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PRECLINICAL STUDY

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# Histological evaluation of osseointegration between conventional and novel bone-level tapered implants in healed bone—A preclinical study

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## Abstract

**Aims:** To histologically compare osseointegration and crestal bone healing between newly introduced tapered, self-cutting bone-level test implants and tapered bone-level control implants in sites with fully healed sites.

**Methods:** Sixty-six implants (33 test, 33 control) were placed 1 mm subcrestally in a minipig model and underwent qualitative histologic and quantitative histometric analyses after 3, 6 and 12 weeks of submerged healing. The primary and secondary outcomes were the bone-to-implant contact (BIC) and first bone-to-implant contact (fBIC). Outcomes between the test and control implants were statistically compared.

**Results:** The BIC values of the test implants were comparable and non-inferior over the time points studied, except for the 12 weeks time point which showed statistically significantly higher BIC values of the test (88.07 ± 5.35%) compared to the control implants (80.88 ± 7.51%) ($p = .010$). Similarly comparable and non-inferior were the fBIC values, except for the 6-week outcome, which showed statistically higher values for the test (−546.5 ± 450.80 μm) compared to the control implants (−75.7 ± 100.59 μm). fBIC results for the test implants were qualitatively more stable and consistent between test time points.

**Conclusion:** Novel self-cutting bone-level test implants demonstrated superior osseointegration and similar bone levels compared to conventional bone-level implants after a healing period of 12 weeks in healed ridges.

KEYWORDS
animal model, crestal bone formation, histology, histometry, implant geometry, osseointegration

Jean-Claude Imber and Andrea Roccuzzo contributed equally to the manuscript and shared the first author position.

## 1 | INTRODUCTION

Dental implant therapy has recently experienced a pronounced shift towards early and immediate procedures.[1–4] Unlike staged procedures, immediate procedures offer a range of distinct advantages, like, for example, shorter treatment duration, reduced number of surgical sessions and the possibility to deliver immediately fixe d restorations.[5,6] While comparable in terms of clinical success and survival rates, immediate procedures, particularly those with immediate loading, compared to more conservative approaches, may also support the preservation of bone and soft tissue contours, thereby positively influencing aesthetic outcomes.[7–10]

Technical progress in implant design and surgical workflows and an enhanced understanding of appropriate case selection have rendered immediate procedures clinically, biologically and aesthetically successful.[11–15] The shift into immediate procedures has also reinforced the importance of primary stability as one of the main parameters for successful implant osseointegration.[16] Primary stability is affected by multiple factors, including bone density, surgical technique and implant design.[16–20]

Implant tapering has evolved as a preferred design strategy for attaining primary stability, especially in complex or challenging situations like extraction sockets and type 4 (low-density) bone.[15,21] Recently, an optimized novel tapered implant design for immediate placement and low bone density situations has been presented.[22] This novel self-cutting implant concept was designed with a pronounced and extended double-thread geometry for apical engagement in trabecular bone. This novel concept extended the conventional tapered implant concepts that primarily achieve stability in host bone via a lateral compression of cortical bone with the coronal implant aspect.[15,17,22,23] In vitro studies have shown that the described novel implant type results in high primary stabilities irrespective of bone quality.[17,24]

Although both implant types can be classified as tapered implants, the differences in placement philosophy and bone engagement characteristics raise the question of how comparable the two implant types can be in terms of osseointegration and crestal bone healing and apposition. Furthermore, it is unknown whether this novel tapered implant design represents a valuable treatment option in sites with fully healed bone—type 4 implant placement.[25] Therefore, the aim of this study was to compare osseointegration and crestal bone healing between newly introduced tapered self-cutting bone-level test implants and tapered bone-level control implants in sites with fully healed bone.

### Clinical Relevance

#### Background

This study compared the osseointegration and crestal bone healing between newly introduced bone-level test implants and bone-level control implants in sites with fully healed bone. Both implant types used in this study can be classified as tapered implants, but the differences in placement philosophy and bone engagement characteristics raise the question of how comparable the two implant types can be in terms of osseointegration and crestal bone healing and apposition.

#### Added Value of This Study

It is unknown whether the novel implant design, primarily intended for immediate implant placement and low bone density situations, represents a valuable treatment option in sites with fully healed hard bone.

#### Clinical Implications

Within the limitations of a preclinical model, the results of this study provide evidence that novel self-cutting bone level implants can be placed in fully healed sites without compromising osteointegration or crestal bone level compared to conventional bone level tapered implants.

## 2 | METHODS

### 2.1 | Study design—animal model

This non-randomized controlled preclinical study histometrically compared the osseointegration of commercial, novel tapered, self-cutting bone-level test implants (Figure 1B, Straumann® BLX, Ø3.75×8 mm, Roxolid®, SLA®, Straumann AG) to long-term available tapered bone-level control implants (Figure 1A, Straumann® BLT, Ø3.3×8 mm, Roxolid®, SLA®) as part of a submerged healing regimen at different time points (3, 6 and 12 weeks) in fully healed sites.

Thirteen female Ellegaard Goettingen Minipigs (A/S) aged between 20 and 23 months and a body weight of 31–50 kg were used. The study design included four animals per time point and one animal to compensate for possible dropouts. The animal and implantation site allocation per animal was defined prior to surgery and is illustrated in Figures S1 and S2. The primary outcome of this study was the bone-to-implant contact (BIC). The sample size was determined based on previous animal studies with similar readouts in which a sample size calculation determined a minimum of $n=6$ was necessary; this study aimed at a minimum of $n=9$ to adhere to the ISO10993-6 which details the minimum number of samples per group for a medical device study. The study design is schematically illustrated in Figures S1 and S2.

### 2.2 | Animal care and anesthesia

The study was conducted at Ellegaard Göttingen Minipigs A/S, Dalmose, Denmark. The study protocol was approved by the local ethics committee of the Ministry of Food, Agriculture and Fisheries, Copenhagen, Denmark (approval number 2021-15-0201-00876).

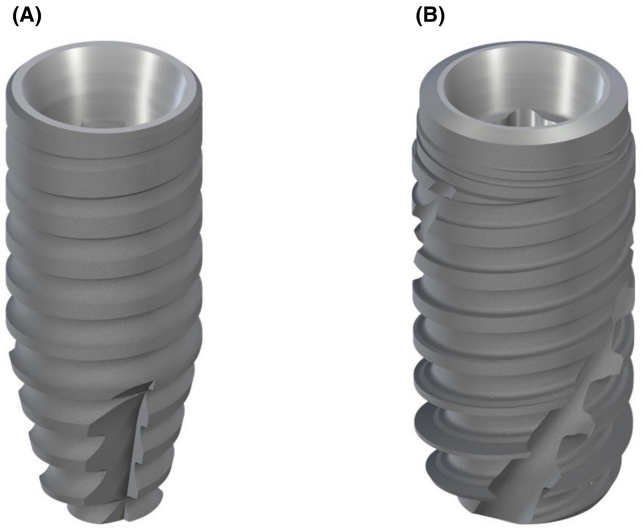


FIGURE 1 Study devices. Side-by-side comparison of schematic representations of control, established Bone Level Tapered implants (A) and novel tapered, self-cutting bone level test implants (B). Both implant types are shown from a lateral and oblique aspect.

It respected the Danish Animal Protection Law, adhered to the ARRIVE Guidelines,[26] and was designed and performed under consideration of the 3R (Replace, Reduce, Refine) guidelines for animal experimentation.

All surgical interventions were carried out under general anaesthesia. Before the surgery, an intramuscular injection of Streptocillin (0.1 mL/kg) was given. Anaesthesia was induced with intra-muscular injection of Zoletil mixture XKB* (0.1 mL/kg). After intubation, the animals received Atropine (1 mg/mL, at a dose of 0.04 mL/kg, I.M.), Metacam (20 mg/mL, at a dose of 0.02 mL/kg, I.V.) and propofol (10 mg/mL, at a dose of 0.1–0.2 mL/kg) to maintain anaesthesia. Vital parameters were monitored continuously. Before starting the surgical interventions, local anaesthesia was administered (Xylopin + noradrenalin, 20 mg/mL + 12.5 µg/mL, at 1.8 mL per hemi-mandible).

Post-operation, the animals received Vetergesic (0.3 mg/mL, at a dose of 0.1 mL/kg, I.V./I.M.). All animals received an oral suspension of Streptocillin (0.1 mL/kg, I.M) and until day 2 post-surgery and Metacam (15 mg/mL, at a dose of 0.03 mL/kg) until day 5 post-surgery.

## 2.3 | Surgical procedure

Prior to implant placement, mandibular premolars (P2–P4) and first mandibular molars (M1) were extracted bilaterally. After a healing period of 12 weeks, a total of 66 implants were placed accordingly to a type 4 implant placement protocol[25] by two experienced surgeons (J.-C. I. + A.R.). After full-thickness mucoperiosteal flap elevation, surgeons were instructed on the location of the test and control implants. Both implant types were used according to the manufacturer's instructions following corresponding hard bone protocols (Figure 2). In brief, implant placement was performed sequentially per hemi-mandible and according to the manufacturer's guidelines. For both implant types, osteotomies were prepared using the Velodrill set (VeloDrills™, Straumann AG) at 800 rpm, involving pilot drilling using needle drills and extending the osteotomy diameter using sequential drilling. For the control implants, the osteotomy preparation was completed by tapping and profiling.

Test and control implants were placed 1 mm subcrestally at 15 rpm using a motorized handpiece. The maximum insertion torque values (maxIT) were measured using a torque wrench. Implants were subsequently equipped with implant closure caps (for BLT: NC Closure cap-Ø 3.1 mm, H 0.5 mm, Titanium and for BLX: RB Closure Cap-H 0.4 mm, Titanium) before primary wound closure (Vicryl 4–0).

## 2.4 | Termination

Four animals each were sacrificed 3 and 6 weeks after surgery and five animals after 12 weeks. An intra-cardiac arrest was induced by injecting a 20% pentobarbital solution (Euthanimal 400 mg/mL, Pentobarbitalnatrium, Alfasan Nederland B.V).

Block sections of the mandibular implantation sites were obtained. Sections were fixed in formalin for at least 2 weeks before histological processing.

## 2.5 | Histological processing

After fixation, all samples were dehydrated in an ascending series of ethanol and embedded in methylmethacrylate. After polymerization, the specimens were sectioned in a mesiodistal plane along the implant axis using a slow-speed diamond saw with coolant, as previously described in preclinical studies.[27,28] Thereafter, two approximately 600-µm-thick ground sections per implant were mounted on Plexiglas slabs and ground and polished (Knuth-Rotor-3; Struers, Rodovre/Copenhagen) to a final thickness of 150 µm. Finally, the sections were superficially stained with toluidine blue/McNeal combined with basic fuchsin. Photography was performed using a digital camera (AxioCam MRc; Carl Zeiss) connected to a light microscope (Axio Imager M2; Carl Zeiss).

## 2.6 | Quantitative histometry

The relevant aspects related to the histometric evaluation are illustrated in Figure 3. The most central section (largest implant diameter) per implant was chosen for quantitative histological evaluation. Histometric parameters were evaluated on central mesiodistal sections of the implant. Histometric parameters comprised the BIC as defined by the relative percentage of the perimeter of the endosseous part of the implant in contact with Bone (Figure 3B) and the first bone-to-implant contact (fBIC) as defined by the distance

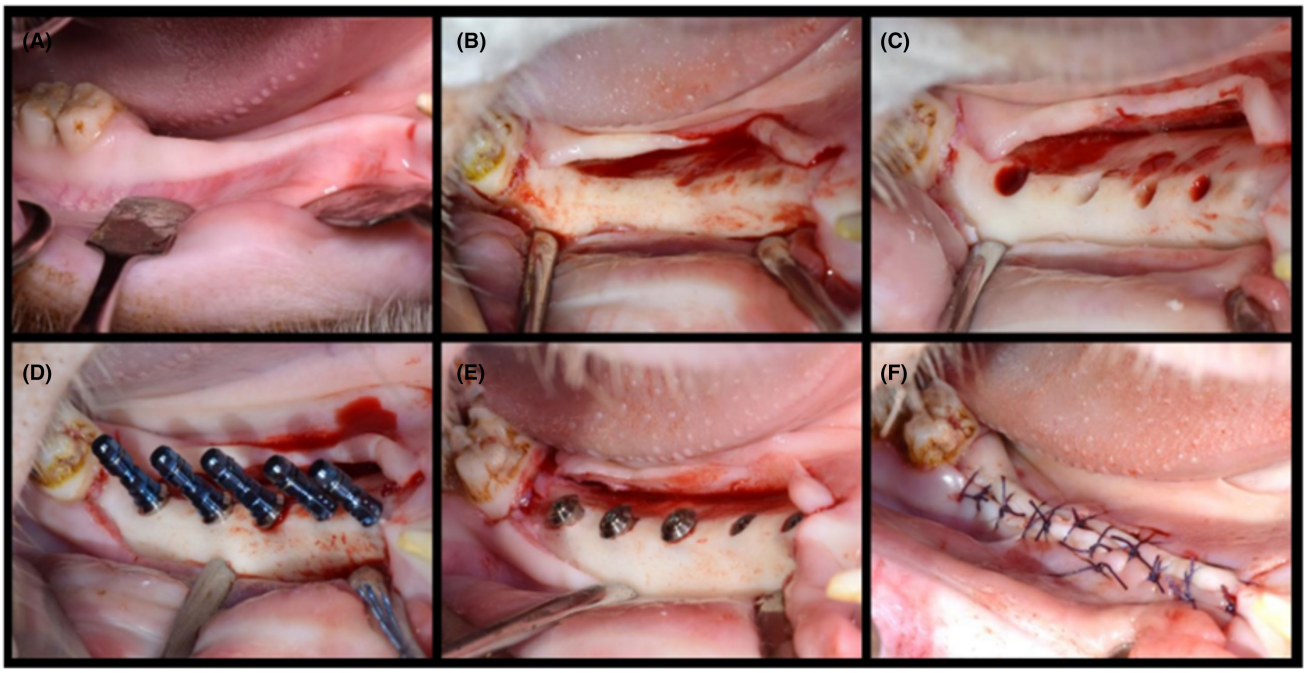


FIGURE 2 Illustration of the surgical procedure. Illustration of the surgical procedure: (A) Lateral view of the exposed healed mandibular ridge prior to implantation. (B) Prepared implantation site after mucoperiosteal flap elevation and flatting of the alveolar bone crest. (C) Implantation sites after osteotomy preparation. (D) Situation after implant placement with transfer pieces in place. 5 implants were placed per hemi-mandible (E) Situation after installation of healing caps before and (F) after primary wound closure and suturing for submerged healing. The tissue level implants were used for another experiment.

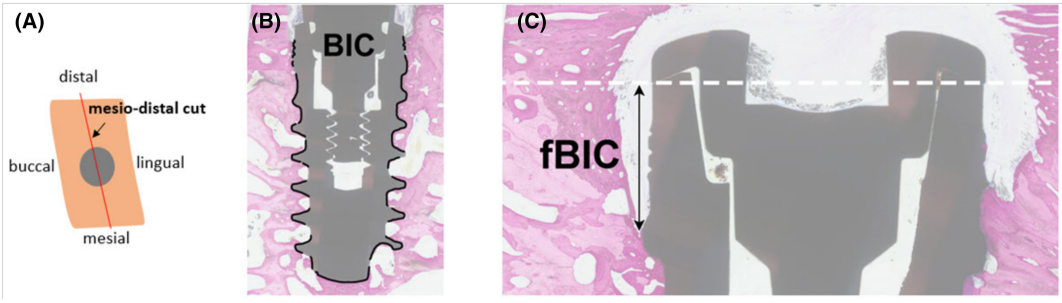


FIGURE 3 Illustration of the histometric parameters. (A) Illustration of the orientation of the histological axis when looking onto the mandible from a superior aspect. Histologic slices were prepared in a mesiodistal direction through the center of the implants. (B) Bone-to-implant contact (BIC, black line) as the percentage of the implant perimeters endosteal microrough surface in contact with bone. (C) First bone-to-implant contact (fBIC) in the apical direction was measured from the coronal implant shoulder (interrupted line) to the most coronal aspect of bone in direct contact with the implant surface (black double-arrow). Mesial and distal values were used to calculate reported averages (mesiodistal).

between the coronal implant platform to the most apical level of crestal bone in contact with the implant surface (Figure 3C). The important histologic landmarks (implant shoulder and fBIC) were identified and discussed by two experienced investigators (J.-C. I. + D.D.B.). The fBIC values were reported as the average of the values derived from the mesial and distal aspects, indicating negative values for crestal bone levels more apical to the reference implant shoulder. Since the macro design of the test and control implants was not similar, it was not possible to achieve blinding of the investigators.

## 2.7 | Statistical evaluation

BIC and fBIC outcomes were summarized as means, standard deviations and interquartile ranges. BIC, fBIC and maxIT between test and control samples were compared using the Wilcoxon-signed rank tests. The pairing was performed by the animal and mandibular position.

Adjusted comparisons were performed using a mixed linear regression model that adjusted for animal effect, side of the mandible and position of test and control implants. The animal effect was introduced

in the model as a random effect. All other factors were set as fixed effects. A $p$ value of <.05 was considered statistically significant. For the hypothesis of non-inferiority of the test device compared to a control device, the average effect and its two-tailed 90% confidence interval (equivalent to a one-tailed 95% confidence interval) were calculated. The lower confidence interval limit served as the tolerance range (T.R.) for supporting the null hypothesis. The detailed results of the mixed regression models and results relevant to the non-inferiority testing are provided as part of the Tables S1–S4–S3.

Non-inferiority testing of BIC between test and control implants was performed based on the following null and alternative hypotheses ($H_0$ and $H_1$):

**H0.** : Average BIC (test) ≤ T.R.

**H1.** : Average BIC (test) > T.R.

Non-inferiority testing of fBIC between implants of specific subgroups was performed with the following null and alternative hypotheses ($H_0$ and $H_1$):

**H0.** : Average fBIC (test) ≤ T.R.

**H1.** : Average fBIC (test) > T.R.

## 3 | RESULTS

All animals recovered from surgeries in a predictable and uneventful manner. No specific surgical, peri- or post-operative complications or signs of inflammation were registered during the healing period.

### 3.1 | Qualitative histological characterization

From all 66 implants, one or two sections were available for descriptive histological evaluation. The representative histological sections in Figure 4 illustrate the peri-implant healing and crestal bone apposition around test and control implants within their respective osteotomies. As evidenced by the micrograph after 3 weeks of healing in Figure 4A, the placement of control implants into size and geometry matching osteotomies resulted in a relatively intimate connection between the implant perimeter and the osteotomy walls with small and narrow gaps between the implant surface and the osteotomy walls (Figure 4A). As the healing progressed, these spaces were gradually filled with newly formed bone at subsequent time points (Figure 4B,C). After 6 weeks of healing, a more advanced stage of healing was observed, characterized by a significant amount of newly formed bone and a relatively high level of implant osseointegration (Figure 4B). Ongoing remodelling closely associated with the implant surface could be observed at this stage. Histological micrographs taken at later healing time points depicted a relatively mature and advanced stage of healing, with tight and complete osseointegration of the implants along the entire implant perimeter (Figure 4C).

In contrast, test implants in their corresponding osteotomies exhibited a distinct feature, wherein the tips of the implant threads engaged with the straight vertical walls of the osteotomy. This engagement was primarily observed in the central and apical segments of the implant (Figure 4D). Notably, the early healing stages were characterized by significant new bone formation at the tips of the implant threads. The microscopic images also revealed that the specific tapering of the implant's lower core and the osteotomy's vertical walls led to the formation of voids with increasing volume towards the apex (Figure 4D). As the healing progressed, these voids gradually filled with newly formed bone (Figure 4E,F). In the later time points, the test implants were once again distinguished by complete osseointegration, with newly formed bone intricately contacting the entire circumference of the implant (Figure 4F).

### 3.2 | Quantitative histological evaluation

Sample dropouts during histological processing due to wrong cutting directions (one implant of the control group at 3 weeks and two implants of the control group at 12 weeks), causing samples to become unusable for histometric evaluation. Therefore, the sample size was reduced the sample sizes per group and time point to the numbers reported in Table 1. From initially 66 implants, 63 were available for histomorphometry (Table 1).

### 3.3 | Bone-to-implant contact—BIC

Figure 5A, Tables 1 and S4 compare the BIC values of test and control implants for the different time points and reports the outcomes of the statistical evaluation and non-inferiority tests performed (Tables S1–S4–S3), respectively. BIC values of control implants increased from (78.44 ± 8.12%) after 3 weeks to (83.2 ± 12.63%) after 6 weeks and (80.88 ± 7.51%) after 12 weeks, respectively. BIC of test implants, on the other hand, showed a steadier increase from (75.84 ± 8.87%) after 3 weeks to (80.22 ± 8.84%) after 6 weeks to (88.07 ± 5.35%) weeks after 12 weeks. Direct comparisons of average BIC values and corresponding linear regression model-adjusted outcomes indicated significantly higher BIC of the test compared to control implants after 12 weeks of healing ($p$ = .010 and .024, respectively). Adjusted average BIC of test implants were also consistently higher compared to the defined T.R., that is, the lower 95% confidence interval range of control implants supporting the alternative hypothesis of test implants being non-inferior compared to control implants in terms of BIC at all studied time points.

### 3.4 | First bone-to-implant contact—fBIC

The temporal evolution of mesiodistal fBIC values around test and control implants is illustrated in Figure 5B and reported in Table 1, respectively. Direct comparisons of average values and

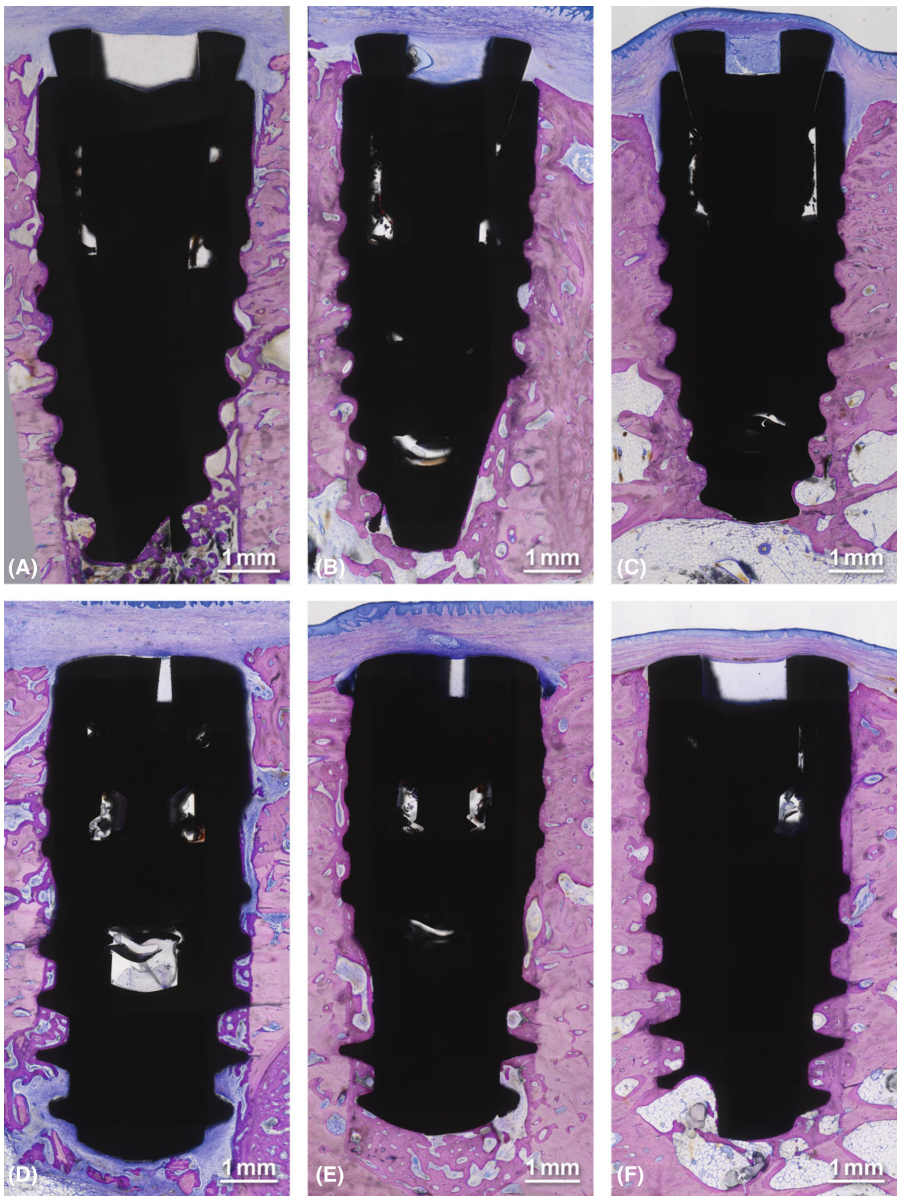


**FIGURE 4** Histology. Representative histological cross sections illustrating the osseointegration and crestal bone apposition and healing around control implants (A–C) and test implants (D–F) after 3 weeks (A,D), 6 weeks (B,E) and 12 weeks (C,F) of healing.

adjusted comparisons using linear regression models are reported in Tables S4 and S1–S4–S3, respectively. The fBIC values of test and control implants were overall comparable, except for the 6 weeks healing time point that showed significantly different values (test: −547 ± 451 µm vs. control: −76 ± 101 µm, $p = .0039$). Adjusted comparisons confirmed the statistically significantly different outcome ($p = .0023$). After 12 weeks of healing, comparable mean fBIC values of (−1084 ± 665 µm) and (−716 ± 512 µm) were measured for control and test implants, respectively. Differences at this time point remained below the significance thresholds ($p = .148$). Comparison of the linear regression adjusted fBIC values of test implants with the lower 95% confidence interval of control implants indicated non-inferiority of fBIC values of the test compared to control implants for the 3 and 12 weeks time points. The corresponding comparison for the 6 weeks time point failed to support the alternative hypothesis indicating inferior fBIC test values compared to control implants at the 6 weeks time point.

### 3.5 | Maximum insertion torque—maxIT

As evidenced by the averaged maxIT value of both implant types (Table 2, Figure 5C), primary stability was high and well above the recommended minimum manufacturers' recommendations for the corresponding test and control implants. MaxIT values of test implants remained significantly higher (60.5 ± 22.5 Ncm) compared to control implants (43.1 ± 19.8 Ncm, $p < .0001$).

## 4 | DISCUSSION

The present preclinical study has histometrically evaluated the osseointegration of novel tapered, self-cutting bone-level implants compared to established, equally surface-functionalized bone level-tapered control implants, both placed according to a type 4 placement protocol. Although both implants may be categorized as bone

**TABLE 1** Bone-to-implant contact—BIC and first bone-to-implant contact—fBIC.

| Time-point (weeks) | Group | *N* | Average BIC ± SD, (%) | BIC range(%) | Average fBIC ± SD (μm) | fBIC range (μm) |
|---|---|---|---|---|---|---|
| 3 | Test | 10 | 75.84 ± 8.87 | 60.74–87.52 | −717.35 ± 342.16 | −1306 to −187 |
| | Control | 9[a] | 78.44 ± 8.12 | 68.34–94.63 | −571.67 ± 473.45 | −1491 to −50 |
| | *p*-value | | .570 | | .359 | |
| 6 | Test | 10 | 80.22 ± 8.84 | 62.50–91.08 | −546.5 ± 450.80 | −1449.5 to 0 |
| | Control | 10 | 83.2 ± 12.63 | 53.58–93.73 | −75.7 ± 100.59 | −275.5 to 0 |
| | *p*-value | | .557 | | .004* | |
| 12 | Test | 13 | 88.07 ± 5.35 | 78.00–94.96 | −715.96 ± 511.64 | −1386 to 0 |
| | Control | 11[a] | 80.88 ± 7.51 | 68.30–93.79 | −1084 ± 665.29 | −2134.5 to −121 |
| | *p*-value | | .010* | | .148 | |

*Note*: Descriptive statistics of histometric-derived bone-to-implant contact (BIC) and first bone-to-implant contact (fBIC).

Abbreviations: *N*, sample number; SD, standard deviation.

[a]One control implant in the 3 weeks group and two control implants in the 12 weeks group could not be measured due to histological processing errors.

*Statistically significant.

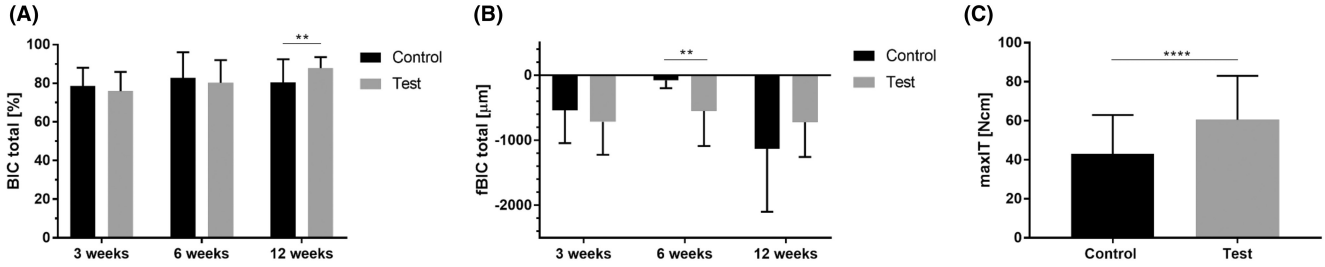


**FIGURE 5** Histometric measurements and maximum insertion torque. Comparison of (A) total bone-to-implant contact (BIC), (B) first bone-to-implant contact (fBIC) and (C) maximum insertion torque (maxIT) values between Control and Test implants after 3, 6 and 12 weeks, respectively. Bars represent mean values, and whiskers represent standard deviation. Horizontal bars and asterisks designate compared pairs with statistically significant differences as determined by Wilcoxon signed rank tests paired by implant site and animal: ** for $p \leq .01$ and **** for $p < .0001$.

**TABLE 2** Maximum insertion torque—maxIT.

| Group | *N* | Average ± SD | Median (IQR) | Range |
|---|---|---|---|---|
| Test | 29 | 60.52 ± 22.53 Ncm | 65 (40–80) | 15–90 |
| Control | 29 | 43.10 ± 19.84 Ncm | 45 (27.5–52.5) | 10–95 |
| *p*-value | | <.0001* | | |

*Note*: Descriptive statistics of maximum insertion torques (maxIT).

Abbreviations: *N*, sample number; SD, standard deviation; IQR, interquartile range (from first to third quartile).

*Statistically significant.

level-tapered implants, the test and control implants exhibited significant disparities in the implant design concepts and macro-design elements, particularly in thread design and placement protocols. However, other design-related parameters, such as material type and surface functionalization, remained consistent between the study devices. The dimensions and shapes of implant osteotomies in relation to implant dimensions, particularly platform diameters, and implant geometry varied notably between the two types of implants. These differences carried significant implications for their engagement mechanism in the host bone, crucial for achieving mechanical primary stability. Similarly, such variations in the placement mechanism likely impacted the interaction with the host bone, influencing implant osseointegration and healing. This encompassed factors such as compression and stress distribution within the native bone and contributed to variations in the void spaces between the implant and osteotomy walls, affecting bone regeneration. Substantial evidence indicates that all these parameters, in conjunction with host bone quality, significantly influence primary stability, osseointegration, marginal bone formation and crestal bone healing.[16,17,20,29–32] To fully understand the results reported here, a comprehensive analysis is needed to account for the discrepancies in the design of the test and control implants, along with their related workflows.

The most important design aspects of test implants were related to the self-cutting, fully tapered implant core and distinctively protruding double-thread geometry. This feature caused test implants to engage with the host bone through the tips of the thread geometry and mainly via the apical portion of the implant.[22] In vitro implantation simulation tests have indicated that this placement mechanism results in high primary stability

irrespective of the host bone quality.[17,18,22] Similarly, simplified drilling protocols adopting a hard bone protocol for this implant were used for osteotomy preparation according to the manufacturer's instructions. The resulting osteotomies displayed a 3.7 mm and 3.5 mm diameter in the coronal 4 mm and apical aspect, respectively. Consequently, the implant osteotomy was coronally slightly overprepared compared to the 3.5 mm platform diameter, causing the implant to mainly engage into the host bone via the apical threads extending with an apical core diameter of 3.75 mm. Core tapering of the implant body in the apical direction further implied an increasing distance between the implant core and osteotomy walls in the apical direction, generating intra-thread voids with increasing volume in the apical direction of the implant. These implant-to-osteotomy geometric considerations suggest that osseointegration of test implants was likely to be characterized by a combination of bone remodeling at the thread tips and de novo bone formation in the inter-thread voids. In contrast, control implants were inserted into equally sized osteotomies tailored to precisely correspond to the implant design geometry following a diameter-matched profile and tap drilling. This particular placement technique has been described as creating a "press fitting" scenario, primarily stabilizing the implant through lateral compression of the coronal osteotomy walls, which are predominantly composed of resistant cortical bone.[33] The absence of larger void spaces between the implant and osteotomy wall and the strong contact between bone and the implant suggests that implant osseointegration may have proceeded mainly via bone remodeling.

One additional interesting finding with consequent relevant clinical impact is the detection of a higher mean maxIT in the tests compared to the controls (i.e. 60 Ncm vs. 43 Ncm): despite some preclinical evidence showing an increased pattern of peri-implant bone resorption following implant placement with high ITs,[34] it is clinical experience that surgeons look for high ITs in order to reduce healing phase prior to loading. Consequently, in order to minimize such risk, it is of paramount importance that implant bed preparation must be scrupulously performed taking into account all variables including bone quality and quantity.

The notable disparities in the primary interaction between the implant and the osteotomy walls in the test and control implants were evident from the significantly varied implant insertion torques, aligning well with or exceeding the limits specified in the manufacturer's placement instructions. Correspondingly, considering the documented interaction with the host bone, it seems plausible to infer that the divergent implant design and placement approaches in the test and control implants would likely contribute to differences in the temporal progression of osseointegration and crestal bone healing and integration. Specifically, the temporal evolution of BIC was characterized by a constant increase around test implants resulting in higher values compared to control implants after 12 weeks of healing. On the other hand, BIC levels around control implants plateaued after the 6 weeks healing time point. It remains speculative whether these differences could be attributed to variations in the mechanistic aspects of osseointegration, particularly distinguishing between remodeling and de novo bone formation among the different implant types. The stability of crestal bone levels is crucial for preserving and supporting peri-implant soft tissues. Thus, comparing these parameters in the context of various implant designs and placement methodologies becomes both intriguing and relevant.[35,36] Amongst the different factors affecting crestal bone healing and stability, the implant position relative to the alveolar crest, the macro-design of the cervical area (platform-switching vs platform-matching designs), as well as the surface topography at the implant neck have all been reported to influence peri-implant bone stability.[37–39] With this regard, the current study design was based on a comparison of crestal bone changes involving a subcrestal placement, which was compared to equicrestal placement described more favourable in a recent systematic review by Valles and coworkers.[39] Likewise, this subcrestal placement method was indirectly confirmed for the test implants in a recent study by Francisco et al. They exhibited comparable crestal bone levels when comparing the loaded transgingival approach to the potentially more advantageous submerged healing regimens.[23]

From a design and placement modality point of view, test implants, compared to control implants, were placed in coronally slightly over-prepared osteotomies to minimize cortical compression and potentially reduce associated risks for bone resorption.[22,29,31,40] Drilling protocols in the herein-applied hard bone model were also designed to specifically minimize buccal cortical stresses accounting for the relatively low compressibility and the associated limited ability of this bone type to dissipate lateral compression forces during implant insertion. Well-defined studies have shown that considerably larger lateral crestal defects around implants tend to heal spontaneously and resolve. Specifically, the authors showed that even much larger lateral marginal bone implant gaps of up to 2.25 mm fully resolved after 4 months of healing.[41–43] In this respect, it is interesting to note that the fBIC values around the test and control implants were comparable overall, except for the fBIC values after 6 weeks of healing, which showed significantly inferior values for the test implants compared to the control implants.

Although not specifically investigated, it was also interesting that fBIC levels around test implants were consistent and stable compared between healing time points. In contrast, fBIC values of control implants showed marked positive and negative variations between individual study time points. Further dedicated studies may investigate if this qualitative observation may be related to differences in healing mechanisms, including differently pronounced levels of slowly remodelling cortical and potentially faster de novo bone apposition due to the mentioned differences in placement modality between test and control implant types.[43]

Finally, it is important to note that the model system used here and its associated physiological and bone-metabolic characteristics related to implant placement have been documented to be comparable to those found in humans.[44,45] Of specific relevance, the applied Göttingen minipig mandibular bone has been reported to intra- and inter-animal consistently manifest as bone type and density I according to Lekholm & Zarb[46] and Misch class D1 respectively.[44,47]

Consequently, the herein-reported results and comparisons are strictly valid only in the herein-investigated context and may vary depending on the type of host bone. Therefore, additional studies with lower bone density, closer to the clinical scenario of primary indication of this newly developed implant, as also type 1 implant placement should be performed to confirm the obtained positive results. Furthermore, it has to be underlined that the focus of this investigation was set on the hard tissue healing sequence prior to loading and that consequently, potential differences in the pattern of peri-implant bone resorption between the two groups resulting from different prosthetic loading protocols, could not be investigated.

## 5 | CONCLUSION

Within the limitations of this preclinical model, novel self-cutting bone level test implants demonstrated superior osseointegration and similar bone levels compared to conventional bone-level implants after a healing period of 12 weeks in healed ridges. These results suggest that the different design and placement approaches of the two tested implant types, potentially related to different healing and osseointegration mechanisms, result in similar overall performance outcomes in terms of osseointegration and crestal bone levels when implants are placed in fully healed bone. Consequently, the novel test implants may be considered in type 4 implant placement procedures.

### AUTHOR CONTRIBUTIONS

J.-C.I., A.R. and B.P. conceived the ideas; J.-C.I. and A.R. performed the clinical procedures; J.-C.I., D.I., B.B. and B.P. collected the data; J.-C.I., B.B., D.D.B., A.S. and B.P interpreted the data; J.-C.I., A.R. and D.I. led the writing. All authors read and approved the final version of the manuscript.

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### CONFLICT OF INTEREST STATEMENT

The study was funded by Institut Straumann AG. B.P. and B.B. are employees of the Institut Straumann AG. The other authors report no other conflict of interest related to this study.

### DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials. Further data that support the findings of this study are available from the corresponding author (J.-C.I.) upon reasonable request.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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