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CLINICAL RESEARCH

Impact of macrogeometry on the primary stability and bone markers of dental implants: A prospective, controlled, randomized, split-mouth clinical study

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ABSTRACT

Statement of problem. With advances in implant dentistry, interest in macrogeometries such as healing chambers, and surface treatments designed to improve or accelerate osseointegration has been growing; however, clinical evidence regarding the impact of macrogeometry on the osseointegration process is lacking

Purpose. The purpose of this randomized, double-blind, split-mouth clinical trial was to evaluate the impact of dental implants with modified macrogeometry with healing chambers on peri-implant bone repair by analyzing resonance frequency compared with conventional macrogeometry implants.

Material and methods. Eighteen participants with bilateral posterior edentulism were enrolled and received an implant with modified macrogeometry (test group) or a conventional implant (control group). Insertion torque was recorded at the time of surgery. Primary stability was measured immediately after implant placement and at 45 and 90 days. Peri-implant fluids were collected at 7, 14, 30, and 90 days to analyze bone markers. Insertion torque was analyzed by using the paired *t* test (α=.05). Generalized linear mixed models for time repeated measures were used to analyze the implant stability quotient (ISQ) and immunoenzymatic variables (α=.05).

Results. Insertion torque was significantly lower in the test group ($P<.05$), but no significant difference in primary stability was found between the groups ($P>.05$). Regarding bone markers, Necrosis Factor-Alpha (TNF-α) levels were significantly lower in the test group ($P<.05$), with no statistically significant differences for the other markers analyzed ($P>.05$).

Conclusions. The modified macrogeometry of dental implants performed similarly to conventional macrogeometry in terms of the primary stability and temporal evolution of osseointegration, even at lower initial insertion torque levels. The reduction in TNF-α levels observed in the test group suggested lower osteoclastic activity, which may represent a more favorable biological environment for peri-implant bone repair. (J Prosthet Dent xxxx;xxx:xxx-xxx)

Dental implants have been widely used to replace missing teeth in partially and completely edentulous patients. High long-term success rates for dental implants have been reported,[1–5] with about 99% success in the mandible and 90% in the maxilla over a 10- to 15-year period.[1–3] While implant survival rate refers to the

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Clinical Implications

Implants with modified macrogeometry may achieve stability and clinical performance similar to those of conventional designs, even with a lower insertion torque.

percentage of implants remaining in the mouth, regardless of complications,[6,7] the definition of success encompasses factors that include biological stability, characterized by the absence of soft and hard tissue loss associated with infection or overload, mechanical stability, a reflection of the lack of fractures, loosening, or damage to prosthetic components, and hygiene accessibility.[6]

Primary stability has been reported to be crucial for implant success,[8–13] particularly in areas of low bone density, in early loading protocols, and in individuals with systemic diseases. Primary stability refers to the absence of micromovements and is influenced by the intimate contact between the implant surface and bone[4,5,14–16] and depends on factors that include bone density, implant macrogeometry, surface characteristics, and osteotomy technique.[17–20] Previous studies[19,21,22] have identified implant macrogeometry as a key determinant of primary stability, particularly where bone volume is limited. Systemic factors may also negatively affect osseointegration quality,[23] either through medication use or metabolic disorders.

The primary stability conferred by implant macrogeometry has been reported to be gradually replaced by secondary stability resulting from osseointegration.[12,24] The primary stability decreases 2 to 4 weeks after implant placement, while secondary stability has not yet fully developed, resulting in a temporary reduction in overall stability.[17,21,25] However, there is also evidence that macrogeometry can positively influence secondary stability,[24] as certain macrogeometries can create spaces, referred to as healing chambers, between the implant and the surgical bed; these can reduce bone compression, minimizing trauma to the site.[25–27] After placement, these chambers are immediately filled with blood clots and have been considered biologically valuable for secondary stability as they promote earlier osteogenic activity.[24,25,28] The nature of the repair process in these chambers and the strategies to enhance primary and secondary stability have been demonstrated in implants with modified macrogeometry.[19,25] Bone regeneration in these situations has been reported to occur via intramembranous ossification, enabling direct new bone formation on the implant surface and thereby reducing the need for appositional bone formation.[29]

However, as evidence regarding the impact of macrogeometry on the osseointegration process is limited, this study compared the effect of modified implant macrogeometry and conventional implant designs on peri-implant bone repair. The null hypothesis was that the peri-implant bone repair of dental implants with modified macrogeometry with healing chambers would not differ from those with conventional macrogeometry.

MATERIAL AND METHODS

This clinical study followed a randomized, double-blind, split-mouth design to evaluate implant stability in participants with bilateral missing teeth during a 3-month evaluation period at Universidade Paulista (UNIP) (ReBEC identifier: RBR-63jtrzs). This study followed the Consolidated Standards of Reporting Trials (CONSORT) guidelines.[30] The selection and treatment of the participants were carried out following the ethical requirements established by the university's Research Ethics Committee (12461319.9.0000.5512). Eighteen participants were enrolled from those who sought treatment at the Postgraduate Clinics of UNIP.

The inclusion criteria were participants of either sex between 18 and 75 years old, with partial bilateral edentulism of the mandible or maxilla and with sufficient bone volume and height for implant placement. The exclusion criteria were the use of medications such as antibiotics, continuous anti-inflammatory agents, phenytoin, cyclosporine, or bisphosphonates within the 6 months prior to the study; the presence of systemic alterations and diseases that prevented the surgical procedure (such as infectious diseases, diabetes, heart disease, or hepatitis), history of radiotherapy in the head or neck region, history of treatment with bisphosphonates, smoking, pregnancy, breastfeeding, or lack of prosthetic height. The risks and benefits of the research were explained to each participant (Resolution No. 196 of October 1996 and the Code of Professional Dental Ethics 179/93), and the participants signed formal consent to participate in the study.

The participants received 2 implants following the split-mouth design. The side to receive the test implant was allocated randomly within each group using a computer-generated list and was stored in an opaque brown envelope in the care of an individual (R.M.M.-M.) different from the operator (M.Z.C.) and the evaluator (A.M.C.). Only the operator knew which implant was inserted on each side. The participants and the evaluator remained blind to the location of the implants, allowing the study to be characterized as double-blind following the CONSORT standards.[30] At the initial clinical visit, all participants were screened, including a medical and dental history questionnaire and a clinical assessment. Cone beam computed tomography (CBCT) scans were obtained for all participants to assess the anatomic suitability of the edentulous sites for implant placement.

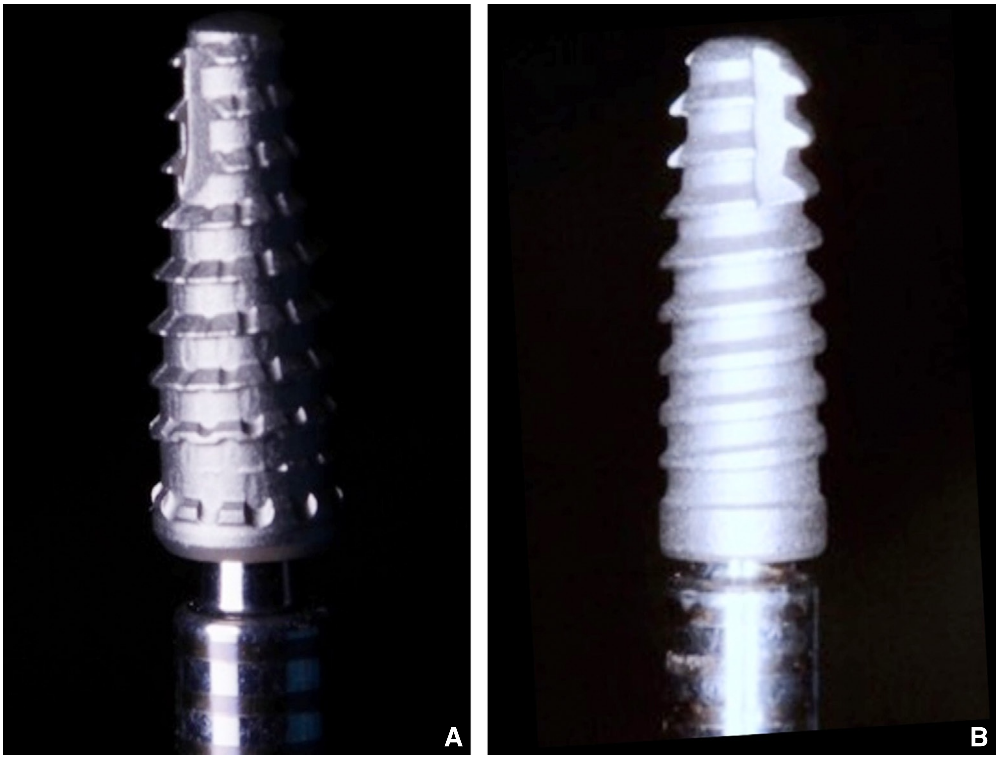

Figure 1. Types of implants used. A, With modified macrogeometry. B, With conventional macrogeometry.

A power analysis to determine the significance of the sample was performed using the *t* test with a software program (G*Power 3.1.9.7; Heinrich-Heine-Universität Düsseldorf). The sample size calculation was based on the results of a previous study[28] using the means and standard deviation at 7 days for the primary variable, the implant stability quotient (ISQ), with an 80% power, and a 5% alpha error. It indicated the need for 14 participants, and 20% was added due to the risk of loss of follow-up, totaling 18 participants.

Each participant received 2 dental implants with Morse taper connections. The implants were manufactured from commercially grade IV pure titanium (ASTM F67; Implacil de Bortoli). The surfaces were airborne-particle abraded with titanium (approximately 150 μm), and after ultrasonic cleaning in organic solvents and acids, they were rinsed with pure water under cleanroom conditions. The 2 groups were the test group (n=18) – Morse cone implants with modified macrogeometry (Maestro Implant; Implacil de Bortoli) that featured a thread design with healing chambers (Fig. 1A) and the control group (n=18) **–** Morse cone implants with conventional macrogeometry that exhibited a conventional thread design without healing chambers (Due Cone Implant; Implacil de Bortoli) (Fig. 1B). In both groups, implants with diameters of 3.5 mm or 4.0 mm and lengths ranging from 7 mm to 10 mm were used according to the bone availability at the site.

Under local anesthesia, the implant beds were prepared according to the manufacturer's instructions (Fig. 2). The surgeries were performed by the same experienced operator (M.Z.C.). After measuring the ISQ and insertion torque at the baseline, healing caps were inserted so that the gingival level was positioned apically at the total height of the healing cap. The site was sutured with nylon suture (4.0 Ethicon; Ethicon US, LLC), which was removed after 7 days. Supragingival biofilm control was performed with 0.12% chlorhexidine mouthwash for 10 days after the surgical procedure. Presurgical anti-inflammatory therapy (dexamethasone 4 mg, single dose, 1 hour before the procedure), presurgical antibiotic (amoxicillin 2 g 1 hour before the procedure)[31] and postoperative analgesia (sodium dipyrone 500 mg every 4 hours for 2 days) were provided. The insertion torque measurements were obtained during implant installation and were performed in triplicate on all implants by the same calibrated examiner (A.M.C.). Additionally, the primary stability was assessed using resonance frequency analysis (Osstell; Integration Diagnostics AB) after implant installation and repeated 45 and 90 days after the implant installation surgery. The measurements were obtained in ISQ.[32–34]

The peri-implant fluid collection was performed by the same professional (A.M.C.) in each group for the immunoenzymatic analysis. Two sites were selected per implant (mesial and distal), with 2 implants on each side and the gingival fluid samples were collected at 7, 14, 30, and 90 days after implant installation. The gingival fluids were

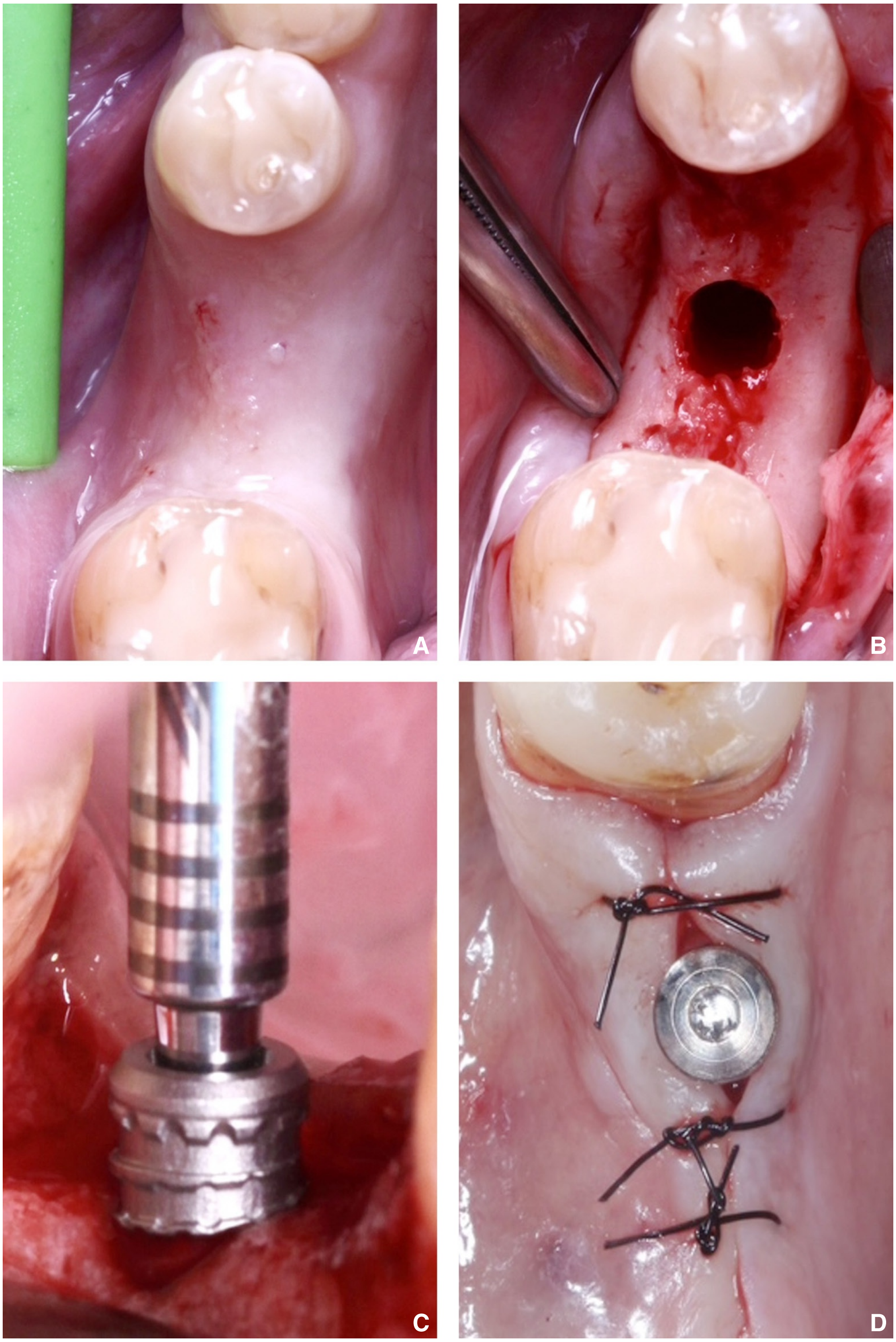

Figure 2. Operative sequence. A, Preoperative. B, Recipient bed. C, Implant insertion. D, Sutured.

obtained using paper strips (Periopaper; Oraflow Inc) inside the periodontal tissue interface for 30 seconds.[35] Aliquots of each gingival fluid sample were analyzed for detection of Dickkopf-1 (DKK1), Tumor Necrosis Factor-Alpha (TNF-α), osteoprotegerin (OPG), osteocalcin (OC), osteopontin (OPN), osteonectin, Tartrate-Resistant Acid Phosphatase 5 (TRAP-5), Tumor Necrosis Factor-Like Weak Inducer of Apoptosis (TWEAK), and Receptor Activator of Nuclear Factor Kappa B Ligand (RANKL) (HRNKLMAG-31K-0; Millipore Corp) using the LUMINEX/MAGpix platform. The mean concentration of each biomarker was calculated and expressed as pg/mL. Samples with quantification below the detection limit of the analysis were recorded as zero, and samples above the quantification limit of the standard curve were recorded with a value equal to the highest value of the curve.

Descriptive and exploratory data analyses were performed. Based on these analyses, the statistical methodologies applied for the inferential analysis of each variable were defined. Insertion torque was compared between sides (implant type) using the paired *t* test. Generalized linear mixed models for time repeated measures were used to analyze the ISQ and immunoenzymatic variables. The main effects of treatment (implant type) and time, as well as the interaction between them, were evaluated in the models. The models accounted for the dependence between evaluations, that is, the fact that both treatments were evaluated in the same participants using a split-mouth approach. Thus, in all models, the participant was treated as an experimental unit (plot), and the participant's sides were subplots. The treatment effect was specified as a within-patient factor (dependent or correlated observations), and the time factor as a repeated measures factor assessed in the same subplots. All analyses were performed in a statistical software package (R; The R Foundation for Statistical Computing) (α=.05).

Table 1. Descriptive analysis of patient's profile variables (n=16)

Sex, n (%)	
Feminine	10 (62.5%)
Masculine	6 (37.5%)
Age	
Mean Age (standard deviation)	45.6 years (11.7)
Minimum and maximum age	27 to 68 years
Adult, n (%)	14 (87.5%)
Elderly, n (%)	2 (12.5%)
Test Teeth (modified macrogeometry), n (%)	
Maxillary right first premolar	2 (12.5%)
Maxillary left second premolar	1 (6.2%)
Mandibular left first premolar	1 (6.2%)
Mandibular left second premolar	1 (6.2%)
Mandibular left first molar	1 (6.2%)
Mandibular right first premolar	1 (6.2%)
Mandibular right second premolar	1 (6.2%)
Mandibular right first molar	8 (50%)
Control Teeth (conventional macrogeometry), n (%)	
Maxillary right second premolar	1 (6.2%)
Maxillary left first premolar	2 (12.5%)
Mandibular left first premolar	1 (6.2%)
Mandibular left second premolar	1 (6.2%)
Mandibular left first molar	8 (50%)
Mandibular right first premolar	1 (6.2%)
Mandibular right second premolar	1 (6.2%)
Mandibular right first molar	1 (6.2%)
Implant dimensions, n (%)	
3.5×7 mm	2 (6.2%)
3.5×9 mm	18 (56.2%)
4×10 mm	12 (37.5%)

RESULTS

Two implants were lost in each group because of failed osseointegration, giving an 88.9% implant survival rate in each group. For the statistical analysis, 16 participants were considered (Fig. 3). Table 1 presents the descriptive analysis of the sample profile variables, the distribution of sites (teeth) in each group and the implant dimensions. No statistically significant interaction was found between implant and time (P>.05) in any assessed variable. The mean torque was significantly greater in the control group (P<.05) (Table 2). In the ISQ analysis,

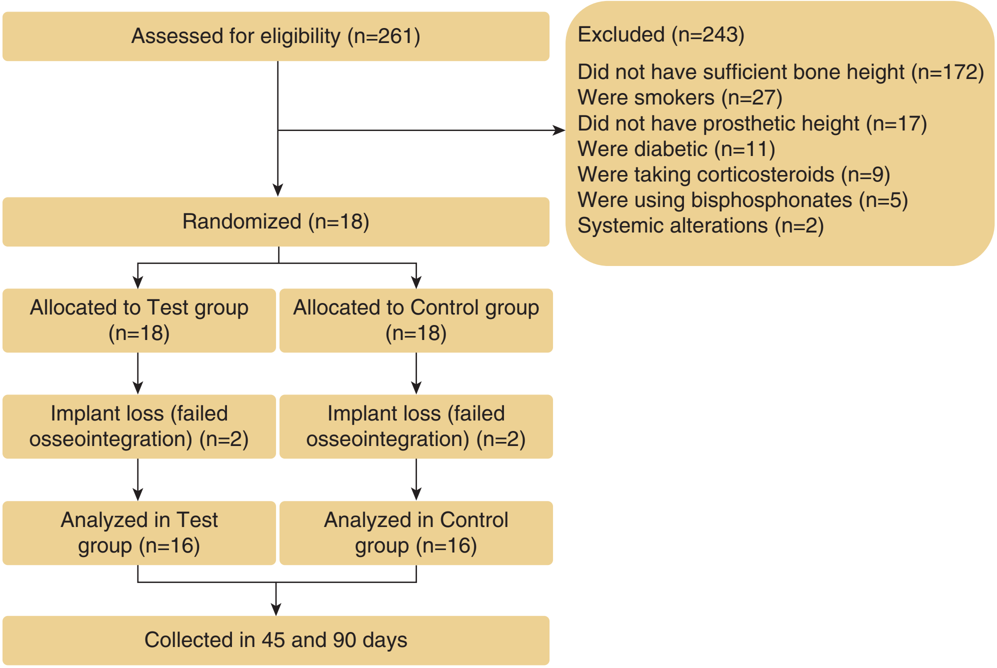

Figure 3. CONSORT flow diagram of participant assessment throughout trial.

Table 2. Insertion torque (N) detected in both groups

	Test	Control
Mean (standard deviation)	25.75 (11.15) B	32.25 (11.78) A
Quartile 25%	15.00	25.00
Median	20.00	30.00
Quartile 75%	35.00	35.25

Different letters indicate statistically significant differences (*P*=.014).

the baseline time was considered as a covariate in the model, and no significant differences were observed between the groups or time points (*P*<.05) (Table 3). Table 4 presents the results of the immunoenzymatic analysis. Regardless of the group, the levels of DKK1, TRAP-5, and TWEAK were significantly higher at 90 days than at the previous time points (*P*<.05). TNF-α levels were significantly lower in the test group (*P*<.05). In both groups, the TNF-α levels decreased at 14 days and increased again at 90 days (*P*<.05). The OPG level, in both groups, increased significantly at 30 and 90 days (*P*<.05). It was also observed that the OC and RANKL levels increased significantly at 14 and 90 days (*P*<.05), regardless of the group. The OPN level increased significantly over time (*P*<.05) in both groups. Furthermore, it was observed that the osteonectin level increased at 30 and 90 days, also in both groups (*P*<.05).

DISCUSSION

The present study provided valuable insights by evaluating the early peri-implant healing response in humans by analyzing mechanical parameters and bone-related biomarkers. While previous studies have assessed implant macrogeometry in preclinical models, few have explored this issue clinically, particularly from a molecular perspective.[25,32,33] The use of peri-implant crevicular biomarkers, such as those related to osteoimmunology, enabled a deeper understanding of the cellular dynamics underlying osseointegration.[4,35] The interest in macrogeometries and surface treatments designed to improve or accelerate osseointegration has been growing.[15,25] Hence, the present study compared the insertion torque, primary stability, and levels of bone biomarkers of implants with modified and conventional macrogeometries. The null hypothesis that the peri-implant bone repair of dental implants with modified macrogeometry with healing chambers would not differ from those with conventional macrogeometry was rejected since the modified macrogeometry demonstrated a reduction in TNF-α levels and a significantly lower insertion torque (*P*<.05).

Insertion torque has been closely related to primary stability and, consequently, to the success of osseointegration.[8,15] However, excessive torque may compress the blood vessels surrounding the implant, potentially impairing or delaying early osseointegration[8,33] because of initial bone necrosis followed by remodeling. Torque levels have also been reported to influence the release of angiogenic and bone remodeling markers,[4] suggesting that implants inserted with lower torque may accelerate osseointegration. Implants inserted with torque up to 30 Ncm were shown in an animal study to have greater contact with mineralized bone.[16] Conversely, another study has reported increased expression of bone formation markers at later healing stages (120 days) in implants inserted at a torque above 45 Ncm.[4] Implants with modified macrogeometry, such as the Maestro design used in the present study, incorporate interthread spaces referred to as healing chambers, which reduce the need for high insertion torque by limiting implant-bone compression and preserving vascular integrity.[9,32] These features have been reported to allow the maintenance of bone vitality at the implant interface and to facilitate new bone formation within the healing chambers.[4,25,26] Consequently, lower insertion torque in this context does not compromise osseointegration; instead, it may enhance early bone healing and accelerate the biological progression of osseointegration as evidenced by the higher removal torque values reported in an early animal study.[32] Overall, the biological benefit is primarily driven by implant design rather than torque alone, emphasizing the synergistic role of macrogeometry and mechanical stimulus in optimizing peri-implant bone repair.[4]

Although no statistically significant difference in primary stability was observed between implants, the test implants achieved similar stability values with significantly lower insertion torque. These findings were consistent with those of previous studies which supported lower torque as being beneficial during the early phases of healing.[10,11] While insertion torque and primary stability have traditionally been associated with long-term success, the literature remains inconclusive

Table 3. Resonance Frequency Analysis - ISQ (N/cm) data, considering baseline time as covariate in model.

	Test		Control	
	Mean (Standard Deviation)	Median (Quartile 25% and Quartile 75%)	Mean (Standard Deviation)	Median (Quartile 25% and Quartile 75%)
45 days	68.43 (8.34) Aa	72.00 (62.00; 73.83)	72.45 (6.48) Aa	73.17 (68.33; 77.33)
90 days	69.95 (8.04) Aa	69.50 (64.66; 77.50)	72.41 (6.15) Aa	72.83 (68.83; 77.33)

Different uppercase letters in row indicate statistically significant intergroup differences (*P*<.05). Different lowercase letters in column indicate statistically significant intragroup differences (*P*<.05). *P*(implant)=.363; *P*(time)=.316; *P*(interaction)=.291.

Table 4. Results of immunoenzymatic analysis

	Time (Days)	Test		Control		*P* value
		Mean (Standard Deviation)	Median (Quartile 25% and Quartile 75%)	Mean (Standard Deviation)	Median (Quartile 25% and Quartile 75%)	
DKK1	7	22.87 (17.45) Ab	20.21 (10.98; 30.01)	19.12 (14.3) Ab	18.28 (4.78; 30.74)	*P*(implant)=.680
	14	31.58 (31.55) Ab	29.9 (1.44; 51.31)	28.47 (28.48) Ab	16.84 (6.82; 47.22)	*P*(time)=.012
	30	21.35 (20.14) Ab	13.57 (2.83; 37.02)	31.62 (27.00) Ab	18.38 (14.61; 56.80)	*P*(interaction)=.222
	90	89.01 (60.91) Aa	68.17 (44.78; 162.21)	214.65 (192.98) Aa	176.66 (27.87; 368.43)	
TNF-α	7	4.19 (4.89) Bb	1.6 (0.61; 7.09)	13.16 (19.14) Ab	5.2 (1.71; 10.94)	*P*(implant)=.042
	14	1.69 (1.94) Bc	1.29 (0.49; 2.31)	4.11 (5.31) Ac	1.41 (0.91; 6.73)	*P*(time)=.008
	30	1.69 (2.94) Bc	0.82 (0.57; 1.29)	3.41 (4.64) Ac	1.63 (1.03; 3.52)	*P*(interaction)=.418
	90	23.72 (25.21) Ba	20.11 (2.51; 34.3)	77.86 (97.87) Aa	32.78 (2.43; 120.79)	
OPG	7	2.20 (3.43) Abc	0.46 (0.21; 3.48)	4.13 (5.48) Abc	2.18 (0.29; 6.99)	*P*(implant)=.156
	14	1.68 (1.91) Ac	1.04 (0.71; 1.81)	1.97 (2.31) Ac	1.05 (0.65; 2.26)	*P*(time)=.015
	30	2.75 (2.95) Ab	1.47 (1.07; 3.67)	4.78 (4.92) Ab	2.95 (2.08; 6.70)	*P*(interaction)=.356
	90	16.37 (14.52) Aa	13.21 (6.52; 20.36)	13.97 (16) Aa	7.28 (2.70; 19.86)	
OSTEOCALCIN	7	0.47 (0.27) Ac	0.43 (0.27; 0.54)	0.52 (0.29) Ac	0.41 (0.30; 0.66)	*P*(implant)=.199
	14	0.96 (0.94) Ab	0.80 (0.33; 0.96)	0.58 (0.26) Ab	0.58 (0.41; 0.74)	*P*(time)=.001
	30	1.05 (0.76) Ab	0.78 (0.63; 1.8)	0.73 (0.41) Ab	0.67 (0.49; 0.87)	*P*(interaction)=.412
	90	3.94 (4.52) Aa	1.62 (1.31; 5.48)	3.16 (2.42) Aa	2.42 (1.33; 4.14)	
OSTEOPONTIN	7	0.32 (0.16) Ad	0.25 (0.20; 0.39)	0.26 (0.17) Ad	0.20 (0.15; 0.29)	*P*(implant)=.571
	14	0.42 (0.19) Ac	0.43 (0.27; 0.55)	0.55 (0.44) Ac	0.47 (0.24; 0.68)	*P*(time)=.006
	30	0.57 (0.35) Ab	0.47 (0.33; 0.78)	0.77 (0.58) Ab	0.57 (0.46; 1.33)	*P*(interaction)=.570
	90	1.99 (1.98) Aa	1.29 (0.93; 2.13)	2.90 (3.47) Aa	1.63 (1.14; 2.63)	
OSTEONECTIN	7	0.21 (0.12) Ac	0.15 (0.13; 0.27)	0.25 (0.30) Ac	0.14 (0.10; 0.25)	*P*(implant)=.300
	14	0.28 (0.16) Ac	0.21 (0.14; 0.42)	0.40 (0.34) Ac	0.34 (0.13; 0.52)	*P*(time)=.025
	30	0.43 (0.28) Ab	0.38 (0.22; 0.53)	0.53 (0.38) Ab	0.44 (0.23; 0.62)	*P*(interaction)=.368
	90	2.76 (3.91) Aa	0.92 (0.53; 3.23)	1.38 (1.29) Aa	0.89 (0.69; 1.70)	
TRAP-5	7	50.24 (50.53) Ab	36.32 (3.38; 101.72)	50.3 (44.87) Ab	37.36 (15.82; 81.36)	*P*(implant)=.889
	14	54.49 (66.11) Ab	31.32 (7.86; 74.87)	37.80 (36.57) Ab	25.59 (13.77; 57.05)	*P*(time)=.015
	30	31.15 (52.53) Ab	12.59 (3.27; 27.8)	42.69 (61.22) Ab	18.09 (12.43; 33.66)	*P*(interaction)=.816
	90	413.28 (382.8) Aa	242.59 (110.37; 703.63)	296.94 (273.84) Aa	219.76 (108.45; 481.23)	
TWEAK	7	0.13 (0.16) Ab	0.07 (0.04; 0.14)	0.12 (0.14) Ab	0.07 (0.04; 0.18)	*P*(implant)=.188
	14	0.19 (0.3) Ab	0.11 (0.06; 0.2)	0.12 (0.15) Ab	0.07 (0.05; 0.14)	*P*(time)=.002
	30	0.10 (0.08) Ab	0.08 (0.04; 0.11)	0.11 (0.07) Ab	0.08 (0.06; 0.16)	*P*(interaction)=.382
	90	0.95 (0.86) Aa	0.85 (0.36; 1.03)	0.83 (0.84) Aa	0.54 (0.28; 1.06)	
RANKL	7	7.41 (3.21) Ac	6.88 (5.39; 8.76)	6.31 (3.76) Ac	4.61 (3.7; 9.53)	*P*(implant)=.448
	14	14.86 (14.98) Ab	8.8 (7.07; 16.98)	14.66 (9.97) Ab	13.2 (6.61; 20.44)	*P*(time)=.0004
	30	19.19 (23.31) Ab	11.27 (7.45; 19.85)	16.77 (11.97) Ab	11.13 (8.47; 25.05)	*P*(interaction)=.820
	90	43.61 (36.49) Aa	31.29 (19.24; 75.52)	39.03 (25.86) Aa	29.25 (23.44; 43.70)	

Different uppercase letters in row indicate statistically significant intergroup differences (*P*<.05). Different lowercase letters in column indicate statistically significant intragroup differences (*P*<.05).

because of the limited precision of current measurement techniques, which may not fully reflect histological healing.[12,33] These findings corroborate those of previous randomized clinical trials that reported that modified macrogeometry did not influence primary stability or peri-implant health in 42[28] and 90[24] days. Although statistical differences were not found between the implants, the clinical benefit of modified implants may still be relevant because the healing chambers may enhance osseointegration and allow for earlier prosthetic loading.[28] However, this results must be interpreted with caution, because in situations with compromised bone quality or immediate loading protocols, a minimum threshold of mechanical stability must be achieved to ensure successful osseointegration.[17] Thus, while lower torque may be advantageous in standard treatments, its indication in demanding clinical scenarios requires further investigation.

Although gingival crevicular fluid primarily reflects soft tissue activity, it has been increasingly recognized as a valuable source of biomarkers of peri-implant bone remodeling.[4,35] By analyzing it at 7, 14, 30, and 90 days, the temporal dynamics of bone formation and remodeling was captured along with the implant stability induced by each implant design,[4,35] especially considering that torque and stability values can vary based on bone density.[17] In the present study, only TNF-α levels were significantly lower in the test group, suggesting a reduced early inflammatory response, reduced osteoclastic activity, and a more favorable environment for bone repair.[4,35] Furthermore, a previous study[35] has reported that elevated TNF-α levels can negatively influence implant stability and osseointegration as they enhance osteoclastic activity.

The progressive increase in OPG and RANKL levels in both groups reflects the activation of bone remodeling pathways. This dynamic underscores the role of the OPG/RANKL axis in regulating osteoclast differentiation, consistent with the transition from early inflammatory phase toward tissue remodeling.[4] Similarly, DKK1 levels, which peaked later in the timeline in both groups, highlight its role as a Wnt signaling antagonist secreted by osteocytes during the shift from initial bone formation to remodeling.[4] In parallel, the gradual rise in OPN and OC, also in both groups, indicated the ongoing mineral deposition and maturation of bone matrix. Osteonectin followed the same trajectory, with a marked elevation at 90 days, supporting its involvement in late-stage matrix organization. TNF-α decreased more rapidly in the test group compared with the control at 14 and 30 days, suggesting a faster resolution of inflammation, although both groups again displayed an increase by 90 days. This may reflect a transient modulation of the inflammation in the test group that could be biologically advantageous. The absence of significant intergroup differences for most biomarkers suggested a comparable molecular response between the groups and demonstrated similar temporal osseointegration patterns, characterized by an early inflammatory phase followed by progressive mineralization and matrix maturation. These findings suggest that osseointegration involves a regulated balance between pro- and anti-osteogenic signals.[35]

It is possible that the 90-day follow-up period was insufficient to capture divergence between groups, especially for late-stage remodeling markers such as OPG.[35] Additionally, even with the lower levels of TNF-α in the test group, no significant differences were found in the primary stability between implant design. However, a previous study showed that TNF-α high levels are related to lower implant stability.[35] While this study did not identify this correlation, it remains plausible that individual variations in inflammatory or bone metabolic responses may influence stability. Previous studies have suggested that molecular changes may precede gains in mechanical stability.[4,35] Thus, correlational analyses in larger samples could provide insights and contribute to individualized planning.

The findings from this study are also consistent with those of previous studies using synthetic bone blocks, which reported higher residual bone fragments around implants with modified macrogeometry.[32] These fragments, transported into the healing chambers during implant insertion, may support early bone regeneration and enhance primary stability. This may have contributed to the comparable stability observed in the test group despite the lower torque and suggests that implant macrogeometry can compensate for limitations in surface treatment or low bone density.[32,34] Also, all participants in this study were healthy, which may have limited the detection of differences. In participants with systemic conditions, such as diabetes or those who smoke, macrogeometry may play a critical role, since certain medications and diseases negatively influence early osseointegration.[13] A previous randomized clinical trial reported that macrogeometry modification in implants with nonactivated surfaces led to the higher production of bone and angiogenic markers in smokers, positively impacting early stabilization.[34]

Limitations of the study included the short follow-up period, which may have reduced the power to detect subtle differences, particularly for biomarker levels. Moreover, the biomarker analysis was restricted to a finite number of bone markers. These limitations underscore the need for future clinical studies to incorporate broader biomarker panels, including histological or microtomographic assessments, to confirm clinical observations and better characterize tissue responses associated with different implant macrogeometries and extended follow-up periods.

CONCLUSIONS

Based on the findings of this randomized clinical trial, the following conclusions were drawn:

1. The modified macrogeometry demonstrated clinical performance comparable with that of conventional designs in terms of primary stability and osseointegration dynamics, even at lower insertion torque levels.
2. The observed reduction in TNF-α levels in the test group may indicate a more favorable biological response, potentially promoting balanced bone remodeling.

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