

Hinweis in eigener Sache

Auf den folgenden Seiten finden Sie die Studie der Heinrich Heine-Universität, Düsseldorf über das Keramik-Implantat **ZV3**. Dieses Implantat wird seit 2018 von uns, Champions-Implants GmbH, unter dem Produktnamen **BioWin!** vertrieben. Wir weisen daraufhin, dass dieses Implantat völlig identisch mit dem in der Studie erwähnten Implantat ist – inkl. der Produktion und dem Zubehör.

Clinical performance of two-piece zirconium implants in the posterior mandible and maxilla. A prospective cohort study over two years.

Jürgen Becker¹, Gordon John¹, Kathrin Becker², Saskia Mainusch¹, Gabriele Diedrichs³, and Frank Schwarz¹

¹Department of Oral Surgery, Heinrich Heine University, Düsseldorf, Germany

²Department of Prosthodontics, Heinrich Heine University, Düsseldorf, Germany

³Department of Orthodontics, Heinrich Heine University, Düsseldorf, Germany

Corresponding address: Dr. Kathrin Becker

Department of Oral Surgery

Westdeutsche Kieferklinik

Heinrich-Heine-University

D-40225 Düsseldorf, Germany

Tel: +49 211 8118151

e-mail: Kathrin.Becker@med.uni-dueseldorf.de

Short title: Two-piece zirconia implants

Key Words: Clinical research, Clinical trials, Bone implant interactions, Patient centered outcomes

Source of Funding

The study was supported by an unrestricted grant of ZV3 Zircon Vision GmbH, Wolfratshausen, Germany.

Conflict of Interests

The authors declare that they have no conflict of interests related to this study.

Abstract

Objectives: To assess the clinical performance of customized two-piece zirconium implants over a period of up to 2 years.

Material & Methods: A total of 52 patients with single tooth gaps in the posterior mandible or maxilla received the same type of a two-piece zirconium implant system. Fibreglass abutments were cemented and restored with fixed all-ceramic single crowns. The cumulative survival rate (primary outcome) was calculated according to the life table method and illustrated with kaplan–meier survival curves. Covariates (gender, implant position, implant diameter/ length, oral surgeon) were estimated using log-rank tests.

Results: A total of two target implants in 2 patients were lost after a functioning time of 8 months. The cumulative survival rate was 95.8% and the mean survival time amounted to 32.9 months. Log-rank tests revealed a significant association for the covariate “oral surgeon” ($P=0.047$). All implant sites revealed a marked creeping attachment and gain of keratinized tissue at 24 months.

Conclusion: This two-piece zirconium implant/ fibreglass abutment system can be successfully used in the clinical indication investigated.

Introduction

With the development of high-strength zirconia, new ceramics were supposed to serve as an alternative material for dental implants. In particular, yttria-stabilized tetragonal zirconia polycrystal (Y-TZP) reveals a high flexural strength, good hardness, a favorable fracture toughness and suitable weibull modulus, thus overcoming major drawbacks associated with previous aluminium oxide based ceramics (Depprich et al. 2014). Moreover, Y-TZP ceramics are tooth-colored, highly biocompatible (Hempel et al. 2010) and reported to be less prone to bacterial colonization (Rimondini et al. 2002), thus offering potential advantages over titanium.

Preclinical studies performed in various animal models provide some evidence that surface-modified zirconia implants were commonly associated with a bone-tissue response and removal torque similar to that noted for moderately rough titanium implants (Sennerby et al. 2005; Gahlert et al. 2010, 2012). However, these outcomes were depending on the surface treatments, thus suggesting that the microtopography seems to be a critical determinant for the osseointegration of zirconia implants (Manzano et al. 2014).

The currently available clinical data are limited but point to inferior survival (74-98% after 12-56 months) and success rates (79.6-91.6% after 6-12 months) when compared with those values noted for commonly used titanium implants (Depprich et al. 2014). It is important to emphasize that the latter systematic review was mainly based on studies reporting on one-piece implants, and the available literature on two-piece zirconia systems is still scarce (Nevins et al. 2011; Cionca et al. 2014; Payer et al. 2014).

Therefore, the aim of the present prospective cohort study was to assess the clinical performance of customized two-piece zirconium implants restored with cemented fibreglass abutments and all-ceramic crowns in the posterior mandible and maxilla over an observation period of up to 2 years.

Materials and Methods

Study design and participants

This is a prospective cohort study aimed at investigating the survival rates (primary outcome) as well as biological, technical, and mechanical complications (secondary outcomes) of two-piece zirconia implants restored with fibreglass abutments in the posterior mandible and maxilla. The study population consisted of 60 partially edentulous patients suffering from at least one missing tooth in the premolar/ molar regions of either the upper or lower jaw and were in need of a fixed dental prosthesis (Table 1). If the patient was in need of more than one implant, the most anterior position was defined as target site. Each patient was given a detailed description of the procedure and was required to sign an informed consent before participation. The study was in accordance with the Helsinki Declaration of 1975, as revised in 2013 and the study protocol was approved by the ethics committee of the Heinrich Heine University, Düsseldorf, Germany. Treatments have been provided between November 2011 and April 2012.

Inclusion criteria

For patient selection, the following inclusion criteria were defined:

1) age ≥ 18 and ≤ 80 years, 2) tooth extraction at least 6 weeks prior to implant placement, 3) no need of more than 4 implants, 4) full mouth bleeding on probing (FMBOP) and full mouth plaque score (FMPS) $\leq 25\%$, 5) no systemic diseases which could influence the outcome of the therapy (e.g. diabetes ($HbA1c < 7$), osteoporosis), 6) no intake of medications which may have an effect on bone turnover and mucosal healing (i.e. steroids, antiresorptive therapy), 7) no pregnancy or breastfeeding women, 8) no physical or mental handicaps that would interfere with the ability to perform adequate oral hygiene, 9) non-smoker or light smoking habits (< 10 cigarettes per day), 8) treated chronic periodontitis and proper periodontal maintenance care, 10) no history of

mucosal diseases or oral lesions, 11) no history of bruxism or clenching habits, 12) no history of adverse reactions to the materials used in this study, and 13) no general contraindications for surgical interventions.

Investigational devices

The two-piece, screw-type and surface-modified (tetragonal pattern, surface roughness $R_a =$ approx. 7 microns / $R_z =$ approx. 40 microns) zirconium implant system (ZV3, Zircon Vision GmbH, Wolfratshausen, Germany) was provided in two different diameters (4.5 mm or 5.0 mm) and 3 different lengths (9, 11, or 13 mm). The transmucosal machined part of the implant allowed for the fixation of a fiberglass abutment (ZV3) serving as retention for the prosthetic reconstruction. Each implant was customized to ensure that the crown margin was located epimucosal. The glass fiber abutments were fixed using a dual-cure resin cement and a self-adhesive primer (Panavia F2.0, Kuraray Europe GmbH, Hattersheim am Main, Germany) and subsequently allowed for a conventional crown preparation. The abutment was part of the implant and certified as such. All implant system components were delivered sterile sealed in peel pouches and were opened immediately before application. Finally, impressions were taken and all-ceramic single crowns (IPS e.-max crowns, Ivoclar Vivadent, Ellwangen, Germany) were fixed using the same resin cement. After cementation, the implant-abutment connection was completely covered by the crown margins.

Surgical Procedure

Under local anesthesia, midcrestal and bilateral vestibular releasing incisions were made and mucoperiosteal flaps elevated to expose the respective sites for implant insertion. Implant sites were prepared using a low-trauma surgical technique under copious irrigation with sterile 0.9 % physiological saline. Each implant had to be inserted with good primary stability (i.e. lack of clinical implant mobility) and in a way so that the borderline between the transmucosal and intrabony part at best coincided with the lingual bone crest (Fig. 1a). The respective diameter and length of the implants was chosen according to the individual clinical and radiological situation. Simultaneous grafting of buccal dehiscence-type defects (Geistlich BioOss[®], Geistlich Biomaterials AG, Wolhusen, Switzerland + Geistlich BioGide[®], Geistlich Biomaterials AG) and internal sinus floor elevations were accomplished when necessary. External sinus floor elevation was associated with a staged implant placement at 4 to 6 months after grafting (BioOss[®], BioGide[®]). All implants were left to heal in a transmucosal position without providing any temporization (Fig. 1b). Implant loading was accomplished after a healing period of about 12 weeks in the maxilla and 10 weeks in the mandible (Fig. 1c). All procedures were accomplished by 3 experienced and previously calibrated oral surgeons.

Postoperative Care

Postoperative maintenance care included a supramucosal-/ gingival professional implant/tooth cleaning, local pocket irrigation using chlorhexidine digluconate, and reinforcement of oral hygiene. Maintenance care was provided according to individual needs at 3, 6, 12, 18 and 24 months after therapy.

Clinical measurements

The following clinical parameters were assessed immediately before therapy (baseline), and after 6, 12, and 24 months using a periodontal probe (PCP 12, Hu-Friedy, Tuttlingen – Moehringen, Germany): 1) plaque index (PI) (Löe 1967), 2) bleeding on probing (BOP), 3) probing depth (PD) – measured from the mucosal margin to the probeable pocket, and 4) mucosal recession (MR) – measured from the crown margin to the mucosal margin. All measurements were performed at 6 aspects per implant: mesiobuccal (mb), midbuccal (b), distobuccal (db), mesiooral (mo), midoral (o), and distooral (do) by two previously calibrated investigators. Implant mobility was measured by manual palpation.

Matrix-metalloproteinase-8

At 6, 12, and 24 months and after a gentle supramucosal cleaning, peri-implant sulcus fluid was collected at the deepest aspect of each target implant site by means of sterile paper points (i.e. each was left in place for 30 seconds). These samples were sent to a commercial provider of laboratory services (Bioscentia MVZ Berlin) and analysed for active matrix-metalloproteinase-8 (aMMP-8).

Survival and Complications

Implants were considered as survivals if they were present at the final follow-up examination after 24 months. Mechanical complications were considered to be all events affecting the integrity (e.g. fractures) of the implant and the fibreglass abutment. Technical events were considered to be those affecting the cemented crown. Biological complications considered the presence of peri-implantitis (i.e. BOP and/ or suppuration, changes in the radiographic bone level) (Lang & Berglundh 2011; Sanz et al. 2012) at the target implants.

Statistical analysis

A commercially available software program (IBM SPSS Statistics 22.0, IBM Deutschland GmbH, Ehningen, Germany) was used for the statistical analysis. The cumulative survival rate was calculated according to the life table method and illustrated with Kaplan–Meier survival curves. The log-rank test was used to estimate the association between study variables (gender, implant position, implant diameter, implant length, augmentation, oral surgeon) and time to event (i.e. implant-failure). A binary logistic regression analysis was used to correlate the event biological complications with the following factors: gender (male/ female), implant position (upper/ lower jaw), augmentation (yes/ no), and PI (<33%/ ≥33%). The final model was established by the backward elimination (Wald) of non-significant factors. Odd ratio (OR) estimates and 95% confidence intervals (95% CI) were retrieved from the intercept of each factor.

Moreover, descriptive statistics were calculated for PI, BOP, PD, and MR values. The data rows were examined with the Kolmogorow-Smirnow. The paired t- test was used for within group comparisons from baseline to 6, 12 and 24 months at the patient level. The alpha error was set at 0.05.

Results

No primary stability could be achieved in eight out of 60 patients. Accordingly, a total of 52 patients received the final prosthetic reconstructions. During the course of the study, four patients were lost to follow-up. Demographic data of the remaining 48 patients are presented in Table 1. Target implants were mainly placed in the lower jaws (72.9%) and most frequently revealed a diameter of 5.0 mm (64.6%) and length of 11 mm (93.8%). Multiple implants were only provided

in 15 patients (31.3%), with a frequency of 20.8% for two-, and 10.4% for three implants. A simultaneous grafting of buccal dehiscence-type defects and internal sinus floor elevation was indicated at 25.0% and 12.5% of the target implant sites. An external sinus floor elevation and staged implant placement was accomplished in one patient (2.1%). The mean observation time was 25.5 ± 5.8 months (Table 1).

The postoperative wound healing was considered as generally uneventful in all patients (Fig. 2). No complications such as allergic reactions or abscesses were noted throughout the study entire period.

Implant survival and study variables

A total of two target implants in 2 patients were lost after a functioning time of 8 months. The cumulative survival rate was 95.8% and the mean survival time amounted to 32.9 months (Fig. 3a). Even though both patients were male and both implants revealed a diameter of 5.0 mm, a length of 11 mm and were located in the lower jaw, the log-rank test failed to reveal a significant association between implant survival and gender ($P=0.054$), implant diameter ($P=0.290$), implant length ($P=0.934$), or implant position ($P=0.384$). Similarly, implant survival was also not influenced by the need of an augmentation procedure ($P=0.761$) (Figs. 3b-f). However, a significant association was noted for the study variable oral surgeon ($P=0.047$; log-rank test) (Fig. 3g).

Clinical measurements and biological complications

Mean PI, BOP, PD and MR values at baseline, 6, 12 and 24 months at the patient level are summarized in Table 2. In particular, mean PI values obtained at baseline slightly increased over

time and reached statistical significance at 24 months ($P=0.001$; paired t-test). Mean BOP values significantly increased at 6 and 12 respectively ($P<0.01$, $P<0.001$; paired t-test, respectively).

According to the given definition, 18 patients were diagnosed for initial peri-implantitis between 12 and 24 months. The Kaplan-meier estimates of biological complications amounted to 37.5%.

These patients were assigned to nonsurgical treatment procedures (data on the clinical efficacy of therapy will be presented elsewhere). At 24 months, these interventions were associated with a marked reduction of mean BOP scores, almost reaching the baseline values at respective implants ($P=0.124$; paired t-test). Mean PD values significantly increased at 6, 12, and 24 months ($P<0.001$; paired t-test) (Table 2). In all patients investigated, MR values decreased over time, even reaching statistical significance at 24 months ($P<0.05$; paired t-test) (Table 2). In patients exhibiting a mucosal recession at baseline, this creeping attachment resulted in an almost complete coverage of the former soft tissue defect area (Fig. 2).

The binary logistic regression analysis failed to identify any significant correlations between the event biological complications and the factors investigated ($P>0.05$, respectively).

Matrix-metalloproteinase-8

The frequency of aMMP-8 levels <8 ng/ml (no inflammation), 8-20 ng/ml (mild inflammation), and >20 ng/ml (severe inflammation) was 37.5% (18 sites), 31.3% (15 sites), and 29.2% (14 sites) at 6 months, respectively. These frequencies were 20.8% (10 sites), 25.0% (12 sites), and 45.8% (22 sites) at 12 months and 25.0% (12 sites), 29.2% (14 sites), and 33.32% (16 sites) at 24 months (Table 3).

Mechanical and technical complications

Over the entire observation period, mechanical complications were only observed in 1 patient. At 23 months, a fracture affected the fibreglass abutment of the respective target implant. This was also associated with a technical complication (i.e. fracture) of the cemented crown. The Kaplan-meier estimates of mechanical and technical complications amounted to 2.1%. The fibreglass fragment could be removed and a new prosthetic restoration cemented which was successful during the further follow up.

Discussion

The present cohort study was designed to investigate the clinical performance of customized two-piece zirconium implants restored with cemented fibreglass abutments and all-ceramic crowns in the posterior mandible and maxilla. The statistical analysis has pointed to a high cumulative survival rate of 95.8% and a mean survival time of 32.9 months. Implant survival was neither affected by gender nor by implant diameter, implant length, implant position, or augmentation thus indicating that this particular system may be safely used in any of the clinical indications investigated. Moreover, mechanical and technical complications were only observed at one target implant and therefore underline the stability and clinical applicability of the fibreglass abutments. Basically, the survival rates noted in the present study are within the range of those data reported in prospective studies on single tooth replacements by surface-modified one- (Oliva et al. 2010; Borgonovo et al. 2011; Cannizzaro et al. 2012; Kohal et al. 2012) and two-piece zirconium implants (Cionca et al. 2014; Payer et al. 2014). In particular, after an observation period of 24 months, the reported survival rate for two-piece zirconia implants amounted to 93.3%, while this value was 100% for titanium implants (Payer et al. 2014). In contrast, Cionca et al. (2014)

reported on a lower cumulative survival rate (87%) at 1 year after loading of two-piece zirconia implants restored with cemented zirconia abutments and full-ceramic crowns. Implant failures were mainly attributed to an „aseptic“ loosening (Cionca et al. 2014). A two-year clinical study on 26 one-piece zirconia implants placed in a total of 16 patients reported on a survival rate of 96.16% (Borgonovo et al. 2011). A similar cumulative survival rate of 95.4% at 1 year was also noted after an immediate temporization of one-piece zirconia implants (Kohal et al. 2012). However, the failure rate (12.5%) was obviously higher for immediately loaded one-piece zirconia implants placed in post-extraction sites (Cannizzaro et al. 2012). All these recently published data, taken together with the results of the present study point to high survival and low complication rates of surface-modified zirconia implants used for single-tooth replacements. However, time to loading, including temporization of the implant during the initial healing period, should be critically considered and its impact on the outcome of therapy needs to be carefully addressed in future studies. When further analysing the present data, it was also noted that 18 patients were diagnosed for peri-implantitis after an observation period of 12.3 months, corresponding to a biological complication rate of 37.5%. The bivariate linear regression analysis failed to identify any correlation with the independent factors investigated.

The incidence of patients diagnosed for peri-implantitis is basically within the range of those prevalences reported for titanium implants, ranging from 14 – 30% (Derks & Tomasi 2015). In this context, however, it must also be realized that the high variability noted in the latter systematic review was mainly due to heterogeneous case definitions (Tomasi & Derks 2012). While in some studies, peri-implantitis was merely defined by BOP and PD thresholds, others have used varying amounts of interproximal bone loss (e.g. from >0.4 mm to >5 mm) in addition to inflammation. Moreover, some studies also diagnosed implants with BOP and a radiographic bone loss of < 3 threads for peri-implant mucositis (Derks & Tomasi 2015). Accordingly, it is not

feasible to compare data derived from studies lacking a reasonable case definition to those using a more sensitive threshold for bone loss, as previously recommended by the European Federation of Periodontology (Lang & Berglundh 2011, Sanz et al. 2012).

When further analyzing the present data, it must also be emphasized that the respective target implants merely revealed minor crestal bone level changes not exceeding the upper 25% of the implant length. This observation was supported by the moderate PD values noted at these sites. Recent studies also reported on a pronounced bone loss at zirconia implants during the remodeling phase (Cannizzaro et al. 2012; Kohal et al. 2012; Payer et al. 2014). In particular, the mean radiographic bone loss adjacent to one-piece implants after 1 year amounted to 1.31 mm, but about 34% of the implant sites had lost at least 2 mm, and 14% even more than 3 mm (Kohal et al. 2012). Since the present study did not consider the longitudinal assessment of interproximal radiographic bone level changes (restrictions due to the EURATOM directive), it is impossible to estimate to what extent a more pronounced remodeling process may have contributed to the incidence of biological complications. However, the immunological analysis has pointed to elevated aMMP-8 levels over the entire observation period of 24 months. Previous studies provide some evidence that aMMP-8 is associated with the extracellular degradation of collagen, and is positively correlated with plaque scores at mucositis sites (Basegmez et al. 2012; Schwarz et al. 2014). Since PI values were not increased after 6 and 12 months of healing, it seems to be rather unlikely that the elevated BOP and aMMP-8 levels were caused by bacterial plaque biofilms. However, aMMP-8 has also been shown to modulate the collagen metabolism of the oral mucosa (Korpi et al. 2009), and therefore, one may speculate that the elevated levels were associated with the marked creeping attachment and gain of keratinized tissue noted over the entire observation period of 24 months. In order to clarify this issue, the remodeling of soft- and hard tissues adjacent to zirconia implants needs further investigation.

Within the limitations of the present cohort study, it was concluded that this two-piece zirconium implant/ fibreglass abutment system can be successfully used in the clinical indication investigated.

Acknowledgements

The authors would kindly thank Dres. Ahmad R Hakimi and Thore Santel (formerly Department of Oral Surgery, Heinrich Heine University, Düsseldorf, Germany) for their support in conducting the surgical procedures as well as Dr. Andreas Künzel (Department of Oral Surgery, Heinrich Heine University, Düsseldorf, Germany) for his support in performing the prosthetic rehabilitations.

References

- Basegmez, C., Yalcin, S., Yalcin, F., Erganli, S. & Mijiritsky, E. (2012) Evaluation of periimplant crevicular fluid prostaglandin E2 and matrix metalloproteinase-8 levels from health to periimplant disease status: a prospective study. *Implant Dentistry* **21**: 306-310.
- Borgonovo, A., Censi, R., Dolci, M., Vavassori, V., Bianchi, A. & Maiorana, C. (2011) Use of endosseous one-piece yttrium-stabilized zirconia dental implants in premolar region: a two-year clinical preliminary report. *Minerva Stomatologica* **60**: 229-241.
- Cannizzaro, G., Leone, M., Ferri, V., Viola, P., Federico, G. & Esposito, M. (2012) Immediate loading of single implants inserted flapless with medium or high insertion torque: a 6-month follow-up of a split-mouth randomised controlled trial. *European Journal of Oral Implantology* **5**: 333-342.
- Cionca, N., Muller, N. & Mombelli, A. (2014) Two-piece zirconia implants supporting all-ceramic crowns: A prospective clinical study. *Clinical Oral Implants Research* doi: 10.1111/clr.12370.
- Depprich, R., Naujoks, C., Ommerborn, M., Schwarz, F., Kubler, N. R. & Handschel, J. (2014) Current findings regarding zirconia implants. *Clinical Implant Dentistry and Related Research* **16**: 124-137.
- Derks, J. & Tomasi, C. (2015) Peri-implant health and disease. A systematic review of current epidemiology. *Journal of Clinical Periodontology*.
- Gahlert, M., Rohling, S., Wieland, M., Eichhorn, S., Kuchenhoff, H. & Kniha, H. (2010) A comparison study of the osseointegration of zirconia and titanium dental implants. A biomechanical evaluation in the maxilla of pigs. *Clinical Implant Dentistry and Related Research* **12**: 297-305.
- Gahlert, M., Roehling, S., Sprecher, C. M., Kniha, H., Milz, S. & Bormann, K. (2012) In vivo performance of zirconia and titanium implants: a histomorphometric study in mini pig maxillae. *Clinical Oral Implants Research* **23**: 281-286.
- Hempel, U., Hefti, T., Kalbacova, M., Wolf-Brandstetter, C., Dieter, P. & Schlottig, F. (2010) Response of osteoblast-like SAOS-2 cells to zirconia ceramics with different surface topographies. *Clinical Oral Implants Research* **21**: 174-181.
- Kohal, R. J., Knauf, M., Larsson, B., Sahlin, H. & Butz, F. (2012) One-piece zirconia oral implants: one-year results from a prospective cohort study. 1. Single tooth replacement. *Journal of Clinical Periodontology* **39**: 590-597.
- Korpi, J. T., Astrom, P., Lehtonen, N., Tjaderhane, L., Kallio-Pulkinen, S., Siponen, M., Sorsa, T., Pirila, E. & Salo, T. (2009) Healing of extraction sockets in collagenase-2 (matrix metalloproteinase-8)-deficient mice. *European Journal of Oral Science* **117**: 248-254.
- Lang, N. P. & Berglundh, T. & Working Group 4 of Seventh European Workshop on, P. (2011) Periimplant diseases: where are we now?--Consensus of the Seventh European Workshop on Periodontology. *Journal of Clinical Periodontology* **38 Suppl 11**: 178-181.
- Löe, H. (1967) The Gingival Index, the Plaque Index and the Retention Index Systems. *Journal of Periodontology* **38**: Suppl:610-616.

- Manzano, G., Herrero, L. R. & Montero, J. (2014) Comparison of clinical performance of zirconia implants and titanium implants in animal models: a systematic review. *International Journal of Oral and Maxillofacial Implants* **29**: 311-320.
- Nevins, M., Camelo, M., Nevins, M. L., Schupbach, P. & Kim, D. M. (2011) Pilot clinical and histologic evaluations of a two-piece zirconia implant. *International Journal of Periodontics and Restorative Dentistry* **31**: 157-163.
- Oliva, J., Oliva, X. & Oliva, J. D. (2010) Five-year success rate of 831 consecutively placed Zirconia dental implants in humans: a comparison of three different rough surfaces. *International Journal of Oral and Maxillofacial Implants* **25**: 336-344.
- Payer, M., Heschl, A., Koller, M., Arnetzl, G., Lorenzoni, M. & Jakse, N. (2014) All-ceramic restoration of zirconia two-piece implants - a randomized controlled clinical trial. *Clinical Oral Implants Reserach*.
- Rimondini, L., Cerroni, L., Carrassi, A. & Torricelli, P. (2002) Bacterial colonization of zirconia ceramic surfaces: an in vitro and in vivo study. *International Journal of Oral and Maxillofacial Implants* **17**: 793-798.
- Sanz, M., Chapple, I. L. & Working Group 4 of the, V. E. W. o. P. (2012) Clinical research on peri-implant diseases: consensus report of Working Group 4. *Journal of Clinical Periodontology* **39 Suppl 12**: 202-206.
- Schwarz, F., Mihatovic, I., Golubovic, V., Eick, S., Iglhaut, T. & Becker, J. (2014) Experimental peri-implant mucositis at different implant surfaces. *Journal of Clinical Periodontology* **41**: 513-520.
- Sennerby, L., Dasmah, A., Larsson, B. & Iverhed, M. (2005) Bone tissue responses to surface-modified zirconia implants: A histomorphometric and removal torque study in the rabbit. *Clinical Implant Dentistry and Related Research* **7 Suppl 1**: S13-20.
- Tomasi, C. & Derks, J. (2012) Clinical research of peri-implant diseases--quality of reporting, case definitions and methods to study incidence, prevalence and risk factors of peri-implant diseases. *Journal of Clinical Periodontology* **39 Suppl 12**: 207-223.

Figure Legends

Fig. 1 Surgical procedures at baseline

- a.** The posterior mandible or maxilla was selected as experimental site for implant placement in all patients. Situation after placement of the two-piece zirconium implant.
- b.** All sites were left to heal in a transmucosal position.
- c.** Situation after fixation of the fibreglass abutment and cementation of an all-ceramic single crown (Baseline).

Fig. 2 Soft tissue wound healing

- a.** Baseline situation after crown cementation revealed a soft tissue dehiscence at the buccal aspect.
- b.** Situation at 18 months showing a creeping attachment and complete soft tissue coverage of the exposed implant neck.

Fig. 3 Kaplan Meier survival curves

- a.** Cumulative survival rate
- b.** Cumulative survival rate - factor gender
- c.** Cumulative survival rate - factor jaw
- d.** Cumulative survival rate - factor implant diameter
- e.** Cumulative survival rate - factor implant length
- f.** Cumulative survival rate - factor augmentation
- g.** Cumulative survival rate - factor surgeon

Tables

Table 1.

Patient demographics and implant site characteristics

Patient number (n)	48
Female	31
Male	17
Age (years)	47.6 ± 13.4
Observation period (months)	25.5 ± 5.8
Patients with multiple implant sites	15
Patients with 1/ 2/ 3 implants	33/ 10/ 5
Patients treated by surgeon 1/ 2/ 3	7/ 29/ 12
Target implant sites	48
Location Upper Jaw	13
Location Lower Jaw	35
Implant diameter (4.5/ 5.0 mm)	17/ 31
Implant length (9/ 11/ 13 mm)	2/ 45/ 1
Target implant sites with augmentation	19
Simultaneous grafting of a dehiscence-type defect	12
Internal sinus floor elevation	6
External sinus floor elevation	1

Table 2.

Clinical parameters (mean \pm SD and median) at baseline, 6, 12 and 24 months (n=48/ 46/ 45 patients).

	Baseline		6 Months		P*	12 Months		P*	24 Months		P*
<i>Plaque index</i>	0.08 \pm 0.24	0.0	0.05 \pm 0.14	0.0	0.617	0.04 \pm 0.14	0.0	0.411	0.34 \pm 0.41	0.2	0.001
<i>Bleeding on probing (%)</i>	21.3 \pm 26.2	25.0	38.3 \pm 27.5	25.0	0.003	64.1 \pm 27.2	75.0	0.000	13.9 \pm 15.7	0.0	0.124
<i>Probing depth (mm)</i>	1.8 \pm 0.7	1.7	2.3 \pm 0.7	2.2	0.001	2.8 \pm 0.7	2.7	0.000	3.1 \pm 0.5	3.2	0.000
<i>Mucosal recession (mm)</i>	0.2 \pm 0.3	0.0	0.1 \pm 0.2	0.0	0.864	0.1 \pm 0.2	0.0	0.621	0.0 \pm 0.1	0.0	0.025

*Within group comparisons (paired t-test) at P<0.05

Table 3.

Frequency distribution of MMP-8 levels at 6, 12 and 24 months

	6 Months	12 Months	24 Months
<i>no inflammation</i>	18 (37.5%)	10 (20.8%)	12 (25.0%)
<i>mild inflammation</i>	15 (31.3%)	12 (25.0%)	14 (29.2%)
<i>severe inflammation</i>	14 (29.2%)	22 (45.8%)	16 (33.3%)
<i>not analysed</i>	1 (2.1%)	4 (8.3%)	6 (12.5%)

aMMP-8: no inflammation (<8 ng/ml); mild inflammation (8-20 ng/ml); severe inflammation (>20 ng/ml)

Figures

Fig 1.



a.



b.



c.

Fig 2.

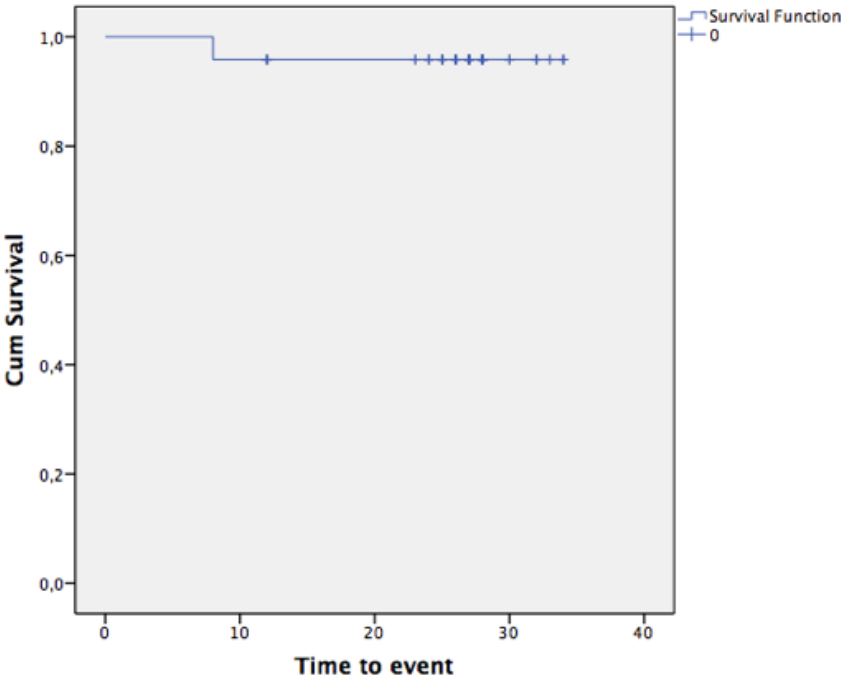


a.

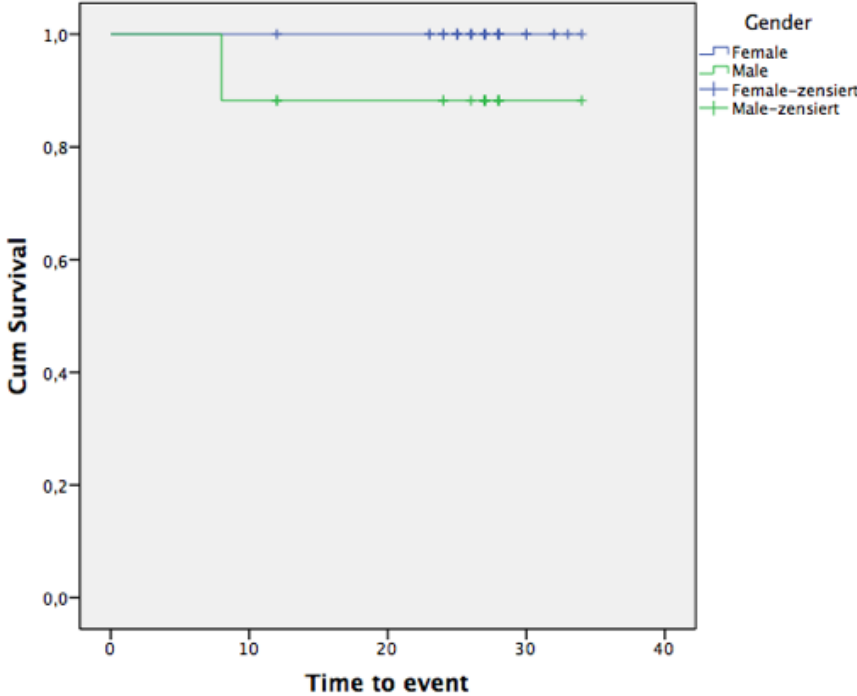


b.

Fig 3.

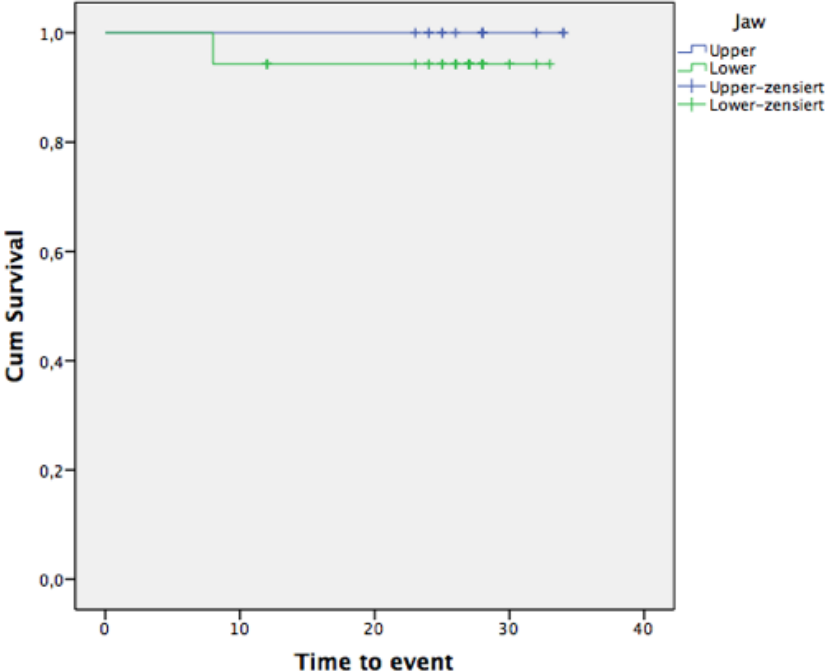


a.

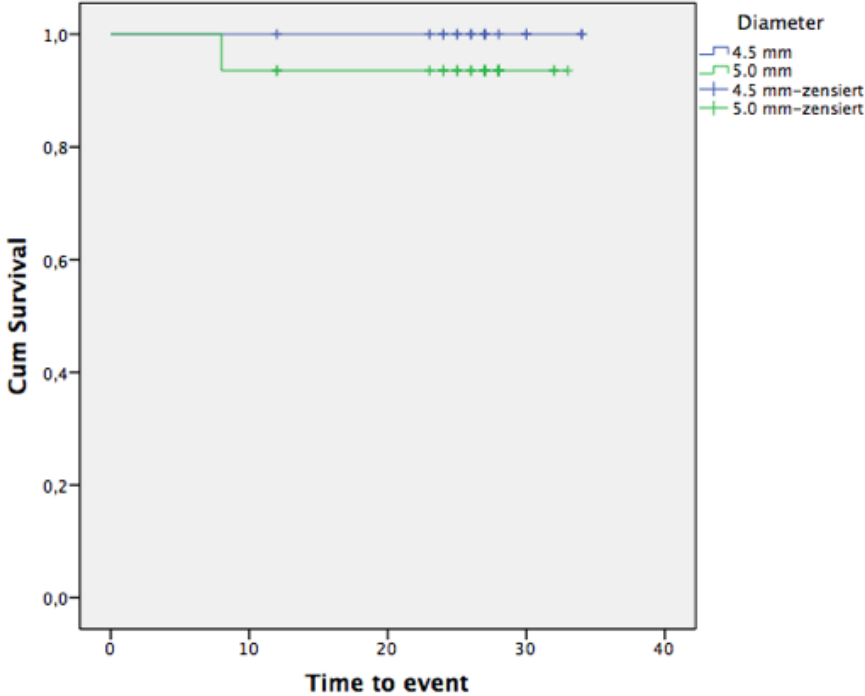


b.

Fig 3.

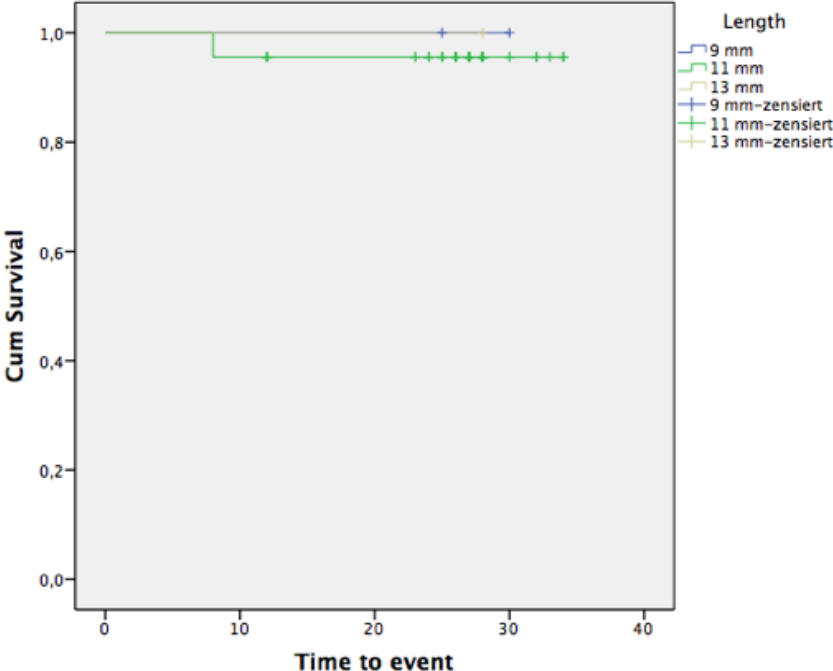


c.

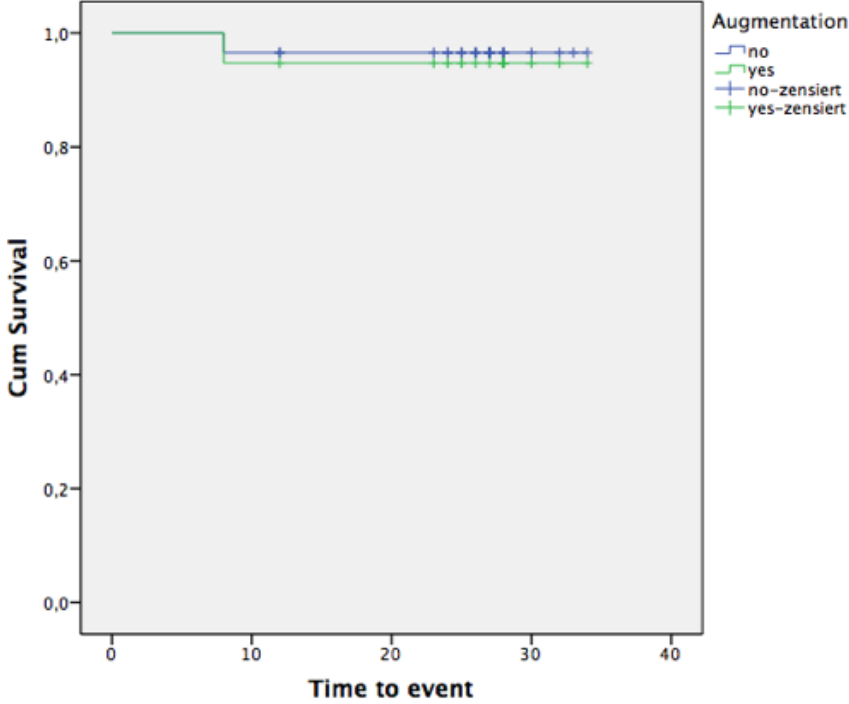


d.

Fig 3.

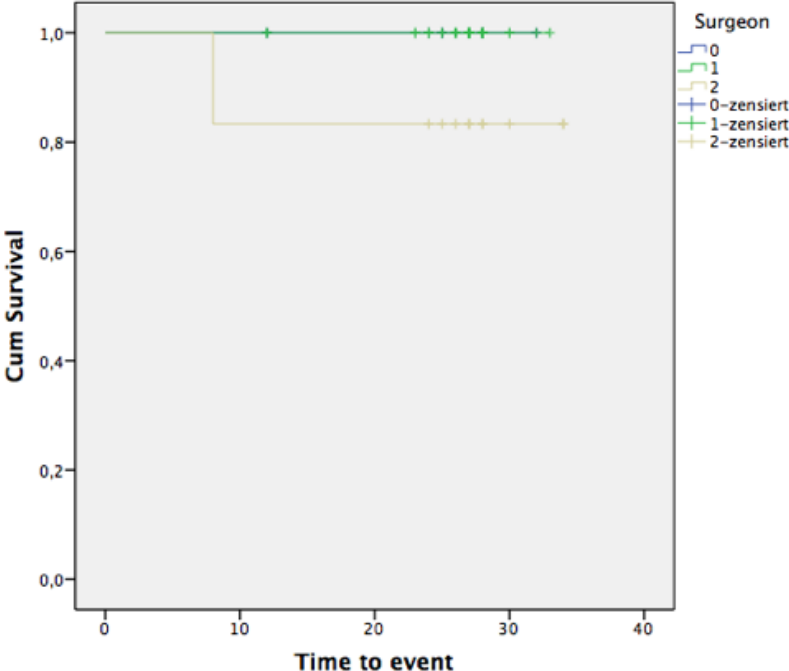


e.



f.

Fig 3.



88