

# Comparison of Clinical and Histologic Outcomes of Zirconia Versus Titanium Implants Placed in Fresh Sockets: A 5-Month Study in Beagles

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**Purpose:** This study evaluated the clinical and histomorphometric results of titanium (Ti) and custom-made zirconia (Zr) implants placed into fresh extraction sockets in beagles that did not receive oral hygiene attention or a softened diet during postoperative healing. **Materials and Methods:** The roughness of the Ti and Zr implant surfaces was assessed by confocal microscopy. In eight beagle dogs, four implants each (two Ti and two Zr) were placed in the distal sockets of the third and fourth premolars with the implant shoulder at the bone crest and subjected to submerged healing. Standardized radiographs were taken after placement and 5 months after placement (at sacrifice). Histologic and histomorphometric measurements were performed on nondecalcified histologic sections. The main outcome measures included implant survival, bone-implant contact (BIC), and bone loss on the buccal and lingual plates. **Results:** Topographic analysis showed significant differences between the Zr and Ti surfaces. Roughness was higher for Ti than for Zr implants, kurtosis was close to 3 for Ti, and skewness was negative for Zr. After 5 months, the mean BIC was similar for the Zr ( $57.0\% \pm 15.2\%$ ) and Ti ( $56.5\% \pm 14.4\%$ ) implants, and the most severe bone loss site was observed on the buccal wall. The risk of failure was significantly higher for the Zr (43.8%) than for the Ti (12.5%) implants. **Conclusion:** The implant failure rate for the Zr implants was 3.5 times higher than that of the Ti implants. This may be partially explained by the less favorable topography of the Zr implants, which had, on average, significantly lower roughness ( $Ra = 0.85 \pm 0.04 \mu\text{m}$ ), negative skewness of the surface profile ( $-1.56 \pm 0.27$ ), and higher kurtosis ( $7.88 \pm 1.99$ ). INT J ORAL MAXILLOFAC IMPLANTS 2015;30:773–780. doi: 10.11607/jomi.3668

**Key words:** histomorphometry, immediate implant, osseointegration, titanium, zirconia

The materials of choice for dental implants have been and continue to be commercially pure titanium (Ti)

and Ti alloys because of their biocompatibility and excellent mechanical properties.<sup>1,2</sup> Commercially pure Ti has different degrees of purity (grades 1 to 4), which are dependent on the content of oxygen, iron, and carbon. Most implants are made of Ti grade 4, since this is stronger than the other grades.<sup>3</sup> Zirconia (Zr) has been proposed as an alternative to titanium for implants for esthetic reasons<sup>4</sup>: when Ti implants are used, especially in anterior sites, poor esthetics may result because of their greyish color, implant body exposure resulting from soft tissue recession, or the presence of thin gingiva. In recent years, several ceramic implant systems made of yttrium-stabilized tetragonal Zr polycrystals (Y-TZP) have become commercially available. The flexural strength of Y-TZP ranges between 900 and 1,200 MPa, its Young's modulus lies between 200 and 210 GPa, and its fracture resistance is between 7 and 10 MPa.<sup>5</sup> Many studies have shown that the biocompatibility of Zr is equal to that of Ti, since no negative effects on hard or soft tissues have been observed, and the accumulation of plaque is lower than with titanium implants.<sup>4,6–8</sup> The results from animal studies in which the osseointegration of both Ti and Zr implants was

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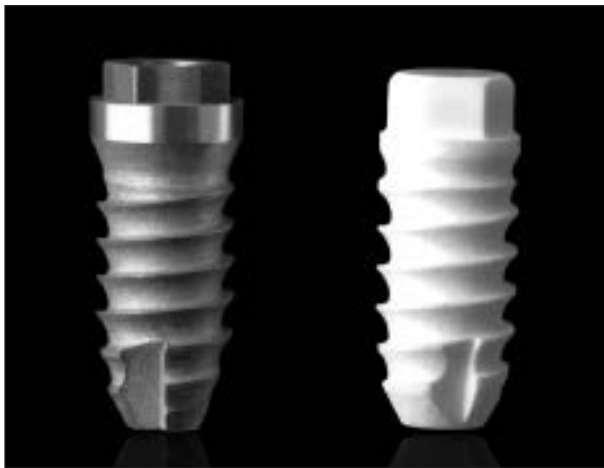
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**Fig 1** Macroscopic geometric design of the Ti implants (Microdent) and Zr implants (Metoxit AG).

compared by removal torque tests or bone-to-implant contact (BIC) revealed that the bone reacted with Zr implants similarly as with Ti implants<sup>9-12</sup> or even better during early healing.<sup>13,14</sup> However, to the authors' knowledge, there are no animal studies comparing the performance of Ti and Zr implants after insertion in fresh extraction sockets, although immediate implant placement is a clear indication for implant therapy to minimize the unavoidable dimensional reduction of the alveolar process after tooth extraction<sup>15,16</sup> and to decrease the time and costs involved with implant treatment. Immediate implant placement has been shown to be a reliable clinical procedure.<sup>17,18</sup>

Furthermore, clinicians must sometimes deal with patients who do not follow postoperative instructions in terms of oral hygiene or employ prudent chewing forces at implant sites during healing, and dentists know that this behavior could put implant survival/success at risk. However, no animal studies have focused on the clinical performance of postextraction implants in less than ideal conditions (in terms of plaque and diet control during the postoperative period), in spite of the wide recognition that optimal oral hygiene and proper occlusal forces are critical for the osseointegration and long-term success of dental implants.<sup>19,20</sup> For this purpose, the beagle dog has been demonstrated to be a valid experimental model in which the dimensional ridge changes after tooth extraction and after inserting implants have been properly described.<sup>15,16</sup>

The aim of this split-mouth study was to compare the clinical performance (survival rate) and the histomorphometric results (BIC and bone loss) of Ti and Zr implants after placement into fresh extraction sockets in beagles that did not receive oral hygiene or a softened diet during 5 months of postoperative follow-up.

## MATERIALS AND METHODS

### Topographic Assessment

The Ti implants investigated in this study were made of Ti grade 4 (M380, Microdent), and the Zr implants were made of a machined bioceramic composed of 80% Y-TZP and 20% alumina (Ziralident, Metoxit). Both implants were identical in dimensions (3.8 mm in diameter and 8.0 mm in length) and shape (screw-type with six buttress threads separated by 1.08 mm). The Ti implants featured an external hexagon that was 0.7 mm above the platform and had a polished collar of 1 mm, whereas the Zr implants had an external hexagon that was 1.7 mm above the platform and did not have a polished collar (Fig 1). The topography of the implant surfaces was assessed by white light confocal microscopy (PLμ, Sensofar-Tech) on a scanning area of  $292 \times 216 \mu\text{m}^2$ ; six scans were performed per surface. The study topography parameters were: average roughness (Ra); square root roughness (Rq); peak roughness (Rp, maximum relative height); valley roughness (Rv, maximum relative depth); valley absolute height ( $R_t = R_p + R_v$ ); skewness (Rs); and kurtosis (Rk).

### Sample Size Calculation

Because no international guidelines are available for sample size calculations for dental implant studies in beagles, sample size was estimated following the general rule for the standardized difference in a given output variable (eg, clinical and histologic assessment or topographic parameters) between the Zr and Ti groups, considering the implant as the unit of analysis. The estimation was based, using the *t* test for independent groups, on the selection of a standardized difference of 0.8. This gave a size of 16 implants per group for a power of 60% ( $\beta = 0.40$ ), which is lower than the usual 80% (to reduce the number of dogs needed, for ethical reasons), and a two-sided significance level of  $\alpha = .05$ . Specific software was used to estimate the sample size (Sample Power 2.0, IBM).

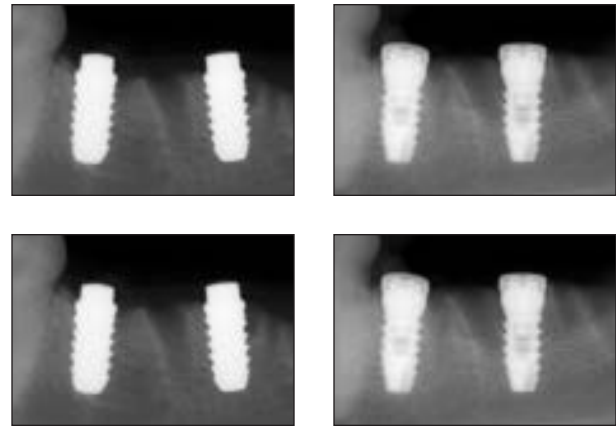
### Surgical Management

Eight beagle dogs (three male, five female) 2 to 8 years old without active periodontal disease were presedated by intramuscular injection using a combination of ketamine (7 mg/kg), diazepam (0.2 mg/kg), and atropine (0.05 mg/kg). This was followed by laryngeal intubation and induction of general anesthesia using a continuous intravenous infusion of propofol (1 mg/kg/min). While under general anesthesia, the dogs inhaled oxygen from the ventilation tube. In addition, submucous injections of articaine hydrochloride (Artinibsa 40 mg/0.01 mg/mL, Laboratorios Inibsa) were infiltrated locally for bleeding control. Then, full-thickness mucoperiosteal flaps were raised adjacent

to the mandibular third and fourth premolars (PM3, PM4) on both sides. These teeth were first sectioned horizontally at the cemento-enamel junction, after which a vertical interradicular osteotomy was performed to divide the mesial and distal roots and to prevent root or alveolar cortical bone fracture during the extractions. This procedure was performed under copious irrigation using a thin carborundum disk mounted on a surgical handpiece. Roots were extracted with elevators and forceps, and in all distal sockets, a screw-type implant was inserted following the manufacturers' surgical protocol (Microdent). All mesial sockets were left to heal spontaneously. In this split-mouth study, all the implants were placed in the distal sockets of PM3 and PM4. Ti implants were inserted on one side and Zr implants were inserted on the other side; the side was changed consecutively between dogs. Thus, in all, 32 implants were inserted (16 Ti and 16 Zr).

In all dogs, the implant platform was placed at the bone level, resulting in a circumferential gap approximately 1 to 2 mm wide between the implant surface and the bone wall. No occlusive membranes were used over the surgical sites to guide tissue regeneration; it was assumed that the flap covering the implant would act as an occlusive barrier against epithelial cell colonization. After the primary stability of the implants was confirmed clinically, the Ti implants were then covered with a 1.0-mm cover screw; those made of Zr were left uncovered because the 1.7-mm hexagon was solid to facilitate transport and surgical insertion. The flaps were closed with single interrupted 3-0 silk sutures, leaving the implants submerged. Radiographic assessments were carried out immediately postoperative and after 5 months of healing (Fig 2) to determine the number of macrothreads in contact with the bone on each side, using a sensor holder (RINN XCP-DS-Posterior, Dentsply); the implants have 12 macrothreads (6 on each side). This evaluation was carried out by three independent observers, who recorded their assessments in whole values.

Postoperative care comprised a daily dose of benzylpenicillin (1 million units) and ketoprofen (3 mg/kg/day) injected intramuscularly for 4 days. Sutures were removed 1 week later. No measures for plaque control (either mechanical or chemical) or diet adaptation were applied during the postoperative maintenance program. Thus, both before and after the experimental work, the dogs had access only to hard pellet food and did not receive oral hygiene treatment. The dogs were followed for 5 months and were then examined clinically and radiographically. Finally, they were sacrificed by an overdose of anesthetic drugs (Propofol Hospira, Hospira Productos Farmacéuticos y Hospitalarios). All procedures relating to animal management were carried out according to the guidelines



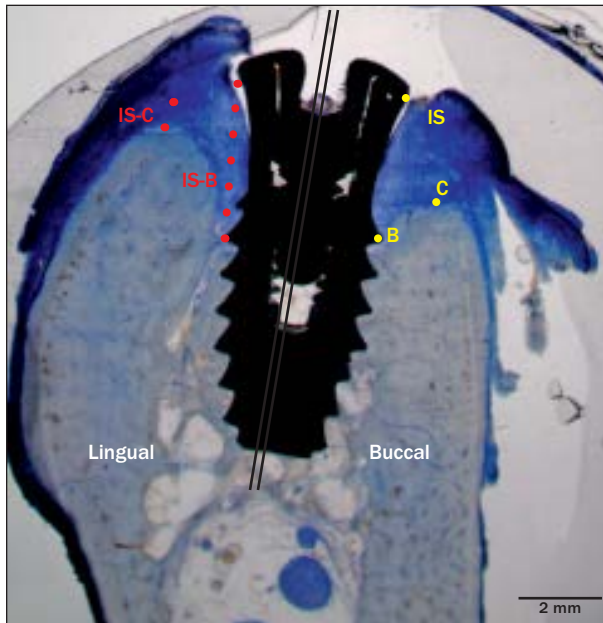
**Fig 2** Typical radiographic assessments of (left) Zr and (right) Ti implants. *Top*: Baseline; *bottom*: 5-month follow-up.

for animal experiments of the Bioethical Committee of the University of Salamanca, Spain. Implants were considered failed if they were mobile or missing in the clinical assessment.

### Histologic Preparation

Tissue blocks containing the implants and the surrounding tissues were obtained and prepared for nondecalcified sectioning. The blocks were fixed in 10% buffered formaldehyde for at least 72 hours and dehydrated in a series of ascending concentrations of ethanol solutions for 24 hours at each stage. Finally, they were embedded in polymethylmethacrylate resin for 3 weeks at room temperature (until the resin had hardened to the touch). Final curing was obtained by placing samples in an oven at 37°C for 72 hours. Then, the blocks were sectioned with a precision cutting machine (Secotom-10, Struers) using diamond wafering blades at initial thicknesses of 200  $\mu\text{m}$  and were carefully buffed by hand on a polishing machine (Labopol 5, Struers) using silicon carbide grit papers in descending grain sizes (from 600- to 4,000-grit papers). With this approach, two to four slices of 100 to 200  $\mu\text{m}$  were obtained buccolingually from the implants for subsequent analyses. The specimens were stained with toluidine blue at ambient temperature. Photomicrographs were taken using a Zeiss-Stemi 2000-C photomicroscope (Carl Zeiss Microimaging) at a magnification of  $\times 100$ .

An image analysis program (MetaMorph, Meta Imaging Series 6.1) was used to quantify the percentage of BIC along the implant surface. To determine the amount of resorption of the alveolar crest during remodeling, the location of the implant shoulder in relation to the surrounding bone was considered by identifying the following landmarks: the implant shoulder (IS), the most coronal point of contact between the bone and implant (B), and the top of the adjacent bony crest (C). These topographic references



**Fig 3** Diagram illustrating the landmarks for the histologic evaluation. IS = implant shoulder; B = most coronal bone-to-implant contact; C = top of alveolar crest.

were used to measure the vertical distance between IS and C and the distance between IS and B (Fig 3).

### Data Analysis

Mean values and standard deviations (SDs) were calculated for each outcome variable. The differences between the Ti and Zi implants were analyzed using the Student *t* test for paired observations. Odds ratios and the relative risk of failure were calculated for paired comparisons. A logistic regression was performed using failure/survival as the dependent variable. The level of significance was set at .05. Descriptive statistics (means, SDs, and percentages) were calculated with SPSS for Windows (version 20, SPSS Inc). Comparisons were calculated with SUDAAN v. 7.5 (RTI International) to account for clustering (ie, multiple implants within the mouth).

### RESULTS

The topographic data are shown in Table 1. The topographic analysis showed that Ra, Rq, Rp, and Rt values were higher for the Ti implants than for the Zr implant. Rv was similar for both surfaces. Rs was positive for the Ti implant (hard surface) and negative for the Zr implant (porous surface). Rk analysis showed that the Ti surface follows a Gaussian behavior ( $Rk \approx 3$ ) and Zr is a leptokurtic surface ( $Rk > 3$ ). Figure 4 shows representative images of the two implant surfaces evaluated.

Thirty-two implants (16 Ti and 16 Zi) were placed in eight dogs (four implants per dog). Although all implants were completely submerged, at the 5-month follow-up, all implant sites showed soft tissue dehiscence. Initially, the implants had, on average,  $11.4 \pm 1.3$  threads in contact with bone, but after healing, among the remaining implants, this value decreased to an average of  $7.0 \pm 1.9$  threads. There were no differences between the Ti and Zr implants in this change, although the Zr implants tended to have fewer threads in contact with the bone at baseline (Student *t* test = 1.387;  $P = .18$ ), as shown in Table 2. On average, the distances IS-C and IS-B revealed more bone loss on the buccal plate. The mean BIC was  $56.7\% \pm 14.4\%$ . No significant differences were found between implant groups for any of these values (Table 2).

Regarding survival rates, at follow-up, nine implants (28.1%) had been lost or were mobile; the remaining implants were clinically fixed (Table 3). The implant survival rate was 3.5 times higher for the Ti implants (87.5%) than for the Zr implants (66.2%), representing a significant difference. The initial implant threads radiographically in contact with bone and the position of the implant tended to be associated with the failure rates, but not significantly. A logistic regression performed with SUDAAN revealed that only the type of implant was a significant predictor of failure.

### DISCUSSION

To the authors' knowledge, this is the first experimental study in which Ti and Zr were inserted into fresh extraction sockets of beagles using a split-mouth randomized scheme. The findings show that the implant material (roughened Ti versus machined Zr) was a significant predictor of implant failure when implants were inserted into fresh extraction sockets without any plaque control or diet adaptation: the failure rates were 3.5 times higher for Zr implants than for Ti implants.

A higher than usual failure rate is probably to be expected because of the lack of control of oral hygiene and diet during the follow-up period, which is not the case in most experimental studies of immediate implants, in which these potential prognostic factors are controlled. However, significant differences between the implant materials were not expected (null hypothesis), and the authors expected better performance of the Zr implants within this septic environment, since Zr seems to accumulate less bacteria than Ti,<sup>4,6-8</sup> mainly because of its smoother surface (as observed here) (Table 1, Fig 4).

It is notable that, despite the lower survival rates of the Zr implants (Table 3), the remaining Zr and Ti implants displayed a similar degree of bone loss and

**Table 1 Topographic Parameters of the Ti and Zr Implants**

Implant	Ra (μm)	Rq (μm)	Rp (μm)	Rv (μm)	Rt (μm)	Rs (–)	Rk (–)
Titanium	1.59 (0.10)*	1.96 (0.13)*	8.44 (2.12)*	–8.18 (1.89)	16.61 (4.01)*	0.27 (0.03)*	2.89 (1.49)*
Zirconia	0.85 (0.04)*	1.17 (0.10)*	3.12 (2.00)*	–7.99 (2.03)	11.11 (2.22)*	–1.56 (0.27)*	7.88 (1.99)*

Means (SDs) shown.

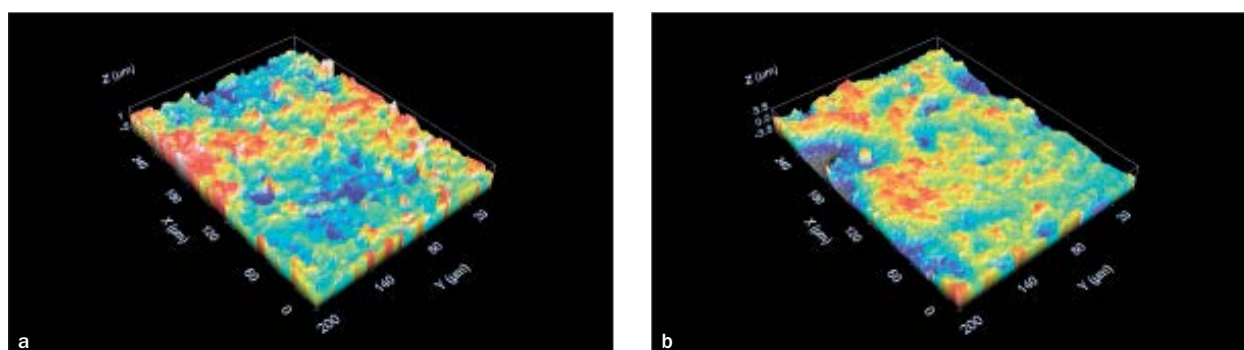
\*Values in the same column with asterisks are statistically significantly different ( $P < .05$ ; Student *t* test).

**Table 2 Clinical and Histologic Parameters (Means ± SDs) for Zirconia and Titanium Implants**

Variable	Zirconia (n = 16)*	Titanium (n = 16)	P value†
Implant threads contacting bone in the radiograph			
Baseline	11.1 ± 1.6	11.8 ± 0.8	.083
Follow-up	7.1 ± 2.3	6.9 ± 1.7	.780
Change	–4.7 ± 2.2	–4.9 ± 2.1	.837
Histologic parameters			
BIC (%)	57.0 ± 15.2	56.5 ± 14.4	.940
IS-C (mm) buccal	2.7 ± 1.2	3.1 ± 1.1	.494
IS-C (mm) lingual	1.5 ± 0.8	1.8 ± 0.7	.319
IS-B (mm) buccal	3.9 ± 1.2	4.5 ± 1.3	.305
IS-B (mm) lingual	3.8 ± 0.8	4.3 ± 1.1	.330

\*Subgroup sample sizes at baseline. At follow-up, sample sizes were n = 9 (Zr) and n = 14 (Ti) because of implant failures.

†Student *t* test corrected for clustering (multiple implants in the mouth) using the DESCRIPT procedure in SUDAAN.



**Fig 4** Visualization by white light confocal microscope of (a) titanium surface and (b) zirconia surface.

achieved similar BIC (Table 2). This fact supports the hypothesis that, around machined Zr, new bone formation is delayed, but when an implant is osseointegrated, the histologic parameters of the remaining implants are comparable to those of the Ti implants. This finding is supported by a recent systematic review that compared the clinical performance of Zr and Ti implants in animal models.<sup>21</sup>

The distinct topography of the implants tested here most likely contributed to the higher failure rate of the Zr implants, since a moderately rough surface, rather than a smooth surface such as the Zr implants, significantly increases cell adhesion and accelerates the tissue response,<sup>22,23</sup> resulting in more and better quality bone formation around implants.<sup>24,25</sup> It is well known that the surface topography and roughness influence the rate and quality of new tissue formation around

**Table 3 Risk Factors for Implant Failure (n = 32)**

Factors	Placed	Failed (%)	RR	P value*
All	32	9 (28.1)		
Surface				.011
Zr	16	7 (43.8)	3.50	
Ti	16	2 (12.5)	1.00	
Initial no. of threads				.079
< 12 threads in BIC	7	4 (57.1)	2.86	
12 threads in BIC	25	5 (20.0)	1.00	
Position				.197
PM3	16	6 (37.5)	2.00	
PM4	16	3 (18.8)	1.00	

RR = relative risk.

\*Chi square corrected for clustering (multiple implants in the mouth) with the CROSSTAB procedure in SUDAAN. In a logistic model with a  $P$  value  $< .05$  to enter a variable and  $P > .10$  to exclude a variable (LOGISTIC procedure in SUDAAN), only the implant variable would be included.

an implant.<sup>25</sup> Appropriate surface roughness on the nanoscopic and microscopic scale can lead to successful implant osseointegration.<sup>26</sup> A moderate increase in surface roughness increases osteoblast differentiation and proliferation, extracellular matrix production, and gene expression, as well as the production of local growth factors and cytokines.<sup>22,23,27</sup> It was demonstrated that an increase in implant surface roughness enhances the mechanical anchorage in bone and reduces the failure rate.<sup>25</sup> The greater roughness of the Ti implants may have contributed to their lower failure rate versus Zr implants. This finding is supported by evidence indicating that Zr implants perform clinically worse (survival and success rates) than Ti implants.<sup>22</sup> In a clinical study,<sup>22</sup> the Zr implant had lower roughness ( $R_a = 0.598 \mu\text{m}$ ) than the Ti implant ( $R_a = 1.77 \mu\text{m}$ ), supporting the hypothesis that the greater the roughness, the lower the failure rate. Skewness ( $R_s$ ) describes the symmetry of the profile about the mean line. A surface with symmetric height distribution has zero  $R_s$ . Profiles with peaks removed or deep scratches have negative  $R_s$  values. Profiles with valleys filled in or high peaks have positive  $R_s$ . It seems that the  $R_s$  values can influence the biologic response. A recent experimental animal study found that a positive  $R_s$  surface is associated with higher BIC values than a negative  $R_s$  surface.<sup>27</sup> The current results are in accordance with this study, since a higher failure rate was observed when  $R_s$  was negative (Zr implant surface). Kurtosis ( $R_k$ ) describes the sharpness of the profile. Surfaces with  $R_k$  above 3 have sharp "peaks" (leptokurtic), whereas surfaces with  $R_k$  below 3 have more rounded "peaks" with wider "shoulders" (platykurtic). In this study, the Ti surface obtained an  $R_k$  close to 3, and the  $R_k$  of the Zr surface was close to 8. There is some evidence that  $R_k$  values of about 3.6 obtain the highest cell adhesion<sup>27</sup> and  $R_k$  values of about 5 provide the highest bone retention. In the current study, the  $R_k$  values of the Ti implants (Table 1) were closer to the bone retention threshold than the Zr implants, another trait that could explain the higher Ti implant survival rate. Several authors recently reported weaker clinical performance of Zr implants in comparison to Ti implants when machined Zr is used<sup>28</sup> as well as when the Zr surface is roughened by sandblasting.<sup>29</sup> Thus, other prognostic factors apart from the roughness could be responsible for the unexpectedly high failure rate observed here.

It should be remarked that the custom-made Zr implants used in this study were composed of 20% alumina in an attempt to reduce the low-temperature degradation of Y-TZP, as suggested elsewhere.<sup>4</sup> Nevertheless, this component ( $\text{Al}_2\text{O}_3$ ) has shown, on average, lower survival rates (ranging from 23% to 98%) than pure Y-TZP in several clinical conditions.<sup>4</sup>

Furthermore, a well-conducted meta-analysis showed that the survival rates of immediate implants are slightly lower than those observed for implants placed in healed sites, especially for minimally rough implants,<sup>30</sup> again supporting the findings of the present study. There are only a few studies of Zr implants placed in fresh sockets, but the results were poorer than expected, mainly when the implants were subjected to some degree of loading. Cannizzaro et al<sup>31</sup> sought to determine whether avoiding direct occlusal contact with implant-supported provisional crowns might decrease the risk of early failures of immediately loaded one-piece Zr implants. They found that 40% of postextraction Zr implants had failed by 2 months and that this factor was significant, unlike the type of occlusal loading.<sup>31</sup> More dramatically, Pirker and Kocher noted the loss of all root-analog Zr implants roughened by sandblasting within the first 2 months.<sup>32</sup>

In contrast, promising results were observed when Zr implants were inserted in healed sites,<sup>11,33,34</sup> even when they were loaded immediately. However, when implants are placed immediately, a gap between the implant and bone is almost unavoidable because of the differing sizes and morphologies of the sockets (pseudoconical) and implants (pseudocylindric). Thus, in this situation, in spite of the use of screw-type dental implants (Fig 1), only the apical part of the implant provides primary stability. This primary stability is logically weaker than if those implants had been inserted into mature bone, and in this clinical situation, the topographic parameters could be a key prognostic factor. In the current study, all the bone-to-implant gaps were smaller than 2 mm; usually, a circumferential gap approximately 1 mm wide occurred between the implant surface and the bone wall. In this situation, it has been demonstrated that a screw-type dental implant placed into a fresh extraction socket, without the use of barrier membranes or other regenerative materials, could achieve a clinical outcome and a degree of osseointegration similar to those of implants placed in healed mature bone.<sup>35</sup>

As may be seen in Table 3, it is noteworthy that failures occurred twice as often in the PM3 sites as the PM4 sites. Both failed Ti implants and four of the seven failed Zr implants were in the PM3 region. This finding could be explained by the fact that bone dimensions and socket wall thickness are clearly greater for PM4 than for PM3, allowing better bone support to stabilize implants and providing more bone for socket regeneration. The thinner the bone wall is, the greater the crestal resorption will be, in agreement with other authors.<sup>36</sup> However, although there are plausible reasons for considering this factor as relevant, it proved to be nonsignificant after multivariate logistic analysis was performed on implant survival (Table 3). Future

studies with larger sample sizes should be done to verify whether the PM3 location was in fact a significant predictor of implant failure in the beagle model.

Crestal resorption has been shown to be even more extensive around immediate implants placed in multiple contiguous extraction sites (as was done here) as compared to immediate implants placed in single extraction sites.<sup>37</sup> In addition, the diameter and length of the implants used in the present study were smaller than in most studies, reducing the area available for primary stability and to distribute forces.<sup>38</sup>

The BIC and the other histometric measurements obtained in the present study are worse than those reported by other authors regarding postextraction Ti implants, even with immediate loading,<sup>33</sup> but are in agreement with similar studies.<sup>11,16</sup> Some surgical explanations could be advanced to explain these results. Other beagle experiments have demonstrated that, after tooth extraction, the socket and the surrounding bone tissue undergo substantial alterations, characterized by a marked degree of hard tissue resorption (in particular on the buccal aspect),<sup>15</sup> and the placement of implants apparently failed to interfere with the process leading to bone loss. After 3 to 4 months of healing, the marginal portion of the implant displayed no bone contact.<sup>16</sup> Some authors have suggested that the placement of implants in fresh extraction sockets not only fails to stop remodeling of the socket walls but may eventually contribute to more pronounced bone resorption, mainly at the buccal walls.<sup>39</sup> Moreover, during the initial phase of regeneration, the flap elevation performed to carry out tooth extractions and implant placement impairs the vascular supply to the healing site, hampering initial wound healing and possibly exerting a long-lasting effect in a dimensional reduction of the supporting bone.<sup>40</sup> Despite this, it was recently observed that a flapless approach in immediate implants did not substantially contribute to preventing alveolar bone resorption<sup>41</sup>; hence, this issue should be addressed in future studies.

Additionally, the implants were inserted at the bone level, but they were all gradually exposed to the oral environment (Fig 2), in contrast to what would have been desirable.<sup>16,40</sup> This probably occurred because the dogs were not fed a soft diet during the experiment, and it may reflect the fact that all the implants were exposed to early occlusal loading of an unknown but presumably high magnitude. Even today, a healing period without loading is often considered a prerequisite for osseointegration. On the other hand, through this mucosal opening, the colonization of bacteria close to the bone-implant interface would induce an inflammatory response and bone resorption.<sup>42,43</sup> It has been estimated that implants gradually exposed to the oral cavity by mucosal defects carry a greater risk

of severe alveolar bone loss as a result of peri-implant inflammation than submerged implants.<sup>44</sup> To compare the osseointegration of the Zr and Ti implants in a dog model, it would be desirable to implement proper oral hygiene and a soft diet during postoperative healing, because both factors seem to be responsible for the suboptimal results reported here. In fact, it was recently stated that the major causes of implant failure are plaque-induced inflammation and overloading, with poor primary stability and a machined surface the main predictors of early implant failure.<sup>45</sup>

The main limitations of the present study are the lack of objective quantification of primary stability at baseline and follow-up, with the macroscopic evaluation of the threads in contact with bone used as a robust proxy; the low number of observations during follow-up, which prevented the analyses of survival times; and possibly the lack of microbiologic measurements on the surfaces of both implant types.

Future research should address these potentially related prognosis factors for a thorough analysis of the clinical outcomes of Zr implants placed in fresh sockets in less than ideal conditions.

## CONCLUSIONS

Within the limitations of this experimental study, the failure rate of custom-made machined zirconia implants was 3.5 times higher than that of titanium implants. This may be partially explained by the less favorable topography of the zirconia implants, which had significantly lower average roughness ( $0.85 \pm 0.04 \mu\text{m}$ ), negative skewness of the surface profile ( $-1.56 \pm 0.27$ ), and higher kurtosis ( $7.88 \pm 1.99$ ).

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