Prospective Clinical Multicenter Study Evaluating the 5-Year Performance of Zirconia Implants in Single-Tooth Gaps

Michael Gahlert, DDS, PhD¹/Heinz Kniha, MD, DDS, PhD²/Sabine Laval, DDS³/
Nils-Claudius Gellrich, MD, DDS, PhD⁴/Kai-Hendrik Bormann, DDS, PhD⁵

Purpose: In recent years, ceramic implants made of zirconia have secured a niche position next to established titanium implants, due partly to new scientific findings and positive clinical experience with the handling of ceramic implants. The aim of this study was to assess the clinical and radiographic data for monotype ceramic implants that have remained in place for 60 months under masticatory loading. Materials and Methods: In 2011, this prospective clinical study included patients with a single-tooth gap in the maxilla and mandible. Monotype ceramic implants (Straumann) were used according to a standard protocol. Provisional prostheses were placed after 3 months, followed by final prostheses 3 months later. Patients were invited for a 60-month follow-up. Implant survival was analyzed from lifetime data. Success rates and crestal bone levels were evaluated from implant placement to 6, 12, 36, and 60 months after surgery. Results: From the initial 44 patients recruited, 36 were analyzable for the 60-month follow-up. With one implant lost before the 6-month follow-up, the success rate after 60 months was 97.7%, and the mean survival time was 58.7 months. Sixty months after implant placement, the success rate was 97.2% (95% confidence interval = 84.6% to > 99.9%). Mean bone loss after 60 months was 0.99 (± 0.59) mm. Conclusion: After 60 months, monotype ceramic implants made of zirconia achieved success and survival rates comparable with those reported for titanium implants in selected patient populations. Ceramic implants can be used as an alternative to titanium implants at the request of patients and if specifically indicated, for example, due to titanium intolerance. Int J Oral Maxillofac Implants 2022;37:804–811. doi: 10.11607/jomi.9289

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Various scientific and clinical studies have demonstrated the biocompatibility and impressive survival and success rates for titanium implants.¹⁻³ However, drawbacks of titanium implants such as peri-implant infections, implant intolerance, and esthetic shortcomings have also been reported.⁴⁻⁶ Zirconium dioxide (zirconia, ZrO₂) ceramic implants represent a completely new material group as an implant material and have been scientifically investigated and used clinically as an alternative to titanium implants for many years.⁷⁻⁸ Ceramic implants are similar to titanium implants in that they possess microrough surfaces, ensuring that osseointegration in the early healing phase is just as likely to be achieved as their titanium counterparts; however, they are toothlike in color.⁹¹⁰ In the latest in vivo scientific studies, ceramic implants showed advantages in terms of bone loss and artificially generated peri-implant infections.¹¹ A meta-analysis comparing titanium and ceramic implants in clinical trials found that the fracture rates of ceramic implants improved significantly, from 3.4% to 0.2%, between 2004 and 2017.⁷ However, variations in terms of the industrial manufacturing process of ceramic implants, study protocols, and implant shapes makes it difficult to compare the various zirconia products.⁸¹² Therefore, this study is designed to establish the clinical success and survival rates 5 years after implant placement for a specific implant system made from zirconia.

MATERIALS AND METHODS

This was a prospective clinical multicenter study investigating implants after 60 months of follow-up. The study
has been performed to provide long-term evidence on the safety and clinical performance of ceramic implants. The 1- and 3-year results have already been published, and the study is registered at www.clinicaltrials.gov (study no. NCT02163395).\textsuperscript{13,14}

**Patient Population**

Patient eligibility was verified against predefined criteria. The main inclusion criteria were single-tooth gaps in the mandible or maxilla, whereas the neighboring teeth of the implant sites had to be natural and healthy. In addition, the implant sites had to be substantially healed for at least 8 weeks after extraction. If necessary because of insufficient bone volume, bone augmentation procedures had to be performed at least 12 weeks prior to or simultaneous with implant placement. Patients not meeting the inclusion criteria were excluded from the study. Further exclusion criteria were defined as follows:

- Uncontrolled diabetes
- Mucosal diseases
- Untreated periodontitis or gingivitis
- Endodontic lesions
- Patients who smoked more than 10 cigarettes a day
- Probing pocket depth of at least 4 mm on a neighboring tooth
- Inadequate oral hygiene
- Severe bruxism
- History of local irradiation therapy

Additionally, patients were excluded from the study if primary implant stability could not be achieved during surgery or if the implants could not be placed in an appropriate prosthetically driven position.

**Implants**

All patients received a monotype ceramic implant (Straumann PURE Ceramic Implant) with a sandblasted, large-grit, acid-etched surface (ZLA). Implants were monotype yttria-stabilized zirconia (Y-TZP) with abutments already integrated into the implant design (abutment heights of 4 or 5.5 mm). This design ensures there is no microgap between the implant and abutment. Implants had a diameter of 4.1 mm, and the lengths ranged between 8 and 12 mm.

**Surgical and Restorative Procedure**

Implant placement surgeries were performed according to a standardized procedure. Based on the monotype design, all implants healed unloaded in a transmucosal position. Optionnally, to avoid soft tissue overgrowth on the implant shoulder, protective caps were placed on the abutments. In cases where no protective cap was placed, if necessary, the implant shoulder was uncovered prior to insertion of the provisional prosthesis. Sutures were removed 1 to 2 weeks after surgery, a provisional prosthesis was placed at 11 to 13 weeks, and a final prosthesis was placed at 24 to 28 weeks after implant placement. The clinicians used their standard procedures to place prosthetics; no specific prosthetic procedure was required by the protocol. Lithium disilicate glass-ceramic or zirconia ceramic crowns were used in most cases due to the monotype implant design. Crowns were directly cemented onto the implant abutment with permanent glass-ionomer luting cement. To avoid excessive cement during the cementation procedure, the ceramic crowns were designed with a cement-draining hole on the occlusal side. Crown cementation was done according to a defined clinical protocol. This included a moderate/thin application of the cement using a small dental brush.

In addition, submarginal cement excess was removed with a special dental floss (Superfloss, Oral B) during the hardening procedure. The absence of excess cement was clinically and radiographically confirmed. Periapical radiographs were taken after implant placement and after crown insertion.

Figures 1 to 6 illustrate one of the treated cases. This involved the replacement of a maxillary left first premolar, which had been extracted 3 months previously, by a monotype ceramic implant. After the alveolar ridge was exposed, a monotype ceramic implant was placed according to the previously established surgical protocol and using positioning indicators to check the correct implant position and angulation during surgery. The selected abutment height of the implant was determined on an ad hoc basis with the aid of gauges during the surgical phase. After 7 days, the sutures were removed, leaving the implant to integrate unloaded in the bone over the next 3 months. Following that, the soft tissues were shaped during the exposure surgery, and a provisional restoration prepared chairside was used to form the gingiva. The final crown was subsequently prepared after a corresponding impression was taken, and this was cemented definitively in place with glass-ionomer cement. The follow-up radiographs shown here are the standardized radiographs directly after implant placement and after the restoration had been in place for over 5 years (Fig 6).

**Clinical and Radiographic Examination**

Patients were invited for a clinical and radiographic checkup 12, 24, 36, and 60 months after implant placement. Clinically, the presence of plaque and sulcus bleeding were assessed around the implants and the neighboring teeth. In addition, adverse events (AEs) regarding the patients’ general health condition (eg, altered medications, general diseases like heart attacks or diabetes that have been diagnosed during the...
study) and implants, including technical complications regarding the implant body and the prosthetic restoration (chipping, fractures, or debonding), were monitored during the observation period. Moreover, it was evaluated whether the patients had experienced any complications (eg, pain, bleeding) since the previous checkup. Biologic complications like peri-implant soft tissue complications (eg, swelling, fistulas, mucositis) and peri-implantitis were also monitored.

To evaluate marginal peri-implant bone remodeling, standard periapical radiography using individual, customized radiographic stents was performed at baseline (implant placement) and at 12, 24, 36, and 60 months after implant surgery. Peri-implant bone remodeling was evaluated as shown in Fig 7, measuring the vertical distance from the implant shoulder to the first visible bone-to-implant contact (BIC) by means of a single, independent specialist on the standardized periapical radiographs. The margin of

Fig 1 Initial clinical situation with an edentulous gap at the maxillary left first premolar and a healthy adjacent canine and second premolar.

Fig 2 Monotype ceramic implant in situ.

Fig 3 Healed situation before prosthetic restoration.

Fig 4 Fully shaped gingiva for definitive prosthetic restoration.

Fig 5 All-ceramic crown cemented onto a monotype ceramic implant with glass-ionomer cement (Ketac Cem, 3M) in the first premolar site.
the implant shoulder was identified as the transition point from the implant shoulder to the cemented crown. This measurement was taken at the distal and mesial sides of the implant, and the mean value was calculated. Measurements were normalized against the known thread pitch of the implants to adjust for any imaging distortions. Over time, mean bone level changes were evaluated by subtracting the average bone level at the respective study visit (5-year follow-up) from the average bone level at implant placement. Distortions based on changes on the radiograph from the true implant dimensions were taken into account. The measurements were performed using ImageJ software.15

**Implant Survival**
Implant survival was defined as retention of the implant at the 60-month follow-up.

**Implant Success**
Implant success was defined according to previously described criteria.16 Implants were considered successful if there was no: pain, foreign body discomfort, dysesthesis, recurrent peri-implant infection with suppurative, implant mobility, or continuous peri-implant radiolucency. Implant failure was defined as implant loss after insertion.

**Statistical Analysis**
DMSYS data management software (version 5.3) was used for data management, and IBM SPSS statistical software (version 21, IBM) was used for statistical analysis.

Descriptive summary statistics were calculated for all documented parameters, including mean values and standard deviations (SDs). The analyses included all patients who received an implant and were not lost to follow-up (intention to treat, ITT).

To account for the patients lost to follow-up, survival rates of the implants were estimated using lifetime data based on the Kaplan-Meier estimator with 95% confidence intervals (CIs). To evaluate success rates, patients lost to follow-up at 60 months were excluded. Success rates were calculated at each follow-up visit as number of patients meeting all the success criteria divided by patient population at this follow-up visit.
At each follow-up visit, average bone level was subtracted from average bone level at baseline to calculate mean bone level change. Positive change represents bone gain from baseline to follow-up and negative change represents bone loss. Missing values of the ITT population were imputed and replaced with the mean values of the remaining patients for the specific measurement and point of time. Sensitivity analysis was conducted for the imputed data set.

Further statistical analysis details are provided in the prior publications of the study.13,14

RESULTS

The present paper only reports the clinical and radiographic data after 60 months of follow-up. The data after 12- and 36-month follow-ups have been previously published.12,13

Patient Population

The first patient was enrolled in October 2011, and the last patient completed the 60-month follow-up in October 2017.

From the initial set of 46 screened and 44 enrolled patients, 10 were not available for the 60-month follow-up investigation and had to be excluded from the analysis: 5 patients terminated the study early, 3 patients were lost to follow-up after 12 and 24 months, one patient withdrew consent after 3 months, and one experienced an AE that lead to loss of the implant after 6 months. Consequently 36 patients (21 female; median age: 53 years, age range: 24–83 years) receiving 36 implants were available for the 60-month follow-up.

In patients included in the 5-year follow-up, the majority of implants were placed in the maxilla (33 implants; 91.7%), with just 3 implants (8.3%) placed in the mandible (Table 1). Bone augmentation during implant placement was necessary in 36.1% of the cases (13 out of 36 sites). In each of these cases, augmentation occurred in the esthetic zone and was performed simultaneously with implant placement. All augmentations were considered to be non-major.

Clinical and Radiographic Examination

From the analyzable population, plaque was observed in 13 (36.1%) patients during the study, mostly at screening (n = 7, 53.8%), at month 60 (n = 8, 61.5%), and at month 12 (n = 6, 46.2%). Until month 24, plaque occurrence was only recorded for the adjacent tooth or teeth, whereas at month 36, three of the eight occurrences were reported for the implant site (Fig 8). At the 60-month follow-up, plaque was only present at two adjacent teeth, whereas no plaque occurrence was detected at the implant sites.

In the population, bleeding was detected in 14 (38.9%) patients since baseline. The majority of bleeding was noted at month 60 (n = 11, 78.6%). At month 36, bleeding was detected in eight patients (57.1%), at month 24 in six patients (42.9%), at month 12 in seven patients (50.0%), and at screening in two patients (14.3%). Bleeding occurred at the implant site, the adjacent teeth, or at both locations (Fig 9). At the 60-month follow-up, bleeding occurred at five implant sites, at two adjacent teeth, and at four implant sites and adjacent teeth. Bleeding was not associated with peri-implantitis.

At the 60-month follow-up, a total of five additional AEs were reported. All were deemed not to be related to the study device. Since implant placement, a total of 63 AEs were reported by the patients returning to the 60-month follow-up (N = 36). From these, 22 AEs (34.9%) were deemed to be related to the placed implants or study treatment: pain (n = 15); bleeding, swelling, inflammation/infection (n = 4); and unfulfilled implant success criteria (n = 3). None of these seven AEs were deemed to be related to the study device or study treatment.

Peri-implant bones levels were derived from the patient population (N = 36) using imputed data for missing values. At 60 months, 88.89% of implant sites (n = 32) demonstrated bone loss of < 1.5 mm or bone gain (Fig 10). In general, bone loss was most pronounced in the first 6 months after implant surgery (0.95 ± 0.88 mm). In contrast, the mean bone level remained stable (minimal gain of 0.04 [± 0.61] mm) between 12 and 60 months. Overall bone loss between

### Table 1 Distribution of Implants Placed in the 60-Month Follow-Up Population FDI

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implant surgery and 60 months was 0.99 (± 0.58) mm. Bone levels at 6, 12, 24, 36, and 60 months were significantly different from baseline at implant surgery ($P < .001$; Fig 11). The ranges of bone loss were 0.7 to 4.4 mm, 0.11 to 4.6 mm, 0.1 to 4.7 mm, −0.8 to 3.0 mm and −0.4 to 2.4 at 6, 12, 24, 36, and 60 months after the implant surgery, respectively.

**Implant Survival**

From the initial 44 patients who received a study implant, 39 patients reached the 36-month endpoint of the study (5 patients dropped out in this period for several reasons). Another 3 patients were lost to follow-up for the 5-year study visit, leaving 36 patients for this endpoint. Over the entire period from implant loading until the 5-year follow-up visit, one implant was lost before final implant loading (date of surgery: 25 July 2012; date of implant loss: 26 October 2012).

Figure 12 shows the Kaplan-Meier curve for implant survival over the entire 60-month observation period. Due to one implant loss 3 months after implant loading, the probability for implant survival declined to 97.7% but remained unchanged for the rest of the observation. Accordingly, the mean survival time amounted to 58.7 months (95% CI: 56.2 to 61.2 months).
Implant Success
By the 60-month follow-up period, four implants in total were considered to be “not successful.” Three of them were reported in the first 24 months. At the 6-month follow-up period, in two patients a mucositis was present, and one of these patients also exhibited continuous radiolucency around the implant. At the 24-month follow-up, one patient’s implant was considered “not successful” as the patient exhibited mucositis as well as pain and foreign-body discomfort or dysesthesia. Thereafter, at the 60-month follow-up, recurring peri-implant infection was detected in one of the remaining 36 patients. This resulted in a 97.2% success rate (95% CI = 84.6% to >99.9%).

DISCUSSION
From the standpoint of materials science, today’s ceramic implants made from zirconia are not comparable to earlier ceramic implants made from alumina in terms of the requirements for an implant material. A meta-analysis by Roehling et al compared the stability of ZrO2 implants with that of titanium implants and concluded that the fracture rates for ZrO2 implants improved during the period between 2004 and 2017 from 3.4% to 0.2%. This situation is certainly attributable to the advances made in industrial manufacturing processes, which crucially affect the stability of the material and the design of microrough surfaces on modern ceramic implant systems. These two features of ceramic implant systems are responsible for osseointegration. According to another meta-analysis by Roehling et al, the osseointegration achieved with ZrO2 implants is almost equivalent to that obtained with comparable titanium implants with a microrough surface. To this end, the authors reviewed preclinical studies that investigated ceramic and titanium implants in regard to their behavior in soft and hard tissues. Distinctions were made between various animal species and loaded and unloaded implants. Of 31 evidence-based and relevant studies, no significant differences were observed in 21 studies between titanium and ZrO2 implants regarding BIC. Significant differences were observed in 10 studies for unloaded implants: significantly higher values were recorded for ZrO2 in five studies and for titanium in the other five studies. These statistically significant differences were attributable to the different surface properties of the implants, with increased surface roughness in ceramic implants being associated with increased BIC values.

The meta-analysis also brought forth statements concerning the removal torque-out values of implants and teeth. The torque-out value gives an indication of the strength of implants in the bone after defined healing periods. Ten studies satisfied the requirements of the meta-analysis in this connection. The analysis revealed no significant differences between ZrO2 and titanium in three studies, significantly higher torque-out values for titanium implants in six studies (five of the studies with unloaded implants, one study with loaded implants), and significantly higher torque-out values for unloaded ceramic implants in one study. In these cases, an increased surface roughness of ceramic implants was associated with increased removal torque values.

Statements concerning the soft tissue integrity of titanium and ceramic implants and based on evaluated evidence-based data were also encountered. Six studies were analyzed, and these showed that the maturation process for the epithelial and connective tissues around ZrO2 implants was faster compared to titanium implants. No significant differences between titanium and ZrO2 were observed regarding biologic width.

A statement concerning the data from long-term studies with ZrO2 implants was also examined during the meta-analysis. Commercially available monotype ZrO2 implants showed survival rates of 98.3% and 97.2%, respectively, after 1 and 2 years.

In previously published studies investigating the same patient population after 1 and 3 years of functional loading, implant success was defined according to the criteria described by Buser et al. Consequently, the same success criteria were applied in the present investigation.

In the present study, implant survival and success rates of 97.5% and 97.2% were evaluated after a mean follow-up period of 58.7 months. However, all monotype implants were placed in correct and appropriate positions according to the prosthetic requirements. It should be noted that placing the implants in inappropriate positions might have negatively influenced the results.

Regarding peri-implant marginal bone levels, a mean bone loss of 0.99 (± 0.59) mm was found 60 months after implant placement. In single cases, the statistical analysis has also shown some bone gain around the polished implant shoulder (see Fig 10). This may be a result of the highly biocompatible material characteristics of zirconia. However, in some cases, the transition point from the implant shoulder to the cemented prosthetic restoration was difficult to identify because the implant margin became obscured with the ceramic crown and the used cement. This fact must be considered when interpreting the results. The presently used method for the evaluation of peri-implant marginal bone loss has previously been described in clinical studies.

The presently evaluated values for implant survival and marginal bone loss are in accordance with previously published data investigating a different kind
of monotype zirconia implant after a mean follow-up period of 5.6 years. The authors of the latter studies reported an implant survival rate of 98.4% and a mean peri-implant bone loss of 0.7 mm for 71 implants placed in 60 patients.17,18

A previously published meta-analysis has shown that ongoing market availability and physical properties of zirconia implants must be considered when interpreting results from clinical studies because this fact has a significant impact on implant survival.7 The zirconia implants that were investigated in the present study are commercially available. The currently evaluated survival and success rates of > 97% are higher compared to results from clinical studies investigating two-piece zirconia implants that are no longer commercially available on the market. The authors of the latter studies reported survival rates of only 83% and 85.7% after functional loading of 5 years and more.19,20

CONCLUSIONS

Within the limitations of this study, including limited patient and implant numbers and possible inaccuracy regarding the radiographic analysis, the results have shown reliable implant survival and success rates of > 97% and low peri-implant marginal bone loss of < 1 mm after 5 years of functional loading for monotype zirconia implants. Additionally, the clinical and radiographic evaluation has shown no signs of peri-implantitis. The study results presented in this paper confirm the trend indicating that zirconia implants show similar survival and success rates compared to published data on titanium implants.

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