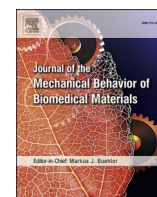




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Research Paper

Avaliação biomecânica e histológica de quatro implantes com diferentes macrogeometrias na fase inicial do processo de osseointegração: um estudo animal *in vivo*

Biomechanical and histological evaluation of four different implant macrogeometries in the early osseointegration process: An in vivo animal study

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RESUMO

Este estudo teve como objetivo avaliar os efeitos da macrogeometria de implantes no período inicial do processo de osseointegração, comparando quatro diferentes modelos de implantes por meio de análises biomecânicas e histológicas após implantação em tíbias de coelhos. No estudo foram utilizados 20 coelhos New Zealand, avaliados em dois momentos distintos (21 e 28 dias) após a instalação do implante. Oitenta implantes de titânio com 4 macrogeometrias diferentes foram divididos em quatro grupos (n = 20 por grupo):

Grupo STRc: implante cilíndrico BoneLevel de 4,1 mm de diâmetro e 8 mm de comprimento, fabricado pela Straumann (Basel, Suíça). Esses implantes apresentam tratamento de superfície por jateamento com micropartículas de óxido de alumínio mais condicionamento ácido. Em seguida, as superfícies de SLA são enxaguadas sob nitrogênio e armazenadas em solução salina, produzindo uma superfície SLActive (SLActive®, Basel, Suíça);

Grupo STRt: Implante cilíndrico-cônico BoneLevel Ø4,1 mm e 8 mm de comprimento, fabricado pela Straumann (Basel, Suíça). Esses implantes apresentam tratamento de superfície SLActive (SLActive®, Basel, Suíça);

Grupo NOBt: Replace Select cônico implante Ø4,3 mm e 8 mm de comprimento, fabricado pela Nobel Biocare AB (Gotemburgo, Suécia). Esses implantes apresentam tratamento de superfície obtido por método de anodização (TiUnite®, Nobel Biocare, Suécia);

Grupo MAEt: Implante Maestro cônico com câmaras de cicatrização de Ø4,0 mm e 8 mm de comprimento, fabricado pela Implacil De Bortoli (São Paulo, Brasil). Esses implantes apresentam tratamento de superfície por jateamento com micropartículas de óxido de titânio mais condicionamento ácido (ácido maleico).

Dez amostras de cada grupo foram analisadas em cada momento proposto. O quociente de estabilidade inicial do implante (ISQ) foi medido por análise de frequência de ressonância (Osstell), tanto no momento da instalação quanto no momento do sacrifício. Nas seções histológicas, a porcentagem de contato osso-implante (BIC%), osso neoformado, matriz osteóide e espaços medulares foram medidos na porção óssea cortical e medular pré-determinada para cada amostra. Os três grupos de implantes cônicos (STRt, NOBt e MAEt) apresentaram valores superiores para os parâmetros analisados no período de osseointegração inicial, em comparação com o grupo de implantes cilíndricos (STRc). Em todos os parâmetros, os três grupos cônicos não apresentaram diferença entre si ($p > 0,05$); entretanto, os três grupos cônicos apresentaram diferenças significativas, quando comparados ao grupo cilíndrico ($p < 0,05$). Nenhuma correlação foi detectada entre os parâmetros analisados. Dentro das limitações do presente estudo, em todos os parâmetros analisados, os implantes cônicos demonstraram resultados superiores quando comparados aos implantes cilíndricos.

Comentários do autor, Sergio Gehrke



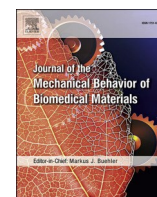
É importante levar em conta que o presente estudo comparou o novo implante Maestro com as duas marcas mundiais mais conceituadas e mais respeitadas (implantes Nobel Biocare e Straumann), os quais, com sua alta tecnologia, são os mais referenciados mundialmente. Isso é importante porque o estudo demonstrou que o implante Maestro está no mesmo nível em comparação com os implantes considerados mundialmente de ponta. E é gratificante ver que a tecnologia aplicada pela empresa Implacil no projeto desse novo implante (implante Maestro) foi acertada.





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Research Paper

Biomechanical and histological evaluation of four different implant macrogeometries in the early osseointegration process: An *in vivo* animal study

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ABSTRACT

This study aims to evaluate the effects of implant macrogeometry on the early period of the osseointegration process, comparing four different implant models through biomechanical and histological analysis after implantation in rabbit tibiae. Twenty New Zealand rabbits were used, evaluated at two different times (21 and 28 days) after installation of the implant. Eighty implants with different macrogeometries were used, forming four groups ($n = 20$ per group): cylindrical implants Ø4.1 mm and 8 mm in length (STRc group); cylindrical-conical implants Ø4.1 mm and 8 mm in length (STRt group); tapered implants Ø4.3 mm and 8 mm in length (NOBt group); and tapered implants with healing chambers Ø4.0 mm and 8 mm in length (MAEt group). Ten samples from each group were analyzed at each proposed time. The initial implant stability quotient (ISQ) was measured by resonance frequency analysis, both at the time of installation and at the time of sacrifice. In the histological sections, the percentage of bone-implant contact (BIC%), newly formed bone, osteoid matrix, and medullary spaces were measured in the pre-determined cortical and medullary bone portion for each sample. The three tapered implant groups (STRt, NOBt, and MAEt) showed higher values for the analyzed parameters in the early osseointegration period, in comparison with the cylindrical implant group (STRc). In all parameters, the three tapered groups showed no difference ($p > 0.05$); however, all three tapered groups presented significant differences, when compared to the cylindrical group ($p < 0.05$). No correlation was detected between the parameters analyzed. Within the limitations of the present study, in all parameters analyzed, the tapered implants demonstrated greater results when compared to the cylindrical implants.

1. Introduction

At present, the use of osseointegrated implants for the rehabilitation of missing teeth is a widely used tool in dentistry, due to its high success rate (Moraschini et al., 2015; Corbella et al., 2021). Thus, the research and development of new implant models (micro- and macro-design) have increased significantly in recent decades (Valente et al., 2019; Hong and Oh, 2017). With the advances of knowledge regarding the biological behavior of these materials when implanted in living tissues, a great search for morphological changes at the macrogeometric,

microgeometric, and even nanogeometric levels began, in order to accelerate the osseointegration process of the implants, thus making it possible to reduce the time needed for the rehabilitation treatment (Smeets et al., 2016; Vivan Cardoso et al., 2015; Yeo, 2019).

Modifications in the surface treatment of the implants is one of the most frequently proposed changes to improve the osseointegration process, in terms of quality and time reduction (Smeets et al., 2016; Yeo, 2019; Gaviria et al., 2014). On the other hand, in recent years, several authors have presented important studies demonstrating that the surgical technique used for the osteotomy of the implant installation site

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can directly influence the biological events of osseointegration, mainly regarding the diameter of the bone drilling, in relation to the diameter of the implant to be inserted (Gehrke et al., 2018a,b; Marin et al., 2016; Campos et al., 2012; Jimbo et al., 2014).

Regarding the implant macrogeometry (implant shape), cylindrical and conical shapes are the most commonly used (Esposito et al., 2014); however, a multitude of models are being marketed on the world market, with different types of shape designs (implant body), thread sizes (pitch and depth), and being self-tapping or not, among other characteristics (Smeets et al., 2016). In general, there is currently a trend towards conical-shaped implants, as studies have shown that this type of design can reduce the surgical trauma caused during the installation of the implants, consequently benefitting the tissue repair process (Samieirad et al., 2019). This is probably due to the type of drilling used for osteotomy for which, in a system of tapered implants, the sequence of drilling cutters used is much less aggressive to the bone tissue (Gehrke et al., 2020b). Moreover, regarding the macrogeometry and considering these related current concepts, implants with the presence of healing chambers have been developed and tested, which have shown excellent results, in terms of quality improvement and decreasing osseointegration time (Gehrke et al., 2020a).

Thus, the present *in vivo* study sought to evaluate the effects on the acceleration of the osseointegration process, by comparing four different implant macrogeometries, through biomechanical and histological analyses after implantation in the cortical and medullary bone of rabbit tibiae. The suggested hypothesis was that different implant macrogeometries can promote different effects on the early osseointegration process.

2. Materials and methods

2.1. Sample descriptions and group formation

Eighty titanium implants with four different macrogeometries were used in the present study, forming four groups ($n = 20$ per group), as follows:

- STRc group: BoneLevel cylindrical implant 4.1 mm in diameter and 8 mm in length, manufactured by Straumann (Basel, Switzerland). These implants present surface treatment by sandblaster with microparticles of aluminum oxide plus acid conditioning. Then, the SLA

surfaces are rinsed under nitrogen and stored in a saline solution, yielding an SLActive surface (SLActive®, Basel, Switzerland);

- STRt group: BoneLevel cylindrical–conical implant Ø4.1 mm and 8 mm in length, manufactured by Straumann (Basel, Switzerland). These implants present SLActive surface treatment (SLActive®, Basel, Switzerland);
- NOBt group: Replace Select tapered implant Ø4.3 mm and 8 mm in length, manufactured by Nobel Biocare AB (Gothenburg, Sweden). These implants present surface treatment obtained by an anodization method (TiUnite®, Nobel Biocare, Sweden);
- MAEt group: Maestro tapered implant with healing chambers Ø4.0 mm and 8 mm in length, manufactured by Implacil De Bortoli (São Paulo, Brazil). These implants present surface treatment by blasting with microparticles of titanium oxide plus acid conditioning (maleic acid).

All implant models used in this study are available for sale on the world market. Fig. 1 shows images of the implant macrogeometries used in each group.

2.2. Animal management and sample distribution

Twenty New Zealand female adult rabbits with weight of 4.5 ± 0.3 Kg were used. The rabbit animal model represents a test system commonly used in orthopedics (Mapara et al., 2012), and the tibia was selected as the implant site, due to the simplicity of the surgical access and to its anatomical characteristics (proportion of cortical and medullary bone). The study protocol was analyzed and approved by the animal committee of the University of Rio Verde (Rio Verde, Brazil), with the number 02-17/UnRV. The international guidelines for animal studies were followed, and the animals received a care and management protocol based on our conventional protocol used in other studies (Gehrke et al., 2018a,b; de Lima Cavalcanti et al., 2019). The present experiment was performed in accordance with relevant guidelines and regulations, and the ARRIVE guidelines were followed. The implant samples ($n = 40$ per group) were installed in both tibiae ($n = 2$ per tibia). The distribution of the implant samples in each tibia (proximal or distal) was designed using a free internet software (available at www.randomizer.org). The implants were installed in the most proximal and central portions of both tibiae (~10 mm from the joint), seeking to avoid differences with respect to the amount of medullary and cortical bone. This portion of the tibia has more medullary bone and less cortical bone,



Fig. 1. Representative images of the implant macrogeometries used for each group: (STRc) Straumann Bone Level cylindrical; (STRt) Straumann Bone Level tapered; (NOBt) Nobel Biocare Replace Select tapered; and (MAEt) Implacil De Bortoli Maestro tapered with healing chambers.

as shown in Fig. 2.

Initially, intramuscular anesthesia was applied using 0.35 mg/kg of ketamine (Ketamina Agener®; Agener União Ltda., São Paulo, Brazil) plus 0.5 mg/kg of xylazine (Rompum® Bayer S.A., São Paulo, Brazil). Then, an incision at ~30 mm was made from the proximal articulation to distal direction. The bone was exposed, and the perforations were performed using a drilling sequence and speed recommended by the manufacturer of each implant model used, as demonstrated in Fig. 3. All osteotomies were performed under intense irrigation with physiological solution at ambient temperature ($23 \pm 2^\circ\text{C}$).

All implant installation was carried out manually using a surgical torquemeter ratchet, which obtained a torque of ~20 Ncm. A distance of 10 mm was observed between the implant samples. After the implantations, a suture was performed using a simple point with Ethicon nylon 4-0 (Johnson & Johnson Medical, New Brunswick, USA). As post-operative care, the animals received an intramuscular injection with a single dose of 0.1 ml/kg of Benzetacil (Bayer, São Paulo, Brazil) plus three doses (one per day) of 3 mg/kg of ketoprofen (Ketoflex, Mundo Animal, São Paulo, Brazil). The sacrifice was performed using an overdose of anesthesia at 21 and 28 days after the surgery ($n = 10$ per time). The tibia portions were removed and immediately immersed in a 4% formaldehyde solution, remaining 7 days for the start of the treatment sequence of these samples.

2.3. Implant stability quotient (ISQ) measurement

The Osstell device (Osstell AB, Gothenburg, Sweden) was used for measurement of the initial implant stability quotient (ISQ). A magnetic sensor (SmartPeg, Gothenburg, Sweden) was installed and torqued for each implant at 10 Ncm (Salatti et al., 2019), as follows: type 54 for STRc and STRt groups, type 13 for the NOBt group and, type 49 for the MAEt group. For all samples, two measurements in two different directions were performed: proximo-distal and antero-posterior. Then, a mean was calculated for each sample. The ISQ measurement was made two times for each sample: immediately after implant installation and immediately after the animal sacrifice.

2.4. Histomorphometric and histological analysis

Seven days after the immersion and conservation of the samples in the fixing solution, the samples were dehydrated using an ethanol sequence (50, 60, 70, 80, 90, and 100%), remaining 72 h in each solution/concentration. Then, the samples were immersed into historesin (Technovit 7200 VLC, Kultzer & Co, Wehrhein, Germany) and submitted to polymerization. All obtained pieces were cut in the central portion of each implant, using a metallographic machine (Isomet 1000; Buehler, Germany). After the cuts, the slices were fixed and submitted to

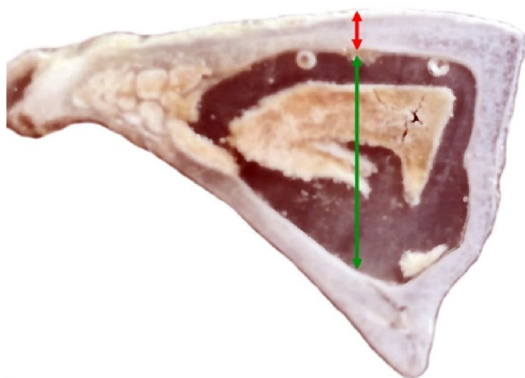


Fig. 2. Image of the proximal tibia area used to install the implants, showing the cortical and medullary bone proportions. Cortical bone in red, medullary bone in green.

polishing (Polipan-U, Panambra Zwick, São Paulo, Brazil) using the following abrasive paper sequence: 180, 320, 600, 1000, and 1200 mesh. The slides were again subjected to an ethanol sequence for rehydration (100–50%), plus a 100% ethanol solution and hydrogen peroxide 10 vol in a 50:50 ratio. Finally, the sample slices were stained by Mayer's hematoxylin (for 8 min) and eosin (for 30 s). A series of images was captured using light optical microscopy (Nikon E200, Tokyo, Japan). The percentage of bone-implant contact (BIC%) was measured using the ImageJ software (National Institute of Health, Bethesda, USA) in the cortical and medullary bone portion, using a pre-determined central area at 1 mm for the cortical bone and 2 mm for the medullary bone, as shown in Fig. 4. The region of interest was determined in the most central portion of the cortical and medullary areas, assuming that there was internal, newly formed bone growth.

In these same bone areas (cortical and medullary), we measured the new bone formed, osteoid matrix, and medullary spaces in a 0.5 mm of distance from the implant surface to the native bone in the same locale where the BIC% was measured, as shown in Fig. 5. The percentage area occupancy of each parameter was measured and calculated proportionally the total area (0.5×1 mm for the cortical portion and 0.5×2 mm in the medullary portion), using the ImageJ software (National Institute of Health, Bethesda, USA). To perform measurements using the software, the program was initially calibrated using the recognized measurements of each portion of the implant. Then, using a color recognition tool for each pre-determined parameter, the "measure area" function was activated.

2.5. Power of samples calculation and statistical analysis

We considered a sample size with a power of 85% to obtain a p -value of 0.05, as calculated using SigmaStat 4.0 software (Systat Software Inc, San Jose, USA). Thus, for a power level of 85% with differences between the means and standard deviations of each group, the calculated minimum sample size for each group at the two proposed times resulted in 8 samples. However, 10 samples were used, in order to ensure this minimum sampling condition.

The D'Agostino-Pearson omnibus normality test was applied to analyze the normal distribution. Once normality was verified, the parametric generalized linear model for repeated measures was applied at a 5% significance level. The one-way ANOVA statistical test was used to determine the difference between the four groups in the same measured time for each parameter analyzed. The t -test was used to evaluate statistical differences in each parameter analyzed inside of each group among the two proposed times. The Bonferroni multiple comparison test was used to detect differences between the groups for each parameter and each time. Pearson's correlation test was used to evaluate the correlation between the ISQ values and BIC%, ISQ values and new bone formed, and BIC% and new bone formed. For all statistical tests, we used the GraphPad Prism software version 5.01 (GraphPad Software, San Diego, USA), considering the result significant when $p < 0.05$.

3. Results

After the two times proposed for the evaluation (at 21 and 28 days), all implants showed clinical signals of osseointegration: no mobility, no inflammation, and absence of infection. Then, all implant samples could be used for the analysis ($n = 20$ implants per group). In all parameters analyzed, statistical differences ($p < 0.05$) were detected in each group, when the values between the times were analyzed.

3.1. Implant stability quotient (ISQ) results

The collected ISQ values, measured immediately after the implantations for all groups, did not show any statistical differences ($p = 0.9887$); these data are presented graphically in Fig. 6a. However, the ISQ values measured at 21 and 28 days after the implantations showed



Fig. 3. Images of the drill sequence and maximum speed recommended by the manufacturer of each implant model used.

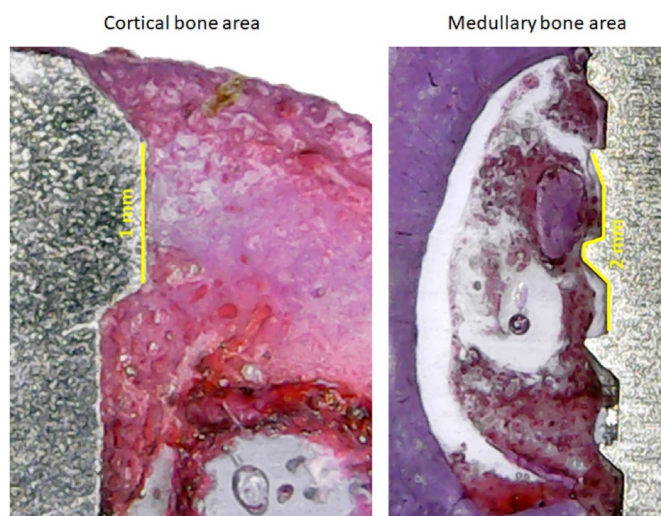


Fig. 4. Schematic image showing the pre-determined area used to measure the BIC% in the cortical and medullary bone (yellow line).

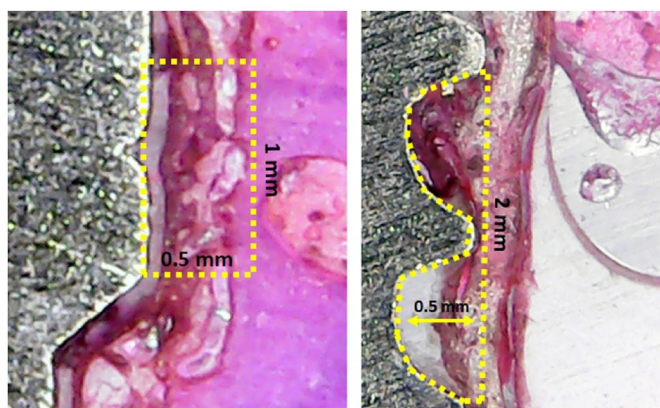


Fig. 5. Representative image showing the bone area considered to measure the new bone formed, osteoid matrix, and medullary spaces in the cortical and medullary bone, respectively.

statistical differences between the four groups ($p = 0.0086$). At the time of 21 days, the STRc group showed statistical differences from the NOBt and MAEt groups, as presented graphically in Fig. 6b. At the time of 28 days, the STRc group showed statistical differences compared to the

STRt, NOBt, and MAEt groups, as presented graphically in Fig. 6c.

3.2. Histomorphometric results

At the time of 21 days after the implantations, the cortical bone healing for the STRt, NOBt, and MAEt groups showed a better initial process of bone neoformation, in comparison to the STRc group. With regards to the measured BIC% in the pre-determined cortical area for this time, the STRt, NOBt, and MAEt groups showed similar values between them ($p > 0.05$), and the STRc group showed a smaller value, with a statistical difference from the other three groups ($p < 0.05$). Meanwhile, in the medullary bone, the healing was more intense for the MAEt group, in comparison with the other three groups (STRc, STRt, NOBt) at the time of 21 days, and showed higher BIC%. Fig. 7 shows the comparative measured data between the groups and the statistical differences of the cortical and medullary measured areas.

At the time of 28 days after implantation, a similar behavior for the cortical bone at the first time (21 days) was observed between the four groups, with regard to the measured BIC% values. In the medullary bone portion, the BIC% measured for the STRt, NOBt, and MAEt groups showed similar values ($p > 0.05$). Furthermore, the STRc group showed a lower value, with statistical differences for the other three groups ($p < 0.05$). Fig. 8 shows the comparative measured BIC% values between the groups and the statistical differences (when significant) for the cortical and medullary portions.

3.3. Morphological results

Different quantities of new bone formation, osteoid matrix, and medullary spaces were observed between the four analyzed groups at the two proposed times. At the time of 21 days, the three groups of tapered implants (STRt, NOBt, and MAEt groups) showed more advanced stage signals of bone formation stimuli (new bone formation and osteoid matrix parameters), in comparison with the STRc group of cylindrical implants. The comparison data between the four groups in the cortical and medullary bone portions used for the measurements are presented in Fig. 9. For both cortical and medullary bone portions, the parameters measured in the STRt, NOBt, and MAEt group samples showed values without statistical differences between groups ($p > 0.05$); however, the STRc group showed lower values for new bone formed and osteoid matrix, in comparison with the other three groups, with a statistical difference ($p < 0.05$).

Histological section images of the cortical and medullary bone area of each group at the time of 21 days are shown in Fig. 10.

All groups showed evolution in the measured parameters, with statistical differences ($p < 0.05$) between the data, when compared inside of the groups among the two times. At the second evaluation time (28

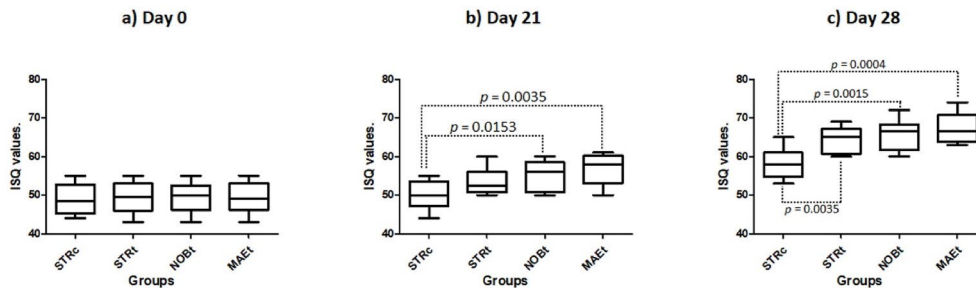


Fig. 6. ISQ values measured for each group at the three different evaluation times, showing the p -value for the groups that presented statistical differences.

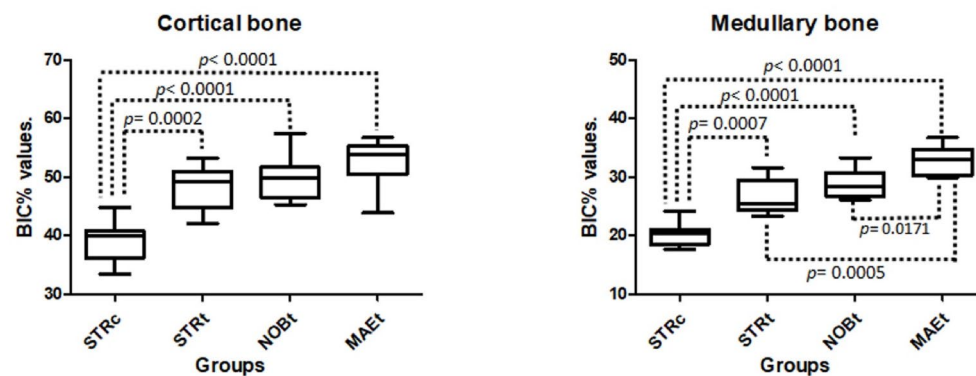


Fig. 7. Box plot graphs showing the BIC% values for each group measured in the cortical and medullary bone area 21 days after implantation. The groups that showed statistical differences between them are shown by the lines with corresponding p -values. In all other cases, no statistical differences were found ($p > 0.05$).

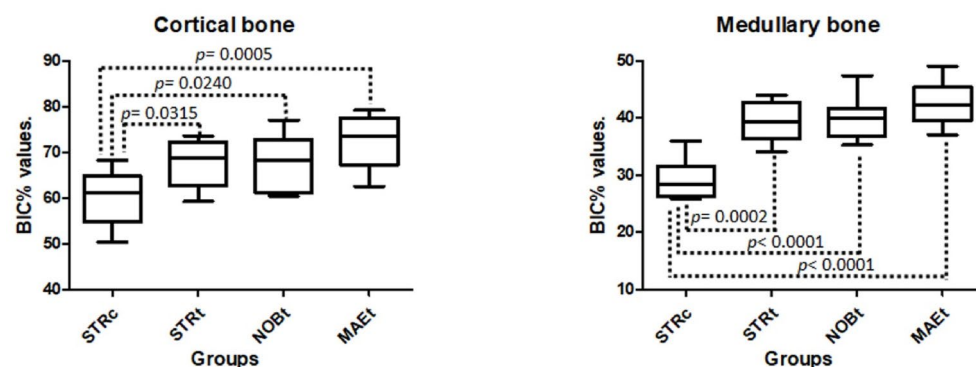


Fig. 8. Box plot graphs showing the BIC% values for each group, measured in the cortical and medullary bone areas 28 days after implantation. The groups that showed statistical differences between them are identified by the lines, with p -values presented. In all other cases, no statistical differences were found ($p > 0.05$).

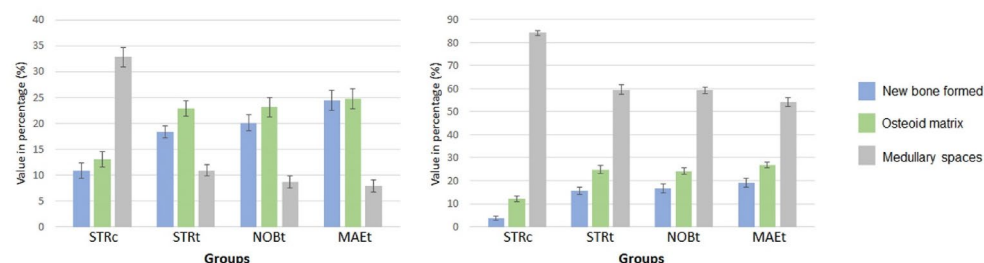


Fig. 9. Bar graph of the data (mean and standard deviation) of measured parameters analyzed for all groups at 21 days.

days), the tapered implants (STRt, NOBt, and MAEt groups) showed better values for all proposed parameters, in comparison with the STRc group of cylindrical implants ($p < 0.05$). The comparison data between

the four groups in the cortical and medullary bone portion used for the measurements are presented in Fig. 11. Comparing the STRt, NOBt, and MAEt groups, we found statistical differences between them in the new

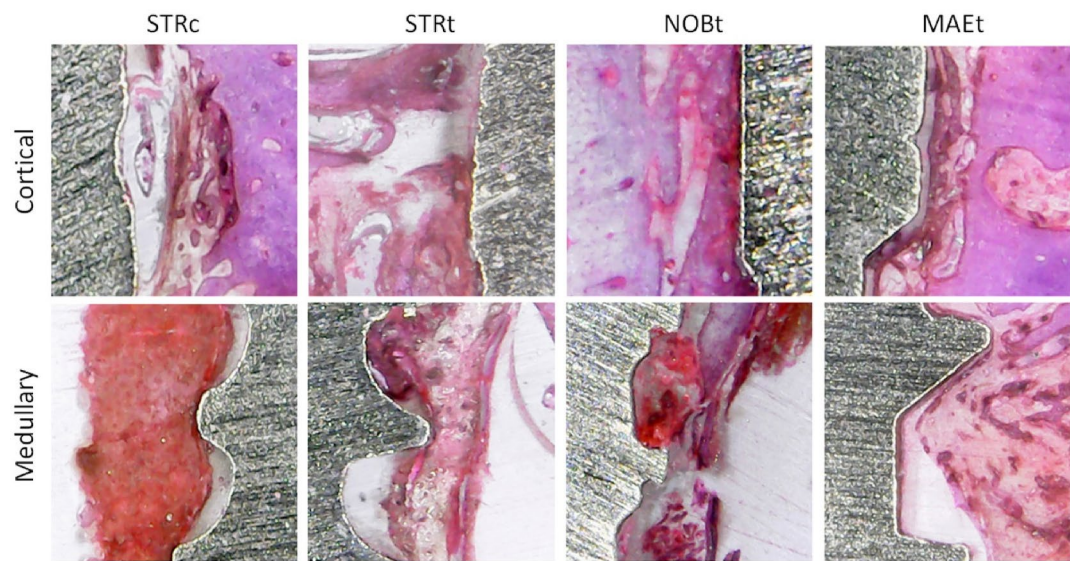


Fig. 10. Section images of samples of the cortical and medullary bone areas of each group at 21 days after implantation.

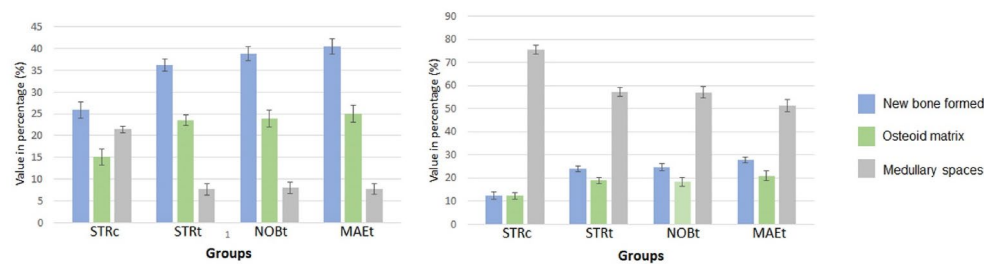


Fig. 11. Bar graph of the data (mean and standard deviation) of measured parameters analyzed for all groups at 28 days.

bone formed values ($p < 0.05$), in both bone portions measured (cortical and medullary), at 28 days.

Histological section images of the cortical and medullary bone area of each group at 28 days are shown in Fig. 12.

3.4. Correlation data analysis

When analyzing possible correlations between BIC% and ISQ values, BIC% and new bone formed, and ISQ values and new bone formed, in all cases tested, no correlation was detected.

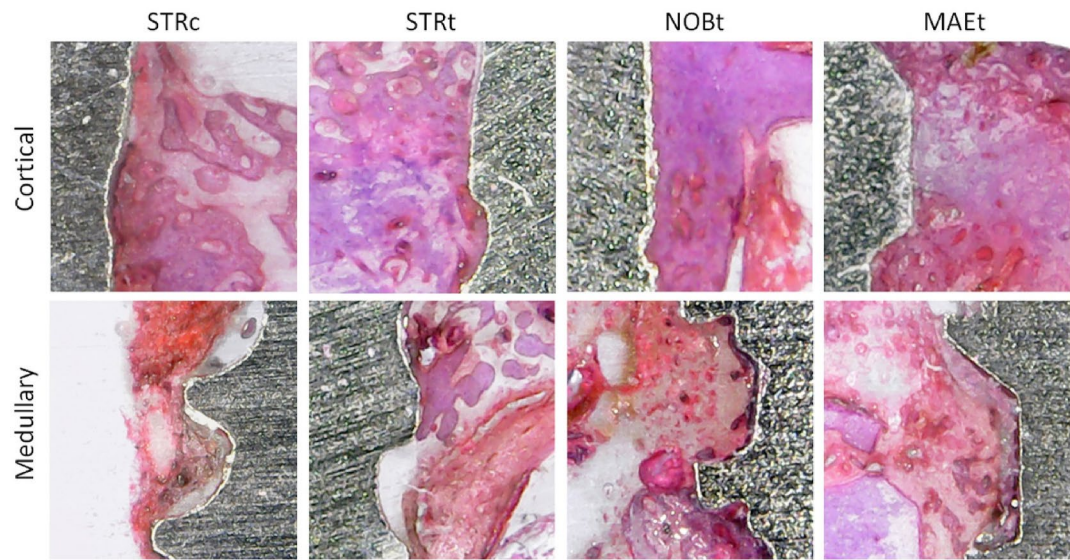


Fig. 12. Section images of samples of the cortical and medullary bone areas of each group at 28 days after implantation.

4. Discussion

In the present study, we analyzed and compared four different commercialized macrogeometries of dental implants and its effects on the early osseointegration process, at 21 and 28 days after their insertion into rabbit tibiae. The results showed that the tapered implant macrogeometries promoted acceleration in the osseointegration process, in comparison with the cylindrical implant macrogeometry, as well as promoting adequate stimulation in the formation of bone tissue in the medullary portion. Changes in the implant surface and/or in the implant macrogeometry, to promote the acceleration of the osseointegration process, is one of the main objectives of current implantology research (Smeets et al., 2016; Gehrke et al., 2019, 2020a; Carmo Filho et al., 2018). In this sense, Scarano and Collaborators have demonstrated that blood vessel formation is stimulated by the presence of the concavities in the implant threads (Scarano et al., 2014a), and higher percentages of bone were observed in the concavities (Scarano et al., 2014b). In addition, another objective of implant design modification has been to improve the predictability of treatment with implants in patients with systemic or local weaknesses (low quality bone), which may hinder the osseointegration process (Jimbo et al., 2014; Nobles et al., 2021).

However, the topic of ideal or adequate micro- or macro-geometry of the implant to accelerate or improve osseointegration remains controversial in the literature (Matos, 2021; Aldahlawi et al., 2018). In our present study, the implants were installed in a low-quality type of bone, corresponding to the area of the proximal tibia, where we found a large amount of medullary bone and a small amount of cortical bone. With regards to our initial hypothesis—that the implant micro- and macro-geometry can improve the osseointegration events on the cortical and medullary bone—the results confirmed that this hypothesis is true.

The surgical technique used for the osteotomy, such as drill design, can promote different intensities of trauma on the bone tissue, thus affecting the healing process. Recently, Gehrke et al. (2020b), comparing the drill design (cylindrical vs. conical drill), showed that conical drills promote a better healing of the bone tissue after the osteotomy. On the other hand, it has been shown, in other studies, that the intensity of the inflammatory response is directly related to the trauma produced during osteotomy (Salles et al., 2018). The influence of these described factors—that is, the design of the drills for osteotomy and the consequent trauma produced during this event—was corroborated by the results of the present study, where the three groups of tapered implants (STRt, NOBt, and MAEt groups) presented similar, better results in all the proposed evaluations, in comparison with the group using cylindrical implants (STRc group).

The initial implant stability is considered a fundamental condition for achieving adequate osseointegration (Gehrke et al., 2020b; Nobles et al., 2021; Javed et al., 2013). This condition is obtained through suitable mechanical seating of the implant into the bone, which minimizes the micro-movements among these structures, allowing for the possibility of bone formation on this interface. The limit proposed for the micro-movements is 50–150 μm (Elias et al., 2012, 2015). The initial stability is dependent on the surgical technique, implant design, and bone morphology (Javed et al., 2013; Coelho et al., 2011), which can be measured through the insertion torque value and/or frequency resonance analysis. In the rabbit animal model, due to the tibia bone characteristics, the installation of the implants cannot reach a high torque value, as it can cause fracturing. Thus, all implants were installed with a controlled torque values of approximately 20 N, and this method (insertion torque value) was not used to ensure the initial stability. Thus, an Osstell device was used to measure the initial stability, which performs a frequency resonance analysis, thus generating the ISQ values. The ISQ values measured for all groups were very similar at this time (i. e., immediately after the implant installation), without statistical differences, showing that all implant systems evaluated in our study presented an adequate relationship between implant and drill design.

All sample groups showed evolution of the ISQ values between the

three moments that the stability was measured. However, the ISQ values obtained at the second measured time (at 21 days) were higher for the three tapered groups (STRt, NOBt, and MAEt groups), in comparison to the cylindrical group (STRc group). At 28 days after implantation, the same differences in ISQ value evolution presented at 21 days was observed between the four groups (STRt, NOBt, and MAEt > STRc). Other studies have shown higher ISQ values for tapered implants, compared with cylindrical implants, in the early osseointegration period, corroborating the results obtained in the present study (O'Sullivan et al., 2004; Lozano-Carrascal et al., 2016). On the other hand, other studies have shown that there are no statistically significant differences between the ISQ values for cylindrical and tapered implants, both in studies in animals and in humans (Cochran et al., 2016; Waechter et al., 2017; Carmo Filho et al., 2019).

With regards to the histomorphometric analysis (BIC%, new bone formed, osteoid matrix, and medullary spaces), both in the cortical and medullary bone, we observed higher values for the three tapered implant groups (STRt, NOBt, and MAEt groups), in comparison to the cylindrical group (STRc group), for both evaluation times. Such behavior of tapered implants, compared with cylindrical implants, at the early period of osseointegration, has been observed in other studies (Jimbo et al., 2014; Lozano-Carrascal et al., 2016). In our view, these results are related to the macrogeometry of the implants; this is because, although the three tapered implants presented different surfaces, when we compare both the STRc and STRt groups—which had the same surface treatment (SLActive surface)—the results were better for the tapered implant. In addition, this difference in results was similar to the difference found between the STRc group and the two other groups of tapered implants (NOBt and MAEt groups).

As for the limitations of our animal study, the number of animals authorized for use by the ethics committee (20 animals) reflect the number of samples tested in each group and at each time (10 samples), despite the power test having presented an adequate representation of samples for this study. On the other hand, it is important to emphasize that the results of studies in rodent animal species cannot be directly translated to humans, which typically shows only ~70% correlation (Hartung, 2008). However, the rabbit animal model appears as a first-hand choice for fundamental implant design studies, due to their ease of handling, short life span, and economical aspects in purchasing and sustaining (Stübinger and Dard, 2013). Another important limitation is the location where the samples were tested (tibia), which differs greatly from their typical use in the conditions presented by the oral cavity. Furthermore, in the present study, the mechanical properties of the newly formed bone were not evaluated, which would require a larger number of animals and samples to be able to be carried out, through the analysis of the removal torque of the implants after osseointegration. For this reason, other clinical studies should be designed to corroborate these results.

5. Conclusions

Within the limitations presented for the present study, the results found demonstrated that implant macrogeometry can produce a significant increase in the early osseointegration for both cortical and medullary bone. In all parameters analyzed (implant stability, bone-implant contact, new bone formed, osteoid matrix, and medullary spaces), the tapered implants showed more effective results, in comparison to the cylindrical implants.

Ethical approval

The present study was approved by the Animal Experimentation Committee (Number 02-17UnRV), University of Rio Verde (Rio Verde, Brazil). All applicable international, national, and/or institutional guidelines for the care and use of animals were followed.

Author contributions

Sergio Alexandre Gehrke: Conceptualization, data curation, formal analysis, investigation, methodology, writing—original draft, writing—review & editing. Jaime Aramburú Júnior: Investigation, methodology, writing—original draft. Tiago Luis Eirles Treichel: Investigation, methodology, writing—original draft. Berenice Anina Dedavid: Conceptualization, data curation, writing—review & editing.

Authors' statement

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Declaration of competing interest

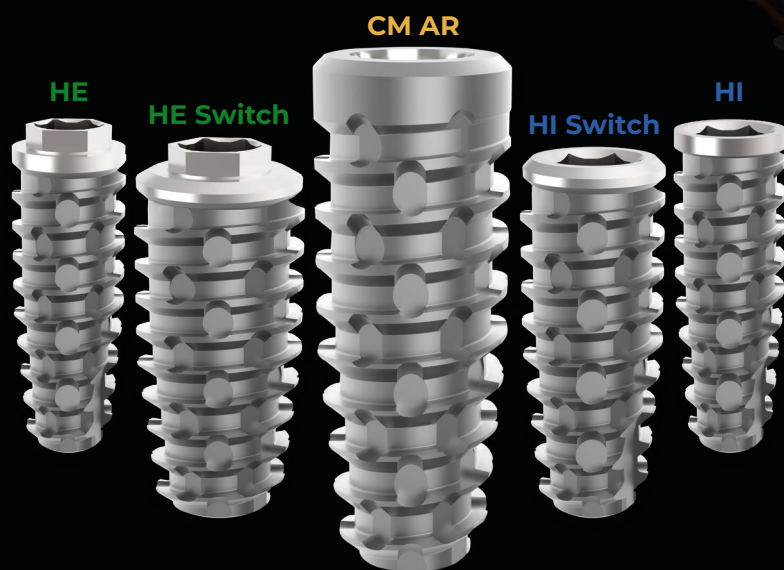
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- Aldahlawi, S., Demeter, A., Irinakis, T., 2018. The effect of implant placement torque on crestal bone remodeling after 1 year of loading. *Clin. Cosmet. Invest. Dent.* 9, 203–209.
- Campos, F.E., Gomes, J.B., Marin, C., Teixeira, H.S., Suzuki, M., Witek, L., Zanetta-Barbosa, D., Coelho, P.G., 2012. Effect of drilling dimension on implant placement torque and early osseointegration stages: an experimental study in dogs. *J. Oral Maxillofac. Surg.* 70, e43–50.
- Carmo Filho, L.C.D., Faot, F., Madruga, M.M., Marcello-Machado, R.M., Bordin, D., Del Bel Cury, A.A., 2019. Effect of implant macrogeometry on peri-implant healing outcomes: a randomized clinical trial. *Clin. Oral Invest.* 23, 567–575.
- Carmo Filho, L.C.D., Marcello-Machado, R.M., Castilhos, E.D., Del Bel Cury, A.A., Faot, F., 2018. Can implant surfaces affect implant stability during osseointegration? A randomized clinical trial. *Braz. Oral Res.* 32, e110.
- Cochran, D., Stavropoulos, A., Obrecht, M., Pippenger, B., Dard, M., 2016. A comparison of tapered and nontapered implants in the minipig. *Int. J. Oral Maxillofac. Implants* 31, 1341–1347.
- Coelho, P.G., Granato, R., Marin, C., Teixeira, H.S., Suzuki, M., Valverde, G.B., Janal, M. N., Lilin, T., Bonfante, E.A., 2011. The effect of different implant macrogeometries and surface treatment in early biomechanical fixation: an experimental study in dogs. *J. Mech. Behav. Biomed. Mater.* 4, 1974–1981.
- Corbella, S., Alberti, A., Calciolari, E., Francetti, L., 2021. Medium- and long-term survival rates of implant-supported single and partial restorations at a maximum follow-up of 12 Years: a retrospective study. *Int. J. Prosthodont.* (IJP) 34, 183–191.
- de Lima Cavalcanti, J.H., Matos, P.C., Depes de Gouvêa, C.V., Carvalho, W., Calvo-Guirado, J.L., Aragonese, J.M., Pérez-Díaz, L., Gehrke, S.A., 2019. In vitro assessment of the functional dynamics of titanium with surface coating of hydroxyapatite nanoparticles. *Materials (Basel)* 12 (5), 12.
- Elias, C.N., Rocha, F.A., Nascimento, A.L., Coelho, P.G., 2012. Influence of implant shape, surface morphology, surgical technique and bone quality on the primary stability of dental implants. *J. Mech. Behav. Biomed. Mater.* 16, 169–180.
- Elias, C.N., Fernandes, D.J., Resende, C.R., Roestel, J., 2015. Mechanical properties, surface morphology and stability of a modified commercially pure high strength titanium alloy for dental implants. *Dent.* 31, e1–e13.
- Esposito, M., Ardebili, Y., Worthington, H.V., 2014. Interventions for replacing missing teeth: different types of dental implants. *Cochrane Database Syst. Rev.* 7, CD003815.
- Gaviria, L., Salcido, J.P., Guda, T., Ong, J.L., 2014. Current trends in dental implants. *J. Korean Assoc. Oral Maxillofac. Surg.* 40, 50–60.
- Gehrke, S.A., Aramburú, J. Júnior, Pérez-Díaz, L., do Prado, T.D., Dedavid, B.A., Mazon, P., N De Aza, P., 2020a. Can changes in implant macrogeometry accelerate the osseointegration process?: an in vivo experimental biomechanical and histological evaluations. *PLoS One* 15, e0233304.
- Gehrke, S.A., Aramburú Júnior, J., Pérez-Díaz, L., Treichel, T.L.E., Dedavid, B.A., De Aza, P.N., Prados-Frutos, J.C., 2019. New implant macrogeometry to improve and accelerate the osseointegration: an in vivo experimental study. *Appl. Sci.* 9 (15), 3181.
- Gehrke, S.A., Bettach, R., Aramburú Júnior, J.S., Prados-Frutos, J.C., Del Fabbro, M., Shibli, J.A., 2018a. Peri-implant bone behavior after single drill versus multiple sequence for osteotomy drill. *BioMed Res. Int.* 9756043, 2018.
- Gehrke, S.A., Maté Sánchez de Val, J.E., Fernández Domínguez, M., de Aza Moya, P.N., Gómez Moreno, G., Calvo Guirado, J.L., 2018b. Effects on the osseointegration of titanium implants incorporating calcium-magnesium: a resonance frequency and histomorphometric analysis in rabbit tibia. *Clin. Oral Implants Res.* 29, 785–791.
- Gehrke, S.A., Treichel, T.L.E., Aramburú Júnior, J., de Aza, P.N., Prados-Frutos, J.C., 2020b. Effects of the technique and drill design used during the osteotomy on the thermal and histological stimulation. *Sci. Rep.* 10, 20737.
- Hartung, T., 2008. Thoughts on limitations of animal models. *Park. Relat. Disord.* 14 (Suppl. 2), S81–S83.
- Hong, D.G.K., Oh, J.H., 2017. Recent advances in dental implants. *Maxillofac. Plast. Reconstr. Surg.* 39, 33.
- Javed, F., Ahmed, H.B., Crespi, R., Romanos, G.E., 2013. Role of primary stability for successful osseointegration of dental implants: factors of influence and evaluation. *Interv. Med. Appl. Sci.* 5, 162–167.
- Jimbo, R., Tovar, N., Anchieta, R.B., Machado, L.S., Marin, C., Teixeira, H.S., Coelho, P. G., 2014. The combined effects of undersized drilling and implant macrogeometry on bone healing around dental implants: an experimental study. *Int. J. Oral Maxillofac. Surg.* 43, 1269–1275.
- Lozano-Carrascal, N., Salomó-Coll, O., Gilabert-Cerdà, M., Farré-Pagés, N., Gargallo-Albiol, J., Hernández-Alfaro, F., 2016. Effect of implant macro-design on primary stability: a prospective clinical study. *Med. Oral Patol. Oral Cir. Bucal* 21, e214–e221.
- Mapara, M., Thomas, B.S., Bhat, K.M., 2012. Rabbit as an animal model for experimental research. *Dent. Res. J.* 9, 111–118.
- Marin, C., Bonfante, E., Granato, R., Neiva, R., Gil, L.F., Marão, H.F., Suzuki, M., Coelho, P.G., 2016. The effect of osteotomy dimension on implant insertion torque, healing mode, and osseointegration indicators: a study in dogs. *Implant Dent.* 25, 739–743.
- Matos, G.R.M., 2021. Surface roughness of dental implant and osseointegration. *J. Maxillofac. Oral Surg.* 20, 1–4.
- Moraschini, V., Poubel, L.A., Ferreira, V.F., Barboza Edos, S., 2015. Evaluation of survival and success rates of dental implants reported in longitudinal studies with a follow-up period of at least 10 years: a systematic review. *Int. J. Oral Maxillofac. Surg.* 44, 377–388.
- Nobles, K.P., Janorkar, A.V., Williamson, R.S., 2021. Surface modifications to enhance osseointegration-Resulting material properties and biological responses. *J. Biomed. Mater. Res. B Appl. Biomater.* 109 (11), 1909–1923.
- O'Sullivan, D., Sennerby, L., Meredith, N., 2004. Influence of implant taper on the primary and secondary stability of osseointegrated titanium implants. *Clin. Oral Implants Res.* 15, 474–480.
- Salatti, D.B., Pelegrine, A.A., Gehrke, S., Teixeira, M.L., Moshaverinia, A., Moy, P.K., 2019. Is there a need for standardization of tightening force used to connect the transducer for resonance frequency analysis in determining implant stability? *Int. J. Oral Maxillofac. Implants* 34, 886–890.
- Salles, M.B., Allegrini, S., Yoshimoto, M., Pérez-Díaz, L., Calvo-Guirado, J.L., Gehrke, S. A., 2018. Analysis of trauma intensity during surgical bone procedures using NF-κB expression levels as a stress sensor: an experimental study in a wistar rat model. *Materials* 12 (12), 11.
- Scarano, A., Perrotti, V., Artese, L., Degidi, M., Degidi, D., Piattelli, A., Iezzi, G., 2014a. Blood vessels are concentrated within the implant surface concavities: a histologic study in rabbit tibia. *Odontology* 102, 259–266.
- Scarano, A., Degidi, M., Perrotti, V., Degidi, D., Piattelli, A., Iezzi, G., 2014b. Experimental evaluation in rabbits of the effects of thread concavities in bone formation with different titanium implant surfaces. *Clin. Implant Dent. Relat. Res.* 16, 572–581.
- Samieirad, S., Mianbandi, V., Shiezhadeh, F., Hosseini-Abrishami, M., Tohidi, E., 2019. Tapered versus cylindrical implant: which shape inflicts less pain after dental implant surgery? A clinical trial. *J. Oral Maxillofac. Surg.* 77, 1381–1388.
- Smeets, R., Stadlinger, B., Schwarz, F., Beck-Broichsitter, B., Jung, O., Precht, C., Kloss, F., Gröbe, A., Heiland, M., Ebker, T., 2016. Impact of dental implant surface modifications on osseointegration. *BioMed Res. Int.* 6285620, 2016.
- Stübinger, S., Dard, M., 2013. The rabbit as experimental model for research in implant dentistry and related tissue regeneration. *J. Invest. Surg.* 26, 266–282.
- Valente, M.L.D.C., Castro, D.T., Shimano, A.C., Reis, A.C.D., 2019. Influence of an alternative implant design and surgical protocol on primary stability. *Braz. Dent. J.* 30, 47–51.
- Vivan Cardoso, M., Vandamme, K., Chaudhari, A., De Rycker, J., Van Meerbeek, B., Naert, I., Duyck, J., 2015. Dental implant macro-design features can impact the dynamics of osseointegration. *Clin. Implant Dent. Relat. Res.* 17, 639–645.
- Waechter, J., Madruga, M.M., Carmo Filho, L.C.D., Leite, F.R.M., Schinestock, A.R., Faot, F., 2017. Comparison between tapered and cylindrical implants in the posterior regions of the mandible: a prospective, randomized, split-mouth clinical trial focusing on implant stability changes during early healing. *Clin. Implant Dent. Relat. Res.* 19, 733–741.
- Yeo, I.L., 2019. Modifications of dental implant surfaces at the micro- and nano-level for enhanced osseointegration. *Materials* 13, 89.

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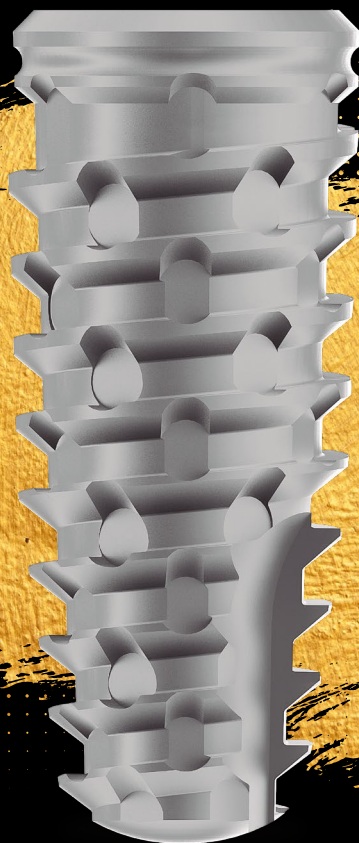
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