ANODIZATION OF Ti-BASED MATERIALS FOR BIOMEDICAL APPLICATIONS: A REVIEW

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Abstract
Commercially pure titanium (cpTi) and titanium alloys are the most commonly used metallic biomaterials. Biomedical requirements for the successful usage of metallic implant materials include their high mechanical strength, low elastic modulus, excellent biocompatibility and high corrosion resistance. It is evident that the response of a biomaterial implanted into the human body depends entirely on its biocompatibility and surface properties. Therefore, in order to improve the performance of biomaterials in biological systems modification of their surface is necessary. One of most commonly used method of implant materials surface modification is electrochemical anodization and this method is reviewed in the present work. Aim of the presented review article is to explain the electrochemical anodization process and the way in which the nanotubes are formed by anodization on the metallic material surface. Influence of anodizing parameters on the nanotubes characteristics, such as nanotube diameter, length and nanotubular layer thickness, are described, as well as the anodized nanotubes influence on the material surface properties, corrosion resistance and biocompatibility.

Keywords: Titanium-based materials, implant material bioactivation, anodization, anodization conditions, nanotubular layer

Introduction
Titanium (Ti) and titanium alloys are considered to be one of the most significant biomaterials due to their resistance to body fluid effects, great tensile strength,

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flexibility, high corrosion resistance and specific combination of strength and biocompatibility [1]. Numerous applications of titanium-based materials can be found in biomedicine, for instance in devices for artificial hearts, structural applications such as screws and dental implant pins, and dental and orthopedic prostheses [2]. Commercially pure titanium (cpTi) is considered to be one of the best biocompatible metallic materials for dental applications, because its surface properties result in the spontaneous formation of a stable passive oxide layer. On the other hand, the Ti-6Al-4V alloy, as α+β type titanium alloy, has been used as structural biomaterial for manufacturing orthopedic prostheses and dental implants owing to its excellent specific strength, corrosion resistance, and biocompatible characteristics. However, it has been recently reported that the release of vanadium ions from the alloy during its use might cause health problems due to their toxicity [3]. For this reason, there is growing research activity on developing vanadium-free titanium alloys for biomedical applications with a good combination of biocompatibility, corrosion resistance and mechanical properties similar to those of Ti-6Al-4V.

Recently, β type Ti alloys containing Nb, Zr, Ta, Mo, Sn, etc. have attracted considerable attention especially for orthopedic implants applications [1]. Their unique combination of mechanical properties, low elastic modulus, superior corrosion resistance, no allergic problems, and excellent biocompatibility make them attractive material of modern age. Moreover, it is found that their elastic modulus can be significantly reduced by adjusting the concentration of β stabilizing elements influencing in that way stress shielding effect avoidance.

Titanium and its alloys, due to their self-organized oxide layer, which protects the surface from corrosion and prevents ion release, are widely accepted as metallic implant materials [4,5]. Titanium is a reactive material and has a very high affinity for oxygen, which means that if the metal is in the presence of air or oxidizing media, as is the case in a biological system when a bioliquid surrounds the metal, the protective thin oxide film (about 3-8 nm in thickness) is formed spontaneously and instantly and its disruption or damage is repaired immediately [4,6]. The nature, composition and thickness of the protective oxide layers formed on titanium-based materials depend on the environmental conditions and alloy composition [6], while the stability of this layer depends strongly on its composition, structure and thickness [7]. Usually, the composition of the protective oxide film is based mainly on TiO₂, Ti₃O₅ or TiO.

It is important to underline that the behavior of the implant material is not only governed by the bulk material (critical in determining the biological performance), but also by its surface properties (surface chemistry and structure), which are crucial factors in the interactions of the material with the surrounding tissue.

**Surface modification of titanium and its alloys**

The surface of an implant often needs some kind of modification to optimize the properties of the implant and to maximize its bioactivity when interfacing with natural tissue. These methods are known as surface treatments or modifications, and can be classified into four categories: mechanical, physical, chemical and biochemical surface modifications. Chemical surface modifications include chemical treatment (with acid, hydrogen peroxide and alkaline solutions), electrochemical processes i.e. anodic oxidation, the sol-gel process and chemical vapor deposition [8].
Primarily, surface treatments of implant titanium alloys are needed in order to achieve better and more rapid bonding to bone [9]. The goal is to improve bioactivity, biocompatibility, wear and corrosion resistance of titanium-based materials for their biomedical applications. In most of the cases electrochemical surface modifications are performed by connecting a metallic implant device to the positive pole of the electrical circuit followed by its immersion in an electrolytic solution containing ion substance or oxidants. This methodology can lead to the deposition or installation of some ions on the material surface with the possibility to change the surface properties [10]. Electrochemical surface modification is initially galvanostatic process with a constant current density until the system reaches the desired voltage, after which the process continues at the same voltage during definite time. The electrochemical cell consists of one power supply and two electrodes: platinum or pure graphitic cathode as the control electrode and one titanium sample serving anode as the working electrode. Before the experiment starts titanium samples are polished with SiC paper (from 180 to 2000 grit) and cleaned in distilled water. As a result of the anodic oxidation nanotube oxide layer is obtained. The morphology and structure of obtained nanotubular layer depends on the substrate characteristics, solution composition and parameters of the electrochemical anodizing process.

Portan et al. [11] examined titanium dioxide nanotube layers, which were obtained by the electrochemical anodizing method. The surface modification process lasted 8 h at 25 V and in a 1 wt.% hydrofluoric acid solution. Schematic overview of this anodization process is presented in Figure 1.

**Fig. 1. Schematic overview of the anodizing process [11].**

**Anodization conditions influence on titanium nanotubes formation**

The most commonly used electrolytes in titanium anodizing are strong acids, e.g. H\(_2\)SO\(_4\), H\(_3\)PO\(_4\), HNO\(_3\), and HF, present in the form of: (i) an aqueous acidic solution containing F\(^-\) ions; (ii) an aqueous buffered solution; or (iii) a non aqueous electrolyte containing F\(^-\) ions with or without a trace amount of H\(_2\)O [8]. The type of electrolyte used and electric conditions applied during anodization process can affect the surface morphology, chemical composition, and crystalline structure of the oxide films formed.
by anodic oxidation [12]. When strong acids are used as electrolytic solutions, the oxide layer will be dissolved. The dissolution of the oxide layer creates micro or nano pores on titanium surface. In order to form self-ordering nanotubular oxide layers, presence of the fluoride (F-) ions in the electrolyte is desired [13]. A key feature of the F- ions is their ability to form soluble metal-fluoride complexes. The metal-fluoride complex helps the prevention of metallic oxides (MOx) layers formation at the tubular bottom, but it also leads to mild but steady chemical dissolution of the MOx. Another important factor is that F- ions are very small and can compete with O2- migration through the oxide layer. It has been noted that F- ions can migrate at a rate twice that of O2- ions through oxide layer, resulting in a fluoride layer formation at the metal-oxide interface [13]. When the anodizing is performed at an acidic pH value most of the F- ions are in the HF form. The diameter of the TiO2 nanotubes that grow in an HF electrolyte was reported to be between 15 nm and 140 nm [8].

The time of successful anodization increases with increasing the electrolyte pH; in fact, formed nanotubes are longer when obtained in alkaline environment compared to nanotubes formed in electrolytes with a lower pH [14]. Also, it was shown that the slightly acidic pH value influences the formation of long and smooth tubes [15]. The titanium-based layers are more hydrophobic than other layers formed in a buffered electrolyte. The hydrophilic value at the interface between the implant material surface and the living tissue is a crucial factor in cell adhesion. An organic electrolyte has a small quantity of oxygen in comparison to an aqueous solution. Nanotubes with a diameter of 20-160 nm were obtained at an applied potential varied between 30 and 120 V using an organic electrolyte [16].

Potential difference and current density applied during the anodization process can vary within an extensive range of values [17]. The polarization potential varies between few volts and 250 V depending on the desired oxide characteristics. In fact, low potential (1-130 V) leads to the achievement of a smooth, amorphous and about 3-100 nm thick oxide film [17]. Contrary, the high potentials (100-250 V) combined with high current densities, lead to the formation of an oxide layer whose thickness vary between few tens to hundreds micrometers. The surface oxide film formation includes several steps [8]. Initially, the natural TiO2 particles are grown, joined together forming a smooth surface. After that, in some surface areas cracks are developed and surface layer becomes porous. With increasing voltage values, the film breaks down locally, and regions of original and modified film develop simultaneously, with the latter occupying more of the surface as the voltage rises. When the voltage is high, TiO2 film formation occurs because of the migration of O2- ions into the metal/film interface and migration of the Ti4+ ions from metallic Ti to the film/electrolyte interface [8].

The applied voltage and the anodizing time also affect the shape of the formed nanotubes [18,19]. For example, in a water-free electrolyte consisting of acetic acid and NH4F, under low potential conditions diameter of the formed nanotubes is about 20 nm while their maximum length is 100 nm [20]. At lower anodizing voltages, the thickness of the obtained oxide layer does not exceed 300 nm [21]. The mean increase of the oxide layer thickness on the Ti-13Nb-13Zr alloy surface is 3-4 nmV⁻¹. The increase of the voltage to 140 V causes the increase of the oxide layer thickness to more than 1 μm [21]. Some studies have shown that the increase of voltage from 10 V to 25 V can
bring out the pore diameter from 30 nm to 150 nm, but above 30 V the nanotubular structure is completely destroyed [22].

It was observed that the nanotube diameter increases with increasing voltage, but that is not affected by time [23]. The nanotube diameter can be increased linearly with the applied potential increase if the electrolyte pH value remains constant. The tube diameter is pH independent if the applied potential remains constant. Saji et al. [24] showed that the diameters of the tubes may vary in the range of 25-110 nm. The average of the smallest and largest nanotubes diameter increases from 25 nm and 60 nm to 40 nm and 110 nm, respectively, when the potential was increased from 10 V to 25 V. In the above mentioned study, the average length of the nanotubes was 2 μm.

Minimal time necessary to create the nanotubular surface structure is between 30 min and 120 min [22]. However, the anodizing time also influences the thickness of the nanotubular layer. The anodizing time increase can increase the thickness of the formed nanotube oxide layer [8]. However, if anodizing is carried out for extended periods of time, nanotubular walls are thinned out [13]. Ossowska et al. [22] increased anodizing time from 0.5 h to 1 h and showed that the anodizing time had small effect on the nanotubes, mainly increasing their length. A TiO$_2$ nanotube layer, which has a maximum layer thickness of 1 μm was formed in an acidic electrolyte consisting of fluoride salt at an applied potential of 20 V [25]. Beranek et al. [26] showed that with the optimal voltage of 20 V and the optimal anodizing time of 12 h in the H$_2$SO$_4$ and H$_3$PO$_4$ electrolyte the TiO$_2$ nanotube maximum length of 500 nm can be achieved. On the other hand, TiO$_2$ nanotubes with a diameter of 70-100 nm can be formed in less than 2 h when anodization occurs at an applied potential of 20 V in the electrolyte which consists of HF [27,28].

Properties of nanotubes formed on Ti-based materials for biomedical applications

Electrochemical anodization technique under optimized conditions is an efficient and economic approach for the production of self-ordered nanotubular structure on biomaterial surface [29,30]. TiO$_2$ nanotubes with different diameters (from 15 nm up to 300 nm) and different lengths can be grown by anodization of titanium or its alloys. TiO$_2$ nanotubes can be obtained on all titanium alloys containing transition metals, such as Ti-6Al-7Nb, Ti-6Al-4V and Ti-Zr alloys with different Zr concentrations or on other alloys developed or tested for biomedical applications. During anodization TiO$_2$ nanotubes that are open at the top and closed at the bottom, and are of different sizes, can be formed by changing the concentration and type of electrolyte and the anodizing time and voltage [8]. In addition, the size and shape of nanostructured materials can be tuned to the desire dimensions.

In general, after anodization the composition of the formed oxide layer is consistent with the alloy composition and alloying elements ratio [23,31]. For instance, the anodic oxide nanotubular layers on Ti-Al alloys are composed of TiO$_2$ and Al$_2$O$_3$, and in the case of Ti-6Al-7Nb alloy the surface layer is composed of TiO$_2$, Al$_2$O$_3$, and Nb$_2$O$_5$ [21]. The fraction of these types of oxides is the respective fraction of Ti, Al and Nb in the base alloys. Mosiálek et al. [21] showed that the chemical composition of the electropolished Ti-13Nb-13Zr alloy surface (Ti/Zr/Nb = 4.0:0.55:1) is similar to the composition of the alloy (Ti/Zr/Nb = 5.6:1:1), but that the surface is depleted in titanium and zirconium. The chemical composition of the surface oxide layer formed at
100 V (Ti/Zr/Nb = 12.6:1:1) is similar to air-formed native oxide layer on that alloy (Ti/Zr/Nb = 12.7:1.2:1), which is composed mainly of TiO$_2$, ZrO$_2$, and Nb$_2$O$_5$, with a small amount of TiO and Ti$_2$O$_3$ [24]. Anodization of the Ti-13Nb-13Zr alloy surface at lower potential (10V) resulted in formation of the spongy-porous oxide layer with pore sizes in the range of 10-20 nm. At higher potential (40V), compact porous oxide layer with pore size in the range of 50-100 nm was obtained. Chemical analysis of the formed nanotubes showed that nanotubes were composed of three constituent elements of the alloy and the presence of Nb and Zr oxides in the nanotubes was confirmed [32]. Thus it can be believed that the nanotubes formed on alloy may have enhanced mechanical properties and adhesion to the substrate.

Nanotubular oxide layer significantly increases the osteoblasts or bone cell adhesion to the titanium-based material surfaces compared to their non-anodized counterparts [7]. The nanotube layer plays a major role in improving the implant osseointegration through the adhesion improvement of hydroxyapatite (HAP) coating. Also, there are many studies dealing with the effect of the nanotube length and wall thickness on the surface roughness, corrosion resistance and biocompatibility of the metallic implant materials [33-37]. Detailed overview of already published research results regarding the effect of electrochemical anodization process on the Ti-based materials properties is given in Table 1.
Table 1. The effects of electrochemical anodization process on the Ti-based materials properties [7,12,17,21,22,24,32,36-44].

| Reference             | Implant material | Anodization conditions                                      | Examined properties of anodized material                                      | Obtained research results                                                                 |
|-----------------------|------------------|------------------------------------------------------------|-------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| N.A. Al-Mobarak et al. [7] | cpTi             | Electrolyte: 1M Na$_2$SO$_4$ + 0.5wt.% NaF, 1 M H$_3$PO$_4$ + 0.8wt.% NaF, 0.5 wt.% HF | Corrosion resistance (electrochemical measurements)                           | The electrochemical measurement results indicate that the electrochemical stability of the nanotubular surface depends on the formed TiO$_2$ nanotubes diameter. Larger nanotube diameter decreases corrosion resistance. |
| N.A. El-Wassef et al. [12] | cpTi (grade 2)  | Electrolyte: 1M H$_2$SO$_4$, Voltage: 200 V, Time: 5 min | Surface characterization (AFM, SEM)                                           | Anodization increased the surface roughness. Also, the surface area increased linearly with increasing the anodization time |
| M.V. Diamanti et al. [17] | cpTi (grade 2)  | Electrolyte: 0.25-2M H$_2$SO$_4$, Current: 100-1080 A/m$^2$, Voltage: 10-150 V | Surface characterization (XRD)                                                 | Surface oxide conversion to anatase is promoted either by an increase in current density or by a decrease in sulphuric acid concentration. |
| M. Mosialek et al. [21] | Ti-13Nb-13Zr     | Electrolyte: H$_3$PO$_4$, Surface characterization (SEM, XPS) | Corrosion resistance (electrochemical measurements)                         | The alloy oxide layer shows very high corrosion resistance. |
| Reference           | Implant material | Anodization conditions | Examined properties of anodized material | Obtained research results |
|---------------------|------------------|------------------------|------------------------------------------|---------------------------|
| A. Ossowska et al. [22] | Ti-13Nb-13Zr     | Electrolyte: 1M H₃PO₄ + 0.3% or 0.5% HF, Voltage: 20 V, Time: 0.5 or 1 h, Temperature: room temperature | Surface characterization (SEM, EDS) Corrosion resistance (electrochemical measurements) Nanohardness and microhardness measurements Young's modulus determination Nanoscratch tests | The length of nanotubes ranges between 1 μm and 2 μm, while their diameter is in the range between 40 nm and 120 nm. The nanotubular oxide structure is observed to increase the corrosion resistance of the alloy. Nanohardness, microhardness and Young's modulus values are significantly lower. The Young's modulus of the nanotubular layer can be 36-43 GPa. The results of nanoscratch tests show that the TiO₂ layer is removed from the substrate earlier for non-anodized sample. |
| V. Saji et al. [24] | Ti-13Nb-13Zr     | Electrolyte: 1M H₃PO₄ + 0.5wt.% NaF, Voltage: different voltages, Time: different duration, Temperature: room temperature | Surface characterization (SEM, XRD, TEM) | Nanotubes with diameter in the range of 25-110 nm can be formed on alloy surface. |
| Reference                      | Implant material | Anodization conditions | Examined properties of anodized material | Obtained research results                                                                                                                                                                                                 |
|-------------------------------|------------------|------------------------|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| V. Saji et al [32]            | Ti-13Nb-13Zr     | Electrolyte: 1M H₃PO₄ + 0.5wt.% NaF | Surface characterization (SEM, XRD, TEM) Corrosion resistance (electrochemical measurements) | Anodization of the Ti-13Nb-13Zr alloy decreases its corrosion resistance. The alloy after nanotubular oxide layer formation exhibited significantly higher corrosion current density than the bare alloy. The lower corrosion resistance of the nanotubular alloy was suggested to be associated with the distinctly separated barrier oxide/concave shaped tube bottom interface. |
| J. Park et al. [38]           | cpTi (grade 3)   | Electrolyte: 0.5% H₃PO₄, 1% H₃PO₄, 2% H₃PO₄ | Surface characterization (SEM, XRD, optical profilometry, contact angle, surface energy) ICP-MS Biocompatibility | Phosphoric acid as an electrolyte increases the biocompatibility of the alloy by improving the osteoblasts binding to the medium surface.                                                                                      |
| A. Ossowska et al. [39]       | Ti-13Nb-13Zr     | Electrolyte: 2M H₃PO₄ + 0.3wt.% HF, Time: 30 min or 1 h | Corrosion resistance (electrochemical measurements) | Anodization of the Ti-13Nb-13Zr alloy increases its corrosion resistance.                                                                                                                                               |
| Reference          | Implant material | Anodization conditions                  | Examined properties of anodized material                | Obtained research results                                                                                                                                 |
|--------------------|------------------|----------------------------------------|--------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| A. Zielinski et al. [40] | Ti-13Zr-13Nb     | Electrolyte: 1M H₃PO₄ + 0.5% HF, Voltage: 20V, Time: 60 min, Temperature: 24 °C | Surface characterization (AFM)                           | Nanotubes with diameter in the range of 80-120 nm and 1 mm in length can be formed on the alloy surface. Hydroxyapatite coated sample shows an initial failure as the hydroxyapatite coating is likely delaminated from the TiO₂ layer. Later, the TiO₂ layer became penetrated in another separate event. The nanomeasurements show that the nanotubular oxide layers formed on the Ti-13Zr-13Nb alloy surface by anodization in the presence of hydrofluoric acid demonstrate high mechanical properties. |
| X. Zhu et al. [36] | cpTi (grade 2)    | Electrolyte: H₃PO₄, calcium-glycerophosphate (Ca-GP) + calcium acetate (CA) | Biocompatibility (osteoblasts response)                 | Surface roughness becomes lower in 0.2M H₃PO₄ but enhances in 0.03M Ca-GP and 0.15M CA. Anodized surfaces showed micro-pores with diameters up to 0.5 mm in 0.2M H₃PO₄ and up to 2 mm in 0.03M Ca-GP and 0.15M CA. Cell attachment increased as anodizing voltage, thickness of oxides, number and size of micro-pores, and roughness increased. |
| Reference                  | Implant material | Anodization conditions | Examined properties of anodized material | Obtained research results |
|----------------------------|------------------|------------------------|-----------------------------------------|---------------------------|
| S. Eraković et al. [41]   | cpTi             | Electrolyte: Fluorid electrolyte (fluorid concentration 0.05-0.3 mol/dm³) | Possibility of HAP application on the surface of titanium nanotubular layer | The anodizing acidic environment allows the obtainment of shorter nanotubes, which have proved to be a better substrate for the application of HAP coatings. After the anodization, plates of titanium were heat-treated and a more defined structure of nanotubular TiO₂ layer was obtained. |
| J.U. Kim et al. [37]      | Ti-29Nb-xZr      | Electrolyte: 1M H₃PO₄ + 0.8wt.% NaF | Corrosion resistance (electrochemical measurements) | Anodization increases corrosion resistance of the alloy. The nanotube oxides formed on the Ti-29Nb-xZr alloy surface show lower corrosion current density compared to non-treated sample. |
| E.J. Kim et al. [42]      | Ti-35Ta-xZr      | Electrolyte: H₃PO₄ + 0.8wt.% NaF; Temperature: room temperature | Nanotubular layer characterization (FE-SEM, EDX, XRD) | Nanotubes with a wide range of diameters (approximately 150-200 nm) and lengths (approximately 4-10 μm) can be formed on alloy surface. |
| V. Saji et al. [43]       | Ti-35Nb-5Ta-7Zr, Ti-13Nb-13Zr | Electrolyte: 1M H₃PO₄ + 0.5wt.% NaF | Nanotubular layer characterization | Heat treatment had significant influence on the nanotube oxide interface. |
Biocompatibility is one of the most important features of the implant materials. Investigations regarding the influence of titanium nanotubes characteristics on the cellular response to the implant surface showed significant effect of the nanotubes diameter. It was observed that titanium nanotubes with diameters of 15-20 nm are optimal for increased cell adhesion [45,46]. In addition, research results showed that nanotubes with a diameter of about 15 nm considerably increase the cellular adhesion, while higher nanotubes diameter of about 100 nm led to programmed cell death (apoptosis) [45,47]. This effect was confirmed for different substrate materials such as TiO₂ and ZrO₂ [47]. Park et al. [38] investigated biocompatibility of commercially pure titanium (cp Ti), after anodization in phosphoric acid. This study showed that the anodizing process increases implant material biocompatibility in a manner that improves the binding of the osteoblasts to the implant surface.

Nanotubes diameter also influences the corrosion properties of the implant materials. Electrochemical measurements, performed in different environments, revealed that the material after anodization shows better corrosion resistance compared to material which is not subjected to anodization [21,22,39,40]. Al-Mobarak et al. [7] showed that the electrochemical stability of the nanotubular surface depends on the TiO₂ nanotube diameter and that larger diameter decreases corrosion resistance of the anodized implant material. For instance, Ossowska et al. [39] investigated electrochemical behavior of Ti-13Nb-13Zr alloy before and after anodization and found
that the $j_{corr}$ value is lower for anodized alloy and that anodization of the alloy increases its corrosion resistance. Contrary to this study, Saji et al. [32] indicated that anodization of the Ti-13Nb-13Zr alloy decreases its corrosion resistance since the empty spaces present between nanotubes may be considered as corrosion weak spots.

For the hard tissue implant, the low Young's modulus of titanium and its alloys is considered an important factor because it leads to less stress shielding compared with other materials, and in the same time induces faster and healthier bone regeneration. Zielinski et al. [40] investigated mechanical properties of the nanotubular oxide layers formed on the Ti-13Zr-13Nb alloy by anodization in the presence of hydrofluoric acid and demonstrated their high mechanical properties. Ossowska et al. [22] showed that the value of Young’s modulus is significantly lower for Ti-13Zr-13Nb alloy after anodization. The Young’s modulus of the nanotubular oxide layer can be approximately 36-43 GPa, which is very close to the Young's modulus of bone.

One of the latest trends in the production of nanotubes is to combine a variety of substances in order to improve their characteristics and make them easier to apply to the implant material surface [48]. Investigations of TiO$_2$ nanotubes are mainly concentrated on the aspects related to their diameter and height. These types of nanotubes typically grow in mono-layers. The formation of multi-layer TiO$_2$ nanotubes by electrochemical anodization is not often mentioned in the literature. Some studies have reported that multi-layered nanotubes can be formed using two different electrolytes or by adjusting the anodization voltage [49,50]. Case studies showed that a two-step anodization process by changing voltage from high to low can effectively grow high-aspect-ratio TiO$_2$ nanotube arrays [49,50]. As a consequence of high voltage and low-voltage application, large diameter nanotubes are formed at the top, while small diameter nanotubes are formed below.

**Conclusion**

Anodization of titanium or its alloys results in formation of surface TiO$_2$ nanotubes with different diameters (from 15 nm up to 300 nm) and different lengths. The diameter and the length of TiO$_2$ nanotubes depend on the conditions of electrochemical anodization, such as concentration and pH of the electrolyte, applied potential and anodization time. The time of successful anodizing process increases with increasing the pH of the electrolyte, while the alkaline environment presence results in the formation of nanotubes with a longer length. Applied current density and potential can vary within an extensive range of values. Low potential (1-130 V) application leads to the obtainment of a smooth, about 3-100 nm thick oxide layer. Contrary to that, the high potentials (100-250 V) combined with high current densities, lead to the formation of an oxide layer which thickness can vary between few tens to hundreds micrometers. The nanotube diameter increases with increasing anodization voltage, but is not affected by anodization time. The tube diameter can be increased by increasing the applied potential if the electrolyte pH value remains constant, while the tube diameter is pH independent if the applied potential remains constant. The tube length or the thickness of the formed nanotubular layer increases with the increase of anodization time, but there is always a point at which the thickness remains constant with any further increase.
Nanotubes fabricated on the implant material surface, offer great potential in improving cell adhesion, as well as corrosion resistance, biocompatibility and mechanical properties of Ti-based materials developed for biomedical applications.

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