

## Review article

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

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## 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.

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

(continued on next page)

Table 1 (continued)

| Study No. | Investigated material    | Surface modification                                                                                       | <i>In vivo/in vitro</i> study | Bioactivity evaluation/conclusion                                                                                                                                                                   | Contact angle                              | Roughness                                            | Ref.  |
|-----------|--------------------------|------------------------------------------------------------------------------------------------------------|-------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|------------------------------------------------------|-------|
| 14        | Y-TZP; NANOZR            | Coated with silk fibroin                                                                                   | <i>in vitro</i>               | 1. A silk fibroin electrogel coating had sufficient bonding strength<br>2. The biocompatibility of zirconia was improved.                                                                           |                                            |                                                      | [132] |
| 15        | ZrO <sub>2</sub>         | Coated with polydopamine (PDA)                                                                             | HGFs <i>in vitro</i>          | 1. Cell attachment and proliferation were increased;<br>2. Bacterial adhesion was reduced.                                                                                                          | Before: 78 ± 4°;<br>After: 64 ± 1°         | Before: 0.065 ± 0.022 μm;<br>After: 0.071 ± 0.026 μm | [137] |
| 16        | ZrO <sub>2</sub>         | Coated with chitosan                                                                                       | HGFs <i>in vitro</i>          | 1. HGF-1 cells were shown to attach and proliferate well                                                                                                                                            | –                                          | –                                                    | [143] |
| 17        | Y-TZP                    | Coated by RGD-containing peptide                                                                           | <i>in vitro</i>               | 1. Cell adhesion was significantly enhanced.                                                                                                                                                        | –                                          | –                                                    | [150] |
| 18        | Y-TZP                    | RGD peptidic biofunctionalization and laser micro-patterns                                                 | <i>in vitro</i>               | 1. Migration was greatly enhanced along the grooves;<br>2. No effects on cell migration were found for the peptidic platform;<br>3. Cell number and area were increased after biofunctionalization. | –                                          | –                                                    | [151] |
| 19        | ZrO <sub>2</sub>         | A multi-step research cleaning method                                                                      | HGFs <i>in vitro</i>          | 1. Surface contact angle was reduced; 2. HGF viability was enhanced.                                                                                                                                | Before: 98.7 ± 4.5°;<br>After: 69.9 ± 6.4° | After: 0.079 ± 0.017 μm                              | [154] |
| 20        | ZrO <sub>2</sub>         | Reagent (PK) and vacuum plasma cleaning                                                                    | HGFs <i>in vitro</i>          | 1. Initial HGF attachment was affected;<br>2. Gene expression of type I collagen was increased.                                                                                                     | –                                          | –                                                    | [155] |
| 21        | CAD/CAM ZrO <sub>2</sub> | Ultrasonic cleaning                                                                                        | –                             | 1. Surface contamination was reduced.                                                                                                                                                               | –                                          | –                                                    | [153] |
| 22        | ZrO <sub>2</sub>         | Coated with sol–gel derived TiO <sub>2</sub> or ZrO <sub>2</sub>                                           | HGFs <i>in vitro</i>          | 1. Fibroblast proliferation was reduced in ZrO <sub>2</sub> -coated specimens.                                                                                                                      | –                                          | –                                                    | [164] |
| 23        | ZrO <sub>2</sub>         | Coated with a sol-gel-derived TiO <sub>2</sub>                                                             | HGK <i>in vitro</i>           | 1. Epithelial cell attachment and proliferation were improved.                                                                                                                                      | –                                          | –                                                    | [107] |
| 24        | ZrO <sub>2</sub>         | Polished/polished and heat-treated/machined/machined and heat-treated/sandblasted, etched and heat-treated | HGF-1 <i>in vitro</i>         | 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 anodic films 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<sup>4+</sup> to Zr<sup>3+</sup> 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  $0^\circ$ , 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),  $\beta$ -tricalcium phosphate ( $\beta$ -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 customized 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 customized 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 micro-cracking, 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

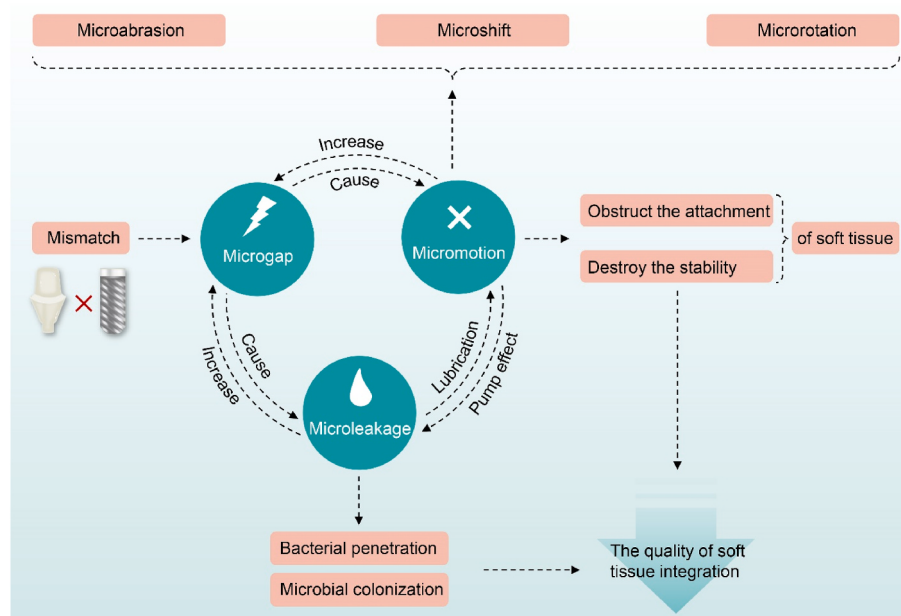


Fig. 2. The relationship between microgap, microleakage and micromovement and their harmful effects on soft tissue integration.

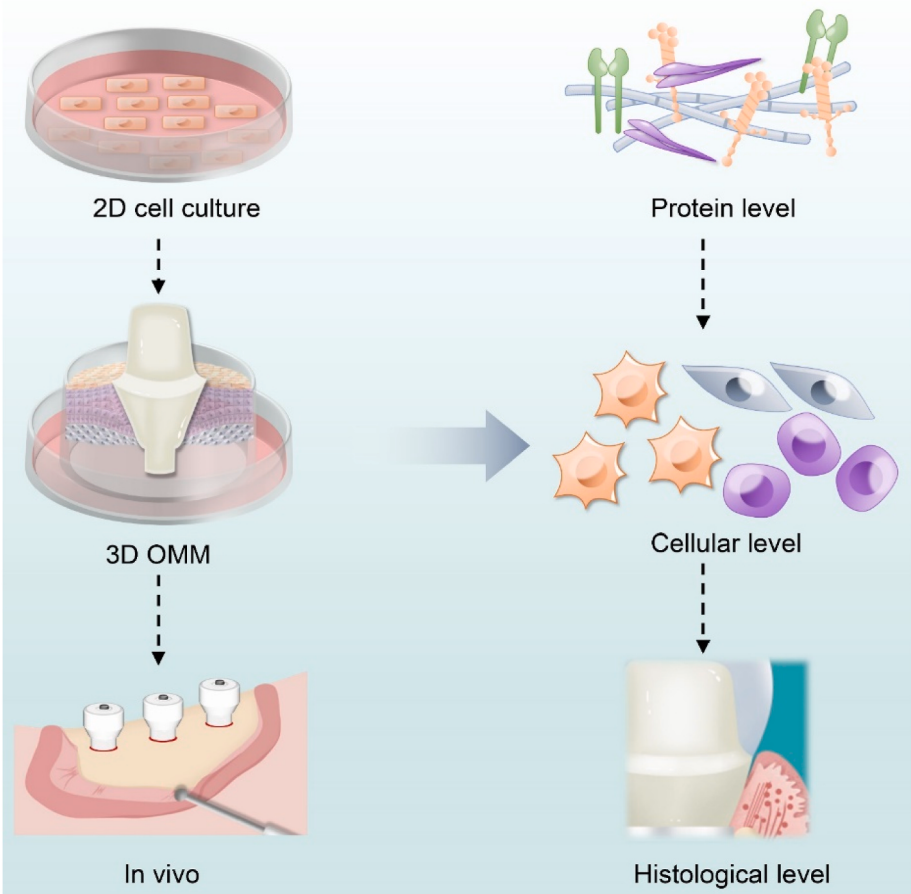


Fig. 3. Schematic of models and evaluation levels related to soft tissue adhesion around abutments.

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.                                                                                |
|                         | Surface chemical composition         | Rough surfaces                                                                                          | More vertically oriented collagen fibers formation and embedment.                                                        |
|                         |                                      | UV treatment (photofunctionalization)                                                                   | The wettability was increased, surface C/O and C/Zr ratios were decreased, and soft tissue cell attachment was enhanced. |
|                         | Surface coating                      | Plasma processing                                                                                       | The wettability was increased, hydroxyl (OH) groups were increased, and soft tissue cell attachment was enhanced.        |
|                         |                                      | Silk fibrin 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.

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#### Availability of data and materials

Not applicable.

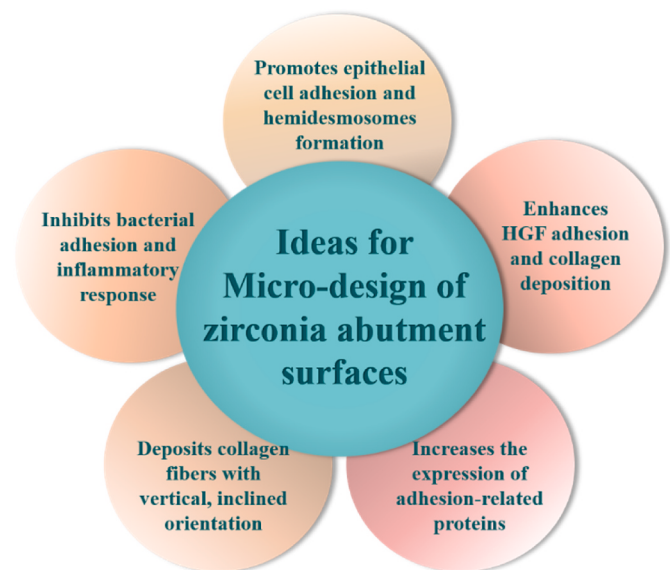


Fig. 4. Ideas for the micro-design of zirconia abutment surfaces.

#### 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.

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#### 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 |

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