Influence of Restorative Design on the Progression of Peri-implant Bone Loss: A Retrospective study

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Abstract

Background and Aim: Clinical data on the restorative designs affecting the early progression of peri-implantitis is scarce. The aim of this retrospective study was to evaluate the influence of several restorative factors (e.g., restoration emergence angle, and internal screw length/diameter) on the marginal bone loss around implants with peri-implantitis.

Materials and methods: Implants diagnosed with peri-implantitis having 1- (T1) and 2-year (T2) follow-ups were included. In addition, within 6 months pre-diagnosis (Tb), all cases required to have full documentation in which no evidence of peri-implantitis was not indicated. Changes in marginal bone levels (MBLs) from Tb to T1 and from T1 to T2 were evaluated. The effect of several variables on MBLs changes was assessed via uni- and multi-variate generalized estimating equations.

Results: Eighty-three bone-level implants from 65 patients were selected. The mean follow-up before peri-implantitis diagnosis was 99.47 ± 47.93 months. The radiographic mean marginal bone loss was 1.52 ± 1.33 mm (Tb to T1) and 0.58 ± 0.52 mm (T1 to T2). Restoration emergence angle and frequency of maintenance visits significantly affected MBLs from Tb to T1. Besides, 66.3% of the included implants' bone levels were in a zone within 1 mm of the apical end of the internal screw at T1 and remained in this zone during the second follow-up year.

Conclusion: Significant marginal bone loss occurred in the early post-diagnosis period of peri-implantitis, which could be affected by the restoration emergence angle. Peri-implant MBLs were frequently located in a zone within 1 mm of the apical end of the internal screw.

1. Introduction

Over the last decades, dental implants have become an increasingly popular modality of treatment when replacing missing teeth[1, 2]. Although traditional periodontal regeneration around teeth with severely compromised periodontal support remains a viable approach [3, 4], many clinicians today are more inclined to extract these teeth, perform socket grafting procedures [5-7], and replace them with dental implants[8-10]. This is due to their high satisfactory results in terms of patient's function, esthetics, as well as long-term survival rate [11-17]. Nonetheless, implant's long-term success rates are not as promising as their survival rate due to their associated biomechanical and biological complications [17-20].

Peri-implantitis is defined as plaque-associated pathological condition occurring in tissues around dental implants, characterized by inflammation in the peri-implant mucosa and subsequent progressive loss of supporting bone [21]. Its prevalence has been reported to range from 1-47% [22]. So far, research has mainly focused on peri-implantitis in terms of the prevention, development, and treatment of this emerging disease. Patients having factors such as a history of severe periodontitis, poor plaque control, and no regular maintenance care after implant therapy have been shown to be more prone to this disease [21]. Other factors such as implant position, smoking, diabetes, the presence of periodontitis at time of placement, restoration emergence angle, amount of keratinized mucosa, presence of residual cement, titanium particles, have also been linked to peri-implantitis but require more evidence [23-30]. However, only a little importance has been given to the factors that may increase the progression of peri-implant bone loss once peri-implantitis has developed. Currently, peri-implantitis associated bone loss has been reported to progress in a non-linear, accelerating pattern in the absence of treatment [17, 18, 31-33].

It has been shown that the extent of bone loss around implants with peri-implantitis could significantly impact its treatment [34]. When evaluating the outcomes of a surgical procedure based on pocket elimination and bone re-contouring for the treatment of peri-implantitis, Serino and colleagues found that implants that presented with minor initial bone loss had a higher chance of becoming healthy when compared to the ones that presented with more bone loss [34].

Therefore, studying the early disease progression pattern of peri-implantitis and the factors that could affect peri-implantitis associated bone loss is critical. In addition, most of the early studies evaluating factors associated with peri-implantitis focused on biological associated events[35-37], however, recently, studies are featuring the restorative aspect as well [23, 24]. In a study evaluating the effect of prosthetic features on peri-implantitis, Yi et al found that implants with restoration emergence angle ≥ 30° had significantly more marginal bone loss compared to implants with restoration emergence angle < 30°, 5 years following functional loading [24]. When implants are in function, occlusal forces propagate from the occlusal surfaces to the implant-abutment connection and further to the internal screw of the implant [38, 39]. If occlusal overload occurs, the internal screw may be prone to fracture or loosening [40-42]. However, if the loosening or fracture does not occur, the stress might be transmitted from the internal screw to the implant body, implant-bone interface, and surrounding bone [38, 39]. Whether the force transmitted from the internal screw has an influence on the bone level surrounding the implant remains unknown. Due to ethical reasons, however, conducting human randomized clinical trials to investigate the association of occlusal overload with the implant-related complication and peri-implant bone loss is not feasible [43].

Hence, the purpose of this retrospective study was to evaluate the early progression of peri-implant bone loss in patients with peri-implantitis and assess potential restorative factors (e.g., restoration emergence angle, as well as internal screw length and diameter) that can affect it.

2.Materials and methods

2.1. Study design

The current investigation was designed according to the principles presented in the Helsinki Declaration of 1975, as revised in 2000 for biomedical research involving human subjects. The study was approved by the Institutional Review Board for Human Studies (HUM00146121), School of Dentistry, University of Michigan, Ann Arbor, MI. to be conducted at the Graduate Periodontics program within the same institution.

This retrospective study selected all patients that presented with peri-implantitis [21] from 2007 to 2017 at the School of Dentistry, University of Michigan. All paper files and digital charts of patients presenting with peri-implantitis were carefully scanned and analyzed by two independent and pre-calibrated investigators (JM, HA). The current research was prepared in compliance with the STROBE guidelines (see Supplementary Table 1 in online Journal of Periodontology).

2.2. Inclusion criteria

To investigate the early progression of bone loss in peri-implantitis, included patients must have had at least one functionally loaded, single dental implant diagnosed with peri-implantitis (B) when:

(1) No evidence of peri-implantitis was documented during a maintenance visit undergone ≤ 6 months prior to its diagnosis (Dx) (investigators confirmed the diagnosis by complete clinical and radiographic documentation according to the 2017 AAP/EFP world workshop [21]). This maintenance visit was defined as the baseline time-point (Tb).

(2) Included implants must have had clinical and radiographic documentation on file at the loading, one year after loading, ≤ 6 months pre-diagnosis (Tb), also 12 ($\pm$2) months (T1), and 24 ($\pm$2) months (T2) following peri-implantitis diagnosis.

(3) Patients must have been on maintenance protocols (evidence of at least one session of cleaning per 12 months) while having had no surgical intervention for the affected implant site.

(4) Included implants must have been bone level implants (In order to homogenize our results).

Figure 1 represents the study design including the time-points at which clinical and radiographic documentation was evaluated.

2.3. Exclusion criteria

Patients were excluded from the study if the patient had the following conditions:

(1) Medically compromised patient or taking medications that are known to interfere with the normal healing response process (e.g., bisphosphonates, anti-cancer therapy, etc.).
(2) Lack or incomplete information regarding peri-implant conditions (clinical and radiographic documentation at the required study time-points).
(3) Did not meet the 2017 AAP/EFP world workshop definition for peri-implantitis[21] .
(4) Insufficient follow-up after peri-implantitis diagnosis.
(5) Surgical treatment on the study implants during the first 2 years after peri-implantitis diagnosis.
(6) Tissue level implants.
(7) Signs of peri-implantitis development during the first year following functional loading.
(8) Multiple unit implants or implants with splinted crowns.

2.4. Peri-implant health, peri-implant mucositis and peri-implantitis diagnosis:

According to 2017 AAP/EFP world workshop case definition and diagnostic considerations [21], for an implant to be considered healthy, absence of erythema, bleeding on probing, swelling and suppuration, should be documented; peri-implant mucositis was diagnosed when bleeding on gentle probing, swelling and/or suppuration but with the absence of bone loss beyond initial bone remodeling; finally, peri-implantitis was diagnosed when bleeding and/or suppuration on gentle probing was combined with increased pocket depth and radiographic bone loss compared to previous examinations.

2.5. Data collection and Classification

The following information was obtained for all qualified individuals: 1) patient-related factors (such as age, gender, etc.); 2) medical history (including documentation of smoking, diabetes, other systemic or local diseases; as binary outcomes); 3) location of the implant (mandible/maxilla); 4) implant characteristics (length and diameter); 5) bone augmentation procedures with simultaneous implant placement; 6) self-reported parafunctional habits/bruxism (confirmed according to the application of a bite-splint); 7) type of restoration (cement- or screw-retained); 8) frequency of maintenance visits during each follow-up year; and 9) all radiographs during the included time-points. Since this is a retrospective study so the data was anonymized for the study.

At every stage, after examining the gathered data, in case of a disagreement, a discussion was held by the two reviewers (JM, HA). If a resolution was not possible, a senior author (HLW) was consulted to reach a consensus.

2.6. Study outcomes: The study outcomes of the present project were as follows:

a. To evaluate peri-implant bone loss progression, changes in marginal bone levels (MBLs) from Tb to T1 and from T1 to T2 were assessed.

b. Additionally, the influence of clinical and radiographic variables was assessed on the peri-implant bone loss progression results.

2.7. Assessment methods

2.7.1. Peri-implant bone loss progression

To assess the progression of peri-implant bone loss, changes in marginal MBLs from Tb to T1 and from T1 to T2 were assessed (Figure 1); this was performed to evaluate the early bone level changes associated with peri-implantitis. All digital radiographs subjected to analysis were taken using a long-cone paralleling technique with a Rinn-type film holder at all time-points, ensuring standardization of our measurements. Implant MBL was considered as the distance between the implant platform and the most coronal point of the implant body in contact with bone. For each radiograph, the MBL was measured by two authors (JM, HA) at the mesial and distal aspects of the effected implants using a digital Image J software † and calibrated by referring to the known height and diameter of each implant. The most apical bone level was used in our statistical analysis[44]. Interclass correlation values were calculated for the mesial and distal measurements of the implants to assess inter-examiner reliably among the examiners.

2.7.2. Clinical factors influencing peri-implant bone loss progression

The influence of clinical variables extracted from the patient files such as gender, age, smoking, diabetes, frequency of maintenance visits, bruxism, location of the implant (maxilla/mandible), the use of grafting material, implant characteristics, and type of restoration were assessed on the MBL results.

2.7.3 Radiographic assessment of potential factors influencing peri-implant bone loss progression

Finally, radiographic measures of the restoration emergence angle, internal screw length and diameter were calculated and their influence on the MBLs was assessed. The angle between a line parallel to the implant long axis, drawn at the outer collar of the implant and another line tangent to the height of the proximal contour of the restoration was used to measure the restoration emergence angle [23, 45]. Implants were placed into two groups: those with interproximal surface with > 30°, and those with interproximal surface measuring ≤ 30° [23]. The Internal screw length was considered as the distance between the implant platform level to the most apical part of the internal screw. Finally, the internal screw diameter was measured from the most mesial apical to the most distal apical radiographic points of the internal screw in contact with the internal part of the implant (Figure 2).

2.8 Data management and Statistical analysis

In this study, all statistical analyses were done using a software program ‡. For the description of data, the number of observations (N), percentage (%), mean, and standard deviation (SD) were presented. For the analysis of potential factors influencing peri-implant MBL changes, the univariate generalized estimation equation (GEE) was performed due to cluster-correlated data; that is, each subject had a different number of implants (1-4 implants) [46]. A further multivariate GEE analysis was utilized in the model including the explanatory variables with a value of $p<0.20$ in the univariate GEE analysis [47]. Regarding the value of MBL change, based on restoration emergence angle (≤30° and >30°), data normality was checked by the Kolmogorov-Smirnov test, and the equality of variance was assessed by Levene's Test. Mann-Whitney U test was used to compare the change of MBL between these two groups. A p-value <0.05 was considered statistically significant.

3. Results:

3.1. Study population

A total of 233 patient charts were retrieved and screened as a result of the initial search. Subsequently, 168 were excluded due to the following reasons: incomplete clinical or radiographic information at any of the required time-points (61), did not meet the 2017 AAP/EFP world workshop definitions of peri-implantitis [21] (40), failed to comply with at least one session of cleaning/prophylaxis per 12 months (10), surgical treatment of the affected implant within 2 years following diagnosis of peri-implantitis (41), or its diagnosis within 1 year of functional loading (16).

As a result, a total of 83 bone-level implants from 65 patients (28 males and 37 females; mean age of 64.2 ± 9.4 years) were included in this study. Supplementary Table 2 (see Supplementary Table 2 in online Journal of Periodontology) presents details on the characteristics of the selected dental implants. All implants had been placed in healed sites and restored with fixed dental prostheses under a delayed loading protocol. Out of the 83 implants, 74 were restored with Zirconia prostheses and only 9 implants were restored with porcelain fused to metal prosthesis. The mean follow-up before peri-implantitis diagnosis was 99.47 ± 47.93 months. At Tb, 18 out of the included implants had also presented with signs leading to a diagnosis of peri-implant mucositis. At Dx, a mean pocket depth of 6.74 ± 1.29 mm was observed. The average maintenance visits for the included patients was 2.43 ± 1.43 and 2.40 ± 1.30 during the first and second follow-up year after peri-implantitis diagnosis, respectively. Table 1 presents details on the characteristics of the selected patients.

3.2. Clinical factors influencing peri-implant bone loss progression

From Tb to T1, the mean marginal bone loss was 1.52 ± 1.33 mm, whereas, from T1 to T2, the additional mean marginal bone loss was 0.58 ± 0.52 mm (see Supplementary Table 3 in online Journal of Periodontology). Outcomes from the regression models investigating the relationships between the gathered variables and MBL changes were presented in Tables 2A and 2B. Within the included subjects, marginal bone loss (Tb to T1, and T1 to T2) did not seem to be affected by any of the clinical characteristics (gender, age, smoking habits, diabetes, bruxism, the site of the treated implant, type of restoration and whether a grafting material with simultaneous implant placement was used or not) (Tables 2A and 2B).

3.3. Radiographic assessment of restorative factors influencing the progression of peri-implant bone loss

When evaluating radiographic restorative factors related to changes in MBLs, outcomes from the multivariate GEE analysis from Tb to T1, showed significant negative correlation between bone loss and the frequency of maintenance visits ($p=0.039$) and positive relationships between marginal bone loss and restoration emergence angle ($p=0.001$) (Table 2A). In fact, from Tb to T1, implants with a restoration emergence angle of >30° had 2.33 ± 1.20 mm marginal bone loss, whereas implants with a restoration emergence angle of ≤ 30° had 0.59 ± 0.71 mm marginal bone loss ($p<0.001$) (Figure 3). Finally, from T1 to T2, outcomes from the regression models failed to show any relationship between marginal bone loss and other recorded radiographic parameters (Table 2B). The mean internal screw length was 4.89 ± 1.43 mm, whereas the internal screw diameter was 1.56 ± 0.28 mm. Both the Internal screw length and diameter did not seem to impact marginal bone loss. However, a pattern was observed: bone levels from Tb to T1 and from T1 to T2 were on the same level with the apical end of the internal screw. In fact, in 66.3% of the cases the marginal bone levels were in a zone within 1 mm of the apical end of the internal screw (AEIS Zone) 1 year after peri-implantitis diagnosis and remained in this same zone during the second follow up year (Figure 2 and figure 4A, scenario 2).

The calculated intraclass correlation values of the measurements amounted to 91.4 (95% CI [86.9, 95.8]) for measurements on the mesial and 92.5 (95% CI [89.7, 95.3]) for measurements on the distal of the implants.

4. Discussion

4.1. Principal findings

Factors contributing to the development of peri-implantitis have been widely investigated [21, 33]. However, the present study aimed to determine restorative related factors that might influence the early stage of peri-implant bone loss and focused on the first two years of disease progression after peri-implantitis signs have developed. Knowing the factors that affect changes in MBLs in the early stage of peri-implantitis is critical, as it could allow us to prevent or slow down the continuing loss of supporting bone. When a patient presents with peri-implantitis, the exact onset of this disease is challenging to determine. For this reason, in the present study, clinical and radiographic evidence of absence of peri-implantitis ≤ 6 months before the diagnosis of disease was required for inclusion. This suggests that patients included in this study developed signs of peri-implantitis somewhere between Tb and diagnosis (Dx). Furthermore, this study also looked at the first (T1), and the second (from T1 to T2) years after the development of peri-implantitis signs. It is, therefore, important to point out that all of the patients included in this study attended their scheduled maintenance therapy regularly (2.43 ± 1.43 and 2.40 ± 1.30 maintenance visits for the first and second year after a diagnosis of peri-implantitis, respectively). The number of maintenance visits was recorded and evaluated for a potential effect on the levels of bone loss, and we found that this factor significantly affected MBL from Tb to T1. Thus, our study provides additional data to the literature highlighting the importance of attending regular maintenance visits to prevent peri-implant bone loss progression [48-51].

In order to homogenize our results, data more than 2 years of follow-up was not included in our analyses even when it was available. This is because several patients were lost to follow-up or have received surgical therapy. The rationale behind exclusion of cases with surgical treatment was that the treatment itself would add additional variability to the study outcomes, particularly when coupled with the addition of bone substitutes. These surgical interventions would have influenced the measurements of radiographic MBLs.

A marginal bone loss of 1.52 ± 1.33 mm during the first year after the development of peri-implantitis and 0.58 ± 0.52 mm from 1 to 2 years following the diagnosis of peri-implantitis was found. This indicates that 2 years following the diagnosis of peri-implantitis 2 mm of marginal bone loss had already occurred. Data from this study also found that, during the first year after the development of peri-implantitis, implants with restoration emergence angles of > 30° had around 1.74 mm more peri-implant bone loss than when restoration emergence angle were ≤ 30°. This is in support of findings from other studies [23, 24]. Katafuchi and colleagues identified that a restoration emergence angle > 30° in bone level implant was a significant risk indicator for peri-implantitis [23]. Yi et al found that restoration emergence angle ≥ 30° had significantly more marginal bone loss compared to implants with restoration emergence angle 5 years following functional loading [24]. In fact, having dental implants with over-contoured restorations may negatively impact proper oral hygiene by limiting accessibility to cleaning, especially when aiming to debride deep bony defects around implants with peri-implantitis, leading to further disease progression [52].

To the best of our knowledge, the influence of the internal screw length on implant MBL has not yet been evaluated. Hence in the present study, the length of the internal screw was radiographically measured in all implants and its effect on marginal bone loss was evaluated.

Although no statistical significant association between the length or the diameter of the internal screw and implant MBL was found; It was observed that in 66.3% of the cases the bone levels were in a zone within 1 mm of the apical end of the internal screw (AEIS Zone) 1 year after peri-implantitis diagnosis and remained in this same zone during the second follow up year (Figure 2 and figure 4A, scenario 2). Therefore, the internal screw might play an important role in the progression of bone loss in the presence of peri-implantitis. This is probably due to the fact that when implants are in function, occlusal forces are dissipated through the occlusal surfaces, prosthetic structure, implant-abutment connection, internal screw, implant body, implant-bone interface, and surrounding bone [38, 39]. In fact, when transverse occlusal forces are applied on an implant, bending of the implant components occurs and only a reduced portion of the supporting bone is involved in counteracting the load; leading to higher stress levels in particular portions of the implant-bone interface [53]. This phenomenon can be explained by the transition of internal forces from the apical end of the internal screw to the supporting bone on the external side of the implant body (Figure 4B). This could lead to a faster progression of peri-implant bone loss in the presence of peri-implantitis until the bone level reaches the AEIS Zone [54] (Figure 4A, scenario 2). This is supported by the fact that in 66.3% of the cases the MBLs were in the AEIS Zone 1 year after peri-implantitis and they also remained in this zone 2 years after the diagnosis. We presume that once the MBLs reaches the AEIS Zone, the occlusal forces transmitted from the AEIS to the implant will not be opposed by bone on the external surface of the implant anymore. At this point, the progression of peri-implant bone loss would slow down. This might explain why in the present study, MBL was less pronounced from T1 to T2 since in many cases MBLs were already in the AEIS zone at T1. However, it should be noted that our study has a short follow-up period following peri-implantitis diagnosis, and further research should investigate bone loss progression for a longer period of time to determine whether bone loss would progress apically to the AEIS zone. Finally, the present study does not claim that occlusion is a risk factor for peri-implantitis development but raise a question on the possible influence of occlusion on the peri-implant bone loss or even peri-implantitis progression.

4.2. Limitations

Among the limitations of this study is the retrospective nature of the study design. Additionally, lack of knowledge on the exact timing of onset of peri-implantitis, nonetheless, we believe that peri-implantitis signs developed from Tb to Dx (within 6 months). Besides, the radiographs used in the present study were not ideally standardized, however, all digital radiographs that were subjected to analysis were taken using a long-cone paralleling technique with a Rinn-type film holder to ensure standardization of our measurements. Finally, the emergence angle might be affected by the variability in the macrostructural design of the implant body, future studies in this area are strongly encouraged.

4.3. Conclusion

Within the limitations of this study, it was concluded that the restoration emergence angle of more than 30° were found to be significantly associated with early stage (up to 2 years) of peri-implant marginal bone loss in peri-implantitis. Following peri-implantitis associated bone loss, there seems to be a relationship between the implants' bone levels and a zone within 1 mm of the apical end of the internal screw.

Footnotes

† National Institutes of Health, Bethesda, MD

‡ SPSS, version 23.0, SPSS Inc., Chicago, IL, USA

Conflict of interest and source of funding

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Figure Legends

Figure 1. Schematic illustration representing the time-points at which clinical and radiographic documentation was required.

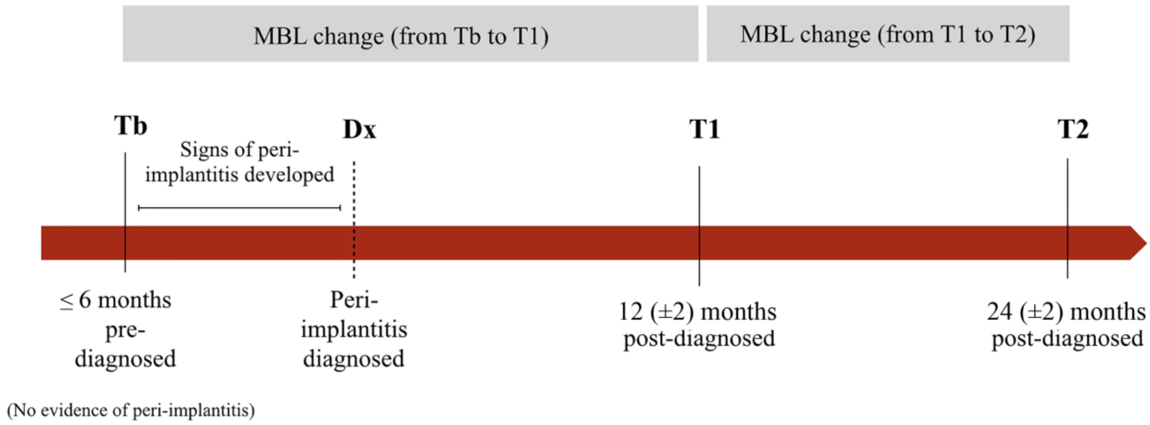


Figure 2. Example of the restoration emergence angle (Yellow), internal screw length (Blue) and diameter (Purple) measurements on a peri-apical radiograph. Note how the MBL is in proximity with the apical end of the internal screw.

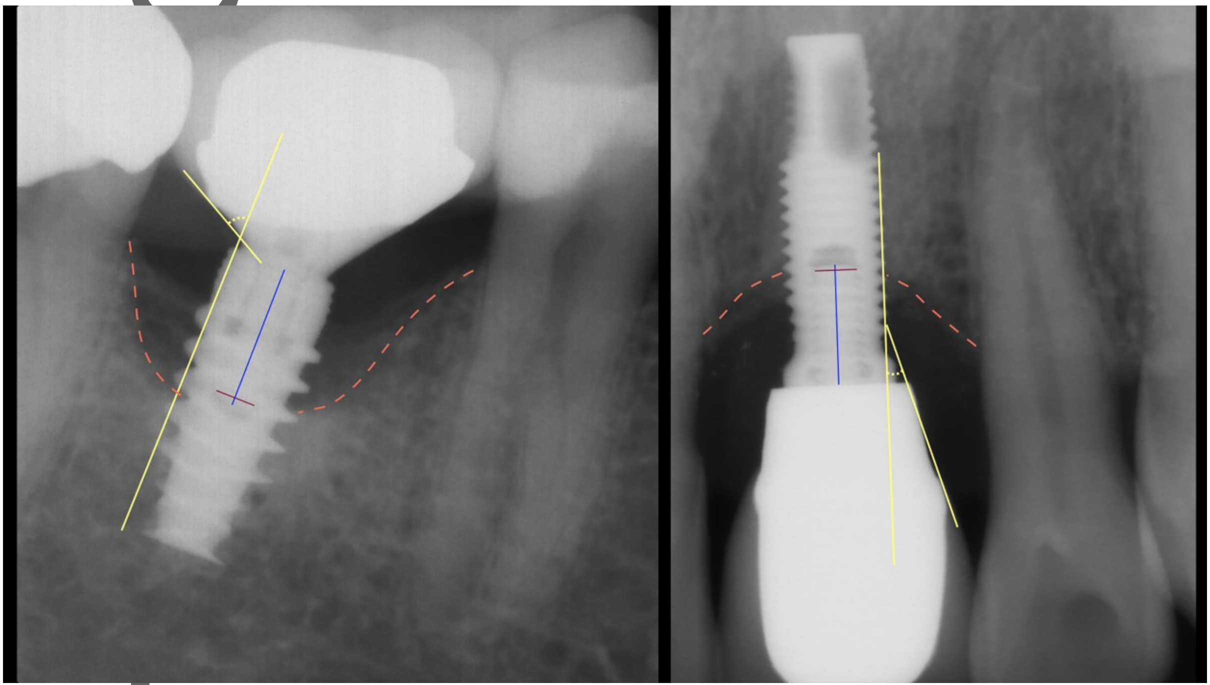


Figure 3. Box plot of marginal bone loss from Tb to T1 (one year following peri-implantitis diagnosis) in implants with restoration emergence angle ≤ 30° and > 30°.

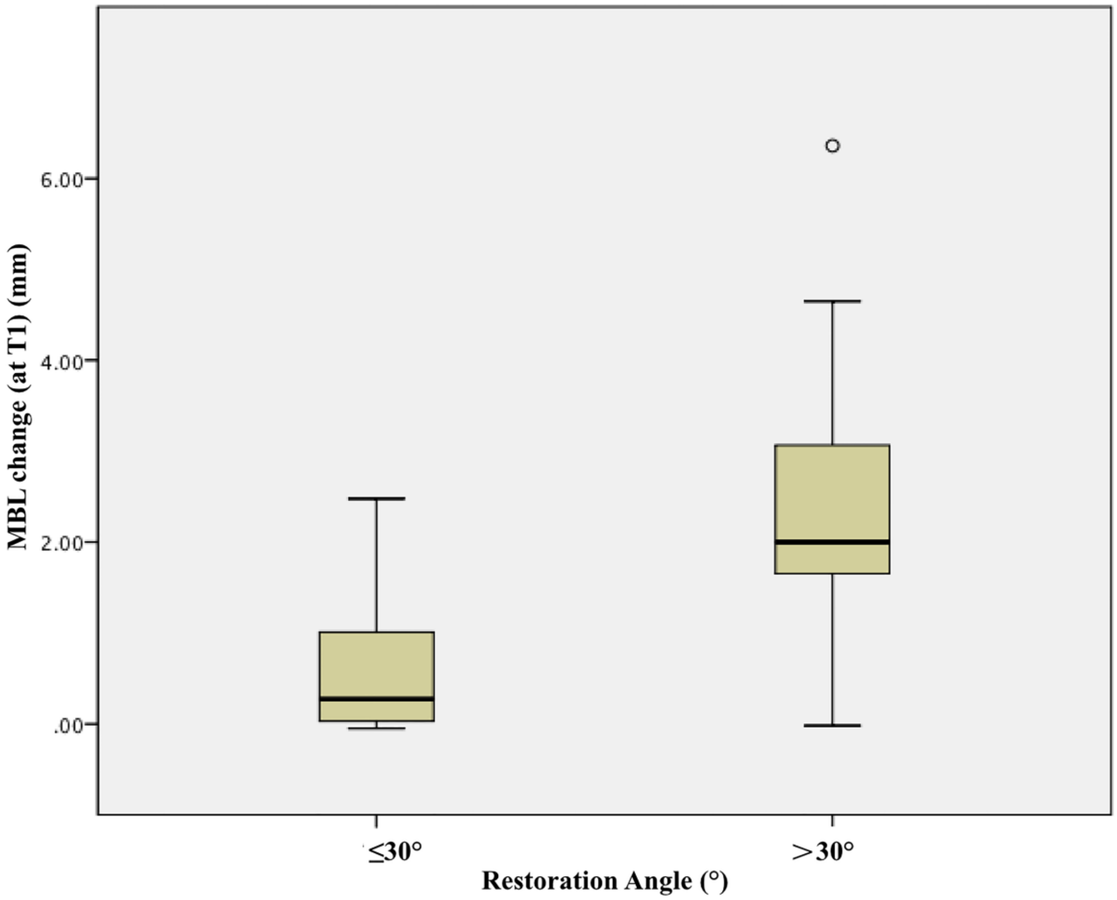
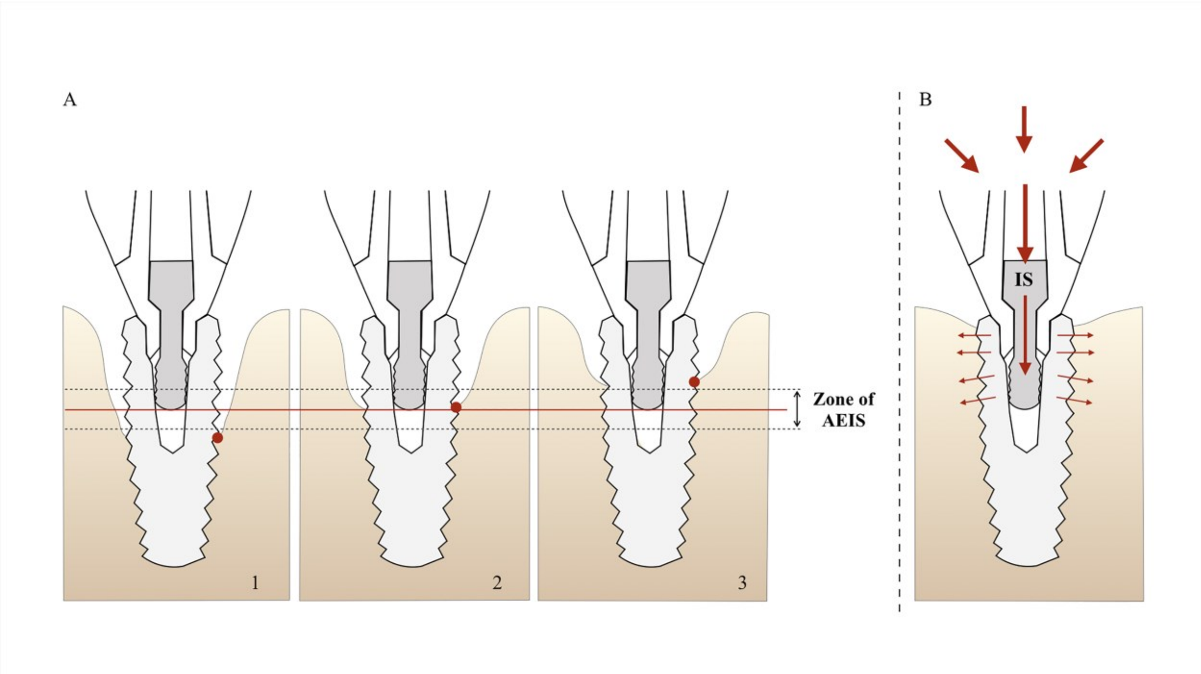


Figure 4. Schematic illustration representing a dental implant and its components. (3A) represents 3 different scenarios: In scenario 1, marginal bone levels (MBLs) are apical to the apical end of the internal screw (AEIS zone), in scenario 2 MBLs are in the AEIS zone and in scenario 3, MBLs are coronal to the AEIS zone. (3B) represents the occlusal forces traveling through the implant system.



Tables

Table 1. Characteristics of the included patients (mm, mean (SD))

Table 2A. Results of generalized estimating equations (GEE) evaluating effect of different variables on marginal bone loss 1-year following diagnosis (from Tb to T1)

Table 2B. Results of generalized estimating equations (GEE) evaluating effect of different variables on marginal bone loss in the second follow-up year (T1 to T2)

Supplementary tables:

Supplementary Table 1**.** STROBE Statement

Supplementary Table 2**.** Characteristics of the included implants

Supplementary Table 3**.** Changes in marginal bone levels at several time-points

Table 1. Characteristics of the included patients (mm, mean (SD))

Variable	**Levels**	**N**	**%**
Gender	Male	28	43.1
	Female	37	56.9
Smoking	Smoker	24	36.9
	Non-Smoker	41	63.1
Diabetes	Yes*	9	13.8
	No	56	86.1
Bruxism	Yes	21	32.3
	No	44	67.7
Implant location	Maxilla	42	50.6
	Mandible	41	49.4
Grafting material use	Yes	20	24.1
	No	63	75.9
Type of restoration	Cement-retained	66	79.5
	Screw-retained	17	20.5
Type of implant connection	Internal	41	49.4
	External	42	50.6
Implant supported prosthetic material	Zirconia	74	89.2
	Porcelain-fused-to-metal	9	10.8
Opposing dentition	Natural tooth	54	65.1
	Tooth supported prosthesis	17	20.5
	Implant supported prosthesis	12	14.4
Restoration emergence angle	> 30°	44	53.0
	≤ 30°	39	47.0

N: number; SD: standard deviation; *All subjects with diabetes were controlled type II diabetics

Table 2. Results of generalized estimating equations (GEE) evaluating effect of different variables on marginal bone loss 1-year following diagnosis (from Tb to T1)

Variables	Univariate GEE			Multivariate GEE			
	Estimate	95% CI	*p*-value[a]	Estimate	Std. Error	95% CI	*p*-value[b]
Gender (female)	-0.227	-0.879, 0.425	0.495				
Age (years)	**-0.032**	**-0.069, 0.006**	**0.096**	-0.019	0.017	-0.052, 0.015	0.272
Implant location (mandible)	0.369	-0.240, 0.978	0.236				
Smoking (non-smoker)	-0.217	-0.785, 0.351	0.454				
Diabetes (non-diabetes)	-0.096	-1.350, 1.158	0.881				
Bruxism (non-bruxism)	0.101	-0.540, 0.742	0.758				
Grafting (non-grafted)	0.048	-0.365, 0.461	0.822				
Implant diameter (mm)	0.267	-0.413, 0.947	0.442				
Implant length (mm)	0.031	-0.189, 0.250	0.784				
Type of restoration (cement-retained)	0.081	-0.558, 0.719	0.804				

Frequency of maintenance visits (times)	**-0.278**	**-0.496, -0.059**	**0.013**	**-0.139**	**0.068**	**-0.272, 0.007**	**0.039**
Restoration emergence angle (°)	**0.053**	**0.026, 0.079**	**<0.001**	**0.045**	**0.013**	**0.019, 0.071**	**0.001**
Internal screw diameter (mm)	**0.969**	**0.030, 1.909**	**0.043**	0.761	0.483	-0.186, 1.708	0.115
Internal screw length (mm)	0.055	-0.130, 0.240	0.559				

GEE, generalized estimating equations; Bold signifies statistical significance (a, cut-off level of significance used was 0.2 for the entry of the multivariate model; b, α=0.05); CI, confidence intervals

Table 3. Results of generalized estimating equations (GEE) evaluating effect of different variables on marginal bone loss in the second follow-up year (T1 to T2)

Variables	Univariate GEE			Multivariate GEE			
	Estimate	95% CI	*p*-value[a]	Estimate	Std. Error	95% CI	*p*-value[b]
Gender (female)	0.115	-0.119, 0.350	0.335				
Age (years)	0.001	-0.015, 0.017	0.866				
Implant location (mandible)	0.119	-0.110, 0.347	0.308				
Smoking (non-smoker)	**-0.180**	**-0.444, 0.069**	**0.152**	-0.213	0.1289	-0.465, 0.040	0.099
Diabetes (non-diabetes)	**-0.223**	**-0.510, 0.064**	**0.128**	-0.266	0.1313	-0.523, -0.009	0.053
Bruxism (non-bruxism)	-0.085	-0.347, 0.176	0.522				
Grafting (non-grafted)	-0.131	-0.059, 0.322	0.177				
Implant diameter (mm)	0.116	-0.100, 0.333	0.291				
Implant length (mm)	0.033	-0.034, 0.101	0.335				
Type of restoration (cement-retained)	-0.002	-0.310, 0.306	0.991				
Frequency of maintenance visits (times)	-0.006	-0.076, 0.064	0.858				

Restoration emergence angle (°)	0.002	-0.005, 0.009	0.624
Internal screw diameter (mm)	-0.245	-0.746, 0.256	0.338
Internal screw length (mm)	-0.041	-0.109, 0.027	0.241

GEE, generalized estimating equations; Bold signifies statistical significance (a, cut-off level of significance used was 0.2 for the entry of the multivariate model; b, α=0.05); CI, confidence intervals