Clinical and patient-reported outcomes of a zirconia oral implant: three-year results of a prospective cohort investigation

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Abstract: The objective of this study was to determine the clinical, radiographic, and patient-reported outcomes of a 1-piece alumina-toughened zirconia implant restored with single crowns (SCs) or 3-unit fixed dental prostheses (FDPs) after 3 y of observation. Forty patients received 53 implants, placed in a 1-stage operation with immediate temporization. Finally, 50 implants were restored with 24 SCs and 13 FDPs. To evaluate peri-implant bone loss, standardized radiographs were taken at implant insertion, at final restoration delivery, and after 1 and 3 y. Additionally, several soft tissue parameters and patient-reported outcome measures were evaluated. Linear mixed models with random intercept for each patient and patients as clusters were used to compare subgroups. Three patients did not receive a SC due to early implant loss, and 1 patient died. As a result, 36 patients with 49 implants were followed-up for 3 y, giving a cumulative survival rate of 94.2%. The average marginal bone loss amounted to 0.79 mm (SCs, 0.47 mm; FDPs, 1.07 mm; $P < 0.001$). After the delivery of the final prosthetic restoration, further bone loss was not statistically significant (0.09 mm; $P = 0.700$). Probing depth, clinical attachment level, and modified bleeding index increased significantly at the implant sites, whereas gingival recession decreased significantly. Compared with the pretreatment questionnaires, the patient-reported outcome measures showed a permanently improved perception of function, aesthetics, sense, speech and self-esteem. The survival rate of the investigated ceramic implant system seems to be comparable to reported survival rates of titanium implants when immediately restored. The recorded parameters suggest its potential for clinical utilization.

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Tissue-related and patient-reported outcome of a zirconia oral implant: Three-year results of a prospective cohort investigation

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Abstract

Objective: To determine the clinical, radiographic and patient-reported outcomes of a one-piece alumina-toughened zirconia (ATZ) implant restored with single crowns (SC) or three-unit fixed dental prostheses (FDP) after three years of observation.

Materials and Methods: Forty patients received 53 implants, placed in a one-stage surgery with immediate temporization. Finally, 50 implants were restored with 24 SCs and 13 FDPs. To evaluate peri-implant bone loss, standardized radiographs were taken at implant insertion, at final restoration delivery, and after one and three years. Additionally, several soft tissue parameters and patient-reported outcome measures (PROMs) were evaluated. Linear mixed models with random intercept for each patient and patients as clusters were used to compare subgroups.

Results: Three patients did not receive a SC due to early implant loss and one patient died. As a result, 36 patients with 49 implants were followed-up for three years giving a cumulative survival rate of 94.2%. The average marginal bone loss amounted to 0.79 mm (SCs: 0.47mm; FDPs: 1.07mm; $p<0.001$). After the delivery of the final prosthetic restoration, further bone loss was not statistically significant (0.09mm; $p=0.700$). Probing depth, clinical attachment level and modified bleeding index increased significantly at the implant sites, whereas gingival recession decreased significantly. Compared with the pre-treatment questionnaires, the PROMs showed a permanently improved perception of function, esthetics, sense, speech and self-esteem.

Conclusion: The survival rate of the investigated ceramic implant system seems to be comparable to reported survival rates of titanium implants when immediately restored. The recorded parameters suggest its clinical utilization.

(249/250 words)

Introduction

Clinical long-term results reported for titanium implants have made titanium the "gold standard" material for the fabrication of oral implants (Jung et al. 2012; Pjetursson et al. 2012). Nevertheless, there are still concerns that titanium might evoke an unwelcome host reaction. However, it remains unproven and difficult to certainly diagnose whether titanium is causal for allergic reactions in patients with dental or even orthopedic implants of a larger dimension (Hallab et al. 2001; Javed et al. 2013). Even so, the rising popularity of metal-free reconstructions motivates clinicians to offer implants of alternative materials, e.g. ceramic implants made of zirconia. Aside from possibly favorable tissue health considerations, one of the main advantages of whitish ceramic implant/abutment materials might be an esthetic benefit in the presence of a thin soft tissue biotype (Cosgarea et al. 2015; Jung et al. 2007). Especially in the occurrence of buccal hard tissue recession in anterior cases resulting in subgingival implant surface exposure, the compensation potential of solely ceramic abutments might be limited. Yttria-stabilized zirconia (Yttria-stabilized tetragonal zirconia polycrystal, Y-TZP) seems to be the favorable ceramic for the manufacturing of dental implants. The material is characterized by a dense, monocrystalline homogeneity. Y-TZP shows a high flexural strength and high fracture toughness (Table 1). These characteristics are based on a phase transformation toughening mechanism (Christel et al. 1989). Pre-clinical laboratory investigations revealed that implants made of Y-TZP may withstand long-term oral chewing forces (Andreiotelli and Kohal 2009). In vitro, in vivo and animal experiments proved their potential for a successful clinical application (Andreiotelli et al. 2009). Besides Y-TZP, another ceramic composite with a modified toughening mechanism (alumina-toughened zirconia = ATZ) proved to be a promising implant material (Spies et al. 2015a). ATZ ceramics seem to be advantageous compared with Y-TZP regarding their susceptibility to the tetragonal to monoclinic ($t \rightarrow m$) phase transformation and, therefore, aging induced fatigue (Kohorst et al. 2012; Schneider et al. 2008).

The data on the clinical application of zirconia implants is limited (Depprich et al. 2014). Regarding the use of ATZ as implant material, only one short-term investigation is available (Spies et al. 2015b). Therefore, the aim of the present prospective clinical investigation was to determine the survival and success rate including the peri-implant bone loss, soft tissue parameters, and patient-reported outcome measures of a one-piece ATZ ceramic implant after five years. This article presents the currently available results after three years of observation.

Materials and Methods

Study design

Considering the inclusion and exclusion criteria, patients were consecutively included having signed an informed consent form. The patients had to be systemically healthy and in need of an implant-supported single tooth or terminally attached three-unit bridge restoration. Only one reconstruction per patient was allowed. The primary outcome was the survival and success rate of the ceramic implant including the radiographic evaluation of peri-implant bone loss. In addition, secondary outcomes were the clinical evaluation of the peri-implant soft-tissue and patient-reported outcome measures, respectively. The investigation was approved by the ethics committee of the University's Medical Center (investigation number: 337/04; 02/22/2008) and performed considering the STROBE Statement for cohort studies (Strengthening the reporting of observational studies in epidemiology; http://www.strobe-statement.org).

Study implants and implant placement

The CE-marked implants (Ziraldent® FR1; Metoxit AG, Thayngen, Switzerland), the pre-surgical evaluations and surgical procedures as well as the peri-operative medications were described in detail elsewhere (Spies et al. 2015b). Implants were placed in healed and fresh extraction sites. When implant sites presented bone fenestrations or dehiscences, regenerative procedures according to the principles of GBR using a resorbable membrane (Bio-Gide®, Geistlich Pharma AG, Wolhusen, Switzerland) and a bovine bone substitute (Bio-Oss®, Geistlich Pharma AG) were performed. For the immediate temporization of the implants, a primary stability of at least 30 Ncm was mandatory. This insertion torque value was chosen on the basis of the positive implant survival results of immediately loaded titanium implants published by several authors (Crespi et al. 2008; Schincaglia et al. 2008; Testori et al. 2007). Occlusal and approximal contacts were removed to avoid excessive forces on the implants. In order to monitor the marginal bone loss at implants and neighboring teeth, an individualized intraoral X-ray film holder was constructed after implant placement to facilitate the making of standardized radiographs. After 7 to 10 days, sutures were removed and the surgical area inspected for any healing problems.

Prosthesis insertion

The patients wore the provisional restorations for at least six weeks in the lower jaw and for at least 14 weeks in the upper jaw. The final prosthetic reconstructions consisted of all-ceramic single-crowns (IPS e.max® CAD LT, Ivoclar Vivadent, Schaan, Liechtenstein) and the three-unit bridges (IPS e.max® ZirCAD & IPS e.max® ZirPress LT, Ivoclar Vivadent).

Clinical follow-ups

Follow-ups were scheduled for 1, 2, 3, 4 and 5 years after implant installation. The follow-ups involved the soft tissue parameters probing depth (PD), clinical attachment level (CAL), gingival recession (GR), the modified bleeding index (mBI) and modified plaque index (mPI), the latter two according to Mombelli (1987). Teeth adjacent to the implants served as reference and the same soft tissue parameters were collected. The parameters PD, CAL and GR were measured to the nearest millimeter with a periodontal probe (PCP 12; Hu Friedy, Rotterdam, Netherlands). In the presence of reference teeth, the papilla height measurement was performed according to Jemt (1997).

Bone loss/bone remodeling

After implant placement, standardized radiographs were taken using a customized film holder. Further radiographs were taken after final crown/bridge insertion and at the one and three-year follow-up (Supplemental figure 1). The radiographs from the timepoint of implant installation served as marginal bone level baseline. The differences between the marginal bone level at baseline and the subsequent follow-ups were calculated at the implant sites and at the neighboring teeth (Supplemental figure 2). All radiographs were independently examined at the University of Zurich (MB).

Patient reported outcome measures (PROMs)

The patients' appraisal of function, esthetics, sense, speech and self-esteem have been assessed at the pre-treatment examination, at the delivery of the final prosthetic restoration, and at the follow-up sessions applying visual analogue scales (VAS). To permit a standardized procedure, the patients were asked to mark on a line (10 cm, no scale) the point that corresponds most with their subjective perception. The left end point represented "poor satisfaction" (0%), the right one "excellent satisfaction" (100%). Patients' markings were measured with a ruler (1 mm corresponds to 1%).

Implant success criteria

A successful implant showed no local or systemic allergic, toxic or other negative reactions. Furthermore, it was not mobile and still supporting the prosthetic reconstruction. Regarding success related to bone loss, the recommendations of the group of Östman et al. (2007) where adopted that not more than 2 mm of bone loss during the first year was acceptable for one-piece implants that were immediately temporized. A success grade I was applied to implants with ≤ 2 mm of bone loss after three years. A success grade II was applied to implants showing no further pathology but a bone loss/resorption of ≤ 3 mm (Östman et al. 2007; Sennerby et al. 2008). If one or more negative reactions towards an implant were observed but the implant and its superstructure were still in situ in a stable condition, the implant was rated as "surviving". Fractures or removed implants were rated as "failure".

Statistical analyses

For the soft- and hard-tissue evaluation, linear mixed models with random intercepts were fitted for each patient to assess time, position (mesial tooth, implant site, distal tooth) and treatment (SC/FDP) effects on the response variables (Bone loss; PD, CAL, GR, mBI, mPI). In consequence of the collected data at three positions (mesial tooth, implant site, distal tooth) per patient, the patients were considered as clusters. This clustering was performed separately for each response variable. Furthermore, multiple pairwise comparisons between the different positions were done. Therefore, the Tukey-Kramer method was applied to correct for the multiple testing problem (adjustment of p-values).

For the PROMs, linear and logistic mixed models with random intercepts were fitted for each patient to evaluate time (restoration independent) and treatment (SC/FDP) effects on the response variables.

The calculations were performed with the statistical software STATA 13 (StataCorp LT, College Station, TX, USA) using "xtmixed" and SAS 9.3 (SAS Institute Inc., Cary, NC, USA). The probability level for statistical significance was set to $p < 0.05$.

Results

Forty patients (20 women and 20 men) were included in this investigation and in total 53 ceramic ATZ Ziraldent® implants were inserted (Supplemental table 1). 51 implants were placed in healed and two implants in fresh extraction sites. All inserted implants showed a primary stability of at least 30 Ncm and were therefore immediately temporized. All single implants were opposed by teeth. Furthermore, except one implant-supported single crown distal to a single tooth replacement, all single implants were mesially and distally bordered by teeth. The FDPs were entirely bordered by teeth (9/13 only on the mesial; 4/13 on the mesial and distal) and opposed by solely teeth (8/13), a combination of teeth and an implant-supported single crown (1/13), partially removable dental prostheses (2/13) or a combination of teeth and a partially removable dental prosthesis (2/13).

Status of follow-up and life table analysis

Of the 53 inserted implants, 50 were finally restored: 24 with all-ceramic single crowns and 26 with (13) terminally attached all-ceramic three-unit bridges. Three posterior single implants failed to osseointegrate and had to be removed prior to their final prosthetic reconstruction (i.e. 3-4 weeks after implant surgery). These three implants were considered as failures. Since one patient died after the 1 year follow-up due to a malign tumor diagnosed after study inclusion, 36 of the remaining 37 patients with 49 implants showed up at the three-year follow-up appointment. From the delivery of the final restoration to the three-year follow-up, no additional implant losses were observed leading to cumulative survival rate of 94.2% after 3 years.

Peri-implant soft tissue conditions

The peri-implant soft tissue conditions over time are illustrated in Figure 1. The corresponding data including detailed information on the statistical analyses are listed in the appendices (Supplemental tables 2 and 3). In brief: Probing depth ($p<.001$), clinical attachment level ($p=.002$) and bleeding index ($p=.002$) increased significantly over time at the implant sites whereas the plaque index remained stable ($p=.096$). Furthermore, gingival recession decreased significantly ($p<.001$). Compared to prosthetic delivery, papilla growth reached statistical significance ($p<.001$) at the one-year and the three-year follow up, respectively.

Marginal bone remodeling

The peri-implant bone remodeling is illustrated in Figure 2. The corresponding data including detailed information on the statistical analyses are listed in the appendices (Supplemental table 4). Of the 49 radiographically evaluated implants, four implants (8.2%) gained some bone from insertion to the three-year follow-up, whereas two implants (4.1%) lost more than 2 mm of bone (Table 2). A bone loss of more than 3 mm was not found at any implant site. According to the success criteria from Östman et al. (Östman et al. 2007; Östman et al. 2008), 95.9 % of the implants were assigned to success grade I and 100 % to success grade II at the three-year follow-up.

In summary, an average bone loss of 0.79 mm was observed from implant insertion to the three-year follow-up. The restoration type seemed to have a significant effect on bone resorption after three years of observation (SCs: 0.47 mm; FDPs: 1.07 mm; $p<.001$; Figure 2b). After the delivery of the final restoration, the bone levels showed no statistical significant changes over time (0.09 mm; $p=.700$). Gender ($p=.751$), location (anterior/posterior; $p=.844$), jaw ($p=.913$), implant platform (3/4/5 mm; $p=.227$), implant length (9/12/14 mm; $p=.128$), bone quality (1-4 according to Lekholm and Zarb (1985); $p=.112$), bone quantity (A-E according to Lekholm and Zarb (1985); $p=.849$), grafting procedure (GBR/no grafting; $p=.542$), flap design (with/without releasing incisions; $p=.494$) and bone anchorage (mono/bi-cortical; $p=.429$) had no significant influence on the marginal bone level changes over time.

Patient-reported outcome measures (PROMs)

The PROMs are illustrated in Figure 3. The corresponding data including detailed information on the statistical analyses are listed in the appendices (Supplemental table 5). Compared to the pre-treatment situation (33.9-85.1%), all follow-up assessments revealed significantly improved average VAS values at the delivery of the prosthetic restorations (81-97.7%; $p<.038$). Whereas the improvement of sense and self-esteem remained stable over the course of the follow-ups ($p=.128$), subjective patients' perceptions of function, esthetics and speech still increased over time ($p<.022$).

Discussion

Clinical parameters can only provide an objective, however, limited understanding of oral health outcomes in dental implant therapy. Therefore, it is strongly recommended to consider PROMs in (dental implant) research as well (McGrath et al. 2012). To date, this is the first clinical evaluation of zirconia oral implants reporting on clinical parameters and several PROMs. Throughout, an increased satisfaction of the participants could be observed immediately after the treatment (i.e. the delivery of the prosthetic restorations). The ongoing assessments at the follow-up appointments showed no reduction of the positive effect (i.e. continuously improved VAS values) over the course of the years. Thus, from the patients' point of view, the presented treatment using zirconia oral implants for the replacement of missing teeth has proved to address their needs with a lasting positive effect.

Most of the currently available evaluations of zirconia oral implants are short to mid-term reports up to 4 years of observation (Borgonovo et al. 2015; Borgonovo et al. 2013; Borgonovo et al. 2012; Brüll et al. 2014; Cannizzaro et al. 2010; Cionca et al. 2015; Gahlert et al. 2015; Kohal et al. 2012; Kohal et al. 2013; Payer et al. 2013; Payer et al. 2015). These reports include a variety of superstructures from single tooth replacements to full-arch fixed dental prosthesis at both augmented and non-augmented sites. Furthermore, they are adopting different success criteria (Albrektsson et al. 1986; Buser et al. 1990; Naert et al. 1992; Östman et al. 2007; Snauwaert et al. 2000) hampering the comparability of the mentioned studies. The importance of reporting parameters like marginal bone loss (MBL) around implants has been shown in the investigations of Kohal et al. (Kohal et al. 2012; Kohal et al. 2013). Although, an implant survival rate of 95%/98% after one year was reported, the implant success rate at the one-year follow-up decreased considerably when the success criteria "bone remodeling/loss" was included. According to the success criteria described by Östman et al. (2007), the implant success rates were as low as 66%/60% applying grade I and 86%/72% applying grade II, respectively. Reported implant survival rates of the above mentioned publications vary between 87% (Cannizzaro et al. 2010; Cionca et al. 2015) after one year and 100% (Borgonovo et al. 2015; Borgonovo et al. 2013; Borgonovo et al. 2012) after up to 4 years of observation. In the current investigation, three implants were lost prior to the delivery of the final prosthetic restorations giving an implant survival rate of 94.2% after three years. Therefore, the presented result is located in the range of the above-mentioned investigations. The three implants that failed to osseointegrate have been removed within the first four weeks after implant placement. After the delivery of the prosthetic

restorations, there was no further failure. The early failure can possibly be accounted to the specific requirements of the treatment with immediately temporized one-piece implants (Östman et al. 2007; Ottoni et al. 2005; Roccuzzo et al. 2009). Especially in the initial healing period, the mentioned treatment is highly dependent on a good patient compliance and the individual expertise of the clinician. The MBL reported for zirconia oral implants ranges from 0.1 mm (up to three years of observation) to 2.1 mm (up to four years of observation). Thus, the MBL observed in the present investigation (0.79 mm after 3 years) and the absence of further statistically significant MBL after the delivery of the prosthetic restorations are promising. As a consequence, high success rates of 96%/100% could be calculated according to the criteria of Östman et al. (2007). Like in the majority of the mentioned investigations, minor GBR was performed during implant surgery (28 implant sites) if necessary. Therefore, in some post-surgical radiographs the margin of the bone substitute could be differentiated from the surrounding pristine bone. In those cases, the upper margin of the bone substitute was used as initial reference for the following bone loss measurements. The statistical analysis of the MBL measurements showed no difference between augmented and non-augmented implant sites, suggesting a good tolerance of the current implant system for GBR during implant placement. The grafted sites in the present investigation were distributed to implants supporting SCs and FDPs as follows: 16 of 23 (70%) implants installed for a single tooth replacement and 12/26 (46%) implants installed to support a FDP reconstruction received a GBR. However, the restoration type showed to have a significant influence on the MBL in the present investigation, especially within the first months after implant surgery until final prosthesis installation (SCs: 0.39 mm; FDPs: 1.03 mm; Figure 2b). This is in accordance with former results of Kohal and colleagues who also observed higher MBL at zirconia one-piece implants when immediately restored with provisional three-unit FDPs (2 mm of MBL after one year) (2013) compared with immediate provisional single implant restorations (1.3 mm of MBL after one year) (2012) and might be owed to a higher load during the healing period. In most cases, provisional FDP restorations were installed without distal bordering teeth and received, therefore, less protection during mastication or against tongue and cheek pressure even if direct static and dynamic occlusion was avoided. Nevertheless, the MBL of implants used for FDP reconstructions in the present investigation was still acceptable. In summary, the results of the present investigation are consistent with the available literature regarding success and survival rates of zirconia dental implants.

Immediate implant placement was not an exclusion criterion of the present investigation. However, only 2 of 53 implants were immediately installed in extraction sockets suggesting their omission from the study resulting in an implant population solely installed in healed ridges. The two implants installed in extraction sockets consisted of a single tooth replacement (a first premolar in the lower jaw) and a mesial attachment of a bridge restoration (a second premolar in the lower jaw). The former failed to osseointegrate prior to prosthetic delivery and was, therefore, one of the three mentioned failures. The latter is still in situ without showing any complications or abnormalities (0.7 mm marginal bone loss at the 3y follow-up). Omitting these two patients after their initially proper inclusion to the study would raise the overall survival rate from 94.2% (49/52 implants) to 95.9% (47/49 implants) and, therefore, violate the ICH guideline for Good Clinical Practice (GCP).

The restorative rehabilitation of one-piece zirconia implants has its limits. The need for esthetics on one side and the cementation difficulty of the restoration have to be considered. The distance of the implant shoulder to the point where the implant exits the bone is 3 mm (height of neck) and the built-in emergence profile can hardly be altered. This in turn means that if an implant is placed to shallow in relation to the soft tissue, the emergence profile of the crown might look unfavorable. This does not pose any problems usually in the non-visible posterior areas, but certainly in the esthetic zone of upper anteriors and premolars. In order to create an esthetically pleasing emergence profile, the implant has therefore to be placed deeper in relation of the soft tissue for developing a positive emergence profile. This in turn may lead to the problem of cement removal after crown cementation (Linkevicius et al. 2013). This double bind can only be overcome using two piece zirconia implants with screw-retention. Efforts are undertaken to fabricate such two-piece implants.

Conclusions

Considering the survival rate and the average bone loss of 0.79 mm after three years of observation, the investigated implant system shows promising results and can be recommended for clinical usage. However, it remains to be seen whether the 5-year follow-up confirms the positive three-year results.

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Tables

Table 1: Material properties according to the manufacturer.

Characteristics	**Unit**	**Yttria-stabilized tetragonal zirconia polycrystal (Y-TZP)**	**Alumina-toughened zirconia (ATZ)**
Components		ZrO_2/Y_2O_3	$ZrO_2/Al_2O_3/Y_2O_3$
Composition	wt%	95/5	76/20/4
Density	g/cm^3	6.05	5.5
Grain size	µm	0.4	0.4
Bending strength	MPa	1.000	2.000
Compressive strength	MPa	2.000	2.000
Young's modulus	GPa	200	220
Fracture toughness	MPa√m	8	8

Table 2: Marginal bone remodeling after 3 years of observation.

Bone resorption [mm]	***n***	**%**
< 0 mm	4	8.2
0 mm	2	4.1
0.1 mm - 0.5 mm	10	20.4
0.6 mm - 1.0 mm	19	38.8
1.1 mm - 1.5 mm	10	20.4
1.6 mm - 2.0 mm	2	4.1
2.1 mm - 2.5 mm	1	2.0
2.6 mm - 3.0 mm	1	2.0
Σ	**49**	**100**

Figure legends

Figure 1: Box plot diagrams of the soft tissue evaluations (a: Probing depth; b: Clinical attachment level; c: Gingival recession; d: Plaque index; e: Bleeding index) sorted by position (mesial reference teeth, implant sites, distal reference teeth) at prosthetic delivery (0) and the follow-up appointments (1: 1 year follow-up; 3: 3 year follow-up).

Figure 2: (a) Box plot diagram of bone resorption sorted by position (mesial reference teeth, implant sites, distal reference teeth) at prosthetic delivery (0) and the follow-up appointments (1: 1 year follow-up; 3: 3 year follow-up).
(b) Illustration of the mean bone resorption stratified by the restoration type (Single crowns; Fixed dental prostheses) from implant insertion to the 3-year follow-up (3).

Figure 3: Box plot diagrams of patient-reported outcome measures (Visual analogue scales [%]; a: Function/Eating; b: Esthetic/Appearance; c: Sense; d: Speech; e: Self-esteem) sorted by restoration type (Fixed dental prostheses; Single crowns) before treatment (Pre), at prosthetic delivery (Delivery) and the follow-up appointments (1: 1 year follow-up; 3: 3 year follow-up).

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