Bioactive Materials 27 (2023) 348–361

Contents lists available at ScienceDirect

Bioactive Materials

journal homepage: www.keaipublishing.com/en/journals/bioactive-materials

Review article

The integration of peri-implant soft tissues around zirconia abutments: Challenges and strategies

Kai Tang [a], Meng-Lin Luo [b], Wei Zhou [a], Li-Na Niu [a], Ji-Hua Chen [a,*], Fu Wang [a,**]

[a] National Clinical Research Center for Oral Diseases & State Key Laboratory of Military Stomatology &Shaanxi Key Laboratory of Stomatology, Department of Prosthodontics, School of Stomatology, The Fourth Military Medical University, Xi'an, Shaanxi, 710032, China
[b] Institute of Stomatology & Oral Maxilla Facial Key Laboratory, The First Medical Center, Chinese PLA General Hospital & Department of Stomatology, The First Medical Center, Chinese PLA General Hospital, Beijing, China

ARTICLE INFO

Keywords:
Zirconia
Implant abutment
Surface modification
Soft tissue adhesion

ABSTRACT

Stable soft tissue integration around the implant abutment attenuates pathogen penetration, protects underlying bone tissue, prevents peri-implantitis and is essential in maintaining long-term implant stability. The desire for "metal free" and "aesthetic restoration" has favored zirconia over titanium abutments, especially for implant restorations in the anterior region and for patients with thin gingival biotype. Soft tissue attachment to the zirconia abutment surface remains a challenge. A comprehensive review of advances in zirconia surface treatment (micro-design) and structural design (macro-design) affecting soft tissue attachment is presented and strategies and research directions are discussed. Soft tissue models for abutment research are described. Guidelines for development of zirconia abutment surfaces that promote soft tissue integration and evidence-based references to inform clinical choice of abutment structure and postoperative maintenance are presented.

1. Introduction

Implant therapy has been successfully used in tooth replacement, constituting a "third set of teeth". The long-term success of implants depends on good osseointegration and the sealing quality of peri-implant soft tissues [1]. Decreased sealing around the implant allows bacterial penetration, causing peri-implantitis and loss of the implant. Varying reports of peri-implantitis incidence have been made. A meta-analysis of 47 studies gave frequencies of approximately 19.83% [95% confidence interval (CI): 15.38, 24.27] for subjects and 9.25% (95% CI: 7.57, 10.93) for implant sites [2]. The formation of an effective barrier by peri-implant soft tissue reduces the occurrence of complications [1,3].

The abutment is the primary transmucosal part of the implant and determines the level of soft tissue attachment around the implant. Titanium abutments have been previously regarded as the "gold standard" but are limited by gingival discoloration [4,5] and potential cytotoxicity issues [6]. Zirconia abutments are "metal free" and have excellent aesthetic properties [7–9], outstanding biocompatibility and favorable mechanical properties [10,11], producing low incidence of technical and biological complications and high patient satisfaction in 10–11 year follow-up studies [12].

Zirconia is bio-inert and may cause marsupialization, epithelial downgrowth and infection after implant placement, defects associated with poor integration of the implant with surrounding soft tissues [13]. The proliferation of soft tissue cells and epithelial closure remain inferior to titanium materials [14–20] on which most pre-existing studies have focused. Peri-implant soft tissues lack hemidesmosome structures, vertical collagen fibers and an effective blood supply and zirconia surface characteristics pose challenges to the improvement of biocompatibility and soft tissue integration.

Advances in micro and macro processing factors influencing soft tissue integration on the zirconia abutment surface are explored in the present review. The first section presents the physiology of peri-implant soft tissues and characteristics of zirconia abutments. The next section describes common zirconia surface treatment methods and other macroscopic design factors and their influence on the quality of soft tissues, followed by an overview of research models. The final section summarizes controversial issues and challenges for consideration in future research.

Peer review under responsibility of KeAi Communications Co., Ltd.
* Corresponding author.
** Corresponding author.
E-mail addresses: jhchen@fmmu.edu.cn (J.-H. Chen), Wangfu99@fmmu.edu.cn (F. Wang).

https://doi.org/10.1016/j.bioactmat.2023.04.009
Received 3 January 2023; Received in revised form 23 March 2023; Accepted 9 April 2023

2. Physiology of peri-implant soft tissues

Peri-implant soft tissue attachments, including epithelial (barrier epithelium) and fibrous connective tissues, result in biocontainment and are a consequence of wound healing [21,22].

The adhesion of peri-implant epithelium (PIE) to the implant is mediated by hemidesmosome structures [23–25], although their occurrence has sometimes been disputed [26,27] or reported to be confined to the lower area. Insufficient hemidesmosomes might result in weak PIE attachment [28,29].

Subepithelial connective tissue around the implant has a high collagen fiber content with a predominance of type-V collagen [30]. The collagen fibers are mostly parallel to the implant surface with a few annular and perpendicular or obliquely oriented to the rough abutment surfaces treated by anodic oxidation [24]. Collagen fibers are embedded in the natural cementum at one end and fan-shaped in gingiva at the other connecting the tooth with the connective tissue. Gingival connective tissue is supplied by the supraperiosteal artery and periodontal vessels while the implant is supplied only by the branches of the superior periosteal artery [31].

The structure of peri-implant soft tissue is similar to that of natural periodontal tooth [32] but is actually more similar to scar tissue in terms of composition, collagen fiber orientation and vascular system distribution [33–37]. Strong soft tissue attachment is the first barrier against the invasion of bacterial pathogens. However, the structure and higher permeability of peri-implant soft tissue increase the risk of bacterial adhesion [1,33,38–40], exacerbating inflammation relative to periodontitis. Immune complexes in gingival tissue of the patients with periodontitis, who are most likely to requre implant surgery, may also increase peri-implantitis risk [39,41,42]. Therefore, abutment surfaces should be designed and optimized for better soft tissue attachment and sealing.

3. Zirconia abutments

Zirconia is a high-strength ceramic which has three crystalline patterns: monoclinic, cubic and tetragonal phases. The tetragonal phase is stabilized at room temperature by mixing with metal oxides, such as MgO, CaO and Y_2O_3 or CeO_2. Cracks may be avoided by the transformation of the crystalline phase during sintering and cooling [43], giving high strength and wear resistance. The most significant advantage of zirconia as an abutment material is its aesthetic properties with more natural color than titanium [4,5,7–9,44] and zirconia is recommended for patients with anterior teeth and thin gingival biotype [5]. Fibroblast viability, adhesion and proliferation are superior on zirconia relative to titanium and other materials [45], resulting in stronger mucosal sealing [46,47], better healing of surrounding soft tissues [48] and higher soft tissue integrity [45]. Inflammatory infiltration of soft tissues is lower than that around titanium abutments [49,50]. Zirconia also has antimicrobial properties, and bacterial adhesion and the thickness of plaque biofilm are reduced compared with titanium abutments, including the anaerobic biofilm responsible for peri-implantitis [41,51–54]. Bacteria compete with soft tissue cells for the surface [55] and reduced bacterial adhesion increases soft tissue adhesion, reducing risk of peri-implantitis [56–58]. Zirconia thus fulfils clinical requirements of an implant abutment material.

4. Surface modification of zirconia abutments

Surface roughness, surface micromorphology, chemical composition, hydrophilicity, surface energy and surface cleanliness affect soft tissue adhesion (Fig. 1). Surface modification of zirconia abutments is reviewed in the following section (Table 1).

Fig. 1. Surface modification of zirconia abutment.

4.1. Optimization of surface micromorphology

Formation of micron-scale surfaces (e.g., microgrooves by laser) and nano-scale surfaces (e.g., nano-pores, nano-tubes and nano-nets by anodic oxidation), airborne-particle abrasion and etching, thermal etching and surface oxidation have been used to modify titanium surfaces and affect bone integration and the quality of peri-implant soft tissues [59–65]. Sandblasting, acid etching, polishing and laser modifications have been used to modify zirconia surfaces.

Laser etching has been used to form microgrooves or porous surfaces on zirconia abutments. Based on the results of *in vivo* experiments, the attachment of connective tissues in the surrounding soft tissues was found to be enhanced [66], and the expression of collagen fiber-related genes in the connective tissue region was up-regulated by 2 times [67]. Collagen fibers were embedded vertically or obliquely into the abutment surface [68–71] and annular fibers surrounding the abutments were observed in the transverse section [69]. The difference in collagen fiber orientation between abutments and natural teeth may lead to poor sealing of peri-implant soft tissues. More vertical or oblique fibers improve connective tissue adhesion to the abutment surface, preventing epithelial downgrowth and saucerization [68,69,71]. Annular fibers enhance the stability of soft tissue. Changes to surface morphology may alter expression levels of junctional epithelium-related genes to promote development [67]. Gingival fibroblast attachment was increased at the cellular level [68,72,73] and mean optical density values in MTT assays were increased for grooved zirconia surfaces after 48 h of HGF adhesion relative to smooth zirconia surfaces without microgrooves [72]. The microstructure (repeating nano-structure) produced by laser etching maximized contact area and enhanced integration of cellular pseudopods and collagen micro-fibrils [73]. Changing substrate topography increased cell spreading and migration and decreased focal contacts among cells, promoting proliferation and mitosis and enhancing adhesion [73]. Fibroblasts are also “rugophobic” cells, stimulated to repopulate the material surface following a controlled and orientated geometry (microgrooves) by “contact guidance” [72,74–76]. However, laser etching may cause mechanical damage to zirconia abutments [77].

Increasing surface roughness at the microscopic level promotes osseointegration but excessive roughness may increase the risk of peri-implantitis while nano-level modification seems to facilitate soft tissue

Table 1
Summary of the current micro-design of zirconia abutment surfaces.

Study No.	Investigated material	Surface modification	*In vivo/in vitro* study	Bioactivity evaluation/conclusion	Contact angle	Roughness	Ref.
1	ZrO_2	UV-A (382 nm, 25 mW cm^{-2}) and UV-C (260 nm, 15 mW/cm^2) treatment	–	1. The hydrophilicity and wettability were increased.; 2. Its efficiency was dependent on the specific material and surface.	94.1 ± 2.1 (UV-A); 27.4 ± 8.6 (UV–C)	0.87 ± 0.08 μm;	[105]
2	Zr1 (compound); Zr2(Y-TZP)	UV-light treatment for 15 min	–	1. A decrease in surface carbon content was observed; 2. A conversion of the hydrophilic status; 3. The monoclinic content of one material was increased.	Before: 56.4°–69°; After: 2.5°–14.1°	–	[106]
3	Y-TZP	UV-light and argon or oxygen plasma treatment for 12 min	*In vitro* (L929 murine fibroblast cells; HGFs)	1. Cell attachment, proliferation and viability were improved; 2. Minor effects on the cytocompatibility (argon plasma treatment).	–	–	[100]
4	ZrO_2 (smooth and rough)	UV-light treatment (17 mW/cm^2) for 24 h	HGFs *in vitro*	1. The behavior of HGFs was affected (varying with surface roughness).	Smooth: 51.98°–33.76°; Rough: 63.87°–36.15°	Smooth groups: 0.05 ± 0.01 μm; Rough groups: 0.19 ± 0.03 μm.	[102]
5	Y-TZP; ATZ (alumina-toughened zirconia)	UV-light treatment (0.05 mW/cm^2 and 2 mW/cm^2) for 12 min	3D OMM *in vitro*	1. Photofunctionalization enhanced the soft tissue cell attachment	–	Y-TZP: 246.48 ± 27.04 nm ATZ: 256.65 ± 35.59 nm	[108]
6	Y-TZP	UV-light treatment (19 mW/cm^2) for 20 min; large-grit sandblasting and hydrofluoric acid etching (blastedHF)	Wistar rats *in vivo*	1. The area of soft-tissue attachment of the perpendicular collagen fibers was the (significantly) largest for blasted HF + UV implants.	Before: 68.75 (2.91)°; UV: 12.29 (2.92)°; BlastedHF: 6.35 (1.18) °; BlastedHF + UV: 0.00 (0.00) °	Before: 3.23 (1.14) nm; UV: 3.09 (3.65) nm; BlastedHF: 351.80 (42.44) nm; BlastedHF + UV: 322.00 (41.91) nm	[92]
7	TZP	UV-light treatment (19 mW/cm^2) for 2 h; low-energy oxygen plasma at room temperature for 10 min	Human oral keratinocytes *in vitro*	1. The initial attachment and migration capability of HOK were promoted.	Before: 51.5 ± 2.3°; After: 0°	Before: 0.067 ± 0.003 μm	[110]
8	ZrO_2	UV-A (365 nm, 550 μW cm^{-2}) for 15 min, 3 h, 24 h; UV-C (243 nm, 490 μW cm^{-2}) for 15 min, 3 h, 24 h	–	1. The color, surface free energy, and surface chemistry of zirconia changed; 2. UV-C (but not UV-A) irradiation change the aesthetic in color.	Before: 70.7 ± 0.3°; After: 24 h UV-C: 17.3 ± 1.1°; 24 h UV-A: 58.3 ± 2.7°	–	[99]
9	ZrO_2	UV-light treatment (17 mW/cm^2) for 24 h; atmospheric room temperature plasma temperature for 60 s.	HGFs *in vitro*	1. He plasma had the better effect on cell adhesion, proliferation, and on collagen synthesis than UV light treatment.	Before: 78.03°; After plasma: 49.94°; After UV: 35.62°	Before: 0.05 ± 0.01 μm; After: no significant difference	[109]
10	Y-TZP	Cold atmospheric plasma (CAP) treatment for 5 min	HGFs *in vitro*	1. Cell surface covering was improved.	Before: 97°; After: 26–36°	251 ± 21 nm	[16]
11	Y-TZP	Helium CAP treatment for 30 s, 60 s or 90 s	*S. mutans* and *P. gingivalis in vitro*	1. The hydrophilicity was increased; 2. The surface chemistry was altered; 3. The surface topography was not affected; 4. Bacterial adhesion and growth were inhibited.	Before: 80.98 ± 0.51°; After:90 s plasma: 25.70 ± 2.06°	–	[80]
12	ZrO_2	Helium atmospheric-pressure dielectric-barrier-discharge plasmas for 30, 60 or 90 s	HGFs *in vitro*	1. The biological behavior of fibroblasts was enhanced; 2. The expression of attachment-related genes was increased; 3. The cell density was improved; 4. The surface morphology and roughness remained no change; 5. The hydrophilicity was increased; 6. The surface C/O ratio was decreased.	Before: 78.31°; After: 43.71°	0.05 ± 0.01 μm	[118]
13	Y-TZP containing 5% HA or 5% β-TCP	Bioactive modified	HGFs *in vitro*	1. HGF adhesion, viability, and proliferation were decreased.	Before: 70.59°; After: 70.82°, 65.04°	1.45–1.86 μm	[121]

(*continued on next page*)

Table 1 (*continued*)

Study No.	Investigated material	Surface modification	*In vivo/in vitro* study	Bioactivity evaluation/conclusion	Contact angle	Roughness	Ref.
14	Y-TZP; NANOZR	Coated with silk fibroin	*in vitro*	1. A silk fibroin electrogel coating had sufficient bonding strength 2. The biocompatibility of zirconia was improved.			[132]
15	ZrO_2	Coated with polydopamine (PDA)	HGFs *in vitro*	1. Cell attachment and proliferation were increased; 2. Bacterial adhesion was reduced.	Before: 78 ± 4°; After: 64 ± 1°;	Before: 0.065 ± 0.022 μm; After: 0.071 ± 0.026 μm	[137]
16	ZrO_2	Coated with chitosan	HGFs *in vitro*	1. HGF-1 cells were shown to attach and proliferate well	–	–	[143]
17	Y-TZP	Coated by RGD-containing peptide	*in vitro*	1. Cell adhesion was significantly enhanced.	–	–	[150]
18	Y-TZP	RGD peptidic biofunctionalization and laser micro-patterns	*in vitro*	1. Migration was greatly enhanced along the grooves; 2. No effects on cell migration were found for the peptidic platform; 3. Cell number and area were increased after biofunctionalization.	–	–	[151]
19	ZrO_2	A multi-step research cleaning method	HGFs *in vitro*	1. Surface contact angle was reduced; 2. HGF viability was enhanced.	Before: 98.7 ± 4.5°; After: 69.9 ± 6.4°	After: 0.079 ± 0.017 μm	[154]
20	ZrO_2	Reagent (PK) and vacuum plasma cleaning	HGFs *in vitro*	1. Initial HGF attachment was affected; 2. Gene expression of type I collagen was increased.	–	–	[155]
21	CAD/CAM ZrO_2	Ultrasonic cleaning	–	1. Surface contamination was reduced.	–	–	[153]
22	ZrO_2	Coated with sol–gel derived TiO_2 or ZrO_2	HGFs *in vitro*	1. Fibroblast proliferation was reduced in ZrO_2-coated specimens.	–	–	[164]
23	ZrO_2	Coated with a sol-gel–derived TiO_2	HGK *in vitro*	1. Epithelial cell attachment and proliferation were improved.	–	–	[107]
24	ZrO_2	Polished/polished and heat-treated/machined/machined and heat-treated/sandblasted, etched and heat-treated	HGF-1 *in vitro*	1. A smooth surface with exposed grains might be suggested as the optimal substrate for human gingival fibroblasts.	–	–	[88]

integration [76]. Anisotropic nanogeometry may be produced by electrochemical anodization and the resulting nano-pores, nano-tubes and nano-webs regulate HGFs, resulting in increased cell adhesion, activity and deposition of collagen fibers [74,76]. The diameter and composition of nano-pores affect biological activity [76,78]. An *in vitro* study demonstrated that small nano-pores promoted cell adhesion and deposition while large nano-pores induced apoptosis. The 15-nm pore has been deemed optimal [78] but the exact pore size remains unclear due to divergence in preparation and cell culture methods. New nano-pitted anodicfilms exhibit better mechanical properties and reproducibility compared to nanotubes and are not easily peeled off when applying lateral forces [79].

Effects of modified rough surfaces remain controversial. *In vitro* studies have suggested superior attachment of soft tissue cells (epithelial cells and gingival fibroblasts) to smooth (machined or polished) surfaces [80,81]. Decreased zirconia surface roughness increased proliferation, adhesion and migration of soft tissue cells, especially keratin-forming cells, and increased collagen deposition [82–84]. The rough surface seems to be more conducive to bacterial retention and plaque accumulation [85–87]. Smooth zirconia surfaces with exposed particles (machined/heat-treated for 1 h) were more conducive to soft tissue cell attachment than completely smooth polished surfaces [88,89]. Rough transmucosal surfaces produced by surface micromorphology modification appear more conducive to the formation of vertically oriented collagen fibers and more mature and organized connective tissue areas, preventing loss of marginal bone *in vivo* [66,68–71,90–92]. Greater plaque formation has been shown *in vivo* on rough surfaces [90] and the rough plasma-treated, sandblasted or acid-etched hydrophilic surface was more conducive to macrophage-mediated immune regulation, increasing release of anti-inflammatory factors, attenuating inflammatory responses, promoting stem cell recruitment *in vitro* [93,94] and creating a favorable environment for soft tissue healing. A threshold roughness of Ra = 0.2 μm balanced bacterial adhesion with soft tissue attachment in clinical studies. Roughness below Ra = 0.2 μm did not reduce plaque accumulation or change the microbial composition but negatively affected epithelial sealing [89,95,96]. Surface hydrophilicity may influence soft tissue integration and biological behavior *in vivo* more significantly than roughness [37,61,62] but correlations between surface roughness and soft tissue cell proliferation and adhesion have not been established [97].

Morphological modification of the zirconia surface at the micro or nano level seems to adjust the attachment of soft tissues around the implant but effects remain controversial. Moreover, the influence of salivary pellicle in the oral environment may mask the modified surface morphology [64] and subtractive treatment may introduce microcracks and defects into the zirconia surface, increasing the risk of mechanical complications [98]. Therefore, surface modification by additive treatment, such as biomimetic coating, should be considered to customize the surface while preserving biofilm and salivary proteins effects [43].

4.2. Photofunctionalization

Photofunctionalization or photochemical modification uses ultraviolet irradiation to modify the abutment surface. UV light treatment of zirconia may improve surface bioactivity via “biological activation” [99]. UV treatment reduced cytotoxicity [100], enhanced protein adsorption, cell proliferation, adhesion and differentiation [101–103] and inhibited oxidative stress (reactive oxygen species production) and inflammatory responses [104]. UV treatment requires simple equipment and procedure, is easy to implement, has a low cost and is not restricted by type of abutment material, including titanium, zirconia and polyether ether ketone (PEEK) [100–103,105,106].

Zirconia has semiconductor and photocatalytic activities [107]. UV irradiation increases surface oxygen vacancy at the bridging sites and photocatalytic reactions transform Zr^{4+} to Zr^{3+} sites with increased wettability. UV light excites an electron from the valence to the

conduction band, resulting in negative-electron (e^-) and positive-hole (h^+) pairs. The positive holes on the zirconia surface increase surface free energy, making it more electropositive and favorable for attaching to negatively charged cells and proteins [106,108]. Surface characterization revealed that UV treatment did not change either surface morphology [106] or crystalline phase [99,109] but changed the elemental composition, decreasing carbon, increasing oxygen and decreasing C/O and C/Zr ratios. Contamination with carbon may hinder protein and cell adhesion and photolysis of carbon by UV light results from the photocatalytic properties of zirconia [109].

UV-treated zirconium oxide surface has increased wettability with a water contact angle approaching 0°, producing a superhydrophilic surface. Generally, the more hydrophilic the surface, the more proteins and other macromolecules may attach, promoting cell adhesion, spreading, proliferation and differentiation [92,110]. Hydrophilic surfaces also create an anti-inflammatory microenvironment, promoting stem cell recruitment, reducing inflammatory factor secretion [94,111–113] and provide conditions for soft tissue healing [114]. In addition, hydrophobic surfaces can partially deform proteins by disrupting their tertiary structure, leading to a decrease in cell adhesion [115]. This process is also known as "surface conditioning" [116]. The hydrophilic surface is not retained for long and "rehydrophobic" phenomena may occur in air [88]. However, the UV-induced superhydrophilic surface is more durable [117]. Thus, the bioactivity enhancement of zirconia produced by photofunctionalization may augment the superhydrophilic surface and decrease surface carbon.

Zirconia surface roughness seems to affect UV treatment, unlike titanium [101]. HGF differentiation and formation of denser vertically oriented collagen fibers were improved on hydrophilic surfaces [76,92] but UV treatment of the smooth polished surface may produce the opposite *in vitro* result [102,109], probably due to the larger rough surface (after air-abrasion) area for UV light absorbance and the greater smooth surface hydrophilicity and wettability. Surface roughness and hydrophilicity may be synergistic *in vitro* [93], although differences in surface morphology, material properties, surface chemical composition, UV irradiation wavelength, treatment timing and mode have led to varied results [101,105]. However, it is unclear why zirconia surface roughness varies by UV treatment effects and there is no consensus on wavelength and time of UV irradiation. Zirconia also differs from titanium in UV irradiation requirements. Zirconia requires UV energy greater than 5.82 eV to induce photocatalytic activity, to excite electrons from the valence to the conduction band while titanium has a forbidden bandwidth of 3.2 eV, implying that more energy is required to induce photocatalytic activity on zirconia surfaces [110].

UV-C treatment of zirconia for 24 h results in optimal biological properties but a visible color change is found in UV-C irradiated compared with UV-A irradiated zirconia [99]. Such discoloration may affect aesthetic properties. Nevertheless, photochemical modification by UV irradiation is promising for enhancing soft tissue integration.

4.3. Plasma processing

Plasma treatment improves surface wettability and promotes protein and cell interactions [100,101]. The plasma-treated surface is more conducive to HGF adhesion and collagen release [109] and facilitates the initial adhesion of oral keratin-forming cells [110] while UV treatment results in better zirconia surface wettability. Plasma is a partially or fully ionized gas appropriate for treatment of heat-sensitive surfaces. Free electrons and ions interact with molecules on the treated surface, producing nitric oxide and reactive oxygen species [16]. Plasma treatment of the zirconia surface alters its chemistry and the peak value of surface hydroxide is detected by X-ray photoelectron spectroscopy [80,109]. Most proteins are negatively charged in a neutral environment and positively charged hydroxyl groups on the zirconia influence protein adsorption and cell attachment [110], indicating the greater impact of hydroxide or hydroxyl groups produced by plasma treatment over the decreased carbon content caused by UV treatment. Hence, changes in surface chemistry play a more significant role in improving cell behavior than the enhancement of wettability.

Plasma treatment technology has been widely used in food packaging and biomedicine. The operating gas temperature is similar to that of the oral environment, saving time and labor and conferring disinfection. Residual cuttings and colonized microorganisms on the surface of factory-finished abutments may interfere with soft tissue healing. Plasma treatment may remove these low-energy surface contaminants, cleaning and increasing surface free energy and improving cell adhesion kinetics [16,22]. HGF adhesion is promoted [22] and bacterial adhesion, growth and number decreased [22]. Helium low temperature plasma treatment for 60 s enhanced HGF behavior *in vitro* while 90 s inhibited it [118]. Therefore, treatment conditions should be optimized. Differences in plasma generation devices, gases used, experimental conditions, cell strains and material surfaces make it difficult to draw a firm conclusion. Plasma treatment may be performed under atmospheric pressure or vacuum conditions and air, nitrogen, oxygen and argon may be used. Helium generates more stable, mild and uniform glow discharges at atmospheric pressure than other gases [80,118] but is expensive. Thus, more cost-effective gases that produce stable glow discharge plasma should be developed in the future.

4.4. Construction of biomimetic coating and biofunctionalization

Bionic surface coatings, such as hydroxyapatite (HA), β-tricalcium phosphate (β-TCP), collagen and chitosan, may promote soft tissue formation around zirconia abutments. However, soft tissues reacted inconsistently towards these coatings [46,119–124] and they gave desirable results on titanium surfaces but not on zirconia [121]. Biomimetics, silk protein and polydopamine (PDA), have also been investigated to construct surface coatings [125].

Silk is composed of fibroin and sericin [126]. Fibroin accounts for 70–80% and has been widely used due to good biocompatibility, mechanical properties, controlled degradation rate, easy accessibility, ability to promote cell adhesion, spreading, proliferation and inherent antibacterial properties [127–131]. Fibroin has been introduced as a carrier for dental implants and provides amino acid side chains that can functionally be modified. Qu et al. [132] applied silk fibroin gel to the zirconia surface in 2019 with no toxic effects *in vitro*, indicating its feasibility. Silk fibroin coating modified with bone morphogenetic peptides accelerated osteogenic differentiation and maturation of osteoblast-like cells [129] and promoted cell adhesion and reduced bacterial retention [133]. The slow degradation of silk fibroin ensures its continuous action, giving sufficient time for soft and hard tissue healing [132]. The weak basic and acidic groups of the fibroin membrane allow it to act as an amphoteric ion exchanger. Molecules passing through the membrane may be controlled by pH adjustment and alkaline pH regulates peri-implant disease [87]. Therefore, silk fibroin is a pH-sensitive drug delivery material for drug release in the peri-implantitis environment [130]. Sericin is a hydrophilic "glue" component of silk proteins [134] and promotes proliferation, migration and adhesion of keratinocytes and fibroblasts, increases collagen production and accelerates wound healing around dental implants [135,136]. Sericin is used for fabricating hydrogels in tissue engineering and shows promise for the optimization of zirconia surfaces. Osseointegration has been investigated but promotion of soft tissue healing requires further attention.

Polydopamine (PDA) is a synthetic polymer inspired by the invertebrate mussel and adheres to different substrates with high bonding strength even under wet conditions. PDA coatings on the hydrophobic and biologically inert surface of implant materials improve hydrophilicity, promoting protein adsorption, cell adhesion, spreading and proliferation. An *in vitro* study by Liu et al. [137] demonstrated that PDA-modified zirconia promoted adhesion, proliferation and differentiation of HGFs and reduced bacterial adhesion, showing promise for clinical applications in improving soft tissue integration around zirconia

abutments.

PDA coatings have many advantages: 1). simple and efficient preparation by impregnating zirconia into alkaline dopamine solution; 2). non-toxic, good biocompatibility; 3). enriched in catechol and amino groups for secondary surface-mediated reactions via Michael addition or Schiff base chemistry [137]; 4). not limited by the substrate material, regardless of shape and size [138]. PDA coating may be achieved by simple dip treatment [139–141]. However, PDA coatings formed by conventional polymerization under alkaline conditions are unstable and inhomogeneous and the high local pH in the vicinity of vesicular self-assemblies formed by a series of acetal-based cationic amphiphiles may be conveniently used to form more uniform and stable nanostructured PDA coating in a gradual manner [142].

Chitosan coating (CS) is produced by partial deacetylation of the natural polysaccharide, chitin, and promotes cell attachment and proliferation [127]. However, some *in vitro* studies have shown that alumina appears to be more suitable as a CS-coating material than zirconia [143]. In addition, CS has a high degree of cell selectivity, since osteoblasts and osteocytes adhere strongly and whereas fibroblasts adhere weakly [144].

Biofunctionalization, or biomimetic surface modification, anchors organic components, such as proteins and peptides, onto the material surface to modify biochemical and biological responses [43]. Collagen [138], adhesion-related proteins [145], fibroblast growth factor (FGF) [146] and RGD peptide sequences [147,148] have been investigated.

However, biomimetic surface modification of zirconia surfaces has received little attention. The Arginine-Glycine-Aspartic (RGD) tripeptide exists in the extracellular matrix (ECM) and regulates cell adhesion by binding to integrins. Covalently immobilized RGD peptides on activated zirconia surfaces promote cell adhesion and spreading with improved mucosal closure [149–151]. This biomimetic coating may also act as a carrier. Yang et al. [152] immobilized RGD on the zirconia surface by PDA coating and improved the biological activity of HGFs and reduced adhesion of *Porphyromonas gingivalis* and *Streptococcus mutans in vitro*. Biomimetic coating-assisted immobilization (indirectly) can effectively improve the anchoring of biomolecules compared with the conventional immobilization (directly) [152].

Biomimetic coatings are rapidly developing [125]. Subtracted zirconia treatment by preparation of grooves or porous surfaces may have a negative impact on mechanical properties but additional treatments (overcoating) do not [121]. However, zirconia is biologically inert and some coatings have exhibited poor adhesion [43,137]. Therefore, further research on long-term stability and *in vivo* effect is required.

4.5. Zirconia abutment surface decontamination

Wear particles, debris, organic and inorganic contaminants occur on the surface of laboratory-fabricated zirconia abutments [153] and their location between implant and soft tissue may stimulate soft tissue and facilitate bacterial adhesion. Surface decontamination increases surface energy for HGF attachment and biological sealing [154,155]. Indeed, the removal of low-energy contaminants implies increased cell adhesion kinetics [22]. Cleaning approaches for zirconia abutments include immersion in antiseptic solutions (chlorhexidine, octreotide and ethanol), steam cleaning, ultrasonic cleaning, plasma cleaning and other newly developed cleaning reagents. Matthes et al. found that preservatives used in traditional cleaning can be retained on the implant surface which leads to a negative impact on cell metabolism, viability and spreading *in vitro* [16]. Ultrasonic cleaning is more effective in decontaminating zirconia surfaces than steam cleaning [153].

The choice of cleaning solution depends on abutment material. Plasma cleaning of zirconia surfaces has no effect on cell adhesion but combination with proteinase K reagent seems to be more effective [16,155].

4.6. Anti-bacterial adhesion

Gristina has described the challenge for advanced surface modification as the “race for the surface” between soft tissue integration and bacterial colonization [55]. However, whereas soft tissue cell adhesion must be promoted, bacterial adhesion and proliferation must be inhibited [46] and research on this area continues.

Zirconia abutment surface properties, such as roughness, free energy and charge density affect bacterial adhesion [52,117,156]. In general, higher roughness (Ra) increases and hydrophobicity is usually the main driver of bacterial adhesion [117]. Bacteria may contribute or gain electrons from the substrate, the former adhering more successfully [52] but bacterial adhesion to zirconia abutments remains controversial [157,158]. Zirconia exhibits lower bacterial adhesion, plaque biofilm density and thickness than titanium *in vitro*. Moreover, anaerobic biofilms of *Porphyromonas gingivalis* and *Clostridium nucleatum*, responsible for peri-implantitis, are also significantly reduced [41,51–54]. Some studies have shown no significant advantage of zirconia abutments in bacterial adhesion [159,160]. Diverse results may stem from differences in measurement metrics, such as total amount of plaque biofilm formation, thickness or percentage surface area covered, implying that the degree of bacterial coverage on the material surface only represents the initial bacterial adhesion event and does not evaluate plaque accumulation [52]. Secondly, different experimental conditions, including differences in strains, presence or absence of experimental protein films and saliva conditions, may also have an impact. Additionally, differences in zirconia storage conditions may affect results [88].

Antibacterial surfaces include antibiotic, nano-silver, photocatalytic, nano-, bionic and smart bioresponsive antibacterial coatings [86,161] which produce different antibacterial effects [161]. Research on the construction of antimicrobial surfaces for zirconia abutments is still lacking. Zirconia surfaces with active oxygen or nitrogen components produced by plasma treatment inhibit the growth of *Porphyromonas gingivalis* and *Streptococcus pyogenes* [80]. PDA coatings are also used and have been demonstrated to inhibit *Escherichia coli* [142,162] *Staphylococcus aureus* [142] and *Streptococcus in vitro* [163]. “Bifunctional abutment” surfaces would have antibacterial function in addition to promoting soft tissue adhesion, such as enzyme-functionalized bifunctional silk fibroin to reduce biological complications after implantation, promote cell adhesion and reduce bacterial (e.g., *Staphylococcus aureus*) damage [133].

Further research on bacterial inhibition by zirconia abutments is required.

4.7. Other approaches

The introduction of titanium dioxide coating on zirconia does not affect the flexural strength of zirconia [164] but promotes adhesion and viability of epithelial cells [107]. Nanostructured titanium dioxide layers are prepared by surface modification, enriched with more anatase crystalline phases compared with those naturally formed, and have enhanced adhesion capacity, attachment strength and cellular activity of HGFs [63,165]. Both animal and clinical studies have confirmed the advantages for increased soft tissue attachment and reduced bone resorption [65,166]. Nano-porous titanium dioxide coatings reduced oral bacterial adhesion on the surface of zirconia abutments [63,64] but HGF proliferation may be reduced relative to titanium surfaces [164].

5. Structure design of zirconia abutments

The implant-abutment connection and the abutment geometry can affect soft tissue healing. Zirconia abutments have higher fracture rates due to the difference in mechanical properties between zirconia and metal. The internal connection method reduces the center of rotation, improving mechanical stability, sealing, reducing the occurrence of technical problems, such as fracture [167,168], and attenuating

marginal bone loss over a short-to-medium duration [168]. The internal connection method may be an ideal approach for zirconia abutments.

Implant-abutment marginal adaptation must be considered. Marginal adaptation refers to the size of the microgap between the implant-abutment interface. The microgap allows blood, saliva, toxic by-products and bacterial pathogens to leak into the implant cavity and lubricate the components [169] and micro-movements, including microabrasion, microshift and microrotation, of the superstructure may occur when subjected to masticatory forces. Micromovements may increase the microgap size, increasing the risk of microbial leakage. The three negative concepts, microgap, microleakage and micromovement, work together to increase the risk of microbial growth and accumulation. Microgaps also interfere with attachment of soft tissues and their stability, resulting in peri-implantitis (Fig. 2) [86]. Microgap formation may be affected by surface machining defects, fabricating methods (prefabricated or customed abutments, conventional fabrication technique and CAD/CAM technique), mismatch between the mechanical properties of abutments and implant materials and loading. Marginal adaptation or microgap may be assessed qualitatively and quantitatively using silicone impressions, scanning electron microscopy or micro-CT techniques [170–172].

The mechanical load is concentrated on the implant-abutment interface [167] and the inconsistent stiffness of titanium and zirconia means that deformation energy is distributed to the material with the lower Young's modulus, resulting in wear at the implant interface. The zirconia abutment-titanium implant interface has been shown to form a 3-7-fold larger gap than the titanium abutment-titanium implant interface [139,171]. Masticatory forces lead to greater wear of the titanium implant than the zirconia abutment [170] and the manufacturing process of CAD/CAM zirconia abutment has not yet been standardized. CAD/CAM zirconia abutments appear to produce a larger microgap than prefabricated abutments [172] and should be carefully considered when selecting abutments for clinical purposes.

In order to improve marginal adaptation, clinicians recommend:

1. a "hybrid abutment" protocol that uses a titanium base to ensure the adaptation between the abutment and the implant, combined with a customed zirconia abutment to meet aesthetic needs [172].
2. avoidance of zirconia abutments with a hexagonal connection which is more likely to cause wear at the zirconia abutment interface [170].

6. Models and evaluation methods related to soft tissue adhesion around abutments

Research models may be divided into *in vitro* and *in vivo* (Fig. 3). *In vitro* research models are mainly 2D cellular models [17,46,100,173–175] while *in vivo* approaches rely on animal models [18,19,35,71,176]. 3D reconstructed human gingival models (RHG) have enabled the same evaluation parameters to be applied to *in vitro,* animal and clinical studies [177–179]. 3D RHG consists of several layers of epithelial cells and an underlying connective tissue component, into which the target implant abutment is inserted [180–182].

Soft tissue adhesion to the surface of modified abutments may be evaluated by three criteria: cell adhesion-related protein levels, soft tissue cell function and tissue level. Assessment of tissue level involves dimensions, proportion of connective tissue, direction of collagen fiber formation [92,183] and soft tissue closure analysis [18,176,184]. Soft tissue adhesion strength is the most clinically relevant indicator to evaluate integration of soft tissue with the implant and assess abutment surface modifications, although deficiencies remain [181]. Most studies have focused on HGFs but the relation of fibroblast adhesion to histological results has been questioned [54,155], as rapid cell attachment does not necessarily lead to the induction of differentiation and inverse relationships between cell proliferation and differentiation have been implied [185]. HGFs may impede soft tissue attachment to the implant surface and loss of keratinocyte colonization may lead to the formation of parafunctional junction epithelium [169]. The gap between *in vitro* and *in vivo* experiments appears greater for fibroblasts than for epithelial cells. However, *in vitro* data does not always translate to the clinic [83]. Therefore, modified zirconia abutments must be validated by *in vivo* histological experiments.

Furthermore, modification of zirconia by sandblasting or acid etching treatment may alter mechanical properties or lead to microcracking, increasing the risk of mechanical complications after implant surgery [121]. Hence, evaluation of the mechanical properties should be undertaken. Zirconia is too brittle for tensile tests and compression or bending tests must be performed to evaluate fracture toughness, flexural strength, hardness and modulus of elasticity [11,43,98].

The inert zirconia surface is difficult to modify and bond strengths of the functionalized coating must be measured by shear and tensile bonding strengths. The two coating samples are stacked together with

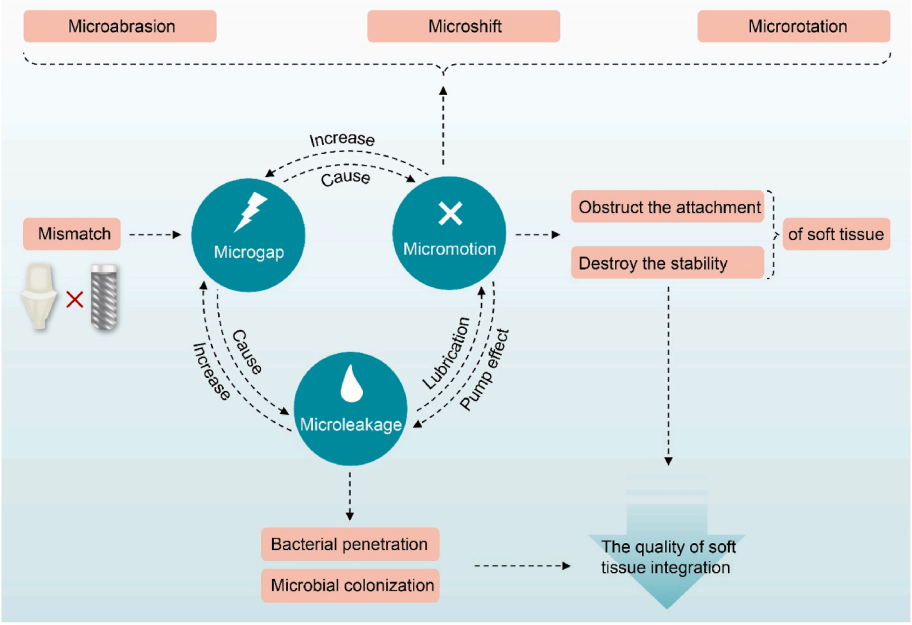

Fig. 2. The relationship between microgap, microleakage and micromovement and their harmful effects on soft tissue integration.

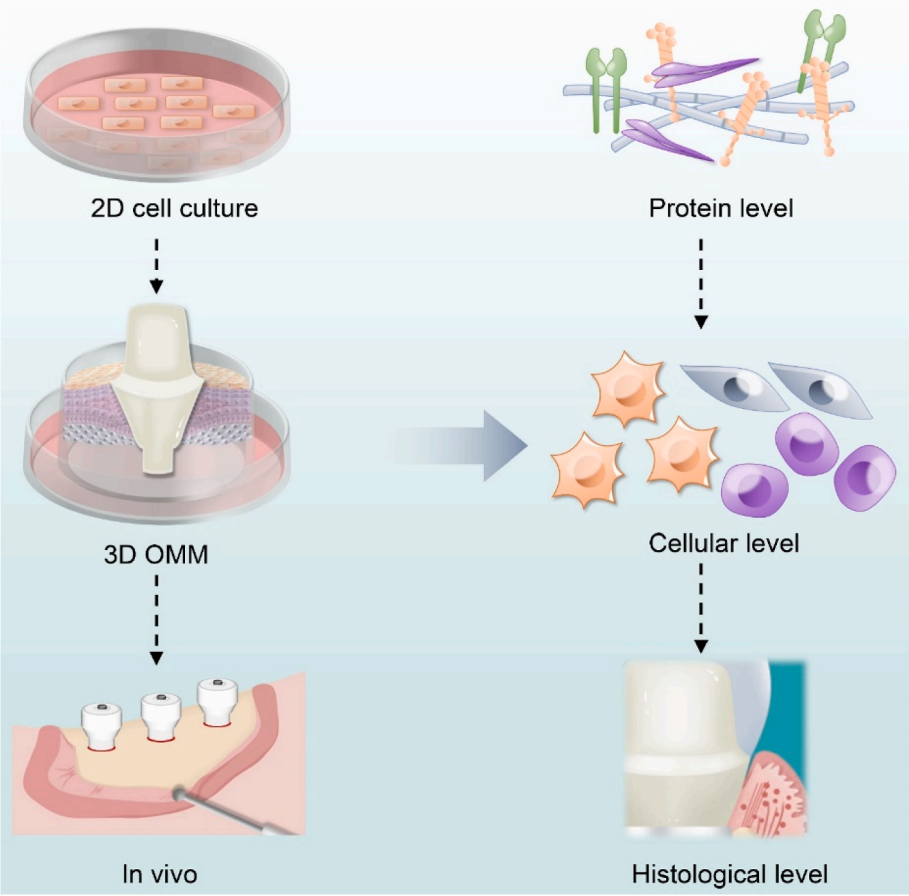

Fig. 3. Schematic of models and evaluation levels related to soft tissue adhesion around abutments.

wet-coating surfaces facing each other and bond strengths are measured at room temperature using a material testing machine in shear and tensile modes until complete separation occurs. Debonding modes may be divided into adhesive (peeling occurs at the coating-substrate interface) and cohesive (peeling occurs inside the coating). The adhesive/cohesive ratio is usually determined by measuring adhesive and cohesive areas. A lower ratio of adhesive failure indicates more fragments located inside the coating rather than at the interface, thus reflecting higher adhesion of the coating to the surface of implant material [132].

7. Conclusions and future perspectives

Zirconia abutments increasingly represent a preferable aesthetic alternative. The quality of soft tissue integration is crucial for prognosis

Table 2
Factors affecting the soft tissue integration of zirconia abutments and the corresponding optimization strategies.

Factors		Recommendation strategies	Results
Surface modification	Surface roughness (still in dispute)	Smooth zirconia surfaces with exposed particles	Soft tissue cell attachment was enhanced.
		Rough surfaces	More vertically oriented collagen fibers formation and embedment.
	Surface chemical composition	UV treatment (photofunctionalization)	The wettability was increased, surface C/O and C/Zr ratios were decreased, and soft tissue cell attachment was enhanced.
		Plasma processing	The wettability was increased, hydroxyl (OH) groups were increased, and soft tissue cell attachment was enhanced.
	Surface coating	Silk fibrorin coating	Cell attachment was enhanced, and it served as a versatile platform.
		Polydopamine coating	Cell attachment was enhanced, bacterial adhesion was reduced, and it served as a versatile platform.
	Surface decontamination	Plasma cleaning	Surface energy was increased, cell tissue integration was enhanced, and bacterial adhesion was reduced.
	Biofunctionalization	Fixed RGD tripeptide	Cell adhesion was promoted.
Structure design	Connection structure	The internal connection methods	Mechanical stability was improved and the occurrence of technical problems was reduced.
	Geometric form	Custom zirconia abutments for simulating soft tissue contours	Biological width and stable Pink Esthetic Score were maintained.
	Marginal adaption	Selection of abutments matching with implants	Microgap was reduced.
		Selection of “hybrid abutment”	Microgap was reduced.
		Avoidance of abutments with a hexagonal connection	Wearing at the zirconia abutment interface was avoided.

and analysis of influencing factors and optimization strategies is of great clinical interest. Surface modifications of zirconia abutments focus on morphology, wettability and roughness, taking into account surface coating construction. Macroscopic design of the connection, geometry and marginal adaptation are also influential factors (Table 2)The design of zirconia abutment surfaces to promote soft tissue adhesion can be considered from the following aspects (Fig. 4):

1. Promoting the adhesion of HGFs to deposit more collagen;
2. Improving the adhesion and spreading of keratinocytes by hemidesmosome promotion;
3. Enhancing the quality of soft tissue adhesion by promoting the expression of adhesion-related proteins;
4. Increasing PIE adhesion or the proportion of peri-abutment connective tissues;
5. Promoting the burial of collagen fibers in the abutment surface in vertical and oblique directions to form “rings” to stabilize soft tissues;
6. Blocking inflammatory pathways, decreasing release of pro-inflammatory factors, reducing bacterial adhesion and inhibiting bacterial growth.

Current trends are:

1. Improving the soft tissue integration properties of zirconia surfaces through bifunctional or multifunctional coating constructions (especially biomimetic coatings);
2. Use of 3D OMM as a preclinical model instead of monolayer 2D cell culture to mimic the soft tissue response to different surfaces through interfacial soft tissue morphology analysis.

Current obstacles to clinical translation are:

1. Subtractive treatment and cutting processes cause microcracks and defects on the zirconia surface;
2. Modification of the inert zirconia surface to ensure long-term stability;
3. Zirconia fatigue or aging with decreased wettability with storage in air [88] and crystalline phase and cellular reaction changes [17,186];
4. Mismatching of non-standardized custom CAD/CAM zirconia abutments with titanium implants.

Optimization of the macroscopic and microscopic design of zirconia abutment surfaces has great potential to promote soft tissue integration but studies are in their infancy and fall short of clinical applications. Thus, soft tissue integration around zirconia abutments with variability of bacterial plaque biofilm, oral saliva and immune cell microenvironment should be considered in future experimental studies. In addition, the question of whether improved adhesion of epithelial cells and fibroblasts represents an increase in soft tissue integration on the zirconia surface should be clarified. It is hoped that the aesthetic zirconia abutment will have good soft tissue confinement and resist the adhesion of plaque biofilm, allowing soft tissue cells to win the race, thus supporting the clinical development of zirconia abutments.

Funding

This work was supported by the National Nature Science Foundation of China (grants 81720108011,82071169, 82100971).

Availability of data and materials

Not applicable.

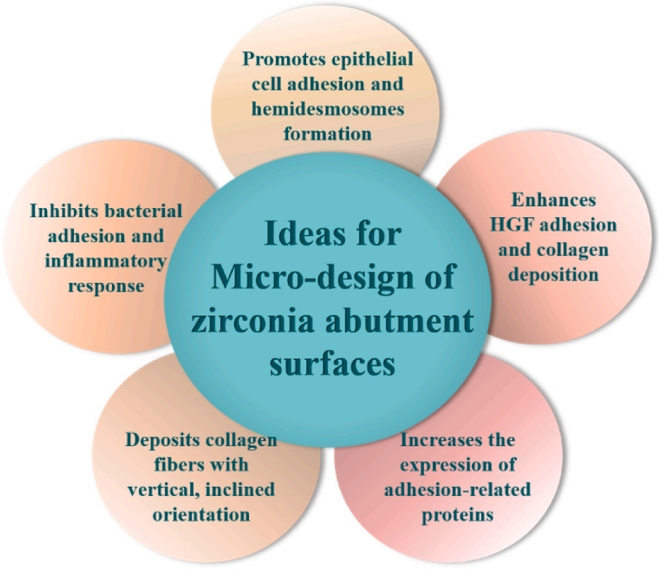

Fig. 4. Ideas for the micro-design of zirconia abutment surfaces.

Authors’ contributions

KT, JHC, LNN and FW conceived the overall topics of discussion. KT wrote the manuscript. JHC, MLL, WZ, LNN and FW reviewed and revised the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Declaration of competing interest

The authors declare that they have no competing interests.

Acknowledgements

The authors would like to express their gratitude to EditSprings (https://www.editsprings.cn) for the expert linguistic services provided.

List of commonly used abbreviations

PIE	Peri-implant epithelium
HGFs	Human gingival fibroblasts
HA	Hydroxyapatite
β-TCP	β-tricalcium phosphate
PDA	Polydopamine
RGD	Arginine-Glycine-Aspartate
ECM	Extracellular matrix
CAD	Computer aided design
CAM	Computer aided manufacturing
PEEK	Polyether ether ketone
2D	Two dimensional
3D RHG	Three dimensional reconstructed human gingival model

References

[1] W.L. Chai, K. Moharamzadeh, I.M. Brook, R. Van Noort, A review of histomorphometric analysis techniques for assessing implant-soft tissue interface, Biotech. Histochem. 86 (2011) 242–254, https://doi.org/10.3109/10520291003707916.

[2] C.T. Lee, Y.W. Huang, L. Zhu, R. Weltman, Prevalences of peri-implantitis and peri-implant mucositis: systematic review and meta-analysis, J. Dent. 62 (2017) 1–12, https://doi.org/10.1016/j.jdent.2017.04.011.

[3] Y. Wang, Y. Zhang, R.J. Miron, Health, Maintenance, and recovery of soft tissues around implants, Clin. Implant Dent. Relat. Res. 18 (2016) 618–634, https://doi.org/10.1111/cid.12343.

[4] A. Kim, S.D. Campbell, M.A. Viana, K.L. Knoernschild, Abutment material effect on peri-implant soft tissue color and perceived esthetics, J. Prosthodont. 25 (2016) 634–640, https://doi.org/10.1111/jopr.12360.

[5] D. Lops, E. Stellini, L. Sbricoli, N. Cea, E. Romeo, E. Bressan, Influence of abutment material on peri-implant soft tissues in anterior areas with thin gingival biotype: a multicentric prospective study, Clin. Oral Implants Res. 28 (2017) 1263–1268, https://doi.org/10.1111/clr.12952.

[6] M. Noronha Oliveira, W.V.H. Schunemann, M.T. Mathew, B. Henriques, R. S. Magini, W. Teughels, J.C.M. Souza, Can degradation products released from dental implants affect peri-implant tissues? J. Periodontal. Res. 53 (2018) 1–11, https://doi.org/10.1111/jre.12479.

[7] H. Cai, J. Chen, C. Li, J. Wang, Q. Wan, X. Liang, Quantitative discoloration assessment of peri-implant soft tissue around zirconia and other abutments with different colours: a systematic review and meta-analysis, J. Dent. 70 (2018) 110–117, https://doi.org/10.1016/j.jdent.2018.01.003.

[8] R. Cosgarea, C. Gasparik, D. Dudea, B. Culic, B. Dannewitz, A. Sculean, Peri-implant soft tissue colour around titanium and zirconia abutments: a prospective randomized controlled clinical study, Clin. Oral Implants Res. 26 (2015) 537–544, https://doi.org/10.1111/clr.12440.

[9] J. Pitta, C. Zarauz, B. Pjetursson, I. Sailer, X. Liu, G. Pradies, A systematic review and meta-analysis of the influence of abutment material on peri-implant soft tissue color measured using spectrophotometry, Int. J. Prosthodont. (IJP) 33 (2020) 39–47, https://doi.org/10.11607/ijp.6393.

[10] A.M. Pabst, C. Walter, A. Bell, M. Weyhrauch, I. Schmidtmann, H. Scheller, K. M. Lehmann, Influence of CAD/CAM zirconia for implant-abutment manufacturing on gingival fibroblasts and oral keratinocytes, Clin. Oral Invest. 20 (2016) 1101–1108, https://doi.org/10.1007/s00784-015-1598-x.

[11] T. Hanawa, Zirconia versus titanium in dentistry: a review, Dent. Mater. J. 39 (2020) 24–36, https://doi.org/10.4012/dmj.2019-172.

[12] A. Ekfeldt, B. Furst, G.E. Carlsson, Zirconia abutments for single-tooth implant restorations: a retrospective and clinical follow-up study, Clin. Oral Implants Res. 22 (2011) 1308–1314, https://doi.org/10.1111/j.1600-0501.2010.02114.x.

[13] Y. Zhu, D. Liu, X. Wang, Y. He, W. Luan, F. Qi, J. Ding, Polydopamine-mediated covalent functionalization of collagen on a titanium alloy to promote biocompatibility with soft tissues, J. Mater. Chem. B 7 (2019) 2019–2031, https://doi.org/10.1039/C8TB03379J.

[14] M.S. Lang, D.R. Cerutis, T. Miyamoto, M.E. Nunn, Cell attachment following instrumentation with titanium and plastic instruments, diode laser, and titanium brush on titanium, titanium-zirconium, and zirconia surfaces, Int. J. Oral Maxillofac. Implants 31 (2016) 799–806, https://doi.org/10.11607/jomi.4440.

[15] J. Hu, I. Atsuta, Y. Ayukawa, T. Zhou, I. Narimatsu, K. Koyano, Effect of titanium or zirconia implant abutments on epithelial attachments after ultrasonic cleaning, J. Oral Sci. 62 (2020) 331–334, https://doi.org/10.2334/josnusd.19-0332.

[16] R. Matthes, L. Jablonowski, B. Holtfreter, T. Gerling, T. von Woedtke, T. Kocher, Fibroblast growth on zirconia ceramic and titanium disks after application with cold atmospheric pressure plasma devices or with antiseptics, Int. J. Oral Maxillofac. Implants 34 (2019) 809–818, https://doi.org/10.11607/jomi.7285.

[17] M. Rigolin, P.A. Barbugli, J.H. Jorge, M. Reis, G.L. Adabo, L.A. Casemiro, C. Martins, O.J. de Lima, J.F. Mollo, Effect of the aging of titanium and zirconia abutment surfaces on the viability, adhesion, and proliferation of cells and the adhesion of microorganisms, J. Prosthet. Dent 122 (2019) 564.e1–564.e10, https://doi.org/10.1016/j.prosdent.2019.08.027.

[18] I. Atsuta, Y. Ayukawa, A. Furuhashi, I. Narimatsu, R. Kondo, W. Oshiro, K. Koyano, Epithelial sealing effectiveness against titanium or zirconia implants surface, J. Biomed. Mater. Res. A. 107 (2019) 1379–1385, https://doi.org/10.1002/jbm.a.36651.

[19] J. Blanco, L. Caneiro, A. Liñares, P. Batalla, F. Muñoz, I. Ramos, Peri-implant soft tissue analyses comparing Ti and ZrO(2) abutments: an animal study on beagle dogs, Clin. Oral Implants Res. 27 (2016) 1221–1226, https://doi.org/10.1111/clr.12729.

[20] A. Furuhashi, Y. Ayukawa, I. Atsuta, Y.D. Rakhmatia, K. Koyano, Soft tissue interface with various kinds of implant abutment materials, J. Clin. Med. 10 (2021), https://doi.org/10.3390/jcm10112386.

[21] C. Tomasi, F. Tessarolo, I. Caola, J. Wennstrom, G. Nollo, T. Berglundh, Morphogenesis of peri-implant mucosa revisited: an experimental study in humans, Clin. Oral Implants Res. 25 (2014) 997–1003, https://doi.org/10.1111/clr.12223.

[22] L. Canullo, C. Cassinelli, W. Gotz, D. Tarnow, Plasma of argon accelerates murine fibroblast adhesion in early stages of titanium disk colonization, Int. J. Oral Maxillofac. Implants 28 (2013) 957–962, https://doi.org/10.11607/jomi.2664.

[23] H. Ikeda, T. Yamaza, M. Yoshinari, Y. Ohsaki, Y. Ayukawa, M.A. Kido, T. Inoue, M. Shimono, K. Koyano, T. Tanaka, Ultrastructural and immunoelectron microscopic studies of the peri-implant epithelium-implant (Ti-6Al-4V) interface of rat maxilla, J. Periodontol. 71 (2000) 961–973, https://doi.org/10.1902/jop.2000.71.6.961.

[24] P. Schupbach, R. Glauser, The defense architecture of the human periimplant mucosa: a histological study, J. Prosthet. Dent 97 (2007) S15–S25, https://doi.org/10.1016/S0022-3913(07)60004-3.

[25] T. Inoue, T. Takeda, C.Y. Lee, Y. Abiko, Y. Ayukawa, T. Tanaka, M. Yoshinari, M. Shimono, Immunolocalization of proliferating cell nuclear antigen in the peri-implant epithelium, Bull. Tokyo Dent. Coll. 38 (1997) 187–193.

[26] J.A. Jansen, J.R. de Wijn, J.M. Wolters-Lutgerhorst, P.J. van Mullem, Ultrastructural study of epithelial cell attachment to implant materials, J. Dent. Res. 64 (1985) 891–896, https://doi.org/10.1177/00220345850640060601.

[27] K. Shioya, T. Sawada, Y. Miake, S. Inoue, T. Yanagisawa, Ultrastructural study of tissues surrounding replanted teeth and dental implants, Clin. Oral Implants Res. 20 (2009) 299–305, https://doi.org/10.1111/j.1600-0501.2008.01644.x.

[28] Y. Ayukawa, I. Atsuta, Y. Moriyama, Y. Jinno, K. Koyano, Localization of integrin beta-4 subunit at soft tissue-titanium or zirconia interface, J. Clin. Med. 9 (2020), https://doi.org/10.3390/jcm9103331.

[29] N.G. Fischer, C. Aparicio, Junctional epithelium and hemidesmosomes: tape and rivets for solving the "percutaneous device dilemma" in dental and other permanent implants, Bioact. Mater. 18 (2022) 178–198, https://doi.org/10.1016/j.bioactmat.2022.03.019.

[30] G.E. Romanos, C. Schröter-Kermani, D. Weingart, J.R. Strub, Health human periodontal versus peri-implant gingival tissues: an immunohistochemical differentiation of the extracellular matrix, Int. J. Oral Maxillofac. Implants 10 (1995) 750–758.

[31] T. Berglundh, J. Lindhe, K. Jonsson, I. Ericsson, The topography of the vascular systems in the periodontal and peri-implant tissues in the dog, J. Clin. Periodontol. 21 (1994) 189–193, https://doi.org/10.1111/j.1600-051x.1994.tb00302.x.

[32] T. Berglundh, J. Lindhe, I. Ericsson, C.P. Marinello, B. Liljenberg, P. Thomsen, The soft tissue barrier at implants and teeth, Clin. Oral Implants Res. 2 (1991) 81–90, https://doi.org/10.1034/j.1600-0501.1991.020206.x.

[33] A. Sculean, R. Gruber, D.D. Bosshardt, Soft tissue wound healing around teeth and dental implants, J. Clin. Periodontol. 41 (2014) S6–S22, https://doi.org/10.1111/jcpe.12206.

[34] T. Berglundh, I. Abrahamsson, M. Welander, N.P. Lang, J. Lindhe, Morphogenesis of the peri-implant mucosa: an experimental study in dogs, Clin. Oral Implants Res. 18 (2007) 1–8, https://doi.org/10.1111/j.1600-0501.2006.01380.x.

[35] C. Mehl, V. Gassling, S. Schultz-Langerhans, Y. Acil, T. Bahr, J. Wiltfang, M. Kern, Influence of four different abutment materials and the adhesive joint of two-piece abutments on cervical implant bone and soft tissue, Int. J. Oral Maxillofac. Implants 31 (2016) 1264–1272, https://doi.org/10.11607/jomi.5321.

[36] D. Buser, H.P. Weber, K. Donath, J.P. Fiorellini, D.W. Paquette, R.C. Williams, Soft tissue reactions to non-submerged unloaded titanium implants in beagle dogs, J. Periodontol. 63 (1992) 225–235, https://doi.org/10.1902/jop.1992.63.3.225.

[37] F. Schwarz, M. Herten, M. Sager, M. Wieland, M. Dard, J. Becker, Histological and immunohistochemical analysis of initial and early subepithelial connective tissue attachment at chemically modified and conventional SLA titanium implants. A pilot study in dogs, Clin. Oral Invest. 11 (2007) 245–255, https://doi.org/10.1007/s00784-007-0110-7.

[38] I. Atsuta, Y. Ayukawa, R. Kondo, W. Oshiro, Y. Matsuura, A. Furuhashi, Y. Tsukiyama, K. Koyano, Soft tissue sealing around dental implants based on histological interpretation, J Prosthodont Res 60 (2016) 3–11, https://doi.org/10.1016/j.jpor.2015.07.001.

[39] Y. Takamori, I. Atsuta, H. Nakamura, T. Sawase, K. Koyano, Y. Hara, Histopathological comparison of the onset of peri-implantitis and periodontitis in rats, Clin. Oral Implants Res. 28 (2017) 163–170, https://doi.org/10.1111/clr.12777.

[40] H. Ikeda, M. Shiraiwa, T. Yamaza, M. Yoshinari, M.A. Kido, Y. Ayukawa, T. Inoue, K. Koyano, T. Tanaka, Difference in penetration of horseradish peroxidase tracer as a foreign substance into the peri-implant or junctional epithelium of rat gingivae, Clin. Oral Implants Res. 13 (2002) 243–251, https://doi.org/10.1034/j.1600-0501.2002.130303.x.

[41] E.D. de Avila, M.J. Avila-Campos, C.E. Vergani, D.M. Spolidório, F.A.J. Mollo, Structural and quantitative analysis of a mature anaerobic biofilm on different implant abutment surfaces, J. Prosthet. Dent 115 (2016) 428–436, https://doi.org/10.1016/j.prosdent.2015.09.016.

[42] T. Koyanagi, M. Sakamoto, Y. Takeuchi, M. Ohkuma, Y. Izumi, Analysis of microbiota associated with peri-implantitis using 16S rRNA gene clone library, J. Oral Microbiol. 2 (2010), https://doi.org/10.3402/jom.v2i0.5104.

[43] M.F. Kunrath, S. Gupta, F. Lorusso, A. Scarano, S. Noumbissi, Oral tissue interactions and cellular response to zirconia implant-prosthetic components: a critical review, Materials 14 (2021), https://doi.org/10.3390/ma14112825.

[44] A. Perez, A. Caiazzo, N.A. Valente, P. Toti, F. Alfonsi, A. Barone, Standard vs customized healing abutments with simultaneous bone grafting for tissue changes around immediate implants. 1-Year outcomes from a randomized clinical trial, Clin. Implant Dent. Relat. Res. 22 (2020) 42–53, https://doi.org/10.1111/cid.12871.

[45] E. Okabe, Y. Ishihara, T. Kikuchi, A. Izawa, S. Kobayashi, H. Goto, Y. Kamiya, K. Sasaki, S. Ban, T. Noguchi, T. Kawai, A. Mitani, Adhesion properties of human oral epithelial-derived cells to zirconia, Clin. Implant Dent. Relat. Res. 18 (2016) 906–916, https://doi.org/10.1111/cid.12369.

[46] D.J. Lee, J.S. Ryu, M. Shimono, K.W. Lee, J.M. Lee, H.S. Jung, Differential healing patterns of mucosal seal on zirconia and titanium implant, Front. Physiol. 10 (2019) 796, https://doi.org/10.3389/fphys.2019.00796.

[47] A. Liñares, L. Grize, F. Muñoz, B.E. Pippenger, M. Dard, O. Domken, J. Blanco-Carrión, Histological assessment of hard and soft tissues surrounding a novel ceramic implant: a pilot study in the minipig, J. Clin. Periodontol. 43 (2016) 538–546, https://doi.org/10.1111/jcpe.12543.

[48] M. Welander, I. Abrahamsson, T. Berglundh, The mucosal barrier at implant abutments of different materials, Clin. Oral Implants Res. 19 (2008) 635–641, https://doi.org/10.1111/j.1600-0501.2008.01543.x.

[49] O. Andrukhov, C. Behm, A. Blufstein, C. Wehner, J. Gahn, B. Pippenger, R. Wagner, X. Rausch-Fan, Effect of implant surface material and roughness to the susceptibility of primary gingival fibroblasts to inflammatory stimuli, Dent. Mater. 36 (2020) e194–e205, https://doi.org/10.1016/j.dental.2020.04.003.
[50] P. Serichetaphongse, W. Chengprapakorn, S. Thongmeearkom, A. Pimkhaokham, Immunohistochemical assessment of the peri-implant soft tissue around different abutment materials: a human study, Clin. Implant Dent. Relat. Res. 22 (2020) 638–646, https://doi.org/10.1111/cid.12942.
[51] C.D. Nascimento, M.S. Pita, F. Fernandes, V. Pedrazzi, J.R. de Albuquerque, R. F. Ribeiro, Bacterial adhesion on the titanium and zirconia abutment surfaces, Clin. Oral Implants Res. 25 (2014) 337–343, https://doi.org/10.1111/clr.12093.
[52] A. Scarano, M. Piattelli, S. Caputi, G.A. Favero, A. Piattelli, Bacterial adhesion on commercially pure titanium and zirconium oxide disks: an in vivo human study, J. Periodontol. 75 (2004) 292–296, https://doi.org/10.1902/jop.2004.75.2.292.
[53] S. Roehling, M. Astasov-Frauenhoffer, I. Hauser-Gerspach, O. Braissant, H. Woelfler, T. Waltimo, H. Kniha, M. Gahlert, In vitro biofilm formation on titanium and zirconia implant surfaces, J. Periodontol. 88 (2017) 298–307, https://doi.org/10.1902/jop.2016.160245.
[54] I. Sanz Martín, I. Sanz Sánchez, A. Carrillo De Albornoz, E. Figuero, M. Sanz, Effects of modified abutment characteristics on peri-implant soft tissue health: a systematic review and meta-analysis, Clin. Oral Implants Res. 29 (2018) 118–129, https://doi.org/10.1111/clr.13097.
[55] A.G. Gristina, Biomaterial-centered infection: microbial adhesion versus tissue integration, Science 237 (1987) 1588–1595, https://doi.org/10.1126/science.3629258.
[56] C. Mikolai, N. Kommerein, A. Ingendoh-Tsakmakidis, A. Winkel, C.S. Falk, M. Stiesch, Early host-microbe interaction in a peri-implant oral mucosa-biofilm model, Cell Microbiol. 22 (2020), e13209, https://doi.org/10.1111/cmi.13209.
[57] S. Renvert, M. Quirynen, Risk indicators for peri-implantitis. A narrative review, Clin. Oral Implants Res. 26 (2015) 15–44, https://doi.org/10.1111/clr.12636.
[58] J.H. Fu, H.L. Wang, Breaking the wave of peri-implantitis, Periodontol 84 (2020) 145–160, https://doi.org/10.1111/prd.12335, 2000.
[59] L. Canullo, M. Annunziata, P. Pesce, G. Tommasato, L. Nastri, L. Guida, Influence of abutment material and modifications on peri-implant soft-tissue attachment: a systematic review and meta-analysis of histological animal studies, J. Prosthet. Dent 125 (2021) 426–436, https://doi.org/10.1016/j.prosdent.2020.01.025.
[60] F. Rupp, L. Liang, J. Geis-Gerstorfer, L. Scheideler, F. Hüttig, Surface characteristics of dental implants: a review, Dent. Mater. 34 (2018) 40–57, https://doi.org/10.1016/j.dental.2017.09.007.
[61] F. Schwarz, D. Ferrari, M. Herten, I. Mihatovic, M. Wieland, M. Sager, J. Becker, Effects of surface hydrophilicity and microtopography on early stages of soft and hard tissue integration at non-submerged titanium implants: an immunohistochemical study in dogs, J. Periodontol. 78 (2007) 2171–2184, https://doi.org/10.1902/jop.2007.070157.
[62] F. Schwarz, A. Sculean, M. Wieland, N. Horn, E. Nuesry, C. Bube, J. Becker, Effects of hydrophilicity and microtopography of titanium implant surfaces on initial supragingival plaque biofilm formation. A pilot study, Mund-, Kiefer-Gesichtschirurgie 11 (2007) 333–338, https://doi.org/10.1007/s10006-007-0079-z.
[63] I. Demetrescu, C. Pirvu, V. Mitran, Effect of nano-topographical features of Ti/TiO (2) electrode surface on cell response and electrochemical stability in artificial saliva, Bioelectrochemistry 79 (2010) 122–129, https://doi.org/10.1016/j.bioelechem.2010.02.001.
[64] M. Dorkhan, J. Hall, P. Uvdal, A. Sandell, G. Svensäter, J.R. Davies, Crystalline anatase-rich titanium can reduce adherence of oral streptococci, Biofouling 30 (2014) 751–759, https://doi.org/10.1080/08927014.2014.922962.
[65] A. Wennerberg, V. Fröjd, M. Olsson, U. Nannmark, L. Emanuelsson, P. Johansson, Y. Josefsson, I. Kangasniemi, T. Peltola, T. Tirri, T. Pänkäläinen, P. Thomsen, Nanoporous TiO(2) thin film on titanium oral implants for enhanced human soft tissue adhesion: a light and electron microscopy study, Clin. Implant Dent. Relat. Res. 13 (2011) 184–196, https://doi.org/10.1111/j.1708-8208.2009.00207.x.
[66] G. Iglhaut, K. Becker, V. Golubovic, H. Schliephake, I. Mihatovic, The impact of dis-/reconnection of laser microgrooved and machined implant abutments on soft- and hard-tissue healing, Clin. Oral Implants Res. 24 (2013) 391–397, https://doi.org/10.1111/clr.12040.
[67] A. Leong, I. De Kok, D. Mendonca, L.F. Cooper, Molecular assessment of human peri-implant mucosal healing at laser-modified and machined titanium abutments, Int. J. Oral Maxillofac. Implants 33 (2018) 895–904, https://doi.org/10.11607/jomi.6367.
[68] B.H. Zhao, F.Z. Cui, Y. Liu, C.F. Deng, Histomorphometrical and clinical study of connective tissue around titanium dental implants with porous surfaces in a canine model, J. Biomater. Appl. 27 (2013) 685–693, https://doi.org/10.1177/0885328211422414.
[69] H.H. Chien, R.L. Schroering, H.S. Prasad, D.N. Tatakis, Effects of a new implant abutment design on peri-implant soft tissues, J. Oral Implantol. 40 (2014) 581–588, https://doi.org/10.1563/AAID-JOI-D-12-00313.
[70] R. Neiva, N. Tovar, R. Jimbo, L.F. Gil, P. Goldberg, J.P. Barbosa, T. Lilin, P. G. Coelho, The effect of laser-etched surface design on soft tissue healing of two different implant abutment systems: an experimental study in dogs, Int. J. Periodontics Restor. Dent. 36 (2016) 673–679, https://doi.org/10.11607/prd.2940.
[71] D.B.R. Martins, M.M. Provinciatti, V.A. Muglia, A.J. Novaes, The effect of laser-lok abutments on fiber orientation and buccal bone remodeling: a histomorphometric study, Int. J. Periodontics Restor. Dent. 40 (2020) 73–81, https://doi.org/10.11607/prd.4426.
[72] A. Pae, H. Lee, H.S. Kim, Y.D. Kwon, Y.H. Woo, Attachment and growth behaviour of human gingival fibroblasts on titanium and zirconia ceramic surfaces, Biomed. Mater. 4 (2009), 025005, https://doi.org/10.1088/1748-6041/4/2/025005.
[73] N. Esfahanizadeh, S. Motalebi, N. Daneshparvar, N. Akhoundi, S. Bonakdar, Morphology, proliferation, and gene expression of gingival fibroblasts on laser-lok, titanium, and zirconia surfaces, Laser Med. Sci. 31 (2016) 863–873, https://doi.org/10.1007/s10103-016-1927-6.
[74] K. Gulati, H.J. Moon, P. Kumar, P. Han, S. Ivanovski, Anodized anisotropic titanium surfaces for enhanced guidance of gingival fibroblasts, Mater Sci Eng C Mater Biol Appl 112 (2020), 110860, https://doi.org/10.1016/j.msec.2020.110860.
[75] S. Ferraris, V. Guarino, A. Cochis, A. Varesano, I.C. Maya, C. Vineis, L. Rimondini, S. Spriano, Aligned keratin submicrometric-fibers for fibroblasts guidance onto nanogrooved titanium surfaces for transmucosal implants, Mater. Lett. 229 (2018) 1–4, https://doi.org/10.1016/j.matlet.2018.06.103.
[76] M.A. Llopis-Grimalt, A.M. Amengual-Tugores, M. Monjo, J.M. Ramis, Oriented cell alignment induced by a nanostructured titanium surface enhances expression of cell differentiation markers, Nanomaterials 9 (2019), https://doi.org/10.3390/nano9121661.
[77] F.H. Schünemann, M.E. Galárraga-Vinueza, R. Magini, M. Fredel, F. Silva, J.C. M. Souza, Y. Zhang, B. Henriques, Zirconia surface modifications for implant dentistry, Mater Sci Eng C Mater Biol Appl 98 (2019) 1294–1305, https://doi.org/10.1016/j.msec.2019.01.062.
[78] J. Park, S. Bauer, K. von der Mark, P. Schmuki, Nanosize and vitality: TiO2 nanotube diameter directs cell fate, Nano Lett. 7 (2007) 1686–1691, https://doi.org/10.1021/nl070678d.
[79] M. Weszl, K.L. Tóth, I. Kientzl, P. Nagy, D. Pammer, L. Pelyhe, N.E. Vrana, D. Scharnweber, C. Wolf-Brandstetter, F.Á. Joób, E. Bognár, Investigation of the mechanical and chemical characteristics of nanotubular and nano-pitted anodic films on grade 2 titanium dental implant materials, Mater Sci Eng C Mater Biol Appl 78 (2017) 69–78, https://doi.org/10.1016/j.msec.2017.04.032.
[80] Y. Yang, M. Zheng, Y. Yang, J. Li, Y.F. Su, H.P. Li, J.G. Tan, Inhibition of bacterial growth on zirconia abutment with a helium cold atmospheric plasma jet treatment, Clin. Oral Invest. 24 (2020) 1465–1477, https://doi.org/10.1007/s00784-019-03179-2.
[81] B. Grossner-Schreiber, M. Herzog, J. Hedderich, A. Duck, M. Hannig, M. Griepentrog, Focal adhesion contact formation by fibroblasts cultured on surface-modified dental implants: an in vitro study, Clin. Oral Implants Res. 17 (2006) 736–745, https://doi.org/10.1111/j.1600-0501.2006.01277.x.
[82] Y. Akiyama, F. Iwasa, Y. Hotta, T. Matsumoto, Y. Oshima, K. Baba, Effects of surface roughness of ceria-stabilized zirconia/alumina nanocomposite on the morphology and function of human gingival fibroblasts, Dent. Mater. J. 40 (2021) 472–480, https://doi.org/10.4012/dmj.2019-435.
[83] B. Klinge, J. Meyle, Soft-tissue integration of implants. Consensus report of working group 2, Clin. Oral Implants Res. 17 (Suppl 2) (2006) 93–96, https://doi.org/10.1111/j.1600-0501.2006.001366.x.
[84] N. Tan, A. Khan, E. Antunes, C.M. Miller, D. Sharma, The effects of physical decontamination methods on zirconia implant surfaces: a systematic review, J Periodontal Implant Sci 51 (2021) 298–315, https://doi.org/10.5051/jpis.2005080254.
[85] M. Petrini, A. Giuliani, E. Di Campli, S. Di Lodovico, G. Iezzi, A. Piattelli, S. D'Ercole, The bacterial anti-adhesive activity of double-etched titanium (DAE) as a dental implant surface, Int. J. Mol. Sci. 21 (2020), https://doi.org/10.3390/ijms21218315.
[86] S. Veerachamy, T. Yarlagadda, G. Manivasagam, P.K. Yarlagadda, Bacterial adherence and biofilm formation on medical implants: a review, Proc. Inst. Mech. Eng. H 228 (2014) 1083–1099, https://doi.org/10.1177/0954411914556137.
[87] E.D. de Avila, B.A. van Oirschot, J. van den Beucken, Biomaterial-based possibilities for managing peri-implantitis, J. Periodontal. Res. 55 (2020) 165–173, https://doi.org/10.1111/jre.12707.
[88] N. Rohr, B. Zeller, L. Matthisson, J. Fischer, Surface structuring of zirconia to increase fibroblast viability, Dent. Mater. 36 (2020) 779–786, https://doi.org/10.1016/j.dental.2020.03.024.
[89] C.M. Bollen, W. Papaioanno, J. Van Eldere, E. Schepers, M. Quirynen, D. van Steenberghe, The influence of abutment surface roughness on plaque accumulation and peri-implant mucositis, Clin. Oral Implants Res. 7 (1996) 201–211, https://doi.org/10.1034/j.1600-0501.1996.070302.x.
[90] D.L. Cochran, M. Obrecht, K. Weber, M. Dard, D. Bosshardt, F.L. Higginbottom, T. J. Wilson, A.A. Jones, Biologic width adjacent to loaded implants with machined and rough collars in the dog, Int. J. Periodontics Restor. Dent. 34 (2014) 773–779, https://doi.org/10.11607/prd.1990.
[91] G. Littuma, M.B. Sordi, C.R. Borges, A. Aragones, C.A. Da, R.S. Magini, Titanium coated with poly (lactic-Co-glycolic) acid incorporating simvastatin: biofunctionalization of dental prosthetic abutments, J. Periodontal. Res. 55 (2020) 116–124, https://doi.org/10.1111/jre.12695.
[92] Y. Iinuma, M. Hirota, T. Hayakawa, C. Ohkubo, Surrounding tissue response to surface-treated zirconia implants, Materials 13 (2019) 30, https://doi.org/10.3390/ma13010030.
[93] K.M. Hotchkiss, G.B. Reddy, S.L. Hyzy, Z. Schwartz, B.D. Boyan, R. Olivares-Navarrete, Titanium surface characteristics, including topography and wettability, alter macrophage activation, Acta Biomater. 31 (2016) 425–434, https://doi.org/10.1016/j.actbio.2015.12.003.
[94] K.M. Hotchkiss, N.M. Clark, R. Olivares-Navarrete, Macrophage response to hydrophilic biomaterials regulates MSC recruitment and T-helper cell

populations, Biomaterials 182 (2018) 202–215, https://doi.org/10.1016/j.biomaterials.2018.08.029.
[95] M. Quirynen, C.M. Bollen, W. Papaioannou, J. Van Eldere, D. van Steenberghe, The influence of titanium abutment surface roughness on plaque accumulation and gingivitis: short-term observations, Int. J. Oral Maxillofac. Implants 11 (1996) 169–178.
[96] E.G. Kleinschmidt, D.D. Schlaepfer, Focal adhesion kinase signaling in unexpected places, Curr. Opin. Cell Biol. 45 (2017) 24–30, https://doi.org/10.1016/j.ceb.2017.01.003.
[97] S. Paul, O. Hanisch, D. Nesic, Human gingival fibroblast proliferation on materials used for dental implant abutments: a systematic review, Int. J. Prosthodont. (IJP) 34 (2021) 811–828, https://doi.org/10.11607/ijp.7388.
[98] M. Yoshinari, Future prospects of zirconia for oral implants -A review, Dent. Mater. J. 39 (2020) 37–45, https://doi.org/10.4012/dmj.2019-151.
[99] A. Han, H. Ding, J. Tsoi, S. Imazato, J.P. Matinlinna, Z. Chen, Prolonged UV-C irradiation is a double-edged sword on the zirconia surface, ACS Omega 5 (2020) 5126–5133, https://doi.org/10.1021/acsomega.9b04123.
[100] L. Guo, R. Smeets, L. Kluwe, P. Hartjen, M. Barbeck, C. Cacaci, M. Gosau, A. Henningsen, Cytocompatibility of titanium, zirconia and modified PEEK after surface treatment using UV light or non-thermal plasma, Int. J. Mol. Sci. 20 (2019), https://doi.org/10.3390/ijms20225596.
[101] L. Canullo, T. Genova, M. Tallarico, G. Gautier, F. Mussano, D. Botticelli, Plasma of argon affects the earliest biological response of different implant surfaces: an in vitro comparative study, J. Dent. Res. 95 (2016) 566–573, https://doi.org/10.1177/0022034516629119.
[102] Y. Yang, J. Zhou, X. Liu, M. Zheng, J. Yang, J. Tan, Ultraviolet light-treated zirconia with different roughness affects function of human gingival fibroblasts in vitro: the potential surface modification developed from implant to abutment, J. Biomed. Mater. Res. B Appl. Biomater. 103 (2015) 116–124, https://doi.org/10.1002/jbm.b.33183.
[103] T. Tuna, M. Wein, B. Altmann, T. Steinberg, J. Fischer, W. Att, Effect of ultraviolet photofunctionalisation on the cell attractiveness of zirconia implant materials, Eur. Cell. Mater. 29 (2015) 82–94, https://doi.org/10.22203/ecm.v029a07. ; discussion 95-6,.
[104] S. Komasa, S. Takao, Y. Yang, Y. Zeng, M. Li, S. Yan, H. Zhang, C. Komasa, Y. Kobayashi, H. Nishizaki, H. Nishida, T. Kusumoto, J. Okazaki, Effects of UV treatment on ceria-stabilized zirconia/alumina nanocomposite (NANOZR), Materials 13 (2020), https://doi.org/10.3390/ma13122772.
[105] Q.M. Al, Y. Wu, S. Spintzyk, P. Krieg, A. Killinger, E. Schweizer, I. Stephan, L. Scheideler, J. Geis-Gerstorfer, F. Rupp, UV-A and UV-C light induced hydrophilization of dental implants, Dent. Mater. 31 (2015) e157–e167, https://doi.org/10.1016/j.dental.2015.04.011.
[106] T. Tuna, M. Wein, M. Swain, J. Fischer, W. Att, Influence of ultraviolet photofunctionalization on the surface characteristics of zirconia-based dental implant materials, Dent. Mater. 31 (2015) e14–e24, https://doi.org/10.1016/j.dental.2014.10.008.
[107] S. Riivari, K. Shahramian, I. Kangasniemi, J. Willberg, T. Närhi, TiO2-Modified zirconia surface improves epithelial cell attachment, Int. J. Oral Maxillofac. Implants 34 (2019) 313–319, https://doi.org/10.11607/jomi.6862.
[108] M. Razali, W.C. Ngeow, R.A. Omar, W.L. Chai, An in-vitro analysis of peri-implant mucosal seal following photofunctionalization of zirconia abutment materials, Biomedicines 9 (2021), https://doi.org/10.3390/biomedicines9010078.
[109] Y. Yang, M. Zheng, Y. Liao, J. Zhou, H. Li, J. Tan, Different behavior of human gingival fibroblasts on surface modified zirconia: a comparison between ultraviolet (UV) light and plasma, Dent. Mater. J. 38 (2019) 756–763, https://doi.org/10.4012/dmj.2018-101.
[110] K. Kobune, T. Miura, T. Sato, M. Yotsuya, M. Yoshinari, Influence of plasma and ultraviolet treatment of zirconia on initial attachment of human oral keratinocytes: expressions of laminin Gamma2 and integrin Beta4, Dent. Mater. J. 33 (2014) 696–704, https://doi.org/10.4012/dmj.2014-087.
[111] K.M. Hotchkiss, N.B. Ayad, S.L. Hyzy, B.D. Boyan, R. Olivares-Navarrete, Dental implant surface chemistry and energy alter macrophage activation in vitro, Clin. Oral Implants Res. 28 (2017) 414–423, https://doi.org/10.1111/clr.12814.
[112] Y. Wang, Y. Zhang, A. Sculean, D.D. Bosshardt, R.J. Miron, Macrophage behavior and interplay with gingival fibroblasts cultured on six commercially available titanium, zirconium, and titanium-zirconium dental implants, Clin. Oral Invest. 23 (2019) 3219–3227, https://doi.org/10.1007/s00784-018-2736-z.
[113] C.J. Oates, W. Wen, D.W. Hamilton, Role of titanium surface topography and surface wettability on focal adhesion kinase mediated signaling in fibroblasts, Materials 4 (2011) 893–907, https://doi.org/10.3390/ma4050893.
[114] F. Schwarz, M. Wieland, Z. Schwartz, G. Zhao, F. Rupp, J. Geis-Gerstorfer, A. Schedle, N. Broggini, M.M. Bornstein, D. Buser, S.J. Ferguson, J. Becker, B. D. Boyan, D.L. Cochran, Potential of chemically modified hydrophilic surface characteristics to support tissue integration of titanium dental implants, J. Biomed. Mater. Res. B Appl. Biomater. 88 (2009) 544–557, https://doi.org/10.1002/jbm.b.31233.
[115] C.J. Wilson, R.E. Clegg, D.I. Leavesley, M.J. Pearcy, Mediation of biomaterial-cell interactions by adsorbed proteins: a review, Tissue Eng. 11 (2005) 1–18, https://doi.org/10.1089/ten.2005.11.1.
[116] S. Gibbs, S. Roffel, M. Meyer, A. Gasser, Biology of soft tissue repair: gingival epithelium in wound healing and attachment to the tooth and abutment surface, Eur. Cell. Mater. 38 (2019) 63–78, https://doi.org/10.22203/eCM.v038a06.
[117] R.A. Gittens, L. Scheideler, F. Rupp, S.L. Hyzy, J. Geis-Gerstorfer, Z. Schwartz, B. D. Boyan, A review on the wettability of dental implant surfaces II: biological and clinical aspects, Acta Biomater. 10 (2014) 2907–2918, https://doi.org/10.1016/j.actbio.2014.03.032.
[118] M. Zheng, Y. Yang, X.Q. Liu, M.Y. Liu, X.F. Zhang, X. Wang, H.P. Li, J.G. Tan, Enhanced biological behavior of in vitro human gingival fibroblasts on cold plasma-treated zirconia, PLoS One 10 (2015), e0140278, https://doi.org/10.1371/journal.pone.0140278.
[119] M. Welander, I. Abrahamsson, E. Linder, B. Liljenberg, T. Berglundh, Soft tissue healing at titanium implants coated with type I collagen. An experimental study in dogs, J. Clin. Periodontol. 34 (2007) 452–458, https://doi.org/10.1111/j.1600-051X.2007.01073.x.
[120] H. Lin, V.S. Van'T, C.P. Klein, Permucosal implantation pilot study with HA-coated dental implant in dogs, Biomaterials 13 (1992) 825–831, https://doi.org/10.1016/0142-9612(92)90175-n.
[121] M. Cruz, J.F. Marques, B.F. Fernandes, M. Costa, G. Miranda, A. Mata, J. Carames, F.S. Silva, Gingival fibroblasts behavior on bioactive zirconia and titanium dental implant surfaces produced by a functionally graded technique, J. Appl. Oral Sci. 28 (2020), e20200100, https://doi.org/10.1590/1678-7757-2020-0100.
[122] U.T. Kalyoncuoglu, B. Yilmaz, S.G. Koc, Z. Evis, P.U. Arpaci, G. Kansu, Investigation of surface structure and biocompatibility of chitosan-coated zirconia and alumina dental abutments, Clin. Implant Dent. R. 20 (2018) 1022–1029, https://doi.org/10.1111/cid.12665.
[123] H. Lin, J. Chen, Osteoblast differentiation and phenotype expressions on chitosan-coated Ti-6Al-4V, Carbohydr. Polym. 97 (2013) 618–626, https://doi.org/10.1016/j.carbpol.2013.05.048.
[124] M. Welander, I. Abrahamsson, E. Linder, B. Liljenberg, T. Berglundh, Soft tissue healing at titanium implants coated with type I collagen. An experimental study in dogs, J. Clin. Periodontol. 34 (2007) 452–458, https://doi.org/10.1111/j.1600-051X.2007.01073.x.
[125] D. Chopra, A. Jayasree, T. Guo, K. Gulati, S. Ivanovski, Advancing dental implants: bioactive and therapeutic modifications of zirconia, Bioact. Mater. 13 (2022) 161–178, https://doi.org/10.1016/j.bioactmat.2021.10.010.
[126] F. Ahsan, T.M. Ansari, S. Usmani, P. Bagga, An insight on silk protein sericin: from processing to biomedical application, Drug Res. 68 (2018) 317–327, https://doi.org/10.1055/s-0043-121464.
[127] M.S. Zafar, F. Amin, M.A. Fareed, H. Ghabbani, S. Riaz, Z. Khurshid, N. Kumar, Biomimetic aspects of restorative dentistry biomaterials, Biomimetics 5 (2020), https://doi.org/10.3390/biomimetics5030034.
[128] Z. Kang, Y. Wang, J. Xu, G. Song, M. Ding, H. Zhao, J. Wang, An RGD-containing peptide derived from wild silkworm silk fibroin promotes cell adhesion and spreading, Polym. Bull. (Heidelberg, Ger.) 10 (2018) 1193, https://doi.org/10.3390/polym10111193.
[129] C. Wang, S. Wang, Y. Yang, Z. Jiang, Y. Deng, S. Song, W. Yang, Z.G. Chen, Bioinspired, biocompatible and peptide-decorated silk fibroin coatings for enhanced osteogenesis of bioinert implant, J. Biomater. Sci. Polym. Ed. 29 (2018) 1595–1611, https://doi.org/10.1080/09205063.2018.1477316.
[130] S. Kapoor, S.C. Kundu, Silk protein-based hydrogels: promising advanced materials for biomedical applications, Acta Biomater. 31 (2016) 17–32, https://doi.org/10.1016/j.actbio.2015.11.034.
[131] F. Wang, Y. Pang, G. Chen, W. Wang, Z. Chen, Enhanced physical and biological properties of chitosan scaffold by silk proteins cross-linking, carbohyd, Polym 229 (2020), 115529, https://doi.org/10.1016/j.carbpol.2019.115529.
[132] Y. Qu, G. Hong, L. Liu, K. Sasaki, X. Chen, Evaluation of silk fibroin electrogel coating for zirconia material surface, Dent. Mater. J. 38 (2019) 813–820, https://doi.org/10.4012/dmj.2018-228.
[133] L. Nilebäck, M. Widhe, J. Seijsing, H. Bysell, P.K. Sharma, M. Hedhammar, Bioactive silk coatings reduce the adhesion of Staphylococcus aureus while supporting growth of osteoblast-like cells, ACS Appl. Mater. Interfaces 11 (2019) 24999–25007, https://doi.org/10.1021/acsami.9b05531.
[134] H. Teramoto, K. Nakajima, C. Takabayashi, Preparation of elastic silk sericin hydrogel, Biosci. Biotechnol. Biochem. 69 (2005) 845–847, https://doi.org/10.1271/bbb.69.845.
[135] L. Lamboni, M. Gauthier, G. Yang, Q. Wang, Silk sericin: a versatile material for tissue engineering and drug delivery, Biotechnol. Adv. 33 (2015) 1855–1867, https://doi.org/10.1016/j.biotechadv.2015.10.014.
[136] L. Shi, N. Yang, H. Zhang, L. Chen, L. Tao, Y. Wei, H. Liu, Y. Luo, A novel poly (Γ-Glutamic acid)/silk-sericin hydrogel for wound dressing: synthesis, characterization and biological evaluation, Mater. Sci. Eng. C 48 (2015) 533–540, https://doi.org/10.1016/j.msec.2014.12.047.
[137] M. Liu, J. Zhou, Y. Yang, M. Zheng, J. Yang, J. Tan, Surface modification of zirconia with polydopamine to enhance fibroblast response and decrease bacterial activity in vitro: a potential technique for soft tissue engineering applications, Colloids Surf. B Biointerfaces 136 (2015) 74–83, https://doi.org/10.1016/j.colsurfb.2015.06.047.
[138] Y. Zhu, D. Liu, X. Wang, Y. He, W. Luan, F. Qi, J. Ding, Polydopamine-mediated covalent functionalization of collagen on a titanium alloy to promote biocompatibility with soft tissues, J. Mater. Chem. B 7 (2019) 2019–2031, https://doi.org/10.1039/C8TB03379J.
[139] M. Stimmelmayr, D. Edelhoff, J.F. Güth, K. Erdelt, A. Happe, F. Beuer, Wear at the titanium-titanium and the titanium-zirconia implant-abutment interface: a comparative in vitro study, Dent. Mater. 28 (2012) 1215–1220, https://doi.org/10.1016/j.dental.2012.08.008.
[140] H. Lee, S.M. Dellatore, W.M. Miller, P.B. Messersmith, Mussel-inspired surface chemistry for multifunctional coatings, Science 318 (2007) 426–430, https://doi.org/10.1126/science.1147241.
[141] S.H. Ku, J. Ryu, S.K. Hong, H. Lee, C.B. Park, General functionalization route for cell adhesion on non-wetting surfaces, Biomaterials 31 (2010) 2535–2541, https://doi.org/10.1016/j.biomaterials.2009.12.020.

[142] A.K. Awasthi, S. Gupta, J. Thakur, S. Gupta, S. Pal, A. Bajaj, A. Srivastava, Polydopamine-on-liposomes: stable nanoformulations, uniform coatings and superior antifouling performance, Nanoscale 12 (2020) 5021–5030, https://doi.org/10.1039/C9NR07770G.
[143] U.T. Kalyoncuoglu, B. Yilmaz, S.G. Koc, Z. Evis, P.U. Arpaci, G. Kansu, Investigation of surface structure and biocompatibility of chitosan-coated zirconia and alumina dental abutments, Clin. Implant Dent. Relat. Res. 20 (2018) 1022–1029, https://doi.org/10.1111/cid.12665.
[144] S.W. Hsiao, D.V. Thien, M.H. Ho, H.J. Hsieh, C.H. Li, C.H. Hung, H.H. Li, Interactions between chitosan and cells measured by AFM, Biomed. Mater. 5 (2010), 054117, https://doi.org/10.1088/1748-6041/5/5/054117.
[145] E.C. Kim, D.Y. Lee, M.H. Lee, H.J. Lee, K.H. Kim, R. Leesungbok, S.J. Ahn, S. J. Park, J.H. Yoon, Y.J. Jee, S.C. Lee, S.W. Lee, The effect of fibronectin-immobilized microgrooved titanium substrata on cell proliferation and expression of genes and proteins in human gingival fibroblasts, Tissue Eng. Regen. Med. 15 (2018) 615–627, https://doi.org/10.1007/s13770-018-0153-7.
[146] Q. Ma, W. Wang, P.K. Chu, S. Mei, K. Ji, L. Jin, Y. Zhang, Concentration- and time-dependent response of human gingival fibroblasts to fibroblast growth factor 2 immobilized on titanium dental implants, Int. J. Nanomed. 7 (2012) 1965–1976, https://doi.org/10.2147/IJN.S29538.
[147] H.B. Lin, C. García-Echeverría, S. Asakura, W. Sun, D.F. Mosher, S.L. Cooper, Endothelial cell adhesion on polyurethanes containing covalently attached RGD-peptides, Biomaterials 13 (1992) 905–914, https://doi.org/10.1016/0142-9612(92)90113-3.
[148] G. Vidal, T. Blanchi, A.J. Mieszawska, R. Calabrese, C. Rossi, P. Vigneron, J. Duval, D.L. Kaplan, C. Egles, Enhanced cellular adhesion on titanium by silk functionalized with titanium binding and RGD peptides, Acta Biomater. 9 (2013) 4935–4943, https://doi.org/10.1016/j.actbio.2012.09.003.
[149] U. Hersel, C. Dahmen, H. Kessler, RGD modified polymers: biomaterials for stimulated cell adhesion and beyond, Biomaterials 24 (2003) 4385–4415, https://doi.org/10.1016/S0142-9612(03)00343-0.
[150] E. Fernandez-Garcia, X. Chen, C.F. Gutierrez-Gonzalez, A. Fernandez, S. Lopez-Esteban, C. Aparicio, Peptide-functionalized zirconia and new zirconia/titanium biocermets for dental applications, J. Dent. 43 (2015) 1162–1174, https://doi.org/10.1016/j.jdent.2015.06.002.
[151] J. Minguela, D.W. Müller, F. Mücklich, L. Llanes, M.P. Ginebra, J.J. Roa, C. Mas-Moruno, Peptidic biofunctionalization of laser patterned dental zirconia: a biochemical-topographical approach, Mater. Sci. Eng. C 125 (2021), 112096, https://doi.org/10.1016/j.msec.2021.112096.
[152] Z. Yang, M. Liu, Y. Yang, M. Zheng, Y. Yang, X. Liu, J. Tan, Biofunctionalization of zirconia with cell-adhesion peptides via polydopamine crosslinking for soft tissue engineering: effects on the biological behaviors of human gingival fibroblasts and oral bacteria, RSC Adv. 10 (2020) 6200–6212, https://doi.org/10.1039/c9ra08575k.
[153] P. Gehrke, A. Tabellion, C. Fischer, Microscopical and chemical surface characterization of CAD/CAM zircona abutments after different cleaning procedures. A qualitative analysis, J. Adv. Prosthodont. 7 (2015) 151–159, https://doi.org/10.4047/jap.2015.7.2.151.
[154] V. Rutkunas, R. Borusevicius, D. Liaudanskaite, U. Jasinskyte, S. Drukteinis, V. Bukelskiene, E. Mijiritsky, The effect of different cleaning protocols of polymer-based prosthetic materials on the behavior of human gingival fibroblasts, Int. J. Environ. Res. Publ. Health 17 (2020), https://doi.org/10.3390/ijerph17217753.
[155] K. Nakajima, T. Odatsu, A. Shinohara, K. Baba, Y. Shibata, T. Sawase, Effects of cleaning methods for custom abutment surfaces on gene expression of human gingival fibroblasts, J. Oral Sci. 59 (2017) 533–539, https://doi.org/10.2334/josnusd.16-0681.
[156] G. John, J. Becker, F. Schwarz, Effects of different titanium zirconium implant surfaces on initial supragingival plaque formation, Clin. Oral Implants Res. 28 (2017) e84–e90, https://doi.org/10.1111/clr.12878.
[157] K. Yamane, Y. Ayukawa, T. Takeshita, A. Furuhashi, Y. Yamashita, K. Koyano, Bacterial adhesion affinities of various implant abutment materials, Clin. Oral Implants Res. 24 (2013) 1310–1315, https://doi.org/10.1111/j.1600-0501.2012.02574.x.
[158] H. Herrmann, J.S. Kern, T. Kern, J. Lautensack, G. Conrads, S. Wolfart, Early and mature biofilm on four different dental implant materials: an in vivo human study, Clin. Oral Implants Res. 31 (2020) 1094–1104, https://doi.org/10.1111/clr.13656.
[159] U. Salihoglu, D. Boynuegri, D. Engin, A.N. Duman, P. Gokalp, K. Balos, Bacterial adhesion and colonization differences between zirconium oxide and titanium alloys: an in vivo human study, Int. J. Oral Maxillofac. Implants 26 (2011) 101–107.
[160] E.M. Lima, H. Koo, S.A. Vacca, P.L. Rosalen, B.C.A. Del, Adsorption of salivary and serum proteins, and bacterial adherence on titanium and zirconia ceramic surfaces, Clin. Oral Implants Res. 19 (2008) 780–785, https://doi.org/10.1111/j.1600-0501.2008.01524.x.
[161] C. Montoya, L. Roldan, M. Yu, S. Valliani, C. Ta, M. Yang, S. Orrego, Smart dental materials for antimicrobial applications, Bioact. Mater. 24 (2023) 1–19, https://doi.org/10.1016/j.bioactmat.2022.12.002.
[162] Z. Iqbal, E.P.C. Lai, T.J. Avis, Antimicrobial effect of polydopamine coating on Escherichia coli, J. Mater. Chem. 22 (2012), 21608, https://doi.org/10.1039/c2jm34825j.
[163] M. Liu, J. Zhou, Y. Yang, M. Zheng, J. Yang, J. Tan, Surface modification of zirconia with polydopamine to enhance fibroblast response and decrease bacterial activity in vitro: a potential technique for soft tissue engineering applications, Colloids Surf. B Biointerfaces 136 (2015) 74–83, https://doi.org/10.1016/j.colsurfb.2015.06.047.
[164] K. Shahramian, H. Leminen, V. Meretoja, P. Linderback, I. Kangasniemi, L. Lassila, A. Abdulmajeed, T. Narhi, Sol-gel derived bioactive coating on zirconia: effect on flexural strength and cell proliferation, J. Biomed. Mater. Res. B Appl. Biomater. 105 (2017) 2401–2407, https://doi.org/10.1002/jbm.b.33780.
[165] V.V. Meretoja, S. Rossi, T. Peltola, L.J. Pelliniemi, T.O. Narhi, Adhesion and proliferation of human fibroblasts on sol-gel coated titania, J. Biomed. Mater. Res. A. 95 (2010) 269–275, https://doi.org/10.1002/jbm.a.32829.
[166] H. Paldan, S. Areva, T. Tirri, T. Peltola, T.C. Lindholm, L. Lassila, L.J. Pelliniemi, R.P. Happonen, T.O. Närhi, Soft tissue attachment on sol-gel-treated titanium implants in vivo, J. Mater. Sci. Mater. Med. 19 (2008) 1283–1290, https://doi.org/10.1007/s10856-007-3234-z.
[167] B.E. Pjetursson, C. Zarauz, M. Strasding, I. Sailer, M. Zwahlen, A. Zembic, A systematic review of the influence of the implant-abutment connection on the clinical outcomes of ceramic and metal implant abutments supporting fixed implant reconstructions, Clin. Oral Implants Res. 29 (Suppl 18) (2018) 160–183, https://doi.org/10.1111/clr.13362.
[168] R. Caricasulo, L. Malchiodi, P. Ghensi, G. Fantozzi, A. Cucchi, The influence of implant-abutment connection to peri-implant bone loss: a systematic review and meta-analysis, Clin. Implant Dent. Relat. Res. 20 (2018) 653–664, https://doi.org/10.1111/cid.12620.
[169] L. Canullo, P.H. Rossetti, D. Penarrocha, Identification of Enterococcus faecalis and Pseudomonas aeruginosa on and in implants in individuals with peri-implant disease: a cross-sectional study, Int. J. Oral Maxillofac. Implants 30 (2015) 583–587, https://doi.org/10.11607/jomi.3946.
[170] D.A. Queiroz, N. Hagee, D.J. Lee, F. Zheng, The behavior of a zirconia or metal abutment on the implant-abutment interface during cyclic loading, J. Prosthet. Dent 124 (2020) 211–216, https://doi.org/10.1016/j.prosdent.2019.09.023.
[171] M. Baldassarri, J. Hjerppe, D. Romeo, S. Fickl, V.P. Thompson, C.F. Stappert, Marginal accuracy of three implant-ceramic abutment configurations, Int. J. Oral Maxillofac. Implants 27 (2012) 537–543.
[172] I. Ramalho, L. Witek, P.G. Coelho, E. Bergamo, L.F. Pegoraro, E.A. Bonfante, Influence of abutment fabrication method on 3D fit at the implant-abutment connection, Int. J. Prosthodont. (IJP) 33 (2020) 641–647, https://doi.org/10.11607/ijp.6574.
[173] L. Guida, A. Oliva, M.A. Basile, M. Giordano, L. Nastri, M. Annunziata, Human gingival fibroblast functions are stimulated by oxidized nano-structured titanium surfaces, J. Dent. 41 (2013) 900–907, https://doi.org/10.1016/j.jdent.2013.07.009.
[174] N. Rohr, B. Zeller, L. Matthisson, J. Fischer, Surface structuring of zirconia to increase fibroblast viability, Dent. Mater. 36 (2020) 779–786, https://doi.org/10.1016/j.dental.2020.03.024.
[175] T.Y. Peng, Y.H. Shih, S.M. Hsia, T.H. Wang, P.J. Li, D.J. Lin, K.T. Sun, K.C. Chiu, T.M. Shieh, In vitro assessment of the cell metabolic activity, cytotoxicity, cell attachment, and inflammatory reaction of human oral fibroblasts on polyetheretherketone (PEEK) implant-abutment, Polymers 13 (2021), https://doi.org/10.3390/polym13172995.
[176] I. Atsuta, Y. Ayukawa, Y. Ogino, Y. Moriyama, Y. Jinno, K. Koyano, Evaluations of epithelial sealing and peri-implant epithelial down-growth around "Step-Type" implants, Clin. Oral Implants Res. 23 (2012) 459–466, https://doi.org/10.1111/j.1600-0501.2011.02163.x.
[177] L. Shang, D. Deng, J.K. Buskermolen, M.M. Janus, B.P. Krom, S. Roffel, T. Waaijman, C. van Loveren, W. Crielaard, S. Gibbs, Multi-species oral biofilm promotes reconstructed human gingiva epithelial barrier function, Sci. Rep. 8 (2018), 16061, https://doi.org/10.1038/s41598-018-34390-y.
[178] L.M. Cardoso, T.N. Pansani, J. Hebling, C.C. de Souza, F.G. Basso, Photobiomodulation of inflammatory-cytokine-related effects in a 3-D culture model with gingival fibroblasts, Laser Med. Sci. 35 (2020) 1205–1212, https://doi.org/10.1007/s10103-020-02974-8.
[179] E.R. Shamir, A.J. Ewald, Three-dimensional organotypic culture: experimental models of mammalian biology and disease, Nat. Rev. Mol. Cell Biol. 15 (2014) 647–664, https://doi.org/10.1038/nrm3873.
[180] W.L. Chai, I.M. Brook, L. Emanuelsson, A. Palmquist, R. van Noort, K. Moharamzadeh, Ultrastructural analysis of implant-soft tissue interface on a three dimensional tissue-engineered oral mucosal model, J. Biomed. Mater. Res. A. 100 (2012) 269–277, https://doi.org/10.1002/jbm.a.33245.
[181] S. Roffel, G. Wu, I. Nedeljkovic, M. Meyer, T. Razafiarison, S. Gibbs, Evaluation of a novel oral mucosa in vitro implantation model for analysis of molecular interactions with dental abutment surfaces, Clin. Implant Dent. Relat. Res. 21 (Suppl 1) (2019) 25–33, https://doi.org/10.1111/cid.12750.
[182] M. Razali, W.C. Ngeow, R.A. Omar, W.L. Chai, An in-vitro analysis of peri-implant mucosal seal following photofunctionalization of zirconia abutment materials, Biomedicines 9 (2021), https://doi.org/10.3390/biomedicines9010078.
[183] R.A. Delgado-Ruiz, J.L. Calvo-Guirado, M. Abboud, M.P. Ramirez-Fernandez, D.V. J. Maté-Sánchez, B. Negri, G. Gomez-Moreno, A. Markovic, Connective tissue characteristics around healing abutments of different geometries: new methodological technique under circularly polarized light, Clin. Implant Dent. Relat. Res. 17 (2015) 667–680, https://doi.org/10.1111/cid.12161.

[184] J. Hu, I. Atsuta, Y. Ayukawa, T. Zhou, I. Narimatsu, K. Koyano, Effect of titanium or zirconia implant abutments on epithelial attachments after ultrasonic cleaning, J. Oral Sci. 62 (2020) 331–334, https://doi.org/10.2334/josnusd.19-0332.
[185] H. Kweon, S. Lee, B. Hahn, Y. Lee, S. Kim, Hydroxyapatite and silk combination-coated dental implants result in superior bone formation in the peri-implant area compared with hydroxyapatite and collagen combination-coated implants, J. Oral Maxillofac. Surg. 72 (2014) 1928–1936, https://doi.org/10.1016/j.joms.2014.06.455.
[186] P. Pandoleon, A. Bakopoulou, L. Papadopoulou, P. Koidis, Evaluation of the biological behaviour of various dental implant abutment materials on attachment and viability of human gingival fibroblasts, Dent. Mater. 35 (2019) 1053–1063, https://doi.org/10.1016/j.dental.2019.04.010.