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Morphology and Severity of Peri-implantitis Bone Defects

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Abstract

Background: Peri-implant defect morphology has shown to potentially impact upon the reconstructive outcomes for the management of peri-implantitis. Given the role that defect morphology plays upon the decision-making in the treatment of peri-implantitis, the present study aimed at assessing the morphology and severity of peri-implantitis bone defects and to insight on the patient-, implant- and site-related variables associated to these.

Material and methods: A cone-beam computed tomography study was carried out to classify peri-implantitis defects according to the type of defect, number of remaining bony walls and severity according to the extension of vertical bone loss. Three major defect categories were proposed: class I - infraosseous; class II - horizontal; class III - combined of class I and II. These were then sub-classified into: a. dehiscence; b. 2/3-wall; and c. circumferential - type defect. According to the severity the defects were further sub-classified into: A: advanced; M: moderate; and S: slight. In addition, 20 site-, implant- and patient-related variables were analyzed by generalized estimating equations (GEEs) of multilevel logistic regression models.

Results: Based on an *a priori* power calculation, 332 implants were screened in 47 peri-implantitis patients. Of these, 158 peri-implantitis implants were eligible. The most prevalent defect morphology type was class Ib (55%) followed by class Ia (16.5%) and class IIIb (13.9%). On the contrary, the less frequent defect was class II (1.9%). The most frequent degree of severity was M (50.6%) with S (10.1%) being the least prevalent. Buccal bone loss was significantly greater compared to the other bony walls in class I and class III defects. Age was

associated with the type of defect. Age and smoking habit were associated with the morphology of the defects, while smoking habit, type of prosthesis and distance to adjacent implant were associated with the severity of the defects (vertical bone loss).

Conclusion: Peri-implantitis defects frequently course with an infraosseous component and often with buccal bone loss. Certain patient-, implant- and site-specific variables are related with defect morphology and severity. However, morphological patterns for peri-implantitis bone defects could not be proven. (NCT NCT03777449).

MeSH Keywords: Peri-implantitis, Peri-implant mucositis, Dental implants, Implant stability, Diagnostic, Alveolar bone

Introduction

It has been suggested that the therapeutic outcome of non-surgical and surgical periodontal treatment is associated to defect morphology. In fact, classical studies demonstrated that narrower defect angles were more prone to achieve greater radiographic bone fill.[1, 2] This remarkable finding has been further evidenced in the field of guided bone regeneration.[3] As such, a concavity outlined in the alveolar crest (<150º) was shown to be more predictable to achieve successful lateral ridge augmentation. Alike, the favorable outcome after peri-implant reconstructive therapy for the management of peri-implantitis has further exhibited to be dependent upon the morphological features.[4] Schwarz et al. showed that circumferential peri-implant defects (named as class Ie) were more conducive to reveal higher changes in probing pocket depth and clinical attachment level at 6 and 12 months compared to other defect morphologies.[4] On the contrary, non-contained residual dehiscence defects >1mm at the time of implant placement are at higher risk of developing peri-implant diseases due to

ineffective guided bone regeneration (GBR).[5] These findings pinpoint on the biological criteria to succeed in GBR, as the stability of the fibrin clot was regarded as a critical factor to recruit mesenchymal stem cells capable of osteogenic differentiation.[6, 7]

In light of the importance of defect morphology upon the therapeutic outcomes, several investigations have explored their features. Schwarz et al. studied and classified peri-implantitis defect configuration.[8] Basically, class I referred to the presence of an infra-osseous compartment, class II was proposed for defects with horizontal pattern of bone loss. Interestingly, in humans (55.3%) and dogs (86.6%) the most frequent defect configuration was circumferential, so-called class Ie defects.[8] Likewise, Serino et al. demonstrated that 34% of the defects did not exhibit circumferential bone loss, but rather, bone breakdown in the buccal areas.[9] Garcia-Garcia et al. found upon surgical entry that, ~30% of the defects presented a circumferential configuration (class Ie), while ~25% displayed a circumferential defect combined with a buccal dehiscence-type defect.[10] This is consistent with a recent canine study that demonstrated that peri-implantitis evolve in a more severe and aggressive fashion in the buccal sites compared to the lingual counterparts.[11] In fact, it has been speculated that bone architecture and the proximity of dental implants to the cortical bone might play important roles on the frequency and severity of pathogenic bone loss on the buccal sites rather than the existence of linear resorptive patterns.[10, 12]

The use of radiographic techniques allows to establish the morphology of the peri-implant bone tissues, either with two-dimensional radiographs like intraoral radiology (IR) or panoramic images either with three-dimensional images as computer tomography (CT) and cone beam computer tomography (CBCT).[13] The use of intraoral radiography is the most common in daily practice, but it is limited to two planes and superimposition may mask marginal bone levels.[14] In fact, the absence of 3D information in IR impede the evaluation of peri-implant bone defects and distinction between buccal and lingual bone plates.[15] On the other side, CBCT may ensue some of these limitations by providing 3D images and several orthogonal planes [16] with the advantages of limiting the geometric distortion reported in about 1/3 of the IR and panoramic images.[13, 15] Additionally, the accuracy of CBCT to assess the histological configuration and extension of ligature-induced peri-implantitis defects was previously demonstrated in a canine model.[17]

Hence, given the weight of defect morphology for the achievement of favorable therapeutic outcomes, it was the primary objective of the present radiographic study to assess the morphologic features and severity of peri-implantitis defects. Secondary, it was purposed to insight on the influence of patient- and implant-related characteristics on defect morphology.

Material and Methods

A retrospective study was conducted in accordance with the Declaration of Helsinki on human studies, following approval from the Ethics Committee of the University of Extremadura (Badajoz, Spain, Ref. no. #18002909). The study was also registered and approved by www.clinicaltrials.gov (NCT NCT03777449), and is reported according to the STROBE statement (www.strobe-statement.org).

Study population

All enrolled peri-implantitis subjects had been consecutively evaluated with dental implants in function for a minimum of 36 months after final prosthesis delivery. The clinical and radiographic analyses were carried out by one experienced periodontist (AM). Available baseline x-rays at the time of prosthesis delivery were retrospectively examined to exclude implants with early peri-implant bone loss before function that could lead to misdiagnosis.[18]

Eligibility criteria

The following inclusion criteria were applied: partial or complete edentulous rehabilitated with implant-supported single-crown, fixed prostheses or implant-supported overdentures, patients aged 18-80 years; smokers (HS), light smokers (LS<10 cig/day), former smokers (FS) or non-smokers (NS); absence of infectious disease at the time of implant placement; absence of systemic disorders or medications known to alter bone metabolism. Subjects were excluded if they revealed the following conditions: pregnancy or lactation at the last follow-up, uncontrolled medical conditions such as

uncontrolled diabetes mellitus; and inadequate bucco-lingual implant positioning outside of the bony contour.

Case definition of peri-implantitis

Based on the consensus report of Workgroup 4 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions [19], the diagnosis of peri-implantitis without baseline information required:

- Presence of bleeding and/or suppuration on gentle probing.

- Probing depth ≥ 6 mm.

- Bone level ≥ 3 mm apical to the most coronal portion of the implant or at the rough-smooth interface in tissue-level implants.

Peri-implantitis local confounders assessment

The following site-specific parameters were recorded as part of a routine screening:

- Keratinized mucosa (KM) around dental implants, measured from the free mucosal margin to the mucogingival junction at the mid-buccal position and recorded to the nearest mm using a North Carolina Probe (Hu Friedy, Chiacgo, IL). If unclear, Lugol's iodine was used to stain the mucosa to better discern the mucogingival margin. The presence of keratinized mucosa was classified as ≥2mm and <2mm. The lack of KM was coded as 0.

- Abutment-implant misfit was defined as the presence of a gap (abutment loosening) between the implant and the abutment constatable according to the radiographic assessment. It was coded as "yes" or "no"

- Type of prostheses were classified as "fixed" for implant-supported single-crowns or "removable" for implant-retained overdentures.

- Accessibility for oral hygiene was assigned for those sites that provided access/capability to carry our personalized oral hygiene measures - "yes". The lack of access was recorded as "no". This was recorded during the initial interview with the patients [20].

- The presence of pink porcelain in hybrid prostheses was recorded as "yes" or "no" independently on the capability of access to reach oral hygiene.

- Implant and tooth proximity adjoining the peri-implantitis implant was defined as a minimal distance of 1.5mm to the adjacent tooth and 3mm between dental implants.

Other patient- and implant-related variables were also recorded, these include age, gender, function time, total number of implants, total number of implants within the same arch, type of edentulism (complete/partial), history of periodontitis (yes/no), periodontitis location (generalized/localized) type of periodontitis (chronic/aggressive), loss of support (mild: bone loss<15%/moderate: bone loss ≥15-30%/severe: bone loss>30%) , implant position (mandibular anterior- ma, mandibular posterior- mp, maxillary anterior- MA, maxillary posterior- MP), smoking habit (heavy smoker –

HS≥10cig/day; light smoker – LS<10 cig/day; former smoker – FS and non-smoker – NS) implant type (tissue level – TL or bone level - BL) and implant system.

Radiographic assessment

CBCTs were taken by an experienced radiologist (VC). Image from eligible patients were acquired by CBCT i-CAT Model 17–19 (Imaging Sciences International LLC, Hatfield, PA, USA). The imaging parameters were set at a width and depth of 16x13mm, 120kVp, 20.27mAs, scan time 14.7 s, resolution 0.25 voxel and a field of view (FOV), which varied based on the scanned region. Defect morphology and severity were determined using the Osirix DICOM viewer (Pixmeo, CH-1233 Bernex, Switzerland) by one previously calibrated examiner (RP). The examiner reached an inter-examiner Cohen kappa index >85% after analysing 10% of the sample calculated a priori in the power analysis.

Peri-implantitis bone morphologic and severity classification

The following characterization of the peri-implantitits defects were featured according to the defect morphology and severity (Figure 1). The present classification is a modification of a previously published work done by one of our authors [8]:

- According to the morphology was classified as follows:

- *Class I:* Infraosseous defect

    o Class Ia: Buccal dehiscence

    o Class Ib: 2-3 walls defect

         o   Class Ic: Circumferential defect

- *Class II:* Supracrestal/horizontal defect

- *Class III:* Combined defect

         o   Class IIIa: Buccal dehiscence + horizontal bone loss

         o   Class IIIb: 2-3 walls defect + horizontal bone loss

         o   Class IIIc: Circumferential defect + horizontal bone loss

-    Each implant was sub-classified to defect severity based upon the defect depth from the implant neck and ratio of bone loss/total implant length:

- Grade S: Slight: 3-4mm/<25% of the implant length

- Grade M: Moderate 4-5mm/≥25%-50% of the implant length

- Grade A: Advanced: >6mm/>50% of the implant length

Statistical analysis

     A priori statistical power analysis was performed assuming an intra-class correlation coefficient (ICC) of 0.25, based on the findings from two previous studies [8, 21] to guarantee a confidence interval of 95% and a power of 80% considering "implant" as the statistical unit. This guarantees that a given defect type is not >8% of error regarding the total population.

     The inferential analysis involved estimation by generalized estimating equations (GEEs) of multilevel logistic regression models. Calculations were made to assess any

association between any variable recorded at implant-level in relation the defect morphology and severity. The 95% confidence interval for the coefficients was given from the Wald's Chi^2 statistic. With this model, the correlations between the measurements of implants and the subjects. The level of significance set in the analyses was 5% ($\alpha = 0.05$).

Results

Study population

Based on an *a priori* power calculation, 332 implants were recorded in 47 consecutive peri-implantitis patients (27.7% males: 72.3% females; age: 58.3 ±10.5 years; complete edentulous= 21.3%: partial edentulous= 78.7%) recruited. Of these, 158 implants were diagnosed as having peri-implantitis (73.4%[*], 1.9%[†], 6.3%[‡], 3i=2.5%, 4.4%[§], 8.9%[**], 2.5%[††]; TL=3.9%, BL= 96.1%). The mean value of implants per patient and per arch was 7.1 ±2.9 and 4.7 ±2.0, respectively. The mean function time was 7.7 ±3.0 years. Regarding smoking habit, 66% were NS, 12.8% were FS, 8.5% were LS and 12.8% were HS.

Peri-implantitis local confounders

Half of the peri-implantitis implants (50%) were lacking KM, while in 15.2% and 34.8% were <2mm and ≥2mm. The majority of implant-abutment connections

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fitted (70.9%), while 29.1% were loose. The vast majority were implant-supported fixed prostheses (91.5%) while only a small percentage were removable prostheses (8.5%). Of these, 77.2% reported no cleansability, and only 22.8% reached adequate access for cleansability. These, 45.6% lacked pink porcelain and 54.4% were designed with pink porcelain at the base of the prosthesis. Concerning the three-dimensional position in relation to adjoining teeth/implants, 25.3% and 4.4% were close to adjacent implants and teeth, respectively.

Relationship between local confounders

Type of implant-supported prosthesis (fixed) and the presence of pink porcelain were statistically significant associated with cleansability (p<0.001). Interestingly, the variable KM (0mm, <2mm, ≥2mm) was significantly associated with location (p=0.0007), being ≥2mm in 75% of the peri-implantitis cases in the maxillary anterior and only 7.7% in the posterior mandible. Alike, the variable KM was significantly associated with the close proximity of the adjacent tooth. As such, in 71.4% of the cases when the implant was close to the adjacent dentition the KM was ≥2mm. On the contrary, in 52.3% of the cases were lacking KM (0mm) when the distance to the adjacent dentition was greater ≥1.5mm.

Peri-implantitis defect morphology and severity

At patient-level, the most frequent peri-implantitis defect morphology was class Ib (87%) then IIIb (22%) and with the least frequently on II (3%). Likewise, at implant-level, the most prevalent defect morphology type was class Ib (55%) then Ia (16.5%) and IIIb (13.9%). On the contrary, the least frequent defect was II (1.9%) (Figure 2). Independent of the landmark used to assess defect severity, the most frequent degree of severity was M (50.6% in mm/52.5% according to implant length) and the least prevalent was S (10.1% in mm/10.8% according to implant length).

When combined defect morphology and the degree of severity, it was exhibited that class Ic (60%) defect morphology was more severe than class Ia (11.5%) and Ib (40.2%). Likewise, class Ic (75%) evidenced greater severity than class Ib (31.8%) and Ia (28.6%). However, statistical significance could not be reached (p=0.25 in relation to bone loss in mm and p=0.234 according to implant length) (Figure 3).

Moreover, it was noted that the majority of defect morphologic subtypes, buccal bone loss was more pronounced than any other bony wall. Mean vertical buccal bone loss was 5.76 ±2.16mm, reaching its maximum mean value for class II defects (8.86 ±0.90mm). Conversely, mean vertical lingual bone loss was 4.12 ±1.83mm. Alike, it reached its maximum mean value for class II defects (7.35 ±1.31mm) (Figure 4).

In addition, only age was found to significantly impact upon defect morphology (p=0.016). As such, it was exhibited a significant increase in defects class Ib as age was increased and a decreased in class IIIb and IIIc. Interestingly, when compared defect morphologies in individuals ≤55 years vs. >65 years it was noted high statistical significance (OR=4.81; p=0.004). In this sense, it was worth noting that smoking did

not reach statistical significance but a marginal tendency towards significance was displayed. For instance, defect morphologies in NS were mainly class Ib (50.5%) and Ia (22.5%). Interestingly, 80.8% of HS presented class Ib, while class III was almost non-existent (3.8%). Further, it was no variable that reached statistical significance when associated with the severity of peri-implantitis defects. Nevertheless, partial edentulous patients presented with greater severity (type A) than complete edentulous patients (45.9% vs. 24.5%, respectively).

Three variables yielded significance when associated to severity by means of mean vertical bone loss. HS had more advanced bone loss compared to FS, NS or LS (p=0.014). Likewise, peri-implantitis in implant-supported fixed prostheses were more progressive compared to removable prostheses (p=0.033). In addition, implant proximity was also found to be associated with greater vertical bone loss (p=0.046).

Discussion

Principal findings

The present study has demonstrated using CBCT that peri-implantitis defects frequently course with an infraosseous component and buccal bone loss. Nevertheless, based upon the findings from this study, peri-implantitis might be exhibited in other assorted defect configurations. It was found that defect severity often relies upon defect morphology. It was further illustrated that certain patient-, implant-, and site-related factors are associated with defect morphologic features including severity. Nonetheless,

the establishment of morphologic patterns for peri-implantitis defects could not be proven.

Agreements and disagreements with previous studies

The frequency and morphological characteristics of periodontal defects have been extensively investigated [22-25]. With the concern of the growing rate of biological complications, the examination of peri-implantitis defect morphology and severity has also gained attention. Schwarz et al. initially described the peri-implantitis defect configuration [8]. As such, the defects were classified according to their morphologic pattern in two major categories. In humans (55.3%) and dogs (86.6%) the most prevalent defect configuration was circumferential, so-called class Ie defects [8]. Subsequently, Serino et al. demonstrated that 34% of the defects did not exhibit circumferential bone loss, but rather, bone breakdown in the buccal areas [9]. Alike, Garcia-Garcia et al. showed that, ~30% of the defects presented a circumferential configuration (class Ie). However, it was further exhibited that ~25% displayed a circumferential defect combined with a buccal dehiscence-type defect [10]. Findings from the present study are in partial agreement with these findings. Nevertheless, the rate of peri-implantitis defects displaying in a 2-3-walls infraosseous morphology was slightly greater than the aforementioned studies [8]. Several explanations might be attributed to the differences noted. Firstly, this study reports higher sample size compared to previous studies. Secondly, it might be speculated that implant type (BL vs. TL) might play a role upon defect morphology. For instance, Zhang et al. in a radiographic study

evaluating patients with lower mandibular tissue-level implant-retained overdentures demonstrated that the majority of peri-implant defects were saucer-shaped [21]. These defects might be more conducive to pure circumferential defects when peri-implantitis occurs. Hence, given the fact that the vast majority of the implants assessed in the present study were BL (~96%), these slight discrepancies could be explained. In addition, although it is not well-understood yet, the buccal bone dynamics after implant placement in the lack of sufficient buccal bone (<1.5mm) might contribute to the resorption of the buccal compartment, jeopardizing this the long-term hard tissue stability.[26]

Findings from the present study also showed that 50% of the peri-implantitis implants were lacking KM. Indeed, the significance of KM around dental implants has been subjected to debate [27-29]. However, breaking down this data, it was found that, in the mandibular anterior peri-implantitis implants, 67.7% lacked KM, while peri-implantitis in the maxillary anterior and posterior sites occurred 75% and 46.2%, in areas ≥2mm KM, respectively. In other words, regardless of plaque control that could not be controlled in the present study as a variable, the lack of KM in the buccal site of implants in the mandible might be more incline to disease development than the maxilla (Figure 5). Additionally, in 77.2% peri-implantitis cases, patients reported no capability/access to achieve cleansability were associated with the presence of hybrid prostheses (i.e., presence of pink porcelain). In fact, Serino & Ström highlighted the role of prosthesis design on plaque control and found that 74% of implants evaluated had no access to proper plaque control. These cases were significantly more associated to peri-

implantitis (65% positive predictive value) compared to cases that oral hygiene could be properly carried out [20]. Recent studies have validated such findings [30-32].

Reliability of cone-beam computed tomography (CBCT) to assess peri-implantitis defects

Differences in sensitivity and specificity have been found assessing peri-implant bone defects with IR, CT and CBCT images; some of these differences might be related to resolution, presence of artefacts and location within the jaws [13]. Whereas IR may show a resolution of 10- to 25-line pairs per mm, panoramic images shows 3- to 5- and CBCT only 1- to 2-line pairs. Indeed, the highest and lowest likelihood ratios were found for IR, indicating the best performance for IR in detecting peri-implant bone defects while the lowest specificity was found with CT [13].

It is worth noting that CBCT accuracy is impaired by artifacts caused by metallic implants [33] where blooming artifacts around implants lead to a radiolucent shadow surrounding implants [34]. Moreover, it has been reported that during daily CBCT clinical use, higher accuracy than 0.5 mm cannot be expected [35]. In fact, the use of CBCT may underestimate the dimension of bone structures of less than 1 mm [36]. CBCT also showed a limited accuracy measuring vestibular and lingual bone levels [15]. Accordingly, an overestimation of +0.3 mm of bone levels in the buccal bone and an underestimation of -0.83 mm in lingual area. [15].

The diagnostic outcomes of CBCT imaging of peri-implant bone loss have been related to the type of study and defect morphology [37]. The *ex vivo* studies (cadaver

models) demonstrated good values for sensitivity and specificity for both circumferential and infraosseous defects but lower for dehiscences [38, 39]. Contrastingly, CBCT imaging for defect analysis in *in vivo* animal studies showed positive correlation with histology but have a tendency to over-[17, 35] or under-estimate[15, 40] the size of the defect. In particular, employing the ligature-induced peri-implantitis defect model in the canine, mean differences between CBCT and histological analyses were -0.53 ± 1.48 mm for supracrestal defects, $+0.49 \pm 1.18$ mm for infraosseous defects, and $+0.18 \pm 0.54$ mm for defect width at vestibular aspects, and -0.13 ± 0.44 mm for supracrestal defects, -0.05 ± 0.62 mm for infraosseous defects and $+0.15 \pm 0.48$ mm defect width at the oral aspects, respectively.[17]

Hence, the use of CBCT might not be incorporated to the standard protocol for radiographic peri-implantitis diagnosis, but can have a relevant role when the determination of defect morphology may play an essential role in the therapeutic decision-making [41].

Clinical implications for the management of peri-implantitis

Clinical recommendations based on the present findings cannot be drawn due to the nature of the study. Nevertheless, given the relevance of defect morphology upon the therapeutical modality,[4] findings from this research may indicate that reconstructive therapy must be very selectively indicated. In other words, conceiving circumferential defects as the indication for regeneration, based on the present findings, the majority of defects might not be the most suitable candidates. Hence, with the goal of reducing

probing pocket depth as the therapeutical endpoint, the reconstruction of infraosseous peri-implantitis bone defects might be in need to be complemented with resective therapy. Furthermore, in 3-wall defects missing the buccal wall (class Ib), reconstructive strategies should be applied to build up the missing bony wall. However, data on this is scarce.

Limitations and recommendations for future studies

Weaknesses and strengths must be disclosed for properly understanding findings from the present study. Firstly, the aim of this study was to assess the morphologic features using CBCT. As such, CBCT has been associated to over- and under-estimation compared to other methods .[15, 17, 35, 40] Nevertheless, this radiographic technique enables to examine the three-dimensional bone structure in cases where implant prognosis is hopeless and minimal invasive implant retrieval is desired. Hence, due to the nature of the present study we could be more inclusive compared to previously published studies regarding the severity despite of the treatment plan to manage the peri-implantitis defect. In addition, in future studies it is encouraged to assess the intra- and inter-examiner reproducibility regarding the morphology and severity of the peri-implantitis defects using CBCT.

Owing to the scarce information on defect morphology on the reconstructive therapeutical outcomes, it is recommended to further investigate the influence of defect morphology upon reconstructive and resective outcomes. In this sense, it is also

suggested to inquire on the relevance of local predisposing factors, including soft and hard tissue characteristics on the onset and severity of peri-implantitis.

Conclusion

Peri-implantitis defects course with an infraosseous component and frequently with buccal bone loss. Certain patient-, implant- and site-specific variables are related with defect morphology and severity. However, morphological patterns for peri-implantitis bone defects could not be proven.

References

1.   Tsitoura E, Tucker R, Suvan J, Laurell L, Cortellini P, Tonetti M. Baseline radiographic defect angle of the intrabony defect as a prognostic indicator in regenerative periodontal surgery with enamel matrix derivative. *J Clin Periodontol* 2004;31:643-647.

2.   Tonetti MS, Pini-Prato G, Cortellini P. Periodontal regeneration of human intrabony defects. IV. Determinants of healing response. *J Periodontol* 1993;64:934-940.

3.   Garaicoa C, Suarez F, Fu JH, et al. Using Cone Beam Computed Tomography Angle for Predicting the Outcome of Horizontal Bone Augmentation. *Clin Implant Dent Relat Res* 2015;17:717-723.

4.   Schwarz F, Sahm N, Schwarz K, Becker J. Impact of defect configuration on the clinical outcome following surgical regenerative therapy of peri-implantitis. *J Clin Periodontol* 2010;37:449-455.

5.   Schwarz F, Sahm N, Becker J. Impact of the outcome of guided bone regeneration in dehiscence-type defects on the long-term stability of peri-implant health: clinical observations at 4 years. *Clin Oral Implants Res* 2012;23:191-196.

6.   Wang HL, Boyapati L. "PASS" principles for predictable bone regeneration. *Implant Dent* 2006;15:8-17.

7.   Susin C, Fiorini T, Lee J, De Stefano JA, Dickinson DP, Wikesjo UM. Wound healing following surgical and regenerative periodontal therapy. *Periodontol 2000* 2015;68:83-98.

8.   Schwarz F, Herten M, Sager M, Bieling K, Sculean A, Becker J. Comparison of naturally occurring and ligature-induced peri-implantitis bone defects in humans and dogs. *Clin Oral Implants Res* 2007;18:161-170.

9.   Serino G, Turri A, Lang NP. Probing at implants with peri-implantitis and its relation to clinical peri-implant bone loss. *Clin Oral Implants Res* 2013;24:91-95.

10.   Garcia-Garcia M, Mir-Mari J, Benic GI, Figueiredo R, Valmaseda-Castellon E. Accuracy of periapical radiography in assessing bone level in implants affected by peri-implantitis: a cross-sectional study. *J Clin Periodontol* 2016;43:85-91.

11.   Monje A, Insua A, Rakic M, Nart J, Moyano-Cuevas JL, Wang HL. Estimation of the diagnostic accuracy of clinical parameters for monitoring peri-implantitis progression: An experimental canine study. *J Periodontol* 2018;89:1442-1451.

12.   Serino G, Turri A. Extent and location of bone loss at dental implants in patients with peri-implantitis. *J Biomech* 2011;44:267-271.

13.   Kuhl S, Zurcher S, Zitzmann NU, Filippi A, Payer M, Dagassan-Berndt D. Detection of peri-implant bone defects with different radiographic techniques - a human cadaver study. *Clin Oral Implants Res* 2016;27:529-534.

14.   Steiger-Ronay V, Krcmaric Z, Schmidlin PR, Sahrmann P, Wiedemeier DB, Benic GI. Assessment of peri-implant defects at titanium and zirconium dioxide implants by means of periapical radiographs and cone beam computed tomography: An in-vitro examination. *Clin Oral Implants Res* 2018;29:1195-1201.

15.   Ritter L, Elger MC, Rothamel D, et al. Accuracy of peri-implant bone evaluation using cone beam CT, digital intra-oral radiographs and histology. *Dentomaxillofac Radiol* 2014;43:20130088.

16.   Harris D, Horner K, Grondahl K, et al. E.A.O. guidelines for the use of diagnostic imaging in implant dentistry 2011. A consensus workshop organized by the European Association for Osseointegration at the Medical University of Warsaw. *Clin Oral Implants Res* 2012;23:1243-1253.

17.   Golubovic V, Mihatovic I, Becker J, Schwarz F. Accuracy of cone-beam computed tomography to assess the configuration and extent of ligature-induced peri-implantitis defects. A pilot study. *Oral Maxillofac Surg* 2012;16:349-354.

18.   Schwarz F, Derks J, Monje A, Wang HL. Peri-implantitis. *J Clin Periodontol* 2018;45 Suppl 20:S246-S266.

19.   Berglundh T, Armitage G, Araujo MG, et al. Peri-implant diseases and conditions: Consensus report of workgroup 4 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *J Clin Periodontol* 2018;45 Suppl 20:S286-S291.

20.   Serino G, Strom C. Peri-implantitis in partially edentulous patients: association with inadequate plaque control. *Clin Oral Implants Res* 2009;20:169-174.

21.   Zhang L, Geraets W, Zhou Y, Wu W, Wismeijer D. A new classification of peri-implant bone morphology: a radiographic study of patients with lower implant-supported mandibular overdentures. *Clin Oral Implants Res* 2014;25:905-909.

22.   Gilmore ND. An epidemiological investigation of vertical osseous defects in periodontal disease. Ann Arbor, Michigan; 1970.

23.   Nielsen IM, Glavind L, Karring T. Interproximal periodontal intrabony defects. Prevalence, localization and etiological factors. *J Clin Periodontol* 1980;7:187-198.

24.   Larato DC. Periodontal bone defects in the juvenile skull. *J Periodontol* 1970;41:473-475.

25.   Wouters FR, Salonen LE, Hellden LB, Frithiof L. Prevalence of interproximal periodontal intrabony defects in an adult population in Sweden. A radiographic study. *J Clin Periodontol* 1989;16:144-149.

26.   Monje A, Chappuis V, Monje F, Muñoz F, Wang HL, Urban IA, Buser D. The Critical Peri-implant Buccal Bone Wall Thickness Revisited: An Experimental Study in the Beagle Dog. *Int J Oral Max Implants (under review)*

27.   Monje A, Blasi G. Significance of keratinized mucosa/gingiva on peri-implant and adjacent periodontal conditions in erratic maintenance compliers. *J Periodontol* 2018.

28.   Souza AB, Tormena M, Matarazzo F, Araujo MG. The influence of peri-implant keratinized mucosa on brushing discomfort and peri-implant tissue health. *Clin Oral Implants Res* 2016;27:650-655.

29.   Schwarz F, Becker J, Civale S, Sahin D, Iglhaut T, Iglhaut G. Influence of the width of keratinized tissue on the development and resolution of experimental peri-implant mucositis lesions in humans. *Clin Oral Implants Res* 2018;29:576-582.

30.   Rodrigo D, Sanz-Sanchez I, Figuero E, et al. Prevalence and risk indicators of peri-implant diseases in Spain. *J Clin Periodontol* 2018;45:1510-1520.

31.   Schuldt Filho G, Dalago HR, Oliveira de Souza JG, Stanley K, Jovanovic S, Bianchini MA. Prevalence of peri-implantitis in patients with implant-supported fixed prostheses. *Quintessence Int* 2014;45:861-868.

32.   Kumar PS, Dabdoub SM, Hegde R, Ranganathan N, Mariotti A. Site-level risk predictors of peri-implantitis: A retrospective analysis. *J Clin Periodontol* 2018;45:597-604.

33.   Schulze RK, Berndt D, d'Hoedt B. On cone-beam computed tomography artifacts induced by titanium implants. *Clin Oral Implants Res* 2010;21:100-107.

34.   Codari M, de Faria Vasconcelos K, Ferreira Pinheiro Nicolielo L, Haiter Neto F, Jacobs R. Quantitative evaluation of metal artifacts using different CBCT devices, high-density materials and field of views. *Clin Oral Implants Res* 2017;28:1509-1514.

35. Fienitz T, Schwarz F, Ritter L, Dreiseidler T, Becker J, Rothamel D. Accuracy of cone beam computed tomography in assessing peri-implant bone defect regeneration: a histologically controlled study in dogs. *Clin Oral Implants Res* 2012;23:882-887.

36. Gonzalez-Martin O, Oteo C, Ortega R, Alandez J, Sanz M, Veltri M. Evaluation of peri-implant buccal bone by computed tomography: an experimental study. *Clin Oral Implants Res* 2016;27:950-955.

37. Pelekos G, Acharya A, Tonetti MS, Bornstein MM. Diagnostic performance of cone beam computed tomography in assessing peri-implant bone loss: A systematic review. *Clin Oral Implants Res* 2018;29:443-464.

38. de-Azevedo-Vaz SL, Alencar PN, Rovaris K, Campos PS, Haiter-Neto F. Enhancement cone beam computed tomography filters improve in vitro periimplant dehiscence detection. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2013;116:633-639.

39. Kamburoglu K, Kolsuz E, Murat S, Eren H, Yuksel S, Paksoy CS. Assessment of buccal marginal alveolar peri-implant and periodontal defects using a cone beam CT system with and without the application of metal artefact reduction mode. *Dentomaxillofac Radiol* 2013;42:20130176.

40. Corpas Ldos S, Jacobs R, Quirynen M, Huang Y, Naert I, Duyck J. Peri-implant bone tissue assessment by comparing the outcome of intra-oral radiograph and cone beam computed tomography analyses to the histological standard. *Clin Oral Implants Res* 2011;22:492-499.

41. Bender P, Salvi GE, Buser D, Sculean A, Bornstein MM. Correlation of Three-Dimensional Radiologic Data with Subsequent Treatment Approach in Patients with

Peri-implantitis: A Retrospective Analysis. *Int J Periodontics Restorative Dent* 2017;37:481-489.