Clinical Longevity of Zirconia Implants with the Focus on Biomechanical and Biological Outcome

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Abstract
Purpose of Review The goal of the present review is to update the reader on the scientific background of zirconia ceramic implants. Clinical investigations using zirconia ceramic implants over the last couple of years have brought up some new developments and questions. Can we be confident in placing zirconia ceramic implants given the recently published data? Is there a difference in the application of one- and two-piece implants?
Recent Findings Systematic reviews on preclinical investigations of zirconia implants revealed that one-piece zirconia implants (≥ 4 mm) are sufficiently stable for clinical use. The same is true for some clinically available two-piece implant systems. Osseointegration and soft tissue integration are, according to the reviews, similar between titanium and zirconia implants with similar surface topographies. Regarding the clinical outcome, a meta-review exists evaluating systematic reviews. The findings of the systematic reviews and the meta-review are that there are good short-term clinical results for one-piece zirconia implants. However, the data for two-piece implants is not robust.
Summary In certain applications (single tooth restorations and small bridges), the results of zirconia implants are comparable with titanium implants in short-term studies. Some mid-term investigations support the short-term results. However, according to the current scientific data available, zirconia implants cannot yet be considered an alternative to titanium implants because there are many areas where there is a lack of clinical studies on zirconia implants. Currently, they are an addendum to the titanium implant armamentarium for situations where they are useful (patient request, known hypersensitivity to titanium, or questions of esthetics when titanium might appear inappropriate for a certain situation/condition), but long-term studies are needed. Without a doubt, there is a need for two-piece zirconia implants, but limited research exists to support their clinical use at the moment.

Keywords Dental implants · Zirconia · Review · Artificial mouth · Biocompatibility · Osseointegration · Clinical study · Systematic review · Meta review

Introduction

The global dental implant market in 2016 was approximately US$3.8 billion. Between 2018 and 2024, it is anticipated to grow at a compound annual growth rate (CAGR) of 7.7% to nearly US$6.8 billion (https://www.grandviewresearch.com/industry-analysis/dental-implants-market). In 2016, titanium implants dominated the dental implant market with a portion of approximately 92.5%. The remaining 7.5% of the share was distributed among implants fabricated out of zirconia and other materials. Although not as large as the dominate titanium, the zirconia implant market is estimated to be worth over US$0.4 billion by the end of 2027, with a CAGR of 6.1% (https://www.futurewiseresearch.com/healthcare-market-research/Zirconia-Implant-Market/4254).

These data show that the market of zirconia implants is small in comparison to the titanium implant market at present, but it is growing and accounts for hundreds of millions of dollars. Zirconia oral implants are of particular interest for
our patients because they can positively support an esthetic outcome of a reconstruction due to their tooth-like color [1, 2].

Another argument in favor for ceramic implants is the wish of the patients to be restored without metals. When conventional fixed prosthetic dentistry is unable to deliver a successful long-term solution, and oral implants are necessary for replacing missing teeth, the respective patients can only be helped by using (zirconia) ceramic implants.

A final and obviously very important point is that zirconia lacks titanium particles which might cause adverse effects like hypersensitivity. This topic is discussed widely in the dental implant community [3–8]. Additionally, some investigations showed that zirconia ceramics are less prone to bacterial attachment and peri-implant infection [9–18], although this positive effect was not shown in all investigations [19–22]. Whether an advantage with respect to bacterial adhesion/peri-implant infection is attributable to the zirconia implant has to be questioned since the (ceramic) prosthetic reconstruction (abutment, crown) is in contact with the oral environment. But in the case of peri-implantitis, the implant does become exposed to the bacteria, and the adhesion characteristics can be very important when the implant surface is treated to decontaminate the surface. Besides the material per se, the surface texture characteristics, as well as the surface free energy, influence the bacterial adhesion.

Nevertheless, since there is interest in zirconia oral implants from the patients' and dentists' perspectives, implant companies realized the economic potential and therefore included zirconia implants into their product line. Already, many companies are distributing zirconia ceramic implants (the list in the following does not claim to be complete: Argon Medical Productions; Bredent medical; CeraRoot S.L.; Dentalpoint AG; Fairimplant; General Implants; Incermed; Moje Keramik-Implantate GmbH & Co KG; Metoxit; Natural Dental Implant AG; NobelBiocare; Paris Implants (Peltier); SDS Swiss Dental Solutions AG; Straumann; VITA Zahnfabrik; WITAR; ZV3-ZirconVison GmbH; Z-systems AG; Camlog system).

It should be pointed out that although quite a few companies sell zirconia ceramic implants, only a few commercial implant systems provide data on preclinical and clinical performances. This fact might be a reason why several associations dedicated to zirconia oral implants (e.g., European Society for Ceramic Implantology) have recently been founded with the goal to support preclinical and clinical research of zirconia ceramic implants.

The era of ceramic oral implants actually started with alumina as ceramic implant material [23, 24]. One-piece alumina implants were placed clinically with minor success. The problems with these implants were low stability and a lack of osseointegration. Since the surface treatment of alumina implants was difficult—in the sense of “surface roughening”—only macroscopic surface enlargements were produced. These modifications, however, did not improve the clinical outcome, and therefore, today, there is no alumina ceramic oral implant commercially available any more [24].

The search for a more fracture-resistant ceramic material for oral implant fabrication led to zirconia. This material has been in use for approximately 20 years in dentistry for the fabrication of endodontic posts, crown and bridge frameworks, and implant abutments [25–29]. Zirconia ceramic compositions that are used clinically or have been used in preclinical investigations are yttria-stabilized zirconia tetragonal polycrystal with a small percentage of alumina (Y-TZP-A), alumina-toughened zirconia (ATZ), ceria-partially-stabilized zirconia/alumina nanocomposite (Ce-TZP/Al2O3), or ceria-stabilized zirconia–alumina–aluminate composite ceramics (ZASr-Ce) [30–35]. The implants that have been used in clinical investigations so far were fabricated generally from 3Y-TZP or ATZ [30, 36].

Resistance to Fracture of Zirconia Ceramic Oral Implants

Before oral implants go to market, it would be advisable to test those implants preclinically regarding their fracture stability and biocompatibility. Different approaches have been applied in artificial testing environments to test the resistance to fracture of zirconia implants [37–39]. On the one hand, there is the mandatory testing of ceramic implant devices according to the ISO Standard 14801 by companies. On the other hand, in some published investigations, there are more “free-style” testing methods like using the environment of an artificial chewing simulator where parts of the ISO standard 14801 have been applied [40]. In the present review, only scientific results were considered.

Several laboratory investigations have been published dealing with the biomechanical stability of zirconia ceramic implants. In a recently presented study evaluating one- and two-piece ceramic implants, Riemer [41] showed that both types of implants survived a loading duration of 10,000,000 cycles with a force of 95 N in a hot aqueous environment. The bending moments to fracture of the ceramic implants were not influenced by this treatment. However, the bending moments to fracture (BMF) of both—the one- and two-piece zirconia implants—were significantly lower than the BMF of a titanium-zirconium control group (one-piece 557 Ncm, two-piece 443 Ncm, TiZr 735 Ncm). The authors concluded that both zirconia implant systems can be recommended for clinical use without concern of implant failure due to fracture. In a further investigation of the same group, Spies et al. [42] evaluated a commercially available two-piece zirconia implant regarding its long-term stability in the same chewing simulator. The bending moment to fracture of 614 Ncm was similar to that of a titanium implant (673 Ncm) but significantly lower.
to that of a titanium alloy implant of a similar design. In accordance with the investigation of Riemer [41], Spies et al. [42] concluded that the two-piece zirconia system will be able to resist masticatory forces for a long period.

A systematic review and meta-analysis by Bethke and coworkers [40••] summarized the current available literature regarding the fracture characteristics of zirconia oral implants. The Medline/Pubmed and Embase databases were screened for the review. In total, 731 implants were analyzed. A finding of the review was that the mean bending moment to fracture amounted to approximately 390 Ncm. The one-piece zirconia implants were significantly more fracture resistant (mean 431 Ncm) than the two-piece implants [mean 291 Ncm (p = 0.004)]. The aging of zirconia using steam or hot water was believed to decrease the stability of zirconia due to the low thermal degradation process [43]. However, according to the results of the systematic review of Bethke et al. [40••], neither high-temperature treatment in water nor thermocycling resulted in a statistically significant change in the bending moment to fracture (no treatment 406 Ncm, high-temperature treatment 393 Ncm, thermocycling 356 Ncm). A further interesting aspect which was evaluated in the systematic review was the influence of the prosthetic preparation of the abutment of one-piece implants. When implant abutments have been ground, the bending moment to fracture dropped from 437 to 411 Ncm. Although the difference was statistically significant, the question is allowed of whether the decrease in bending moment to failure (Δ 26 Ncm) due to grinding during prosthetic preparation would lead to a reduction of implant lifetime. The authors stated that “one might consider a minimum fracture resistance of 200 Ncm sufficient to guarantee clinical safety” after taking into account that the highest bending moment in humans has been stated to be 95 Ncm and adding a safety margin of 100% would result in a maximum of 190 Ncm.

The systematic review [40••] included investigations that dealt with commercially available [37, 39, 42, 44–50] and non-commercial prototype [38, 45, 50–56] implants. The authors considered this a limitation of the review. Indeed, some of the prototype implants were delivered without final treatment such as surface topography modifications or sterilization which might influence the fracture stability of the implants. Nevertheless, this comprehensive review showed that one-piece implants are less likely to fracture than two-piece implants. The authors of the present review adds the conclusion to the systematic review that one-piece implants with a regular diameter (≥ 4 mm) are stable enough for clinical function over a long period of time, and this is supported by the available published clinical evaluations (see later in this review). Also, some of the commercially available two-piece implant systems mentioned in the systematic review seem to be biomechanically stable enough to function clinically [41, 42].

A second review dealing with preclinical stability tests was published recently by Nishihara and coworkers [57]. In the paragraph dealing with biomechanical implant stability, the authors mentioned that the stability of one-piece implants seems to be sufficient for the clinical use in the posterior region. This statement was supported by three publications, and two [51, 53] of them were also included in the systematic review by Bethke et al. [40••]. The third publication [58] dealt with “the influence on mouth-motion fatigue reliability and failure.” The ultimate fracture strengths of the experimental one-piece implants with 1023 N and 1112 N were in a comfortable zone of stability.

Regarding the mechanical stability outcomes, it may be concluded from the original works and the (systematic) reviews that one-piece zirconia implants from a certain minimal diameter (≥ 4 mm) in general, as well as some of the two-piece zirconia implants—independent of the retention screw material—are stable enough to withstand normal clinical masticatory forces over an extended time period.

**Biological Outcomes of Zirconia Ceramic Oral Implants**

Besides the biomechanical stability as an important criterion for implant success, the biocompatibility is equally important. To be regarded as successful, zirconia implants should show an osseointegration rate that is similar to that of titanium implants. The bone-to-implant contact is one measure for biocompatibility. In the last 5 years, numerous reviews were published dealing with the biocompatibility of zirconia implants using the bone-to-implant contact as well as biomechanical stability as surrogate parameters [57, 59•, 60]. In the systematic review of Pieralli and coworkers [59•], the authors evaluated the amount of osseointegration of zirconia “implants” in animal investigations. In the end, they included 54 investigations that matched their inclusion criteria. The bone-to-implant contact (BIC) in percent, the removal torque (RTQ) in Newton centimeter, as well as the push-in force in Newton were the outcomes of interest. In their analyses for the bone-to-implant contact over all animal models, the evaluated titanium implants showed a mean BIC of 61%, and the zirconia implants, a BIC between 57 and 63%. The differences were not statistically significant. The authors stratified the dataset. For the differentiated results, the interested reader is referred to the systematic review and meta-analysis [59•]. Regarding the removal torque, no significant difference was found by the authors between titanium implants (103 Ncm) and zirconia.
implants (95 Ncm). In rats—where a removal torque evaluation is difficult/not possible to perform due to the limited size of bones—push-in tests were performed. Again, this parameter did not show significant differences between titanium (52 N) and zirconia implants (54 N). Smooth machined surfaces showed significantly lower RTQ and push-in values.

The authors concluded that within the limits of their systematic review and meta-analysis, there was no significant difference regarding the bone-to-implant contact between titanium and zirconia. However, the animal model and surface modification obviously influenced osseointegration [59].

In a second, more recently published systematic review and meta-analysis on preclinical studies [60], the hard and soft tissue integration of zirconia implants were evaluated. Thirty-seven animal studies were included in that review. Variables of investigation were again the bone-to-implant contact, the removal torque, and the push-in of implants. The BIC for titanium was 59%, and for zirconia, 56%. The RTQ for titanium amounted to 103 Ncm and 72 Ncm for zirconia. Titanium implants showed a push-in resistance of 25 N, while the zirconia implants showed one of 22 N. The BIC values for the two materials are in the range that has been found in the former systematic review [59]. The removal torque for titanium implants was identical in both reviews, whereas a difference of 23 Ncm existed for the RTQ for zirconia implants between the two reviews. Furthermore, Roehling and coworkers [60] found much lower values for the push-in values for titanium and zirconia implants. These differences might obviously be attributed to the different inclusion/exclusion criteria and subsequent selection of the analyzed studies (54 studies vs. 37 studies). Nevertheless, Roehling et al. [60] concluded that their findings point to a similarity in hard and soft tissue integration of (microrough) titanium and zirconia implants.

In a narrative review, Nishihara et al. [57] evaluated zirconia implants regarding mechanical properties (see above in this review) and hard and soft tissue response. Again, BIC and RTQ were the parameters assessed. In the selected studies (42 studies), the interval of BIC for the titanium implants was between 25 and 88% and between 24 and 85% for the zirconia implants. The RTQ values for titanium and zirconia implants were also very similar (titanium 7–74 Ncm; zirconia 9–78 Ncm). The authors were able to localize 5 investigations that explored the soft tissue response toward zirconia implants. In summary, the authors found that the majority of the studies reported no differences between titanium and zirconia implants. The soft tissue cuff around the implant neck consisted in both materials of a similarly sized epithelial layer followed by a connective tissue layer. In one of the selected investigations [61], the soft tissue height was 4.5 mm for the zirconia implants and 5.2 mm for the titanium implants ($p = 0.8327$). The extension of the junctional epithelium was similar between the two materials (2.9 mm). The connective tissue layer, however, showed a slight, but not statistically significant, difference (zirconia 1.5 mm; titanium 2.4 mm). The other investigations disclosed a smaller total soft tissue height in the range of 3 to 4 mm depending on the animal model used [57].

Regarding bacterial accumulation and inflammatory reactions, conflicting data exist (see above). Degidi et al. [10] showed in a clinical setting that the inflammatory infiltrate, the microvessel density, the expression of a certain growth factor (vascular endothelial growth factor-VEGF), and a synthesis producing free radicals (nitric oxide synthase) were higher around titanium healing caps than around zirconia caps. On the other hand, Barwacz and coworkers [19] did not find significant differences in pro-inflammatory cytokine or bone metabolism mediator profiles between titanium and zirconia abutments.

### Clinical Outcome of Zirconia Oral Implants

Preclinical investigations are necessary and valid in order to get early information on stability and biocompatibility of devices that will be applied clinically. Especially, laboratory biomechanical tests (see above) seem to be reasonable at evaluating implant stability (strength) and clinical applicability.

Nevertheless, clinical investigations are the ultimate proof of whether a device is successful on a long-term basis. Regarding zirconia ceramic implants, there are meanwhile some—by far not enough—scientific publications. Besides those, the interested reader will find already a meta-review [62] evaluating systematic reviews reporting on clinical outcomes of zirconia implants.

In a systematic review with meta-analysis, Pieralli and coworkers [30] included 9 studies filtered through certain inclusion criteria. A meta-analysis was performed for marginal bone loss. Two meta-analyses were performed for the survival of zirconia ceramic implants. The total population of the included investigations was 326 patients, with a total of 398 zirconia implants. Of these implants, 104 were restored with fixed dental prostheses, and the remainder, by single crowns. The meta-analysis for 1-year survival rendered a success rate of 96%. The second meta-analysis, based on follow-up times exceeding 1 year, calculated an expected decrease of implant survival of 0.05% per year. Marginal bone loss after 12 months was 0.79 mm in the meta-analysis. No significant differences in marginal bone loss could be found for the type of restorations (single crowns and small bridges), whether or not the implants had been immediately temporized or whether one- or two-piece implants had been inserted. The authors concluded from their systematic review and meta-analysis that within the limits of the review, the survival rate and the marginal bone...
loss after 1 year are comparable to the data of two-piece titanium implants and therefore promising.

Haro Adanez and colleagues [63] similarly performed a systematic review and meta-analysis on the clinical outcome of zirconia implants. With the inclusion and exclusion criteria applied, 17 investigations were included for review. The 17 investigations comprised a number of 1002 patients with a total number of 1704 implants (1521 one-piece implants, 183 two-piece implants). The observation period of the investigations was between 1 and 7 years, and the mean survival rate of the implants was calculated at 95%. One-piece implant survival was 95%, and two-piece implant survival, 94%. The failure rate was 6% for one-piece implants and 14% for two-piece implants over the respective observation times. A meta-analysis of 11 investigations for marginal bone loss found a mean loss of 0.98 mm. The authors reported that the heterogeneity of the included studies regarding implant survival and marginal bone loss was statistically significant. They regarded the clinical outcome of one-piece zirconia implants with the current evidence as good, whereas the evidence so far for two-piece implants does not justify the clinical use of those.

A further systematic review including a meta-analysis [36••] evaluated—interestingly—clinical investigations using commercially available or not commercially available zirconia implants. Their database search ended up with 18 included investigations. Fourteen of the investigations reported on one-piece zirconia implants and 4 on two-piece zirconia implants. Eleven different zirconia implant types from 10 companies were assessed. Nine investigations provided results for commercially available zirconia implants. A total of 1128 zirconia implants in 741 patients were available for analysis. Eighty-five implants failed (7.5%). When focusing only on not commercially available implants in the meta-analysis, the estimated 1-year survival rate was 91%, and when considering only commercially available zirconia implants, the estimated survival rate increased to 98%. Thus, commercially non-available implants showed a significantly lower survival rate compared with commercially available ones. The estimated 2-year survival rate for commercially available implants was calculated with 97%. When it came to marginal bone loss, there was no significant difference between the two groups of zirconia implants. The 1-year bone loss for commercially available implants was 0.78 mm and 0.98 mm for the not commercially available implants. In addition to implant survival and marginal bone loss, the authors reported on 22 zirconia implant fractures in 3 investigations (total fracture rate 1.95%). Eighteen fractures occurred in the investigation from Roehling et al. [64], 3 in the study from Osman et al. [65], and 1 fracture in the study from Brüll et al. [66]. Of the 18 fractures observed in the investigation of Roehling et al. [64], 15 implants were of a narrow diameter of 3.25 mm. These implants showed only an estimated survival rate after 7 years of 59%. According to the authors, this diameter-reduced implant has been taken from the market.

Of the 22 fractured implants, only one fracture occurred in an investigation evaluating 510 commercially available implants (0.2%) [66]. The fracture occurrence of commercially available zirconia implants coincides with the cumulative 5-year complication rate for titanium implant fractures with single crowns on implants of 0.18% [67] and for implants restored by fixed dental prostheses of 0.5% [68].

Roehling et al. [36••] concluded from the results of their systematic review that one-piece commercially available implants seem to be a reliable treatment for replacing missing teeth (except narrow diameter implants) for up to 2 years, whereas there is limited evidence that this is true for two-piece implants.

The conclusions drawn by the authors of the abovementioned meta-review [62] evaluating 9 systematic reviews that were published before December 24, 2018, were that the outcomes of short-term clinical investigations are good. However, the authors also concluded that there is still not enough evidence that either zirconia should be preferred over titanium or that it is an alternative to titanium.

After publication of the systematic reviews (including the meta-review that relates to those), further results on zirconia ceramic implants appeared in the scientific literature (Table 1). Balmer and coworkers [69] and Kohal et al. [73] presented the 5-year data of one-piece zirconia implants. Whereas in the former investigation Y-TZP implants were applied, in the latter, ATZ implants have been utilized. The implant survival rate after 5 years for the Y-TZP implants amounted to 98% with a marginal bone loss of 0.7 mm, whereas the ATZ implants showed a 5-year survival rate of 94% and a marginal bone loss of 0.8 mm [73]. Lorenz et al. [70] reported that after a mean 7.8 years, all one-piece Y-TZP-A-Bio-HIP implants survived (100%). The authors reported that one patient suffered from peri-implantitis around a zirconia implant. The marginal bone loss after the time period was recorded with 1.2 mm. Results of a 3-year follow-up of another one-piece zirconia implant were presented by Bormann et al. [71]. Only 1 implant was lost during the 3 year follow-up which led to a survival rate of 98%. The marginal bone loss from implant surgery to the 3-year follow-up was 0.97 mm. Mate-Sanchez de Val and Siewert [72] analyzed the results of zirconia implants in a clinical investigation after 11 years. Of 164 implants, 18 were lost over time.
(quick calculated survival rate 89%). Unfortunately, in the abstract, no further data (e.g., on marginal bone loss etc.) is provided.

No implant fractures have been reported in these latter studies, and it seems that the initial positive short-term data might be consistent over mid-term.

Conclusions

When summarizing the presented newer investigations, the systematic reviews, and the meta-review, the authors of this narrative literature review would conclude that one-piece zirconia implants are a valid treatment option over a period of up to 5 years with results comparable with those of titanium implants. However, when it comes to two-piece implants, the evidence is not as solid as for the one-piece implants, and the clinical use of those implants is more likely to be questioned due to the missing clinical data. It is therefore necessary that companies selling two-piece implants support sound research projects in order to close this scientific gap. This is for the safety and well-being of our patients.

For the authors of this narrative review, it is not a question at the moment about zirconia implants being preferred over titanium implants nor of being an alternative to those [62] because there are many areas where zirconia implants cannot be used in the same manner as titanium implants. It is rather about having an addendum to the implant armamentarium for situations where they are useful such as patient preferences, hypersensitivity to titanium, and esthetic limitations. If so, these situations should be discussed by the patient-dentist team with consideration of utilizing zirconia implants as a substitute to titanium implants.

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