Variables that Influence the Relationship Between Osseointegration and Bone Adjacent to an Implant

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It is often assumed that there is a direct relationship between the bone density adjacent to an implant, as revealed by radiographs, and the percent histologic osseointegration. Moreover, the lack of standardized methods for evaluation of histologic preparations makes it difficult to compare published studies, especially as little is known about the variables that influence these measurements. In this animal study, computer-assisted lineal analysis was used to evaluate the effects of subject, tooth position, and implant surface site on measured bone density and osseointegration in a bone augmentation experiment. Three sites—coronal lingual, apical lingual, and apical facial—were analyzed around each of 6 (3.75 × 8 mm) threaded machined titanium implants, as well as the apical facial site of 21 other implants placed in the mandibular premolar area of 5 dogs. In all sites, a progressive decrease in bone density was observed from bone adjacent to the implant to that at the titanium implant surface. There was an animal effect on osseointegration, but there were no differences between the mandibular premolar locations (second, third, and fourth). Most importantly, there were significant measurable effects attributable to the surface site examined. The need for carefully standardized histologic evaluations is established. (INT J ORAL MAXILLOFAC IMPLANTS 2000;15:654–661)

Key words: *bone density, endosseous dental implants, histology, histomorphometry, osseointegration*

Emphasis has been placed upon the assessment of alveolar bone as the support for an endosseous implant. This derives from longitudinal studies that have examined the outcome of root-form implant therapy and have reported differences in the quality of the alveolar bone present at the recipient site as assessed clinically.[1] The clinical assessment of the quality of alveolar bone is often determined by routine or computerized radiographic methods, as compared to resistance by drilling. This apparently remains the method of choice, in spite of the errors introduced as a consequence of bone marrow content.[2] Reportedly, bone found in the anterior portion of both dental arches is denser than that found in the posterior portion, and bone found in the mandibular arch is generally denser than that found in the maxillary arch.[3] Histologic verification of these clinical impressions of bone density (quality) has rested on alveolar bone cores harvested as part of the osteotomy implant placement procedure[4,5] or the occasionally retrieved specimen from autopsy or trephine removal.[6,7]

The primary criterion used to define implant failure has been clinical mobility. Usually, this has been determined manually with surgical forceps, with the use of the Periotest device, or by a reverse torque test administered at the time of implant uncovering.[8–10] Inability to perceive rotational movement with a torque wrench establishes the clinical diagnosis of immobility or clinical osseointegration. Clinical osseointegration then implies histologic osseointegration, ie, contiguous contacts of alveolar bone with the implant surface.

A study by Fujimoto et al[11] attempted to relate radiographic bone density, torque removal, and histologic osseointegration in 3 different bone sites within

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the same animal. Bone density in the femur was compared to torque removal data and a descriptive evaluation of histologic osseointegration of implants placed into the rabbit tibia or the mandible. Torque implant removal in the tibia correlated fairly well with radiographic bone density (r = 0.64), but torque removal in the mandible did not (r = 0.11). The histologic description of osseointegration supported the torque removal data. Johansson and colleagues[12] reported that a greater torque removal force was accompanied by greater histologic osseointegration. Caulier and coworkers[13] compared radiographic assessment of implants placed in the maxilla of the goat to Periotest values and histologic osseointegration. No correlation could be found regarding the Periotest data; the radiographic assessment routinely overestimated the histologic osseointegration. Still, it is not known to what extent histologic bone density or histologic osseointegration is responsible for the clinical criterion of implant immobility.

Numerous studies have examined histologic osseointegration as it relates to various aspects of the implant, ie, implant surface material,[14–18] loading,[19–21] or time since placement.[15–17,20,22] The consensus reveals that these factors do, in fact, affect the degree of bone-to-implant interface. For these factors and factors that involve the histomorphometric technique, ie, inter- or intra-analysis error,[23] area of bone density analyzed,[10,15,22,24–26] direction of sectioning,[24] cortical versus cancellous bone,[27] coronal versus apical implant site,[28] buccal versus lingual implant site,[29] and all versus the "best 3" implant threads,[24,30] the results and conclusions are varied, and the ranges are widely diverse according to the conditions or factors imposed.

An earlier study analyzed one efficient method for measuring histologic bone density and histologic osseointegration.[31] The present study evaluated the relationship between the histologic bone density located within the interthread area, within 2 mm of adjacent alveolar structure, and at the implant surface with respect to animals, tooth positions, and implant surface sites.

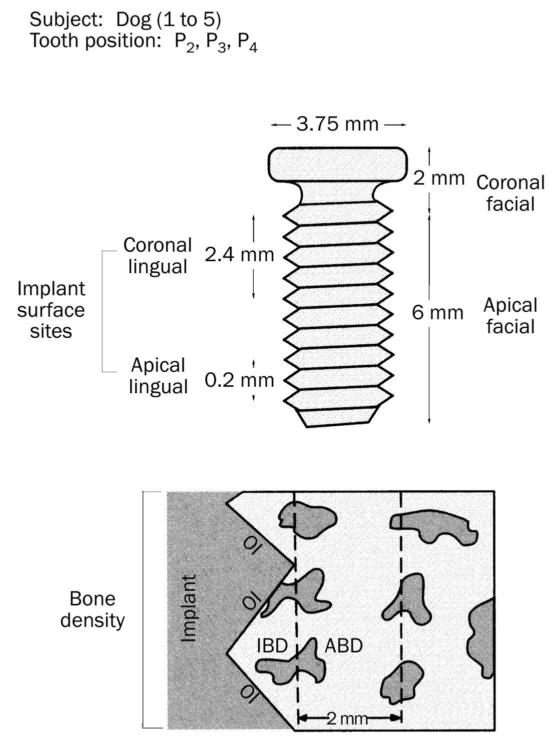

Fig 1 Scope of analyses and parameter definitions. P_2, P_3, P_4 = second, third, and fourth premolars; ABD = adjacent bone density; IBD = interthread bone density; OI = osseointegration.

MATERIALS AND METHODS

The study utilized 5 young adult foxhound dogs, and the protocol was approved by the Institutional Animal Care Committee. Full mucoperiosteal flaps were reflected and the mandibular premolars were extracted. Alveolar bone, measuring 5 by 5 mm, was removed, creating a facial dehiscence defect in the second, third, and fourth premolar mesial root extraction positions. A 3.75 × 8-mm submerged threaded machined titanium implant (Steri-Oss, Yorba Linda, CA) was then placed immediately into this position (n = 6 for each animal). The coronal facial alveolar defect was filled with *(1)* a bioactive bone inductive agent carried in a bioresorbable vehicle, *(2)* vehicle alone, or *(3)* unfilled sham control. The recipient positions were closed by primary intention and allowed to heal for 3 months, at which point the tissues were harvested for histologic preparation. Ground sections were prepared and stained for histologic evaluation. Histomorphometric analysis was accomplished using a computerized lineal analysis method described earlier.[31] The effects of different animals, tooth positions, and implant surface sites on bone densities (percent bone) were examined in 3 different areas: *(1)* at the implant surface (osseointegration [OI]), *(2)* between the thread peaks (interthread bone density [IBD]), and *(3)* surrounding the implant to the lateral extent of 2 mm (adjacent bone density [ABD]) (Fig 1). Twenty-seven implants were available for analysis as described earlier.[31] The parameters chosen for this analysis using the Ribbon software (a computer-assisted lineal

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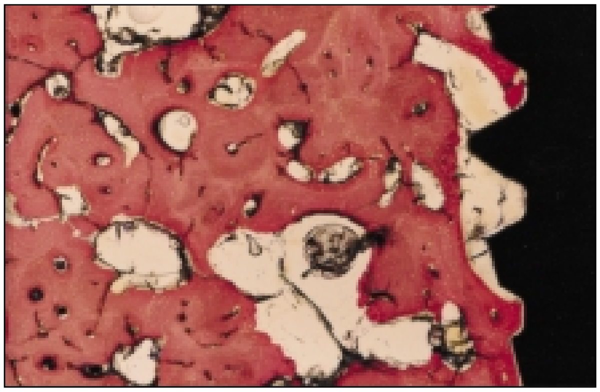

Fig 2 An example of low osseointegration and interthread bone density.

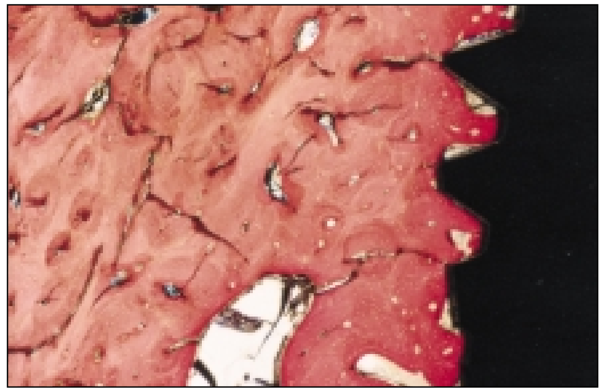

Fig 3 An example of high osseointegration and interthread bone density.

analysis program created at Loma Linda University) created 9 line intersections with the implant surface per groove width (0.59 mm) to estimate osseointegration and 4.5 ribbons (a ribbon consists of 2 horizontal lines 0.05 mm or 8 pixels apart) per groove to analyze bone density (percent bone).

The facial apical aspects of all 27 implant sections and 6 implant sections from the lingual apical and lingual coronal aspects were analyzed. Four grooves between thread peaks were evaluated from the coronal facial site, and 2 grooves between the most apical full peaks were used for the lingual analysis (Fig 1). Data for the treated coronal facial sites will be reported elsewhere.

Statistical Analysis

Analysis of variance (ANOVA) was used to test for differences in bone density among animals, tooth positions, and implant surface sites. Parametric analysis was employed, given that most distributions by group approximated normal, assumptions of homogeneity of variance were generally met, and measurement was on a ratio scale. All ANOVA *F* tests were followed by Bonferroni adjusted post hoc tests for pairwise differences. Given the small sample size, these conservatively adjusted tests were very low in power. Where ANOVA tests were significant and effect sizes (eta^2, defined as the proportion of variance explained by the total variance) were large, interpretation of "where the difference lies" was generally based upon assessment of the graphic representation of the data.

The data were graphed using box plots. The advantage of box plots is that they not only reflect an estimate of central tendency (the middle line represents the median score), but they also provide a representation of variability around the central tendency. The "box" reflects the range of scores from the 25th to the 75th percentile. The error bars show the 10th to 90th percentile. Outliers (data points found 1.5 to 3.0 box lengths above or below the box) were indicated in the present study by O's. Extreme outliers (data points found more than 3.0 box lengths above or below the box) are indicated by asterisks. Differences from one box to the next reflect "variance explained." Variability within boxes represents "variance unexplained" or error.

RESULTS

All Implants

Examples of low and high values of OI and IBD are seen in Figs 2 and 3. In all implants (n = 27), 62% of the variance in bone density could be explained by accounting for the component (OI, IBD, ABD) of the tissue sample analyzed. The ANOVA showed clear significance ($P < .001$). Post hoc pairwise comparisons subjected to a Bonferroni correction enabled the conclusion that ABD (92.6, SD 9.0) was significantly greater than IBD (76.9, SD 16.7; $P < .001$). Interthread bone density values were, in turn, significantly greater than OI (59.2, SD 19.3; $P < .001$) (Fig 4). Thus, for the conditions utilized in placement of the titanium threaded implants, bone was most dense 2 mm exterior to the thread peaks, less dense in the interthread area, and least dense when in direct contact with the titanium surface.

Distribution by Animal

The ABD, IBD, and OI were compared by animal. Analysis of variance for OI established an effect size of 35% ($P < .05$), ie, 35% of the variability within OI values was determined by differences among animals. The post hoc Bonferroni analysis showed that the OI values in the apical facial sites between animals 1 and 5 were significantly different ($P < .05$) (Fig 5). Effect sizes for IBD and ABD by animal were 22.5% and 13.9%, respectively.

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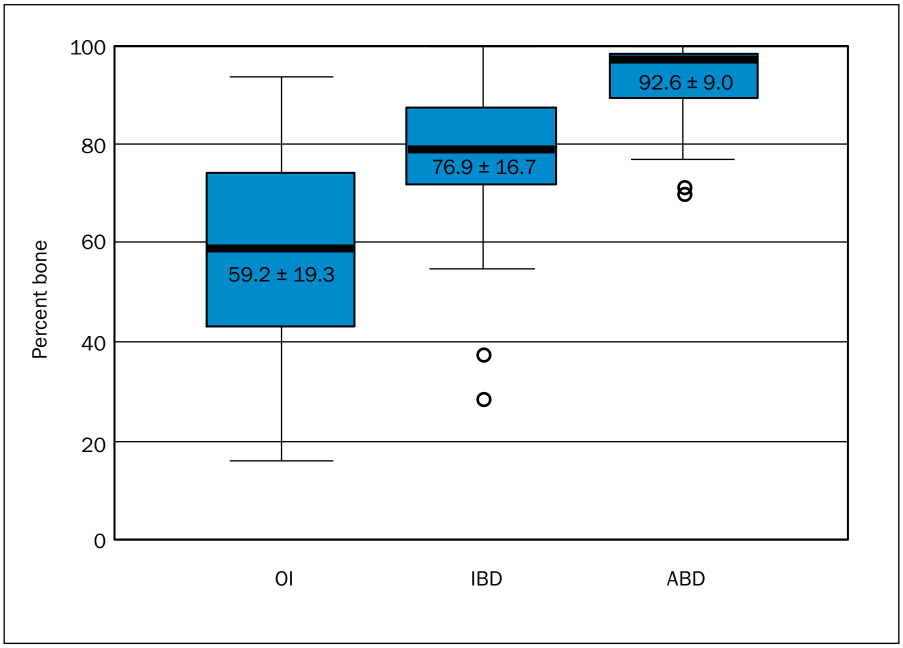

Fig 4 Pooled data from all animals, tooth positions, and implant surface sites (n = 27 for each). Medians, means, and standard deviations are shown. The value for ABD is significantly greater than IBD ($P < .001$); IBD is significantly greater than OI ($P < .001$). O = outliers.

Distribution by Tooth Position

Comparison of ABD, IBD, and OI by tooth position (second, third, or fourth mandibular premolar location) revealed no significant differences by position (Fig 6). Less than 5% of the variance in bone density at OI was accounted for by tooth position. The effect size at IBD was 17%, but this was not statistically significant. Variance explained at ABD was also small (6.5%).

Distribution by Implant Surface Site

Quartile distribution of ABD, IBD, and OI by implant surface site, either apical facial (AF), apical lingual (AL), or coronal lingual (CL) is illustrated in Figs 7 to 9. All tests resulted in significant differences in bone density among the 3 sites (AF, AL, and CL). Results of ANOVA for OI, IBD, and ABD were significant ($P < .05$, $P < .05$, and $P < .01$, respectively). The respective effect sizes were 52%, 50%, and 62%. Clearly, a significant amount of the variability of bone density can be explained by knowledge of the implant site from which a sample was derived. Nevertheless, pairwise adjusted comparison (adjusted using Tukey's HSD correction to protect against family-wise alpha inflation) revealed statistically significant differences only between the adjacent bone densities in the apical facial and coronal lingual sites ($P < .05$).

DISCUSSION

Clinicians have generally agreed that root-form implant success is enhanced by placement of the implant in denser bone, that dental alveolar bone is generally denser in the mandibular than in the maxillary arch, and that bone density decreases as one moves posterior in the respective arch.[3] Experimental studies in animals have provided histologic assessment of the recipient site bone density. Such animal histologic analysis has yielded information regarding osseointegration of the bone to the implant surface subsequent to implant placement. Agreement between studies, however, has been varied. Previous lack of consistency may in part be the result of differences in experimental design and histometric protocols. Data from the current study, under the specific analysis employed, suggest that animal differences and the implant surface site examined may influence results.

Limited knowledge exists regarding the association between the various proximal implant bone densities (ie, adjacent, interthread, and at the implant surface). A unique model has been developed, isolating the interthread area and then making an "outfolded mirror image of the respective thread" extending into the adjacent confining bone.[32] Gottlander and associates[33] used this method and compared the bone densities around 2 types of implants harvested

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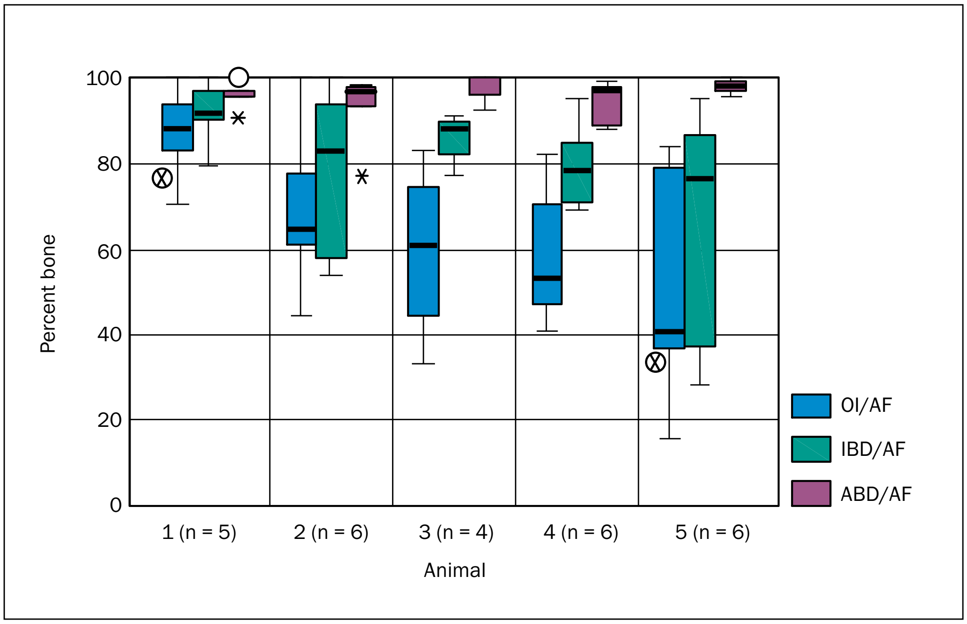

Fig 5 Comparison of apical facial (AF) bone densities by animal. Medians are shown. The OI in animal #1 is significantly greater than OI in animal #5 ($P \leq .05$). *, O = outliers; ⊗ = $P \leq .05$).

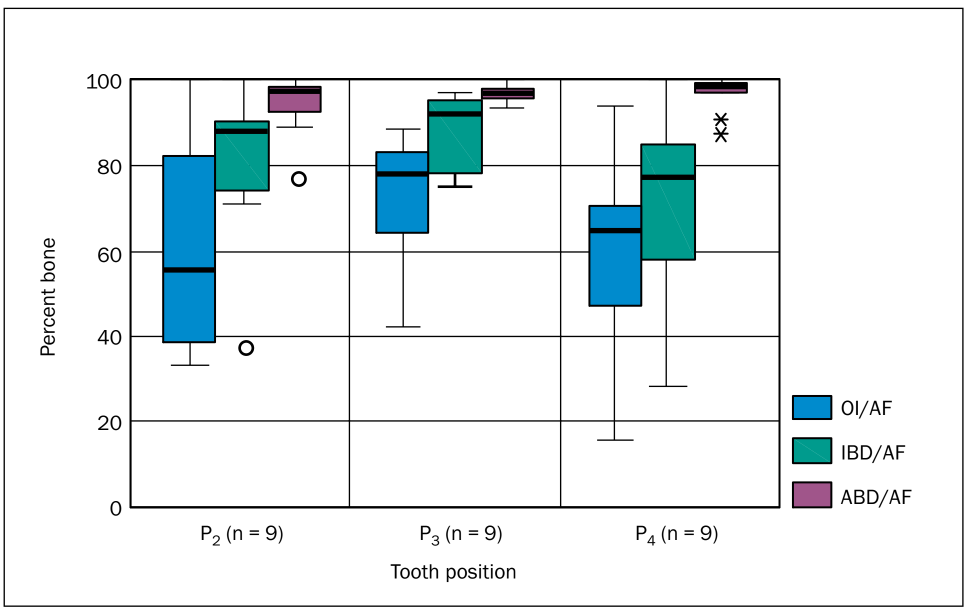

Fig 6 Comparison of apical facial (AF) bone densities by tooth position. Medians are shown. No significant differences were found. *, O = outliers.

at 1 and 6 months after placement in the rabbit femur. At 1 month, the percent interthread bone density was consistently greater than the percent at the implant surface, as reported in the current study. At 6 months, the relationship between the adjacent "mirror image" bone density, the interthread bone density, and density at the implant surface varied according to implant surface type. A recent study using the same "mirror image" method compared implants placed into intact versus chronically reduced alveolar ridges in dogs.[34] The bone density in the "mirror image" area was larger than the associated interthread area. This result is supported by the findings in the current paper.

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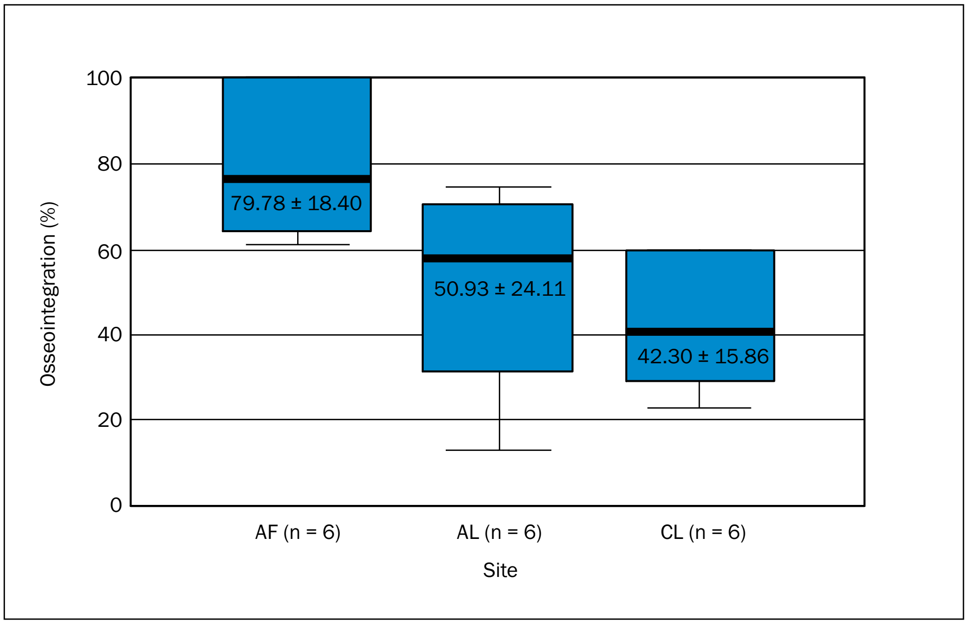

Fig 7 Comparison of osseointegration by implant surface site. Medians, means, and standard deviations are shown. No significant differences were found. AF = apical facial; AL = apical lingual; CL = coronal lingual.

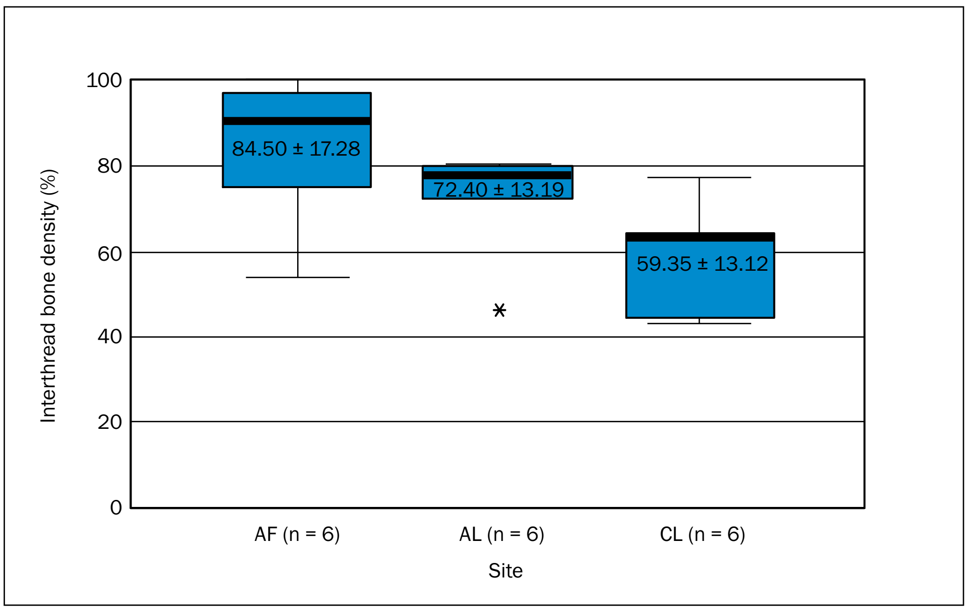

Fig 8 Comparison of interthread bone density by implant surface site. Medians, means, and standard deviations are shown. No significant differences were found. * = outlier.

In the present study, an animal effect was demonstrated on bone density at the implant surface. In contrast, Cochran and coworkers[35] reported no animal effect with bone morphogenetic protein–(BMP) induced bone on smooth titanium implants. Differences in implant design (threaded versus smooth) and type of bone (resident versus BMP-induced) may account for the inconsistency between these studies. The fact that animal individuality can have an influence on osseointegration underlines the need to test for this factor in the analysis of animal implant studies.

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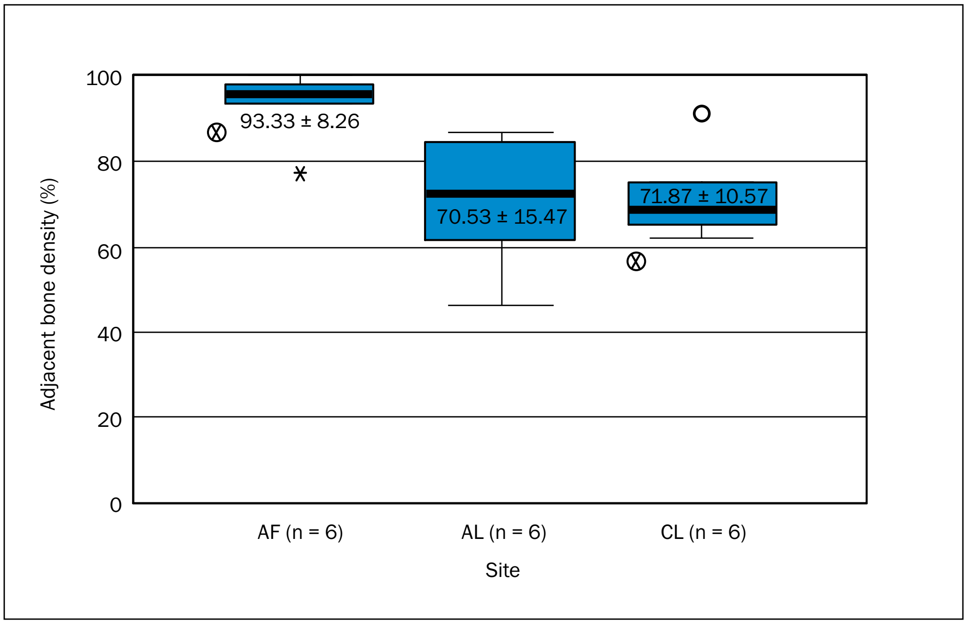

Fig 9 Comparison of adjacent bone density by implant surface site. Medians, means, and standard deviations are shown. Density at the apical facial was significantly greater than at the coronal lingual ($P \leq .05$). *, O = outliers; ⊗ = $P \leq .05$.

Although arch position was addressed in the current study, in actuality differences in positioning were restricted to the mandibular second, third, and fourth premolar locations. Maxillary versus mandibular and anterior versus posterior positions were not part of this study material and must be examined in the future. However, it is apparent from previously well-documented work that bone densities are affected by arch and by position within the arch.[3] The current study demonstrates that animal and surface site of the implant affect bone densities and probably should be considered as part of the experimental design. Therefore, it is important to standardize these factors when comparing different implant protocols.

The finding that the percentage of bone-to-implant contact representing histologic osseointegration is often lower than the percentage of bone density adjacent to the implant is of some interest. It is probable, but not known, that bone density revealed by radiographs most closely correlates with ABD. However, if OI is significantly less than, and poorly correlated with, ABD, then the value of the radiographic evaluation is also called into question. In spite of this uncertainty, titanium threaded implants have a long history of successful clinical osseointegration. It is also not known how loading would influence these relationships, or which and how much peripheral bone is needed to maintain a clinically functional implant. Perhaps with the standardization of experimental design and histometric assessment protocol, these issues can be solved.

CONCLUSION

This study supports the recent work of others[32–34] in that it is important to analyze the association between adjacent implant bone, the interthread bone, and the bone in direct contact with the implant (osseointegration) in the histometric analysis of implants. In addition, the experimental constraints of the current study—ie, animal, arch, position in the arch, and coronal-apical or facial-lingual site—may have an impact on the amount of bone demonstrated. Changes in any of the aforementioned factors may result in totally different associations. This suggests that study designs for implant experimentation should consider these issues.

ACKNOWLEDGMENT

This study was funded by a grant from Atrix Laboratories, Inc.

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