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Article

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Abstract: Objectives: The aim of the present preclinical study, using rabbits as an experimental model, investigated the effects of a new implant design that incorporates specific changes in the cervical portion, using a conventional implant design as a control group. **Materials and Methods:** Ten rabbits and 40 dental implants with two different macrogeometries were used. Two groups were formed (n = 20 per group): Collo group, where implants with a new cervical design were used, which present a concavity (reduction in diameter) in the first 3.5 mm and with this portion of the implant without surface treatment; Control group, where conical implants with conventional design were used, which feature surface treatment throughout the body. All implants present dimensions of 4 mm in diameter and 10 mm in length. The initial implant stability quotient (ISQ) was measured immediately after the implant insertion (T1) and immediately after removing the pieces with the implants. The animals (n=5 animals/time) were euthanized at 3 weeks (T1) and 4 weeks (T2). Histological sections were prepared and, the percentage of bone-implant contact (BIC%) and the tissue area fraction occupancy (TAFO%) were analyzed in the pre-determined cervical area of the first 4 mm from the implant platform. **Results:** The ISQ values showed no statistical differences in T1 and T2 (p = 0.9458 and p = 0.1103, respectively). However, in T3 superior values were found for the Collo group (p = 0.0475). Higher BIC% values were presented in samples from the Collo group compared to the Control group, with statistical differences (3-weeks p = 0.0009 and 4-weeks p = 0.0007). TAFO% (new bone, medullary spaces, and collagen matrix) had statistical differences between the groups at each evaluation time. **Conclusion:** Within the limitations of the present preclinical study, the results of this study suggest that the new implant design with changes in the cervical portion (Collo group) presents significant advantages concerning the conventional implant (Control group), regarding stability in the initial times and osseointegration.

Keywords: dental implants; macrogeometry; pre-clinical study; histomorphometry; implant stability

1. Introduction

Although dental implants generally have high success rates for the rehabilitation of missing teeth, their long-term maintenance directly depends on the health of the adjacent tissues [1,2]. The constant evolution in the field of implant dentistry has provided significant advances in the development of new designs of dental implants, especially with changes in their macrogeometry [3]. As demonstrated in previous studies, the different macrogeometries of implants can bring different responses in the osseointegration process [4]. These changes can be divided into 3 areas of the implant: cervical, body and apical. Among the changes proposed in each area, in the body of the implant we most frequently have new coil designs, in the apical portion the modifications are related to the cutting power and threading of the implant and, in the cervical portion, maintaining the stability of the peri-implant tissues is the main objective. This specific region of the implant (cervical) challenges conventional standards by exploring new configurations that aim to optimize both osseointegration and the aesthetic and functional integration of implants [5].

The stability and maintenance of the health of the peri-implant tissues around the cervical portion (neck) of the implant represent primary objectives in the contemporary practice of implant dentistry [6]. The integrity of the soft and bone tissues in this region not only directly influences the aesthetics and functional comfort of patients but is also crucial for the longevity and success of dental implant treatments [6]. The cervical portion of the implant challenges professionals in the field to constantly seek new approaches and technologies that promote robust osseointegration and healthy adaptation of gingival tissues [1]. The evolution of implant designs has been guided by studies that highlight the importance of characteristics such as shape, surface texture and biomechanical adjustments that minimize the impact on surrounding tissues [7].

Several studies address the design of the implant neck and its relationship with marginal bone loss, but the results are varied in the literature [8]. Studies in human showed that dental implants with triangular neck designs suggest better crestal bone preservation [9]. Extra-short implants with a narrow ring demonstrated less bone loss at the crest, although with similar peri-implant tissue thickness [10]. On the other hand, implants with micro-threads in the neck showed greater bone loss compared to implants with open-thread collars [11]. Authors have indicated superior biomechanical behavior with dental implants that have a divergent neck design, favoring a more efficient stress/strain distribution, in comparison to straight and convergent crest module in ascending order of stress distribution [12]. Furthermore, non-submerged implants with short, smooth collars did not show significant additional bone loss compared to similar but longer collar designs [13].

Recently, a new cervical macrogeometry design was developed as a promising alternative to traditional models [14]. This new design not only aims to facilitate the formation and maintenance of peri-implant tissues, through carefully designed modifications, such as the introduction of a concave area in the cervical portion, and this new approach aims to promote more effective osseointegration and a biological response optimized. This new design generates a clot chamber in the cervical portion of the implant without causing compression in this area when compared to conventional implant designs (**Figure 1**).
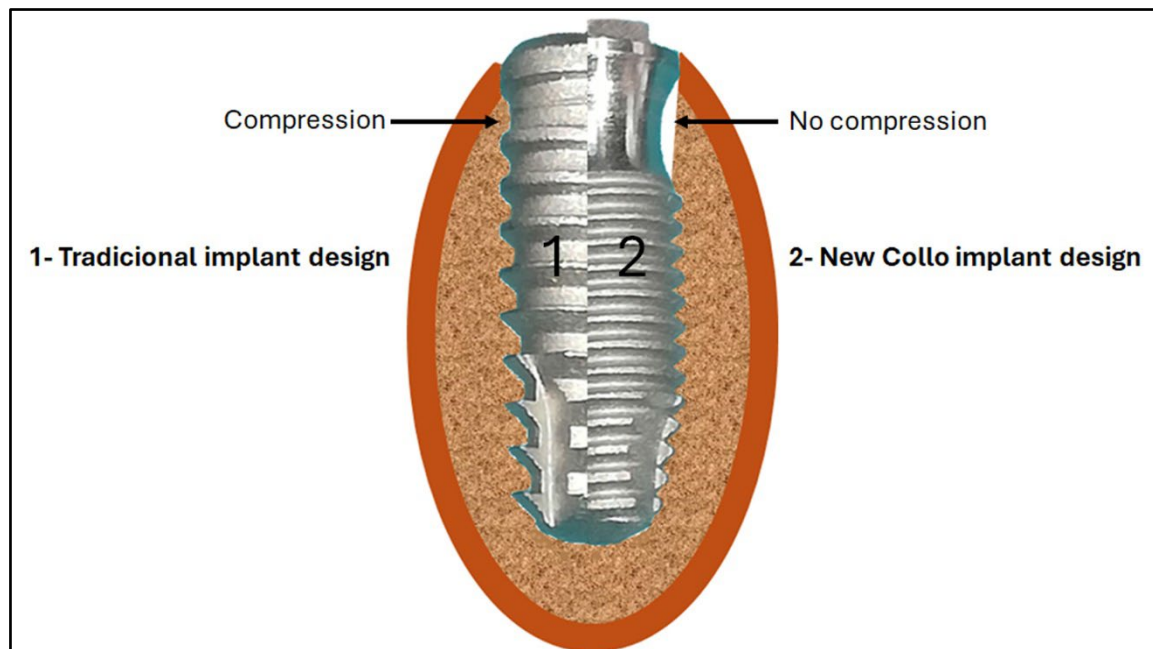
Figure 1. Schematic image showing the difference provided by the macrogeometry of the cervical portion using a traditional implant model (1) and the new Collo implant (2).

Therefore, this preclinical study, using rabbits as an experimental model, investigated a new implant design that incorporates specific changes in the cervical portion, using a conventional implant design as a control group. The main objectives of this experimental study were: (i) to evaluate the stability behavior of this new implant; (ii) evaluate the bone response in the concave area of the implant where the formation of a healing chamber occurs; (iii) analyze and compare the characteristics of the newly formed tissue in the initial stages of healing.

2. Materials and Methods

2.1. Implants and Groups Formation

A total of 40 implants were used in this study. These samples were divided into two groups (n = 20 per group): **Collo group**, where implants with a new cervical design were used, which present a concavity (reduction in diameter) in the first 3.5 mm and with this portion of the implant without surface treatment; **Control group**, where conical implants with conventional design were used, which feature surface treatment throughout the body. Both implants were manufactured by the company Implacil De Bortoli (São Paulo, Brazil), with dimensions of 4 mm in diameter and 10 mm in length. The surface treatment presented by all implants of both groups was blasting with titanium oxide and subsequent acid etching [15]. **Figure 2** presents representative images of the implant models.

Figure 2. Representative images of the implant models used in the present study.

2.2. Animal Model and Care

In the present study, 10 adult rabbits weighing between 4 and 5 kg were used. Initially, the study protocol was analyzed and approved by the animal ethics committee of the University of Rio Verde – UnRV (Rio Verde, Brazil), under number 02-17/UnRV. The rabbit animal model represents a testing system commonly used in orthopedics as it is a model that presents adequate cost for acquisition, ease of handling and care, availability, tolerance to captivity and convenience of housing [16]. Both tibias were selected as the site for installing the implants due to the simplicity of the surgical access and their anatomical characteristics (proportion of cortical and medullary bone). As in previous studies, international guidelines for animal studies were followed, where animals received a care and handling protocol [17]. The present experiment was performed in accordance with relevant guidelines and regulations, and the ARRIVE guidelines were followed. All animals were kept in individual cages, with 12 hours of light and food and water *ad libitium* throughout the experiment.

2.3. Implant Surgery and Distribution

Two implants were installed per tibia in each animal, in a proximal site (approximately 1 cm away from the joint) and another approximately 1 cm distally, as shown schematically in **Figure 3**.
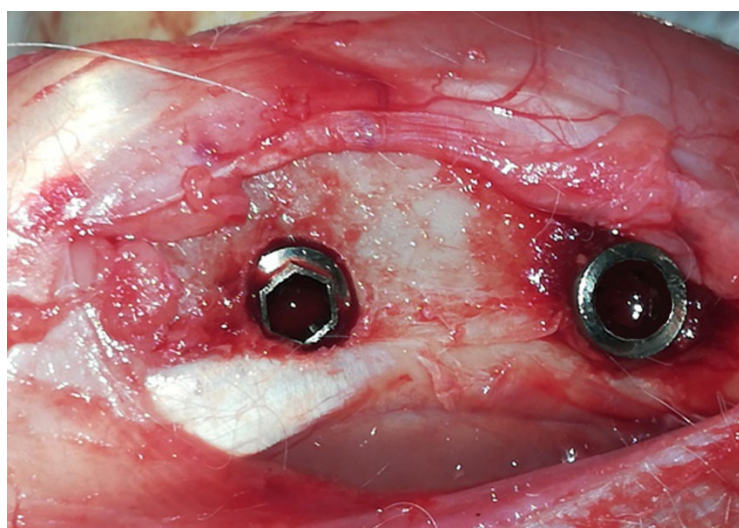
Figure 3. Representative image of the two implants installed in the tibia, in a proximal site (approximately 1 cm away from the joint) and another approximately 1 cm distally.

These implant installation positions were determined to reduce possible differences in the anatomical characteristics of the bone (amount of medullary and cortical bone), as in this area the tibia has a greater amount of medullary bone and less cortical bone [4]. The distribution was determined using free software (available at www.randomizer.org).

All animals were anesthetized with an intramuscular injection of 0.35 mg/kg of ketamine (Ketamina Agener®; Agener União Ltd.a., São Paulo, Brazil) and 0.5 mg/kg of xylazine (Rompum® Bayer S.A., São Paulo, Brazil). Initially, a total incision was made from the proximal joint towards the distal of approximately 4 cm. Afterwards, the bone tissue was exposed, and drilling was carried out using the drill sequence and speed recommended by the manufacturer for each implant design, under intense irrigation with physiological solution. The implants were installed manually using a surgical torque wrench with an approximate torque of 15 Ncm. Finally, the tissues were sutured with a single stitch using a nylon suture (Ethicon 3-0, Johnson & Johnson Medical, New Brunswick, USA). To control postoperative infection, a single intramuscular dose of 0.1 ml/kg of Benzetacil (Bayer, São Paulo, Brazil) was injected. While controlling pain and inflammation, three doses (one per day) of 3 mg/kg of ketoprofen (Ketoflex, Mundo Animal, São Paulo, Brazil) were administered. After a period of 3 and 4 weeks, the animals were sacrificed using an overdose of anesthetics (n = 5 animals per time). Then, both tibias of each animal were removed and duly identified, and these samples were immediately immersed in a 4% formaldehyde solution, where they remained for 7 days to begin the treatment sequence for inclusion in resin.

2.4. Implant Stability Quotient (ISQ) Measurement

Immediately after installation of each implant, a magnetic sensor (SmartPeg, Gothenburg, Sweden) was threaded and manually tightened to measure initial stability: sensor type 49 for Control group and, sensor type 1 for Collo group. These measurements were carried out using the Osstell device (Osstell AB, Gothenburg, Sweden), which indicates a value from 0 to 100 determining the implant stability quotient (ISQ). For each sample, measurements were taken in two directions (proximo-distal and antero-posterior), generating an average between these values. The ISQ was measured at three times for each sample, that is, immediately after installing the implants (Time 1) and immediately after removing the samples (Times 2 and 3).

2.5. Histological Preparation and Measurements

After 7 days of fixing the samples in formaldehyde solution, they were subjected to a sequence of alcohol in progressive concentrations (50-100%), for a period of 72 hours at each concentration, for dehydration. Then, all samples were embedded in historesin Technovit 7200 VLC (Kultzer & Co, Wehrhein, Germany) and polymerized. These historesin blocks containing the samples (bone and implants) were subjected to cutting in the central portion of each implant in a metallographic machine (Isomet 1000; Buehler, Germany), being subsequently fixed on the blades and sanded on a bench polisher (Polipan- U, Panambra Zwick, São Paulo, Brazil) using an abrasive paper sequence (180, 320, 600, 1000, and 1200 mesh). To stain the slides, these slides were rehydrated using a decreasing sequence of alcohol (100–50%), plus a 100% ethanol solution and hydrogen peroxide 10 vol in a 50:50 ratio. Then, all sample slices were stained by Picrosirius red-hematoxylin. Image series were acquired using light optical microscopy (Nykon E200, Tokyo, Japan).

In all samples, the percentage of bone–implant contact (BIC%) parameters were evaluated within 4 mm from the implant platform in the apical direction, as shown schematically in **Figure 4a**. Furthermore, in an area of 4 mm (from the implant platform towards the apical direction) by 0.7 mm (from the implant platform towards the native bone) the tissue area fraction occupancy (TAFO%) with anatomical characteristics of the newly formed tissue were evaluated, i.e., amount of newly formed bone, collagen matrix and medullary spaces present (**Figure 4b**). For both evaluations and measurements, ImageJ software (National Institute of Health, Bethesda, USA) was used.
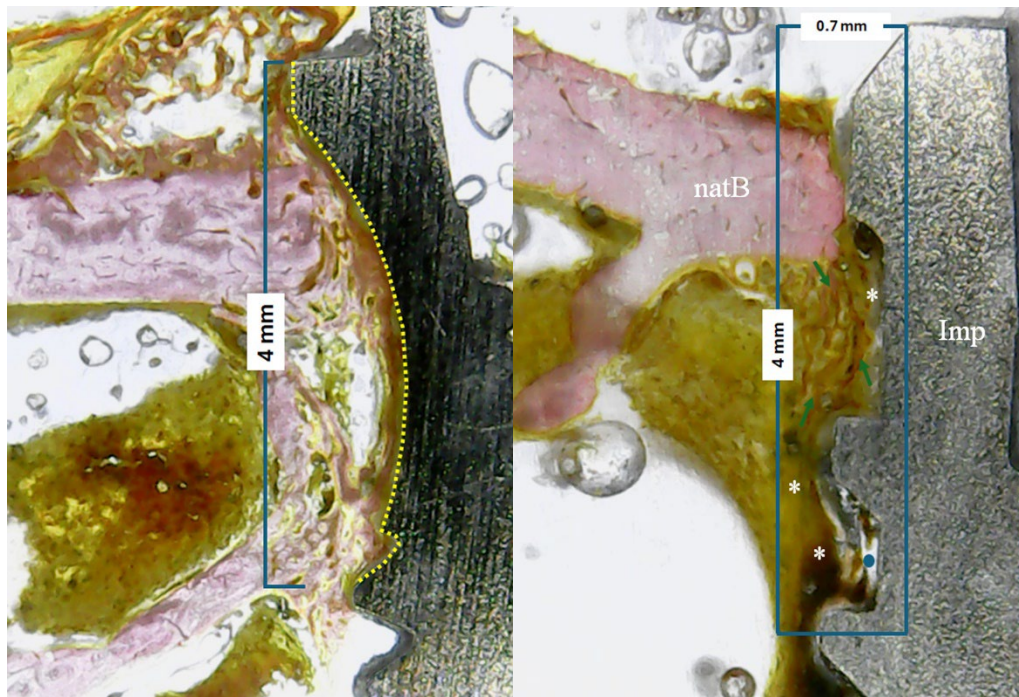
Figure 4. Representative images of the performed measurements. **(a)** BIC% in the 4 mm from the implant platform in an apical direction = yellow line; **(b)** Periimplant tissues occupancy in a rectangular area at 4 x 0.7 mm = inside of blue rectangle (natB = native bone; = new bone; * = collagen matrix; = medullary space).

2.6. Statistical Analysis

3. Results

No adverse events were observed during the healing period, such as inflammation and/or infection in the surgery area. All implants showed clinical stability at the percussion test, and radiographic signs of osseointegration during the predetermined evaluation period (3 and 4 weeks).

3.1. Implant Stability Quotient (ISQ) Results

The implant stability measured using Osstell® in the three evaluation periods is shown comparatively in Figure 5. Statistically, there were differences between the 3 times analyzed in both groups (ANOVA intragroup): for Control group $p = 0.0003$, and for Collo group $p = < 0.0001$. Intergroup (t-test), no statical differences were detected between the groups at Time 1 ($p = 0.9458$), and Time 2 ($p = 0.1103$). However, in the Time 3 $p = 0.0475$, showing statistical differences between the groups.
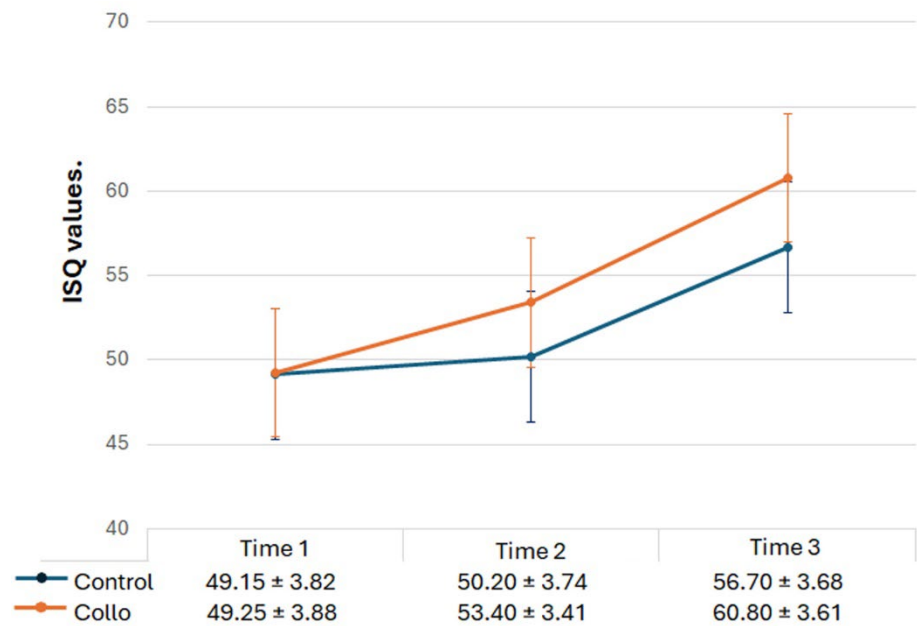
	Time 1	Time 2	Time 3
Control	49.15 ± 3.82	50.20 ± 3.74	56.70 ± 3.68
Collo	49.25 ± 3.88	53.40 ± 3.41	60.80 ± 3.61

Figure 5. Line graph showing the ISQ evolution for both groups at the 3 times predetermined for the evaluation. Time 1 = immediately of implant installation; Time 2 = 3 weeks after the implant installation; Time 3 = 4 weeks after the implant installation. Below are the averages and standard deviation of the values obtained in each group and time.

3.2. Histological Results

Higher BIC% values were presented in samples from the Collo group than in the Control group at both times. The data obtained (mean and standard deviation) and the statistical comparison calculated are graphically presented in Figure 6.
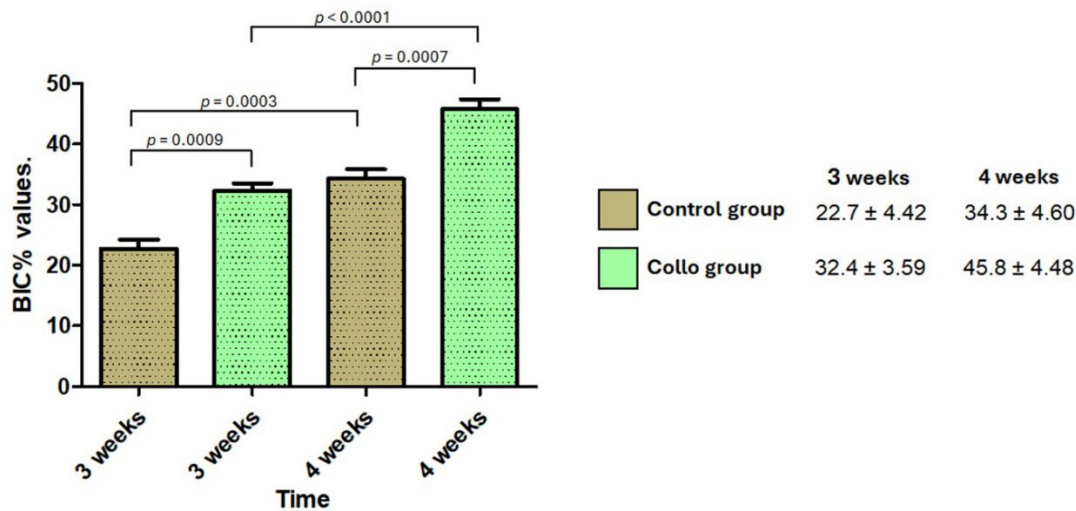

	3 weeks	4 weeks
Control group	22.7 ± 4.42	34.3 ± 4.60
Collo group	32.4 ± 3.59	45.8 ± 4.48

Figure 6. Bar graph showing the BIC% values and statistical differences between the groups. In right, the mean and standard deviation of both groups and times.

Figure 7 presented the mean and standard deviation of TAFO% values of the rectangle area in the cervical position, where the predetermined parameters were measured (new bone, collagen matrix, and medullary spaces). The statistical differences between the groups of the same parameters at each evaluation time are shown in the graph bar **(Figure 7)**.
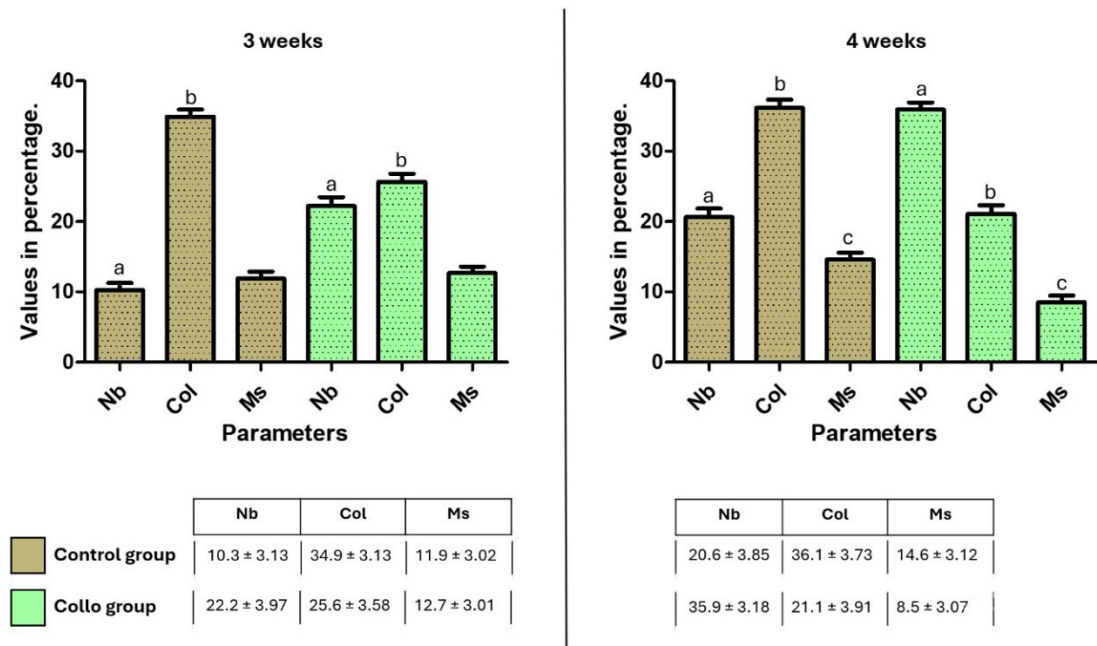
Figure 7. Bar graph showing the TAFO% values and statistical differences between the groups. a, b, and c determine the difference between the groups in the same parameter, in all cases p<0.001. Nb = new bone presence, Col = collagen matrix, Ms = medullary spaces. Below are the averages and standard deviation of the values obtained in each group and time.

4. Discussion

The present study presents a comparative analysis between a new implant design with changes in the cervical portion (Collo group) and a conventional implant (Control group), focusing on the initial stages of osseointegration in a pre-clinical trial. The main parameters evaluated were the initial stability of the implants (measured by ISQ) at the time of installation, in addition to stability at 3 and 4 weeks after installation. Additionally, histological analyzes were performed to evaluate the proportion of bone-implant contact (BIC%) and the tissue area fraction occupancy (TAFO%) of the predetermined cervical portion (initial 4 mm from the platform). The results revealed that the Collo group presented higher stability values (ISQ) both at the time of installation and in subsequent measurements after 3 and 4 weeks, compared to the Control group. Furthermore, histological evaluations demonstrated that the Collo group had a higher proportion of bone-implant contact (BIC%) and a higher rate of new bone formation (TAFO%) at both times analyzed. These findings are consistent with previous studies that suggest that macrogeometric changes in implants can exert a significant influence on the osseointegration process [4,15]. Furthermore, other studies have shown that changes in the macrogeometry and shapes of the external threads of dental implants are still topics that are widely explored in the literature [18–21].

Several studies on macrogeometric changes carried out focused on animal models, and most of them explored the biological mechanisms involved in the healing process with different surface treatments and macrogeometries [22–25]. The macrogeometry of implants is one of the factors that has the greatest influence on the primary stability of implants, on the initial torque and, consequently, promotes optimization of osseointegration [26]. The observation of positive results in tissue neoformation around the cervical portion of the implants in the Collo group in comparison with the Control group corroborates the results of other studies showing that the proposed change in the macrogeometry of the implants can have a significant impact on the osseointegration process [4,15,26]. Specifically, the more accelerated formation of peri-implant tissues was highlighted, attributed to the presence of an area of bone non-compression due to the formation of a healing chamber, as shown in **Figure 1**. Furthermore, previous studies have shown that the presence of clot

chambers in dental implants can optimize osseointegration [4,15,22,28]. These chambers promote an environment conducive to cell differentiation and tissue neoformation around the implant, which are essential for successful long-term osseointegration. Other studies have shown that in conjunction with appropriate surface treatments and adequate macrogeometry, it can accelerate healing and promote more effective osseointegration [27,28].

On the other hand, the bone portion in contact with the cervical area of the implant is characterized by the presence of cortical bone, which is directly related to the initial stability of the implants [29,30]. However, the cortical bone tissue presents anatomical characteristics with little vascularization compared to the medullary bone portion. Therefore, compression of this area (cortical) can cause unwanted effects, such as ischemia, necrosis and bone resorption [31,32]. Mosavar et al. [33] suggested that dense cortical bone, especially the bone adjacent to the first thread, experiences the maximum strain upon insertion and bears maximum compressive force and shear stresses. Thus, the new macrogeometry of Collo implants, forming a compression-free area on the cortical bone tissue, appears to be effective for healing events based on the results obtained.

Regarding stability measured through resonance frequency analysis using Osstell, which is an effective and non-invasive method [34], the initial values were similar for both groups, with no statistical difference between them. These findings demonstrate that the presence of the healing chamber, provided by the cervical design of the Collo group implants, did not reduce the initial ISQ values, as the final part of the implant platform (0.5 mm) is anchored in the cortical bone. In this sense, as demonstrated by other authors, contact with the cervical portion of the implant with the cortical bone favors initial stability [30]. At other predetermined times for measurements (3 and 4 weeks after the implantations), the values were higher for the Collo group compared to the Control group, corroborating findings from other studies that related changes in macrogeometry with the ISQ values obtained [4,15].

Another factor that macrogeometry is capable of influencing is the biomechanics and distribution of chewing loads [35]. However, studies have shown that primary stability may not be directly related to insertion torque [36]. Therefore, some authors question the correlation of high insertion torque with high rates of clinical success of dental implants [37], as it can result in high tension in the peri-implant region and, consequently, can provoke negative responses both biological and secondary stability. Therefore, macrogeometry stands out as one of the factors capable of directly interfering in the osseointegration of dental implants, enabling a reduction in loading time [4,15,38].

Finaly, it is important to highlight that this study is a preclinical trial, and results observed under controlled conditions may vary in a real clinical setting, where additional factors such as individual patient characteristics, oral health conditions and implantation techniques may influence the results. Furthermore, it is essential to consider that this study was conducted in a controlled preclinical environment, and results may vary in real clinical conditions, where factors such as individual patient characteristics and implant installation techniques may influence results. Subsequent clinical studies are needed to confirm the applicability of these findings in everyday dental practice and to evaluate the long-term effectiveness of this new implant design.

5. Conclusions

Within the limitations of the present pre-clinical study, the results of this study suggest that the new implant design with changes in the cervical portion (Collo group) presents significant advantages in relation to the conventional implant (Control group), regarding stability in the initial times and osseointegration. Subsequent clinical studies are needed to validate these findings and verify their large-scale clinical applicability.

Author Contributions: Conceptualization, Sergio Alexandre Gehrke, Marco Aurélio Bianchini and Piedad De Aza; Data curation, Sergio Alexandre Gehrke, Guillermo Cortellari, Marco Aurélio Bianchini, Antonio Scarano and Piedad De Aza; Formal analysis, Sergio Alexandre Gehrke and Marco Aurélio Bianchini; Investigation, Sergio Alexandre Gehrke, Guillermo Cortellari, Jaime Aramburú Júnior and Tiago Luis Eirles Treichel; Methodology, Sergio Alexandre Gehrke, Guillermo Cortellari, Jaime Aramburú Júnior, Tiago Luis Eirles Treichel and Antonio Scarano; Validation, Piedad De Aza; Writing – original draft, Sergio Alexandre Gehrke, Jaime

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