# CLINICAL ORAL IMPLANTS RESEARCH

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Marginal bone loss around implants placed in maxillary native bone or grafted sinuses: a retrospective cohort study

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Fax: +34 958 520658 e-mail : pgalindo@ugr.es Key words: alveolar bone loss, bone grafting, bone resorption, dental implants, maxillary sinus

#### **Abstract**

**Objectives:** To assess differences in marginal bone loss around implants placed in maxillary pristine bone and implants placed following maxillary sinus augmentation over a period of 3 years after functional loading.

Material and methods: Two cohorts of subjects (Group 1: Subjects who received sinus augmentation with simultaneous implant placement; Group 2: Subjects who underwent conventional implant placement in posterior maxillary pristine bone) were included in this retrospective study. Radiographic marginal bone loss was measured around one implant per patient on digitized panoramic radiographs that were obtained at the time of prosthesis delivery (baseline) and 12, 24, and 36 months later. The influence of age, gender, smoking habits, history of periodontal disease, and type of prosthetic connection (internal or external) on marginal bone loss was analyzed in function of the type of osseous support (previously grafted or pristine).

Results: A total of 105 subjects were included in this study. Cumulative radiographic marginal bone loss ranged from 0 mm to 3.9 mm after 36 months of functional loading. There were statistically significant differences in marginal bone loss between implants placed in grafted and pristine bone at the 12-month assessment, but not in the subsequent progression rate. External prosthetic connection, smoking, and history of periodontitis negatively influenced peri-implant

**Conclusions:** Implants placed in sites that received maxillary sinus augmentation exhibited more marginal bone loss than implants placed in pristine bone, although marginal bone loss mainly occurred during the first 12 months after functional loading. Implants with external implant connection were strongly associated with increased marginal bone loss overtime.

Ridge augmentation via bone grafting has become a routine indication to treat alveolar bone deficiencies and facilitate prosthetically driven implant placement. Maxillary sinus floor elevation is not only a predictable surgical procedure to obtain vertical bone augmentation in posterior segments of atrophic maxillae, but also represents an ideal model to investigate healing events following bone grafting (Busenlechner et al. 2009; Price et al. 2011). Clinical, radiographic, and histologic outcomes after maxillary sinus augmentation procedures, applying different grafting materials and surgical techniques, have been extensively reported over the past two decades (Wallace & Froum 2003; Del Fabbro et al. 2004; Pjetursson et al. 2008; Avila et al. 2010; Galindo-Moreno et al. 2011). A critical

bone maintenance, regardless of the type of osseous substrate.

clinical question that has attracted the attention of clinicians and researchers is whether implants placed in grafted sites present higher risk of failure than implants placed in native/pristine maxillary bone. According to various systematic reviews, survival rates for implants partially inserted in grafted maxillary sinuses are similar (Wallace & Froum 2003; Del Fabbro et al. 2004; Pjetursson et al. 2008), or even superior (Olson et al. 2000), to those associated with implants placed in pristine maxillary areas. On the contrary, in a recently published cohort study, it was observed that "...implants placed in augmented sinuses had a lower survival rate compared to implants placed in pristine bone." After a 6-year follow-up period, the mean survival rate for implants placed in

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grafted areas or in native maxillary bone was 86.1% and 96.4%, respectively (Barone et al. 2011). How can these reported differences be explained?

It is generally accepted that, in order to ensure long-term survival of functionally loaded implants placed in augmented sinuses, tantamount to achieving enough ridge volume for straightforward implant placement is to obtain an osseous substrate which intrinsic structural and physiological characteristics resemble those of native bone. While osseous support of implants placed in pristine maxillae is exclusively constituted by native and newly formed bone, in cases that involve maxillary sinus floor elevation remaining graft particles may also be part of the peri-implant tissue. In the latter, marginal support is provided by a variable amount of native bone, depending on the original remaining alveolar bone height (RBH) (Avila-Ortiz et al. 2012). Finite element analysis studies have suggested that load distribution and marginal bone loss (MBL) around implants placed in grafted sinus cavities may be strongly conditioned by the characteristics of the grafting material (Fanuscu et al. 2004; Huang et al. 2009; Inglam et al. 2010). In this regard, it has been observed that when the grafted volume exhibits less stiffness than the native bone, functional loading produces an increased concomitant stress at the level of the crestal bone (Huang et al. 2009), which is typically associated with MBL (Kitamura et al. 2004). Although finite element analysis studies should be cautiously interpreted, to the light of currently available evidence, it can be hypothesized that implant failure and/or peri-implant bone loss in sites that have undergone sinus floor elevation may be associated with inadequate adaptive responses of the supporting tissues to functional loading. Other factors that have been associated with peri-implant MBL, such as history of periodontal disease (Roccuzzo et al. 2010; Koldsland et al. 2011), smoking (Wallace 2000), and the location of the microgap in function of the type of prosthetic connection (Veis et al. 2010) may play a synergistic role. Hence, the primary objective of this study was to assess differences in MBL around implants placed in maxillary pristine bone and implants placed following maxillary sinus augmentation over a period of 3 years after functional loading. The secondary aim was to evaluate the influence that history of periodontitis, smoking, and type of prosthetic connection have on peri-implant bone resorptive events.

## Material and methods

#### Study population

All subjects were selected from a private practice pool following these inclusion criteria: 18-85 years of age, have at least one implant in the posterior maxillary region with a minimum of 3 years of functional loading, physical status according to the American Society of Anesthesiologists (ASA) I or II, absence of systemic diseases or conditions known to alter bone metabolism, periodontally stable and enrolled in a maintenance program. All records contained standardized orthopantomographs obtained at the time of final restoration delivery (baseline), and at 12, 24, and 36 months after functional loading. Subjects were excluded if they had a history of intake of medications known to modify bone metabolism (e.g., bisphosphonates). Likewise, subjects who developed acute or chronic sinus pathology (i.e., sarcoidosis, osteomas, carcinomas, cancer of any kind, or had postoperative complications related to the procedures described in this study were excluded. The study protocol was reviewed and approved by the ethical committee of the University of Granada for studies involving human subjects.

Consecutive patients that fulfilled the inclusion criteria were elected for this study. The study population was divided into two cohorts of subjects. Subjects were assigned to each cohort based on a sinus augmentation classification that indicates delayed implant placement in clinical scenarios where the (RBH) is <5 mm (Wang & Katranji 2008). The first cohort (Group 1) was formed by subjects who presented RBH between 5 and 9 mm, which generally allows for maxillary sinus augmentation with simultaneous implant placement. The second cohort (Group 2) included subjects who presented enough alveolar bone height to allow conventional placement of implants with a length of  $\geq 12$  mm. Subjects received either one of two different implant systems, with internal (Astra Tech AB, Mölndal, Sweden) or external connection (Microdent Implant System, Barcelona, Spain).

## Surgical and restorative procedures

All surgical procedures were conducted under local anesthesia (Ultracain®, Aventis Inc., Frankfurt, Germany). In group 1, sinus augmentation procedures were performed following the bone scraper technique as described elsewhere (Galindo-Moreno et al. 2007). Briefly, all sinus cavities were grafted using autologous cortical bone in combination with anorganic bovine bone particles ranging from

250 to 1000 μm (Bio-Oss® – Geistlich Pharma AG, Wolhusen, Switzerland) in a 1:1 ratio. Prior to bone graft placement, implant osteotomy was performed while protecting the Schneiderian membrane with a blunt metal instrument, according to implant manufacturer's instructions. Then, grafting material was placed to fill the medial half of the sinus cavity, implant/s was/were inserted and the rest of the sinus cavity was filled. A variable volume of bone grafting material, ranging from 3 to 5 cc, was used per sinus. An absorbable collagen membrane (BioGide® -Geistlich Pharma AG, Wolhusen. Switzerland) was trimmed and adapted over the lateral aspect of the bony window. Soft tissues were approximated and sutured. Primary wound closure was achieved in all cases. In subjects that did not require maxillary sinus augmentation (Group 2), implants were installed following a conventional implant placement protocol. All subjects were asked to comply with a pharmacologic regime that included amoxicillin/clavulanic acid tablets (875/125 mg, TID for 7 days) or, if allergic to penicillin, clindamycin tablets (300 mg, TID for 7 days), as well as antiinflammatory medication (Ibuprofen 600 mg, every 4-6 hours as needed to a maximum of 3600 mg per day). Sutures were removed at 2 weeks after sinus surgery (Group 1) or 1 week in belonging to group 2. Subjects were then evaluated at 6-8 weeks intervals, to monitor postoperative healing. Trans-epithelial abutments were placed in a second surgical procedure after a 5-month healing period. Implant-supported prostheses were delivered 4 weeks later. All definitive restorations were screw-retained fixed partial dentures.

# Radiographic evaluation of marginal bone loss

Standardized digital panoramic radiographs (Kodak ACR-2000, Eastman Kodak Company, Rochester, NY, USA) obtained at the time of final restoration delivery (baseline), and at 12, 24, and 36 months after functional loading were digitized and exported to a computer software for further analysis (Dent-A-View v1.0, DigiDent, DIT, Nesher, Israel). To determine MBL, an independent calibrated examiner (A.F-J.) made linear measurements on each panoramic radiograph from the most mesial and distal point of the implant platform to the crestal bone (Figures 1 and 2). Only one implant per subject was analyzed, regardless of the number of implants placed. In order to standardize the measurements and to reduce the influence of anatomical variables, the implant located at





Fig. 1. Radiographic measurements at baseline (a) and 36 months (b) after functional loading in the external connection group



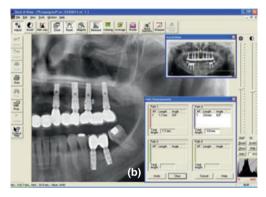


Fig. 2. Radiographic measurements at baseline (a) and 36 months (b) after functional loading in the internal connection group

the site with the shortest RBH was selected, which most often was the first molar position.

## Additional data recorded

Age, sex, smoking, and drinking habits at the time of enrollment in the study, history of periodontal disease, and type of prosthetic connection (internal or external) were recorded for each subject. Smoking habits were classified using the following criteria: Non-smoker: 0 cigarette/day, mild smoker: 0 -10 cigarette/day, and heavy smoker: >10 cigarette/day. Alcohol intake was considered over 10 gr/day (Galindo-Moreno et al. 2005). History of periodontal disease was determined by consulting dental history records. If not available, information was gathered by asking the subject about past dental care and performing a comprehensive periodontal examination.

## Statistical analyses

MBL was expressed as average values (in mm) in function of type of bone, interproximal site, time elapsed since functional loading, and type of prosthetic connection. One-way analysis of variance (ANOVA) was performed to identify the categorical vari-

ables (gender, history of periodontitis, and smoking) significantly associated with MBL. The relationship between MBL and age was determined by calculating the Pearson correlation coefficient. All these results reported below were robust to the general linear model assumptions. The effect of two variables of interest, type of bone (grafted versus pristine) and type of connection (external versus internal), relative to peri-implant bone loss was analyzed using analysis of covariance (ANCOVA). In this analysis, there were two repeatedmeasures factors: elapsed time since surgery (12, 24 or 36 months) and location of the marginal bone loss (mesial or distal). The Greenhouse-Geisser correction was used to correct for violation of the sphericity assumption for all decisions in which repeatedmeasures factors with more than 2 levels were involved. All the analyses were carried out using statistical software (SPSS 15, Armonk, NY, USA).

## Results

One hundred and five subjects (74.2% females) participated in this retrospective cohort study. Age ranged from 32 to 68 years (Mean = 52.37 years). A total of 46

subjects were enrolled in Group 1 and 59 subjects formed Group 2. Therefore, 105 implants were evaluated. Thirty-three implants in Group 1 had internal connection and 13 had external connection. Twenty-five implants with internal connection and 34 with external connection were allocated in Group 2.

Cumulative radiographic MBL ranged from 0 mm to 3.9 mm after 36 months of functional loading. When data from both groups were pooled, 53.3% of mesial and 49.5% of distal sites showed <1 mm of MBL, while 32.4% of mesial and 22.9% of distal sites exhibited no MBL at all. Table 1 shows MBL average values, with the corresponding standard deviation, in function of interproximal site (mesial or distal), elapsed time since functional loading (12, 24 and 36 months), type of prosthetic connection (internal or external), and type of bone (pristine or grafted). Table 2 displays the data that relate to the association between the independent variables and MBL. Independent samples t-tests were used to examine the effects of gender, history of periodontitis, and smoking. Pearson correlation coefficients were computed for age. Smoking independently influenced bone loss during the observed

Table 1. Average [Medians] values in mm (standard deviations) for mesial and distal marginal bone loss (intragroup) around implants placed in pristine and grafted bone (intergroup) in function of elapsed time since functional loading (intragroup) and type of prosthetic connection (intergroup)

Site	Bone	Connection	Marginal bone loss 12 m	24 m	36 m
Mesial	Pristine	Internal External	0.08 [0.01] (0.24) 0.99 [1.09] (0.52)	0.11 [0.01] (0.28) 1.16 [1.19] (0.58)	0.23 [0.01] (0.51) 1.28 [1.3] (0.63)
	Grafted	Internal External	0.59 [0.01] (0.93) 1.37 [1.11] (0.86)	0.71 [0.01] (0.97) 1.51 [1.31] (0.93)	0.78 [0.2] (1.02) 1.55 [1.4] (0.91)
Distal	Pristine	Internal External	0.23 [0.01] (0.48) 1.07 [0.91] (0.61)	0.27 [0.01] (0.52) 1.27 [1.41] (0.64)	0.32 [0.01] (0.54) 1.49 [1.51] (0.71)
	Grafted	Internal External	0.74 [0.31] (0.89) 1.09 [0.91] (0.81)	0.95 [0.53] (0.93) 1.31 [1.21] (0.88)	1.04 [0.51] (0.99) 1.45 [1.51] (0.94)

Table 2. Independent association of marginal bone loss with gender, history of periodontitis, smoking, and age

		Gender	History of periodontitis	Smoking	Age
12 m	Mesial	0.25 [0.70] (0.17)	0.41 [0.90] (0.007)	0.55 [1.10] (0.001)	0.38 (0.001)
	Distal	0.24 [0.41] (0.17)	0.33 [0.45] (0.028)	0.40 [0.50] (0.020)	0.26 (0.008)
24 m	Mesial	0.23 [0.65] (0.23)	0.38 [0.90] (0.022)	0.53 [0.90] (0.001)	0.32 (0.001)
	Distal	0.20 [0.60] (0.29)	0.29 [0.55] (0.074)	0.41 [0.70] (0.020)	0.25 (0.009)
36 m	Mesial	0.19 [0.52] (0.34)	0.36 [1.05] (0.039)	0.47 [1.05] (0.002)	0.30 (0.002)
	Distal	0.20 [0.57] (0.32)	0.29 [0.65] (0.110)	0.40 [0.90] (0.030)	0.28 (0.004)

Differences between averages [Medians], marginal bone loss for gender (females–males), periodontitis (periodontal vs. non-periodontal), and Smoking (smokers vs. non-smokers). Independent samples *t*-test *P*-values are between parenthesis. Last column, Pearson correlation coefficients for age (p-values between parenthesis).

times at both mesial and distal sites. Likewise, an association between history of periodontitis and increased MBL was observed, except on distal sites at 24 and 36 months. Increased MBL was also associated with older age.

The 2 (intergroup, type of bone: pristine vs. grafted) by 2 (intergroup, type of connection: external vs. internal) by 3 (intragroup, Times: 12, 24, and 36 months) by 2 (intragroup, Sites: mesial vs. distal) repeatedmeasures ANCOVA, using history of periodontitis, smoking and age as covariates, revealed that peri-implant MBL was higher in grafted (1.09 mm) than in pristine (0.71 mm) bone [F (1.98)=5.62, p = 0.02]. MBL progression rate was not different between both groups. Interestingly, MBL was significantly higher around implants with external (1.30 mm) than with internal (0.50 mm)connections [F(1,98)=17.23,P < 0.01]. The type of connection by elapsed time interaction was also significant [F (2,196)=4.85, P < 0.01]. Trend analyses of this interaction showed that MBL was steeper overtime for the external than the internal connection implants [F(1,98)=5.51, P=0.02](Slopes were 0.18 mm/year and 0.075 mm/ year, respectively). No other significant effects were observed.

## Discussion

To our knowledge, this is the first long-term retrospective cohort study aimed at determining whether implants placed following maxillary sinus augmentation exhibit more radiographic MBL than implants placed in pristine bone after functional loading. The influence of other variables such as smoking, history of periodontitis, and type of prosthetic connection on MBL incidence was also investigated.

Interestingly, it was observed that MBL is higher around functionally loaded implants placed in augmented sinuses than around implants placed in pristine maxillary bone. Similar findings were reported in a study published in 1999 (Johansson et al. 1999). In that prospective study, it was noticed that implants placed in areas that underwent maxillary sinus grafting presented an average MBL of 1.4 mm after three years of loading, while implants placed in non-augmented posterior maxillary areas showed an average of 1.1 mm of MBL over the same period. These findings may contribute to partially explain the observed higher failure rate of implants placed in augmented sinuses, as compared to implants placed in pristine

bone, reported by Barone and collaborators (Barone et al. 2011). Differences in the biomechanical and biological properties of the tissue that directly interfaces with the implant surface may be the main reason for variations in MBL patterns noticed between both groups in the present study. The effect of biomechanical adaptive responses after functional loading on progressive MBL in the sinus augmentation model has been investigated in several finite element analystudies. Cehreli and collaborators reported that, although sinus augmentation normally results in more vertical bone support, it also gives rise to the appearance of strains in the sinus floor region, at the boundary between the native and the neoformed tissue (Cehreli et al. 2007). In this regard, Inglam et al. noticed that when the stiffness of the grafted area is less than that of the cancellous bone high-level strain is primarily distributed at the crestal level, which may promote MBL. Therefore, grafted areas should ideally have certain stiffness (similar or superior to adjacent native bone), so efficient loading forces distribution can be reached due to the exhibited similar values of strain energy density in the crestal cortical, cancellous, and grafted bone (Inglam et al. 2010). In this study, a composite graft (autologous cortical bone and anorganic bovine bone) was used for maxillary sinus augmentation. Physical properties of anorganic bovine bone (ABB) are comparable with human bone, given their similarities in both crystalline and morphological structure. Compared with normal human cancellous bone, ABB has a slightly higher modulus of elasticity [11 GPa] (Yildirim et al. 2000) and a similar compressive strength of 35 MPa (Scarano et al. 2006). It has been shown that in augmented sinus areas, bovine bone material behaves like autologous chin bone particles, although ABB has a much slower resorption rate than autogenous grafts (Sbordone et al. 2011). Hence, the differences between the used biomaterials were minimal, and no complication that could have affected graft consolidation was noticed during the observational period, but still MBL was higher around implants placed in grafted areas. This indicates that despite careful patient and biomaterial selection, the sequence of healing events following maxillary sinus augmentation may not always lead to obtain implant-supporting tissues with optimal properties. This is possibly related to variations in maturation and consolidation of the grafted area (i.e., reduced stiffness).

In the present study, smoking and history of periodontitis negatively influenced MBL with statistical significance regardless of the type of osseous substrate (grafted or pristine). Nonetheless, this is not surprising because both variables have been reported to play an important detrimental role in the maintenance of peri-implant crestal bone. Multiple studies have demonstrated an increased risk of MBL for smokers compared with nonsmokers, with odds ratio of peri-implantitis in smokers that range from 3.6 to 4.6 (Galindo-Moreno et al. 2005; Nitzan et al. 2005; Heitz-Mayfield & Huynh-Ba 2009). Former smokers also present more MBL when compared with non-smokers (Levin 2008). In a recent meta-analysis, MBL in subjects with history of periodontitis was found to be higher than in periodontally healthy subjects [mean difference = 0.61 mm] (Safii et al. 2010). It has also been shown that the combination of history of periodontitis and smoking increases the risk of peri-implant bone loss (Feloutzis et al. 2003; Wennstrom et al. 2004; Heitz-Mayfield & Huynh-Ba 2009). A recent study has reported that after 10 years, implants placed in tobacco smokers with a history of treated periodontitis yielded higher marginal bone loss compared with implants placed in periodontally healthy smokers, independent of the implant system used (Aglietta et al. 2011). Another study showed that implants in periodontally compromised, but non-smoking subjects who were previously treated for periodontitis had a tendency to exhibit more MBL when compared to those placed in periodontally healthy subjects (Matarasso et al. 2010). Confounding factors between these two variables could be argued because it is evident that tobacco smokers are more prone to develop periodontitis than non-smokers (Heitz-Mayfield 2005). In our study, after analyzing the effect of each variable, tobacco appeared to play a more determinant role in the progression of MBL overtime as compared to the other variables (P < 0.0001).

Interestingly, the variable that showed the strongest association with MBL in this study was the type of prosthetic connection. MBL was higher around implants with external connection than around those with internal prosthetic connection, regardless of bone type (grafted or non-grafted). These differences were sustained over the 36-month observational period. As of 2007, of all dental implant systems presently available in the market, only three had scientific documentation on periimplant MBL reported in two or more 5-year prospective clinical studies (Laurell & Lundgren 2011). These systems showed mean marginal bone loss values over 5 years well below what is hitherto accepted as success (Misch et al. 2008). In the majority of cases. most of the cumulative MBL takes place at early stages, particularly during the interval between abutment connection and crown delivery (Cardaropoli et al. 2006). It was suggested that this phenomena occurs because of the establishment of a peri-implant biological width (Berglundh & Lindhe 1996; Oh et al. 2002). However, it can be inferred that this physiological event does not happen to the same degree around all implants, and it may occur at different points in time. This notion is in accordance with our findings, where external prosthetic connection was associated with increased MBL, in particular during the first 12 months after functional loading. Although strongly significant, the reason for the difference in MBL between systems should be speculated upon a wide array of subjectrelated factors such as implant-supporting bone features (location, nature, or architecture), microbiologic characteristics, and individual inflammatory profiles; implant-related factors such as surface (Abrahamsson & Berglundh 2009), macro- (Hansson 2000; Novaes et al. 2006), or micro-design (Hansson & Werke 2003), roughness at the cervical portion (Hansson & Norton 1999; Aloy-Prosper et al. 2011), platform switching (Vela-Nebot et al. 2006; Canullo et al. 2010; Serrano-Sanchez et al. 2011) and location of the micro-gap (Piattelli et al. 2003; Dibart et al. 2005); or surgical-related factors such as distance between implants (Tarnow et al. 2000; Traini et al. 2010) and delayed versus immediate placement (Herzberg et al. 2006). Future studies should be conducted in order to elucidate the

effect of this plethora of variables on MBL to better understand these phenomena and prevent its appearance.

Despite the efforts made by the investigators to comply with high standards of research quality, this study presents some limitations. First, number of subjects and implants are not equally distributed per group. Also, obtaining radiographic MBL measurements from cone beam computer tomographic (CBCT) scans would have provided more accuracy and the possibility of performing a tridimensional analysis. However, this method was not part of this study due to unavailability in existing dental records.

## Conclusions

Implants placed in sites that received maxillary sinus augmentation exhibited more MBL than implants placed in pristine bone, although MBL mainly occurred during the first 12 months after functional loading. Smoking and history of periodontitis negatively influenced MBL with statistical significance regardless of the type of osseous substrate. Implants with external implant connection were strongly associated with increased MBL overtime.

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## Disclosure

Authors do not have any financial interests, either directly or indirectly, in the products listed in the study.

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