



Review

Is zirconia a viable alternative to titanium for oral implant? A critical review

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ABSTRACT

Purpose: Titanium based implant systems, though considered as the gold standard for rehabilitation of edentulous spaces, have been criticized for many inherent flaws. The onset of hypersensitivity reactions, biocompatibility issues, and an unaesthetic gray hue have raised demands for more aesthetic and tissue compatible material for implant fabrication. Zirconia is emerging as a promising alternative to conventional Titanium based implant systems for oral rehabilitation with superior biological, aesthetics, mechanical and optical properties. This review aims to critically analyze and review the credibility of Zirconia implants as an alternative to Titanium for prosthetic rehabilitation.

Study selection: The literature search for articles written in the English language in PubMed and Cochrane Library database from 1990 till December 2016. The following search terms were utilized for data search: "zirconia implants" NOT "abutment", "zirconia implants" AND "titanium implants" AND "osseointegration", "zirconia implants" AND compatibility.

Results: The number of potential relevant articles selected were 47. All the human in vivo clinical, in vitro, animals' studies were included and discussed under the following subheadings: Chemical composition, structure and phases; Physical and mechanical properties; Aesthetic and optical properties; Osseointegration and biocompatibility; Surface modifications; Peri-implant tissue compatibility, inflammation and soft tissue healing, and long-term prognosis.

Conclusions: Zirconia implants are a promising alternative to titanium with a superior soft-tissue response, biocompatibility, and aesthetics with comparable osseointegration. However, further long-term longitudinal and comparative clinical trials are required to validate zirconia as a viable alternative to the titanium implant.

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1. Introduction

The rehabilitation of edentulous spaces in patients with an osseointegrated dental implant is a scientifically accepted and well-documented treatment modality. Branemark in 1908, first discovered the concept of osseointegration as a serendipity when blocks of titanium placed into the femur of rabbit got ankylosed with the surrounding bone and could not be retrieved. Since then, numerous investigations and clinical studies have established titanium as a reliable biomaterial for oral rehabilitation and reconstruction. Various modifications in the structure, composition, and design of titanium implants have been made since then to

enhance its physical, mechanical and optical properties [1–4]. However, the development of undesirable allergic reactions, cellular sensitization, galvanic current formation and aesthetics gray hue have raised demands for more aesthetic and biocompatible implant material [5–9]. Zirconia is emerging as a promising alternative to conventional Titanium based implant system for oral rehabilitation with superior biological, aesthetic, mechanical and optical properties. Zirconia implant is made from a lustrous, grey-white, strong transition metal named Zirconium (Symbol Zr). Zirconia is the oxide form of zirconium. Jons Jakob Berzelius in 1824 was the first to isolate zirconium in an impure form. Initially, zirconia was used in various orthopedic surgical procedures for manufacturing ball heads for total hip replacements, artificial hips, finger and acoustic implants prosthesis. Later it was introduced in dentistry for fabrication of endodontic posts, crown/bridge, restorations, esthetic orthodontic brackets and implant abutments

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for rehabilitation of partial and complete edentulous arches [10–20]. It was only in 1968, that the first ceramic implant known as the Sigma implant (Sanhause, Incerned, Lausanne, Switzerland) was developed by Sandhaus. Recently the demand for zirconia-based implant system is rising tremendously due to an increased demand for aesthetics. However, it is important to understand the similarities and differences between zirconia and titanium implant system so as to enable the clinician to provide the best treatment outcomes for their patients. This review aims to analyze the credibility of Zirconia as an alternative to replace Titanium based implant system.

2. Material and methods

2.1. Focus question

Is zirconia a viable alternative to titanium for oral implant?

2.2. Search strategy

The following search terms were utilized for data search: “zirconia implants” [All Fields] NOT “abutment” [All Fields], “zirconia implants” [All Fields] AND “titanium implants” [All Fields] AND “osseointegration” [All Fields], “zirconia implants” [All Fields] AND compatibility [All Fields]. Articles written only in English language in PubMed and Cochrane Library database from 1990 till December 2016 were selected.

2.3. Inclusion/exclusion criteria

The inclusion criteria for selecting articles include: type of study design (randomized clinical trial comprising of longitudinal study design, cohort study, case-control study, and cross-sectional study), nature of randomization, risk of bias, sample size and statistical and clinical significance of the outcome. All human in vivo, in vitro, animals' studies, using zirconia implant were included. Case reports and case series were not considered.

2.4. Data collection

The number of potential relevant article identified and screened were 174. Only those articles that fulfilled the criteria of adequate sample size with equal distribution, outcomes across the study with statistical and clinical significance, correct method of randomization, low risk of bias and adequate blinding were selected. Only 47 article were included for review.

3. Results

The result were discussed under the followings sections: Chemical composition, structure and phases of zirconia implants; Physical and mechanical properties; Aesthetic and optical properties; Osseointegration and biocompatibility of zirconia implants; Surface modifications of zirconia implants, Peri-implant tissue compatibility, Inflammation and soft tissue healing around zirconia implants, and long term clinical trials on prognosis.

3.1. Chemical composition, structure, and phases of zirconia implants

The pure form of Zirconia occurs in two major forms: (a) the crystalline zirconia which is soft, white, and ductile, (b) the amorphous form which is bluish-black powder in nature. The powder form of Zirconia is refined and subsequently treated synthetically at high temperatures to yield optically translucent form of crystalline zirconia. After purification, the powder form of zirconium is filled into malleable dies and processed under high

pressure (2000–4000 bar) and temperature molds to form homogenous implants of exact dimension [11–19].

Three crystalline phases occur in zirconia implants: monoclinic (m), tetragonal (t) and cubic (c). The monoclinic phase of Zirconia exists at room temperature and is stable for up to 1170 °C. Above 1170 °C, the monoclinic phase changes to tetragonal phase with 5% decrease in volume. At 2370 °C, the cubic phase starts appearing. Upon cooling, a tetragonal to monoclinic transformation with a 3–4% increase in volume takes place for about 100 °C till 1070 °C. This increase in volume and resultant expansion without a mass transfer upon cooling generates stress and causes it to become unstable at room temperature [17]. To prevent this phenomenon and to generate a Partially Stabilized Zirconia (PSZ) with stable tetragonal and/or cubic phases, various stabilizing oxides [16 mol% magnesia (MgO), 16 mol% of limestone (CaO) or 8 mol% Ytria (Y_2O_3)] are added to zirconia implants [17,20]. This martensitic-like phase transformation toughening significantly increases the crack resistance, fracture toughness, and longevity of zirconia endosseous implant [17,18,21].

Other variants of zirconia implants include 12Ce-TZP (Ceria-stabilized zirconia) and ATZ (Alumina toughened Zirconia). Alumina has also been added to Ytria stabilized-tetragonal Zirconia polycrystal (Y-TZP) in low quantities (0.25 wt%) to yield tetragonal zirconia polycrystal with alumina (TZP-A) with significant improvement in the durability and stability of zirconia crystals under high temperatures and humid environment. This improves the resistance of implant to low temperature degradation (LTD) and “ageing” [22–27]. Studies have shown that implants without alumina when exposed to the artificial mouth have a survival rate of 50%, whereas implants with alumina have a survival rate of 87–100% [19].

3.2. Physical and mechanical and optical properties of Zirconia implants

The mechanical and physical properties of zirconia implants depend upon its composition, nature of crystals, metastable polymorphic structure, ratio of the monoclinic to tetragonal phase, percentage of stabilizing metal oxide, ageing process, macro and microdesign of the implant, nature of the finish line on the implant abutment, characteristics of implant abutment, and amount of occlusal load [19,27–29].

Though transformation toughening improves the fracture strength and toughness of Y-TZP implant, it hampers the phase integrity and makes the implant susceptible to LTD or ageing. An increase in moisture or stress can cause transformation of zirconia crystals to a monoclinic phase with micro crack formation that increases the water penetration, crack propagation, surface deterioration, phase destabilization and decreased resistance to load [30]. The porosity of the material, amount of cubic phase, yttrium segregation, presence of residual stresses, grain size, sintering temperature and duration, stabilizer content of the processed material, dental procedures such as grinding or sandblasting influence the metastability, mechanical properties, extent of ageing, and resistance to LTD of zirconia implant. Although, no clinical evidence of LTD has yet been reported for dental zirconia, the combination of lower-grade powders, high sintering temperatures, and direct exposure to oral fluids has the potential to trigger this slow but autocatalytic phenomenon [27,30–36]. Watanabe et al. assessed the critical grain size for retaining the tetragonal phase and stated that an increase in the grain size from 0.2 to 0.6 μm occurs when the Y_2O_3 content increases from 2 to 5 mol%. The resistance to transformation is also increased if the grain size $<1 \mu\text{m}$, density of 6.1 g/cm^3 and yttrium oxide content of 3 mol% (5.1 wt%) is present [36,37]. Therefore, it is important not to use an implant that has too much reduction in grain size in high stress bearing areas to prevent

loss in metastability. On the contrary, an implant with a grain size larger than 1 μm exhibits a remarkable decrease in strength with large amount of tetragonal-monoclinic transformation. Additionally, implants with low silica content, high aluminum oxide (Al_2O_3) and high stabilizer content are preferred to reduce the incidence of LTD in 3Y-TZP implant systems [38–43].

The amount of occlusal load and characteristics of the implant abutment in function strongly influence the fracture resistance of zirconia implants. Various clinical studies have reported that the flexural strength, fracture toughness, static fracture strength of 3Y-TZP to be 900–1200 MPa, 8–10 $\text{MPa}\cdot\text{m}^{1/2}$ and 725–850 N respectively. ATZ exhibits the highest bending strength among all the ceramics, both at room temperature (1800–2400 MPa) and at high temperatures (>800 MPa at 1000°C). It also shows improved mechanical properties and enhanced thermal shock resistance due to its ability to maintain strength upon rapid cooling [25]. When a heavy occlusal load is placed on the zirconia implant, a subcritical crack growth (SCG) and fracture of the implant abutment is more for one-piece zirconia implants in unloaded than loaded conditions (512.9 N versus 410.7 N) [40–59]. The mean fracture strength was higher for ATZ implants (1064–1734 N) than for TZP implants (516–607 N). Kohal et al. in a pilot in vitro study compared the mechanical properties and effect of loading on one and two-piece zirconia implants and concluded that the fracture strength was lower for two piece zirconia both under loaded and unloaded conditions. Thus, two-piece zirconia should not be recommended in all clinical situations until further longitudinal studies confirm its long-term prognosis [48]. The type and nature of preparation also influenced the fracture resistance of zirconia implant. Silva et al. in an in-vitro study examined the effects of crown preparation on one-piece zirconia implant and found that the fracture strength without abutment preparation was lower as compared to a full crown preparation [47]. When the implants were not prepared, the fracture line was horizontal, at the limit of the embedding resin. In contrast, when the implants were modified by grinding, the fracture was vertically parallel to the long axis. The line of fracture was observed through the implant head in the zirconia implants, whereas a bending/fracture of the abutment screw was observed in the titanium implant group. Kohal et al. also evaluated the effects of cyclic loading and finish line design on the fracture strength of one-piece zirconia implants and concluded that chamfer finish lines along with cyclic loading decrease the fracture strength of zirconia implants [44]. The circumferential preparation depth of 0.5 mm on the zirconia abutments was better than 0.6 mm and 0.7 mm. An increase in the preparation depth by 0.2 mm decreases the fracture load by 68 N and aging and chewing simulations decrease the fracture load to 102 N [46–49]. Thus it was concluded that regardless of the chewing cycle and amount of occlusal load, an appropriate depth of finish line on the zirconia abutment is critical for the survival of zirconia implant abutment. Spies et al. conducted a study in the artificial mouth and evaluated the fracture resistance of different types of two piece zirconia implant system (bonded, screwed) and single piece after the process of thermomechanical cycling in the aqueous environment. The results showed that dynamic loading significantly increased the fracture resistance of single one-piece implants. However, both screwed and bonded zirconia implants showed a significant decrease in fracture resistance as the connecting mechanism of bonded two-piece implants was weak and prone to fracture [50,51].

The macro design of zirconia implants such as the depth of thread, diameter, and implant neck design of the implant are important criteria's that should be evaluated before selecting a zirconia implants system. The thread design of the implant plays a critical role in crack initiation and propagation. A profound thread

depth should be avoided as it may hinder bone clearance during the surgical implant placement and generate unnecessary bending forces on the implant body, especially in the patients with dense bone [52–54]. Any sharp or pointed thread design with a narrow diameter, notched edges, minor scratches, and any surface modifications including grinding, acid etching, sand-blasting etc. should be avoided to prevent local stress concentration, mechanical overloading, and subsequent implant fracture. Since mechanical overloading is considered as one of the main reasons for the implant fracture, zirconia implants with a diameter less than or equal to 3.25 mm are not recommended for clinical use [53,54].

3.3. Aesthetics and optical properties of zirconia (Table 1)

An important advantage of zirconia implant over titanium is in relation to its excellent aesthetics. The optical behavior of zirconia varies with its composition, crystal size, grain distribution and methods of machining. The enhanced aesthetics of zirconia is attributed its ability to mask dark substrates with good opacity in the visible and infrared spectrum and controlled translucency. The masking ability is due to its grain size being greater than the length of light, high refractive index, low absorption coefficient, high density with low residual porosity ($<0.05\%$) even in thin sections, the presence of various additives, stabilizers and pigments [55–57]. Unlike polycrystalline alumina, single crystal alumina is more glassy and translucent in appearance. Alloying Y-TZP with alumina cause a slight reduction in its translucency. Usually “translucent” zirconia blocks are made from Y-TZP and “opaque” zirconia blanks are made up of TZP-A. Therefore, 3Y-TZP blocks of zirconia implants that are pure white in color should be adequately masked with translucent ceramics to simulate the color of natural teeth. In such situations, pre-soaking the sintered implant prosthesis in solutions based on nano-sized pigments of iron oxide or lanthanum help in obtaining a core that is easier to be covered [53–55].

3.4. Osseointegration and biocompatibility of zirconia implants (Table 2)

Zirconia-based ceramics are chemically inert biomaterials with minimal local or systemic adverse reactions; good cell adhesion; excellent tissue response and a high degree of biocompatibility with the surrounding bone and soft tissues. Animal and humans clinical studies have evaluated and confirmed the deposition of newly formed mature bone in close proximity to zirconia implant surfaces with few marrow spaces, minimal inflammation and numerous small actively secreting multinucleated osteoblasts [58–62]. Various in vitro and in vivo studies have revealed the osteoconductive nature of zirconia with no cytotoxic, oncogenic or mutagenic effects on the bone and fibroblasts after implantation into muscles or bones [19,29,60–66]. Scarano et al. demonstrated a good bone response to zirconia implants at four weeks with Bone to Implant contact (BIC) of nearly 68.4% [65]. Dubruille et al. compared the BIC in titanium, alumina, and zirconia implants and found no statistically significant difference between the three types of implants. The BIC was found to be 68% for alumina, 64.6% for zirconia, and 54% for titanium [66].

When osseointegration of zirconia implant is compared to titanium implant, minimal difference in the BIC and distribution of stress patterns were observed [59–70]. However, an animal study done by Hoffmann et al. showed that, though zirconia implants showed a higher degree of bone apposition (54–55%) when compared to titanium implants (42–52%) at the two weeks, bone apposition was higher in titanium (68–91%) as compared to zirconia (62–80%) at four weeks. The initial osseointegration of

Table 1

Physical and mechanical properties of zirconia implant system.

Authors	In vivo/in vitro/animal	Studied material	Result assessment method	Results	Conclusion
In vitro studies					
Kohal et al. [43]	In vitro	Titanium implants with porcelain fused to metal crowns and Zirconia implants with Empress 1 crowns and Procera crowns	Long term fracture test on loaded and unloaded	The mean fracture load without artificial loading: Titanium implant-PFM crown = 531.4 N; Empress-1 = 512.9 N; Procera crown = 575.7 N The mean fracture load with artificial loading: Titanium implant-PFM crowns = 668.6 N; Empress-1 crowns = 410.7 N; Procera crowns = 555.5 N	The fracture values for the PFM and the Procera crowns after artificial loading were statistically significantly higher than that for the loaded
Chai et al. [12]	In vitro	Ten block specimens of YZ CUBES (YZ Zirconia) (Vita Zahnfabrik), and Cercon (Dentsply). IPS Empress 2 (Ivoclar Vivadent as control In-Ceram Zirconia (IZ) In-Ceram 2000	The percentage loss of mass and the loss of mass per unit of surface area for each specimen for uniaxial flexural strength (UFS) and biaxial flexural strength (BFS).	For UFS, YZ Zirconia (899 ± 109 MPa) > Cercon (458 ± 95 MPa) > IZ (409 ± 60 MPa) > Empress 2 (252 ± 36 MPa). For BFS, YZ Zirconia (1107 ± 116 MPa) > Cercon (927 ± 146 MPa) > IZ (523 ± 51 MPa) > Empress 2 (359 ± 43 MPa)	Zirconia-based ceramics possessed significantly higher flexural strengths than the control lithium disilicate ceramic.
Yilmaz et al. [11]	In vitro	6 ceramic core materials [Finesse (F), Cerco (C), IPS Empress (E), InCeram Alumina (ICA), In-Ceram Zirconia (ICZ), Cercon Zirconia (CZ)] ($15 \times 1.2 \pm 0.2$ mm	Biaxial flexural strength, Weibull modulus, Indentation fracture toughness	Indentation fracture toughness: Cercon zirconia: 6.27 MPa (0.05) InCeram zirconia: 5.58 MPa (0.18) InCeram alumina: 4.78 MPa (0.18)	Cercon Zirconia core material showed high values of biaxial flexural strength and indentation fracture toughness when compared to the other ceramics materials
Silva et al. [47]	In vitro	Forty-eight one-piece Y-TZP ceramic implants (Nobel Biocare, Goteborg, Sweden)	The influence on mouth-motion fatigue reliability and failure modes between as-received and after full crown preparation on one-piece ceramic implants.	No differences was found between the groups' reliability. Failure mode for both groups were similar. Cracks initiated mainly at the tensile bending side of the second thread's internal diameter.	Crown preparation did not influence the reliability of one piece ceramic implant. Fatigue did not influence the life time of ceramic implants at loads under 600 N. Failure depended upon the applied load
Animal studies					
Schultze-Mosgau et al. [13]	4 Göttinger pigs	Y-PSZ cone (Friadent) and Titanium cone (Straumann)	Quantitative histomorphometric assessment of the Bone implant Contact (BIC), Bone-fibrous connective tissue contact (BFCC) using Intravital polychrome sequence, Qualitative light microscopic, fluorescence microscopic.	Quantitatively and histomorphometrically, the mean ratio between the total cone/bone contact and the total cone/fibrous tissue contact was 0.95 (SD 1.10) on the titanium surface (n = 38) and 1.47 (SD 1.12) on the ZrO ₂ surface (n = 78; P = .02)	Biocompatibility of ZrO ₂ was similar to that of titanium

zirconia and titanium implants were similar with positive effects on the morphology of osteoblasts, proliferation rate, and synthesis of bone-associated proteins. However, at the end of day three and five, the cell growth and proliferation was significantly higher on the zirconia surfaces than on the titanium surfaces [71,72]. Akagawa et al. examined the initial implant to bone interface in one-stage screw type zirconia implant with different occlusal loading conditions in beagle dogs [59]. At three months, the BIC was higher for the non-loaded group (81.9%) compared to the loaded group (69.8%) with evident crestal bone loss around the loaded implants. Another animal study by Akagawa et al. evaluated the long-term prognosis and stability of osseointegration around one-staged PSZ implants with three different concepts of load (single freestanding implant support; connected freestanding implant support; a combination of implant and tooth support). The results revealed a minimal difference among single freestanding, connected freestanding, and implant tooth supports for PSZ implants [73]. Based on these findings, it was concluded that the zirconia implants have the ability to osseointegrate to the same extent as titanium implants even under load, however initial unloaded conditions is preferable to achieve favorable osseointegration in one-stage zirconia implants [59,67–73].

3.5. Surface modifications of zirconia implants (Table 3)

Various surface modifications such as acid etched Zirconia, sandblasted Zirconia, plasma sprayed, anodized, machined, chemically modified (plasma-anodized), coated (calcium phosphate, bisphosphonate or collagen type I with chondroitin sulphate), nanotechnology surface modified (Calcium phosphate nanolayer) have been developed to enhance the osseointegration of zirconia implants [19,29,74–94]. These surface modifications at microscopic level enhance osseointegration by increasing the roughness, wettability and expression of integrin's alpha5 and beta1 mediated osteoblast-gene expression and osteoblast-like cells adhesion, spreading and migration on the zirconia implant substrates [82–100]. When osteoblast differentiation on two different zirconia surfaces (sandblasted with alumina particles or SLA in a mixture of hydrofluoric acid and sulfuric acid) was compared with standard titanium surface (sandblasted and acid-etched), zirconia substrates showed better osteoblastic adhesion and proliferation compared with titanium [83]. However, in some clinical studies comparable osseous healing and BIC between acid etched titanium and zirconia implants surface have been observed [62,69–77,98]. Bachle et al. evaluated the cell proliferation on

Table 2
Osseointegration around Zirconia implants.

Authors	In vivo/in vitro/animal	Studied material	Result assessment method	Results	Interpretation/conclusion
Animal studies					
Scarano et al. [65]	Animal, white mature male rabbits	Unloaded Zirconia implants	Histology	Percentage of bone-implant contact was $68.4 \pm 2.4\%$. Mature bone, with few marrow spaces and small actively secreting osteoblasts were present in the most coronal and apical portions of the implant. No inflamed or multinucleated cells present	Zirconia implants are highly biocompatible and osteoconductive.
Hoffmann et al. [71]	Animal study (white rabbit)	Commercially available zirconia implants with sandblasted, acid-etched surface titanium implants with	Bone-implant contact at 2 weeks and 4 weeks	A high degree of bone apposition on all implants at both time points. Differences in the percentage of implant surface covered with bone were noted between the 2 time points, with comparable results for both materials.	A similar rate of bone apposition on zirconia and surface-modified titanium implant surfaces during early healing
Stadlinger et al. [61]	Animal study (minipig mandible)	14 one-piece zirconia implants and 7 titanium implants inserted into the mandibles of 7 minipigs. The zirconia implants were alternately placed submerged and non-submerged.	Histomorphometric analysis of the bone-implant contact (BIC) and relative peri-implant bone-volume density (rBVD; relation to bone-volume density of the host bone)	An intimate connection with bone in both submerged zirconia and titanium implants. The BIC of 53% was found in the implant surface. For the non-submerged zirconia implants, crestal epithelial down growth and BIC of 48% was observed. Highest rBVD values for submerged zirconia (80%), followed by titanium (74%) and non-submerged zirconia (63%).	Unloaded zirconia and titanium implants osseointegrate comparably, within the healing period studied.
Gahlert et al. [70]	15 adult pigs, 30 implants	Threaded zirconia implants (+ acid etching versus Titanium implants (sandblasting and acid etching)	Bone-implant contact (BIC) and bone-volume density (rBVD) at 4, 8, and 12 weeks	Zirconia implants revealed mean peri-implant bone density values of 42.3% ($SD \pm 14.5$) at 4 weeks, 52.6% ($SD \pm 5.7$) at 8 weeks and 54.6% ($SD \pm 11.5$) at 12 weeks after implantation, whereas Ti-SLA implants demonstrated mean values of 29% ($SD \pm 10$), 44.1% ($SD \pm 18$) and 51.6% ($SD \pm 8.6$) at corresponding time intervals. The bone-implant contact ratio for zirconia ranged between 27.1% ($SD \pm 3.5$) and 51.1% ($SD \pm 12.4$) and for Ti-SLA, it ranged between 23.5% ($SD \pm 7.5$) and 58.5% ($SD \pm 11.4$).	No statistical difference between implants in osseointegration between modified zirconia and titanium
Dubruille et al. [66]	54 (5 beagle dogs, 18 implants)	Y-TZP (6 implants) Al_2O_3 (6 implants) Titanium grade I (6 implants)	Histomorphometric analysis using SEM for analysis of bone-implant interface	Bone-implant interface for Y-TZP–64%, Al_2O_3 –68%, titanium grade–54%	The mean percentage of implant-bone contact was better for ceramic implants than for titanium implants.
Sennerby et al. [87]	(12 rabbits, 96 implants) Placed in femur and tibia for 6 weeks	Threaded zirconia implants with a diameter of 3.75 mm with either a machined surface (Zr-Ctr): Y-TZP (24 implants); screw type (Zr) (3.75 mm $\times$ 9 mm), surface roughened with pore former A (pfA), surface roughened with pore former B (pfB); and control as screw type titanium (24 implants) (3.75 mm $\times$ 7.5 mm)	Bone-implant contact by Backscatter scanning electron microscopic (BS-SEM) analyses and Removal torque values assessed	The oxidized titanium and Zr-A implants showed the highest surface roughness, followed by the Zr-B implants and Zr-Ctr implants. The non-modified ZrO ₂ implants showed statistically significant lower RTQs than all other implants.	The modified zirconia implants showed a resistance to torque forces similar to oxidized implants and a four- to fivefold increase compared with machined zirconia implants. Surface-modified zirconia implants can reach firm stability in bone.

machined, sandblasted, and Sandblasted, large grit, acid etched (SLA) zirconia surfaces and found that airborne particle abrasion and acid-etching increased the surface roughness of zirconia implants with enhanced cell proliferation compared to machined zirconia implants [85]. Moreover, sandblasting zirconia particles on implant surface significantly improves the peri-implant osteogenesis compared to machined titanium surfaces [79,80]. When chemically modified or coated titanium implant surfaces

(plasma-anodized; calcium phosphate; bisphosphonates; collagen type I or chondroitin sulphate coated) are compared to SLA zirconia implants, pharmacologically and chemically modified titanium implants have a better BIC at eight weeks when compared to zirconia implants with plasma anodized surface [68,78,84]. A coating of 50% hydroxyapatite and 50% zirconia have been tried as a surface coating agent on titanium implants with enhanced osseointegration and specific biologic effects [68,74–78]. The

Table 3

Effects of surface modification and occlusal loading on the osseointegration and mechanical properties of zirconia implants.

Authors	In vivo/in vitro/ animal	Studied material	Surface treatment of studied material	Result assessment method	Observed and analyzed subject with results	Conclusion
In vitro studies						
Depprich et al. [62]	In vitro	12 mm ϕ disks of Commercially pure Titanium, Zirconia and Polystyrene	Acid etching	Photography, select washing, immuno-cytochemistry, SEM	Osteoblastic cells behaviour	Zirconia can be considered biocompatible
Kohal et al. [48]	In vitro pilot	Fracture strength of two-piece cylindrical zirconia implants after aging in a chewing simulator with and without abutment preparation	Different surface topographies and loading: titanium implants were reconstructed with porcelain-fused-to-metal crowns	Survived or fractured	A high number of failures occurred already during the artificial loading in the titanium group at the abutment screw level. The zirconia implant groups showed irreparable implant head fractures at relatively low fracture loads. Bending/fracture of the abutment screw in the titanium group	Zirconia and titanium have comparable osseointegration. Preparation of the abutment has a negative effect on fracture strength.
Animal studies						
Akagawa et al. [59]	Animal: (4 dogs, 12 implants)	Partially stabilized zirconia endosseous implants	Machined, barrel polished, ultrasonically cleaned	Clinical and histologic evaluations of under unloaded and early loaded conditions	Unloaded implants: Bone to implant contact- 82% At 3 months loaded: Bone to implant contact- 70%	Initial unloaded condition is preferable to achieve osseointegration of one-stage zirconia implants
Akagawa et al. [73]	Animal (7 monkeys, 28 implants)	Screw type, loaded Y-TZP implants divided with different loading conditions: Single implants Connected and Tooth connected implants	NA	Clinical, histologic, and histomorphometric evaluations of peri-implant tissues at 12 and 24 months after loading	Histometrically, bone contact ratio ranged between 66% and 81%, and bone area ratio varied between 49% and 78% at 24 months after loading. No difference among single freestanding, connected freestanding, and implant-tooth supports of partially stabilized zirconia implants. The mean height of the soft peri-implant tissue cuff was 5 mm around the titanium implants and 4.5 mm around the zirconia implants. The bone-to-implant contact after 9 months of healing and 5 months of loading amounted to 72.9% (SD: 14%) for the titanium implants and to 67.4% (SD: 17%) for the zirconia implants.	1-stage partially stabilized zirconia implants could maintain direct bone contact for 2 years with all types of loading support.
Kohal et al. [67]	Animal (6 monkeys, 24 implants)	Y-TZP zirconia implants versus titanium within 5 months after extraction and kept unloaded for 3 months	Machined, sand blasted (50 μ m Al_2O_3 bar) versus acid etched (H_2O_2/HF) after sandblasting	Histologic evaluation of the bone-to-implant contact and soft tissues under the light microscope	The bone-to-implant contact after 9 months of healing and 5 months of loading amounted to 72.9% (SD: 14%) for the titanium implants and to 67.4% (SD: 17%) for the zirconia implants. Surface analysis revealed the highest surface roughness for the SLA-implant, followed by ZrO_2r and ZrO_2m . The turned ZrO_2m implants showed statistically significant lower RTQ values than the other two implants types after 8 and 12 weeks, while the SLA implant showed significantly higher RTQs values than ZrO_2r surface after 8 weeks. With respect to the bone-implant contact ratio, the mean values for zirconia ranged between 27.1% (SD 3.5) and 51.1% (SD 12.4) and for Ti-SLA, it ranged between 23.5% (SD 7.5) and 58.5% (SD 11.4).	Custom-made zirconia implants osseointegrated to the same extent as custom-made titanium implants and show the same peri-implant soft tissue dimensions
Gahlert et al. [1]	Animal 13 adult miniature pigs	Unloaded titanium versus Machined acid etched (ZrO_2m) and sandblasted zirconia implants (ZrO_2r)	acid etched and sandblasted	Histologically compare the bone tissue responses and removal torque values	Surface analysis revealed the highest surface roughness for the SLA-implant, followed by ZrO_2r and ZrO_2m . The turned ZrO_2m implants showed statistically significant lower RTQ values than the other two implants types after 8 and 12 weeks, while the SLA implant showed significantly higher RTQs values than ZrO_2r surface after 8 weeks. With respect to the bone-implant contact ratio, the mean values for zirconia ranged between 27.1% (SD 3.5) and 51.1% (SD 12.4) and for Ti-SLA, it ranged between 23.5% (SD 7.5) and 58.5% (SD 11.4).	No difference in osseointegration between the two types of implants. ZrO_2r implants can achieve a higher stability in bone than ZrO_2m implants. Roughening the turned zirconia implants enhances bone apposition and has a beneficial effect on the interfacial shear strength.
Hoffmann et al. [71]	Animal New Zealand white male rabbits	Unloaded implants Titanium and Zirconia implants	Zr: RoughenedTi: Sandblasted, Acid etched	Light microscopic analysis and histomorphometric analysis of the bone-implant contact	A high degree of bone apposition observed on all implants	Similar bone apposition around zirconia implants and around titanium implants
Depprich et al. [2]	Animal Implants placed into the tibia of 12 minipigs.	48 Unloaded implants Titanium and Zirconia implants	Acid etched	At 1, 4 or 12 weeks were examined in terms of histological and	Histological results showed direct bone contact on the zirconia and titanium surfaces. Bone implant	Zirconia implants with modified surfaces result in an osseointegration which is comparable

Table 3 (Continued)

Authors	In vivo/in vitro/ animal	Studied material	Surface treatment of studied material	Result assessment method	Observed and analyzed subject with results	Conclusion
				ultrastructural techniques.	contact as measured by histomorphometry was slightly better on titanium than on zirconia surfaces.	with that of titanium implants.
Langhoff et al. [84]	Animal study in a sheep pelvis model.	Six types of dental implants were tested for osseointegration after 2, 4 and 8 weeks (chemically and two were pharmacologically modified titanium implant versus zirconia)	Chemically modified implants were plasma- anodized or coated with calcium phosphate. The pharmacological coatings contained either bisphosphonate or collagen type I with chondroitin sulphate.	The implants were evaluated using macroscopic, radiographic and histomorphometric methods (Bone to implant contact)	All titanium implants had similar bone implant contact (BIC) at 2 weeks (57–61%); only zirconia was better (77%). The main BIC increase was between 2 and 4 weeks. The pharmacologically coated implants (78–79%) and the calcium phosphate coating (83%) showed similar results compared with the reference implant (80%) at 8 weeks.	No improvement of osseointegration by coated implant surfaces compared to control zirconia implant.
Rocchietta et al. [86]	Animal	Unloaded Zirconia (ZiUnite) implants with addition of two chemical surface modification	Porous surface (ZiUnite) with chemical surface modifications	Removal torque test and bone to implant contact	No significant histological difference between test and control.	Chemical surface modification is not beneficial to interfacial shear strength
Lee et al. [89]	Animal	Unloaded zirconia (ZiUnite) implants with addition of two chemical surface modifications	Porous surface (ZiUnite®) with chemical surface modifications	Histology, SEM, histometric analysis	Bone density around implants, direct bone- implant contact	Addition of CaP nanotechnology to the ZiUnite® surface does not enhance the osteoconductivity displayed by the TiUnite® and the ZiUnite® implant surface
Gahlert et al. [79]	Animal 30 dental implants	Threaded zirconia implants produced using a new low- pressure injection moulding technique and acid etching. Titanium implants sandblasting and acid etching (SLA) served as controls	Acid etched and sandblasted	Histology Histomorphometric analysis at 4, 8 and 12 weeks	Zirconia implants revealed mean peri-implant bone density values of 42.3% (SD ± 14.5) at 4 weeks, 52.6% (SD ± 5.7) at 8 weeks and 54.6% (SD ± 11.5) at 12 weeks after implantation. Ti-SLA implants demonstrated mean values of 29% (SD ± 10), 44.1% (SD ± 18) and 51.6% (SD ± 8.6) at corresponding time intervals. With respect to the bone-implant contact ratio, the mean values for zirconia ranged between 27.1% (SD ± 3.5) and 51.1% (SD ± 12.4) and for Ti-SLA, it ranged between 23.5% (SD ± 7.5) and 58.5% (SD ± 11.4).	No detectable difference in osseointegration between test and control. Not directly applicable to humans
Aboushelib et al. [90]	Animal study 20 implants of each group inserted in 40 adult New Zealand white male rabbits	Osseous healing of selective infiltration-etched (SIE) zirconia implants compared to as- sintered zirconia and titanium implants	Nano-porous selective infiltration etched	Histology, SEM, histometric analysis	SIE zirconia implants had significantly higher BIC and marginally higher bone density.	The addition of this nano-porous selective infiltration etched surface improved osseous healing and bone apposition compared to as- sintered Zirconia implants
Human studies Blaschke and Volz [76]	Human	Loaded Zirconia implants	Sandblasting	Radiological	Crestal bone around implants and soft tissue healing is similar to titanium	Zirconia implants allow a degree of osseointegration and soft tissue response that is superior to titanium dental implants.
Oliva et al. [114]	Human	One-piece zirconia dental implants with 2 different rough surfaces were specially designed	Two different treatments to achieve a porous surface: the noncoated group and mechanically roughened surface and the coated group with a stable bioactive ceramic	Panoramic X ray at 12 months	The overall implant success rate at the 1-year follow-up was 98% in both the coated and non-coated groups. The overall survival rate after the first month post-surgery was 100%.	Zirconia implants may be an alternative for Titanium implants

adhesive, morphologic, and structural properties of the plasma sprayed coatings on titanium and cobalt chromium molybdenum (CoCrMo) implants coated with ZrO_2 (4% CeO_2) and ZrO_2 (3% Y_2O_3) proved that adhesive strength of ZrO_2 (4% CeO_2) coating was higher in comparison to ZrO_2 (3% Y_2O_3) to Titanium implants [81]. Ferguson et al. compared the biomechanical properties of six types of implant surfaces and found that the RTQ values were highest for the SLA titanium (1884 N/mm) followed by SLA and Calcium phosphate (CaP)-coated titanium (1683 N/mm), SLA and bisphosphonate-coated titanium (1835 N/mm), SLA and collagen-coated titanium (1593 N/mm), SLA zirconia (1005 N/mm) and SLA and anodic plasma chemical surface-treated titanium (919 N/mm) [88,91]. Additionally, the RTQ value was four to five fold more for sandblasted zirconia than machined zirconia. Studies have even compared selective infiltration-etched zirconia implants with sintered zirconia implants and titanium implants (sandblasted and acid-etched) and found that selective infiltration-etching zirconia implants showed greater BIC (75%) than both sintered zirconia (62%) and titanium (68%) implants [89–91]. Bioactive glass as a surface coating material has also been tried for zirconia implants with promising results like enhancement of the early osseointegration rate as compared to non-coated implants. Bioactive glass coated Zirconia implants is useful in geriatric patients with poor bone quality or osteoporotic bone as it exhibits a flexural strength (twice that of Y-TZP), greater fracture toughness and reduced low-temperature degradation [92,93].

Lasers, particularly carbon dioxide laser (CO_2 laser), are commonly used to enhance the wettability and decreased surface roughness of zirconia implants. Various studies have also shown comparable degree of early bone apposition around sintered zirconia, laser modified zirconia and sandblasted zirconia implants to surface-modified titanium implants [1,19,87,88–94]. Stubinger et al. analyzed the effects of erbium-doped yttrium aluminum garnet (Er: YAG), carbon dioxide (CO_2), and diode laser on the surface of polished zirconia implants and demonstrated that diode and Er:YAG lasers did not cause any visible alterations on the implant surface. CO_2 laser produced a discrete surface alterations on the zirconia implant surface that enhanced adherence of the osteoblast with increased bone formation. Thus it was concluded that CO_2 laser is best for surface modifications and diode lasers is the only laser system that could be used in patient with peri-implantitis and soft tissue modifications around zirconia implants [95–97].

3.6. Peri-implant tissue compatibility, inflammation and soft tissue healing around zirconia implants (Table 4)

The bio-inert properties of zirconia help in rapid proliferation of the human gingival fibroblasts over the implant surface and formation of a good mucosal barrier [96]. However, various factors such as surface characteristics and design, nature of implant material and degree of roughness influence the nature and amount of the mucosal seal around zirconia implants. A smooth implant surface promotes a good soft tissue seal in comparison to a rough implant surface. Various differences have been observed in the periimplant mucosa around zirconia implants as compared to titanium. The expression of chemical mediators such as integrin α_2 , integrin α_5 and type I collagen are found to be more up-regulated on smooth zirconia implants as compared to titanium [97–107]. However, the pattern of connective tissue adhesion and transgingival collar around zirconia implants is similar to that seen around machined titanium surface (collagen fiber orientation predominantly in a parallel oblique pattern) [108]. The color of the periimplant mucosa, the amount of bleeding on probing and probing depth is similar around zirconia implants as compared to titanium implants [53,98,102–108]. The distance

from the periimplant mucosa to the apical termination of the barrier epithelium is lower for zirconia implants as compared to titanium [96,108–110]. A significantly higher content of collagen and a shorter length of the sulcular epithelium has been observed around zirconia implants (0.76 mm) as compared to titanium implants (1.4 mm). The biological width of 2.3 mm for titanium implants and 2.85 mm for zirconia implants has been recorded. The presence of a long junctional epithelium with a high density of collagen fibers around zirconia implants provides a better soft-tissue integration with less ingress of the bacteria and reduced inflammatory infiltration as compared to titanium implants [108,110]. Zirconia implant has also shown to inhibit bacterial adhesion and biofilm formation on its surface because of its hydrophobicity, bio-inert properties, optimal smoothness, reduced surface free energy and surface wettability [97–101]. Various microbiological and in-vivo studies have reported a reduced number of cocci and rods around zirconia implant (increase in levels of *Streptococcus mutans* with less *Streptococcus sanguis*) as compared to titanium implants. These bioinert properties enhance perio-integration around zirconium implants and in turn prevent the development of peri-implant bone resorption and peri-implant soft inflammation [103–108]. Nascimento et al. in a randomized crossover clinical trial identified and quantified the microbial species in 24-h biofilms on different implant materials (machined titanium; cast and polished titanium; and zirconia) using DNA checkerboard hybridization technique. The results showed that cast and polished titanium showed higher proportions of rods and filamentous bacteria and fewer cocci compared with machined titanium and zirconia. In the cast and polished titanium group, *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis* were detected in 100% and 95% of the samples respectively. In addition, in Zirconia group, *S. mutans* was recorded in 58.34% of samples, while *Streptococcus mitis* and *Staphylococcus pasteurii* were recovered from only 54.17% of samples [108].

Apart from low bacterial colonization, a low inflammatory response around zirconia implant is attributed to increased release of various angiogenic factors and anti-inflammatory cytokines as compared to Titanium [103,110–112]. The inflammatory response is more around titanium implant with higher microvessel density, vascular endothelial growth factor expression, expression of nitric oxide synthase as compared to zirconia [101]. However, in a contraindicating study by Cionca, the levels of pro-inflammatory cytokines in the peri-implant and gingival crevicular fluid around zirconia implant and contralateral teeth were compared. The results showed that interleukin-1RA, Interleukin-8, granulocyte colony-stimulating factor, macrophage inflammatory protein-1beta, Tumor necrosis factor-alpha were significantly higher around zirconia implants as compared to healthy teeth. Implants with restoration that gradually transitioned from the circumferential design of the implant collar to the cervical tooth anatomy demonstrated higher levels of interleukin-1RA and significantly lower levels of interleukin-6 than implants with restorations that did not gradually transition from the circumferential design of the implant collar, adjacent implants with connected supra-structures or with adjacent over/under-contoured implant and/or tooth-supported restorations affecting accessibility for oral hygiene. When zirconia implants are compared to titanium implants, the levels of Interleukin-1RA, Interleukin-8, granulocyte colony-stimulating factor and macrophage inflammatory protein-1beta were similar [101–104]. Nickenig et al. also demonstrated lower expression of two specific cytokines (Interleukin-6 and Tumor necrosis factor alpha) in soft tissues surrounding cover screws coated with zirconia as compared to cover screws made of titanium. The reduced inflammatory response indicates that onset of peri-implantitis would be less with zirconia implants than with

Table 4

Peri-implant soft tissue, inflammation and bacterial colonization around zirconia implants.

Authors	In vivo/in vitro/animal	Studied material	Result assessment method	Bacterial colonization	Soft tissue assessment results	Conclusion
In vitro studies						
Rimondini et al. [104]	In vitro and in vivo study (10 human)	As-fired and rectified tetragonal zirconia polycrystals stabilized with yttrium (Y-TZP) and commercially pure grade titanium (Ti)	Bacterial adhesion on materials quantified by spectrophotometric evaluation of the slime production by the <i>Streptococcus mutans</i> , <i>S. sanguis</i> , <i>Actinomyces viscosus</i> , <i>A. naeslundii</i> , and <i>Porphyromonas gingivalis</i> . Bacterial adhesion in human volunteers with SEM.	In vitro as-fired and rectified Y-TZP showed significantly more adherence to <i>S. mutans</i> than on Titanium disks, while <i>S. sanguis</i> adhere easily to Ti specimens. No differences were noted for <i>Actinomyces</i> spp and <i>P. gingivalis</i> . In vivo Y-TZP accumulated fewer bacteria than Ti.	NA	TZP accumulates fewer bacteria than Ti.
Animal studies						
Tete et al. [108]	Animal study on mandibular bone of adult pigs.	Machined Titanium implant neck and Machined Zr implant neck	Scanning electron microscopic and profilometric analyses to evaluate the different surface morphology. Evaluation of collagen fiber orientation in the connective tissue surrounding the implant necks by polarized light microscopy. Inflammation in the peri-implant soft tissues measured via the Gingival Index.	Limited plaque formation and better esthetics around zirconia as compared to titanium	The mean probing depth around titanium implants = 2.2 ± 0.2 mm and around zirconia = 2.0 ± 0.2 mm with a parallel or parallel-oblique orientation of the collagen fibers and Non osseointegrated implants showed inflammatory infiltrate, whereas healthy connective tissue was found around osseointegrated implants.	Collagen fiber orientation is comparable around titanium and zirconia, which is used as a transgingival collar on some implants, demonstrates
Welander et al. [96]	Animal	Titanium abutment, Zirconia abutment and Au/Pt-alloy abutments	Biopsies containing the implant and the surrounding soft and hard peri-implant tissues were collected and prepared for histological analysis.	NA	The soft tissue dimensions at Ti- and ZrO ₂ abutments remained stable between 2 and 5 months of healing. At Au/Pt-alloy abutment sites, however, an apical shift of the barrier epithelium and the marginal bone occurred between 2 and 5 months of healing.	Soft tissue healing to abutments made of titanium and ZrO ₂ is different to that at abutments made of AuPt-alloy.
Human/in vivo studies						
Glauser et al. [113]	Prospective study on	Twenty-seven patients with 54 single-tooth implants with implant abutment made of densely sintered zirconia	Modified Plaque, Simplified Gingival Indices, peri-implant bone levels	NA	Mean Plaque Index at abutments was 0.4 (SD 0.6) and 0.5 (SD 0.6) at teeth; mean Gingival Index was 0.7 (SD 0.5) at abutments and 0.9 (SD 0.5) at teeth. Mean marginal bone loss measured 1.2 mm (SD 0.5) after 4 years of functional loading.	Zirconia abutments offered sufficient stability to support implant-supported single-tooth reconstruction. The soft and hard tissue reaction toward zirconia was favorable.
Scarano et al. [109]	In vivo study 10 patients	Removable disks of commercially pure titanium and zirconium oxide glued to the buccal aspect of molar-premolar	Characterize the percentage of surface covered by bacteria after 24 hours by scanning electron microscopy for the evaluation of the portion of surface covered by bacteria.	The area covered by bacteria was $19.3\% \pm 2.9$; in titanium disk and $12.1\% \pm 1.96$ in zirconium disk.	NA	Zirconium oxide may be a suitable material for manufacturing implant abutments with a low bacterial colonization potential.
Zembic et al. [112]	In vivo study	Zr abutments and Titanium abutments	Probing pocket depth (PPD), plaque control record (PCR) and bleeding on probing. Bone level (BL) with standardized radiographs. The color of the peri-implant mucosa and gingiva assessed with a spectrophotometer.	NA	Mean PPD (ZrO ₂) = 3.2 ± 1 mm & (Ti) 3.4 ± 0.5 mm), PCR (mPCR (ZrO ₂) = 0.1 ± 0.2 , & (Ti) 0.1 ± 0.2) and mBOP (ZrO ₂) = 0.4 ± 0.4 , & (Ti) 0.2 ± 0.3). Both, zirconia and titanium abutments induced a similar amount of discoloration of the mucosa compared with the gingiva at natural teeth	At 3 years, zirconia and titanium abutments exhibited same survival and technical, biological and esthetical outcomes.
Salihoglu et al. [105]	In vivo	Adhesion and colonization of two periodontal pathogens on abutments made of	Probing depth and gingival biopsy samples analyzed by reverse-transcriptase polymerase chain reaction for <i>Aggregatibacter</i>	No statistically significant differences between the DNA of <i>A. actinomycetemcomitans</i> and <i>P. gingivalis</i> .	No statistically significant differences between probing depths. There was lower surface free energy	Zirconium oxide surfaces have comparable properties to titanium alloy surfaces with similar

Table 4 (Continued)

Authors	In vivo/in vitro/animal	Studied material	Result assessment method	Bacterial colonization	Soft tissue assessment results	Conclusion
		zirconium oxide and titanium and soft tissues.	<i>actinomycescomitans</i> , <i>Porphyromonas gingivalis</i> . The surface free energy of the abutments by sessile water drop		for zirconium abutments than titanium abutments.	tendency of bacterial adhesion and colonization
Van Brakel et al. [102]	In vivo Twenty edentulous subjects	Endosseous mandibular implants (ZrO ₂) and Ti abutment (non-submerged implant)	Sulcular bacterial sampling and the assessment of probing pocket depth, recession and bleeding on probing were performed at 2 weeks and 3 months post-surgery	ZrO ₂ and Ti abutments harbored similar counts of <i>Aggregatibacter actinomycetemcomitans</i> , <i>Porphyromonas gingivalis</i> , <i>Prevotella intermedia</i> , <i>Tannerella forsythia</i> , <i>Peptostreptococcus micros</i> , <i>Fusobacterium nucleatum</i> and <i>Treponema denticola</i> at 2 weeks and 3 months.	Healthy clinical conditions were seen around both ZrO ₂ and Ti abutments at all times, Mean probing depths around Ti abutments were slightly deeper than around ZrO ₂ abutments after 3 months (2.2 SD 0.8 mm vs. 1.7 SD 0.7 mm, P=0.03).	No difference in health of the soft tissues adjacent to ZrO ₂ and Ti abutment surfaces or in early bacterial colonization. Shallow probing depths were observed around ZrO ₂ abutments after 3 month.
Van Brakel et al. [103]	In vivo human study Twenty patients	Mandibular implants either with zirconia or titanium abutment (split mouth study design, left-right randomization).	Compare the health of the soft tissues around zirconia and Titanium by biopsies of soft tissue by histological evaluation. The number of blood vessels per surface unit and an inflammation grading scale score ranging from 1 to 4 were determined.	NA	Well-keratinized stratified squamous epithelium continuous with the barrier (junctional) epithelium faced the abutment surface. The normal epithelial build-up could be recognized with little signs of inflammation between the two implant types. No statistically significant difference in tissues adjacent to zirconia and titanium abutment surfaces were seen with respect to vascular density (20.5 SD 4.4 and 20.7 SD 3.2) or inflammation grading scale scores (3.2 SD 0.7 versus 3.1 SD 0.7).	No differences in soft tissue health were seen in peri-implant mucosa adjacent to zirconia and titanium abutment surfaces.
Siddiqi et al. [69]	In vivo (24 subjects)	Investigate soft and hard tissue response to Titanium and Zirconia implants in edentulous patients.	One-piece ball-abutment implants to support overdentures.	NA	Only 11 (52.4%) of 21 palatal implants survived the follow-up period. Peri-implant health was equivalent for Titanium and Zirconia implants. Statistically significant differences in radiographic bone level between Titanium and Zirconia implant, with Zirconia showing greater bone loss.	Although the failure rates with the one-piece Zirconia implants were higher than with the Titanium ones, However fault may also lie with the novel prosthodontic design which was used.

titanium implants. However, further longitudinal long-term studies comparing the onset, prognosis and severity of peri-implantitis around zirconia and titanium implants are warranted [112].

3.7. Long-term clinical trials on prognosis of zirconia implant

The use of zirconia as a viable alternative to titanium can be established only if it provides good long-term prognosis in patients. Very few clinical trials have evaluated the overall success rate of zirconia implants in terms of its survival, biological and esthetical outcomes [113,114]. Oliva et al. reported the first clinical in vivo study with a one-year follow-up of 100 zirconia implants with different surface roughness and reported an overall success rate of 98% [115]. However, it was concluded that to assess the success rate of zirconia implants at sites where sinus elevation is necessary, further investigation and research is required. Pirker et al. evaluated the prognosis of zirconia implant placed in the maxillary first premolar region after extraction and showed a stable implant with an unchanged peri-implant marginal bone level even at two years follow-up [116]. Osman et al. assessed the

one-year clinical success of one-piece zirconia implants compared with titanium implants with conventional loading protocol and reported no significant difference with a survival rate for titanium and zirconia implants in the mandible being 95.8% and 90.9% respectively. The corresponding values in the maxilla were 71.9% and 55%, respectively. Thus, it was concluded that single-piece zirconia implants should be used with caution for over-denture support and should be limited to cases with proven allergy to titanium [117].

A good marginal bone preservation with a reduced periimplant bone loss under cyclic loading has shown to be a characteristic of zirconia implants. Unlike zirconia, titanium implants have shown higher peri-implant bone resorption; increased bending on the implant, fatigue fracture under increased cyclic loading conditions [116–119]. Borgonovo et al. assessed the health of the soft tissue along with radiographic bone loss around zirconia implants with multiple or single implant restorations and concluded that the mean marginal bone loss around zirconia implant was 1.631 mm at the end of three years. The marginal bone loss during the first year of loading for zirconia implants placed in the posterior molar regions was comparable to implants placed at other sites and no

differences were observed for sites with multiple and single implants restoration. Therefore protection of one-piece zirconia with no occlusal load during the healing phase is a critical step for achieving good prognosis [120–128]. It is also advised to over prepare the osteotomy site to prevent the need for any hand torquing at a later stage, especially in areas where a dense hard-type of bone is present (D1/D2). This helps to evade the transfer of unfavorable bending forces on the implants and promote good osseointegration [117–120]. It is critical to place one-piece zirconia implant in it's surgically and prosthodontically most accurate position to prevent any subsequent modification and load transfer while abutment preparation. The zirconia implant abutment should be placed at a minimum distance of 1.5 mm below the plane of occlusion and not less than 3 mm in height. The implant shoulder should be scalloped to match the gingival contour of the tissues and should favor subgingival placement of the crown shoulder. The recommended shoulder design for zirconia implant is chamfer. The abutment section should be smoothed with no rough margins or areas prior to final impression. The crowns should be placed at a later stage after complete osseointegration and initial loading should be limited. Any immediate modification in the abutment section after implant placement should be performed with an ultrafine diamond bur along with copious irrigation. The abutment should only be prepared to allow for adaptation of the provisional restoration and more definitive modification of the implant shoulder should be done only following soft tissue healing. Additionally, the use of zirconia abutments for single implant-fixed crowns in posterior regions is still questionable due to the absence of long-term data. Few clinical long-term studies have reported an unexpected aseptic mechanical breakdown of the osseointegration and loosening of two-piece zirconia implants without any pain, discomfort and clinical signs of infection or inflammation [126]. Therefore clinicians should be cautious while using zirconia abutments in posterior regions until further clinical evidence shows favorable long-term outcomes [127,128].

4. Conclusion

Many in vitro and in vivo studies have proved zirconia implants as a promising alternative to titanium with a superior soft-tissue response, biocompatibility, and aesthetic with comparable osseointegration. The early fracture of one-piece zirconia implant, especially in the posterior region is a sensitive and critical factor to be considered regarding its use and acceptance in all clinical situations. Since most clinical studies on zirconia implants are short-term, substantial evidence supported by long-term clinical trials are warranted before zirconia based implant systems can completely replace titanium for prosthetic rehabilitation. Further research analyzing the techniques to prevent the ageing, enhancing surface characteristics, structure and osseointegration of zirconia implant are needed. More structured studies that assess the mechanical capacities of different types of zirconia with their exact composition, sintering process and manufacturing process are also needed to set standardized guidelines according to the ASTM (American Society for Testing and Materials) and ISO (International Organization for Standardization) in the manufacturing of zirconia implants.

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