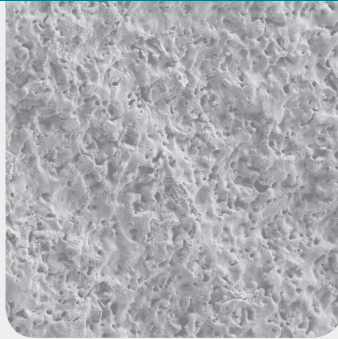
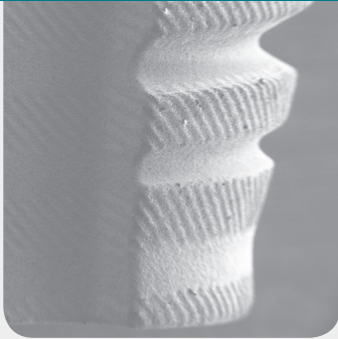




# SCIENTIFIC EVIDENCE



## Colophon

1st Edition, December 2017

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Dear Doctor,

Ceramic dental implants have been first tested in the 1960s – in those early days, alumina was the chosen material and sometimes caused mixed clinical results. Nowadays, and not least thanks to the introduction of zirconia as the best suited material for ceramic implants, these technical shortcomings are apparently overcome, and more and more clinicians worldwide use ceramic dental implants with excellent results. The main driver of their increasing diffusion is patient request – and what could be a better stimulus than that for a modern clinician?

So the application of ceramic implants has become an obviousness for many surgeons – but how is the current situation as far as fundamental research and clinical trials are concerned?

The present document intends to offer you a first, and of course only partial, insight into publications related to ceramic dental implants. Regular updates of this booklet will provide you in the future with even more information.

We wish you an interesting lecture and successful clinical work!

Your Z-SYSTEMS team

E-Mail: [science@zsystems.com](mailto:science@zsystems.com)

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Courtesy by Dr. Ralf Lüttmann, Germany

## CASE STUDIES

## First clinical results of dental screw implants made of zirconium oxide

Mellinghoff J

In the work at hand, clinical results of dental screw implants made of zirconium oxide (type Z3, Z-SYSTEMS AG) have been evaluated for the first time. Altogether, 189 implants were examined by 71 experimentalists. The middle lay days were 8.2 months. One year later the reliability function was 93% according to Kaplan-Meier. The success of the implants was also judged by clinical and x-ray examination parameters as defined by Jahn and d'Hoedt in the success criterion catalogue. A year later the probability of success in this group lay also (44

= n) at 93%. When compared with similar studies to titanium implants, zirconium implants do comparably well in the two residence time analyses. If one takes into account the aesthetic advantages of zirconium oxide in comparison to titanium, the results lead one to assume that zirconium oxide can establish itself alongside titanium in implant dentistry in the future. What importance can be attributed to these first results, clinical long-term studies will have to clarify.

## Erste klinische Ergebnisse zu dentalen Schraubenimplantaten aus Zirkonoxid

In der vorliegenden Arbeit werden erste klinische Ergebnisse von enossalen Schraubenimplantaten aus Zirkonoxid (Typ Z-Look 3, Z-SYSTEMS AG) ausgewertet. Insgesamt wurden 189 Implantate von 71 Probanden untersucht. Die mittlere Liegezeit betrug 8,2 Monate. Nach einem Jahr lag die Überlebenswahrscheinlichkeit nach Kaplan-Meier bei 93%. Der Erfolg der Implantate wurde auch nach klinischen und röntgenologischen Untersuchungsparametern bewertet, wie sie in dem Erfolgskriterienkatalog von Jahn und d'Hoedt [10] definiert sind. Nach einem Jahr lag die Erfolgswahrscheinlichkeit in dieser Gruppe

(n = 44) ebenfalls bei 93%. Verglichen mit ähnlich angelegten Studien zu Titanimplantaten schneiden Zirkonimplantate in beiden Verweildauernanalysen vergleichbar gut ab. Berücksichtigt man die ästhetischen Vorteile von Zirkonoxid gegenüber Titan, so geben die Ergebnisse zu der Vermutung Anlass, dass sich Zirkonoxid in Zukunft neben Titan in der zahnärztlichen Implantologie etablieren wird. Welcher Stellenwert diesen ersten Ergebnissen zuzumessen ist, werden klinische Langzeitstudien klären müssen.

## Zirconium dioxide implants – Practical experience What are the aesthetic benefits of ceramic implants?

Mellinghoff J

Ceramic implants combined with all-ceramic superstructures create a perfect red-white aesthetic, offering care at the highest aesthetic level. In this context, ceramic implants promote the natural appearance of the peri-implant soft tissue.

In addition, traditional titanium implants can achieve excellent results. However, in aesthetically relevant areas, combined with unfavorable initial anatomical conditions, the use of two-piece implants with titanium abutments can be unsightly. In this respect, ceramic implants and ceramic abutments meet an aesthetic need.

## Zirkoniumdioxidimplantate – Erfahrungen aus der Praxis Welche ästhetischen Vorteile haben Keramikimplantate?

Keramikimplantate in Verbindung mit vollkeramischen Suprakonstruktionen schaffen eine perfekte rot-weiße Ästhetik, die eine Versorgung auf höchstem ästhetischem Niveau bietet. Die Keramikimplantate unterstützen in diesem Zusammenhang das natürliche Aussehen der periimplantären Weichgewebe.

Auch mit herkömmlichen Implantaten aus Titan lassen sich ausgezeichnete Ergebnisse erzielen. Aber in ästhetisch relevanten Zonen, kombiniert mit ungünstigen anatomischen Ausgangsbedingungen, können bei der Verwendung von zweiteiligen Implantaten mit Titanabutments unschöne Begleiterscheinungen auftreten. Keramikimplantate und keramische Abutments schließen hier eine ästhetische Lücke.



**Aim**  
Zirconia implants: an alternative to titanium?  
A clinical follow-up examination

**Methods**  
92 zirconia implants (Z-Look3, Z-SYSTEMS AG, 2nd and 3rd generation with standard sandblasted surface) were placed in 34 patients.

**Results**  
All implants successfully osseointegrated, and displayed gingival health and excellent esthetic results.

**Conclusion**  
Rehabilitation with zirconia implants and full ceramic crowns is a very good alternative to titanium implants if patients desire a metal-free solution.

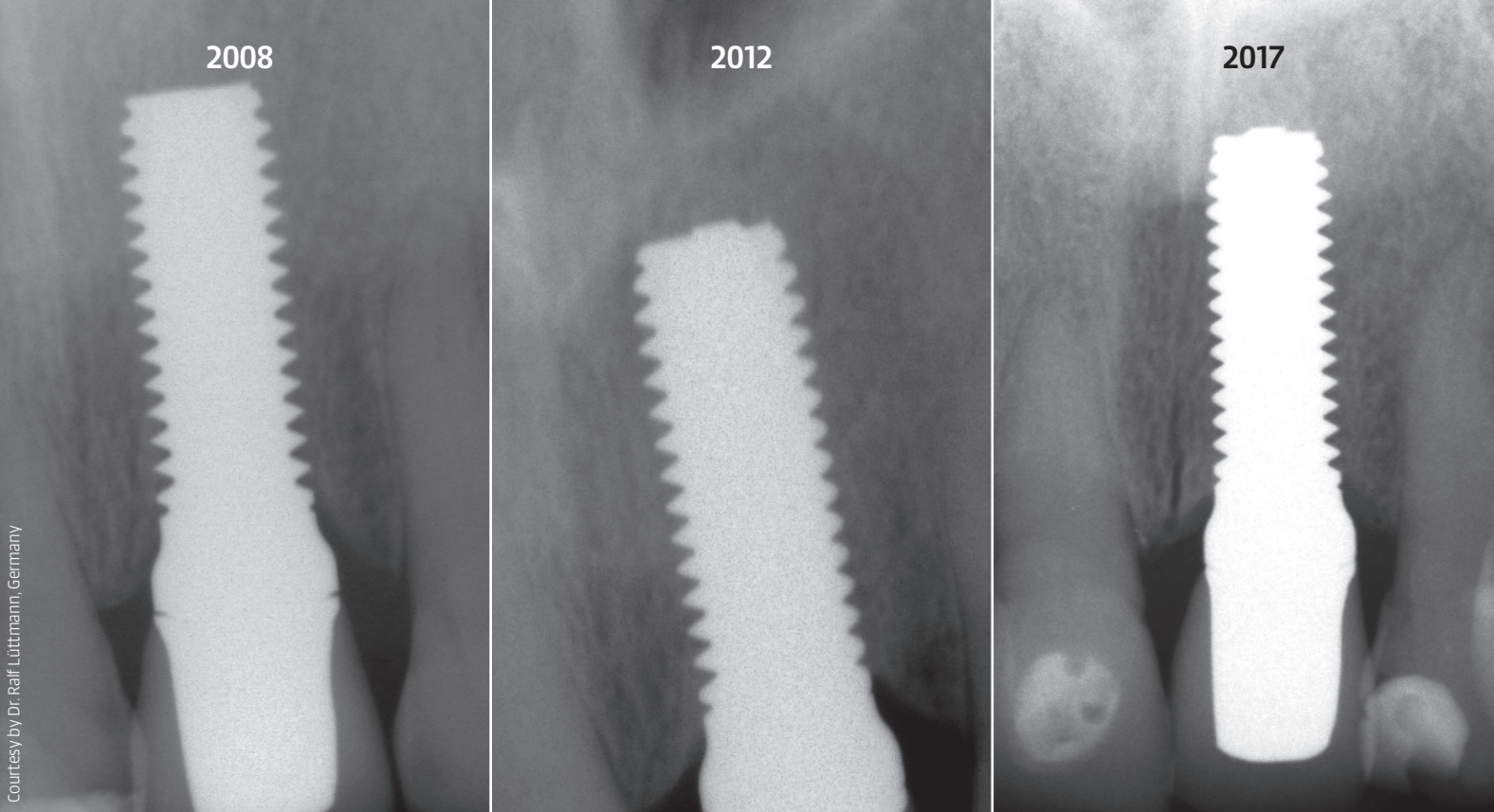
**Zirkondioxidkeramik-Implantate: Eine Alternative zu Titan? Eine klinische Nachuntersuchung**

**Zielsetzung**  
Zirkondioxidkeramik-Implantate: Eine Alternative zu Titan?  
Eine klinische Nachuntersuchung

**Methode**  
92 Zirkondioxid-Implantate (Z-Look3, Z-SYSTEMS AG, 2. und 3. Generation mit standardmäßiger sandgestrahlter Oberfläche) wurden bei 34 Patienten implantiert.

**Ergebnisse**  
Alle Implantate erfolgreich osseointegriert, Patienten zeigten gesunde Gingiva und hervorragende ästhetische Ergebnisse.

**Konklusion**  
Rehabilitation mit Zirkondioxid-Implantaten und Vollkeramik-Kronen ist eine sehr empfehlenswerte Alternative zu Titan-Implantaten für Patienten, die eine metallfreie Lösung wünschen.



LONG TERM DATA

## Zirconia dental implants: a clinical, radiographic, and microbiologic evaluation up to 3 years

Brüll F

### Purpose

To retrospectively evaluate the clinical performance of zirconia endosseous implants.

### Material and Methods

Partially edentulous patients with adequate bone volume to fit yttria tetragonal zirconia polycrystal (Y-TZP) implants at least 3.5 mm wide and 8.0 mm long were included. Full-mouth probing pocket depth (PPDs) and percentage bleeding on probing (BOP) scores around teeth and implant(s) were assessed and compared. Marginal bone loss/gain relative to baseline was measured on intraoral radiographs, and the prevalence and quantities of seven periodontal bacteria were assessed around implants and teeth in the same patient.

### Results

Seventy-four consecutively treated patients with 121 zirconia implants (66 two-piece implants and 55 one-piece implants)

were clinically evaluated after a mean observation period of 18 months. Three implants had failed and had been removed, for a cumulative implant survival rate of 96.5% ( $\pm 2.0\%$ ) after 3 years. The 118 surviving implants demonstrated healthy mucosal conditions, with low mean PPDs ( $1.8 \pm 0.4$  mm) and mean BOP scores ( $4.1\% \pm 4.2\%$ ). PPD and BOP were statistically significantly lower around implants than around teeth. BOP and PPD around implants and teeth were significantly correlated. Stable marginal bone levels were observed (mean bone loss of  $0.1 \pm 0.6$  mm after 3 years). The frequency of isolation of all marker bacteria was similar at tooth and implant sites.

### Conclusion

Zirconia endosseous implants can achieve a 3-year implant survival rate in partially edentulous patients, similar to that of titanium implants, with healthy and stable soft and hard tissues.

## One-piece ceramic implants: A longitudinal study over a two-year observation period

Mellinghoff J, Cacaci C, Detsch F

### Introduction

The greatest risk of one-piece ceramic implants is during their transgingival healing. Loads on the supracrestal implant section can have a negative effect during this phase on osseointegration.

### Materials and Methods

23 patients had altogether 51 Z-Look3 evo implants (Z-SYSTEMS, Oensingen, Switzerland) in two practices, and their success parameters were assessed during the entire treatment period using clinical and X-ray tools. Thus the risk of transgingival healing was carried out in accordance with manufacturer's instructions by ensuring a good bony implant bed and the use of implant protective measures.

### Results

After an average treatment time of about 2.5 years in which the implants were under prosthetic loads for about two years, all implants were in-situ, and were unremarkable from a clinical and X-ray standpoint. The average crestal bone loss (kkv) was 0.63 mm, and correlated significantly with the undershooting of the biological width when placing the implants.

### Summary

Successful prosthetic solutions were implemented with the one-piece zirconium dioxide implants under practice conditions without exception. In order to reduce the risk to transgingival healing, the authors recommend primary stability of at least 35 Ncm and safe implant protection measures.

## Einteilige Keramikimplantate – eine Longitudinalstudie über zwei Jahre Beobachtungsdauer

### Einleitung

Das grösste Risiko für einteilige Keramikimplantate besteht während ihrer transgingivalen Einheilung. Belastungen des subkrestalen Implantatanteils können sich in dieser Phase nachteilig auf die Osseointegration auswirken.

### Material und Methode

In zwei Praxen wurden 23 Patienten insgesamt 51 Z-Look3 Evo Implantate (Z-SYSTEMS, CH-Oensingen) inseriert und während der gesamten Liegezeit anhand klinischer und röntgenologischer Erfolgsparameter bewertet. Dabei wurde dem Risiko der transgingivalen Einheilung entsprechend den Herstellervorgaben durch Sicherstellung eines guten knöchernen Implantatlagers und Verwendung von Implantatschutzmassnahmen Rechnung getragen.

### Ergebnisse

Nach einer mittleren Liegezeit von ca. 2,5 Jahren, in der die Implantate im Durchschnitt ca. 2 Jahre unter Belastung standen, waren alle Implantate in situ und klinisch und röntgenologisch unauffällig. Der durchschnittliche krestale Knochenverlust (kkv) betrug 0,63 mm und korrelierte signifikant mit der Unterschreitung der biologischen Breite beim Versenken der Implantate.

### Fazit

Mit den verwendeten einteiligen Zirkoniumdioxidimplantaten liessen sich unter Praxisbedingungen ausnahmslos erfolgreiche prothetische Lösungen realisieren. Um das Risiko während der transgingivalen Einheilung zu reduzieren, empfehlen die Autoren eine Primarstabilität von mindestens 35 Ncm und sichere Implantatschutzmassnahmen.

## Five-year success rate of 831 consecutively placed Zirconia dental implants in humans: a comparison of three different rough surfaces

Olivia J et al.

### Purpose

The aim of this study was to evaluate the 5-year success rate of zirconia (ZrO<sub>2</sub>) implants with three different kinds of surfaces.

### Material and Methods

One-piece zirconia dental implants (CeraRoot) with three different roughened surfaces were designed and manufactured for this study: coated, uncoated, and acid-etched. Five different implant designs were manufactured. Standard or flapless surgical procedures were used for implant placement. Simultaneous bone augmentation or sinus elevation was performed when bone height or width was insufficient. Definitive all-ceramic restorations were placed 4 months after implant placement (8 months or more for implants when bone augmentation or sinus elevation was performed). The implants were followed up to 5 years (mean, 3.40 +/- 0.21).

### Results

In all, 831 implants were placed in 378 patients with a mean age of 48 years. The overall implant success rate after 5 years of follow-up was 95 % (92.77 % for uncoated implants, 93.57 % for coated implants, and 97.60 % for acid-etched implants). The success rate of the acid-etched surface group was significantly better than that of the other two.

### Conclusion

From this midterm investigation, it can be concluded that zirconia dental implants with roughened surfaces might be a viable alternative for tooth replacement. Further follow-up is needed to evaluate the long-term success rates of the implant surfaces studied.

## Titanium to Ceramic Dental Implants: A Short Communication

Saurabh G

Zirconia ceramics is successfully used to fabricate tooth-supported restorations and this has stimulated clinicians to encompass its application for restorations with implants. CAD/CAM technology combined with zirconia ceramic is gaining more and more popularity in implant dentistry. The introduction of zirconia implants served as an alternative to titanium implants in dental implantology. Zirconia appears to be a proper implant material due to its opacity, low plaque affinity, mechanical properties and biocompatibility.

Gingival recession and apical bone loss connected with implants many a times expose portions of the metal implant, showing the overlying gingiva's bluish discoloration. This complication is avoided by the use of zirconia implants and complies with the request of several patients for metal-free implants. Bone resorption and the inflammatory response caused by ceramic particles are less compared to those caused by titanium particles, signifying the biocompatibility of ceramics.

Nowadays most of the implant manufacturers provide zirconia abutments for restorations with aesthetic implants. Abutments

are offered in customized or prefabricated forms and may be prepared in the dental laboratory by using CAD/CAM techniques or by the technician. Zirconia's biocompatibility toward epithelial and soft connective tissue is vital. Furthermore-TZP abutments can support soft tissue integration, whereas promising peri-implant soft tissues can be achieved clinically adjacent to zirconia healing caps and zirconia implants.

In addition to strength considerations, abutments of Y-TZP implant provide metal-like radio-opacity for improved radiographic assessment, and finally condensed bacterial adhesion, inflammation risk and plaque accumulation. A methodical evaluation revealed that zirconia abutments might maintain a corresponding bone level when compared to aluminum oxide, titanium and gold ones. In one randomized and controlled trial twenty customized, non-HIPed based Zirconia single tooth implant abutment and same number of titanium single tooth implant abutments were observed for three years, with no cases of loosening or fractures in both the groups and reported 100% survival rates.



Courtesy by Dr. Ralf Lüttmann, Germany

## PERI-IMPLANTITIS

Peri-implantitis – onset and pattern of progression

Derks J, Schaller D, Håkansson J, Wennström JL, Tomasi C, Berglundh T

Background

While information on the prevalence of peri-implantitis is available, data describing onset and progression of the disease are limited.

Materials and Methods

A 9-year follow-up examination of 596 randomly selected implant-carrying individuals identified 62 patients with moderate/severe peri-implantitis. Longitudinal assessments of peri-implant marginal bone levels were used to construct a statistical model with bone loss as the dependent variable. A multilevel growth model estimated the pattern of bone loss for each implant/patient. Onset of peri-implantitis was determined by evaluating the cumulative percentage of implants/patients presenting with estimated bone loss at each year following prosthesis delivery.

Results

The analysis showed a non-linear, accelerating pattern of bone loss at the 105 affected implants. The onset of peri-implantitis occurred early, and 52% and 66% of implants presented with bone loss of >0.5 mm at years 2 and 3 respectively. A total of 70% and 81% of subjects presented with ≥1 implants with bone loss of >0.5 mm at years 2 and 3 respectively.

Conclusion

It is suggested that peri-implantitis progresses in a non-linear, accelerating pattern and that, for the majority of cases, the onset occurs within 3 years of function.

A systematic review of the clinical survival of zirconia implants

Hashim D, Cionca N, Courvoisier DS, Mombelli A

Objectives

The aim of this review was to evaluate the clinical success and survival rates of zirconia ceramic implants after at least 1 year of function and to assess if there is sufficient evidence to justify using them as alternatives to titanium implants.

Materials and methods

An electronic search in MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Clinical Trials (CENTRAL) databases was performed in April 2015 by two independent examiners to retrieve clinical studies focusing on the survival rate of zirconia implants after at least 1 year of function. Implant survival was estimated using the overall proportion reported in the studies with a Clopper-Pearson 95% confidence interval (random effect model with a Der-Simonian Laird estimate).

Results

Fourteen articles were selected out of the 1519 titles initially screened. The overall survival rate of zirconia one- and two-piece implants was calculated at 92% (95% CI 87–95) after 1 year of function. The survival of implants at 1 year for the selected studies revealed considerable heterogeneity.

Conclusions

In spite of the unavailability of sufficient long-term evidence to justify using zirconia oral implants, zirconia ceramics could potentially be the alternative to titanium for a non-metallic implant solution. However, further clinical studies are required to establish long-term results, and to determine the risk of technical and biological complications. Additional randomized controlled clinical trials examining two-piece zirconia implant systems are also required to assess their survival and success rates in comparison with titanium as well as one-piece zirconia implants.

Clinical relevance

Zirconia implants provide a potential alternative to titanium ones. However, clinicians must be aware of the lack of knowledge regarding long-term outcomes and specific reasons for failure.

Zirconium dioxide dental implants: Clinical and microbiological assessment

Holländer J

Aim

Clinical and microbiological follow-up examination of zirconia dental implants

Methods

A total of 106 implants (Z-Look3, Z-Systems AG, 3rd generation with standard sandblasted surface) were placed in 38 healthy patients and evaluated clinically and microbiologically.

Results

The implant sites displayed healthy and stable soft tissue conditions with sulcus depths of 2–3 mm, and in 87 % of the cases a width of the keratinized gingiva of 2 mm or more. Interestingly enough, the implant sites demonstrated a significantly lower plaque accumulation when compared to natural teeth.

Dentale Implantate aus Zirkoniumdioxid: Klinische und Mikrobiologische Nachuntersuchung

Zielsetzung

Klinische und mikrobiologische Nachfolgeuntersuchung von Zirkoniumdioxid-Implantaten

Methoden

Bei 38 gesunden Patienten wurden insgesamt 106 Implantate (Z-Look3, Z-Systems AG, 3. Generation mit standardmäßiger sandgestrahlter Oberfläche) platziert und klinisch und mikrobiologisch bewertet.

Ergebnisse

Die Implantatbetten zeigten gesundes und stabiles Weichgewebe mit Sulkustiefen von 2–3 mm und in 87 % der Fälle eine Breite der keratinisierten Gingiva von 2 mm oder mehr. Interessanterweise zeigten die Implantatbetten eine deutlich geringere Plaque-Ansammlung als natürliche Zähne.

Zirconia Dental Implants: Investigation of Clinical Parameters, Patient Satisfaction, and Microbial Contamination

Holländer J, Lorenz J, Stübinger S, Hölscher W, Heidemann D, Ghanaati S, Sader R

Purpose

In recent years, dental implants made from zirconia have been further developed and are considered a reliable treatment method for replacing missing teeth. The aim of this study was to analyze dental implants made from zirconia regarding their clinical performance compared with natural teeth (control).

Materials and Methods

One hundred six zirconia implants in 38 adults were analyzed in a clinical study after 1 year of loading. The plaque index (PI), bleeding on probing (BOP), probing pocket depth (PPD), probing attachment level (PAL), and creeping or recession (CR/REC) of the gingiva were detected and compared with natural control teeth (CT). Furthermore, the papilla index (PAP), Periotest values (PTV), microbial colonization of the implant/dental sulcus fluid, and patient satisfaction were assessed.

Results

The survival rate was 100 %. No statistical significance was observed between implants and teeth regarding BOP, PPD, and

PAL. A statistical significance was detected regarding PI and CR/REC with significantly less plaque accumulation and recession in the study group. Mean PAP was 1.76 ± 0.55, whereas the mean PTV was -1.31 ± 2.24 (range from -5 to +6). A non-statistically significant higher colonization of periodontitis/peri-implantitis bacteria was observed in the implant group. The questionnaire showed that the majority of the patients were satisfied with the overall treatment.

Conclusion

One-piece zirconia dental implants exhibited similar clinical results (BOP, PPD, and PAL) compared with natural teeth in regard to adhesion of plaque (PI) and creeping attachment (CR/REC); zirconia implants performed even better. The favorable results for PAL and CR/REC reflect the comparable low affinity of zirconia for plaque adhesion. Patient satisfaction indicated a high level of acceptance for zirconia implants. However, a long-term follow-up is needed to support these findings.

Quality of the peri-implant soft tissue attachment of zirconia implants (-abutments): Comparison of the results of a literature review with the experiences of dental practitioners

Mellinghoff J

Purpose

In the present work, zirconia implants are discussed solely with respect to their suitability as stock for periimplant soft tissue. The aim of the study was to compare the results of a literature review with the results of five years of clinical use in our dental practice.

Material and Methods

A systematic literature research was conducted in the internet database PUBMED using the keywords ‘zircon\*’, ‘implant’, ‘soft tissue’, ‘bacterial adhesion’, ‘mucosa’, ‘attachment’, ‘connective tissue’, and ‘plaque’. In the clinical part of the work, 65 zirconia implants type Z-Lock-III were inserted in 34 patients according to a surgical protocol, cared for during the healing process using protective measures and examined in annual follow-ups after the placement of the prosthetic superstructure. The mean exposure time was approximately 22 month (min. 1.3 months/ max. 59 months).

Results

In the literature review, 72 hits were generated, with a total of 16 publications that were relevant for our topic. The studies evaluated soft tissue attachment that was histologically examined, plaque adhesion, bacterial colonization with germs associated with periodontal diseases, inflammation factors of the soft tissue, as well as the influence on the color of the periimplant soft tissue. Compared with TiO2, the implants and abutments of zirconia achieved comparable or better results in all studies. At all times in the investigation, the evaluation of the clinical findings showed average probing depths between 2 and 3 mm. Plaque and bleeding results were described as exceptionally good. In addition, esthetically pleasing results could be achieved even with soft tissue in problematic condition.

Qualität des periimplantären Weichgewebeattachments von Zirkondioxid-Implantaten (Abutments): Vergleich der Ergebnisse einer Literaturrecherche mit den Erfahrungen aus der eigenen Praxis

In der vorliegenden Arbeit werden Zirkondioxidimplantate ausschließlich bezüglich ihrer Eignung als periimplantäres Weichteil-lager besprochen. Ziel der Arbeit war es, die Ergebnisse einer systematischen Literaturrecherche mit den Ergebnissen aus fünf Jahren klinischer Anwendung in eigener Praxis zu vergleichen.

Material und Methode

Anhand einer vorrecherchierten Keyword-Liste wurde eine Recherche in der Datenbank „PubMed“ durchgeführt. Im klinischen Teil der Arbeit wurden insgesamt 65 Zirkondioxidimplantate Typ Z-Lock-III von 34 Patienten nach einem festgelegten OP-Protokoll inseriert, mit Schutzmaßnahmen während der Einheilung versorgt und nach Eingliederung der prothetischen Suprakonstruktion im jährlichen Recall nachuntersucht. Die durchschnittliche Liegezeit betrug 22 Monate (min. 1,3 Mon./max. 59 Mon.).

Ergebnisse

Anhand der Literaturrecherche konnten 72 Arbeiten ermittelt werden, von denen 16 für die inhaltliche Auswertung im Hinblick auf die Eingangsfragestellung relevant waren. Die Studien bewerteten das histologisch untersuchte Weichgewebeattachment, die Plaque-adhäsion, die bakterielle Besiedlung mit PA-pathogenen Keimen, die im Weichgewebe gefundenen Entzündungsfaktoren, sowie den Einfluss auf die Weichteilfarbe. Verglichen mit Titandioxid schnitten die Implantate und Abutments aus Zirkondioxid in allen Studien gleich gut oder besser ab. Die Auswertung der klinischen Befunde ergab zu allen Untersuchungszeitpunkten durchschnittliche Sondierungstiefen zwischen 2 und 3 mm. Plaque- und Blutungsbefunde waren als überdurchschnittlich gut zu bezeichnen. Außerdem konnten selbst bei schwierigen Weichgewebeverhältnissen ästhetisch ansprechende Ergebnisse erreicht werden.

Increased Levels of Dissolved Titanium Are Associated With Peri-Implantitis – A Cross-Sectional Study

Safioti LM, Kotsakis GA, Pozhitkov AE, Chung WO, Daubert DM

Background

Peri-implantitis represents a disruption of the biocompatible interface between the titanium dioxide layer of the implant surface and the peri-implant tissues. Increasing preclinical data suggest that peri-implantitis microbiota not only triggers an inflammatory immune response but also causes electrochemical alterations of the titanium surfaces, i.e., corrosion, that aggravate this inflammatory response. Thus, it was hypothesized that there is an association between dissolution of titanium from dental implants, which suggests corrosion, and peri-implantitis in humans. The objective of this study is to compare levels of dissolved titanium in submucosal plaque collected from healthy implants and implants with peri-implantitis.

Methods

Submucosal plaque from 20 implants with peri-implantitis and 20 healthy implants was collected with sterile curets from 30 participants. Levels of titanium were quantified using inductively coupled plasma mass spectrometry and normalized

for mass of bacterial DNA per sample to exclude confounding by varying amounts of plaque per site. Statistical analysis was performed using generalized estimated equations to adjust for clustering of implants per participant.

Results

Implants with peri-implantitis harbored significantly higher mean levels of titanium (0.85 ± 2.47) versus healthy implants (0.07 ± 0.19) after adjusting for amount of plaque collected per site (P = 0.033).

Conclusion

Greater levels of dissolved titanium were detected in submucosal plaque around implants with peri-implantitis compared with healthy implants, indicating an association between titanium dissolution and peri-implantitis. Factors triggering titanium dissolution, as well as the role of titanium corrosion in the peri-implant inflammatory process, warrant further investigation.



## Bacterial adhesion on commercially pure titanium and zirconium oxide disks: an in vivo human study

Scarano A, Piattelli M, Caputi S, Favero GA, Piattelli A

### Background

Little is known about the mechanisms of bacterial interaction with implant materials in the oral cavity. A correlation between plaque accumulation and progressive bone loss around implants has been reported. Bacterial adhesion shows a direct positive correlation with surface roughness. Other surface characteristics also seem to be extremely important with regard to plaque formation. Different adhesion affinities of bacteria have been reported for different materials. The aim of this study was to characterize the percentage of surface covered by bacteria on commercially pure titanium and zirconium oxide disks.

### Methods

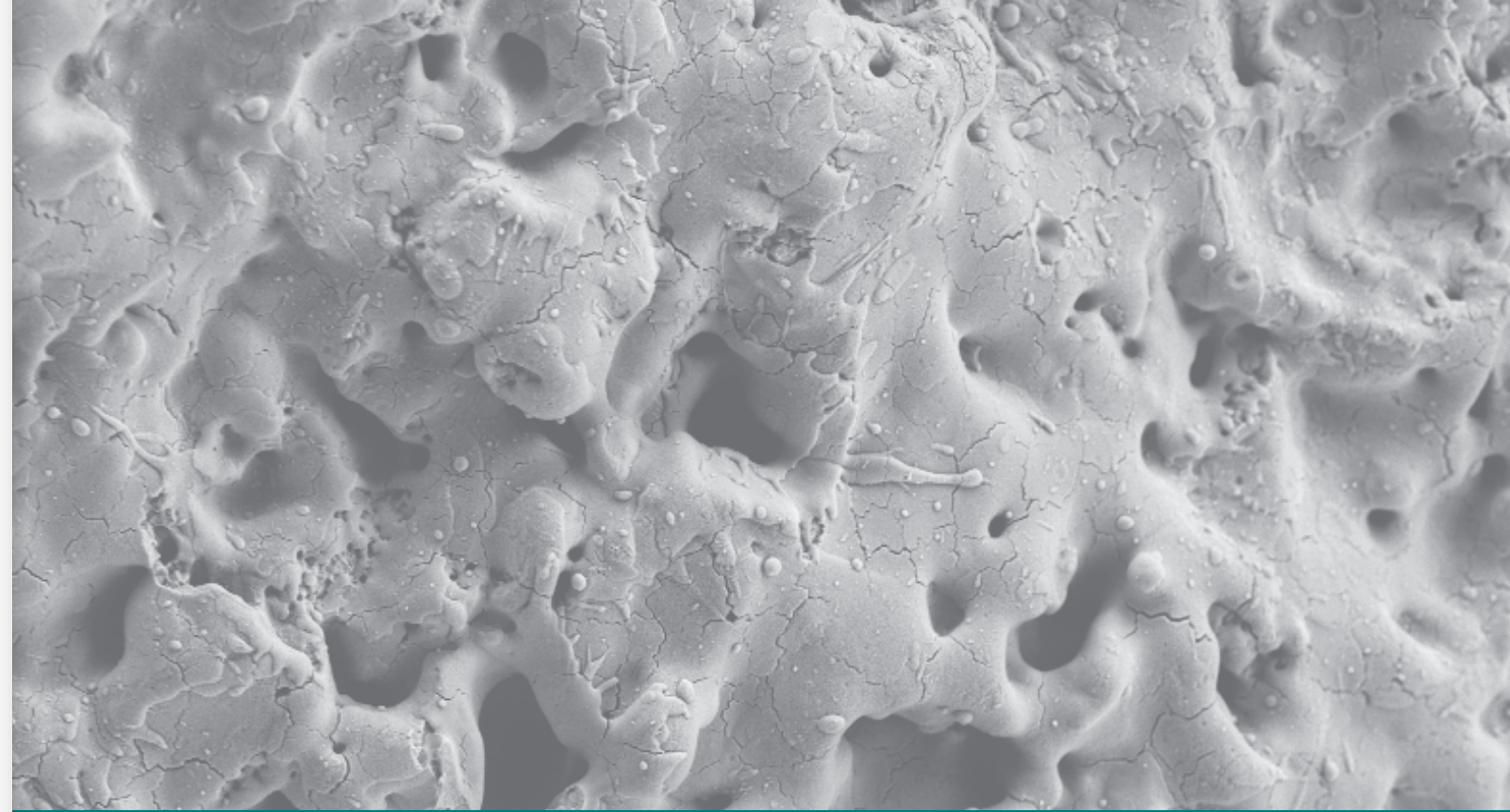
Ten patients participated in this study. A removable acrylic device was adapted to the molar-premolar region, and commercially pure

titanium (control) and zirconium oxide (test) disks were glued to the buccal aspect of each device. The surface roughness of titanium and test specimens was similar. After 24 hours, all disks were removed and processed for scanning electron microscopy, for the evaluation of the portion of surface covered by bacteria.

In control specimens, the area covered by bacteria was 19.3%  $\pm$  2.9; in test specimens, the area was 12.1%  $\pm$  1.96. The disk surface covered by bacteria on test specimens was significantly lower than that of control specimens ( $P = 0.0001$ ).

### Conclusion

Our results demonstrate that zirconium oxide may be a suitable material for manufacturing implant abutments with a low colonization potential.



# MATERIAL SCIENCE



Osseointegration of zirconia implants with different surface characteristics: an evaluation in rabbits

Hoffmann O, Angelov N, Zafiropoulos GG, Andreana S

Purpose

Zirconia ceramics are a viable alternative to titanium for use as dental implants. However, the smooth surface of zirconia means that longer healing periods are needed to accomplish osseointegration compared to roughened titanium surfaces. Surface modifications can be used to increase the roughness of zirconia. The aim of this study was to assess histologically and compare the degree of early bone apposition around zirconia dental implants with sandblasted, sintered, or laser-modified surfaces to that seen around surface-modified titanium implants. Removal torque was also measured and compared.

Materials and Methods

Ninety-six implants – 24 each of four types (sintered zirconia, laser-modified zirconia, sandblasted zirconia, and acid-etched titanium) – were placed in 48 New Zealand White female rabbits. One implant was inserted in each distal femur. Half of the specimens were harvested at 6 or 12 weeks and processed for light microscopic analysis; the area of bone-to-implant contact was measured morphometrically. The other half were evaluated for removal torque at 6 and 12 weeks.

Results

No statistically significant differences existed in bone apposition between the different surfaces at either time point. Differences in removal torque were significantly different between titanium and sandblasted zirconia and between sintered zirconia and sandblasted zirconia, with the first mentioned demonstrating a higher torque value at 6 weeks. At 12 weeks, the only significant difference in removal torque was between titanium and sandblasted zirconia, with titanium demonstrating the higher value.

Conclusion

Comparable rates of bone apposition in the zirconia and titanium implant surfaces at 6 and 12 weeks of healing were observed. Removal torque values were similar for all implants with a roughened surface.

The Impact of In Vitro Accelerated Aging, Approximating 30 and 60 Years In Vivo, on Commercially Available Zirconia Dental Implants

Monzavi M, Noumbissi S, Nowzari H

Background

Despite increased popularity of Zirconia dental implants, concerns have been raised regarding low temperature degradation (LTD) and its effect on micro-structural integrity.

Purpose

This study evaluated the effect of LTD on four types of Zirconia dental implants at 0, 30, and 60 years of artificial aging. The impact of aging on t-m transformation and micro crack formation was measured.

Materials and Methods

Accelerated aging at 15 and 30 hours, approximating 30 and 60 years in vivo, aged 36 Zirconia dental implants: Z-SYSTEMS® (A), Straumann® (B), Ceraroot® (C), and Zeramex® (D). Focused ion beam-scanning electron microscopic analysis determined the micro structural features, phase transformation, and the formation of micro cracks.

Results

At 15 hours, type A implant presented with micro cracks and t-m transformation of 0.9  $\mu\text{m}$  and 3.1  $\mu\text{m}$ , respectively. At 30 hours, micro cracks remained shallow (1  $\mu\text{m}$ ). At 15 hours, type B implant presented micro cracks (0.7  $\mu\text{m}$ ) and grain transformation (1.2  $\mu\text{m}$ ). At 30 hours, these features remained superficial at 0.6 and 1.5  $\mu\text{m}$ , respectively. Type C implant presented surface micro cracks of 0.3  $\mu\text{m}$  at 15 hours. The depth of t-m transformation slightly increased to 1.4  $\mu\text{m}$ . At 30 hours, number of micro cracks increased at the surface to an average depth of 1.5  $\mu\text{m}$ . Depth of t-m transformation increased to an average of 2.5  $\mu\text{m}$ . At 15 hours, micro cracks remained superficial (0.8  $\mu\text{m}$ ) for type D implant and depth of t-m transformation increased to 2.3  $\mu\text{m}$ . At 30 hours, the depth of micro cracks increased to an average of 1.3  $\mu\text{m}$  followed by increased t-m transformation to a depth of 4.1  $\mu\text{m}$ . Conclusion: Depth of grain transformation remained within 1–4  $\mu\text{m}$  from the surface. The effect of aging was minimal for all Zirconia implants.

Stability Assessment of 85 Standblasted and Laser-Etched Surface Zirconia Implant Using the Periotest Method over 4 Months of Bone Integration Time

Noumbissi S, Piconi C

The stability of a series of 85 one-piece zirconia implants performed by the same surgeon between 2011 and 2015 has been analyzed retrospectively. The stability was measured using the Periotest device during 4 months of osseointegration. The implants had two type of endosseous surface: fully sandblasted and laser etched at the crest of the threads. Stability values were assessed starting at the time of placement,

two, four, eight, 12 and 16 weeks. The pattern and timing of osseointegration and implant stability resulted in observations similar to that observed with sandblasted and coated titanium implants. As a result of laser etching, the implants displayed higher roughness with a bone like surface topography and appear to have faster osseointegration and higher values of stability in comparison with sandblasted implants.

Radiation risk estimation based on activity measurements of zirconium oxide implants

Porstendörfer J, Reineking A, Willert HC

**Objective**  
Measuring the specific radioactivity of orthopedic implants (hip joint ball heads) made from zirconia compared to metallic hip joint implants and ball heads made from Al<sub>2</sub>O<sub>3</sub>.

**Method**  
Biological effectiveness of a-radiation (compared to β- or γ-radiation) is about 20 times higher. Therefore a-radiation was measured with the help of γ-spectral analysis determining radionuclides and their mass fractions.

**Result**  
ZrO<sub>2</sub> samples (hip joint ball heads mass-/weight about 100 grams) release on average an effective dose rate (He\*) between 0.13 mSv/year and 0.53 mSv/year\*\* and are thus lower than the limit of 1 mSv/year recommended by ICPR (International Commission on Radiological Protection).

Source or mode	Typical dose (mSv)
10 hour airplane flight	0.03
Chest x-ray	0.05
CT scan	10
Annual dose from natural environment	2.4
Data from: <a href="http://www.unscear.org/faq">www.unscear.org/faq</a> (United Nations Scientific Committee on the Effects of Atomic Radiation), December 2017	
*Effective dose (He): The effective dose (unit: Sievert [Sv]) is an indicator of whole-body dose, measuring the total stochastic risk of radiation re. cancer and leukemia of a person exposed to ionizing Radiation.	
**Given its typical weight of approx. 1 gram, a zirconia implant is supposed to release an effective dose rate between 0.0013 and 0.0053 mSv/year.	

A new testing protocol for zirconia dental implants

Sanon C, Chevalier J, Douillard T, Cattani-Lorente M, Scherrer SS, Gremillard L

Objectives

Based on the current lack of standards concerning zirconia dental implants, we aim at developing a protocol to validate their functionality and safety prior their clinical use. The protocol is designed to account for the specific brittle nature of ceramics and the specific behavior of zirconia in terms of phase transformation.

Methods

Several types of zirconia dental implants with different surface textures (porous, alveolar, rough) were assessed. The implants were first characterized in their as-received state by Scanning Electron Microscopy (SEM), Focused Ion Beam (FIB), X-Ray Diffraction (XRD). Fracture tests following a method adapted from ISO 14801 were conducted to evaluate their initial mechanical properties. Accelerated aging was performed on the implants, and XRD monoclinic content measured directly at their surface instead of using polished samples as in ISO 13356. The implants were then characterized again after aging.

Results

Implants with an alveolar surface presented large defects. The protocol shows that such defects compromise the long-term mechanical properties. Implants with a porous surface exhibited sufficient strength but a significant sensitivity to aging. Even if associated to micro cracking clearly observed by FIB, aging did not decrease mechanical strength of the implants.

Significance

As each dental implant company has its own process, all zirconia implants may behave differently, even if the starting powder is the same. Especially, surface modifications have a large influence on strength and aging resistance, which is not taken into account by the current standards. Protocols adapted from this work could be useful.

Bone tissue responses to surface-modified zirconia implants: A histomorphometric and removal torque study in the rabbit

Sennerby L, Dasmah A, Larsson B, Iverhed M

Background

Zirconia ceramics are biocompatible and have mechanical properties that make them suitable as materials for dental implants. Little is known about how surface modification influences the stability and bone tissue response to zirconia implants.

Purpose

The objective of the investigation was to histologically and biomechanically evaluate the bone tissue response to zirconia implants with two different surface modifications in comparison with machined, nonmodified zirconia implants and oxidized titanium implants.

Materials and Methods

Threaded zirconia implants with a diameter of 3.75 mm with either a machined surface (Zr-Ctr) or one of two surface modifications (Zr-A and Zr-B) were manufactured. Oxidized titanium (Ti-Ox) implants 3.75 mm in diameter were also used. The implants were characterized with regard to surface topography using an interferometer. Twelve rabbits received 96 implants using a rotational scheme, two in each tibia and two in each femur. The implants in six rabbits were subjected to removal torque (RTQ) tests after a healing period of 6 weeks.

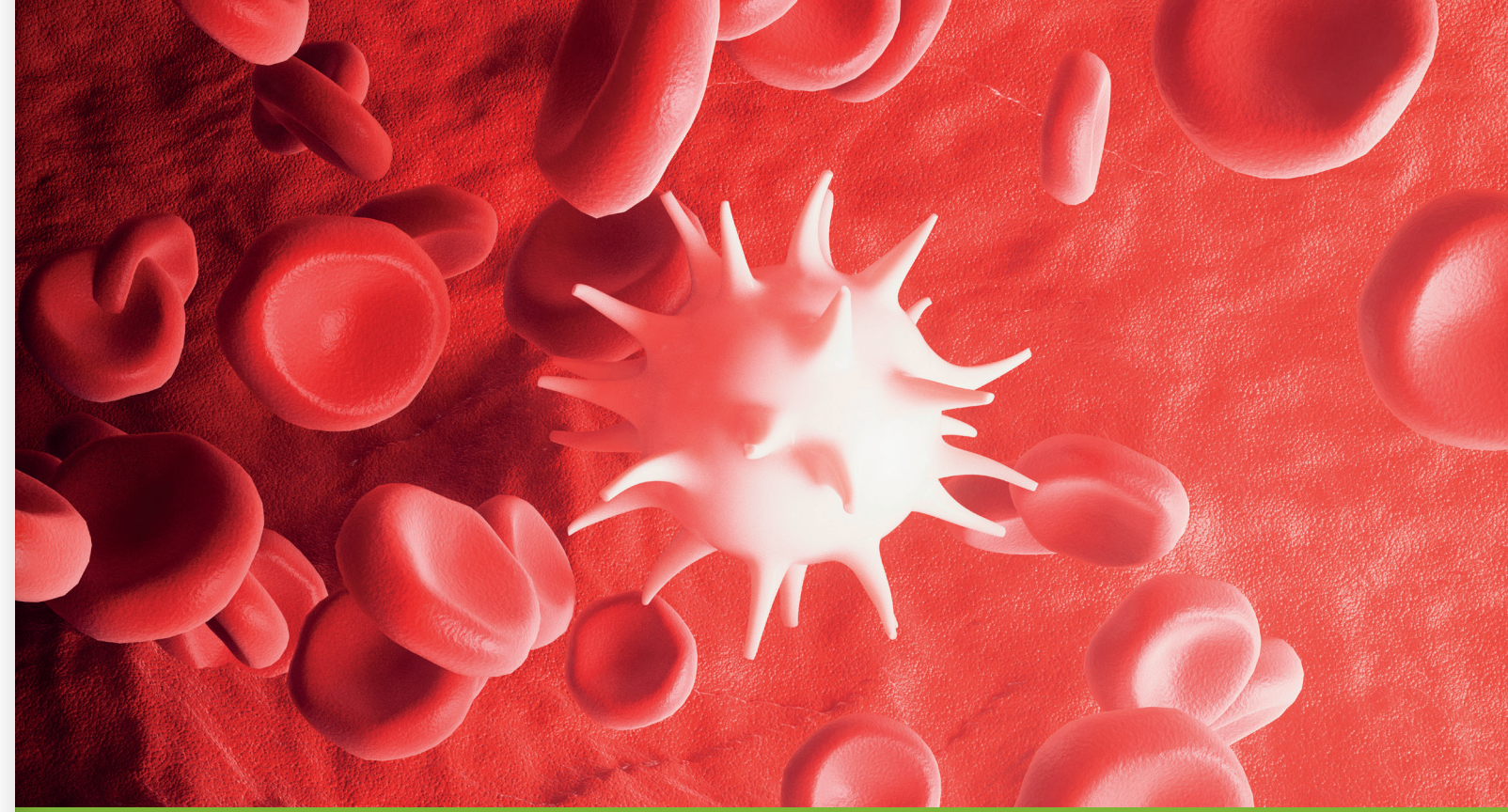
The implants in the remaining six animals were removed en bloc for light microscopic analysis. Back-scatter scanning electron microscopic (BS-SEM) analyses were used to evaluate the state of the bone-implant interface at the modified zirconia implants after RTQ testing.

Results

The Ti-Ox and Zr-A implants showed the highest surface roughness, followed by the Zr-B implants and, finally, the Zr-Ctr implants. The nonmodified ZrO<sub>2</sub> implants showed statistically significant lower RTQs than all other implants. No significant differences in bone-implant contact or bone area filling the threads were observed. BS-SEM showed intact surface layers of the surface-modified implants after RTQ testing and revealed fracture of the interface bone rather than a separation.

Conclusion

The present study showed a strong bone tissue response to surface-modified zirconia implants after 6 weeks of healing in rabbit bone. The modified zirconia implants showed a resistance to torque forces similar to that of oxidized implants and a four- to fivefold increase compared with machined zirconia implants. The findings suggest that surface-modified zirconia implants can reach firm stability in bone.



## IMMUNOLOGY



Patient introduction and material choice with subjectively experienced intolerance to titanium

Bayer G

Goal

Case report about the functional and aesthetic rehabilitation of a central incisor in the upper jaw

Methodology

14 years ago the left, inner upper jaw incisor of the patient was treated endodontically after a trauma. Because of a fistula, the tooth must be classified in the meantime as no longer worthy of preservation. Five months after atraumatic extraction and “socket preservation” the bone situation allowed for the placing of an implant. The implant (Z-Look3, Z-Systems AG, 3rd

generation with standard sandblasted surface) was inserted by hand with a 20 Ncm insertion torque and was provided with a Maryland bridge. After a further four months of healing, the final prosthetic could be integrated: the abutment was grinded in intraorally and the crown was cemented.

Discussion

One-piece Z-Look3 ceramic implants are very suitable for an aesthetically demanding prosthetic treatment because of their white color and their excellent soft tissue ingrowth.

Patientenführung und Materialauswahl bei subjektiv empfundener Titanunverträglichkeit

Ziel

Fallbericht über die funktionelle und ästhetische Rehabilitation eines zentralen Schneidezahns im Oberkiefer

Methodik

Vor 14 Jahren wurde der linke, innere Oberkieferschneidezahn des Patienten nach einem Trauma endodontisch behandelt. Aufgrund einer Fistel muss der Zahn inzwischen als nicht mehr erhaltungswürdig klassifiziert werden. Fünf Monate nach atraumatischer Extraktion und „Socket Preservation“ erlaubte die knöcherne Situation das Setzen eines Implantates. Das Implantat (Z-Look3, Z-Systems AG, 3. Generation mit Standard

sandgestrahlter Oberfläche) wurde von Hand mit 20 Ncm Eindrehmoment inseriert und mit einer Marylandbrücke versorgt. Nach weiteren vier Monaten Einheilzeit konnte die finale Prothetik eingegliedert werden: Das Abutment wurde intra-oral eingeschliffen und die Krone zementiert.

Diskussion

Einteilige Z-Look3 Keramikimplantate sind wegen ihrer weißen Farbe und der hervorragenden Weichgewebseinheilung sehr gut für eine ästhetisch anspruchsvolle prothetische Versorgung geeignet.

Electrical implications of corrosion for osseointegration of titanium implants

Gittens RA, Olivares-Navarrete R, Tannenbaum R, Boyan BD, Schwartz Z

The success rate of titanium implants for dental and orthopedic applications depends on the ability of surrounding bone tissue to integrate with the surface of the device, and it remains far from ideal in patients with bone compromised by physiological factors. The electrical properties and electrical stimulation of bone have been shown to control its growth and healing and can enhance osseointegration. Bone cells are also sensitive to the chemical products generated during corrosion events, but less is known about how the electrical signals associated with corrosion might affect osseointegration. The metallic nature of the materials used for implant applications and the corrosive

environments found in the human body, in combination with the continuous and cyclic loads to which these implants are exposed, may lead to corrosion and its corresponding electrochemical products. The abnormal electrical currents produced during corrosion can convert any metallic implant into an electrode, and the negative impact on the surrounding tissue due to these extreme signals could be an additional cause of poor performance and rejection of implants. Here, we review basic aspects of the electrical properties and electrical stimulation of bone, as well as fundamental concepts of aqueous corrosion and its electrical and clinical implications.



Genetic and immunological markers predict titanium implant failure: a retrospective study

Jacobi-Gresser E, Huesker K, Schütt S

This study evaluates diagnostic markers to predict titanium implant failure. Retrospectively, implant outcome was scored in 109 subjects who had undergone titanium implant surgery, IL1A -889 C/T (rs1800587), IL1B +3954 C/T (rs1143634), IL1RN +2018 T/C (rs419598) and TNFA -308 G/A (rs1800629) genotyping, in vitro IL-1 $\beta$ /TNF- $\alpha$  release assays and lymphocyte transformation tests during treatment. TNF- $\alpha$  and IL-1 $\beta$  release on titanium stimulation were significantly higher among patients with implant loss (TNF- $\alpha$ : 256.89 pg/ml vs. 81.4 pg/ml;  $p < 0.0001$ ; IL-1 $\beta$ : 159.96 pg/ml vs. 54.01 pg/ml;  $p < 0.0001$ ). The minor alleles of the studied polymorphisms showed increased prevalence in the implant failure group (IL1A: 61% vs. 42.6% in controls, IL1B:

53.7% vs. 39.7% in controls, TNFA: 46.3% vs. 30.9% in controls, IL1RN: 58.5% vs. 52.9% in controls). Increasing numbers of risk genotypes of the studied polymorphisms were associated with an increasing risk of implant loss, suggesting an additive effect. Multiple logistic regression analysis showed positive IL-1 $\beta$ /TNF- $\alpha$  release assay scores ( $p < 0.0001$ , OR=12.01) and number of risk genotypes ( $p < 0.046$ , OR=1.57–6.01) being significantly and independently associated with titanium implant failure. IL-1/IL1RN/TNFA genotyping and cytokine release assay scores provide prognostic markers for titanium implant outcome and may present new tools for individual risk assessment.

Dental implants stimulate expression of Interleukin-8 and its receptor in human blood – an in vitro approach

Quabius ES, Ossenkop L, Harder S, Kern M

Interleukin (IL)-8 secreted from osteoblasts and peripheral blood monocytes increases in patients with aseptic hip-implant loss and in patients with mucositis after dental implant insertion. We explored in vitro the possibility of an IL-8-mediated inflammatory response as a consequence of contact between different dental implant surfaces and human blood. Titanium and zirconia implants were incubated in human blood. Nonstimulated blood served as negative, while blood stimulated with bacterial lipopolysaccharides (LPS) served as positive control. After depyrogenization, to examine the possible role of LPS, implants were again submerged in blood. Gene-expression of IL-8 and its receptor was measured by

real-time quantitative polymerase chain reaction. In a receptor mediated, but LPS-independent manner, titanium implants led to a more pronounced increase in IL-8 gene expression when compared with zirconia implants. Depyrogenization resulted after 24 h in zirconia implants in decreased IL-8 gene expression. Altered IL-8 expression could indicate aseptic, at least LPS-independent implant loss, which may be an additional feature in the manifestation of peri-implantitis, possibly triggered by microscopically small implant-particles. Hence, opening a new field of investigations to further understand the possible mechanism underlying the manifestation of implant failure.

Increased frequency of delayed type hypersensitivity to metals in patients with connective tissue disease

Stejskal V, Reynolds T, Bjørklund G

Background

Connective tissue disease (CTD) is a group of inflammatory disorders of unknown aetiology. Patients with CTD often report hypersensitivity to nickel. We examined the frequency of delayed type hypersensitivity (DTH) (Type IV allergy) to metals in patients with CTD.

Methods

Thirty-eight patients; 9 with systemic lupus erythematosus (SLE), 16 with rheumatoid arthritis (RA), and 13 with Sjögren's syndrome (SS) and a control group of 43 healthy age- and sex-matched subjects were included in the study. A detailed metal exposure history was collected by questionnaire. Metal hypersensitivity was evaluated using the optimised lymphocyte transformation test LTT-MELISA(®) (Memory Lymphocyte Immuno Stimulation Assay).

Results

In all subjects, the main source of metal exposure was dental metal restorations. The majority of patients (87%) had a positive

lymphocyte reaction to at least one metal and 63% reacted to two or more metals tested. Within the control group, 43% of healthy subjects reacted to one metal and only 18% reacted to two or more metals. The increased metal reactivity in the patient group compared with the control group was statistically significant (P<0.0001). The most frequent allergens were nickel, mercury, gold and palladium.

Conclusion

Patients with SLE, RA and SS have an increased frequency of metal DTH. Metals such as nickel, mercury and gold are present in dental restorative materials, and many adults are therefore continually exposed to metal ions through corrosion of dental alloys. Metal-related DTH will cause inflammation. Since inflammation is a key process in CTDs, it is possible that metal-specific T cell reactivity is an etiological factor in their development. The role of metal-specific lymphocytes in autoimmunity remains an exciting challenge for future studies.

Titanium allergy: could it affect dental implant integration?

Siddiqi A, Payne AG, De Silva RK, Duncan WJ

Purpose

Degradation products of metallic biomaterials including titanium may result in metal hypersensitivity reaction. Hypersensitivity to biomaterials is often described in terms of vague pain, skin rashes, fatigue and malaise and in some cases implant loss. Recently, titanium hypersensitivity has been suggested as one of the factors responsible for implant failure. Although titanium hypersensitivity is a growing concern, epidemiological data on incidence of titanium-related allergic reactions are still lacking.

Materials and Methods

A computer search of electronic databases primarily MEDLINE and PUBMED was performed with the following key words: ‘titanium hypersensitivity’, ‘titanium allergy’, ‘titanium release’ without any language restriction. Manual searches of the bibliographies of all the retrieved articles were also performed. In addition, a complementary hand search was also conducted to identify recent articles and case reports.

Results

Most of the literature comprised case reports and prospective in vivo/in vitro trials. One hundred and twenty-seven publications were selected for full text reading. The bulk of the literature originated from the orthopaedic discipline, reporting wear debris following knee/hip arthroplasties. The rest comprised osteosynthesis (plates/screws), oral implant/dental materials, dermatology/cardiac-pacemaker, pathology/cancer, biomaterials and general reports.

Conclusion

This review of the literature indicates that titanium can induce hypersensitivity in susceptible patients and could play a critical role in implant failure. Furthermore, this review supports the need for long-term clinical and radiographic follow-up of all implant patients who are sensitive to metals. At present, we know little about titanium hypersensitivity, but it cannot be excluded as a reason for implant failure.

## Titanium immunology: Titanium tolerance – myth or reality?

von Baehr V

It is disputed at present whether titanium causes intolerances in some individuals. True allergies to titanium are rare as compared to other metals, as titanium ions form oxides quickly after their release due to their oxygen affinity. Oxides cannot bind with protein, and therefore no haptens, and therefore do not have an allergic effect. This fact has led to the realization that titanium is often seen as biocompatible. This assumption is not true, however, if one means that titanium is not perceived by the immune system. In this case, bone integration is not possible, as there is a stimulus provided by the material which must be assumed.

The fact is that titanium can be a trigger for titanium-induced periimplantitis over a different immunological mechanism. The cause for this is not allergic mechanisms, but rather overcompensating inflammatory reactions of tissue macrophages after contact with titanium (oxide) particles. This inflammatory response is not based on the presence of specific lymphocytes (and therefore, by definition, this is not an allergy), but rather to a genetically-determined increased susceptibility to inflammation due to non-specific inflammatory cells after contact with titanium particle debris.

This present work address the current state of scientific literature on the topic of „titanium immunology.“

## Die Immunologie des Titans: Titanunverträglichkeit – Mythos oder Realität?

Bis heute ist es umstritten, ob es auf Titan individuelle Unverträglichkeiten gibt. Echte Allergien auf Titan sind im Unterschied zu anderen Metallen selten, da Titanionen durch ihre hohe Sauerstoffaffinität unmittelbar nach Ihrer Freisetzung Oxide bilden. Oxide können keine Proteinbindung eingehen und somit keine haptene und somit keine allergene Wirkung entfalten. Diese Tatsache hat dazu geführt, dass Titan bis heute nicht selten als biokompatibel angesehen wird. Diese Annahme ist aber nicht richtig, wenn man damit meint, dass Titan vom Immunsystem nicht wahrgenommen wird. In diesem Fall wäre eine knöcherne Integration nicht möglich, da diese immer einen Reiz seitens des zu ignorierenden Werkstoffes zur Voraussetzung hat.

Tatsache ist, dass Titan über einen anderen immunologischen Mechanismus Auslöser einer Titaninduzierten Periaparodontitis sein kann. Ursächlich sind sind dafür sind aber nicht allergische Mechanismen, sondern überschießende Entzündungsreaktionen der Gewebemakrophagen nach Kontakt mit Titan(oxid)partikeln. Diese Entzündungsantwort beruht nicht auf der Anwesenheit spezifischer Lymphozyten (somit liegt definitionsgemäß keine Allergie vor) sondern auf einer in der Regel genetisch determinierten gesteigerten Entzündungsbereitschaft der unspezifischer Entzündungszellen nach Kontakt mit partikulärem Titanpartikelabrieb (engl. „debris“).

In der vorliegenden Arbeit soll der aktuelle Stand der wissenschaftlichen Literatur zum Thema „Immunologie des Titans“ wiedergegeben werden.

## NOTES

## NOTES



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