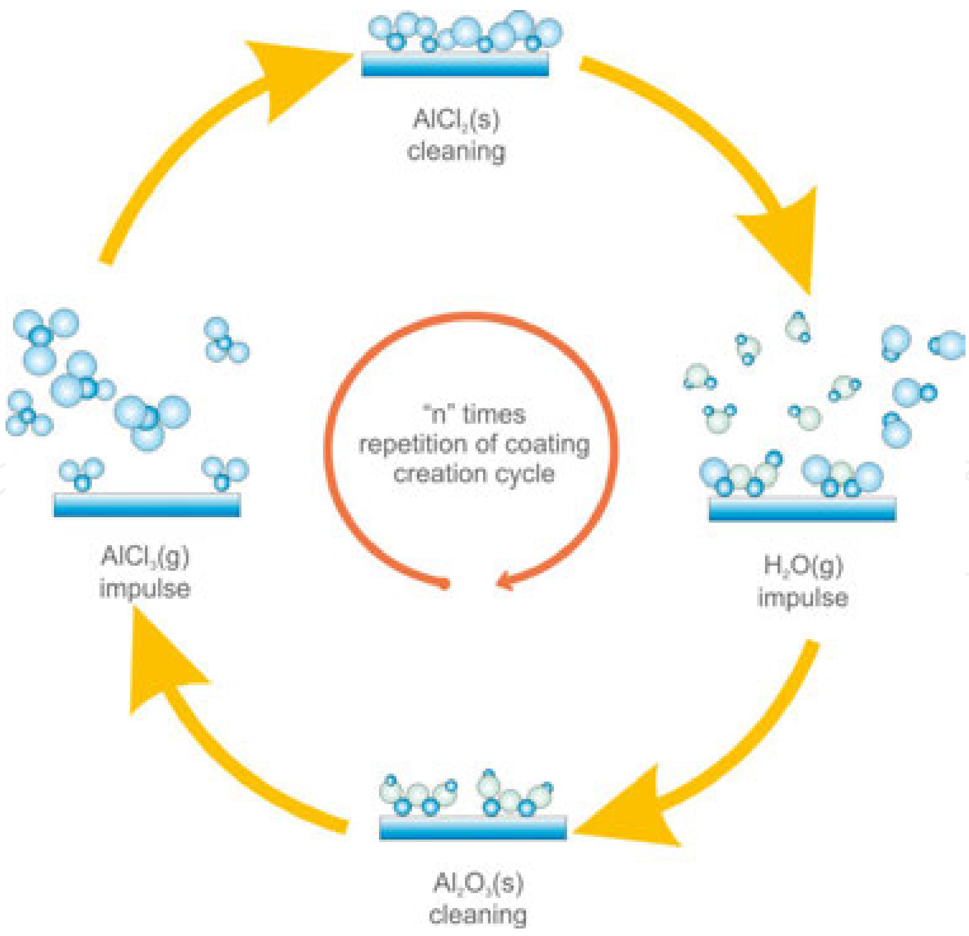

Figure 2. Sequence of the phenomena associated with ALD technology [96].

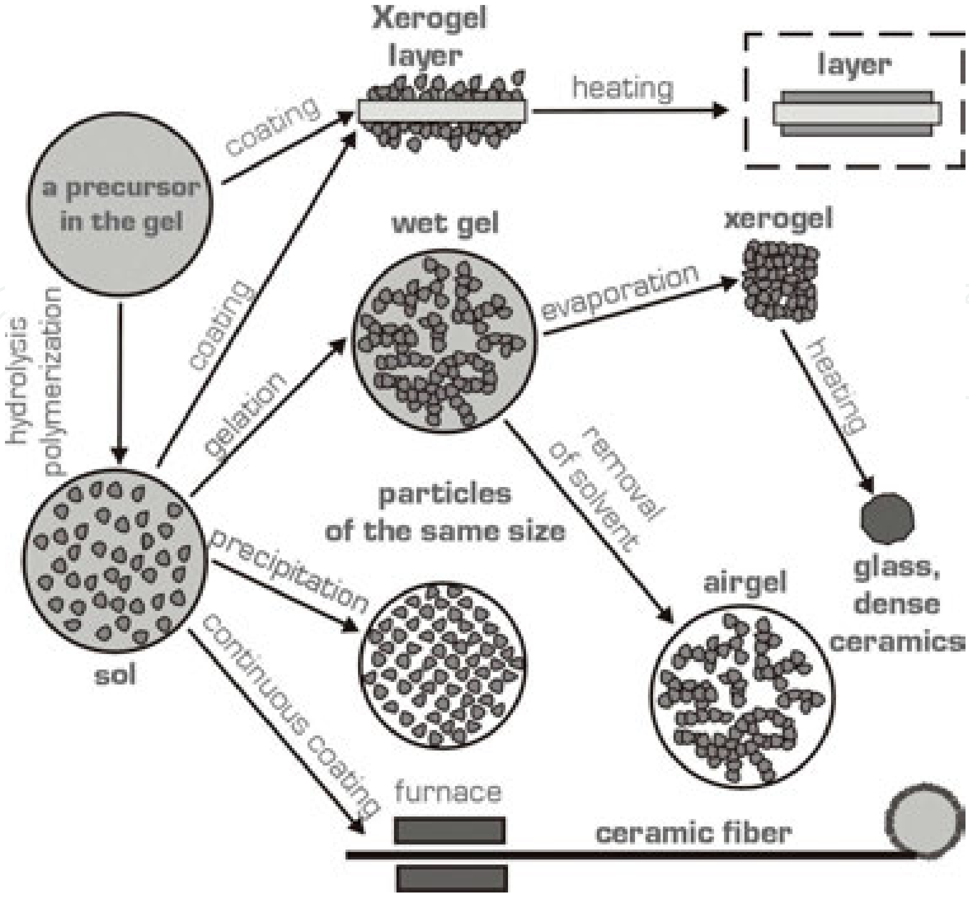

Figure 3. Sequence of the phenomena associated with the sol-gel technology of coating deposition [96].

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 Marcarm 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

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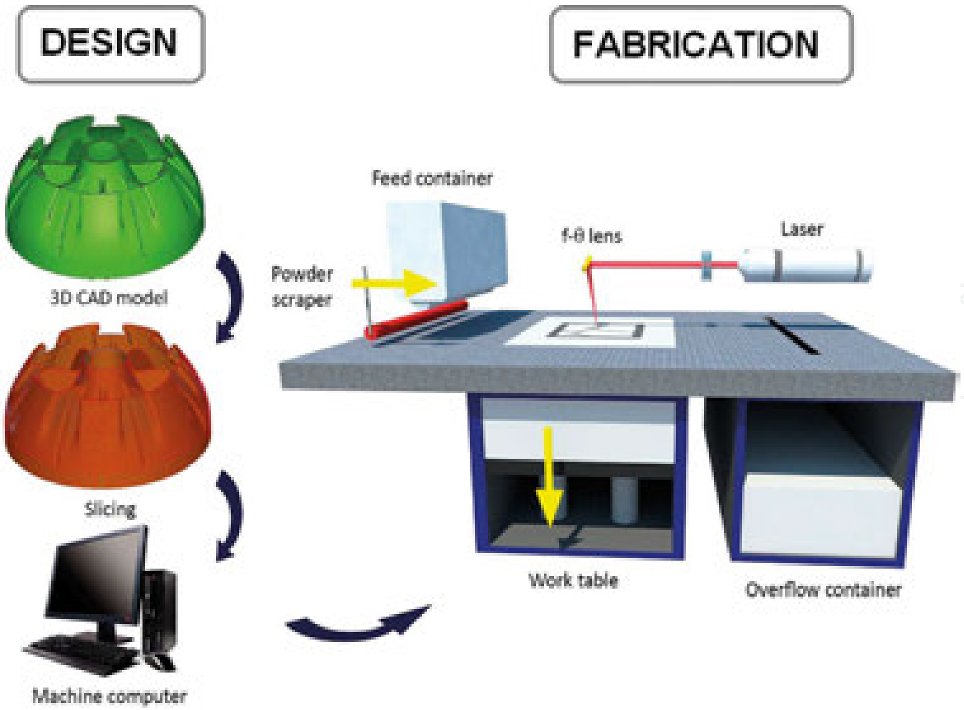

Figure 4. Selective laser sintering technology process diagram [195].

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.

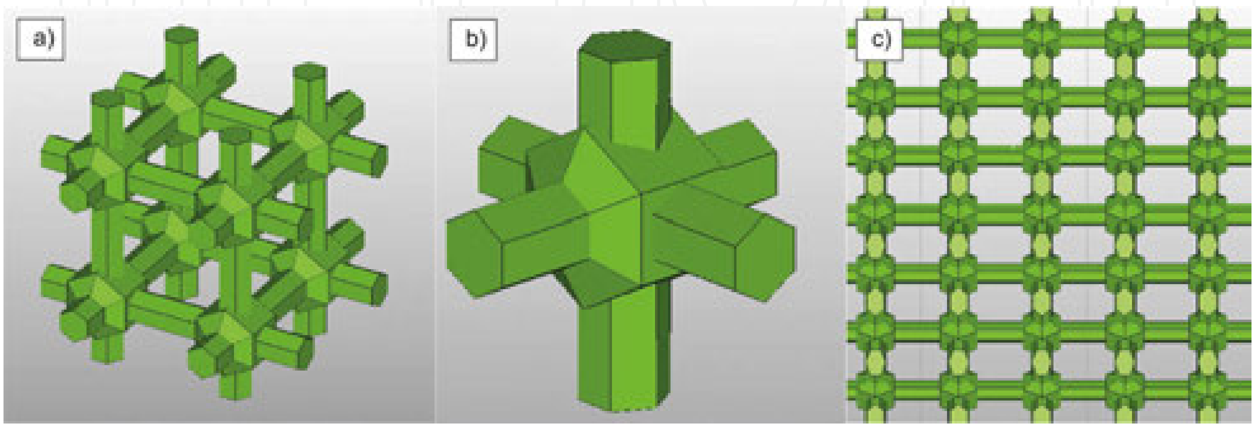

Figure 5. (a, b) Hexagon cross unit cell; (c) image of structure of computer models presenting the arrangement of unit cells in the space of the system of coordinates at the angle of 45° relative to the *x*-axis.

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/cm^3, 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

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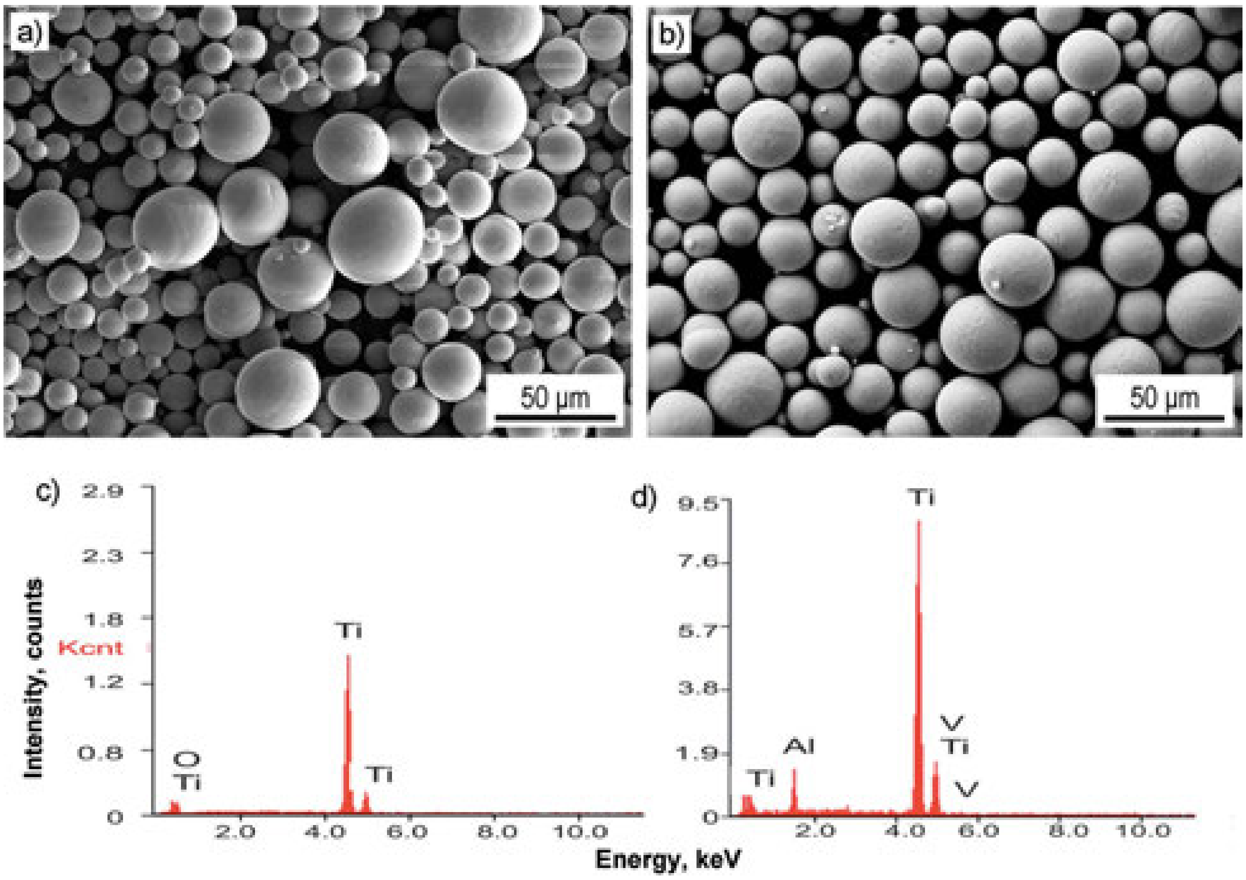

Figure 6. Powder of (a) Ti, (b) Ti6Al4V alloy (SEM), (c, d) relevant diagrams of EDS [119].

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.

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:HNO_3, 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.

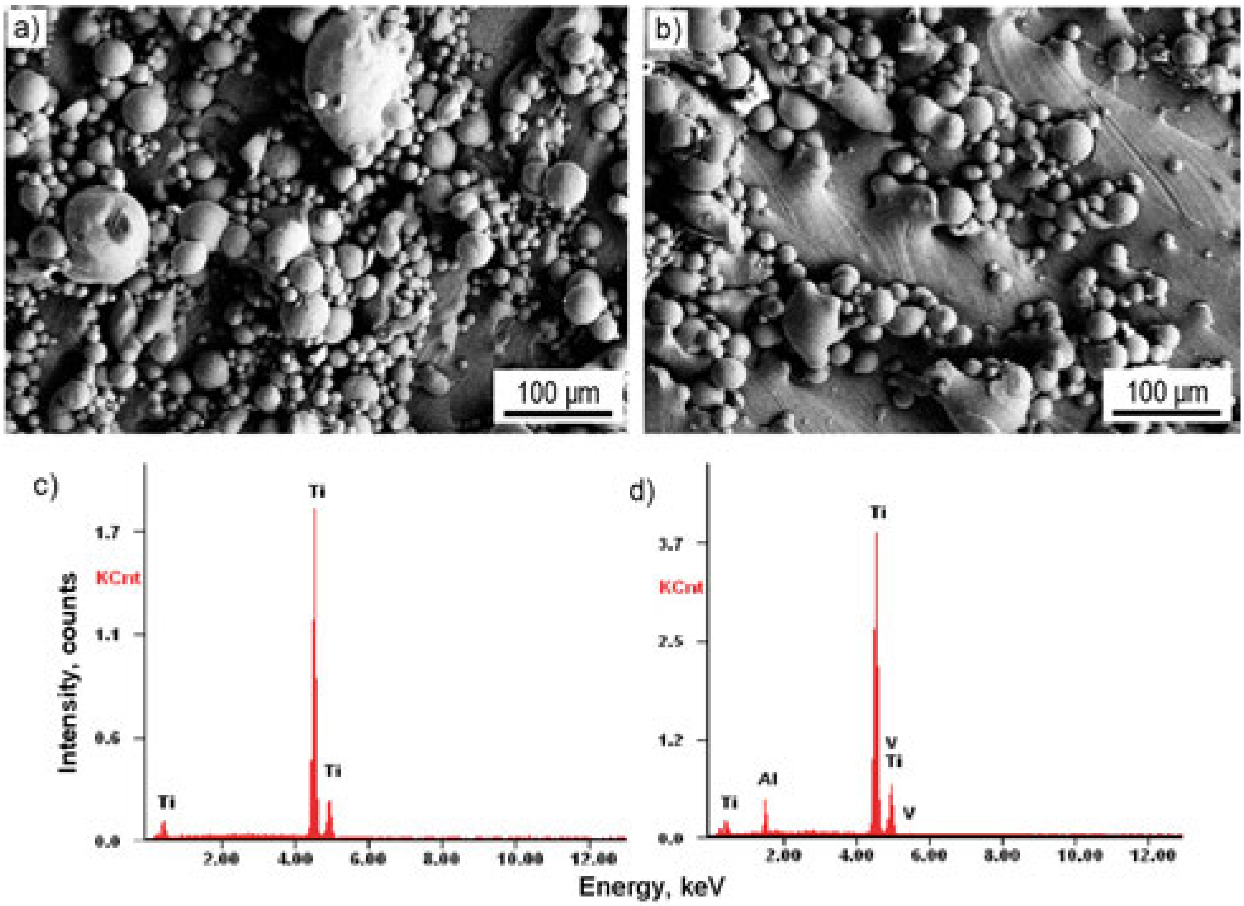

Figure 7. Surface structure of solid samples manufactured by selective laser sintering with the use of laser beam of 50 μm with laser power of 110 W; SEM of (a) solid titanium, (b) Ti6Al4V alloy, (c, d) respectively, EDS charts [119].

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 × 3 × 15 mm, 3 × 10 × 35 mm (for support spacing of 30 mm) and 10 × 10 × 10 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

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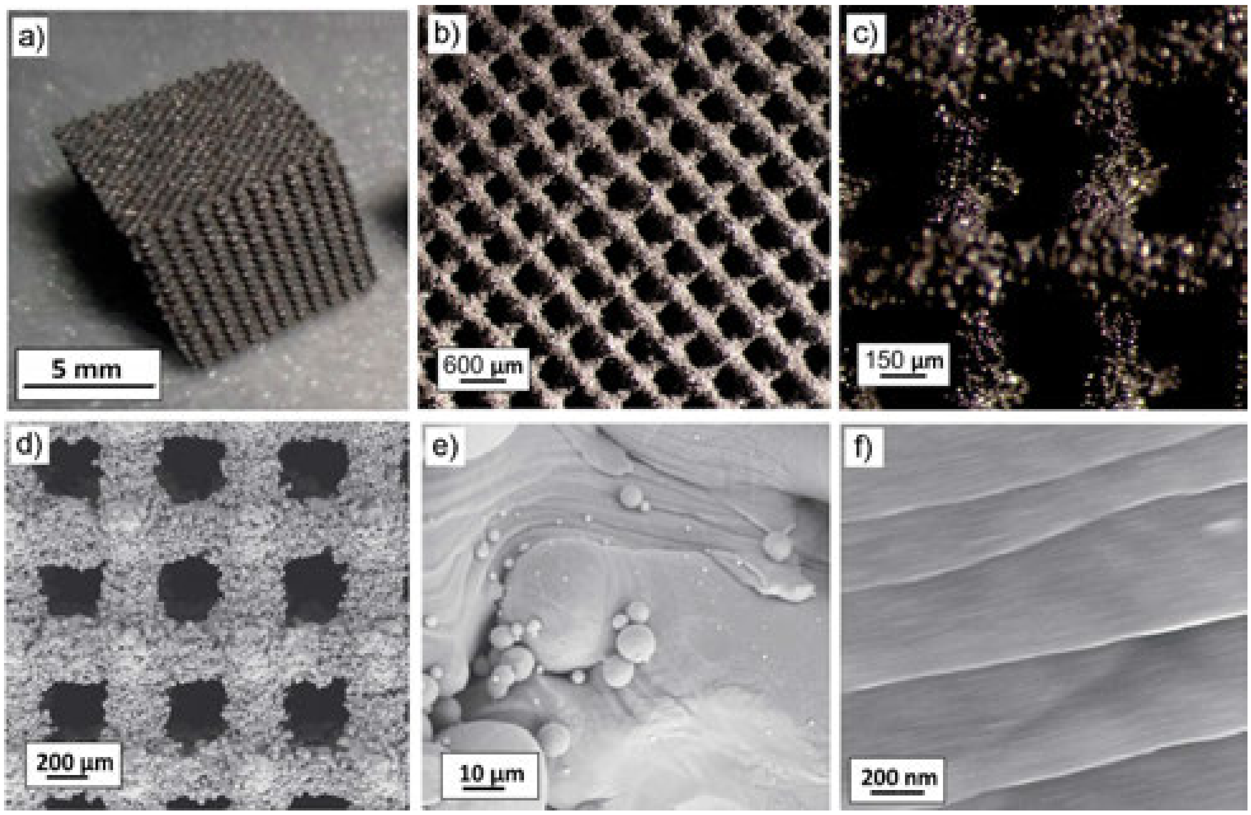

Figure 8. Titanium scaffold (a) visible with bare eye, (b, c) stereoscope microscope, (d–f) SEM.

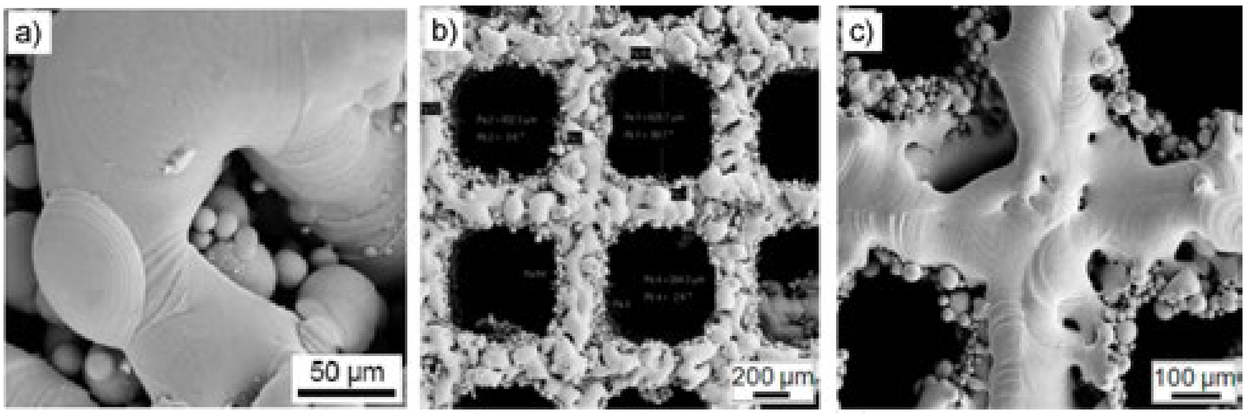

Figure 9. Surface typography of porous titanium skeletons with different pore size: (a) 350 μm, (b) 450 μm, (c) 630 μm; SEM.

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

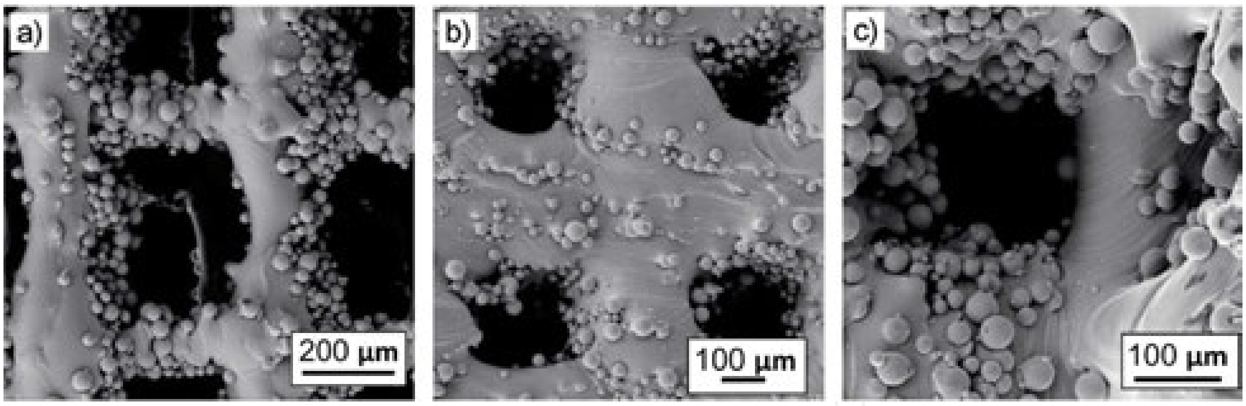

Figure 10. Surface topography of microskeletons made of Ti6Al4V alloy manufactured as multiplication of different unit cells presented with different magnificence (a, b, c); SEM images.

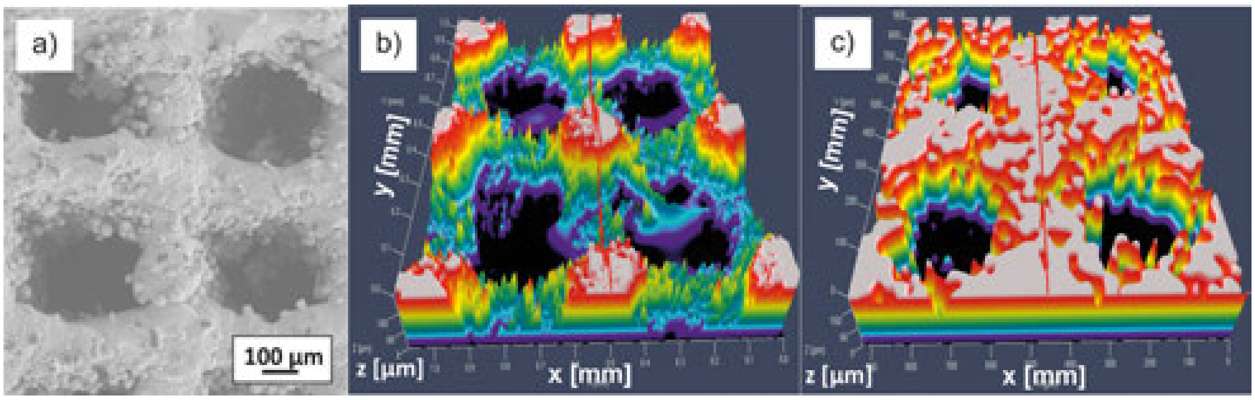

Figure 11. Surface topography of porous titanium skeletons with the pore size of ~450 µm (a) after etching in aqua regia solution (SEM), (b) after ultrasound cleaning, (c) after etching in aqua regia solution; (b, c) laser confocal microscope.

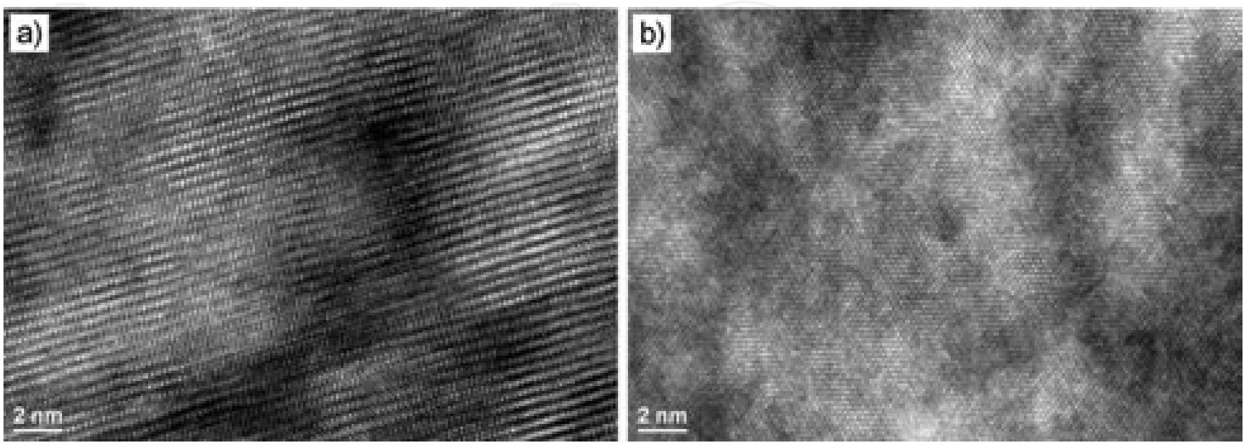

Figure 12. Crystalline structure of: (a) pristine titanium, (b) Ti6Al4V alloy; HRTEM image.

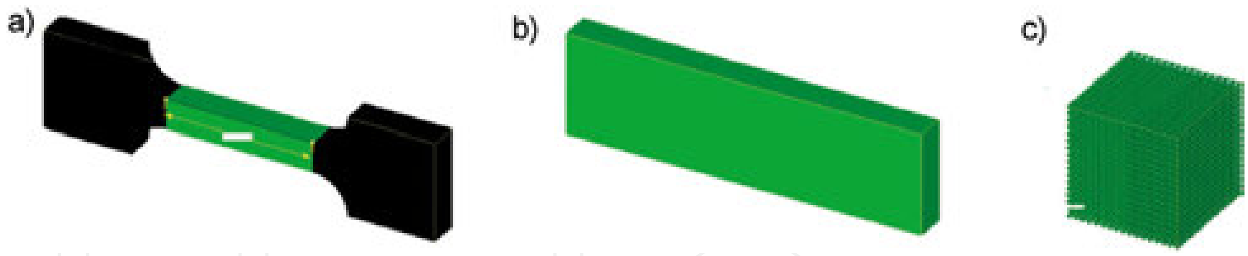

Figure 13. Image of computer model of solid samples for static test: (a) tensile test, (b) three-point bending test, (c) compression test.

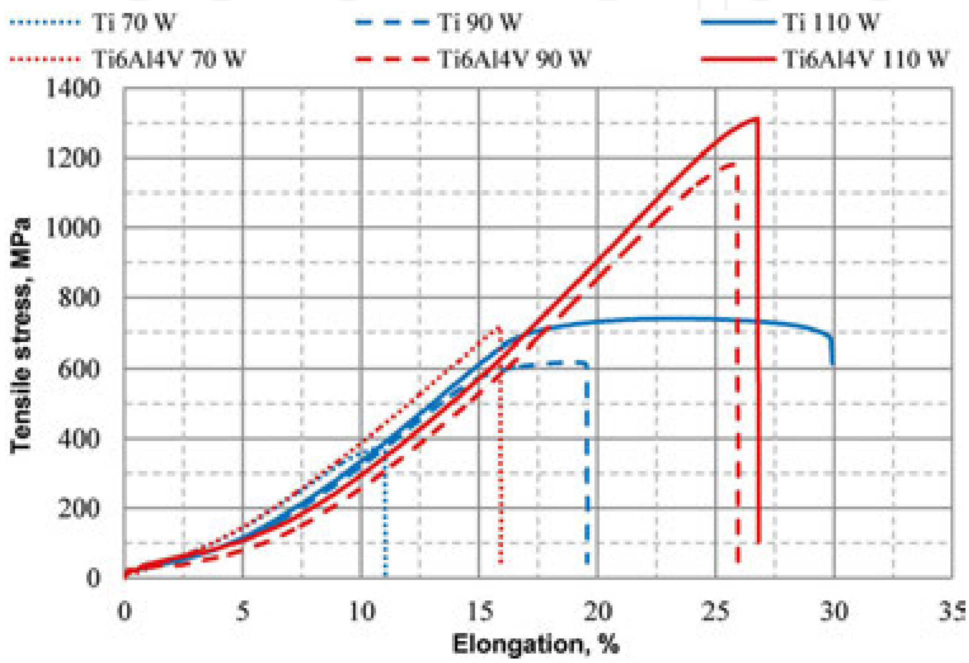

Figure 14. Comparison of diagrams of dependency between tensile stress and elongation for solid samples made of Ti6Al4V alloy and pristine titanium sintered at different laser powers [119].

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.

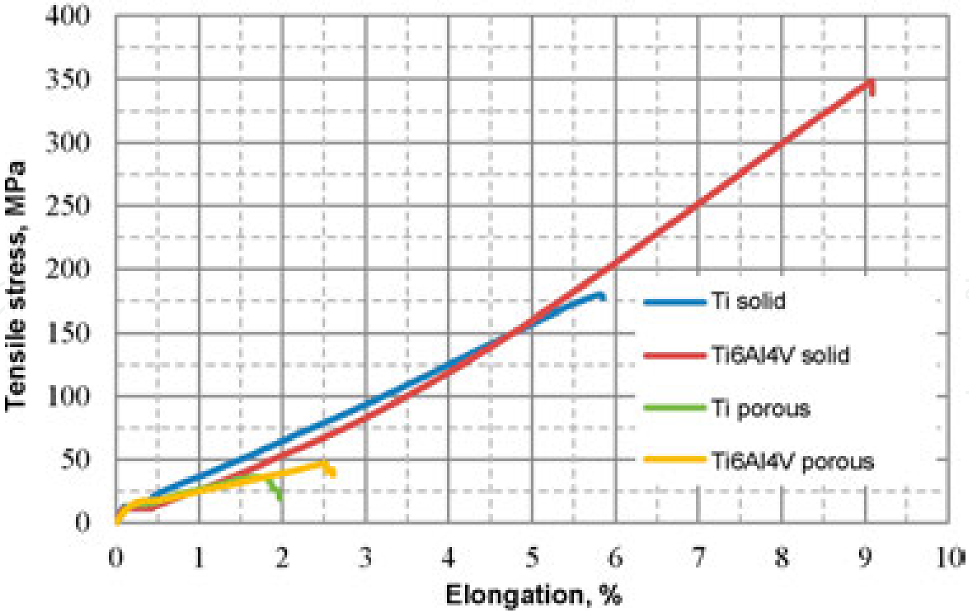

Figure 15. Comparison of diagrams of dependency between tensile stress and elongation for solid and porous laser sintered Ti and Ti6Al4V alloy samples with the pore size of approx. 250 μm [119].

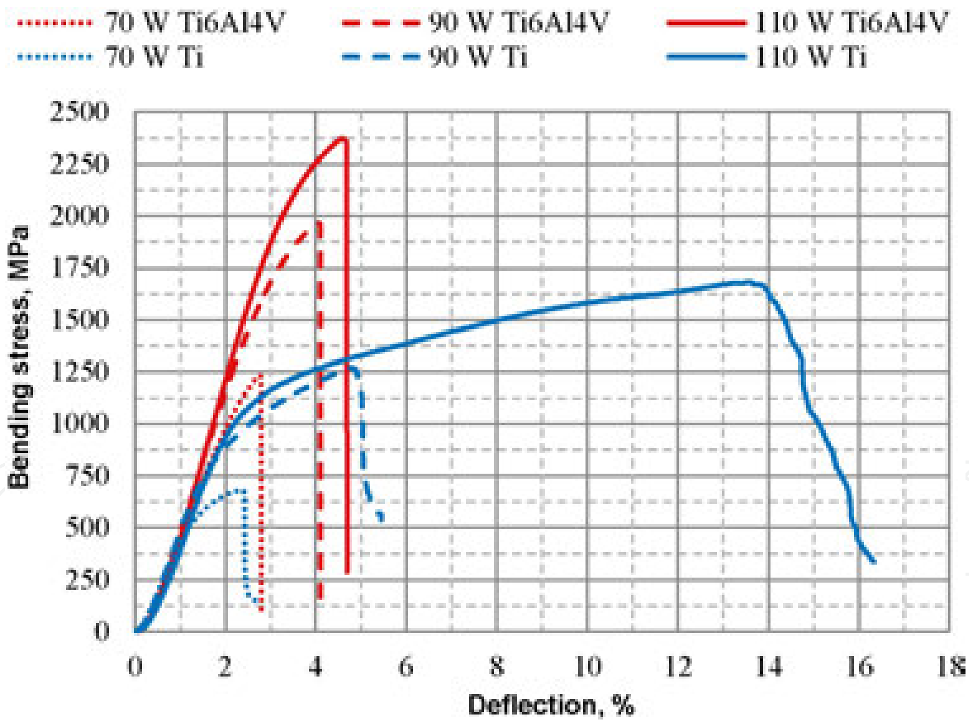

Figure 16. Comparison of diagrams of dependency between bending stress and deflection for solid samples made of Ti6Al4V alloy and pristine titanium sintered at different laser powers [119].

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**).

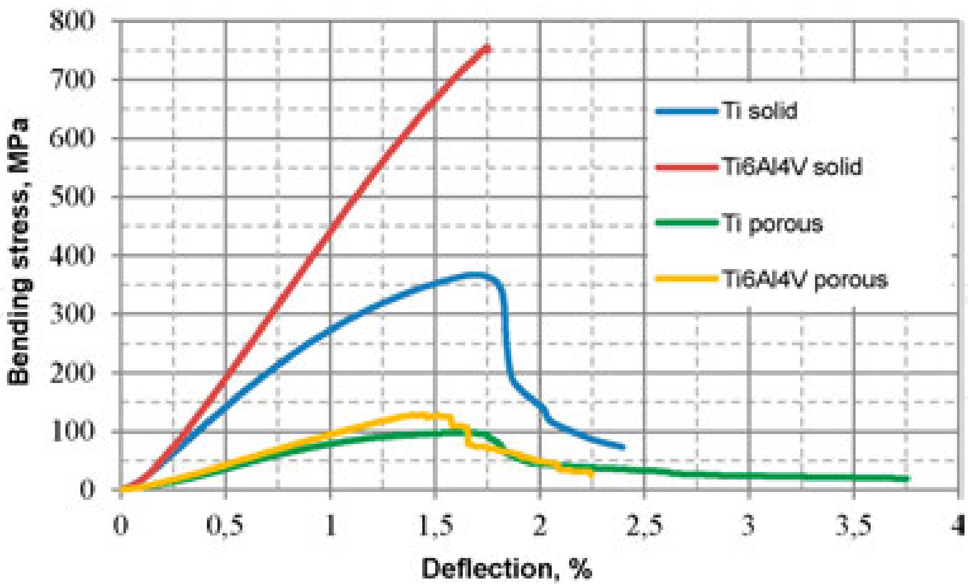

Figure 17. Comparison of diagrams of dependency between bending stress and deflection for solid and porous selectively laser sintered Ti and Ti6Al4V alloy samples with the pore size of approx. 250 μm [119].

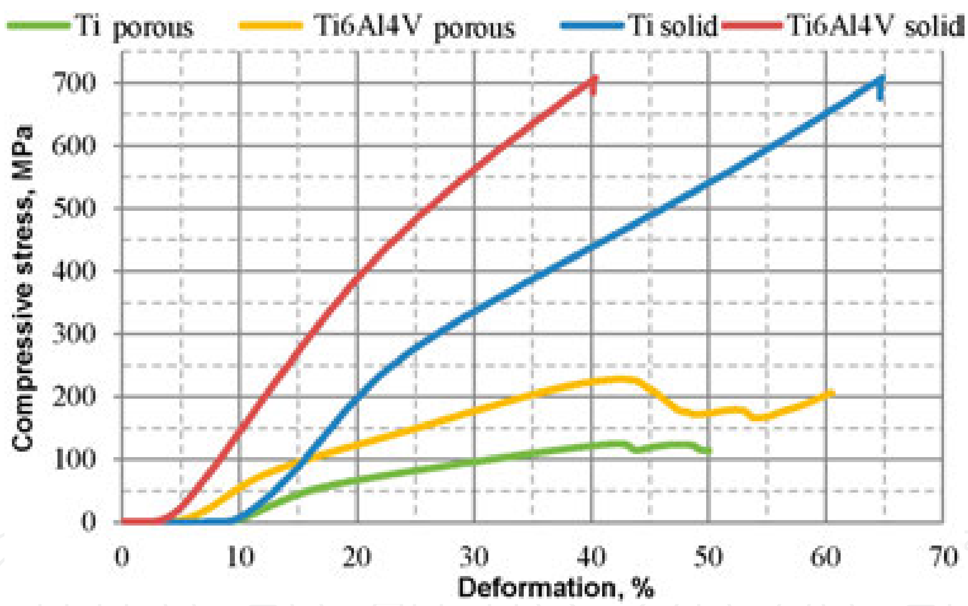

Figure 18. Comparison of diagrams of dependency between compressive stress and deformation for solid and porous selectively laser sintered Ti and Ti6Al4V alloy samples [119].

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 TiO_2 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_2O_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_2O_3 layers were deposited in 500 cycles, are dark brown; such onto which Al_2O_3 layers were deposited in 1000 cycles are navy blue, and such onto which Al_2O_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

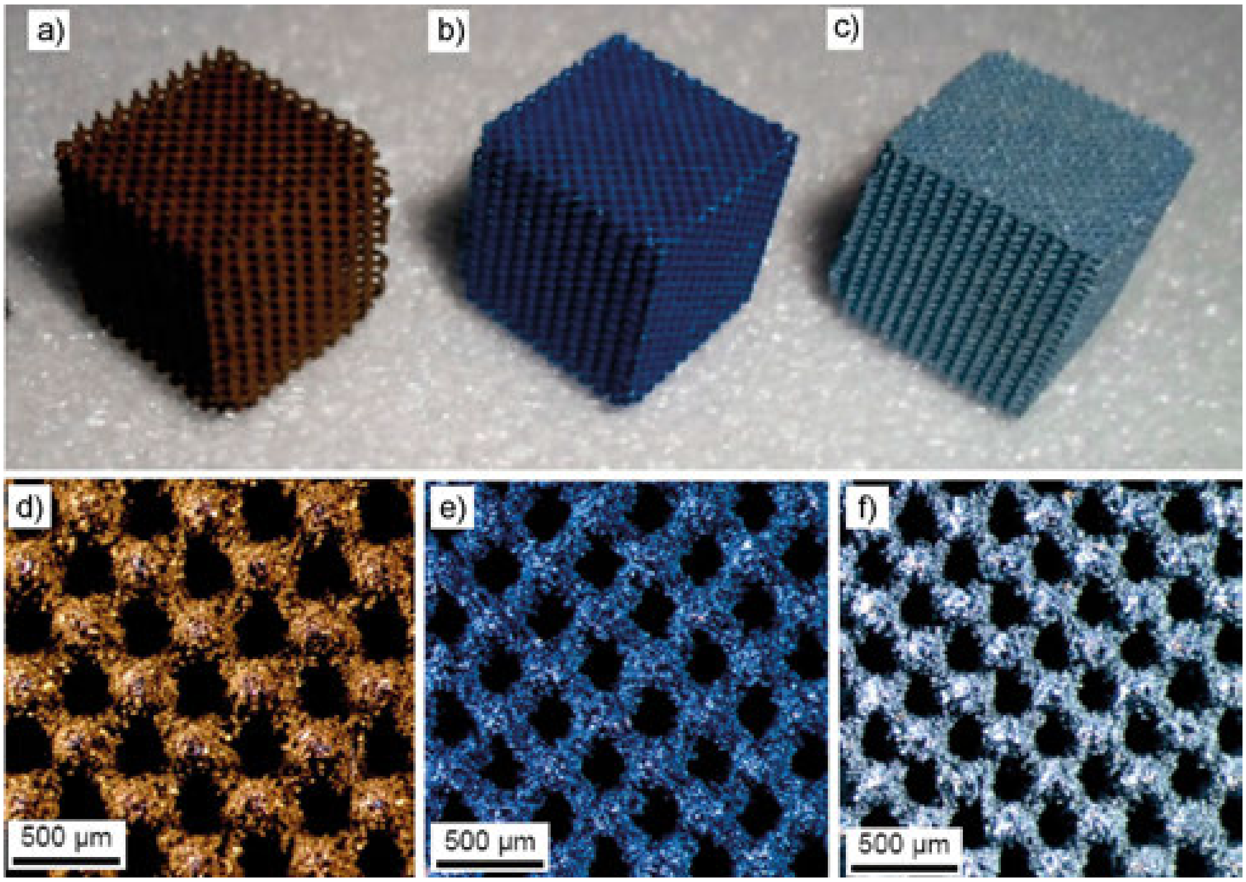

Figure 19. Titanium scaffolds coated with TiO_2 layers deposited by ALD; (a–c) cubic scaffolds viewed with bare eye, (d–f) stereoscopic scaffold images made with the magnification of 32× after: (a, d) 500 cycles, (b, e) 1000 cycles, (c, f) 1500 cycles.

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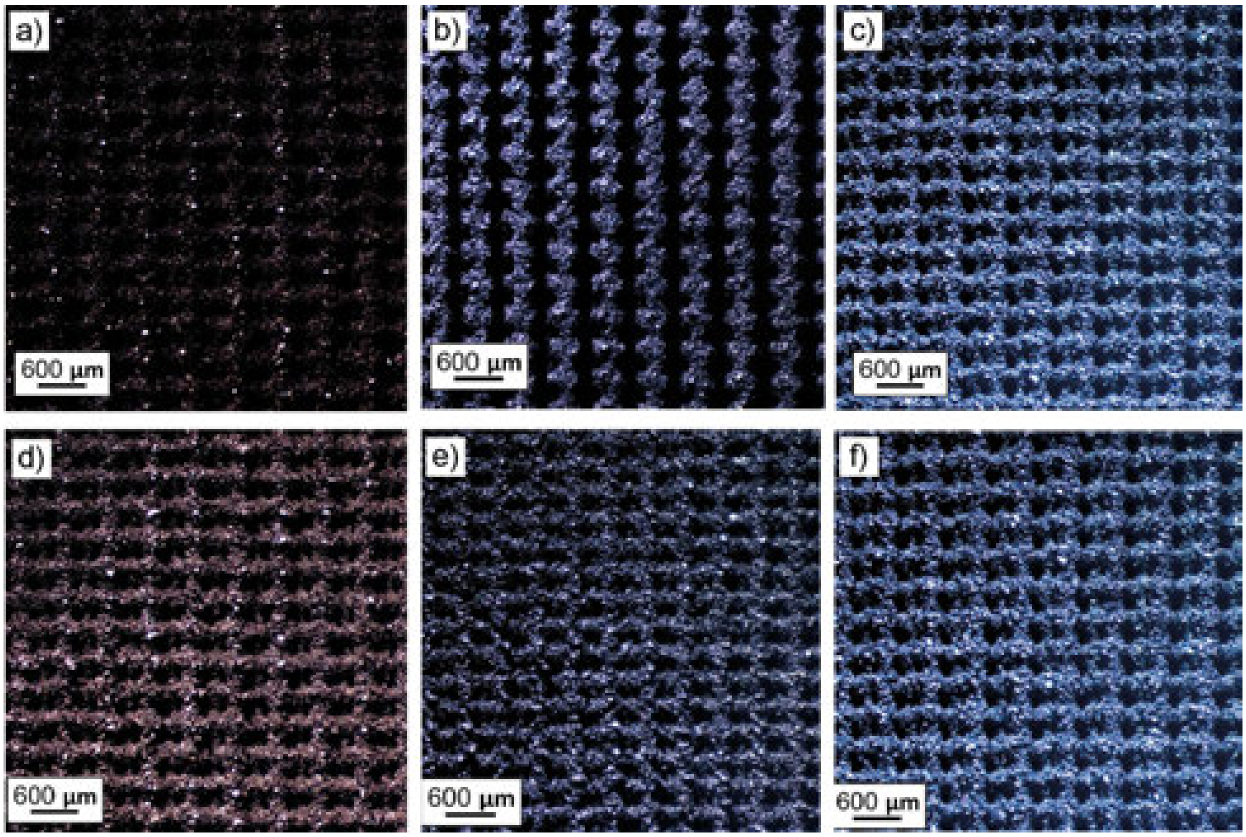

Figure 20. Surface topography of scaffolds manufactured from: (a–c) pristine titanium; (d–f) Ti6Al4V alloy; and coated with a layer of Al_2O_3 in: (a, d) 500; (b, e) 1000; (c, f) 1500 cycles; stereoscope microscope.

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

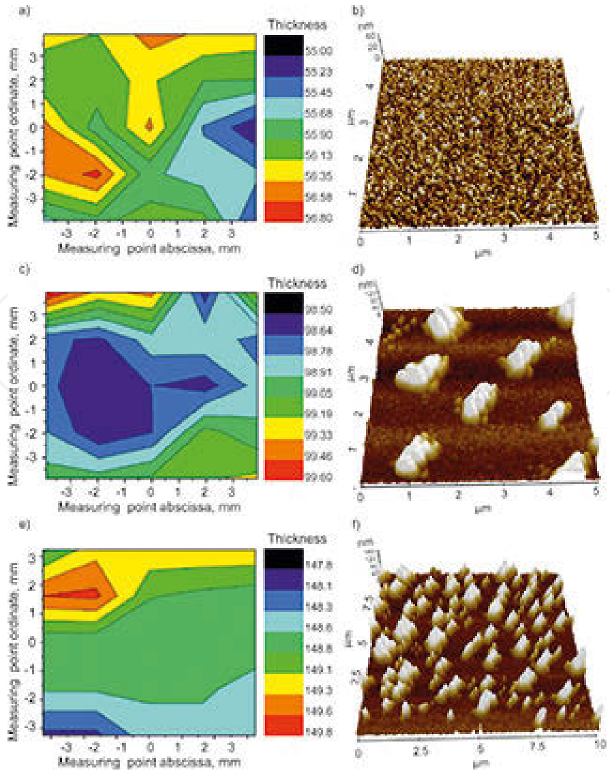

Figure 21. Titanium scaffolds coated with TiO_2 layers deposited by ALD after: (a, b) 500 cycles, (c, d) 1000 cycles, (e, f) 1500 cycles; (a, c, e) thickness deposition maps; (b, d, f) AFM image of 3D surface topography.

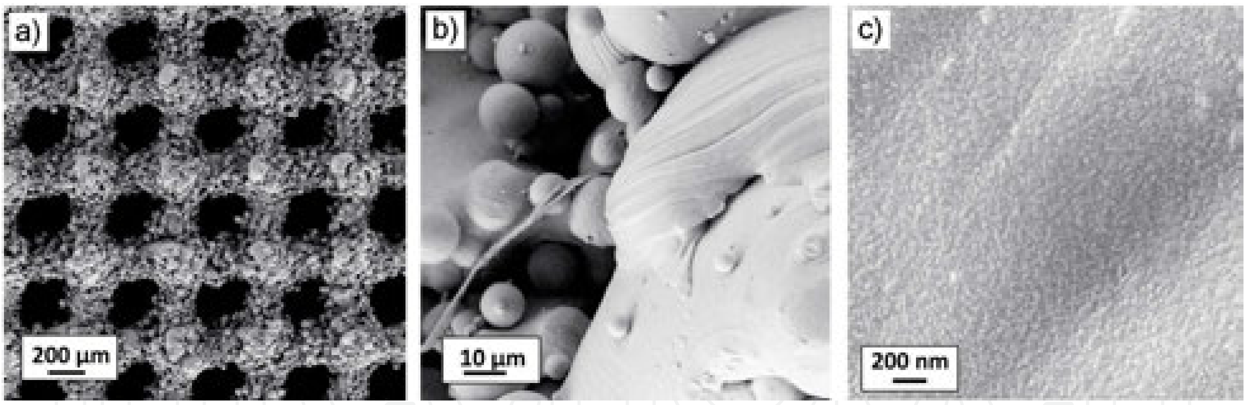

Figure 22. Scaffold surface with TiO_2 layer deposited in 1500 cycles presented with different magnificence (a, b, c); SEM images.

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 TiO_2 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 TiO_2 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.

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_2O_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

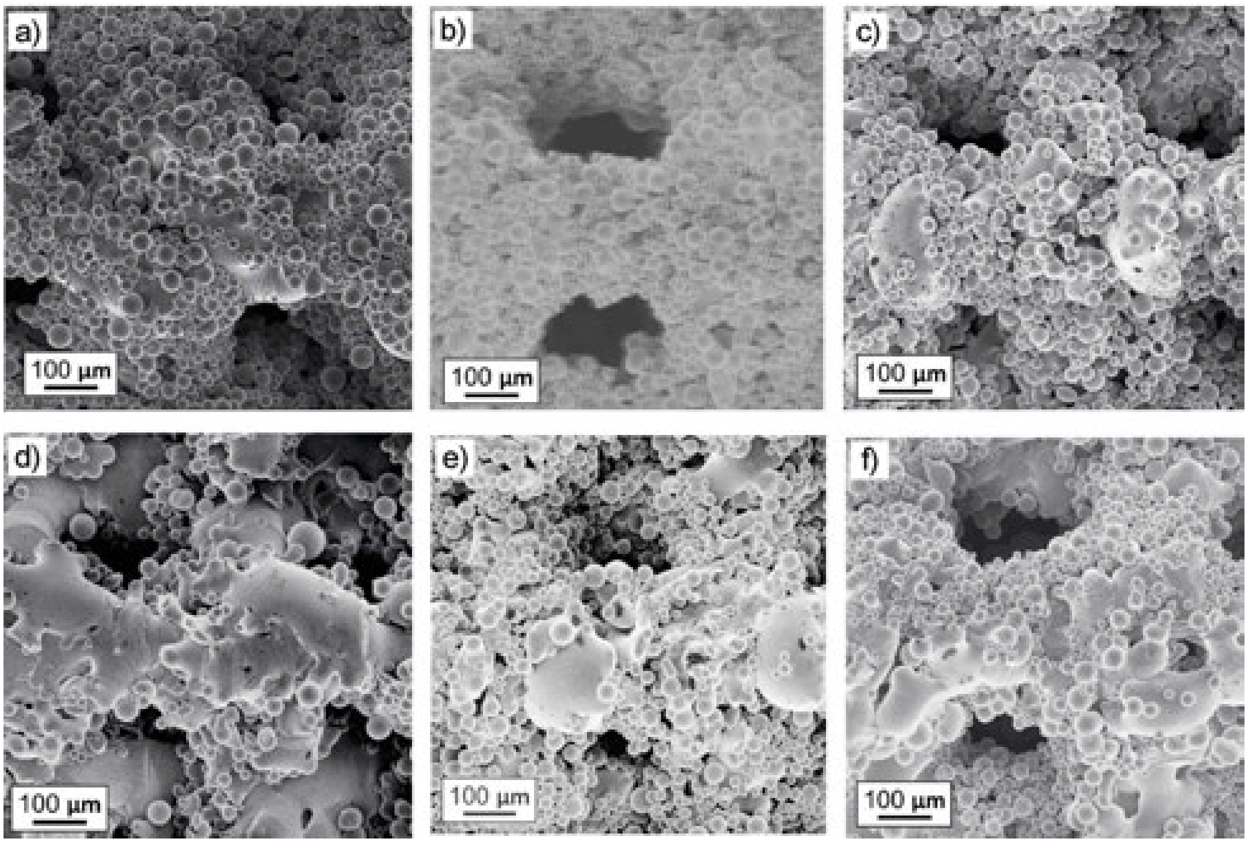

Figure 23. Surface topography of scaffolds manufactured from: (a–c) pristine titanium; (d–f) Ti6Al4V alloy and coated with Al_2O_3 layer in: (a, d) 500; (b, e) 1000; (c, f) 1500 cycles; SEM.

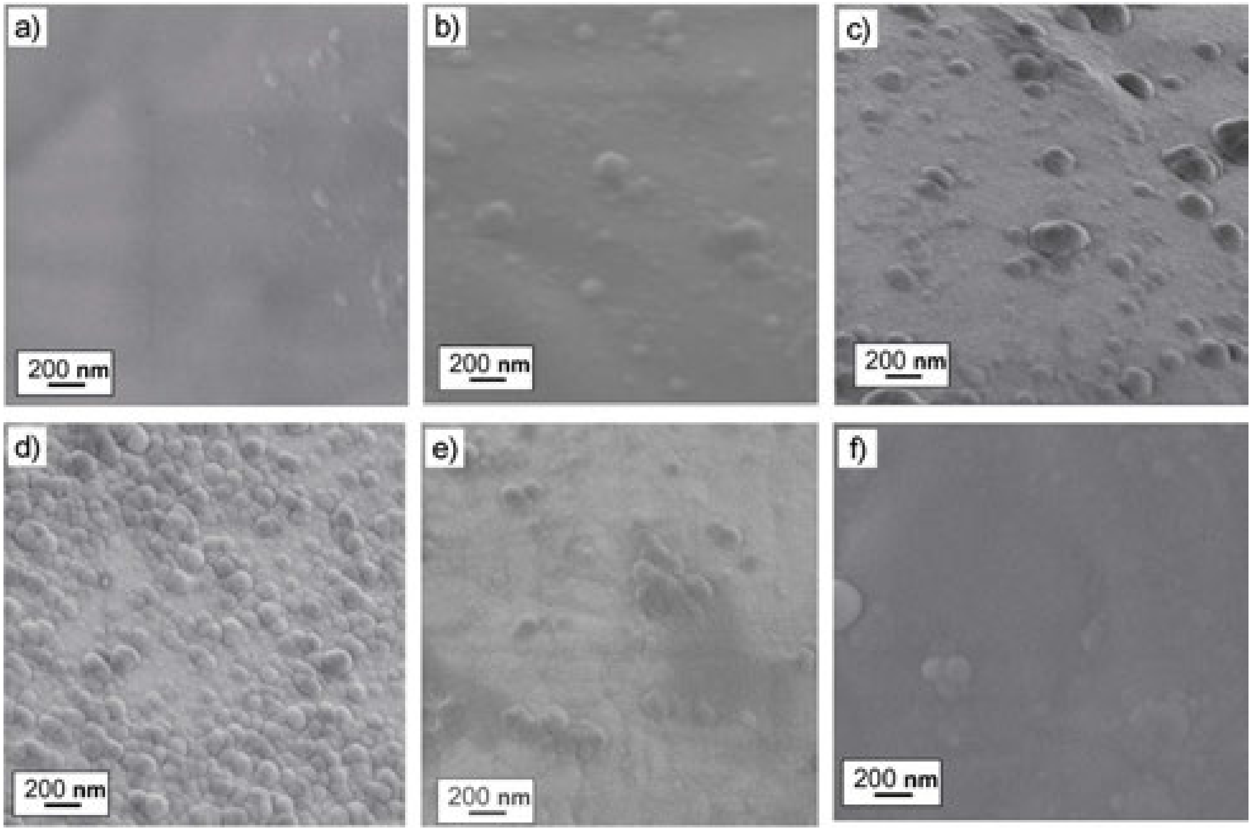

Figure 24. High-resolution surface topography of scaffolds manufactured from: (a–c) pristine titanium; (d–f) Ti6Al4V alloy and coated with Al_2O_3 layer in: (a, d) 500; (b, e) 1000; (c, f) 1500 cycles; SEM.

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

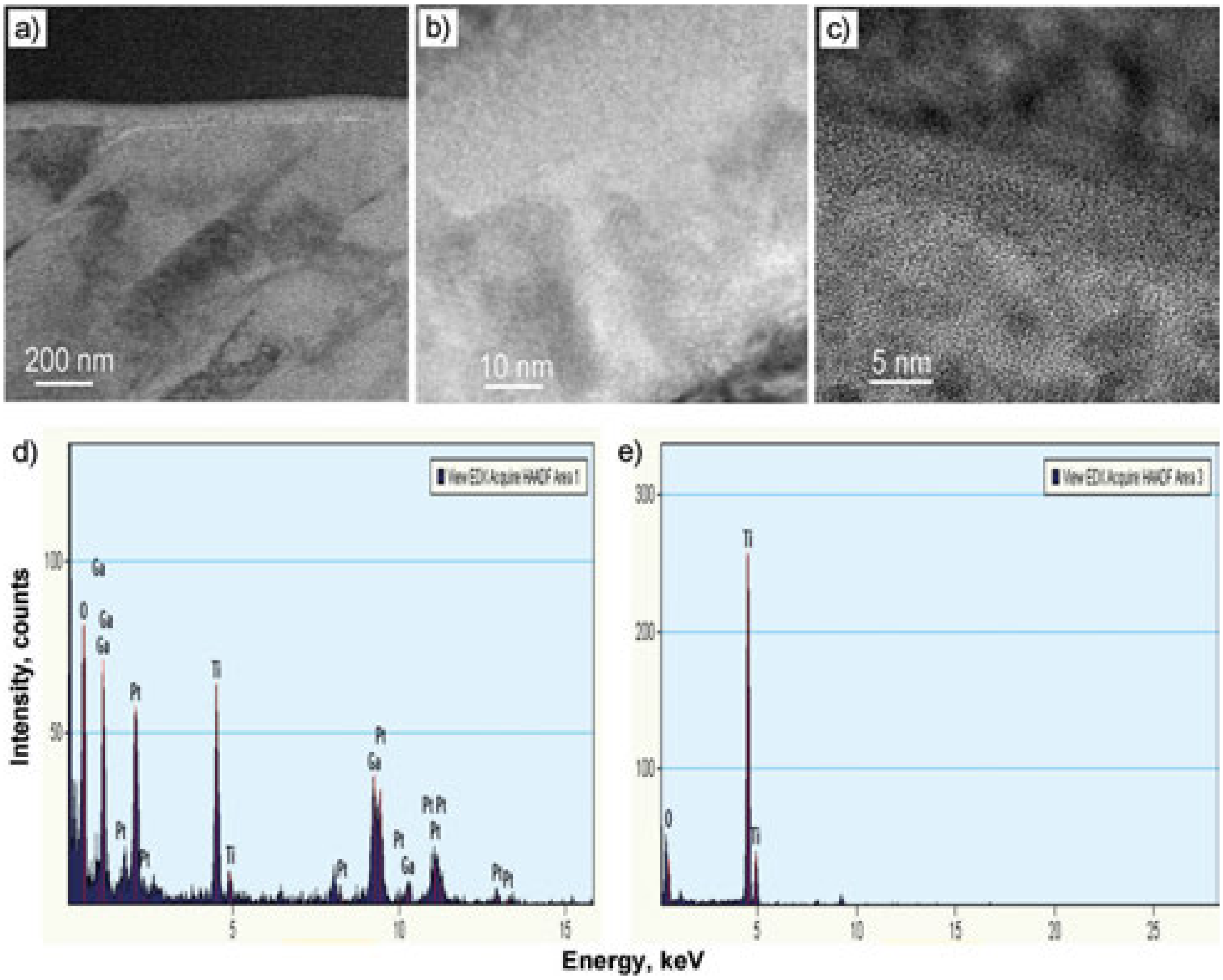

Figure 25. Amorphous TiO_2 layer deposited onto pristine titanium with a crystalline structure in a technological process lasting 1500 cycles; (a–c) HRTEM; (d, e) qualitative analysis of EDS chemical composition of TiO_2 layer: (d) from the peripheral region contiguous to the protective platinum layer; (c) near a titanium substrate.

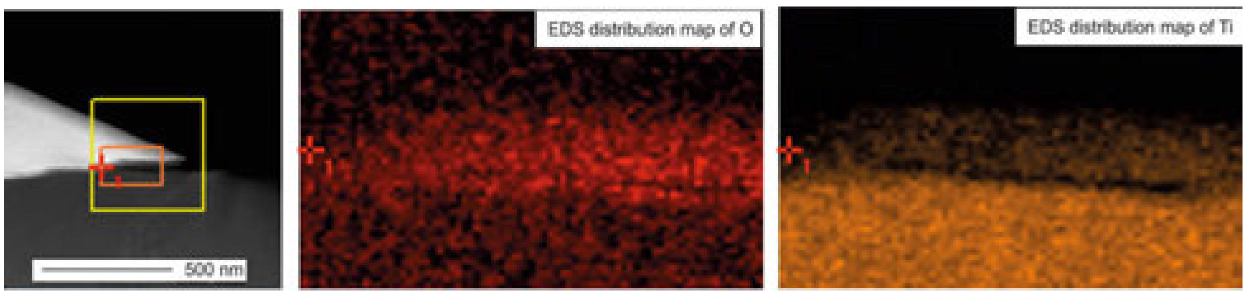

Figure 26. Distribution map of chemical elements present in the TiO_2 layer situated near titanium substrate.

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

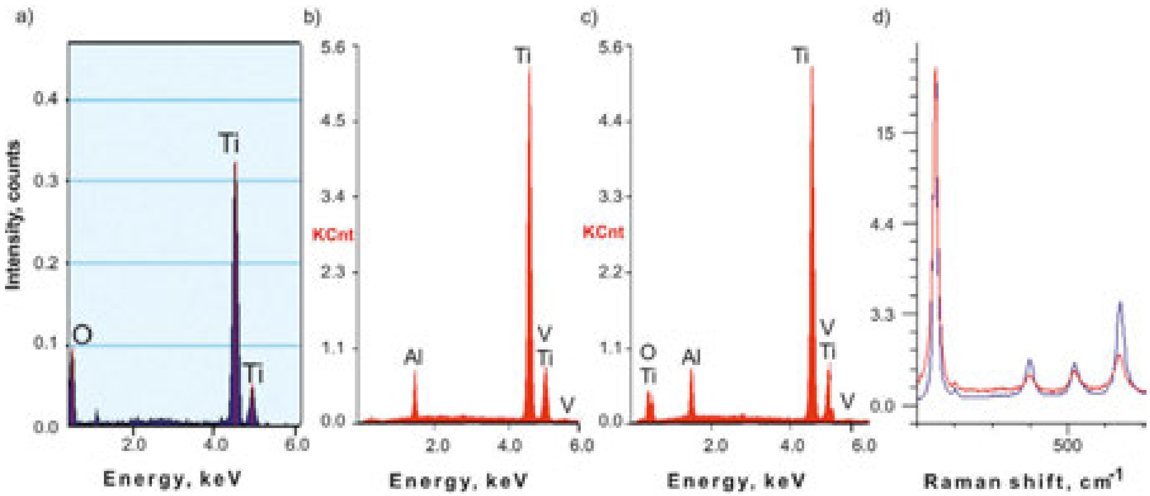

Figure 27. (a) Qualitative analysis of EDS chemical composition of TiO_2 layer; (b, c) results of qualitative analysis of chemical composition of: (b) TiAl6V4 without ALD layer, (c) TiAl6V4 with TiO_2 layer deposited by ALD method after 1500 cycles; (d) Raman spectrum of Ti6Al4V scaffold deposited by ALD method with TiO_2 layer [124].

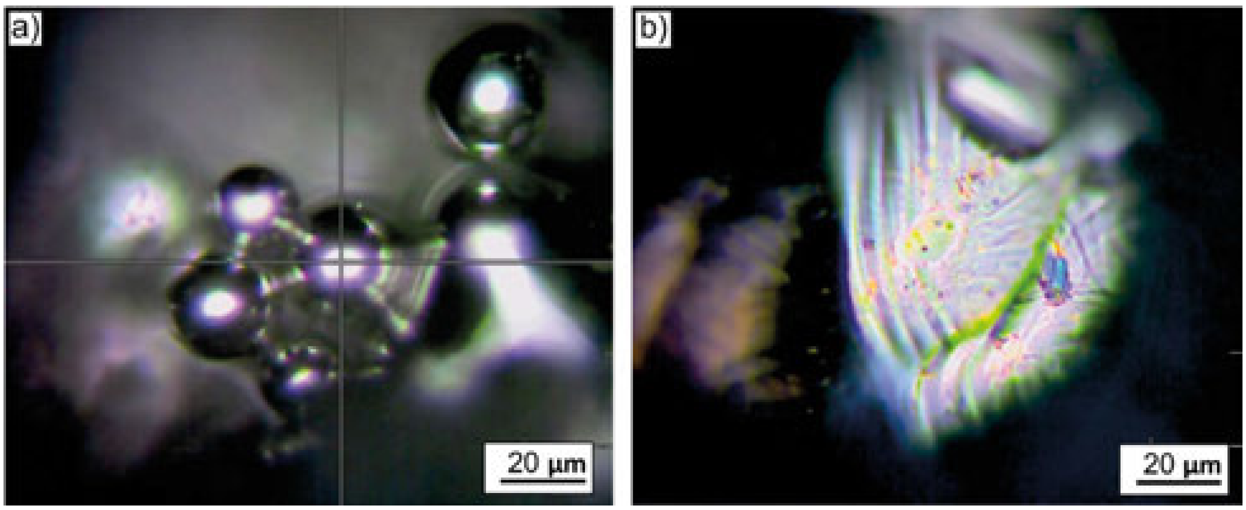

Figure 28. Points where Raman spectra were recorded, originating from: (a) reference Ti6Al4V scaffold, (b) Ti6Al4V scaffold covered with a layer of TiO_2; images coming from a confocal microscope.

points where spectra were recorded, originating from a reference Ti6Al4V scaffold and a scaffold covered with a layer of TiO_2; the images were made with a confocal microscope being a constituent part of the inVia Reflex device.

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, $\lambda = 1.54050 \cdot 10^{-10}$ m) using filtered radiation of a copper lamp with the voltage of 45 kV and a filament current of 35 mA, and the deposited TiO_2 layers were examined with the razing-incidence method due to the small thickness of not more than 150 nm, thus extinguishing

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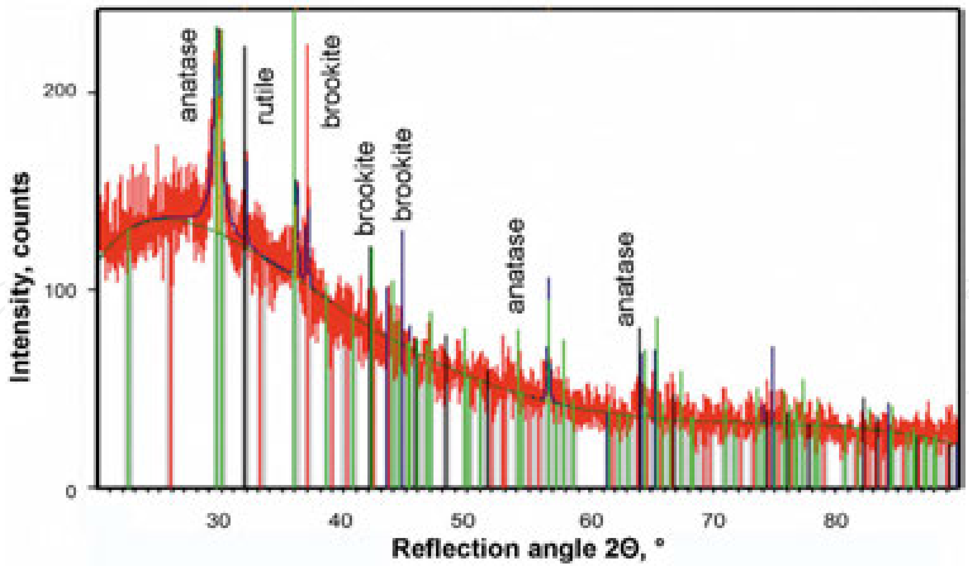

Figure 29. X-ray diffraction pattern of TiO_2 layer applied by atomic layer deposition (ALD) performed with the razing-incidence X-ray diffraction method.

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 Al_2O_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 Al_2O_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

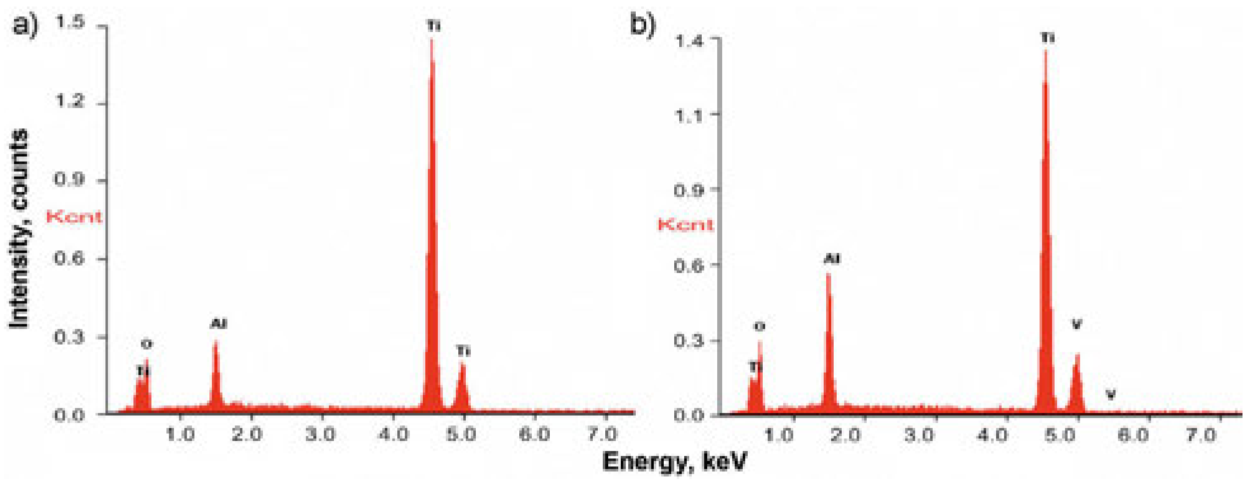

Figure 30. EDS spectrum made for scaffolds manufactured from: (a) pristine titanium; (b) Ti6Al4V titanium alloy; and coated with Al_2O_3 layers in 500 cycles.

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

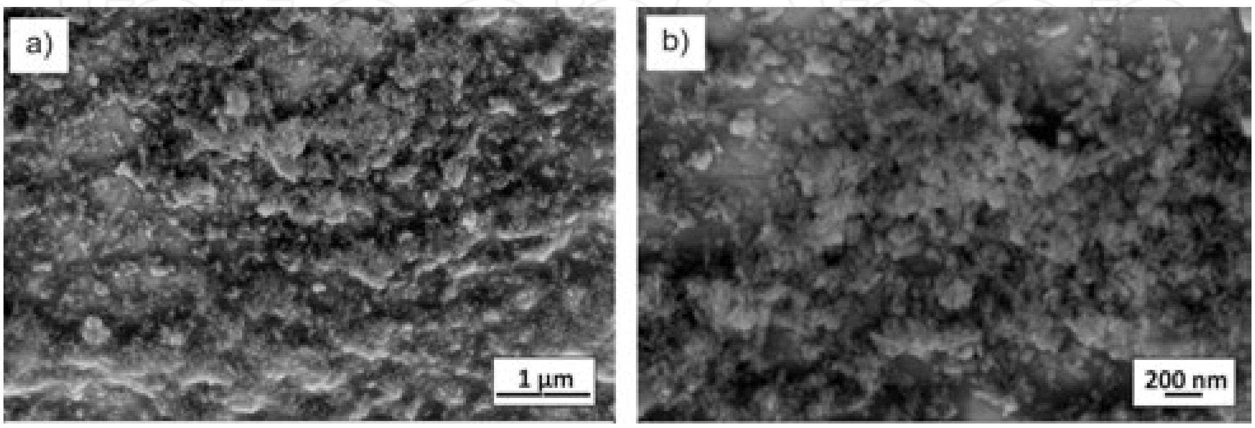

Figure 31. Scaffold made of Ti with the sol-gel layer of hydroxyapatite deposited after 10 immersions presented with different magnificence (a, b); SEM images.

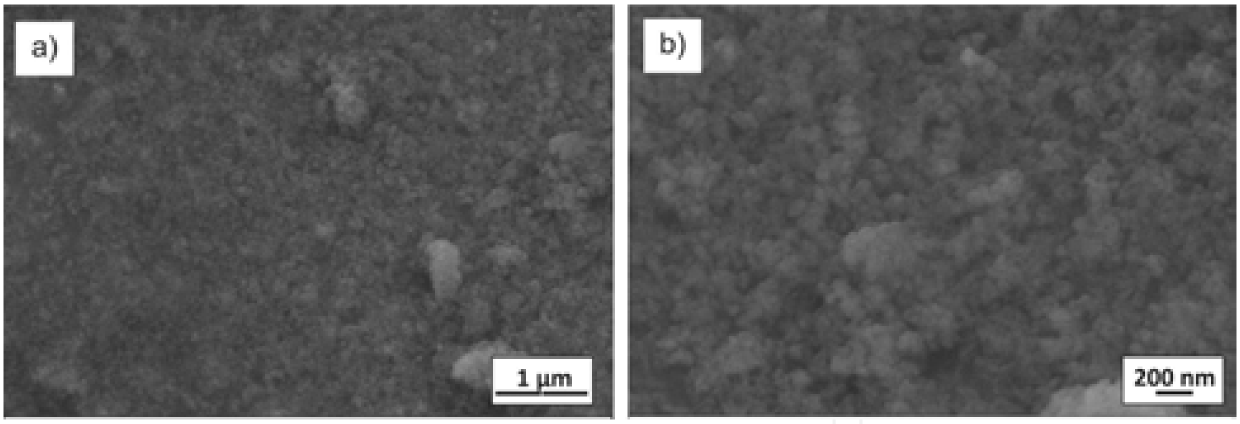

Figure 32. Scaffold made of Ti6Al4V alloy with the sol-gel layer of hydroxyapatite deposited after 10 immersions presented with different magnificence (a, b); SEM images.

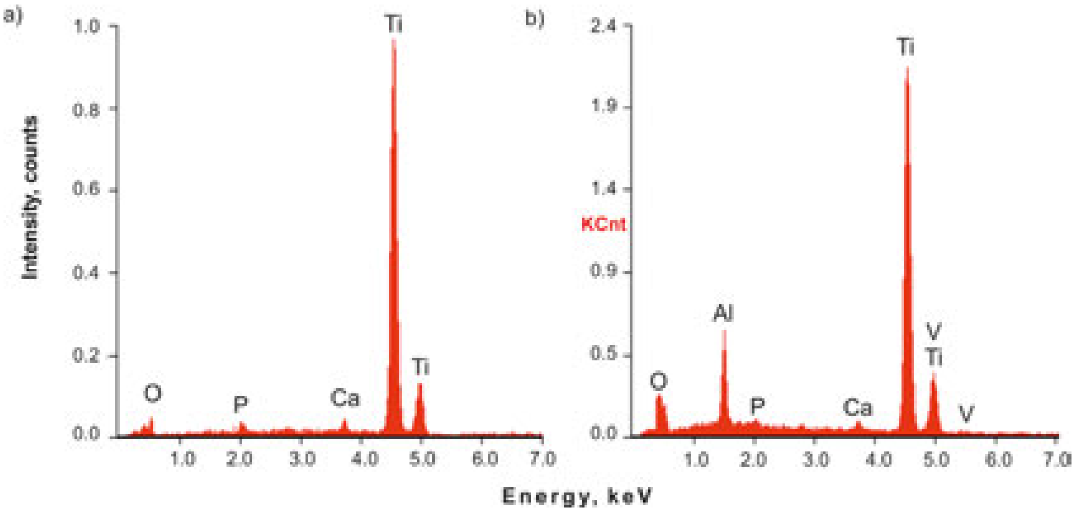

Figure 33. EDS spectrum of scaffold made of: (a) Ti, (b) Ti6Al4V: With a sol-gel layer of hydroxyapatite deposited after 10 immersions.

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**).

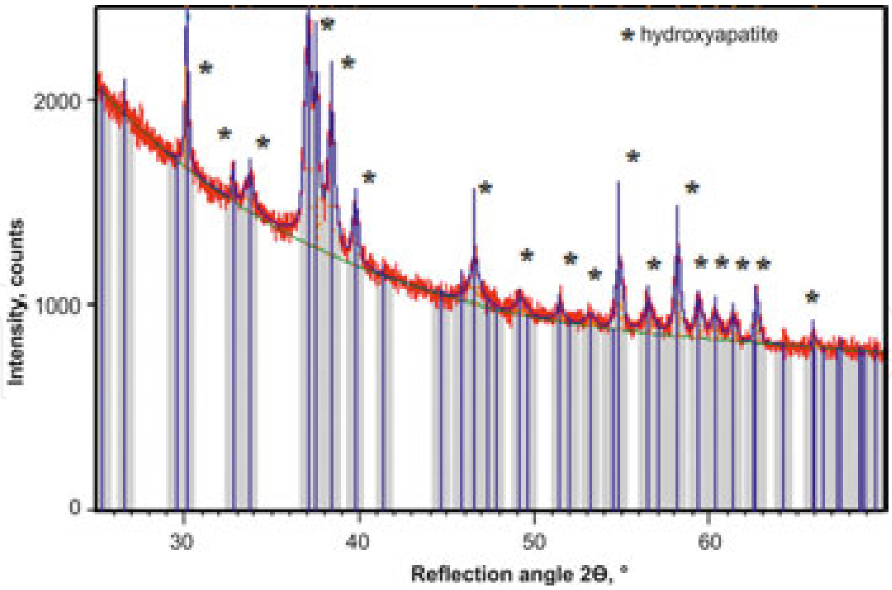

Figure 34. X-ray diffraction pattern of hydroxyapatite layer made with the sol-gel method.

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 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 μm 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 prosthodontics. 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 μm 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.

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