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# Crestal bone response to loaded zirconia and titanium implants: a radiographic and histometric analysis in canines

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## Abstract

**Objectives** To evaluate the crestal bone response to a two-piece zirconia implant compared with a control titanium implant using periapical radiographs (PAs) and histometry.

**Materials and methods** Thirty zirconia and 30 titanium implants were placed in healed posterior mandibles of five canines. Full-ceramic single-tooth restorations were cemented after 6 weeks of healing. Three observers measured the distance between the implant shoulder and the crestal bone (DIB) at placement, loading, and harvesting after 4 or 16 weeks in function. The influence of implant material and loading time on DIB as well as the inter-observer agreement were analyzed. Additionally, histometric distance between implant shoulder and most coronal bone-to-implant contact (IS-cBIC) was compared with DIB.

**Results** Mean DIB values increased between 4 and 16 weeks of loading for both zirconia (from 1.66 to 2.25 mm;  $P < 0.0001$ ) and titanium (from 1.81 to 1.95 mm;  $P = 0.06$ ). Zirconia yielded mean IS-cBIC values of 2.18 mm and 2.48 mm ( $P < 0.001$ ) and titanium 2.23 mm and 2.34 mm ( $P = 0.27$ ) after 4 and 16 weeks, respectively. The raters reached an excellent intraclass correlation coefficient. PAs underestimated the bone loss on average by 0.39 mm.

**Conclusions** Zirconia implants showed a greater increase of DIB during early healing and function than titanium.

**Clinical relevance** Crestal peri-implant tissue dimensions may show more pronounced changes around two-piece zirconia implants during early healing. PAs may underestimate peri-implant bone loss.

**Keywords** Crestal bone · Dental implants · Osseointegration · Radiographic analysis · Zirconia implants

## Introduction

Titanium implants have been successfully used for the replacement of teeth for over 40 years, since the first reports by Brånemark 1969 and Schroeder 1978 [1, 2]. Mechanical and biological stability and excellent long-term results make

titanium the gold standard as an implant material [3, 4]. Demand for metal-free implant materials has recently increased, partially due to more or less founded criticism towards titanium [5, 6] and the potential of optimal esthetic outcomes of white ceramic materials [7]. Among these, recent reports hypothesize a limited impact of bacteria from zirconia

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surfaces on the surrounding tissues [8, 9], whereas bacterial peri-implant infections are known as a main reason for the failure of titanium implants [10–12]. This may be due to a lower bacterial adhesion and plaque formation on ceramic surfaces [9, 13, 14].

Early preclinical studies on implants made of zirconium dioxide ( $ZrO_2$ ; zirconia) appeared in the early 1990s [15], while the first clinical data were published 10 years later [16]. Then, in the last two decades, availability and use of zirconia implants increased. Preclinical data demonstrate that zirconia implants with moderately rough endosseous surface show similar osseointegration to current titanium implants [17]. Clinical studies show promising survival rates for periods of up to 5 years for currently commercially available zirconia implants [18–20]. Most implant failures occur in the first year with a survival rate of 95.6%; then, failure incidence decreases to 0.05% per year with almost constant survival curves [21].

Peri-implant tissue health is characterized by defined dimensions of soft and hard tissue [22]. On the other side, peri-implant infection is mostly associated with crestal bone loss [23] and is an important factor for implant failure [11, 12]. Peri-implantitis can be successfully treated when patients follow a regular supportive care program which results in high implant survival in the medium and long term [24]. In this context, methods for non-invasive, reliable measurement and detection of crestal bone loss are essential. Accordingly, the measurement of the distance between implant shoulder and bone crest (DIB) in periapical radiographs (PAs) is a routinely used diagnostic tool in combination with the clinical examination during the follow-up after implant therapy [25–28]. DIB measurement in PAs around titanium implants has shown good correlation when compared with the histometric measurement of the same dimension (implant shoulder to most coronal bone-to-implant contact; IS-cBIC) [28]. Zirconia implants generate significantly more artifacts than titanium in computed tomography (CT) and cone-beam CT (CBCT) scans [29, 30]. Interestingly, this material-related influence is reversed in magnetic resonance imaging (MRI) scans [31]. The current literature contains no data about the effect of implant material (zirconia vs. titanium) on DIB measurement in PAs.

The purpose of this study was to evaluate the influence of loading time and implant material on crestal bone levels around a two-piece zirconia (test) and well-documented titanium (control) implant under functional loading. Secondary objectives were the reproducibility between the observers and the comparison of the radiographic to the histometric assessment. The null hypothesis was that no statistically significant difference between test and control groups can be found in any measured parameter after 4 and 16 weeks of loading and also among the 3 observers.

## Material and methods

The study was conducted in accordance with the ethical standards of current US federal regulations. The University of Texas Health Science Center at San Antonio Institutional Animal Care and Use Committee approved animal selection, management, and study protocol prior to the start of the experiment (IACUC; ID no. 13005x).

### Study design

The study design has been described previously [17]. In brief, implants were placed in healed edentulous ridges 12 weeks after extraction of all mandibular premolars and first molars in five male, laboratory-bred hound dogs with mean age of 18 months (range 14–24 months). Two different implant materials were compared. The test material was a novel two-piece zirconia implant, with an endosseous diameter of 4.1 mm and endosseous length of 8 mm, featuring a machined collar of 4.8 mm diameter and 1.8 mm height (Institut Straumann AG, Basel, Switzerland). The surface of this yttria-stabilized tetragonal zirconia polycrystal implant was modified with sandblasting (large  $Al_2O_3$  grits of 0.25–0.5 mm) and acid-etched (hydrofluoric acid) up to 0.74  $\mu m$  (micro) and 1.64  $\mu m$  (macro) roughness. The control was a commercially available implant with similar endosseous and collar dimensions as the test (Standard Plus Regular Neck; Institut Straumann AG). This implant made of commercially pure titanium displayed a surface with 1.26  $\mu m$  (micro) and 3.14  $\mu m$  (macro) roughness, obtained with a treatment identical to the control except for the etchant being a mixture of hydrochloric/sulfuric acid. Three test and 3 control implants were inserted in an alternating pattern bilaterally in the healed edentulous ridge, yielding a total of 6 implants per side. Full-ceramic, single-tooth restorations were cemented after 6 weeks of transmucosal healing, allowing for full functional loading of the implants. The crowns all had an identical outer shape and appropriate inner shape for the respective abutment type, i.e., zirconia or titanium. Both sides of the mandible were treated following the same surgical and prosthetic protocols, with the treatment of the randomly chosen first side starting 12 weeks before the second side and thus leading to two different loading periods (4 and 16 weeks, respectively) of the implants at euthanasia and harvesting (Fig. 1). Histometric procedures were performed as described previously [17].

### Radiographic analysis

Periapical radiographs (PAs) were taken immediately after implant placement, after restoration, and at harvesting. For all five canines, customized radiographic stents allowing standardized x-ray projections during the experimental period were prepared. Film-holding bite blocks with a paralleling

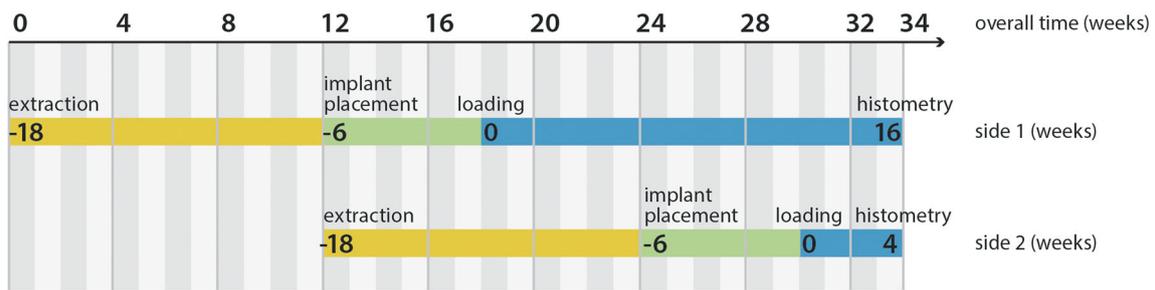


Fig. 1 Timetable of the treatment protocol

beam-guiding device (Rinn-XCP posterior; Dentsply Sirona, York, PA, USA) were adapted by means of light-curing acrylic resin engaging the canines and the second molars (Fig. 2). Each of the digital PAs was assigned a random number allowing a blinded evaluation with regard to the investigational time point. DIB measurements were performed by three observers according to the previously described method [27, 32] (Fig. 3), using digital medical imaging software (Osirix Lite Version 7.0.4; Pixmeo SARL, Bernex, Switzerland). On each PA, the vertical distance between the maximal amount of clearly visible threads of one zirconia implant was used as reference for the computer-assisted calibration. The three observers were trained oral and implant surgeons, well-experienced in dental and maxillofacial radiology. They all were calibrated by means of 10 randomly chosen PAs from the study dataset prior to the assessment of the radiographs.

**Statistical analysis**

The assessment of the data was performed in three consecutive steps.

**Radiographic assessment (primary outcome variables)**

The impact of the implant material (zirconia/titanium) on the main outcome DIB was assessed. As well, it was analyzed if the time point (placement/loading/harvesting) had a significant impact on DIB. Data was analyzed with respect to the loading period (4 or 16 weeks) at harvesting. Because of repeated measurements, all radiographic analyses were done with the help of linear mixed models.

Fig. 2 Customized X-ray holder



**Homogeneity analysis of the observers (secondary outcome variables)**

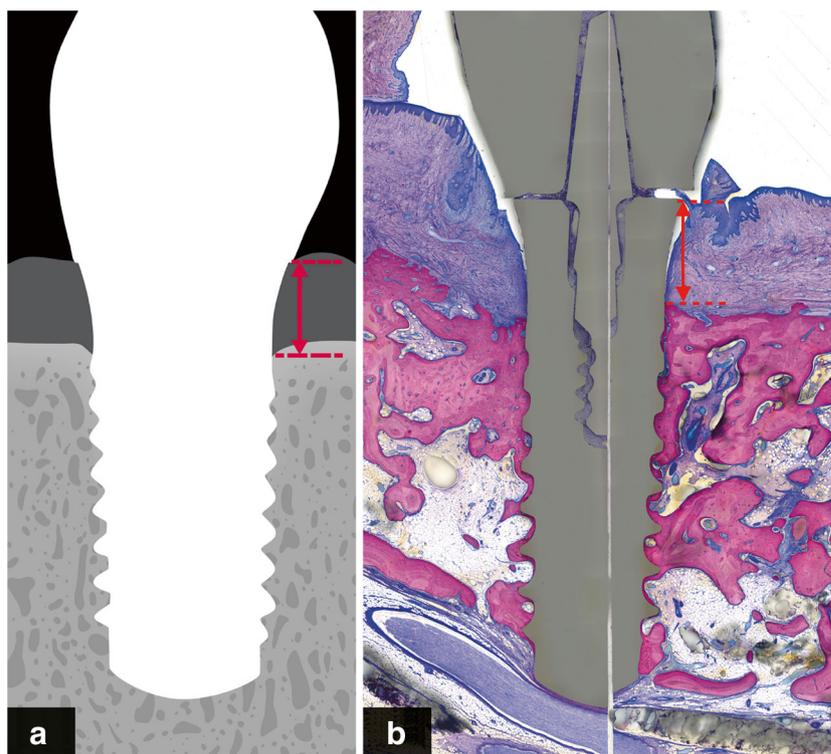
The inter-observer agreement (reproducibility) among the three observers was analyzed. For this purpose, inter-class correlation coefficients (ICC) were calculated and classified according to Cicchetti’s grading system [33] into poor (< 0.40), fair (0.40–0.59), good (0.60–0.74), or excellent (> 0.75). In addition, the average absolute inter-observer error with its 95% confidence interval (95% CI t-interval) as well as its variability was estimated by calculating the mean of the absolute differences between all repeated measurements on the same tooth for each aspect (mesial/distal) and time point (loading/placement/harvesting) separately. This homogeneity analysis was performed chronologically as the first statistical step, in order to assess whether the three measurements of each site may be averaged for the subsequent analyses based on the agreement rate.

**Histometric assessment (secondary outcome variables)**

Histometric data were generated according to the previous study [17]. The outcome (IS-cBIC) was compared with the radiographic data (DIB) at harvesting using again linear mixed models. Except for the previously reported analysis of implant material and loading period [17] that serves in the comparison between histometry and PA, all data presented in this study is new.

As for the linear mixed models, the variables “implant type” (zirconia/titanium), “time point” (placement/loading/harvesting), “loading period” (4 or 16 weeks), and

**Fig. 3** Schematic representation of the distance between implant shoulder and bone crest (DIB) as measured in the PA (a). Distance between implant shoulder and most coronal bone-to-implant contact IS-cBIC in an exemplary histologic specimen (b)



“measurement type” (radiology/histology) were always included as fixed factors whereas the variables “aspect” (mesial or distal) and “tooth-nested-in-canine” were used as random factors. A type III ANOVA *F* test using Satterthwaite’s correction was performed to detect global significant effects while Satterthwaite-corrected *t* tests were performed post hoc to detect group-wise differences. Throughout the mixed models were validated with the help of normality tests (Shapiro-Wilk) on both residuals and random effects. Also, fitted and effective values were plotted against each other to check for possible residual patterns. *P* values less than 0.05 were considered statistically significant. No corrections for *P* values and no sample size calculation were applied due to the explorative nature of this study. All analyses in this report were performed with the statistics software R, version 3.5.0 (R Development Core Team, Vienna, Austria, 2018. URL <https://www.r-project.org/>).

## Results

All 60 implants and 60 restorations were still in function after 4 and 16 weeks of loading in both test and control groups. No implant loss, no implant or abutment fracture, and no chipping at the restorations could be detected. The animals remained healthy throughout the entire study time frame.

## Inter-observer agreement

The inter-observer agreement was graded as “excellent” according to Cichetti [33] at all time points with intraclass correlation values (95% CI) of 0.83 (0.78–0.87) at placement, 0.86 (0.81–0.89) at loading, and 0.83 (0.77–0.87) at harvesting. The average absolute measurement error between observers was almost constantly 0.15 mm with a standard deviation of 0.15 mm (Table 1) and a maximum of 0.88 mm. This again emphasizes the strong agreement. The average measurement difference between observers was close to 0.0 mm, with an almost constant standard deviation of 0.2 mm (Table 1). Also, the overlapping confidence intervals emphasized the strong consensus. Based on the high agreement between the

**Table 1** Summary of average absolute measurement errors (distances) between observers (in mm): grand mean with 95% CI, standard deviation, and range in lines 1 to 3, respectively

	Loading	Placement	Harvesting
Mesial aspect	0.15 (0.19, 0.23)	0.15 (0.19, 0.23)	0.16 (0.20, 0.24)
	0.15	0.15	0.16
	[0.01, 0.74]	[0.01, 0.60]	[0.02, 0.84]
Distal aspect	0.16 (0.20, 0.24)	0.15 (0.20, 0.24)	0.15 (0.19, 0.24)
	0.15	0.17	0.16
	[0.03, 0.81]	[0.01, 0.68]	[0.04, 0.88]

three observers, averaged values of all three observers at each time point were used for further analysis.

### Radiographic assessment

The mean DIB increased for zirconia from placement (1.47 mm) to 16 weeks of loading (2.25 mm) and from 1.33 to 1.95 mm for titanium (Table 2). The implant material (zirconia/titanium) had no effect on the averaged DIB ( $P = 0.33$ ).

The study period from placement to 16 weeks loading showed a highly significant impact on DIB ( $P < 0.0001$ ). Hence, post hoc tests were performed to compare the different time frames. For each implant material (zirconia/titanium), DIB at each time point was compared with DIB at the other time points and then analyzed for whether there was a statistically significant difference (Table 3). For zirconia, all analyzed time frames showed statistically significant differences ( $P \leq 0.004$ ) except between loading and harvesting after 4 weeks of loading ( $P = 0.83$ ). For titanium, the comparisons with placement were statistically significant (all  $P < 0.0001$ ), whereas all time point combinations after loading reached no statistical significance (all  $P \geq 0.06$ ).

### Histometric analysis and comparison to radiography

Histometric (IS-cBIC) values differed from radiographic (DIB) values at both harvesting times ( $P < 0.0001$ ). The overall IS-cBIC was 2.31 mm, whereas the overall DIB reached 1.92 mm (Table 4 and Fig. 4). The effect of loading period was also highly significant ( $P < 0.0001$ ), but this effect was influenced by a significant interaction with implant material ( $P = 0.01$ ). Therefore, post hoc tests were performed to compare each group.

The loading period had a significant impact on IS-cBIC at zirconia implants, with values being higher at 16 than 4 weeks. This effect was revealed in both histometry and PA (both  $P < 0.0001$ ). Histometry and PA thus led to the same result despite their significant difference. Opposingly, when assessing the effect of loading period on titanium implants, the group-wise comparison was close to significant in PAs ( $P = 0.06$ ; Table 4) and far from significant at histometry ( $P = 0.27$ ; Table 4). Similar to zirconia, titanium also yielded a high correlation between the two measurement methods at each time point (both  $P < 0.0001$ ).

In conclusion, when comparing PAs to histometry at zirconia implants, the discrepancy between DIB and IC-cBIC

**Table 3** Changes of DIB between the study time points for zirconia and titanium implants. Comparisons between all combinations of two time points, respectively

Implant material	Time frame comparison	P value
Zirconia	Placement-loading	< 0.0001
	Placement-harvesting 4 weeks	< 0.0001
	Placement-harvesting 16 weeks	< 0.0001
	Loading-harvesting 4 weeks	0.83
	Loading-harvesting 16 weeks	0.004
	Harvesting 4 weeks-harvesting 16 weeks	< 0.0001
Titanium	Placement-loading	< 0.0001
	Placement-harvesting 4 weeks	< 0.0001
	Placement-harvesting 16 weeks	< 0.0001
	Loading-harvesting 4 weeks	0.22
	Loading-harvesting 16 weeks	0.25
	Harvesting 4 weeks-harvesting 16 weeks	0.06

depended on the loading period (Table 4 and Fig. 5): the highest discrepancy was found after 4 weeks (1.66 mm vs. 2.18 mm, respectively) and the lowest at 16 weeks (2.25 mm vs. 2.48 mm). For titanium, the difference between PAs and histometry was more similar between the two time points (Table 4 and Fig. 5).

### Discussion

The present study was designed to evaluate the influence of implant material (zirconia vs. titanium) and loading time (4 vs. 16 weeks) on crestal bone levels measured in PAs and histometry in a canine model. Under these experimental conditions, the zirconia implant showed a more pronounced crestal bone loss than titanium between 4 and 16 weeks of function. DIB measurements performed in the PAs reached high reproducibility. Moreover, PA tended to underestimate the distance between implant shoulder and crestal bone when compared with histometric measurements. The null hypothesis could be confirmed only for the inter-observer agreement. For all other measured parameters, there was a statistically significant difference between test and control groups after 4 and 16 weeks of loading; therefore, the null hypothesis had to be rejected.

The current literature contains a number of studies reporting high long-term survival of titanium implants such

**Table 2** Mean DIB and 95% confidence interval at all time points for zirconia and titanium implants

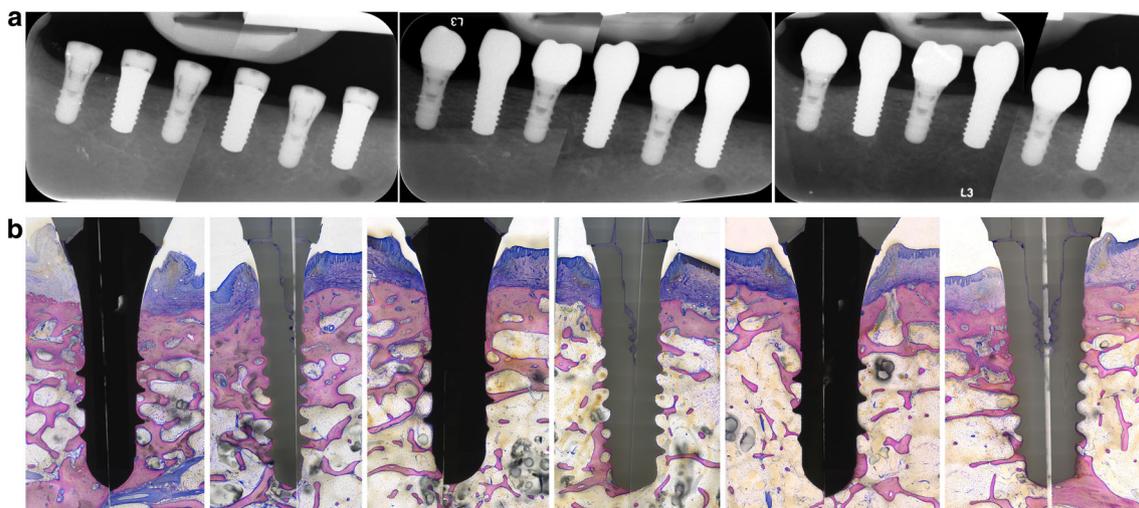
Time point	Zirconia mean DIB (mm) (95% CI)	Titanium mean DIB (mm) (95% CI)
Placement	1.47 (1.38, 1.55)	1.33 (1.22, 1.45)
Loading	1.86 (1.75, 1.98)	1.81 (1.70, 1.93)
Harvesting 4 weeks	1.66 (1.56, 1.76)	1.81 (1.65, 1.98)
Harvesting 16 weeks	2.25 (2.14, 2.35)	1.95 (1.79, 2.11)

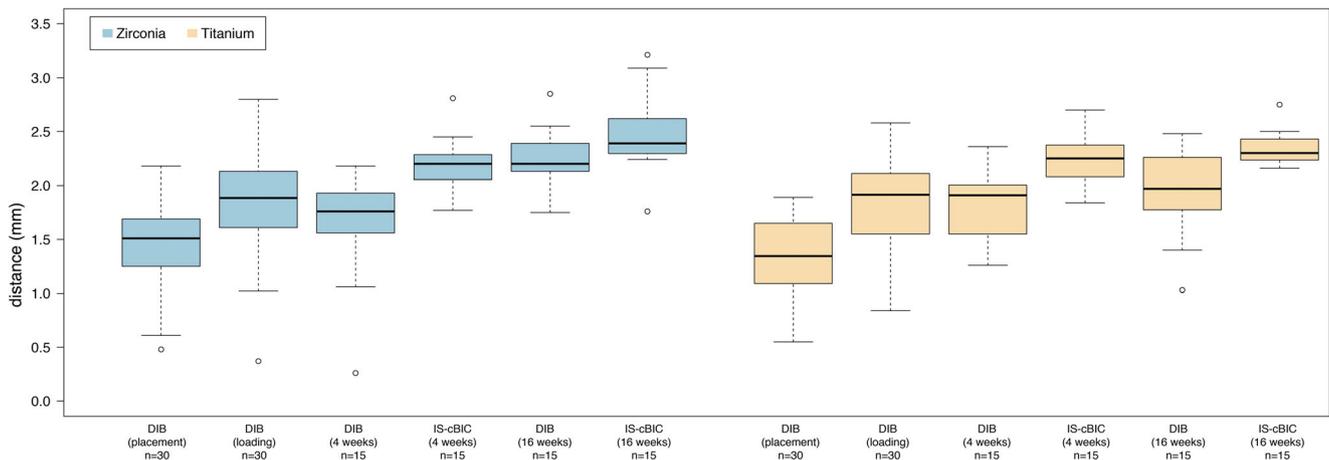
**Table 4** Mean DIB and IS-cBIC for zirconia and titanium implants at harvesting after 4 and 16 weeks of loading, respectively

	Harvesting 4 weeks	Harvesting 16 weeks	<i>P</i> value 4 to 16 weeks
Zirconia mean DIB (mm) (95% CI)	1.66 (1.56, 1.76)	2.25 (2.14, 2.35)	< 0.0001
Zirconia mean IS-cBIC (mm) (95% CI)	2.18 (2.05, 2.31)	2.48 (2.36, 2.60)	< 0.0001
<i>P</i> value zirconia histometry vs. PAs	< 0.0001	< 0.0001	
Titanium mean DIB (mm) (95% CI)	1.81 (1.65, 1.98)	1.95 (1.79, 2.11)	0.06 <i>NS</i>
Titanium mean IS-cBIC (mm) (95% CI)	2.23 (2.11, 2.36)	2.34 (2.22, 2.47)	0.27 <i>NS</i>
<i>P</i> value titanium histometry vs. PAs	< 0.0001	< 0.0001	
Mean overall DIB (mm)	1.92		
Mean overall IS-cBIC (mm)	2.31		

as 98.8% over 10 years for current implant surfaces and 89.5% over 20 years for older implant generations [3, 34]. Published data about long-term survival of commercially available zirconia implants is scarce [35]. The principal cause may be the high turnover rate typical of new medical products, as far as applicable to this relatively young material on the implant market. To the authors' knowledge, only 2 prospective clinical studies assess implant outcome of currently commercially available zirconia implants at 3 or more years of follow-up [20, 36]. Nevertheless, reports on recent—but no longer commercially available—zirconia implants demonstrate that most failures occur in the first year in function, followed by a phase with low to inexistent failure incidence [37–39]. This suggests that early to mid-term implant healing and function may be decisive for long-term outcome. In this context, preclinical *in vivo* analyses are essential (a) to establish diagnostic reference values for healthy implants, such as crestal bone remodeling over time in function, and (b) to validate accordingly non-invasive tools for early diagnosis of peri-implant health and pathology, such as PAs. Apart from the present study, only two preclinical studies using currently commercially available implants under loaded conditions are available to date [8, 40].

The present analysis demonstrated a slight reduction in DIB immediately after loading, followed by an increase between 4 and 16 weeks of function, that was more pronounced at zirconia implants. The existing literature corroborates these findings. A prospective clinical study with 71 zirconia implants found a mean marginal bone loss of 0.78 mm from implant insertion to the 1-year follow-up after the final prosthetic restoration. The peri-implant probing depth increased accordingly from 2.7 to 3.5 mm [41]. An observational clinical study demonstrated crestal bone gain of 0.66 mm between 1 and 3 years after loading, following an initial 0.44 mm loss in the first year [36]. Bone maturation at microrough titanium surfaces shows a similar pattern of BIC increase after implant placement during 4–6 weeks and subsequent decrease and stabilization in the context of bone remodeling [42]. Also, the mentioned study on loaded zirconia implants showed minimal crestal bone changes of 0.15 mm at the control titanium implant between loading and 6 months post-loading [40]. On the other hand, the authors found high variability in crestal bone loss between the 3 test zirconia implants, with a range from 0.42 mm bone gain to 0.82 mm bone loss.

**Fig. 4** PA at implant placement (a), loading (b), and after 16 weeks of loading (c) as well as histology (d) of a representative study region



**Fig. 5** Boxplots showing mean DIB for zirconia (blue) and titanium (yellow) at each time point, as well as mean IS-cBIC at 4 and 16 weeks of loading; the whiskers represent the range

Similarly, a study with unloaded implants found 0.13 mm crestal bone gain at titanium and 0.32/0.60 mm loss at two zirconia implants between 2 and 6 weeks in function [43]. Data about differences between 1- and 2-piece implant types are contradictory, with a clinical observational study showing more bone loss around 2-piece zirconia implants [44] and the mentioned animal study showing bone gain, oppositely [40].

The present investigation found a statistically significant difference between the PAs and the histometry for both materials, with radiographs yielding mean values 0.39 mm smaller than histometry on average. The discrepancy was highest for zirconia at 4 weeks (0.52 mm) and lowest for zirconia at 16 weeks (0.23 mm). A possible explanation for this difference obtained by the same implant at two time points can be searched for in the variations of peri-implant bone radiopacity over the early maturation process, which may show patterns specific to an implant material and surface. To the best of the authors' knowledge, this is the first analysis comparing PA with histometry around loaded zirconia implants. One of the earliest available animal studies with titanium implants reported that the histologic IS-cBIC was 0.85 mm more apical than measured as DIB in PAs [45]. A further analysis demonstrated high, statistically significant correlation between the two measurement methods and PA underestimating bone loss by only 0.1 mm in 73.4% of the cases [28]. When challenged with plaque accumulation and occlusal overload, respectively, DIB and IS-cBIC were on average only 0.5 and 0.1 mm apart in monkeys [46]. Moreover, this study also proved a strong, statistically significant correlation between PA and histometry. In summary, preclinical research shows (a) high reproducibility of DIB measurements in PAs through clear identifiability of crestal bone; (b) discrepancy between PA and histomorphometry of 0.1–0.85 mm, with PA generally underestimating the extent of the bone loss; and (c) sensor or film used for PA having a clear influence on the extent of the discrepancy [47].

The missing histometric analysis at the time points of implant placement and loading may be considered a major limitation of the present study. Moreover, as applicable to animal models in general, results have to be interpreted with caution due to the diverging behavior of the study subject if compared with humans. Finally, the follow-up period of maximally 16 weeks may not be sufficient to draw conclusions valid for the long-term outcome.

## Conclusion

In summary, zirconia implants showed a more pronounced crestal bone loss than titanium implants between 4 and 16 weeks after loading, following initial bone gain. PAs overestimated the bone level around dental implants on average by 0.39 mm. At a closer look, underestimation of bone loss was considerable at 4 weeks for zirconia implants, whereas DIB matched histometry at 16 weeks after further tissue maturation around the same implant. Oppositely, the overestimation of crestal bone level was more linear over time at titanium implants. Bearing the discrepancy between histometry and radiography in mind, these findings further confirm PAs as non-invasive tools for early diagnosis of peri-implant health and pathology around titanium and zirconia implants.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** All applicable international, national, and/or institutional guidelines for the care and use of animals were followed. The study was conducted in accordance with the ethical standards of current US federal regulations. The University of Texas Health Science Center at San Antonio Institutional Animal Care and Use Committee approved animal selection, management, and study protocol prior to the start of the experiment (IACUC; ID no. 13005x).

**Informed consent** For this type of study, no consent other than the IACUC approval was required.

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