

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/361706947>

Impurities in commercial titanium dental implants – A mass and optical emission spectrometry elemental analysis

Article in *Dental materials: official publication of the Academy of Dental Materials* · July 2022

DOI: 10.1016/j.dental.2022.06.028

CITATIONS

0

READS

59

8 authors, including:



Andres Stricker

University Medical Center Freiburg

68 PUBLICATIONS 892 CITATIONS

[SEE PROFILE](#)



Thomas Bergfeldt

Karlsruhe Institute of Technology

57 PUBLICATIONS 983 CITATIONS

[SEE PROFILE](#)



Tobias Fretwurst

University Medical Center Freiburg

64 PUBLICATIONS 1,025 CITATIONS

[SEE PROFILE](#)



Owen Addison

King's College London

140 PUBLICATIONS 2,230 CITATIONS

[SEE PROFILE](#)

Some of the authors of this publication are also working on these related projects:



Elemental analysis from Li to U of special materials [View project](#)



Process Design to Prevent Prosthetic Infections (EP/P02341X/1) (PREVENTION) [View project](#)

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/dental

Impurities in commercial titanium dental implants – A mass and optical emission spectrometry elemental analysis

Andres Stricker^a, Thomas Bergfeldt^b, Tobias Fretwurst^a, Owen Addison^c, Rainer Schmelzeisen^a, René Rothweiler^a, Katja Nelson^a, Christian Gross^{a,*}

^a Department of Oral and Maxillofacial Surgery, Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Hugstetter Str. 55, 79106 Freiburg im Breisgau, Germany

^b Institute of Applied Materials - Applied Material Physics (IAM-AWP), Karlsruhe Institute of Technology (KIT), Hermann-von-Helmholtz-Platz 1, 76344 Eggenstein-Leopoldshafen, Germany

^c Centre for Oral, Clinical & Translational Sciences, Faculty of Dentistry, Oral and Craniofacial Sciences, King's College London, Guy's Hospital, Great Maze Pond, SE1 9RT London, UK

ARTICLE INFO

Article history:

Received 19 February 2022

Received in revised form 19 June 2022

Accepted 22 June 2022

Keywords:

Titanium

Dental implants

Titanium implants

Elemental analysis

ABSTRACT

Objective: Titanium (Ti) is considered bioinert and is still regarded as the “gold standard” material for dental implants. However, even ‘commercial pure’ Ti will contain minor fractions of elemental impurities. Evidence demonstrating the release of Ti ions and particles from ‘passive’ implant surfaces is increasing and has been attributed to biocorrosion processes which may provoke immunological reactions. However, Ti observed in peri-implant tissues has been shown to be co-located with elements considered impurities in biomedical alloys. Accordingly, this study aimed to quantify the composition of impurities in commercial Ti dental implants.

Methods: Fifteen commercial titanium dental implant systems were analyzed using inductively coupled plasma-mass spectrometry (ICP-MS) and optical emission spectrometry (ICP-OES).

Abbreviations: Al, aluminum; As, arsenic; B, boron; Ba, barium; Bi, bismuth; Ca, calcium; Cd, cadmium; Co, cobalt; Cr, chromium; Cu, copper; EDX, energy dispersive X-ray spectroscopy; Fe, iron; Ga, gallium; Ge, germanium; Hf, hafnium; IAM-AWP, Institute of Applied Materials - Applied Material Physics; ICP-MS, inductively coupled plasma mass spectrometry; ICP-OES, inductively coupled plasma optical emission spectrometry; In, indium; K, potassium; KIT, Karlsruhe Institute of Technology; KNMF, Karlsruhe Nano Micro Facility; Li, lithium; Mg, magnesium; Mn, manganese; Mo, molybdenum; Na, sodium; Nb, niobium; Ni, nickel; P, phosphorus; Pb, lead; Rb, rubidium; Re, rhenium; Sb, antimony; Sc, scandium; Se, selenium; SEM, scanning electron microscopy; Sn, tin; SR-XAS, X-ray absorption spectroscopy; SR-XRF, Synchrotron radiation X-ray fluorescence spectroscopy; Sr, strontium; Ta, tantalum; Te, tellurium; Th, thorium; Ti, titanium; Tl, thallium; U, uranium; V, vanadium; W, tungsten; XRF, X-ray fluorescence spectroscopy; ELI, extra low interstitials; Zn, zinc; Zr, zirconium

* Correspondence to: Department of Oral and Maxillofacial Surgery, Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Hugstetter Straße 55, 79106, Germany.

E-mail addresses: andres.stricker@uniklinik-freiburg.de (A. Stricker), thomas.bergfeldt@kit.edu (T. Bergfeldt), tobias.fretwurst@uniklinik-freiburg.de (T. Fretwurst), owen.addison@kcl.ac.uk (O. Addison), rainer.schmelzeisen@uniklinik-freiburg.de (R. Schmelzeisen), rene.rothweiler@uniklinik-freiburg.de (R. Rothweiler), katja.nelson@uniklinik-freiburg.de (K. Nelson), christian.gross@uniklinik-freiburg.de (C. Gross).

<https://doi.org/10.1016/j.dental.2022.06.028>

0109-5641/© 2022 The Authors. Published by Elsevier Inc. on behalf of The Academy of Dental Materials.

CC_BY_NC_ND_4.0

Results: The elemental composition of implants manufactured from commercially pure grades of Ti, Ti-6Al-4V, and the TiZr alloy (Roxolid) conformed to the respective ISO/ASTM standards or manufacturers' data (TiZr/Roxolid). However, all implants investigated included exogenous metal contaminants including Ni, Cr, Sb, and Nb to a variable extent. Other contaminants detected in a fraction of implants included As and the radionuclides U-238 and Th-232.

Significance: Although all Ti implant studies conformed with their standard compositions, potentially allergenic, noxious metals and even radionuclides were detected. Since there are differences in the degree of contamination between the implant systems, a certain impurity fraction seems technically avoidable. The clinical relevance of these findings must be further investigated, and an adaptation of industry standards should be discussed.

© 2022 The Authors. Published by Elsevier Inc. on behalf of The Academy of Dental Materials.

CC_BY_NC_ND_4.0

1. Introduction

Commercially pure (Cp) and alloyed forms of Titanium (Ti) have been considered the “gold standard” biomaterials for endosseous dental implants since the treatment modality was introduced in the 1960s [1,2]. The mechanical and physico-chemical characteristics of these materials are specified by the International Organization for Standardization (ISO) standard 5832 and the American Society for Testing and Materials (ASTM) standard ASTM F67-13 [3–5]. The standards detail the elemental compositions required for the different presentations of Ti alongside technical requirements. Currently, biomedical Ti is available in four commercially pure grades (ASTM I-IV) and several alloys, including Ti-6Aluminum(Al)-4Vanadium(V) (Ti6Al4V; ASTM Grade V). For the four grades of CpTi, ISO 5832-2 and F67-13 specify alongside Ti, the maximum elemental mass fractions of nitrogen (N) (max.: 0.012–0.05 mass%), carbon (C) (max.: 0.03–0.08 mass%), hydrogen (H) (max.: 0.0125 mass%), oxygen (O) (max.: 0.1–0.4 mass%), and iron (Fe) (max.: 0.1–0.5 mass%) contents. The Fe and O fractions increase from Grade I to Grade IV Ti and correlate with the enhancement of the hardness, yield, and tensile strengths but a decrease in corrosion resistance. The elemental composition of Grade IV Ti, the most common commercially pure Grade of Ti used in dental implants, is standardized as follows: N: max. 0.05 mass%; C: max. 0.08 mass%; H: max. 0.0125 mass%; Fe: max. 0.5 mass%; O: max. 0.4 mass%; Ti: balance. No other metal element fractions are specified or limited for CpTi in the respective standards [3,5].

The alpha-beta alloy Ti6Al4V (Grade V) exhibits higher tensile and yield strength (≥ 860 MPa and ≥ 780 MPa, respectively) and is also used for the fabrication of commercial dental implants. When a Ti6Al4V alloy meets below lower limits for O (max. 0.13 mass%) and Fe (max. 0.25 mass%) fractions, it is referred to as “Extra Low Interstitials” (ELI), possesses improved fracture toughness, and is standardized by ASTM F-136 [6]. A binary alloy of ~ 85 mass% Ti and ~ 15 mass% zirconium (Zr) has also been introduced to the dental implant market to achieve higher fatigue and tensile strength values (Roxolid®, Straumann). However, its composition is not currently standardized by ISO or ASTM standards [7–9].

Although Ti and its alloys are considered to have high corrosion resistance under physiological conditions, there is

increasing evidence that Ti ions and particles are released from Ti dental implants and may be associated with local and systemic immunological reactions, such as peri-implant inflammation [10–15]. The final statement of the European Association for Osteointegration (EAO) Consensus Conference 2018 concluded from in vitro studies that Ti particles released into the peri-implant tissues in an acidic environment, such as that induced locally within acidogenic bacterial biofilms, can interfere with bone homeostasis by the activation of osteoclasts and osteoblasts and the secretion of cytokines by lymphocytes and macrophages [16]. Clinical data regarding allergy associated with titanium dental implants is limited to case reports and case series as currently reviewed [10].

A recent study investigated the distribution and chemical speciation of exogenous metal particles found in inflamed tissues adjacent to commercial Ti and ceramic dental implants using Synchrotron radiation X-ray fluorescence (SR-XRF) and X-ray absorption spectroscopy (SR-XAS) [17]. Alongside the detection of Ti and ceramic particles in the peri-implant tissue of the Ti and ceramic implants, the authors reported the presence of potential contaminant elements such as lead (Pb) and arsenic (As). It has been widely accepted that topographical modifications of dental implants, such as airborne particle abrasion or acid etching used to increase surface roughness and enhance osseointegration, can lead to contamination of the Ti surface [18–20]. Several studies have used non-destructive techniques such as scanning electron microscopy (SEM) and energy-dispersive X-ray spectroscopy (EDX) to detect a variety of organic and inorganic contaminants on commercial dental implant surfaces [21–23]. Less attention has been given to characterizing the elemental composition of the implant body. However, analyses of biomedical Ti and Ti alloys have shown the presence of metal elements not described in the standards, such as chromium (Cr), molybdenum (Mo), and copper (Cu) [24].

In a previous study, elemental analysis of commercial yttria-stabilized zirconia dental implants was carried out using chemical digestion and a combination of inductively coupled plasma mass spectrometry (ICP-MS) and inductively coupled plasma optical emission spectrometry (ICP-OES). The techniques enabled the elemental composition of the implants to be determined, including ultra-trace levels (ppb) of

contaminants [25]. Besides Zr, various metal elements were detected, including the radionuclides thorium (Th-232) and uranium (U-238).

Accordingly, the current study aimed to characterize the major, minor and trace elemental compositions for a range of modern commercial Ti-based dental implants.

2. Methods

2.1. Sample acquisition

Fifteen commercial Ti dental implants from twelve dental implant brands were examined. Two implants per implant system were purchased directly from the respective companies (implants $n = 30$; implant systems $n = 15$, brands $n = 12$). After the documented receipt of the sterile packaged implants, the implants were unpacked under a laminar air flow, detached from the insertion posts or screws with plastic tweezers, transferred to threaded glass containers (ARGLAS®, Schott AG, Mainz, Germany), and indexed by a three-digit code. The analytical methodology was designed and conducted by the Institute of Applied Materials - Applied Material Physics (IAM-AWP) of the Karlsruhe Institute of Technology (KIT). During analysis, investigators at IAM-AWP were blinded to the sample designation (only three-digit code = sample blind index). Table 1 summarizes the details of the implants investigated.

2.2. Preanalytical sample procession and digestion

For chemical digestion, the samples were cut using a steel cutting shear (1 BR/6, Peddinghaus, Germany). and then etched with a mixed acid (HCl 35 % subboiled, HNO₃ 65 % subboiled, ultrapure water (OmniaPure, stakpure GmbH, Niederahr, Germany)) and HF 40 % suprapure for one minute. The samples were subsampled in three 80–190 mg portions (weighing accuracy ± 0.25 mg (XP205, Mettler-Toledo, Gießen, Germany), TiMed1, TiMed2, and TiZrRox2: due to a lack of material only two replicates for each sample). Each subsample was completely dissolved in 9 mL of mixed acid (HCl 35 % subboiled, HNO₃ subboiled, ultrapure water) and 1 mL HF 40 % suprapure. All reagents were ultrapure mass spectrometry grade. Each sample container (PFA 50 mL) was heated in a graphite oven at 80 C for two hours. Following heating, the resultant clear acidified solution was diluted to ~ 50 mL with ultrapure water with the exact weight of the solution balanced. Due to a large number of subsamples ($n = 87$) and the partly different chemical composition of some samples, the quantitative measurements were performed in five measurement runs (see different limits of quantification (LOQ) in Appendix Table B).

2.3. Inductively coupled plasma-optical emission spectrometry (ICP-OES)

Each sample solution was diluted several times depending on the concentration of the target elements for analysis. Instead of using volumetric dilution methods, the sample solution and ultrapure water were weighed (XP 205, Mettler-Toledo,

Gießen, Germany) for improved accuracy. Elemental quantification was achieved by using four different calibration solutions and an internal standard (scandium (Sc)) by ICP-OES (iCAP 7600 ICP-OES Duo, Thermo Fisher Scientific Inc., Waltham, MA, USA). For minor and trace elements, the solution was matrix-adapted (Al, Ti, V, Zr, acid). The range of the calibration solutions extended from 0 to 0.2 mg/L. Two or three emission wavelengths of each element were used for the calculation of mass fraction. The instrument settings for the ICP-OES are reported in Table A.1.

2.4. Inductively coupled plasma-mass spectrometry (ICP-MS)

ICP-MS was performed (7500ce ICP-MS, Agilent Technologies Inc., Santa Clara, CA, USA) to measure the concentration of elements with lower detection sensitivity with ICP-OES. Elemental analysis was accomplished with four different matrix-adapted calibration solutions (Al, Ti, V, Zr, acid) and two internal standards (Sc, indium (In)). The range of the calibration extended from 0.01 to 4.0 µg/L (varying by each element) and involved the area of the concentration of the samples. One, two, or three masses of the elements were used for the calculation. The instrument settings for the ICP-MS are reported in Table A.2.

2.5. Quality control

The certified ICP calibration solutions (Aesar, Thermo Fisher (Kandel) GmbH, Karlsruhe, Germany) were controlled with another certified ICP solution from a different producer (Merck, Darmstadt, Germany). Recovery of these standards in matrix-adapted solutions was between 90 % and 110 %.

2.6. Calculations and descriptive statistics

ICP-MS/OES results are reported as mean, standard deviation (SD), and measurement uncertainty (\pm). The respective limit of quantitation (LOQ) for each sample is given (Appendix Table C). The results were visualized in mg/kg (ppm) and mass percent (mass%) in stacked bar graphs. IBM SPSS Statistics (version 25.0, released 2017, IBM Corp., Armonk, NY, USA) was used for descriptive statistics. Results (mean, SD) have been rounded for a better overview.

3. Results

All results of the ICP-MS and ICP-OES elemental analyses are shown in Table B.1–6 and selectively visualized in Figs. 1–4. Element abbreviations are presented in the list of abbreviations.

3.1. Main constituents

Ti was the major component; however, multiple other metal elements were detected in all samples. The normalized non-Ti fraction in the commercially pure implant samples averaged 1009 ppm (SD: 534). The binary TiZr alloy implant samples TiZrRox1 and TiZrRox2 (Roxolid) featured a

Table 1 – Investigated implants.

Brands/Company	S.no.	S.B.In.	S.In.	LOT no.	Sample Name	Material
CAMLOG	1	35K	TiCon1	0020048300	Conelog Screwline Promote Plus	Ti Grade IV
	2	L11	TiCon2	0020048300	Conelog Screwline Promote Plus	
	3	G6A	TiCam1	0010084535	Camlog Progressive Line Promote Plus	Ti Grade IV
	4	HL6	TiCam2	0000080692	Camlog Progressive Line Promote Plus	
BEGO	5	A86	TiBeg1	054774	Semados SC 58174	Ti Grade IV
	6	93F	TiBeg2	054774	Semados SC 58174	
MEDENTIS MEDICAL	7	FF8	TiMed1	20180315-37	ICX-Premium	Ti Grade IV
	8	KL5	TiMed2	20180315-37	ICX-Premium	
NOBEL BIOCARE	9	AA7	TiNoA1	13094202	NobelActive Internal RP	Ti Grade IV
	10	CV9	TiNoA2	13094202	NobelActive Internal RP	
	11	FE7	TiNoU1	12149785	NobelActive TiUltra RP	Ti Grade IV
	12	XC5	TiNoU2	12149785	NobelActive TiUltra RP	
STRAUMANN	13	LA1	TiSLA1	V6988	SLActive Standard Implant	Ti Grade IV
	14	BG7	TiSLA2	Z2550	SLActive Standard Implant	
	15	CC5	TiZrRox1	PY663	ROXOLID Slactive IMPLANT BL Tapered Loxim	85 % Ti 15 % Zr
	16	SB1	TiZrRox2	PY663	ROXOLID Slactive IMPLANT BL Tapered Loxim	
SIC INVENT	17	AV2	TiSic1	622312	SICace Screw Implant	Ti Grade IV
	18	GG8	TiSic2	622312	SICace Screw Implant	
ASTRA TECH/DENTSPLY SIRONA	19	LV4	TiAst1	155273	OsseoSpeed TX	Ti Grade IV
	20	YY6	TiAst2	155273	OsseoSpeed TX	
ANKYLOS/ DENTSPLY SIRONA	21	H4S	TiDen1	B170003533	Ankylos C/X Implant	Ti Grade II
	22	XN3	TiDen2	B170015379	Ankylos C/X Implant	
MIS IMPLANTS/ DENTSPLY SIRONA	23	TZ5	Ti6Al4VMis1	W19010304	C1B-13420	Ti-6Al-4V-ELI (extra low interstitials)
	24	BB1	Ti6Al4VMis2	W19010304	C1B-13420	
NEODENT/STRAUMANN	25	NM4	TiNeo1	800371916	Helix GM	Ti Grade IV
	26	45A	TiNeo2	800371916	Helix GM	
OSSTEM IMPLANT	27	LF9	TiOss1	FUP18C028	USII SA	Ti Grade IV
	28	G2H	TiOss2	FUP18C028	USII SA	
THOMMEN MEDICAL	29	M8A	TiTho1	21113	SPI Contact RC Incell	Ti Grade IV
	30	R3F	TiTho2	12810	SPI Contact RC Incell	
brands n = 12	n = 30				implant systems n = 15	

S.No. = sample number; S.B.In. = Sample blind index; S.In. = sample index; LOT no. = LOT number/batch number.

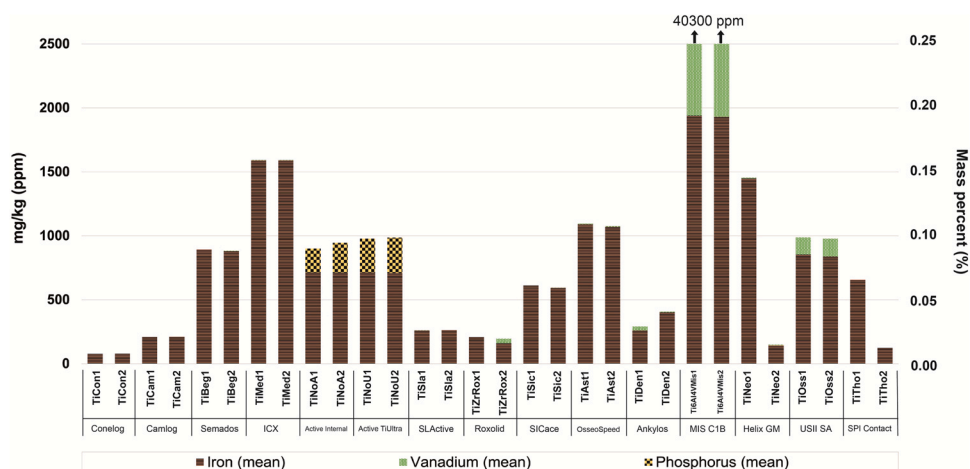


Fig. 1 – Specific contamination with iron (Fe), phosphorus (P) and vanadium (V). Results (absolute; mean) are visualized as stacked bar charts. For a better overview, the left Y-axis is scaled in mg/kg (ppm) and the right Y-axis in mass percent (%). All investigated samples contained contamination with Fe. P was only found in the Nobel Active implants (TiNoA1, TiNoA2, TiNoU1, TiNoU2). The samples Ti6Al4VMis1 and Ti6Al4VMis2 were outliers regarding their V fraction, that is indicated by black arrows.

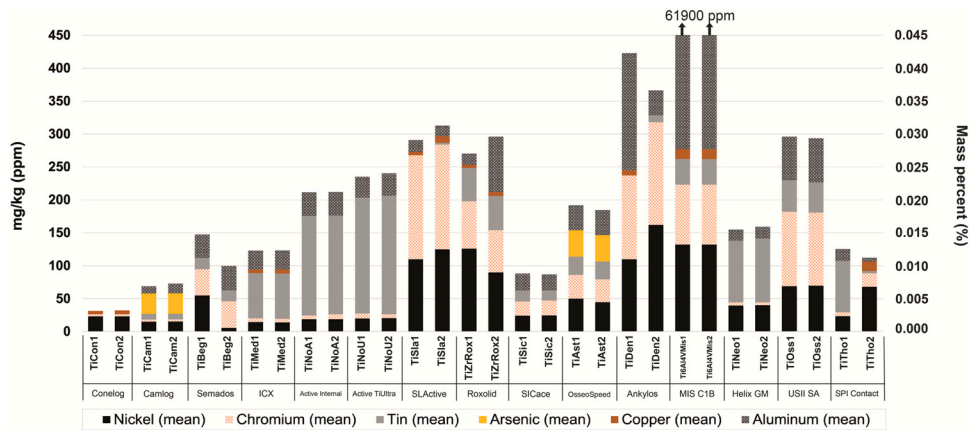


Fig. 2 – Specific contamination with nickel (Ni), chromium (Cr), tin (Sn), arsenic (As), copper (Cu), and aluminum (Al). Results (absolute; mean) are visualized as stacked bar charts. For a better overview, the left Y-axis is scaled in mg/kg (ppm) and the right Y-axis in mass percent (%). Contamination with As was found in two implant systems. The samples Ti6Al4VMis1 and Ti6Al4VMis2 were outliers regarding their Al fraction, that is indicated by black arrows.

normalized Zr fraction with a mean of 14.2 mass% (mean: 142,000 ppm, SD: 6530) and a normalized non-Ti, non-Zr fraction averaging 493 ppm. The Ti6Al4V implant samples Ti6Al4VMis1 and Ti6Al4VMis2 (MIS C1B) featured a normalized Al fraction averaging 6.16 mass% (mean: 61,600 ppm, SD: 44 ppm), a normalized V fraction with a mean of 4.01 mass% (mean: 40,100 ppm, SD: 29 ppm) and a normalized impurity fraction averaging 2260 ppm. Absolute result values for the main constituents and impurity fractions are given in Table B.1–6.

3.2. Minor, trace, and ultra-trace level contamination with metal elements

The largest fraction of the minor constituents was Fe, found in all investigated implant samples and averaged a 0.071 mass% (absolute; mean: 708 ppm; SD: 548 ppm). The Fe

fraction of all implant samples was less than 0.5 mass% as specified by ISO 5832-2 and F67-13 [3,5]. All investigated implant samples contained fractions of nickel (Ni) (absolute; mean: 56 ppm, SD: 46 ppm), chromium (Cr) (absolute; mean: 47 ppm, SD: 53 ppm), antimony (Sb) (absolute; mean: 5.6, SD: 3.7 ppm), and niobium (Nb) (absolute; mean: 4.2, SD: 2.9 ppm). 12 of 28 non-vanadium-doped implant samples comprised a V fraction (absolute; mean: 26.6 ppm, SD: 47.5 ppm). The found fractions of Fe, Cr, Ni and V are visualized in Figs. 1 and 2. 26 of the 28 non-aluminum-doped samples contained Al (absolute; mean: 36.1 ppm, SD: 33.9 ppm). No Al was detected above the LOQ in the samples TiCon1 and TiCon2 (Conellog Screwline implants) (see Fig. 2). 24 of 28 non-zirconium-doped implant samples contained a fraction of Zr (absolute; mean: 3.4 ppm, SD: 3.5 ppm). Four implants (Nobel Active implants: TiNoA1, TiNoA2, TiNoU1, TiNoU2) featured a fraction of phosphorus (P) (absolute;

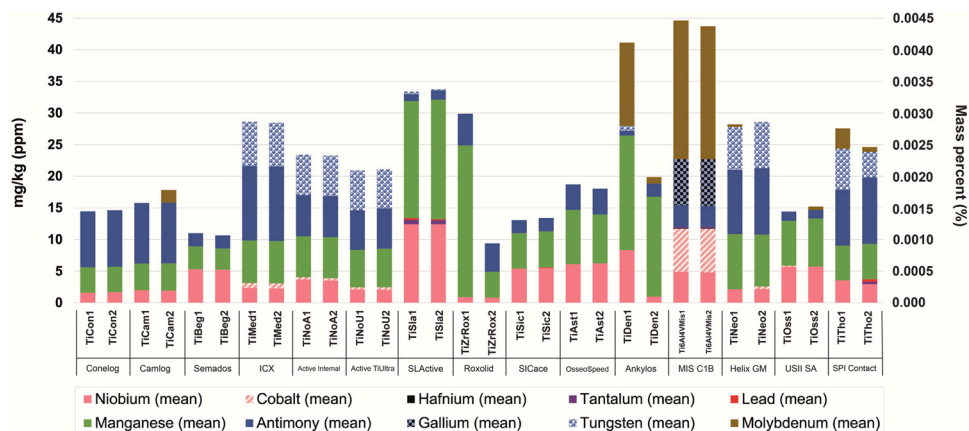


Fig. 3 – Specific contamination with selected metals. Results (absolute; mean) of the niobium (Nb), cobalt (Co), hafnium (Hf), tantalum (Ta), lead (Pb), manganese (Mn), antimony (Sb), gallium (Ga), tungsten (W), and molybdenum (Mo) fractions are visualized as stacked bar charts. For a better overview, the left Y-axis is scaled in mg/kg (ppm) and the right Y-axis in mass percent (%).

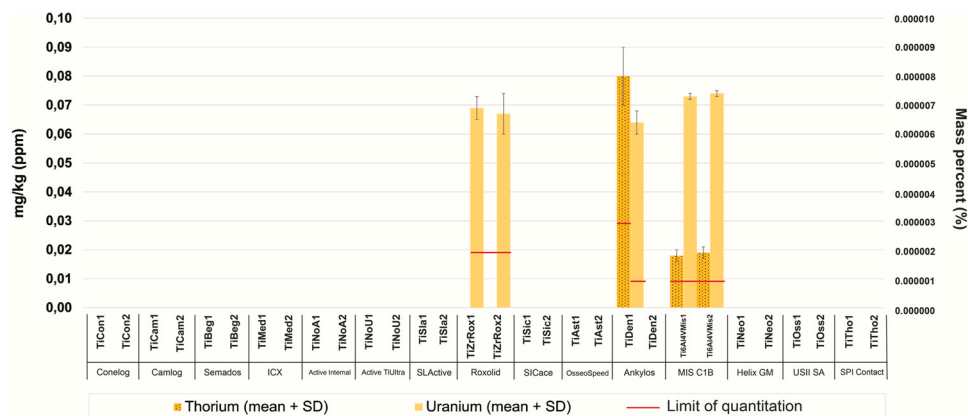


Fig. 4 – Ultra-trace level contamination with Thorium (Th)-232 and Uranium (U)-238. Results (absolute; mean) are visualized as grouped bar charts. The left Y-axis is scaled in mg/kg (ppm) and the right Y-axis in mass percent (%). The red line indicated the limit of quantitation. SD = standard deviation. 5/30 samples showed contamination with radionuclides.

mean: 241 ppm; SD: 40 ppm) (see Fig. 1). Arsenic (As) was found in four samples from two brands (absolute; mean: 35.5 ppm, SD: 5.2 ppm) (see Fig. 2). Further elements detected included manganese (Mn) (28/30 samples), tin (Sn) (26/30 samples), tungsten (W) (13/30 samples), copper (Cu) (12/30 samples), cobalt (Co) (10/30 samples), molybdenum (Mo) (9/30 samples), lead (Pb) (4/30 samples), potassium (K) (5/30 samples), tantalum (Ta) (5/30 samples), gallium (Ga) (2/30 samples) and hafnium (Hf) (2/30 samples). Fig. 1 (Fe, P, V), Fig. 2 (Ni, Cr, Sn, As, Cu, Al), and Fig. 3 (Nb, Co, Hf, Ta, Pb, Mn, Sb, Ga, W, Mo) selectively visualize the found contaminations. For all absolute results, see Table B.

3.3. Ultra-trace level contamination with Thorium (Th-232) and Uranium (U-238)

The ICP-MS analysis revealed that 5 of 30 implant samples contained contamination with U-238 in the parts per billion range (absolute; mean: 69 ppb, SD: 4 ppb), and 3 of 30 samples featured contamination with Th-232 (absolute; mean: 39 ppb, SD: 36 ppb) in the ultra-trace level above the LOQ. Fig. 4 visualizes the Th-232 and U-238 fractions of all samples investigated.

4. Discussion

To aid the interpretation of the presented results, it is important to recognize that the ICP-MS/OES analyses quantified the average elemental composition of the entire implant body. In contrast, most of the previous reports describing impurities of Ti implants have used surface characterization techniques only [21–23]. Ti is a highly reactive metal that rapidly forms a robust surface oxide layer which confers its chemical passivity protecting the implant against corrosion under physiological conditions [26,27]. However, clinically, Ti release from dental implants [17] and extra-oral bone anchorage implants [28] has been demonstrated, with the size and chemical speciation of the released Ti products consistent with those formed by corrosion. To account for these observations, mechanisms have been proposed where high

concentrations of reactive oxygen species (ROS) associated with inflammation [29]; or acidic environments [30] are maintained locally [12,14,31–33]. Biocorrosion due to local ROS release or acidogenic biofilms, and mechanically assisted crevice corrosion associated with relative micromotion of modular components, lead to the break-down of the surface passive layer. Regions of impurity, such as aggregation of Fe at grain boundaries in CpTi, present locations with reduced corrosion resistance that are more likely to propagate before repassivation occurs [34]. In this way, the bulk composition and heterogeneity of distribution of minor and trace elements within the bulk alloy can directly influence corrosion resistance.

A previous SR-XRF/XAS study showed that Ti particles present in peri-implant tissues are predominantly of oxide speciation and are attributed to release due to undermining and detachment from the Ti-oxide surface or, through a precipitation route when bursts of released Ti ions rapidly react with oxygen or water to form insoluble TiO₂ [17]. The abundance of relatively high concentrations of ‘contaminant’ elements in the same location as the observed Ti in the study [17] could be interpreted as consistent with inhomogeneous distributions of impurities with the bulk metal that represent points for higher risk of corrosion.

4.1. Conformance with ISO/ASTM standards and manufacturer’s specifications

All investigated implants fabricated from CpTi conformed to ISO 5832-2 and ASTM F67-13 (Grade II: max. 0.3 mass% Fe; Grade IV: max. 0.5 mass% Fe). In addition, the two implants manufactured from Ti6Al4V ELI (MIS Implant Systems) met the ASTM F136 standard (max. Fe: 0.25 mass%, Al: 5.5–6.50 mass%, V: 3.5–4.5 mass%). Implants fabricated from the binary TiZr alloy (Roxolid, Straumann) are not subject to any standardization regarding the material composition but conformed to the manufacturer’s specifications (Ti: ~85 mass%, Zr: ~15 mass%) and to CpTi Grade IV standards regarding the Fe fraction.

4.2. Contamination with multiple metal elements in all implants

Although all investigated dental implant systems conformed to the respective ISO/ASTM standards or manufacturer's specifications, they all contained contamination with multiple elements. The contaminants found included harmless endogenous trace elements (e.g., Cu, Zn) but also potentially allergenic (e.g., Ni, Co, Cr), potentially poisonous (e.g., As) metals, and even radionuclides (Th-232, U-238) [35]. Ni, Co, and Cr are potent contact allergens with estimated age-standardized sensitization rates of 14.5 %, 2.1 %, and 0.8 %, respectively, in European countries [36]. Due to a low dielectric constant, Ni oxides and Co oxides are likelier to interact with tissue electrolytes than Ti oxide or oxides of the refractory group (e.g., Nb, Ta, V) [24]. Previous studies have identified their presence in biomedical Ti substrates [24], and in this study, Ni and Cr were observed in all samples. Co was found in a third of the samples measured. However, the degree of contamination with Ni (mean: 56 ppm, SD: 46 ppm !), Cr (mean: 47 ppm, SD: 53 ppm !), and Co (mean: 1.7 ppm, SD: 2.7 ppm !) differed among the implant systems, indicating a difference in the quality of source materials and that impurity reduction is not yet technically implemented on a standardized level across the dental implant market.

According to the World Health Organization (WHO), exposure to As is a major public health concern [37]. Although evidence is growing that traces of As, a natural component of the earth's crust, might play a role in human metabolism, it is assumed to be toxic and cancerogenic when chronic exposure occurs to its inorganic forms [38,39]. Therefore, the WHO recommends a limit of 10 µg/L (= 10 ppm) As in drinking water [37]. The present study found consistent As contamination of 30 and 40 ppm respectively in two implant systems, which cannot be extrapolated to a release concentration. However, the kinetics of any release require further scientific clarification. It is to be mentioned that from the present ICP-MS/OES elemental analysis, it is not possible to deduce whether As is locally concentrated or acts as an interstitial element within the Ti bulk. Nevertheless, given the recommendations of the WHO to keep As contamination as low as technically possible and regarding the observations that the majority of the implant systems were manufactured without detectable As contamination, As impurities in dental implants can be considered avoidable.

It has been demonstrated that even purified medical zirconia ceramics can be contaminated with the radionuclides U and Th [40–43]. A previous ICP-MS/OES analysis on commercial zirconia dental implants demonstrated that the majority of the implants investigated featured ultra-trace contamination (in ppb) with U-238 and Th-232 [25]. Therefore, the ultra-trace contamination with U-238 of the TiZr alloy implant system (Roxolid) found in the present study was expected. However, three Ti dental implants also featured contamination with radionuclides, which is not associated with a major zirconia fraction. Clinically relevant radioactivity is not to be expected from this. However, further radiochemical analysis is required to scan for other radionuclides and to determine not only the estimated but the actual radioactivity.

4.3. Sources of contamination

Although abundant in the earth's crust, due to a time-consuming and expensive extraction from various ores, Ti is considered a "rare metal". Many impurities, e.g., Cu, Mn, and Mo, can persist in commercial Ti [44]. However, further contamination can also arise in the course of topographical modifications of the surface, such as chemical etching, airborne particle abrasion, anodization, laser ablation, and surface coating [45,46]. By anodizing the implant's surface in phosphoric acid, the surface roughness can be increased, and it is proposed that cytokine production can be modulated and the osseointegration improved [46,47]. The present study found exclusive contamination of all NobelActive implants with P, which is likely due to the surface treatment with phosphoric acid. A phosphorus signal on the surface of NobelActive implants has also been described by Duddeck et al. in an SEM/EDX study [21].

Except for one implant system (Conelog Screwline), all investigated implants made of CpTi exhibited an Al fraction. Residual Al is a known potential contaminant on the surface of Ti dental implants [21,22,45], most commonly resulting from residues of aluminum oxide used for surface air abrasion on the Ti surface [48,49]. However, the impact of this residual aluminum(oxide) on the osseointegration of the implant is still controversially discussed [50–52].

The current study provides a unique, manufacturer-independent overview of the elemental composition of a fraction (< 10 %) of commercially available Ti implants. Further research should investigate possible cluster formation of impurities within the implant body and between batches. Furthermore, it needs to be clarified to what extent impurities are clinically relevant and whether they may play a role in the intolerances to Ti dental implants. The market for dental implants is growing rapidly and is subject to high fluctuation (market entries and exits); therefore, a complete investigation of all implants on the market is limited. Instead, with the knowledge of the existing elemental composition of the investigated implant systems, an adaptation of the relevant standards, in particular additional limit values for specific contaminants, should be further evaluated and discussed.

5. Conclusion

Based on the results of the present ICP-MS/OES analysis, the following conclusions can be drawn:

1. Although all investigated Ti dental implants conform to the respective standards and manufacturer's specifications, all contain traceable contamination with several metal elements.
2. The contaminants differed between the implant systems and included harmless essential trace elements and potentially noxious metals, e.g., As and radionuclides.
3. Further research must prove generalization on other implant systems and the biological relevance of these contamination. Especially the role of potentially allergenic contaminants, such as Ni, is of clinical interest.

4. Since there are relevant differences in the degree of contamination with metal elements between the implant systems, a certain impurity fraction seems technically avoidable. An adaptation of the relevant standards, particularly additional limit values for contaminants, should be discussed.

Ethics approval and consent to participate

No ethics approval needed as no patients/animals were studied.

Consent for publication

No consent needed, as no patient data/material was used.

Funding

The resources for the experimental part were supported by Karlsruhe Nano Micro Facility (KNMF, <http://www.knmf.kit.edu>), a Helmholtzresearch infrastructure at the Karlsruhe Institute of Technology (KIT) (Proposal 2019-023-028249). The Ti dental implants were commercially acquired from the respective manufacturer/vendors without any funding and without the knowledge of the manufacturers.

Availability of data and material

All data generated or analyzed during this study are included in this published article.

Acknowledgements

The authors thank the Institute of Applied Materials - Applied Material Physics (IAM-AWP) of the Karlsruhe Institute of Technology (KIT) and the Karlsruhe Nano Micro Facility (KNMF, <http://www.knmf.kit.edu>), a Helmholtz research infrastructure at the KIT), for providing and executing the methodology of this study. Many thanks to the KNMF for funding the experimental part of this project.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.dental.2022.06.028](https://doi.org/10.1016/j.dental.2022.06.028).

REFERENCES

- [1] Branemark PI, Hansson BO, Adell R, Breine U, Lindstrom J, Hallen O, et al. Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. *Scand J Plast Reconstr Surg Suppl* 1977;16:1–132.
- [2] Osman R, Swain M. A critical review of dental implant materials with an emphasis on titanium versus zirconia. *Materials* 2015;8:932–58. <https://doi.org/10.3390/ma8030932>
- [3] ISO 5832-2:2018 (Implants for surgery – metallic materials – Part 2: unalloyed titanium). Geneva, Switzerland: International Organization for Standardization; 2018.
- [4] ISO 5832-3:2020 (Implants for surgery – metallic materials – Part 3: Wrought titanium 6-aluminium 4-vanadium alloy). Geneva, Switzerland: International Organization for Standardization; 2020.
- [5] ASTM F67-13, 2017, Standard specification for unalloyed titanium, for surgical implant applications (UNS R50250, UNS R50400, UNS R50550, UNS R50700). West Conshohocken, PA, USA: ASTM International; 2017.
- [6] ASTM F136-13, 2021, e1, Standard specification for wrought titanium-6aluminum-4vanadium ELI (extra low interstitial) alloy for surgical implant applications (UNS R56401). West Conshohocken, PA, USA: ASTM International; 2013.
- [7] Karl M, Krafft T, Kelly J. Fracture of a narrow-diameter roxolid implant: clinical and fractographic considerations. *Int J Oral Maxillofac Implants* 2014;29:1193–6. <https://doi.org/10.11607/jomi.3573>
- [8] Grandin HM, Berner S, Dard M. A review of titanium zirconium (TiZr) alloys for use in endosseous dental implants. *Materials* 2012;5:1348–60. <https://doi.org/10.3390/ma5081348>
- [9] Barter S, Stone P, Brägger U. A pilot study to evaluate the success and survival rate of titanium-zirconium implants in partially edentulous patients: results after 24 months of follow-up. *Clin Oral Implants Res* 2012;23:873–81. <https://doi.org/10.1111/j.1600-0501.2011.02231.x>
- [10] Comino-Garayoa R, Cortés-Bretón Brinkmann J, Peláez J, López-Suárez C, Martínez-González JM, Suárez MJ. Allergies to titanium dental implants: what do we really know about them? A scoping review. *Biology* 2020;9. <https://doi.org/10.3390/biology9110404>
- [11] Mombelli A, Hashim D, Cionca N. What is the impact of titanium particles and biocorrosion on implant survival and complications? A critical review. *Clin Oral Implants Res* 2018;29:37–53. <https://doi.org/10.1111/clr.13305>
- [12] Fretwurst T, Nelson K, Tarnow DP, Wang HL, Giannobile WV. Is metal particle release associated with peri-implant bone destruction? An emerging concept. *J Dent Res* 2017;97:259–65. <https://doi.org/10.1177/0022034517740560>
- [13] Wilson TG. Bone loss around implants—is it metallosis. *J Periodontol* 2020;92:181–5. <https://doi.org/10.1002/jper.20-0208>
- [14] Suárez-López del Amo F, Garaicoa-Pazmiño C, Fretwurst T, Castilho RM, Squarize CH. Dental implants-associated release of titanium particles: a systematic review. *Clin Oral Implants Res* 2018;29:1085–100. <https://doi.org/10.1111/clr.13372>
- [15] Fretwurst T, Muller J, Larsson L, Bronsert P, Hazard D, Castilho RM, et al. Immunohistological composition of peri-implantitis affected tissue around ceramic implants—a pilot study. *J Periodontol* 2021;92:571–9. <https://doi.org/10.1002/JPER.20-0169>
- [16] Schliephake H, Sicilia A, Nawas BA, Donos N, Gruber R, Jepsen S, et al. Drugs and diseases: summary and consensus statements of group 1. The 5th EAO Consensus Conference 2018. *Clin Oral Implants Res* 2018;29:93–9. <https://doi.org/10.1111/clr.13270>
- [17] Nelson K, Hesse B, Addison O, Morrell AP, Gross C, Lagrange A, et al. Distribution and chemical speciation of exogenous micro- and nanoparticles in inflamed soft tissue adjacent to titanium and ceramic dental implants. *Anal Chem* 2020;92:14432–43. <https://doi.org/10.1021/acs.analchem.0c02416>
- [18] Ameen AP, Short RD, Johns R, Schwach G. The surface analysis of implant materials. 1. The surface composition of a titanium dental implant material. *Clin Oral Implants Res* 1993;4:144–50. <https://doi.org/10.1034/j.1600-0501.1993.040305.x>

- [19] Velasco-Ortega E, Ortiz-García I, Jiménez-Guerra A, Núñez-Márquez E, Moreno-Muñoz J, Rondón-Romero JL, et al. Osseointegration of sandblasted and acid-etched implant surfaces. a histological and histomorphometric study in the rabbit. *Int J Mol Sci* 2021;22. <https://doi.org/10.3390/ijms22168507>
- [20] Cervino G, Fiorillo L, Iannello G, Santonocito D, Risitano G, Cicciù M. Sandblasted and acid etched titanium dental implant surfaces systematic review and confocal microscopy evaluation. *Materials* 2019;12. <https://doi.org/10.3390/ma12111763>
- [21] Duddeck, Albrektsson, Wennerberg, Larsson, Beuer. On the cleanliness of different oral implant systems: a pilot study. *J Clin Med* 2019;8. <https://doi.org/10.3390/jcm8091280>
- [22] Dias FJ, Fuentes R, Navarro P, Weber B, Borie E. Assessment of the chemical composition in different dental implant types: an analysis through EDX system. *Coatings* 2020;10. <https://doi.org/10.3390/coatings10090882>
- [23] Semez G, Todea C, Mocuta D, Sas IT, Luca R. Chemical and morphologic analysis of titanium dental implants: X-ray photoemission techniques (XPS) and scanning electron microscopy (SEM) with EDX analysis. *Rev Chim* 2018;69:474–7. <https://doi.org/10.37358/rc.18.2.6130>
- [24] Harloff T, Hönle W, Holzwarth U, Bader R, Thomas P, Schuh A. Titanium allergy or not? “Impurity” of titanium implant materials. *Health* 2010;02:306–10. <https://doi.org/10.4236/health.2010.24045>
- [25] Gross C, Bergfeldt T, Fretwurst T, Rothweiler R, Nelson K, Stricker A. Elemental analysis of commercial zirconia dental implants – is “metal-free” devoid of metals? *J Mech Behav Biomed Mater* 2020;107. <https://doi.org/10.1016/j.jmbbm.2020.103759>
- [26] Souza JCM, Apaza-Bedoya K, Benfatti CAM, Silva FS, Henriques B. A comprehensive review on the corrosion pathways of titanium dental implants and their biological adverse effects. *Metals* 2020;10. <https://doi.org/10.3390/met10091272>
- [27] Noronha Oliveira M, Schunemann WVH, Mathew MT, Henriques B, Magini RS, Teughels W, et al. Can degradation products released from dental implants affect peri-implant tissues. *J Periodontol Res* 2017;53:1–11. <https://doi.org/10.1111/jre.12479>
- [28] Addison O, Davenport AJ, Newport RJ, Kalra S, Monir M, Mosselmans JFW, et al. Do ‘passive’ medical titanium surfaces deteriorate in service in the absence of wear? *J R Soc Interface* 2012;9:3161–4. <https://doi.org/10.1098/rsif.2012.0438>
- [29] Zhang Y, Addison O, Yu F, Troconis BCR, Scully JR, Davenport AJ. Time-dependent enhanced corrosion of Ti6Al4V in the presence of H₂O₂ and albumin. *Sci Rep* 2018;8. <https://doi.org/10.1038/s41598-018-21332-x>
- [30] Yu F, Addison O, Baker SJ, Davenport AJ. Lipopolysaccharide inhibits or accelerates biomedical titanium corrosion depending on environmental acidity. *Int J Oral Sci* 2015;7:179–86. <https://doi.org/10.1038/ijos.2014.76>
- [31] Apaza-Bedoya K, Tarce M, Benfatti CAM, Henriques B, Mathew MT, Teughels W, et al. Synergistic interactions between corrosion and wear at titanium-based dental implant connections: a scoping review. *J Periodontol Res* 2017;52:946–54. <https://doi.org/10.1111/jre.12469>
- [32] Fretwurst T, Buzanich G, Nahles S, Woelber JP, Riesemeier H, Nelson K. Metal elements in tissue with dental peri-implantitis: a pilot study. *Clin Oral Implants Res* 2016;27:1178–86. <https://doi.org/10.1111/clr.12718>
- [33] Blum K, Wiest W, Fella C, Balles A, Dittmann J, Rack A, et al. Fatigue induced changes in conical implant–abutment connections. *Dent Mater* 2015;31:1415–26. <https://doi.org/10.1016/j.dental.2015.09.004>
- [34] Virtanen S, Curty C. Metastable and stable pitting corrosion of titanium in halide solutions. *Corrosion* 2004;60:643–9. <https://doi.org/10.5006/1.3287839>
- [35] Zoroddu MA, Aaseth J, Crisponi G, Medici S, Peana M, Nurchi VM. The essential metals for humans: a brief overview. *J Inorg Biochem* 2019;195:120–9. <https://doi.org/10.1016/j.jinorgbio.2019.03.013>
- [36] Schuttelaar MLA, Ofenloch RF, Bruze M, Cazzaniga S, Elsner P, Gonçalo M, et al. Prevalence of contact allergy to metals in the European general population with a focus on nickel and piercings: the EDEN Fragrance Study. *Contact Dermat* 2018;79:1–9. <https://doi.org/10.1111/cod.12983>
- [37] Guidelines for drinkingwater quality. 4th edition with 1st addendum. WHO Geneva; 2017.
- [38] Hunter P. A toxic brew we cannot live without. *EMBO Rep* 2008;9:15–8. <https://doi.org/10.1038/sj.embor.7401148>
- [39] Nurchi VM, Buha Djordjevic A, Crisponi G, Alexander J, Bjørklund G, Aaseth J. Arsenic toxicity: molecular targets and therapeutic agents. *Biomolecules* 2020;10. <https://doi.org/10.3390/biom10020235>
- [40] Nielsen RH, Wilfing G. Zirconium and zirconium compounds. *Ullmann’s encyclopedia of industrial chemistry*. Electronic release. Weinheim: Wiley-VCH; 2010.
- [41] Vagkopoulou T, Koutayas SO, Koidis P, Strub JR. Zirconia in dentistry: Part 1. Discovering the nature of an upcoming bioceramic. *Eur J Esthet Dent* 2009;4:130–51.
- [42] Piconi C, Maccauro G. Zirconia as a ceramic biomaterial. *Biomaterials* 1999;20:1–25.
- [43] Hurley PM, Fairbairn HW. Abundance and distribution of uranium and thorium in zircon, sphene, apatite, epidote, and monazite in granitic rocks. *Trans Am Geophys Union* 1957;38. <https://doi.org/10.1029/TR038i006p00939>
- [44] Takeda O, Ouchi T, Okabe TH. Recent progress in titanium extraction and recycling. *Metall Mater Trans B* 2020;51:1315–28. <https://doi.org/10.1007/s11663-020-01898-6>
- [45] Dhaliwal JS, David SRN, Zulhilmil NR, Sodhi Dhaliwal SK, Knights J, de Albuquerque Junior RF. Contamination of titanium dental implants: a narrative review. *SN Appl Sci* 2020;2. <https://doi.org/10.1007/s42452-020-2810-4>
- [46] Yeo I-SL. Modifications of dental implant surfaces at the micro- and nano-level for enhanced osseointegration. *Materials* 2019;13. <https://doi.org/10.3390/ma13010089>
- [47] França FL, Honorio-França AC, Honorio MS, Silva FHD, Fujimori M, França EL, et al. Dental implant surfaces treated with phosphoric acid can modulate cytokine production by blood MN cells. *Braz Oral Res* 2019;33. <https://doi.org/10.1590/1807-3107bor-2019.vol33.0040>
- [48] Bahraminasab M, Bozorg M, Ghaffari S, Kavakebian F. Electrochemical corrosion of Ti-Al₂O₃ biocomposites in Ringer’s solution. *J Alloy Compd* 2019;777:34–43. <https://doi.org/10.1016/j.jallcom.2018.09.313>
- [49] Yurttutan ME, Keskin A. Evaluation of the effects of different sand particles that used in dental implant roughened for osseointegration. *BMC Oral Health* 2018;18. <https://doi.org/10.1186/s12903-018-0509-3>
- [50] Lukaszewska-Kuska M, Wirstlein P, Majchrowski R, Dorocka-Bobkowska B. Osteoblastic cell behaviour on modified titanium surfaces. *Micron* 2018;105:55–63. <https://doi.org/10.1016/j.micron.2017.11.010>
- [51] Canabarro A, Diniz MG, Paciornik S, Carvalho L, Sampaio EM, Beloti MM, et al. High concentration of residual aluminum oxide on titanium surface inhibits extracellular matrix mineralization. *J Biomed Mater Res Part A* 2008;87A:588–97. <https://doi.org/10.1002/jbm.a.31810>
- [52] Piattelli A. Residual aluminum oxide on the surface of titanium implants has no effect on osseointegration. *Biomaterials* 2003;24:4081–9. [https://doi.org/10.1016/s0142-9612\(03\)00300-4](https://doi.org/10.1016/s0142-9612(03)00300-4)