



Review Paper



The effect of different surface topographies of titanium implants on bacterial biofilm: a systematic review

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Abstract

To compare the different surface topographies of titanium implants used in dentistry against the formation of bacterial biofilm. To identify relevant studies, the electronic databases PubMed, Science Direct and Springer Link were searched from inception until January 2019. A total of 38 studies were selected for the systematic review ($n=38$). The most commonly used titanium surfaces were machined titanium (16.3%), sandblasted, large-grit, acid-etched titanium (10.9%), untreated or pure titanium (10.9%), polished titanium (9.8%), physically textured titanium (9.8%), acid-etched titanium (8.7%) and anodized titanium (5.4%). The majority of the studies (78.9%) found that surface topographies (with varying degrees of roughness) had a beneficial effect on the ability to allow low bacterial biofilm on the surfaces. A low roughness value (R_a) of below 1 μm was found in 68% of these surfaces. Overall, no specific surface topography was found to be the ideal surface in allowing the least bacterial biofilm attachment. In this study, meta-analysis was not performed. This narrative systematic review provides a summary of the effects of surface topographies for future research and development of new dental implant surfaces and decontamination techniques.

Keywords Titanium · Dental implant · Biofilm · Bacteria · Surface topography · Profilometry · Systematic review · Dental materials · Periimplantitis

1 Introduction

Peri-implantitis is a microbial biofilm-induced inflammatory process which results in the loss of supporting bone around an osseointegrated dental implant [38]. Approximately one-third of patients with dental implants and one-fifth of all dental implants experienced peri-implantitis [31]. Patients with bleeding on gentle probing (BOP) had a 33.8% probability to be diagnosed with peri-implantitis [25]. The reported prevalence of peri-implantitis ranged between 0 and 39.7% within 5 years from the insertion of the dental implant [17]. One study looked at peri-implantitis prevalence at different levels of the implant, finding a range of 1.1–85.0% [20]. The same study reported the

incidence of periimplantitis from 0.4% within 3 years to 43.9% within 5 years [20].

Currently, there is no strong evidence to suggest the most effective treatment for peri-implantitis [48]. Surface topographic features may significantly modify the ability of the titanium surfaces to allow the attachment of bacterial biofilm, hence implying that the roughness of the surfaces were highly correlated with bacterial adhesion [2]. With regards to this, numerous innovative topographic surfaces have been developed and reported in the scientific literature and international patents to prevent the development of microbial biofilm [45–47]. A hypothesis was developed that certain surface topography can provide a surface with minimal bacterial biofilm. Therefore,

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this review focused on the surface topography of the dental implant, highlighting the importance of combating dental implant failures caused by peri-implantitis.

The arithmetical mean roughness (R_a) is used as a parameter to describe the implant surface roughness, which can be measured via stylus profilometry [52]. Differences in surface roughness are sensitive to the different sizes and external membrane compositions of bacterial, mammalian or eukaryotic contaminants [39]. An R_a value of less than or equal to $0.088 \mu\text{m}$ can strongly inhibit bacterial adherence during early biofilm formation [40]. However, an R_a value of $0.2 \mu\text{m}$ has been widely suggested as a threshold surface roughness under which any further surface smoothing (*i.e.* lowering of the R_a value) did not have an impact on the sub- and supra-mucosal microbial composition [7]. This was based on the idea that an increase in the surface roughness and the surface free energy is equal to an increase in the biofilm formation [19]. A high roughness not only provides a large surface area for bacterial adhesion and additional niches, but also reduces shearing forces and therefore, assists bacteria to escape from the host defense mechanisms during the initial adhesion phase [1]. However, a recent study has shown that an R_a value of $0.2 \mu\text{m}$ could not properly predict biofilm formation and did not encourage osseointegration [21]. Therefore, a moderate R_a value of $1\text{--}2 \mu\text{m}$ was suggested as a pre-requisite for the long-term success of implant-supported prostheses [10]. Various methods have been developed to create a moderately rough surface and to promote the osseointegration of implants, such as plasma-spraying, blasting with ceramic particles, acid-etching and anodization using specific instruments and chemical treatments [28].

This systematic review aimed to compare the bacterial biofilm on the different types of dental titanium implant surfaces reported in the literature.

2 Method

A systematic search of the English-language literature indexed in PubMed, Science Direct and Springer Link was conducted from their respective inception up to 1 January 2019. The studies had to be published in English language. The search terms used were “dental” AND “implant” AND “titanium” AND “bacteria” AND “biofilm” AND “treatment” OR “decontamination” OR “eradication” OR “cleaning” OR “remove”. Wildcards such as an asterisk (*), a question mark (?), or other designated symbols of each selected database were applied. Original research papers (*i.e.* experimental studies) that applied titanium-based materials for dental studies were selected for this review. The studies had to report the existence of microbial biofilm and focused on the different types of dental implant surface topographies. Biofilm by both bacteria and fungi were included. The data was extracted and entered into a structured data extraction form using Microsoft Excel facilitating data summarization and the writing of the final report. Data analysis was performed using SPSS Software Version 23 (IBM Corp) and PRISM Software Version 7 (GraphPad Inc.).

3 Results

3.1 Search results

The electronic search yielded four hundred results from three databases ($n=400$, Fig. 1). After removing duplicates and further screening, thirty-eight studies were included in this review ($n=38$, Table 1). These 38 studies specifically focused on the surface topography profiles and modifications of titanium materials, and compared against the amount of bacterial biofilm attachment on the surfaces.

Fig. 1 Flowchart of the study selection process

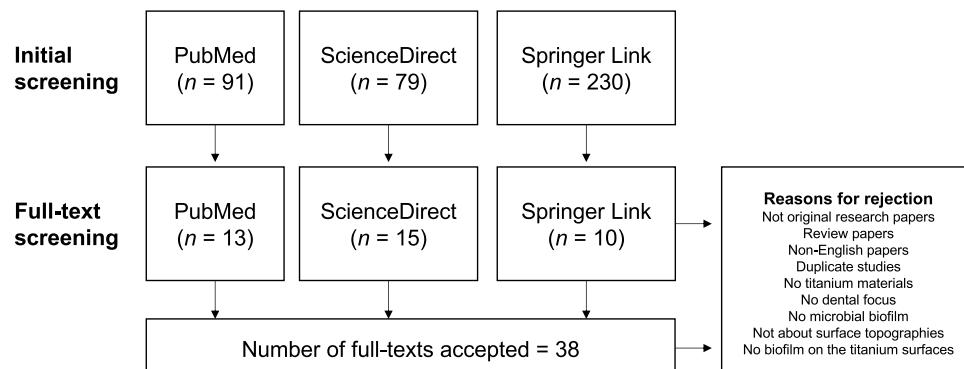


Table 1 Description of the included studies

Author and year	Surface description of titanium	Surface roughness (R_a) of titanium	Did the study compared titanium with other materials?	Bacteria tested	Incubation time with bacteria	Type of surface reported to have less microbial biofilm in the respective study	Were their findings statistically significant? (p value)	Did their findings support that the different surface topographies have an effect on microbial biofilms?
Drago et al. [19]	Sandblasted Laser-modified	–	No	<i>Staphylococcus aureus</i> <i>Pseudomonas aeruginosa</i> <i>Porphyromonas gingivalis</i>	72 h	Laser-modified titanium	$p < 0.001$	Yes
Nascimento et al. [37]	Machined Cast Polished	–	Zirconia	Normal flora (saliva, healthy)	n/a	Zirconia	$p < 0.01$	Yes
de Freitas et al. [13]	Machined (M) Oxide-blasted (OB)	$0.47 \pm 0.17 \mu\text{m}$ (M) $1.00 \pm 0.18 \mu\text{m}$ (OB)	Hydroxyapatite	Normal flora (saliva, healthy)	1, 3, 7, 14, 21 d	n/a	Not significant	No
Groessner-Schreiber et al. [23]	Titanium nitride (TiN) coating	“Close to zero”	Zirconia	Normal flora (saliva, healthy)	60 h	Zirconium nitride-coated glass	–	Yes
Yan Lin et al. [54]	Pickled (PT) Sandblasted, large-grit, acid-etched (SLA)	$0.3 \pm 0.02 \mu\text{m}$ (PT) $1.4 \pm 0.05 \mu\text{m}$ (SLA)	No	<i>Streptococcus mutans</i> C180-2(14) <i>Porphyromonas gingivalis</i> FDC381	1, 3 d	Pickled (PT) titanium	$p < 0.05$	Yes
de Melo et al. [14]	Machined Sandblasted	–	No	Normal flora (saliva, healthy)	24 h	n/a	Not significant	No
Violant et al. [50]	Machined, grade 2 – Modified with Avantblast [®] , grade 2 (Tigr2-t) Machined, grade 4 (Tigr4-C) Modified with Avantblast [®] , grade 4 (Tigr4-t)	–	No	<i>Actinomyces naeslundii</i> ATCC 12104 <i>Veillonella parvula</i> ATCC 10790 <i>Streptococcus gordonii</i> ATCC 10558 <i>Fusobacterium nucleatum</i> ssp. <i>polymorphum</i> ATCC 10953	7 d	Titanium modified with Avantblast [®] , grade 2 (Tigr2-t)	$p < 0.05$	Yes

Table 1 (continued)

Author and year	Surface description of titanium	Surface roughness (R_a) of titanium	Did the study compared titanium with other materials?	Bacteria tested	Incubation time with bacteria	Type of surface reported to have less microbial biofilm in the respective study	Were their findings statistically significant? (p value)	Did their findings support that the different surface topographies have an effect on microbial biofilms?
Martínez-Hernández et al. [34]	Pre-treatment (PT) Sandblasted, large-grit, acid-etched (SLA) Hydrophilic SLA (modSLA)	0.2 µm (PT) 0.8 µm (SLA) – (modSLA)	No	Normal flora (saliva, healthy and periodontitis)	48 h	–	–	No
Cao et al. [8]	Polished (P) Spear-type (S) Pocket-type (PC)	13.2±2.3 µm (P) 195.0±6.5 µm (S) 479.0±15.3 µm (PC)	No	<i>Staphylococcus epidermidis</i> FH8	2, 6 d	Pocket-type (PC) titanium	$p < 0.05$	Yes
Bierbaum et al. [6]	Electropolished (EPOL) Electropolished and anodized (EPOLAN) Electropolished and double anodized (DAN)	0.15±0.05 µm (EPOL) 0.75±0.11 µm (EPOLAN) 0.74±0.1 µm (DAN)	No	<i>Streptococcus sanguinis</i> ATCC 10556	24 h	Electropolished and double anodized (DAN) Titanium	$p < 0.05$	Yes
Karoussis et al. [30]	Acid-etched (AE) AE treated with tricalcium phosphate (TCP) AE treated with bioactive glass (BG)	–	No	Normal flora (saliva, perimplantitis)	48 h	n/a	–	Yes
Rimondini et al. [40]	Polished	0.088–2.142 µm	No	Normal flora (saliva, healthy)	24 h	Smoothest titanium with R_a value of 0.088	$p < 0.05$	Yes
Matos et al. [35]	Machined (M) Sandblasted (Sb) Micro-arc oxidation (MAO) Glow discharge plasma (GDP)	Below 0.5 µm	No	<i>Streptococcus sanguinis</i> IAL 1832 <i>Actinomyces naeslundii</i> OMZ 745 <i>Fusobacterium nucleatum</i> OMZ 596	16.5, 64.5 h	Micro-arc oxidation (MAO) titanium	$p < 0.05$	Yes

Table 1 (continued)

Author and year	Surface description of titanium	Surface roughness (R_a) of titanium	Did the study compared titanium with other materials?	Bacteria tested	Incubation time with bacteria	Type of surface reported to have less microbial biofilm in the respective study	Were their findings statistically significant? (p value)	Did their findings support that the different surface topographies have an effect on microbial biofilms?
Jordan et al. [29]	Machined cobalt Chromium-polished (CoCr) Machined titanium-milled (Ti-milled)	0–0.05 µm (CoCr) 0.15–0.20 µm (Ti-milled)	Cobalt-chrome	<i>Porphyromonas gingivalis</i> NCTC 11834 <i>Fusobacterium nucleatum</i> ATCC 49256 <i>Prevotella intermedia</i> NCTC 13070 <i>Aggregatibacter actinomycetemcomitans</i> DSM 8324	2 h	Machined titanium-milled (Ti-milled)	$p < 0.05$	Yes
Sánchez et al. [43]	Sandblasted, large-grit, acid-etched (SLA)	—	Zirconia, Hydroxyapatite	<i>Streptococcus oralis</i> CECT 9077 <i>Actinomyces naeslundii</i> ATCC 19039 <i>Veillonella parvula</i> NCTC 11810 <i>Fusobacterium nucleatum</i> DMSZ 20482 <i>Porphyromonas gingivalis</i> ATCC 33277 <i>Aggregatibacter actinomycetemcomitans</i> DSMZ 8324	1, 12, 24, 48, 72, 96, 120 h	Zirconia	$p < 0.05$	Yes
Zhang et al. [56]	Pure titanium (Ti–3 wt% Cu (Ti–3Cu))	$0.523 \pm 0.04 \mu\text{m}$ (cp) $0.413 \pm 0.01 \mu\text{m}$ (Ti–3Cu)	No	<i>Staphylococcus aureus</i>	6, 12, 18, 24 h	Ti–3 wt% Cu (Ti–3Cu) titanium alloy	—	Yes
Annunziata et al. [2]	Turned (T) Mildly acid-etched (MA) Direct laser metal formed (DLMF)	$0.283 \mu\text{m}$ (T) $0.369 \mu\text{m}$ (MA) $10.835 \mu\text{m}$ (DLMF)	No	<i>Streptococcus sanguinis</i> ATCC 10556	2, 6, 12 h	Turned (T) titanium	$p < 0.001$	Yes

Table 1 (continued)

Author and year	Surface description of titanium	Surface roughness (R_a) of titanium	Did the study compared titanium with other materials?	Bacteria tested	Incubation time with bacteria	Type of surface reported to have less microbial biofilm in the respective study	Were their findings statistically significant? (p value)	Did their findings support that the different surface topographies have an effect on microbial biofilms?
de Avila et al. [12]	Machined (M)	0.21±0.06 µm	Yttrium-stabilized zirconia (ZrO ₂)	Normal flora (saliva, healthy) <i>Staphylococcus aureus</i> ATCC 25923 <i>Escherichia coli</i> ATCC 25922	16, 48 h	Machined (M) titanium	$p < 0.05$	Yes
Liu et al. [33]	Pure titanium (Ti) Titanium alloy with 5 wt% Cu (Ti-Cu)	–	No	<i>Staphylococcus aureus</i> ATCC 25923	2, 6, 12, 24 h	Titanium alloy with 5 wt% Cu (Ti-Cu)	–	Yes
Al-Ahmad et al. [1]	Machined titanium (Ti-m) Modified titanium (TiUnite)	0.054 µm (Ti-m) 0.544 µm (Ti-Unite)	Zirconia	Normal flora (saliva)	30, 120 min	Machined titanium (Ti-m, Nobel Biocare)	$p < 0.05$	Yes
Ferreira Ribeiro et al. [22]	Machined (M) Acid-etched (AE) Anodized and laser irradiated (AL)	0.8±0.2 µm (M) 0.7±0.2 µm (AE) 1.4±0.4 µm (AL)	No	Normal flora (saliva, healthy)	24 h	n/a	Not significant	No
Kulkarni et al. [32]	Titanium foil (Ti) Titanium dioxide (TiO ₂) nanotubes (NT)	0.019 µm (Ti) 0.011–0.027 µm (NT)	No	<i>Bacillus cereus</i> CCM 2010 <i>Pseudomonas aeruginosa</i> CCM 3955	48 h	Titanium dioxide (TiO ₂) nanotubes (NT)	$p < 0.05$	Yes
Do Nascimento et al. [15]	Pre-machined	–	Zirconia	Normal flora (saliva, healthy)	0, 3, 6 months	Zirconia	$p < 0.05$	Yes
Doll et al. [16]	–	–	Copper	<i>Staphylococcus aureus</i> DSM 20231 <i>Aggregatibacter actinomycetemcomitans</i> MCCM 2474	24 h	Copper	$p < 0.05$	Yes

Table 1 (continued)

Author and year	Surface description of titanium	Surface roughness (R_a) of titanium	Did the study compared titanium with other materials?	Bacteria tested	Incubation time with bacteria	Type of surface reported to have less microbial biofilm in the respective study	Were their findings statistically significant? (p value)	Did their findings support that the different surface topographies have an effect on microbial biofilms?
Sánchez et al. [42]	Sandblasted, large-grit, acid-etched (SLA)	–	Zirconia	<i>Streptococcus oralis</i> CECT 9077 <i>Veillonella parvula</i> NCTC 11810 <i>Actinomyces naeslundii</i> ATCC 19039 <i>Fusobacterium nucleatum</i> DMSZ 20482 <i>Aggregatibacter actinomycetemcomitans</i> DSMZ 8324 <i>Porphyromonas gingivalis</i> ATCC 33277	72 h n/a	n/a	Not significant	No
Zhao et al. [57]	Mirror-polished (P) Ground to mimic the machined part (M) Ground and then acid-etched (MA) Ground and acid-etched (modMA)	0.007 μm (P) 0.1 μm (M) 0.6 μm (MA, modMA)	Zirconia	<i>Streptococcus oralis</i> I22 <i>Streptococcus mitis</i> BMS <i>Streptococcus salivarius</i> HB <i>Staphylococcus aureus</i> ATCC 25923	24 h 24 h, 7 d	Ground and then acid-etched (MA) Ground and acid-etched (modMA)	$p < 0.05$	Yes
de Avila et al. [11]	Machined (M)	0.21 \pm 0.06 μm	Yttrium-stabilized zirconia (ZrO_2)	<i>Porphyromonas gingivalis</i> ATCC 33277 <i>Fusobacterium nucleatum</i> ATCC 25586	24 h, 7 d	Yttrium-stabilized zirconia (ZrO_2)	$p < 0.05$	Yes

Table 1 (continued)

Author and year	Surface description of titanium	Surface roughness (R_a) of titanium	Did the study compared titanium with other materials?	Bacteria tested	Incubation time with bacteria	Type of surface reported to have less microbial biofilm in the respective study	Were their findings statistically significant? (p value)	Did their findings support that the different surface topographies have an effect on microbial biofilms?
Uhlmann et al. [49]	Abrasive blasting (AB) Chemical polishing (P) Microchannels (MC) Microcavities Type 1 (MCV1) Microcavities Type 2 (MCV2) Laser Induced Periodic Surface Structures (LPSS, L)	0.7 μm (AB) 0.3 μm (P) 1.3 μm (MC) 0.6 μm (MCV1) 1.7 μm (MCV2) 0.2 μm (L)	No	<i>Streptococcus mutans</i> DSMZ 20523	72 h	Chemically polished titanium	–	Yes
Dorkhan et al. [18]	Untreated pure titanium (Ti) Anodically-oxidized pure titanium (N1) Anodically-oxidized alloy TiAl6V4 (N2)	–	No	<i>Streptococcus gordonii</i> HC7 <i>Streptococcus mitis</i> BA7 <i>Streptococcus oralis</i> 89C	8 h	Anodically-oxidized pure titanium (N1) Anodically-oxidized alloy TiAl6V4 (N2)	Not significant	No
Caous et al. [9]	Machined Anodized	–	No	<i>Streptococcus sanguinis</i> FC2 <i>Streptococcus mitis</i> CCUG 27741 <i>Actinomyces oris</i> CCUG 33517	2 h	Anodized	$p < 0.05$	Yes
Yue and Yang [55]	Pre-treated titanium (PT) Anodized specimens (AO-Ti) Alkali-heat treatment (AH-Ti) Acid and alkali treatment (AA-Ti)	$0.185 \pm 0.011 \mu\text{m}$ (PT) $0.206 \pm 0.015 \mu\text{m}$ (AO-Ti) $0.204 \pm 0.005 \mu\text{m}$ (AH-Ti) $0.260 \pm 0.015 \mu\text{m}$ (AA-Ti)	No	<i>Staphylococcus aureus</i> ATCC 25923 <i>Escherichia coli</i> ATCC 25922	1, 3, 5 d	Anodized specimens (AO-Ti) titanium	$p < 0.01$	Yes

Table 1 (continued)

Author and year	Surface description of titanium	Surface roughness (R_a) of titanium	Did the study compared titanium with other materials?	Bacteria tested	Incubation time with bacteria	Type of surface reported to have less microbial biofilm in the respective study	Were their findings statistically significant? (p value)	Did their findings support that the different surface topographies have an effect on microbial biofilms?
Bevilacqua et al. [5]	Machined surface (M) Laser-treated surface (LT) Sandblasted surface (SB)	0.5–1 μm (M) Less than 0.4 μm (LT) More than 2.0 μm (SB)	No	<i>Pseudomonas aeruginosa</i> ATCC 27853	1 d, 4 d, 48 h	n/a	Not significant	No
Wang et al. [51]	Pure titanium (T)	0.12±0.01 μm	Machined zirconium oxide	Normal flora (saliva, healthy)	48 h	Machined zirconium oxide	Not significant	No
Schwarz et al. [44]	Polished (P) Acid-etched (A) Chemically modified (modA) Sandblasted large grit and A (SLA) ModSLA	0.04±0.00 μm (P) 0.83±0.05 μm (A) – (modA) 3.22±0.88 μm (SLA) – (modSLA)	No	Normal flora (saliva, healthy)	12, 24, 48 h	Chemically modified (mod) A (modA) titanium	$p < 0.001$	Yes
Hauser-Gerspach et al. [26]	Sandblasted, large-grit, acid-etched (SLA) Polished (P)	1.554±0.029 μm (SLA) 0.012±0.001 μm (P)	Yttria-stabilized zirconia	<i>Streptococcus sanguinis</i> DSM 20068 <i>Porphyromonas gingivalis</i> ATCC 33277	2 h	Polished titanium – Yttria-stabilized zirconia	–	Yes
Rodríguez-Hernández et al. [41]	Pre-treated titanium (PT) Shot-blasted titanium (ST)	0.34±0.03 μm (PT) 2.7–8 μm (ST)	No	<i>Streptococcus sanguinis</i> CECT 480	2 h	Shotblasted titanium (ST)	$p < 0.05$	Yes
Barbour et al. [4]	Unpolished titanium (UT) Polished titanium (PT)	0.25–0.45 μm (UT) 0.21–1.77 μm (PT)	No	<i>Streptococcus mutans</i> NG8 <i>Actinomyces naeslundii</i> NCTC 10301	16 h	Polished titanium (PT)	$p < 0.05$	Yes
Wassmann et al. [52]	Pure titanium (T)	0.09–2.98 μm	Zirconia	<i>Staphylococcus epidermidis</i> AF270147	120 min	Smoothest titanium with R_a value of 0.09 μm	$p < 0.05$	Yes

n/a, not applicable. –, not stated. Not significant studies with p value of more than 0.05

3.2 Types of titanium implant surfaces

In this review, the common types of titanium surfaces being investigated were machined titanium, sandblasted, large-grit, acid-etched titanium (SLA), untreated and pure titanium, polished titanium, physically textured titanium, anodized titanium and laser-modified titanium (Table 2). The machined surfaces had a pattern of unidirectional grooves and showed anisotropic irregularities [57]. The SLA titanium surfaces also had an irregular surface [19], which were found to contain voids and open spaces at the surface [57]. The irregularities of an SLA surface can also be reduced by exposure to nitrogen gas [34]. The untreated and pure titanium were not modified and usually included in the investigations as a control. The polished titanium had a flat surface without evident texture and served as the smoothest surface, regardless of its R_a value, when compared to machined and SLA [8]. Physically textured titanium represented the surfaces with nanostructures

comprising thin spears and uniform nanotubular structures [8, 32]. The anodized titanium surfaces had a bone-like apatite formation on its surface and a rough homogeneous and isotropic structure [9, 55]. The laser-modified surfaces had a controlled geometry consisting of micro-metrical holes symmetrical in dimension, shape and distribution [19].

One of the studies also compared the difference between Grade 2 and Grade 4 titanium as these grades have slight differences in their chemical composition [50] (Table 2). Grade 2 titanium has a content of 0.1% carbon (C), 0.3% iron (Fe), 0.015% hydrogen (H), 0.03% nitrogen (N), 0.25% oxygen (O) and 99.2% titanium (Ti), whereas grade 4 titanium has 0.08% C, 0.5% Fe, 0.015% H, 0.05% N, 0.40% O and 98.9% Ti [24]. These slight chemical differences between titanium purities could have an important effect on surface properties when titanium was treated with different chemical or physical processes, and therefore, also cause an impact on the early bacterial

Table 2 Characteristics of the included studies

Variable	Frequency (%)	References
<i>Physical structure of titanium</i>		
Discs	30 (78.9)	[2, 5, 6, 8, 9, 11, 14, 16, 18, 19, 22, 23, 26, 29, 30, 32, 34, 35, 37, 40–42, 49, 50, 52, 54–57]
Not discs	8 (21.1%)	[1, 4, 12, 13, 15, 32, 44, 51]
Not stated	1 (2.6%)	[33]
<i>Nature of experiment</i>		
In-vitro	27 (71.1%)	[2, 4–6, 8, 9, 11, 12, 16, 18, 19, 26, 29, 30, 32, 33, 35, 41, 42, 49, 50, 52, 54–57]
In-vivo	14 (36.8%)	[1, 2, 5, 13–15, 22, 23, 33, 34, 37, 40, 44, 51]
<i>Types of titanium surfaces</i>		
Machined titanium	15 (16.3%)	[1, 5, 9, 11–14, 22, 29, 35, 37, 50, 57]
Sandblasted, large-grit, acid-etched titanium	10 (10.9%)	[6, 14, 26, 34, 42, 44, 54]
Untreated/pure titanium	10 (10.9%)	[4, 15, 18, 33, 34, 41, 51, 52, 55, 56]
Polished titanium	9 (9.8%)	[4, 6, 8, 26, 37, 40, 44, 49, 57]
Physically textured titanium	9 (9.8%)	[1, 2, 8, 32, 49, 54]
Acid-etched titanium	8 (8.7%)	[2, 22, 30, 44, 57]
Anodized titanium	5 (5.4%)	[9, 18, 22, 55]
Laser-modified titanium	3 (3.3%)	[2, 5, 19]
Other titanium surfaces	22 (24.2%)	[5, 6, 13, 19, 23, 32, 33, 35, 37, 41, 44, 49, 50, 55, 56]
Not stated	1 (1.1%)	[16]
<i>Titanium grade</i>		
Grade 1	1 (1.1%)	[52]
Grade 2	26 (28.6%)	[6, 12, 14, 26, 34, 35, 41, 42, 44, 50]
Grade 4	11 (12.1%)	[16, 19, 40, 50, 57]
Grade 5	17 (18.7%)	[2, 18, 29, 37, 49]
Not stated		[1, 4, 5, 8, 9, 11, 13, 15, 22, 23, 30, 32, 33, 51, 54–56]
<i>Roughness value (R_a)</i>		
0–1 μm	50 (54.9%)	[1, 2, 4–6, 11–13, 22, 23, 26, 29, 32, 34, 35, 40, 41, 44, 49, 51, 52, 54–57]
>1 μm	13 (14.3%)	[2, 5, 6, 8, 13, 22, 26, 41, 44, 49, 54]
Not stated	28 (30.8%)	[9, 14–16, 18, 19, 30, 33, 34, 37, 42, 44, 50]

attachment. Conversely, element alloying by adding copper (Cu) in titanium to develop Ti–Cu alloys, presented a very stable and strong anti-bacterial ability to obstruct biofilm attachment efficiently by damaging bacterial cell walls, better wear resistance, higher mechanical properties and better anti-corrosion resistance than commercially pure titanium [33]. The anti-bacterial rate was found to be greater than 90% when the Cu content in Ti–Cu alloy was at least 3 percent by weight (wt%) [3]. This finding is similar to another included study in this systematic review which confirmed the strong antibacterial property of Ti–3Cu alloy [56].

The titanium surfaces can also be treated with an additional layer of coating, which acts as a physical barrier against early bacterial attachment before the formation of biofilm. For example, one study focused on Avantblast®, a thermal treatment surface that combines an increment in the surface roughness by chemical etching with an increased thickness and crystallinity of the titanium oxide layer [50]. A different study focused on anti-bacterial bioactive glass, which is composed of silica (SiO_2), calcium (Ca), sodium (Na), and phosphorus (P) [30]. This forms a silica-rich hydroxyl carbonated apatite that resembles hydroxyapatite of a bone when in contact with biological fluids [30]. In another investigation, titanium oxide (TiO_2) as a coating of the titanium, was also able to produce a surface with grain size textures to allow improved osseointegration [55]. Titanium nitride (TiN), also as a coating, permitted lower bacterial biofilm compared to pure titanium coating [23].

3.3 Comparison of titanium with other implant surface materials

Fifteen studies compared titanium implants with other implant materials, such as zirconia and copper ($n=15$, 39.5%). Twelve studies in this systematic review compared titanium surfaces with zirconia. Zirconia is an alternative to titanium materials in implant dentistry mainly due to its esthetic properties [37]. In six studies out of thirty with beneficial effects of surface topographies (*i.e.* studies with significant findings in Table 1), zirconia-based implant surfaces resulted in lower bacterial counts than titanium-based surfaces, implying that zirconia reduces the risk of peri-implantitis [11, 15, 23, 26, 37, 43]. However, four of these studies did not disclose the R_a values of the titanium [15, 23, 37, 43]. Therefore, it was difficult to conclude whether the roughness of the surface played an important role in their investigations.

There are four other studies which found titanium to be significantly superior (*i.e.* less bacterial counts) than zirconia, even when their R_a values were similar to one another [1, 12, 52, 57]. Additionally, two studies did not

find significant superiority between titanium and zirconia [42, 51]. When compared to a different dental material called hydroxyapatite, only zirconia, not titanium, displayed superiority in lowering bacterial biofilm on the implant surfaces [13, 43]. In another study, copper-based surfaces exhibited greatly decreased bacterial biofilm compared to titanium [16].

4 Discussion

In this review, all of the tested titanium implant surfaces permitted the formation of bacterial biofilm. However, the bacterial count, depth, morphology or viability differed between the surfaces. Thirty studies found that surface topographies have a beneficial effect on the biofilm formation and in the surface ability to allow lower biofilm attachment ($n=30$, 78.9%). This review did not observe one specific type of titanium surface, which was found to exhibit lower bacterial counts or biofilm mass than the other surfaces. Several studies came to the same conclusion that anodized titanium surfaces exhibited lower bacterial biofilm mass than untreated titanium surfaces [9, 18, 55] and machined titanium had a lower bacterial biofilm than other types of implant materials (*e.g.* zirconia, copper) [1, 12, 29]. Polished titanium surfaces had lower bacterial biofilm than untreated titanium with rougher surfaces [4, 6, 26, 40, 49, 52]. The differences (p value) in the comparisons between the surfaces were not consistent in all of these studies (Table 1). This implies that the superiority of a specific surface may not be concluded.

Sixty-eight percent of the titanium surfaces with beneficial surfaces (*i.e.* studies with significant findings in Table 1, labelled with 'Yes' in the final column) had a roughness value (R_a) of less than 1 μm , 8% had an R_a value of more than 1 μm , while 24% did not disclose the R_a value ($n=68\%$, Tables 1, 2). *In-vivo* experiments confirmed that bacterial colonization starts on sites of surface roughness [5]. Conversely, there are also studies which found that surface topography did not cause any difference to the amount of microbial biofilm (*i.e.* studies with no significant findings in Table 1, labelled with 'No' in the final column). Eight studies found that surface topographies of the dental implants have no significant effect on the formation and attachment of biofilm ($n=8$, 21.1%). Only 16% of the titanium surfaces in these findings had a roughness value (R_a) of more than 1 μm . 50% of the surfaces had an R_a value of less than 1 μm , while no R_a values were disclosed for the remaining 33.3% of the surfaces. Figure 2 shows the R_a values of the titanium implant surfaces. The R_a value in the studies with insignificant findings signifies that a low R_a did not necessarily affect the growth of bacterial biofilm or in reducing the amount of bacterial biofilm.

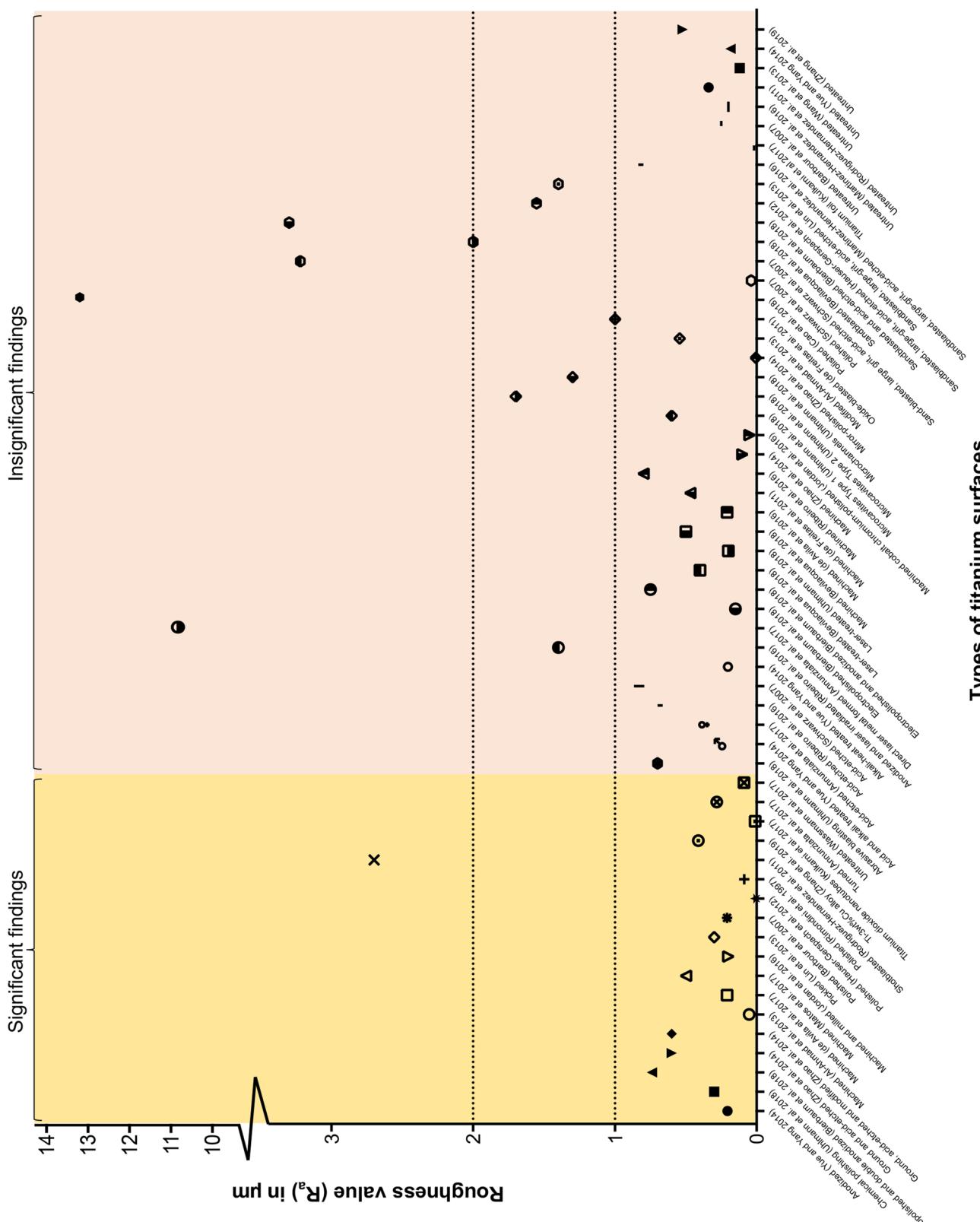


Fig. 2 Roughness of the titanium implant surfaces in this review

Figure 2 shows that there is no definite pattern in the R_a values regarding surface topography and its effects on biofilm counts. R_a values of 1 μm and 2 μm were indicated in Fig. 2 as these values have been considered to be a pre-requisite roughness for the long-term success of implant-supported prostheses [10]. The figure shows that a majority of the titanium surfaces had an R_a value of 1 μm in studies with both significant and non-significant findings, while a minority of the surfaces with non-significant findings had an R_a value of 2 μm (Fig. 2). These studies also suggest that surface topography was not the only important factor for biofilm accumulation. In addition, a study found that different surface treatments of the titanium implants (*i.e.* alkali-heat treatment and anodization) can produce two different surfaces but with approximately the same mean roughness value [55]. In another unrelated studies, 'pickled' and chemically polished titanium implants were both reported to have an R_a value of 0.3 μm , regardless of their dissimilarity in the surface topography. This shows that the mean roughness is not very sensitive against specific changes in surface topography.

A certain surface topography may permit bacterial biofilm growth for a specific structure according to the pattern of roughness. Schwarz et al. [44] showed that microtopography had a highly uneven and unpredictable influence on supragingival plaque biofilm formation [44]. For example, *Staphylococcus aureus* growth (localizing almost completely into the surface holes) was found on laser-modified surfaces, while the biofilm covered the entire disc area as a more homogeneous layer on the sandblasted surfaces [19]. With regards to morphology, the bacterial biofilm was found to form a crater-like architecture on titanium surfaces (mimicking a honeycomb), while zirconium surfaces mimicked a complex cobweb-like structure [43]. In another study, bacterial microcolonies were more abundant along the grooves of machined discs, while in laser-treated discs, they were located within all of the holes formed by laser treatment [5]. In sand-blasted discs, they were randomly distributed on the surface [5].

The rationale for texturing the implant surfaces was to mimic the natural bone architecture, so osteoblast proliferation can be improved [27]. In this review, one study found that the micro-texturing of the titanium surfaces was also able to successfully reduce the attachment of bacteria when compared to the classical abrasive-blasted surfaces [49]. The modification of the titanium surface can increase the thickness of its oxidation layer, which can cause an interference with cell-to-cell communications in biofilm development, leading to a significant reduction in bacterial adhesion in comparison to its unmodified titanium surfaces [19]. However, regardless of the titanium's surface roughness, bacterial colonization of different implant materials was observed to be similar over

time. One study focused on machined and SLA titanium surfaces and found that these surfaces were colonized by similar counts of bacteria after 24 h of exposure to the oral environment. Also, the different surface topographies did not significantly influence the colonizing microbiota [14]. In another investigation, the smoothing of a surface (polishing) did not reduce the ability of bacteria to adhere to metallic surfaces [29]. This is because smooth surfaces were still capable of attracting substantial levels of specific bacteria.

A number of limitations in this review need to be acknowledged. Firstly, 'turned', 'polished' or 'milled' surfaces are also called 'machined' in oral implantology and these machined surfaces are often used as a control since they serve as rougher surfaces [53]. The terminology is inconsistent in the included studies, therefore comparison of the studies could be misleading.

In twelve studies, the actual R_a value was not reported by the authors ('not stated' in Table 1) [9, 14–16, 18, 19, 30, 33, 37, 42, 50]. Therefore, we could not strongly confirm the R_a value of the surfaces which can encourage the lowest bacterial biofilm. The terms 'smooth surfaces' and 'rough surfaces' were employed to represent their differences in the surface roughness in these studies. The microbial composition has been found to differ significantly between individuals who were healthy and those diagnosed with peri-implantitis [38]. However, ten studies in our review performed their biofilm experiments using saliva which were collected from healthy individuals [12–15, 22, 23, 37, 40, 44, 51]. Therefore, whether their established biofilms on the implant surfaces can mimic clinically diagnosed peri-implantitis remains doubtful. Additionally, the composition and the proportion of the species that initially colonize titanium implant surfaces are influenced by the periodontal status than the surface topography of the implant [34]. One study stated that the implant surface chemical properties, surface treatment and titanium purity can also influence early bacterial colonization [50]. Actions can be taken to provoke chemical changes in the oral environment to restrict bacterial adhesion after implant placement in order to promote healing [9]. Additionally, the development of in vitro biofilm was more easily influenced by the surface features of the dental implants than biofilm formed by complex communities in the mouth [5]. This may be because of the presence of a wide range of nutrients and conditions, allowing colonization by bacteria [5]. Therefore, it is important to remember that the differences observed using in vitro experiments in the different implant surface topographies might not represent the in vivo colonization rates. Moreover, surgical techniques, soft and hard tissue characteristics, and residual precipitants (*e.g.* residual cement and residual floss) may also be the predisposing factors to biofilm adherence around

dental implants [36]. Additionally, a high level of protease activity may be a predictive factor for disease progression in peri-implantitis [38]. Rougher implant surfaces were found to cause reduced treatment efficacy, for example in the treatment of biofilm by chlorhexidine, but no influence on the amount of biofilm formation [54].

5 Conclusion

This systematic review compared the amount of bacterial biofilm on the different surface topographies of titanium implants used in dentistry. The roughness value (R_a) of the implants was also discussed and compared to their ability to allow low bacterial attachment and biofilm formation. An R_a value of less than 1 μm constituted the majority of the dental implant surfaces included in this review. A majority of the studies agreed that different surface topographies had an effect on reducing the bacterial biofilm growth. However, due to inconsistent significant findings, it is suggested that more experiments be performed comparing specific types of surface (e.g. polished surfaces against sand-blasted surfaces). Also, more information on the experiments (e.g. R_a values) should be disclosed for a more thorough review. Additionally, existing periodontal health may be a strong predisposing factor for bacterial colonization of implant surfaces.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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