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Multicomponent Alloys for Biomedical Applications

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Abstract

Titanium alloys are considered to be the most advanced materials for orthopedic implants due to the favorable combination of mechanical properties, low density, tissue tolerance, high strength-to-weight ratio, good resistance to corrosion by body fluids, biocompatibility, low density, nonmagnetic properties, and the ability to join with the bone. This is the reason why we decided to assess the resistance of two titanium alloys currently used for orthopedic implants, namely, Ti6Al7Nb and Ti6Al4V, as reference, to cyclic fatigue by dynamic tests with crevice corrosion stimulation. According to the results obtained, the examined electrochemical quantities, the visual and SEM observations, and EDX analysis reveal better corrosion behavior of the prostheses made of Ti6Al4V—anodized series compared to prostheses made of Ti6Al7Nb. The further comparison of two explanted proximal modules, made of Ti6Al7Nb and Ti6Al4V, to the same type of prostheses evaluated by cyclic fatigue dynamic tests with crevice corrosion stimulation reveals that there are significant similarities, in particular with regard to the electrolyte diffusion, deposition of products and corrosion. Cation extraction tests which were carried out for Ti6Al7Nb prostheses that have undergone particular surface treatments show significant differences depending on the surface treatment and demonstrate that orthopedic implant materials are not “inert.”

Keywords: titanium alloys, Ti6Al4V, Ti6Al7Nb, orthopedic implant, cyclic dynamic test, static test, fatigue corrosion, crevice corrosion, localized corrosion, tribocorrosion, biocompatibility

1. Introduction

Starting with the twentieth century, a wide range of alloys have been used in medical applications as surgically implanted medical devices or denture materials, aimed at providing improved physical and chemical properties, such as strength, durability, and corrosion resistance [1, 2].

The classes of alloys used in medical devices and denture materials include stainless steels, cobalt-chromium, and titanium (alloyed and unalloyed) [3].

Orthopedic implants are subjected to heavy and cyclic load bearing, and they work in a bioactive environment. Most parts of hip joint implants are made of metallic materials. Titanium alloys are considered to be the most advanced materials in this type of application. However, Co-Cr-Mo alloys and austenitic stainless steels

as biosteels paired with appropriate metallic alloys, ceramics, and polymers are also being used for hip implant components [4].

The alloys currently accepted for orthopedic implant applications are:

- Stainless steels: 18Chromium-14Nickel-2.5Molybdenum; Nitrogen Strengthened 21Chromium-10Nickel-3Manganese-2.5Molybdenum; Nitrogen Strengthened 23Manganese-21Chromium-1Molybdenum Low-Nickel; Stainless Steel Forgings
- Cobalt chromium alloys: Cobalt-28 Chromium-6 Molybdenum; Cobalt-20Chromium-15Tungsten-10Nickel; Cobalt-28Chromium-6Molybdenum; Cobalt -28Chromium-6Molybdenum Powder
- Cobalt chromium nickel alloys: 40Cobalt-15Nickel-20Chromium-7 Molybdenum-16Iron; 35Cobalt-35Nickel-20Chromium-10Molybdenum; 35 Cobalt-35Nickel-20Chromium-10Molybdenum Forgings
- Titanium & titanium alloys: Unalloyed Titanium; Titanium Alloy in the Alpha Plus Beta Condition; Titanium-6Aluminum-4Vanadium; Titanium and Titanium-6 Aluminum-4Vanadium Alloy Powders; Titanium-6Aluminum-4 Vanadium Casting; Titanium-3Aluminum-2.5Vanadium; Titanium-6 Aluminum -7Niobium; Titanium-13Niobium-13Zirconium; Titanium-12 Molybdenum-6 Zirconium-2 Iron; Titanium-15 Molybdenum; Nickel-Titanium Shape Memory
- Zirconium: Zirconium-2.5Niobium Stabilized Zirconium (Mg-PSZ)
- Tantalum: Unalloyed Tantalum

The biocompatibility of any material in contact with a living tissue is part of the general context of chemical toxicity effects on the human body [5–7]. A biocompatible material may be defined as inert, nontoxic, non-mutagenic, non-recognizing, nonirritating, and non-allergenic [8–9].

Since the early twenty-first century, Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) [7, 10] regulates Europe's approach regarding chemical toxicology to humans, aiming to list the substances present in Europe (manufactured or imported in volumes exceeding one ton) and to control the high-risk substances while reconciling public health and environmental protection.

According to the European Chemicals Agency (ECHA) [11], the list of preregistered substances contains around 143,000 chemicals. Substances that may have serious effects on human health and the environment can be identified as substances of very high concern (SVHCs):

1. CMR group: substances which are carcinogenic, mutagenic, or toxic for reproduction.
2. ED group: substances with endocrine-disrupting (ED) properties.
3. Sensitizers and other equivalent level of concern (ELOC) substances.
4. PBT group: substances that are persistent, bioaccumulative, and toxic, whereas vPvB substances are very persistent and very bioaccumulative [12].

Among the SVHCs incriminated by ECHA, about 4000 substances which can cause a contact allergy are listed. It is estimated that 15–20% of Europe's population are sensitized to allergens. Allergic reactions are a significant and growing health problem affecting large parts of the European population [7, 13].

According to the International Agency for Research on Cancer, metals are classified into three classes:

Class 1: The agent is carcinogenic to humans—Ni derivatives, Cr^{6+} , Cd and its derivatives, and Be and its derivatives.

Class 2: The agent is possibly carcinogenic to humans—metallic Ni and Co.

Class 3: The agent is not classifiable as to its carcinogenicity to humans but reveals mutagenic properties— Sn^{2+} , Cu^{2+} , and Fe^{2+} .

Metals with none or limited references as mutagens are Cu^{1+} , Sn^{4+} , Au, Pt, Ag, Pd, In, and G [8, 9, 14].

Corrosion is an electrochemical reaction characteristic to all metals in contact with biological systems, and its consequence is the formation of metal ions which may trigger hypersensitivity reactions and affect the immune response system [15]. It characterizes the chemical reactivity of metals and alloys, which results in a visible alteration of the material and affects the function of a metallic component or of the entire ensemble [16]. Crevice corrosion is the localized corrosion of a metal surface at, or immediately adjacent to, an area that is shielded from full exposure to the environment because of the close proximity between the metal and the surface of another material (ASTM G15-97). Tribocorrosion refers to all the mechanical and chemical interactions that cause the degradation of solids in relative displacement with or without contact lubricant.

A major characteristic that concerns any metallic material used for medical applications is good resistance to corrosion, and this is the most relevant property when it comes to its biologic safety [8]. The tendency of a metal to corrode is given by its electrode potential.

Conceived for a biological environment, alloys for medical use should essentially be integrated without developing adverse effects, maintaining their function without degrading within an acceptable time limit [17].

The potential systemic and local toxicity, allergy, and carcinogenicity result from releasing elements during the corrosion process. Elements such as Ni and Co are known for their high allergic potential, and prudence dictates that alloys containing these elements should be avoided as much as possible. Several elements are known mutagens, and a few, such as Be and Cd, are known carcinogens in different chemical forms [17].

The potential negative effects on the tissues or on the body at cellular level are precisely induced by the presence of certain components released as degradation products, especially metal cations in solution, due to surface corrosion [9]. The degradation of metallic devices in a biological environment is accompanied by the release of cations such as Cr, Co, Ni, and Ti. Therefore, we deal with a cumulative effect: allergic, irritating, mutagenic, and toxic [7].

Metal ions and debris have been shown to be released from orthopedic implants which are made of stainless steel and Co-Cr alloys [18].

Cr, Mo, Si, Fe, and Mn are the ions released from stainless steel implants, while Ti, Al, V, and Nb are released from titanium alloy implants [19]. The in situ degradation of an implant decreases its structural integrity and also releases products which may trigger an adverse biological reaction [15]. Biological risks associated with the released metal ions have been identified to include those from wear debris, colloidal organometallic complexes, free metal ions, and inorganic metal salts or resulting oxides [20].

The exposure to a variety of chemicals is known as the “cocktail effect” and expresses the way in which different chemicals are released from different sources and affect humans [7, 21]. Individual chemicals can become more dangerous when mixed together and act as an aggravating factor [22].

About 10%–15 female European adults and 1–3% male European adults suffer from Ni contact allergy. Because this is considered an important health problem, the European Union (EU) legislated this matter as follows:

- a. “the Ni release from parts in direct contact with the skin must be lower than 0.5 mg/cm²/week” (European Parliament and council directive 94/27/EC of June 30, 1994) [23] and
- b. “all metallic parts that are inserted into pierced ears and other parts of the human body must not have a nickel release rate greater than 0.2 mg/cm²/week” (Commission directive 2004/96/EC of September 27, 2004) [24].

In dentistry, the percentage of females allergic to Ni is reported to vary from 9 to 20%, and in case of orthodontic patients with pierced ears, 30% are allergic to Ni, Cu, and Cr [2]. In certain countries, nickel-based, cheaper alloys have increasingly been subjected to more and more regulations or even banned [25]. However, piercing of other parts of the body has increased in the last years [26].

Today we find ourselves with a Ni “cocktail effect,” in an allergic population, pierced, tattooed, and with orthodontic devices made of poor stainless steels. The presence of an orthopedic implant, especially a failed metal one, has been shown to predispose patients to dermal sensitivity when compared with the general population [27].

A part of the orthopedic implants is made of alloys which contain Cr, mainly used as an alloying element in steels, where it contributes to hardness, tempering, and resistance to oxidation. Such implants will release Cr ions. Because of the increasing number of arthroplasties in young patients with osteoarthritis, the exposure time to the released chromium may be over 50 years in these cases. Cr⁶⁺ has been labeled as a class 1 human carcinogen by the International Agency for Research on Cancer, signifying carcinogenesis as a potential long-term biological effect in patients with Cr alloy implants [15]. The subsequent chromium ion metabolism is complex. The Cr released during the degradation of the Co-Cr, Co-Cr-Mo, or NiCr alloys is Cr³⁺, but it can be oxidized to Cr⁶⁺ at the cellular level. Cr⁶⁺ is mutagenic and carcinogenic; but its potential biological effects are controversial, as it is metabolized in the cytoplasm and cell’s nucleus in Cr³⁺, which is not involved in DNA and chromosomal damage. Effects as reduction in CD8 lymphocyte levels and possible hypersensitivity reactions (ALVAL) are controversial [15].

ALVAL may represent an immunological response to metal wear debris [28, 29] which may appear in tissues around metallic implants. Such infiltration was reported absent in case of implants without Co, Cr, and Ni [28] and in metal-on-polyethylene implants [30]. The toxic effects of the released metal ions and wear debris affect cells and tissues which are in the proximity and distant from the implant, as well. Histological studies carried out on tissues recovered from explanted metal prostheses revealed areas of necrotic tissue, with visible metal particles [15]. Elevated metal ion concentrations in serum [31, 32], erythrocytes [33], urine [34], whole blood [35, 36], tissue [37, 38], and organs [39] have all been reported in patients with implants [15]. Both Cr⁶⁺ and Cr³⁺ are described as allergens. According to ECHA 130,000 people allergic to Cr⁶⁺ are reported, and their number increases.

Titanium alloys are indicated for orthopedic implants because of the favorable combination of mechanical properties, low density, tissue tolerance, high strength-to-weight ratio, good resistance to corrosion by body fluids, biocompatibility, low density, nonmagnetic properties, and ability to join with the bone. Ti induces the formation of a fibrous tissue barrier when placed in contact with a healthy bone and facilitates subsequent bone growth. Contaminations of Ti alloys with elements like hydrogen and oxygen may occur during melting, thermic treatment, and surface hardening and must be avoided, due to their embrittling effect. Ti alloy corrosion resistance is superior to that of stainless steels [4]. This is the reason why we decided to present part of our research regarding titanium alloys.

2. Resistance evaluation of titanium alloys to cyclic fatigue by dynamic tests with crevice corrosion stimulation

The role of biomaterials is to aid or totally replace the functions of living tissues. In case of orthopedic implants, the loading response has to match the natural bone. The average load on a hip bone, estimated to be thrice the body weight, may increase to a value of 10 times the body weight during heavy exercise [15]. Therefore, the ideal orthopedic implant should manifest appropriate mechanical properties and be highly biocompatible with existing tissues [40]. In case of a metallic implant, the potential corrosion of the material in the body environment has to be considered.

Corrosion fatigue is defined as the process in which a metal fractures prematurely under conditions of simultaneous corrosion and repeated cyclic loading at lower stress levels or fewer cycles than would be required in the absence of the corrosion environment (ASTM G15-97).

The term cyclic dynamic test (fatigue) with crevice corrosion stimulation covers various phenomena, namely, crevice corrosion, fatigue, and tribocorrosion. The term stress corrosion (static) with crevice stimulation covers two entangled phenomena, namely, crevice corrosion and stress corrosion. Stress corrosion cracking is the result of a joint action between corrosion and a constraint of reaction or of static compression, applied or residual.

The aim of our research was to assess the mechanical properties of two titanium alloys currently used for orthopedic implants, namely, Ti6Al7Nb and Ti6Al4V, as reference.

The tested modular prostheses, type PL-06, consist of a distal and a proximal module, interlocked by a screw (**Figure 1**).

Two sample series were used for testing. The main characteristics are given in **Table 1**.

Figure 1.
The modular prostheses used for testing.

	First sample series	Second sample series
Composition	Ti6Al7Nb	Ti6Al4V
Surface	No specific treatment	type 2 (“Ti anodizing”)
Tolerances	Uniforms	Adapted to each cone level

Table 1.
Main characteristics of the sample series.

For each series, four samples were evaluated: three in cyclic dynamic test (fatigue) with crevice stimulation and one constrained with crevice stimulation (static) (**Table 2**).

The organization and coding of the samples subjected to the tests are given in **Table 2**. Samples # 1 and # 2 were used for the cyclic adjustments of the fatigue test machine and verification of electrochemical corrosion programs.

For the fatigue tests, a Walter & Bai AG, Switzerland, LFV 10 KN series machine, adapted for fatigue testing (**Figure 2a**) and research of biomedical implants (hip implant prostheses according to ISO 7206-4 and 6), was used. This compact testing system has a hydraulic power pack integrated in its base. The crosshead features automatic adjustment with hydraulic unlocking and hydraulic moving through two long stroke actuators. The prosthesis, more precisely the distal module, was embedded in a non-conductive composite resin, held by a metal sample holder (**Figure 2b**). The embedding of the tapered shape was up to 1 cm from the boundary between the two modules (distal module/proximal module). The specimens were loaded with an average stress of 1.4 and amplitude of 1.1 mm at a frequency of 10 Hz.

Two types of mechanical tests were conducted, the first one under dynamic loading for 5 million fatigue cycles and the second one under a static force of 981 N, during the equivalent time corresponding to 5 million dynamic fatigue cycles, which correspond to approximately 5 years of walking for a person with a body-weight of 100 kg. The parameters of sample placement followed the requirements of the ISO 7206-6:2013(E) standard.

The potentiostatic measurement technique (controlled-potential coulometry), adapted according to the ASTM F746-87 standard, consists in performing an excitation at a given potential for a very short period of time and then positioning itself on a fixed potential for a certain time. The composition of a measurement cycle is shown

Sample series no.	Code	Mechanical solicitation	Crevice electrochemical test
	#1 #2	Simulation, setting tests	Simulation, test, and control of the corrosion program
1	#3	Fatigue	Yes
1	#4	Fatigue	Yes
1	#5	Fatigue	Yes
1	#6	Constraint	Yes
2	#7	Fatigue	Yes
2	#8	Fatigue	Yes
2	#9	Constraint	Yes
2	#10	Fatigue	Yes

Table 2.
Organization and coding of the samples subjected to the tests.

Figure 2.
The fatigue testing system. (a) The fatigue testing machine and (b) the metal sample holder, specifically adapted to the fatigue testing machine.

Potential type	Level (mV)	Time
Stimulated potential	800	60 s
Preselected potential	600	36 min
Stimulated potential	800	60 s
Preselected potential	650	36 min
Stimulated potential	800	60 s
Preselected potential	700	36 min
Stimulated potential	800	60 s
Preselected potential	750	36 min
Preselected potential	−500	20 min

Table 3.
Composition of an electrochemical measurement cycle.

in **Table 3**. Ten cycles correspond to 1 million cycles of mechanical fatigue. The test was carried out in increments of 1 million cycles for a total of 5 million cycles.

The choice of the measuring technique is motivated by the following considerations:

- The materials the components are made of do not pose any significant problems regarding the general corrosion resistance. On the other hand, electrolyte infiltration into the spaces of the distal/proximal module joint may lead to localized crevice corrosion, accompanied by a tribocorrosion process.
- The values of the electrical potential suggest that no decomposition process of the electrolyte into hydrogen and oxygen takes place.
- A cathode potential equalizer at −500 mV SCE was added in order to analyze the depassivation-repassivation capacity of the materials in the tested areas.
- Using this technique, the electrical charge used for the experiment may be easily measured. For analytical estimations the total electrical charge passed in the experiment is easily related to the concentration of electroactive species in the cell.

The potentiostat used is a model PAR 273A, EG&G (Princeton Applied Research). The electrochemical cell has been specially designed for these types of measurements. It is a cell with three electrodes: working electrode (green wire), platinum counter electrode (red wire), and the saturated calomel reference electrode on the right (**Figure 3a**). It is fitted on the head of the cyclic fatigue machine (**Figure 3b**). The test environment was a solution of NaCl at a concentration of 9 g/l (ASTM F746-1998) in ultrapure water (electrical resistivity 18 MΩ cm).

After the assembly of the two modules, there will always be a space which will allow the diffusion of the fluids (**Figure 4a**). Thus the presence of fluids in the interstice can generate crevice corrosion. After the fatigue corrosion test, it is possible to notice the corrosion by strong staining (**Figure 4b**).

Behavior to localized corrosion of samples #3, #4, and #5 (series 1) during 5 million mechanical fatigue cycles is shown in **Figure 5a**.

Behavior to localized corrosion of samples #7, #8, and #10 (series 2) during 5 million mechanical fatigue cycles is shown in **Figure 5b**. Sample #6 and #9 were evaluated for corrosion resistance without cyclic dynamic forces but under a load of 100 kg (**Figure 5**). The comparative behavior to localized corrosion for samples #6 and #9 is presented in **Figure 6**.

Figure 3.
The electrochemical cell adapted on LFV 10 KN machine.

Figure 4.
Sample #3 before and after testing. (a) (A) Distal module and (B) proximal module. Before testing. (b) Coloration of the two modules after the corrosion test.

Figure 5.
Behavior to localized corrosion of tested samples. (a) Behavior to localized corrosion of samples #3, #4, #5, and #6 (series 1-cyclic fatigue dynamic test) and (b) behavior to localized corrosion of samples #7, #8 #9, and #10 (series 2-cyclic fatigue dynamic test).

Figure 6.
Behavior to localized corrosion of samples #6 and #9 (static).

Figure 7.
Electrical charges accumulated during testing.

By analyzing the sum of the accumulated charges during the total duration of the test, we note a worse behavior of the series 1 samples compared to series 2 (**Figure 7**) (samples #6 and #9 were tested under a stress of 100 kg).

It should be noted that the curves presented in **Figure 5a** and **b** are very different from one series to another. The harmonic shape of the series 2 curves is probably due to the surface treatment.

Since the last stage of the measurement cycle (**Table 3**) is -500 mV vs. SCE; thus a depassivation cathodic plateau, the repassivation capacity of the layer designed for the first series samples shows an ability of slower repassivation. In the first stage (600 mV), one still finds higher amounts of electrical charges compared to the later stage (750 mV) vs. SCE (**Tables 4** and **5**). The curves of the series 2 samples have no correlation with the testing fatigue cyclic motion.

In case of series 1 samples, after about 3 million cycles of the dynamic tests, crystallized sodium chloride can be found in the area of the tightening screws of the modular prostheses (**Figure 8**). This means that there is an electrolyte pumping effect in the assembly space of the two parts, and therefore crevice corrosion is quite possible to occur. For series 2 samples, this process can be noticed earlier, starting from about 2.5 million cycles. In the case of electrochemical static measurements, no phenomena of electrolyte pumping were observed. The quantities of electrical charges consumed in the corrosion process (**Tables 4** and **5**) are greater in series 1 than in series 2 (**Figure 7**).

When interpreting the microscopic observations, it is essential to take into account that the various phenomena involved, namely, crevasse corrosion, fatigue (cyclic dynamic test), stress (static test), and tribocorrosion (cyclic dynamic test), are impossible to be considered separately. These processes are intimately intertwined by complex mechanisms; observation is limited to their combined effects. This is why the presented phenomenon is referred to as corrosion fatigue.

The distal module of sample #3, observed by scanning electron microscopy (SEM) at a $560\times$ magnification, is presented in **Figure 9**.

In the analyzed area, cracks have developed (**Figure 9a**), which are probably due to the cyclic dynamic process (fatigue), accompanied by the corrosion processes (**Figure 9b**).

In case of samples #4 and #5, similar phenomena may be observed. In case of sample 4, the deposition is present at the level of the crevice as well as the interferential colorations (same as in **Figure 4b**). The EDX analysis of the area reveals only Al, Ti, and Nb.

Cycle no.	600 mV	650 mV	700 mV	750 mV	Total
1	108.2	69.7	54.1	50.3	282.3
2	30.9	26.3	25.9	25.3	108.4
3	23.0	18.4	18.9	20.3	80.6
4	19.3	15.4	16.0	16.7	67.4
5	15.7	13.2	13.3	14.8	57.0
6	10.8	10.5	10.2	10.5	42.0
7	10.7	8.3	7.9	8.6	35.5
8	8.7	6.8	7.3	7.8	30.6
9	8.1	6.4	6.4	6.8	27.7
10	7.8	5.7	5.9	6.1	25.5
Total	243.2	180.7	165.9	167.2	757.0

Table 4.
Quantity of electrical charge (mC) consumed for the first million fatigue cycles during testing of sample #4, series 1.

Cycle no.	600 mV	650 mV	700 mV	750 mV	Total
1	37.3	21.9	17.8	16.5	93.5
2	12.3	7.4	7.3	8.1	35.1
3	10.1	5.3	5.1	5.7	26.2
4	8.9	4.1	3.8	4.0	20.8
5	8.4	3.5	3.0	3.3	18.2
6	8.2	3.1	2.7	2.9	16.9
7	7.8	2.9	2.4	2.6	15.7
8	7.9	2.8	2.3	2.5	15.5
9	7.9	2.7	2.2	2.4	15.2
10	8.1	2.7	2.2	0.9	13.9
Total	116.9	56.4	48.8	48.9	271.0

Table 5.
Quantity of electrical charge (mC) consumed for the first million fatigue cycles during testing of sample #10, series 2.

Figure 8.
Sample #3. (a) Salt deposition in sample #3 and (b) crack of the distal module of sample #3.

Figure 9.
Sample #3. Distal module. (a) Sample #3. Distal module. SEM 560× and (b) sample #3. Distal module. SEM 560×.

Sample #5 shows gaps in the distal part (**Figure 10b**) at the level of the crevice as well as coloration at the same level on the proximal module (**Figure 10a**). The spectrum EDX analyses 1, 2, and 3 (**Figure 10c**) reveal depassivation (lack of oxygen in spectrum 1) of the gap interior; the gap’s margins contain Na, Cl, Si, and K.

At the distal/proximal part interface of the distal module, deposits may be observed. The EDX analyses particularly show the presence of elements C, Na, Si, Cl, and K (**Figure 10d**).

Sample #7 reveals the same phenomenon of electrolyte penetration at the interface of the distal/proximal modules. The optical examination establishes the presence of wear and corrosion in this area, revealed by a rough appearance of the proximal module surface, as well as on the distal module but to a lesser extent. Examination of the distal module does not reveal the presence of cracks. The phenomenon is probably due to tribocorrosion and crevice corrosion.

Sample #8 also shows an increase in the roughness of the surface (**Figure 11a and b**). **Figure 11c and d** show the EDX spectrum analysis in the rough zone of the distal modules and reveal the presence of Na, Cl, and Si elements.

In case of sample #9, having undergone only a static test, the electrolyte does not enter the distal/proximal module interface, and no corrosion phenomenon is highlighted. These remarks are also valid for sample #6, which was subjected to the same static test. The EDX analysis does not reveal any traces of corrosion, the chemical composition being the same in the three zones subjected to evaluation.

Figure 12a shows a sectional view of the proximal module of sample #10; as in case of samples #7 and #8, salt deposits and a phenomenon of wear and/or corrosion in the crevice area are present. On the other hand, the distal module (**Figure 12b**) is much less marked by this phenomenon than the distal module of sample # 8. The EDX analysis in **Figure 12d** is measured on the distal module in the crevice area (**Figure 12c**).

According to the results obtained, the electrochemical quantities are examined, and the optical observations reveal a better corrosion behavior on the part of the series 2 samples (Ti6Al4V—anodized type 2) compared to the series 1 samples (Ti6Al7Nb).

Figure 10. Sample #5. (a) Sample #5. Proximal module, (b) sample #5. Distal module, (c) sample #5. Distal module. SEM 230× and (d) spectrum EDX analysis.

Figure 11.
Sample #8. (a) Sample #8. Proximal module. Rough area, (b) sample #8. Distal module. Rough area, (c) sample #8. Distal module. SEM 560 $\times$. Spectrum EDX analysis and (d) sample #8. Distal module. SEM 560 $\times$. Spectrum EDX analysis.

Figure 12.
Sample #10. (a) Sample #10. Proximal module, (b) sample #10. Distal module, (c) sample #10. Distal module. Crevice area and (d) spectrum EDX analysis.

In cyclic dynamic tests with crevice stimulation, the electrolyte enters the interface between the distal and proximal modules, which is not the case during static tests (#6 and #9).

Samples #3 and #4 of series 1 reveal cracks in the distal module. Samples #3 and #5, also series 1, reveal holes in the crevice proximity. Metallic interferential staining of the distal/proximal module interfaces of the series 1 samples (#3, #4 and #5) is indicative of electrolyte reactions with the substrate and helps highlighting the corrosion process. This coloration does not appear in case of series 2 samples.

Series 2 samples (#7, #8, and #10) do not show cracks or holes as observed in case of series 1 samples. On the other hand, at crevice level, the surface of the proximal module and to a lesser extent the surface of the distal module present an increase of roughness after the cyclic dynamic corrosion test with crevice stimulation. This phenomenon is particularly visible on sample #8.

The observation of the samples only subjected to the static test does not reveal any sign of corrosion.

3. Components of Ti6Al7Nb and Ti6Al4V explanted modular prostheses (proximal module)

Two components of modular orthopedic prostheses—proximal module (**Figure 13**)—were explanted after 7 years. The proximal parts are made of Ti6Al7Nb (Lot 02-PL-06, Plus 662, PI 793—Gr. BS, art. 11,940, 1 series, lot 02.1424) and Ti6Al4V (Lot 03-PL-06, Plus 662, Gr. BL, art. 11,973—2 series, lot 03.463).

The aim was to observe and analyze the two components of the explanted modular prostheses (proximal module) and to compare them with the results of the cyclic fatigue dynamic tests with crevice corrosion stimulation (**Figure 14a and b**).

Figure 14a and b show the penetration of biological fluids at the interface of the proximal/distal modules and reveal significant similarities, in particular with regard to the phenomena of electrolyte penetration, product deposition, and corrosion.

Figure 15a reveals the presence of mechanical wear (SEM). The presence of a deposit originating from the biological fluids which have penetrated the interface is noted by the presence of C and Na (**Figure 15b**). Pumping effects of the electrolyte may be observed after 3 million cycles in laboratory tests. This type of effect is also observed on the explanted Ti6Al7Nb prosthesis.

The comparison between **Figure 16a** (explanted Ti6Al4V proximal module) and **Figure 16b** (Ti6Al4V proximal module, sample #8, after the cyclic fatigue

Figure 13.
Proximal module explanted.

Figure 15.
Lot 02-Ti6Al7Nb proximal module explanted. (a) Lot 02-Ti6Al7Nb proximal module explanted (SEM) and (b) lot 02-Ti6Al7Nb proximal module explanted. Spectrum EDX analysis.

Figure 16.
Ti6Al4V proximal module. (a) Lot 03-Ti6Al4V proximal module explanted, (b) Ti6Al4V proximal module, sample #8, prior subjected to cyclic fatigue dynamic test with crevice corrosion stimulation, (c) lot 03-Ti6Al4V proximal module explanted (SEM) and (d) spectrum EDX analysis.

dynamic test with crevice corrosion stimulation) shows that the location of the visible spots on the proximal explanted module approximately corresponds to the electrolyte deposits observed during cyclic fatigue dynamic tests with crevice corrosion stimulation. SEM observation does not reveal obvious localized corrosion in the spots area (**Figure 16c**). In exchange, the EDX analysis (**Figure 16d**) reveals the presence of C and Na, which suggests that biological fluids have penetrated and diffused at the proximal/distal module interface. The evaluation of cyclic dynamic corrosion with crevice stimulation on Ti6Al4V modular prostheses shows a similar analogue phenomenon of electrolyte pumping at the interface of the proximal/distal modules.

The comparison of the explanted proximal parts with modular prostheses of the same type evaluated by cyclic fatigue dynamic tests with crevice corrosion stimulation reveals that there are significant similarities, in particular with regard to the electrolyte diffusion, deposition of products, and corrosion. Thus, these observations justify the use of cyclic fatigue dynamic tests with crevice corrosion stimulation in order to compare and evaluate different types of materials for the development of modular prostheses.

4. Cation extraction

Cation extraction tests were carried out only for Ti6Al7Nb prostheses that have undergone very particular surface treatments. **Table 6** presents the characteristics of the two series of prostheses used.

To minimize the volume/surface ratio, Pyrex glass reactors have been developed and adapted to the prosthesis shape (**Figure 17**). The orthopedic implant has a total area of 115.9 cm². An electrolyte solution of HCl 0.07 N (300 ml) prepared from Titrisol® 1.0 N (Merck) was used. For extraction tests the release solution volume (ml)/total sample surface (cm²) ratio was equal to 3. The choice of electrolyte extraction was based on thermodynamic considerations [40] (solubility). Standards (EN-71-3) concerning bioavailability [41] and constraints of the analysis technique (simple matrix causes no perturbations) were considered.

For washing the glass reactors, concentrated nitric acid was used for 24 h. Afterwards they were thoroughly rinsed with deionized water (18 MΩ cm), in order to completely eliminate the acid and then, finally, dried. The extraction tests were conducted at 37 ± 2°C. The prosthesis were kept in the extraction solution for 168 h and then removed, rinsed, and dried. 50 ml of the extraction solution was used for the analysis using ICP-OES/MS method (PerkinElmer Elan DRC). A blanc solution was measured as a reference. The release of elements in the diluted solution of hydrochloric acid 0.07 N shows significant differences between the two types of

Series	Code	Type	Surface treatment
Series 1	#A	SL-Plus r NT Stem	Corundum blasted + mechanical-chemical cleaning
	#B		
	#C		
Series 2	#D	SL-Plus r Stem	Corundum blasted
	#E		
	#F		

Table 6.
Description of Ti6Al7Nb prosthesis used for cation extraction.

Figure 17.
Glass reactors for cation extraction tests.

Element	Blanc	Series 1				Series 2	
		#A	#B	#C	#D	#E	#F
As	<1	<1	1.4	<1	<1	1.7	2.6
Ba	0.24	0.51	0.24	0.48	0.63	0.8	0.77
Be	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
Br	3.54	6.32	4.89	4.72	4.13	5.73	7
Cd	<0.02	0.18	0.02	<0.02	0.09	<0.02	<0.02
Co	0.02	0.78	0.76	0.79	0.12	0.22	0.16
Hg	0.81	0.62	0.18	0.13	0.1	0.13	<0.05
Li	0.11	0.16	0.16	0.15	0.17	<0.1	0.15
Mo	<0.02	<0.02	<0.02	<0.02	<0.02	<0.02	<0.02
Nb	<0.02	130	110	110	73	55	62
Pb	1.9	0.93	0.46	0.71	0.84	0.95	1.0
Sb	0.06	0.1	0.08	0.08	0.06	0.03	0.07
Sn	0.13	0.13	0.15	0.14	0.12	0.1	0.08
Zr	<0.02	0.03	<0.02	0.04	0.16	0.19	0.15
Al	18	193	143	135	194	180	199
Ca	0.0	0.1	0.0	0.1	0.0	<0.02	<0.02
Cr (total)	<0.5	0.9	0.9	0.9	2.1	1.8	2.2
Cu	<2	<2	<2	<2	<2	6.1	<2
Fe	<2	51.5	36	48.4	32.6	30.1	41.7
Ni	<2	<2	<2	<2	<2	<2	<2
P	<10	<10	<10	<10	<10	<10	<10
S	<0.02	<0.02	<0.02	<0.02	<0.02	<0.02	<0.02
Ti	0.7	1600	1590	1500	1510	1350	1500
V	<0.2	<0.02	<0.02	<0.02	<0.02	<0.02	<0.02
Zn	<2	15.9	4.2	6.9	5.5	5.9	7.7

Table 7.
Cations released in solution.

prostheses (**Table 7**). The following elements, which correspond to the detection limit (Be, Mo, Ni, P, S, and V) as well as those that show a released value identically to the blanc solution (Br, Hg, Pb and Sn), were not taken into account.

The presence of the alloying elements, Ti and Al, is comparable for both series of implants and confirms the literature data [42–45]. Spriano et al. [42] also reported an increase of metal ion concentration after a long time exposure, for the Ti6Al7Nb alloy in a SBF solution. On the other hand, the concentration of Nb cations for series 2 is significantly smaller than for series 1 ($60\text{--}120\ \mu\text{g l}^{-1}$, respectively). The most important impurity is Fe (between 30 and $50\ \mu\text{g l}^{-1}$), almost identical for the two types of prostheses. The samples of series 1 released less chromium than series 2, respectively, 0.9 and $2\ \mu\text{g l}^{-1}$. The prostheses of sample #E released $6\ \mu\text{g l}^{-1}$ Cu. Samples #B, #E and, #F released $1.4\text{--}2.6\ \mu\text{g l}^{-1}$ As. The specimens from series 1 released less Ba than series 2. Series 1 released $0.8\ \mu\text{g l}^{-1}$ Co, $0.03\ \mu\text{g l}^{-1}$ Zr and series 2, $0.2\ \mu\text{g l}^{-1}$ Co and respectively $0.17\ \mu\text{g l}^{-1}$ Zr.

Part of the cations released in solution (Pb and Sn) probably originates from the glass reactor or the HCl composition (according to Merck information). As Cd and Cu are considered to be accidental impurities, their presence is not related to the affiliation of the tested sample to one or the other series of prostheses.

5. Conclusions

Various biomaterials have been used for orthopedic implant manufacturing. Polymeric materials, as a result of their mechanical weakness, have been considered unsuitable for the stress deformation requirements of orthopedic implant components, while ceramics have good biocompatibility but are brittle, and designs should take this into account. Alloys are known for their good mechanical properties, but poorer biocompatibility, due to the systemic release of ions [46]. An orthopedic implant is frequently made of a metallic or ceramic component articulating with a metal, ceramic, or polyethylene surface [19]. Different possible combinations are possible: metal (stainless steel or Co-Cr) on ultrahigh molecular weight polyethylene, metal on metal, ceramic on polyethylene, ceramic on ceramic, or ceramic on metal [47]. Coatings such as bioinert films, which have the main purpose of hindering corrosive processes of the underlying metal and bioactive films, which are capable of improving biological compatibility, avoiding inflammation or implant-associated infection processes, are used more and more often. The ideal coating is a system in which anticorrosion, anti-infection, and osseointegration can be obtained simultaneously [48]. Because of their favorable characteristics, Ti alloys are the first choice material in case of orthopedic implants. Even in case of Co-Cr-Mo alloys, Ti-vacuum-plasma-sprayed (VPS) coatings decrease the release of the substrate elements (Co, Cr, and Mo) considerably, but they do not suppress it completely [49].

Titanium remains the predominant material used for medical implants. Despite its high strength and good resistance to corrosion, multiple studies have demonstrated that degradation products of titanium alloys may be detected in neighboring tissues as well as in distant organs. Titanium particles are released from the implant's surfaces for many reasons, such as mechanical wear, contact with chemical agents, and bacteria embedded in adherent biofilm and inflammatory cells [16].

It is obvious that none of the orthopedic prosthetic materials are “inert”. However the question regarding their toxicological behavior “Which are the long-term consequences for humans?” still stands.

The near future of multicomponent alloys for biomedical applications does not only belong to high-quality Co-Cr, Ti, Ta, or Zr alloys but also to customized orthopedic prostheses, manufactured by 3D printing techniques, based on a CT or MRI scan, which fit perfectly. One can also imagine the not-so-distant future, which seems to belong to the bioprinting techniques, in this case, bone-made orthopedic implants.

Conflict of interest

The authors declare no conflict of interest.

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References

- [1] Ardelean L, Reclaru L, Bortun C, Rusu LC. Assessment of dental alloys by different methods. In: Aliofkhazraei M, editor. *Superalloys*. Rijeka: InTech; 2015. pp. 141-170. DOI: 10.5772/61115
- [2] Reclaru L, Ardelean LC. Alternative processing techniques for CoCr dental alloys. In: Narayan R, editor. *Encyclopedia of Biomedical Engineering*. Vol. 1. Amsterdam: Elsevier; 2019. pp. 1-15. DOI: 10.1016/B978-0-12-801238-3.11100-6
- [3] Wassell RW, Walls AWG, Steele JG. Crowns and extra-coronal restorations: Materials selection. *British Dental Journal*. 2002;**192**:199-211. DOI: 10.1038/sj.bdj.4801334a
- [4] Choroszyński M, Choroszyński MR, Skrzypek SJ. Biomaterials for hip implants-important considerations relating to the choice of materials. *Bio-Algorithms and Med-Systems*. 2017;**13**:133-145. DOI: 10.1515/bams-2017-0017
- [5] Jaishankar M, Tseten T, Anbalagan N, Blessy BM, Beeregowda KM. Toxicity, mechanism and health effects of some heavy metals. *Interdisciplinary Toxicology*. 2014;**2**:60-72. DOI: 10.2478/intox-2014-0009
- [6] Hamann D, Hamann CR, Thyssenn JP. The impact of common metal allergens in daily devices. *Current Opinion in Allergy and Clinical Immunology*. 2013;**13**:525-530. DOI: 10.1097/ACI.0b013e32836457bf
- [7] Ziegenhagen R, Reclaru L, Ardelean LC, Grecu AF. Corrosion resistance of stainless steels intended to come into direct or prolonged contact with the skin. *Materials*. 2019;**12**:987. DOI: 10.3390/ma12060987
- [8] Ardelean LC, Reclaru L, Bortun CM, Ghiban B. Laser welding of different dental alloys. In: Cevik S, editor. *Superalloys for Industry Applications*. London: InTech; 2018. pp. 85-107. DOI: 10.5772/65570
- [9] Reclaru L, Ardelean L, Rusu L. Toxic materials, allergens and mutagens and their impact on the dental field. *Medicine in Evolution*. 2008;**14**:98-102
- [10] Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), Establishing a European Chemicals Agency, Amending Directive 1999/45/EC and Repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as Well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC [Internet]. 2006. Available from: <https://echa.europa.eu/regulations/reach/legislation> [Accessed: 10 October 2018]
- [11] ECHA (European Chemical Agency) [Internet]. Available from: <https://echa.europa.eu/home> [Accessed: 10 October 2018]
- [12] ECHA-Legislation-REACH-Cooperation with authorities and stakeholders-PBT Expert Group [Internet]. Available from: <https://echa.europa.eu/pbt-expert-group> [Accessed: 11 March 2019]
- [13] Diepgen TL, Ofenloch RF, Bruze M, Bertuccio P, Cazzaniga S, Coenraads PJ, et al. Prevalence of contact allergy in the general population in different European regions. *British Journal of Dermatology*. 2016;**174**:319-329. DOI: 10.1111/bjd.14167
- [14] Reclaru L, Eschler PY, Lerf R, Blatter A. Electrochemical corrosion and metal ion release from Co-Cr-Mo

prosthesis with titanium plasma spray coating. *Biomaterials*. 2005;**26**:4747-4756. DOI: 10.1016/j.biomaterials.2005.01.004

[15] Afolaranmi GA, Tettey J, Meek RMD, Grant MH. Release of chromium from orthopaedic arthroplasties. *The Open Orthopaedics Journal*. 2008;**2**:10-18. DOI: 10.2174/1874325000802010010

[16] Noumbissi S, Scarano A, Gupta S. A literature review study on atomic ions dissolution of titanium and its alloys in implant dentistry. *Materials*. 2019;**12**:368. DOI: 10.3390/ma12030368

[17] Wataha JC. Biocompatibility of dental casting alloys: A review. *Journal of Prosthetic Dentistry*. 2000;**83**:223-234. DOI: 10.1016/S0022-3913(00)80016-5

[18] Ingham E, Fisher J. Biological reactions to wear debris in total joint replacement. *Proceedings of the Institution of Mechanical Engineers Part H. Journal of Engineering in Medicine*. 2000;**214**(H1):21-37. DOI: 10.1243/0954411001535219

[19] Sargeant A, Goswami T. Hip implants-paper VI-ion concentrations. *Materials and Design*. 2007;**28**:155-171

[20] MacDonald SJ, McCalden RW, Chess DG, Bourne RB, Rorabeck CH, Cleland D, et al. Metal-on-metal versus polyethylene in hip arthroplasty: A randomized clinical trial. *Clinical Orthopaedics and Related Research*. 2003;**406**:282-296. DOI: 10.1097/01.blo.0000043066.62337.9d

[21] Godfrey A, Abdel-Moneim A, Sepúlveda MS. Acute mixture toxicity of halogenated chemicals and their next generation counterparts on zebrafish embryos. *Chemosphere*. 2017;**181**:710-771. DOI: 10.1016/j.chemosphere.2017.04.146

[22] Polychronis G, Al Jabbari YS, Eliades T, Zinelis S. Galvanic coupling of steel and gold alloy lingual brackets with orthodontic wires: Is corrosion a concern? *The Angle Orthodontist*. 2018;**88**:450-457. DOI: 10.2319/092917-655.1

[23] European Parliament and council directive 94/27/EC of June 30, 1994 [Internet]. Available from: <https://publications.europa.eu/en/publication-detail/-/publication/0a5a20d2-063e-4892-b94d-d82c9b223de0/language-en> [Accessed: 11 March 2019]

[24] Commission Directive 2004/96/EC of 27 September 2004 Amending council directive 76/769/EEC as regards restrictions on the marketing and use of nickel for piercing post assemblies. *Official Journal of the European Union* 2004, L301, 51

[25] Schnuch A, Wolter J, Geier J, Uter W. Nickel allergy is still frequent in young German females—Probably because of insufficient protection from nickel-releasing objects. *Contact Dermatitis*. 2011;**64**:142-150. DOI: 10.1111/j.1600-0536.2010.01841.x

[26] Gutsche P, Schmalz G, Landthaler M. Prevalence of piercing in a German population. *European Journal of Dermatology*. 2008;**18**:26-28. DOI: 10.1684/ejd.2008.0306

[27] Hallab N, Merritt K, Jacobs JJ. Metal sensitivity in patients with orthopaedic implants. *The Journal of Bone and Joint Surgery. American Volume*. 2001;**83A**:428-436

[28] Willert HG, Buchhorn GH, Fayyazi A, Flury R, Windler M, Köster G, et al. Metal-on-metal bearings and hypersensitivity in patients with artificial hip joints. A clinical and Histomorphological Study. *The Journal of Bone and Joint Surgery. American Volume*. 2005;**87**:28-36. DOI: 10.2106/JBJS.A.02039pp

- [29] Roberts P, Grigoris P, Bosch H, Talwaker N. Resurfacing arthroplasty of the hip. *Current Orthopaedics*. 2005;**19**:263-279. DOI: 10.1016/j.cuor.2005.05.004
- [30] Davies AP, Willert HG, Campbell PA, Learmonth ID, Case CP. An unusual lymphocytic perivascular infiltration in tissues around contemporary metal-on-metal joint replacements. *The Journal of Bone and Joint Surgery. American Volume*. 2005;**87**:18-27. DOI: 10.2106/JBJS.C.00949
- [31] Clarke MT, Lee PTH, Arora A, Villar RN. Levels of metal ions after small- and large-diameter metal-on-metal hip arthroplasty. *Journal of Bone and Joint Surgery. British Volume (London)*. 2003;**85B**:913-917
- [32] Rasquinha VJ, Ranawat CS, Weiskopf J, Rodriguez JA, Skipor AK, Jacobs JJ. Serum metal levels and bearing surfaces in total hip arthroplasty. *The Journal of Arthroplasty*. 2006;**21**:47-52. DOI: 10.1016/j.arth.2006.05.005
- [33] MacDonald SJ. Can a safe level for metal ions in patients with metal-on-metal total hip arthroplasties be determined? *The Journal of Arthroplasty*. 2004;**19**:71-77
- [34] Iavicoli I, Gianluca F, Alessandrelli M, Cresti R, De Santis V, Salvatori S, et al. The release of metals from metal-on-metal surface arthroplasty of the hip. *Journal of Trace Elements in Medicine and Biology*. 2006;**20**:25-31. DOI: 10.1016/j.jtemb.2005.10.002
- [35] Hart AJ, Hester T, Sinclair K, Powell JJ, Goodship AE, Pele L, et al. The association between metal ions from hip resurfacing and reduced T-cell counts. *Journal of Bone and Joint Surgery. British Volume (London)*. 2006;**88B**:449-454. DOI: 10.1302/0301-620X.88B4.17216
- [36] Lhotka C, Szekeres T, Steffan I, Zhuber K, Zweymuller K. Four-year study of cobalt and chromium blood levels in patients managed with two different metal-on-metal total hip replacements. *Journal of Orthopaedic Research*. 2003;**21**:189-195. DOI: 10.1016/S0736-0266(02)00152-3
- [37] Hennig FF, Raithel HJ, Schaller KH, Dohler JR. Nickel-, chrom- and cobalt-concentrations in human tissue and body fluids of hip prosthesis patients. *Journal of Trace Elements and Electrolytes in Health and Disease*. 1992;**6**:239-243
- [38] Dorr LD, Bloebaum R, Emmanuel J, Meldrum R. Histologic biochemical, and ion analysis of tissue and fluids retrieved during total hip-arthroplasty. *Clinical Orthopaedics and Related Research*. 1990;**261**:82-95
- [39] Urban RM, Jacobs JJ, Tomlinson MJ, Gavrilovic J, Black J, Peoc'h M. Dissemination of wear particles to the liver, spleen, and abdominal lymph nodes of patients with hip or knee replacement. *The Journal of Bone and Joint Surgery. American Volume*. 2000;**82A**:457-477
- [40] Pourbaix M. Atlas of Electrochemical Equilibria in Aqueous Solutions, National Association of Corrosion Engineers. National Association of Corrosion Engineers: Houston, Texas; 1974. 644 p
- [41] EN-71-3, Safety of toys, part 3: Migration of certain elements, directive 88/378/EEC (C 188, 2005-08-02). 1994. Available from: <https://eur-lex.europa.eu/legal-content/ES/TXT/?uri=LEGISSUM%3A121005> [Accessed: 11 March 2019]
- [42] Spriano S, Bosetti M, Bronzoni M, Vern E, Mainac G, Bergo V, et al. Surface properties and cell response of low metal ion release Ti-6Al-7Nb alloy after multi-step chemical and

thermal treatments. *Biomaterials*.
2005;**26**:1219-1229

[43] Zaffe D, Bertoldi C, Consolo U.
Element release from titanium devices
used in oral and maxillofacial surgery.
Biomaterials. 2003;**24**:1093-1099

[44] Martini D, Fini M, Franchi M,
DePasquale V, Bacchelli B, Gamberini
M, et al. Detachment of titanium
and fluorohydroxyapatite particles
in unloaded endosseous implants.
Biomaterials. 2003;**24**:1309-1316. DOI:
10.1016/S0142-9612(02)00508-2

[45] Wang J, Wicklund B, Gustilo R,
Tsukayama D. Titanium, chromium
and cobalt ions modulate the release of
bone-associated cytokines by human
monocytes/macrophages in vitro.
Biomaterials. 1996;**17**:2233-2240

[46] Katti KS. Biomaterials in total joint
replacement. *Colloids and Surfaces. B,
Biointerfaces*. 2004;**39**:133-142. DOI:
10.1016/j.colsurfb.2003.12.002

[47] Brown C, Williams S, Tipper JL,
Fisher J, Ingham E. Characterisation
of wear particles produced by metal
on metal and ceramic on metal
hip prostheses under standard and
microseparation simulation. *Journal
of Materials Science. Materials in
Medicine*. 2007;**18**:819-827. DOI:
10.1007/s10856-006-0015-z

[48] Cometa S, Bonifacio MA, Mattioli-
Belmonte M, Sabbatini L, De Giglio E.
Electrochemical strategies for titanium
implant polymeric coatings: The why
and how. *Coatings*. 2019;**9**:268. DOI:
10.3390/coatings9040268

[49] Steinemann SG. Titanium—The
material of choice. *Periodontology*
2000. 2007;**17**:7-21. DOI: 10.1111/
j.1600-0757.1998.tb00119.x