Immediate Functional Loading of Single-Tooth TiO_2 Grit-Blasted Implant Restoration. A Controlled Prospective Study in a Porcine Model. Part II: Histology and Histomorphometry

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ABSTRACT

Background: Evidently, there is a fast-moving shift from delayed to immediate implant loading. The hypothesis to be tested was that bone reactions adjacent to single TiO_2-microthreaded implants exposed to immediate masticatory loading for 10 weeks after placement would modulate osseointegration.

Materials and Methods: Cylindrical- and tapered-designed implants (Astra Tech AB, Mölndal, Sweden) replaced first and third mandibular premolars respectively in 12 pigs. The animals were allocated into two groups based on soft and hard diet feeding. Each animal received, at random positions, four different masticatory loading conditions: implant with either (1) a cover screw only, (2) a healing abutment, (3) an implant with a crown without occlusal contact, or (4) an implant with a crown in contact with the antagonistic teeth.

Results: Histomorphometry showed that there were no statistically significant differences in bone-implant contact (BIC), bone mass inside/outside of the threads and soft tissue ingrowth ratio for all the implants at 10 weeks after placement irrespective of masticatory loading condition. Bone loss showed a trend of progressive increase for implants with a healing abutment toward implants with occlusal contact.

Conclusions: The results of this study rejected the hypothesis and could be explained by the fact that grit-blasted acid-etched implants were already placed in dense bone.

KEY WORDS: adaptation, bone-implant interface, immediate loading, masticatory loads, single dental implant

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Success rates with immediate occlusal loading of single implant restorations vary significantly (79–100%)[1] with the majority of the failures occurring early after loading. This variability is attributed to different levels of masticatory/occlusal forces, including parafunction, in relation to both implant design and bone quality.

Current knowledge of the effect of loading on the peri-implant bone[2] indicates that strains in bone around dental implants above osteogenic levels (3,000 $\mu\varepsilon$) should be avoided, as they are considered responsible for bone loss around the implant neck or complete failure of osseointegration.[3,4]

Different loading environments in the oral cavity, based on (1) diet (soft or hard food), (2) implant situation (submerged or not, protruding or not), and (3) single post or prosthetic reconstruction (splinted or not), induce different mechanical environments.[5] Moreover, forces from adjacent soft tissues (lips, cheeks, tongue) in the oral cavity also react upon teeth and implants with different magnitudes and directions.[6]

However, these suggestions have been insufficiently validated in vivo. Furthermore, bone response to TiO_2 grit-blasted microthreaded implants of either a cylindrical or tapered design is well documented.[7]

This study was designed to test bone reactions to TiO_2-blasted implants under different masticatory loading environments.

HYPOTHESIS

Perturbating the load on single implant restorations (either in occlusion or not) immediately after placement by feeding with a diet of hard food will induce osteogenic strains at the bone-implant interface leading to enhancement of the osseointegration.

MATERIALS AND METHODS

The study design has been described in detail elsewhere.[8] The study protocol was approved by the Local Research Ethical Committee and conducted under license in accordance with UK government regulations (Scientific Animal Procedures Act, 1986).

Euthanasia

Euthanasia took place 10 weeks after implant placement. Following disarticulation from the body, each pig head was perfused with a bilateral carotid artery canulation technique. Initially, a warmed heparinized buffered saline solution was administered IV to prevent coagulation of blood, followed by fixation with 10% formalin saline. Mandibular block specimens containing the implants and surrounding soft tissues were dissected from all of the animals and fixed (10% formalin saline) for shipment to the specimen processing laboratory.

Preparation of Specimens

The histological preparation was performed according to the technique described by van der Lubbe and colleagues[9] at the Department of Periodontology and Biomaterials (Radboud University Nijmegen Medical Centre, the Netherlands). All specimens were reduced in size with a band saw, fixed in 4% buffered formalin, rinsed in water, dehydrated in a graded series of ethanol (70, 80, 90, 96, 100%), and embedded in methyl-methacrylate (Acros Organics, Geel, Belgium). Sections (4–6 in total of each specimen) of a thickness of approximately 10 µm each were made for conventional light microscopy. Initially, the block segments were mounted parallel to the sagittal plane and were cut (saw microtome Leica SP 1600, Leica AG, Glattbrugg, Switzerland) along the longitudinal implant axis in a mesio-distal direction so that the implants were approximately halved.

The remaining two halves of each block (because of loss of approximately 300 µm per section due to the saw blade thickness) segment were glued, and two to three more sections were made for each specimen in a bucco-lingual direction. Finally, the sections were stained by methylene blue 0.1% and basic fuchsine 0.3%, and were evaluated histologically and histomorphometrically.

Histologic and Histomorphometric Evaluation

Evaluations were performed by light microscopy (Leica DM RBE, Leica, Zeist, the Netherlands) with a digital imaging equipment (DC-200, Leica) and were coupled to a computer. The transilluminated image from the light microscope was transferred in true color and real time over the video camera to a frame grabber board where it was digitally converted with graphic resolution of 800 × 600 pixels. The image-processing software (Q Win Pro, v2.5, Leica) allowed histomorphometric analysis directly on the digital colored signal on the screen after scale calibration. Implants were highlighted in green, host bone in blue, and newly formed bone in yellow.

Specimens were examined blind by a single independent observer, and for each implant, the histomorphometrical analysis consisted of the following parameters (diagrammatically shown in Figure 1):

- *Bone-implant contact (BIC)* % over the whole implant length (cylindrical part). A coronal area from the upper implant margin (first microthread) toward the apical part (see Figure 1) was defined for measurements. The tapered apical implant part was excluded from the analysis as its contribution to bone remodeling due to loading is considered nonsignificant.[10]
- *Epithelial downgrowth ratio* over the whole implant length in regard to a reference point (first

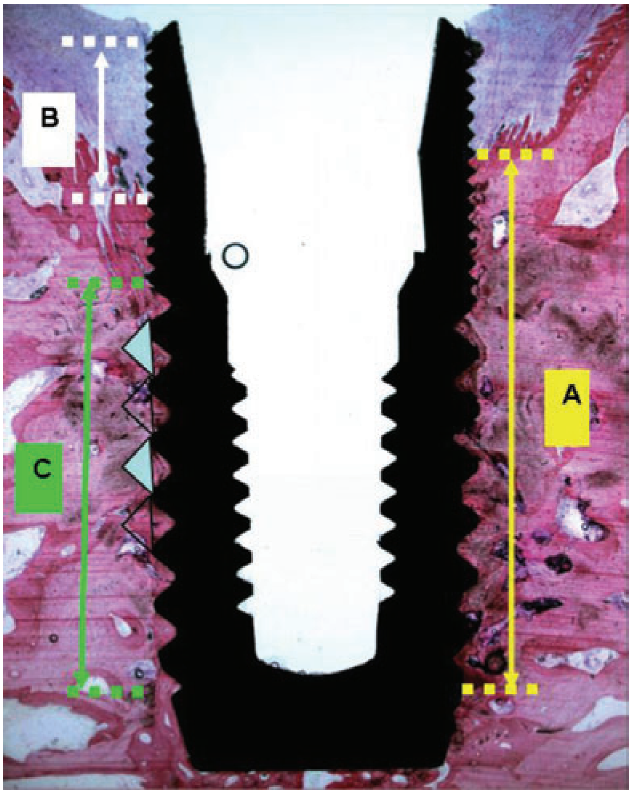

Figure 1 Histomorphometric landmarks for a cylindrical 4.0ST Astra Tech implant of 9-mm length: (A) bone-implant contact (BIC) % over the whole implant length (cylindrical part), (B) epithelial downgrowth ratio over the whole implant length in regard to a reference point (first microthread), (C) difference in bone mass (ΔBM) measured in triangular areas inside and outside the implant-screw macrothreads.

microthread). As the overall implant length is 9 mm, this ratio was also quantified in millimeters.

- *Difference in bone mass* (ΔBM) *measured in triangular areas inside and outside the implant-screw macrothreads.*[11] The measured data were related to the total cancellous bone area inside the macrothread, and this amount of bone mass was quantified in squared millimeters.

$$\text{Bone mass } (BM) = (\text{area of bone in the reference area } (\text{mm}^2)/\text{reference area } (\text{mm}^2)$$

$$\Delta BM = (\text{area of bone inside the tread} - \text{area of bone outside the thread}) \; (\text{mm}^2)$$

All measurements for each of the variables were carried out on the buccal, lingual, mesial, and distal aspects of the implant. For the analysis, mean values for the mesial and distal measurements and also for buccal and lingual were calculated.

Statistical Analysis

The effects of masticatory loading mode (flush, zebra, nonocclusal, occlusal) on the histomorphometric data were evaluated using a nonparametric Kruskal–Wallis one-way analysis of variance (Version 12.1.1, SPSS Inc., Chicago, IL, USA), since the data were not normally distributed in each group. Ideally, a nonparametric Friedman two-way analysis of variance should be performed on these data, but as there were many missing observations, this was not feasible. Results were considered significant if $p < 0.05$. Median values and the minimum and maximum values were used to summarize the data. Data obtained from implants in both groups (soft and hard diet) were combined as no effect of diet had been demonstrated previously.[8] The analysis was repeated excluding the group with occlusal implants, which comprised only three observations (implants).

RESULTS

In vivo Data

Eleven out of 12 animals recovered well after surgery, and no signs of infection were noted at any time during the observation period. Overall, 13 implants of a total of 44 failed in the remaining 11 animals. At euthanasia, the remaining 31 implants demonstrated healthy tissues and clinical stability. Crestal bone loss of the restored implants was evident, irrespective of the presence or absence of occlusal contacts.

Due to chewing habits and parafunctional mastication of the pigs, mucosal dehiscences occured around six 4.0ST implants in the first premolar sites (three flush, one zebra, one nonocclusal, and one occlusal which failed) in three animals. This was attributed to the thinner suture material (3–0 Vicryl, Ethicon, Somerville, NJ, USA) initially used. This was replaced with a thicker suture (2–0 Vicryl, Ethicon), and no more dehiscences were observed. At the time of implant retrieval, no signs of dehiscences or inflammation around the implants were seen anymore.

Histology

Light microscopy demonstrated uneventful healing of all the implants without any sign of inflammatory response. Both cylindrical and tapered geometry implants were completely or partially in direct contact with the host bone. Both the structure of the peri-implant dense trabecular bone and the direct BIC showed little

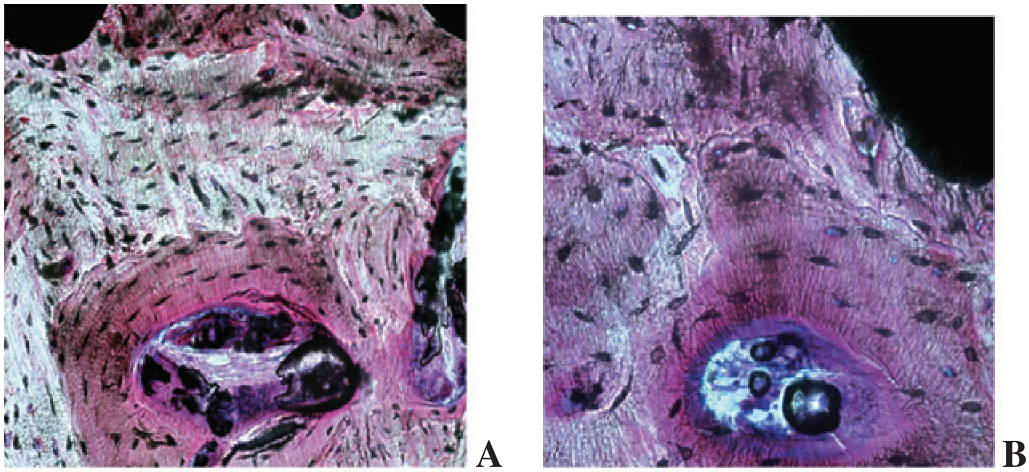

Figure 2 Osteonal remodeling: (A) isolated macrophage (multinucleated giant cell) and (B) osteoclast-like cell in close proximity of a cylindrical implant (flush, ×20 original magnification). Continuum organization and remodeling after 10 weeks can be seen.

dependence on the micromorphology of the implant surface. A few macrophages and isolated multinucleated giant cells could be detected close to the TiO_2 macrothreads comprising definite signs of bone remodeling with bone resorption and osteoid formation at 10 weeks (Figure 2). On sagittal sections, the cancellous bone was of high density, particularly in first premolar sites, and the implants were embedded in dense bone area in

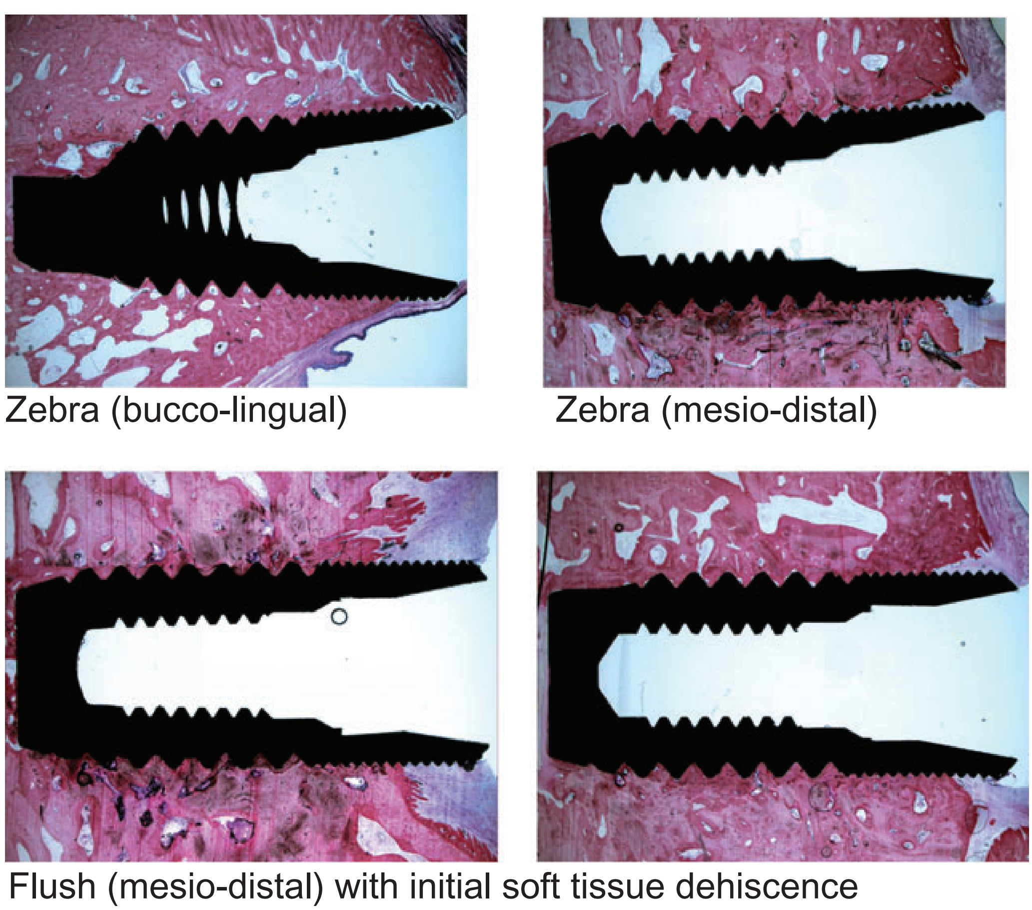

Figure 3 Light photographs of 9-mm cylindrical 4.0ST microthread implants. At 10 weeks of implantation, the implant is almost completely covered with bone (1.6 × 0.9 original magnification ×2).

significant length (Figure 3). The bony apposition revealed a lamellar and, in some parts, a trabecular structure containing woven bone with fingerlike contacts.

There was absence of cortical bone contact around the neck of the restored implants (with crowns either occlusal or not), and the histologic appearance of both occlusal and nonocclusal restored implants was comparable (Figure 4). Epithelial downgrowth could be seen mostly on the cortical alveolar crest around the microthread areas of both cylindrical- (first premolar) and tapered-designed (third premolar) implants (see Figure 4).

Connective tissue with no signs of inflammation, separating the implants from the bone, was evident in the coronal implant part mainly around implants restored with crowns (nonocclusal, occlusal). Isolated strands of collagenous fibers extended vertically to the implant surface (see Figure 4). Two of the implants had their apical parts in contact with the connective tissue instead of the bone (Figure 5).

Histomorphometry

The descriptive data and the analysis outcome are shown in Table 1. Two of the implants (one with a healing abutment and one with a [flush] cover screw) had to be excluded from the statistical analysis due to the poor quality of the sections obtained. Medians for all variables from both mesio-distal and bucco-lingual sections were calculated for all the remaining 29 implants (nine flush, nine healing abutments, eight nonocclusal, and three occlusal) obtained from 11 animals, irrespective of diet group and anatomical position (first or third premolar).

Effect of Loading Environment on BIC, Epithelial Downgrowth Ratio, and Difference in Bone Mass (ΔBM) inside and outside the Implant Macrothreads

Box plots show the distribution of the data in Figure 6, A–C. No statistically significant differences were observed for any of the variables (BIC, epithelial downgrowth ratio, ΔBM inside and outside the implant macrothreads) between implants with flush/healing abutment and implants with nonocclusal/occlusal restorations at week 10 (Tables 2 and 3).

DISCUSSION

Experimental models have been used to compare immediate nonocclusal loading to delayed loading[12] or immediate functional implant loading to nonfunctional implant loading[13,14] with single implants, and multiunit splinted implant restorations.[15,16] However, no basic research has been conducted comparing the putative effect of different masticatory loading environments on implant osseointegration.

In the present study, there was no evidence of a statistically significant difference after an observation time of 10 weeks in any of the histomorphometrical variables including the median crestal bone loss values for implants in all four masticatory loading groups. There were no statistically significant differences even when the analysis was repeated excluding the group with the occlusal implants (see Table 2).

Immediately restored implants (either in occlusion or not) had a similar pattern of crestal bone loss with the top microthreads exposed. However, this bone loss seemed to follow a trend of progressive increase for implants with a healing abutment toward implants with occlusal crowns as the masticatory load increased (see Table 3).

Crestal bone loss was evident around the majority of 4.0ST (cylindrical) and 4.5ST (tapered) unsubmerged implants restored with a crown. This bone loss was most notably not the result of an infectious resorption, since no exudation or signs of inflammation were identified during clinical examinations and histology, thus suggesting a biomechanical etiology. The high soft tissue ingrowth values observed with the flush implants (long and wide cover screw) were attributed to the dehiscences observed initially in three 4.0ST implants in the first premolar sites (see Figure 4). Recent evidence also suggests that abutments/cover screws of larger diameters facilitate microorganism retention in the peri-implant sulci and may lead to crestal bone loss.[17] The rationale of crestal bone loss around dental implants still remains poorly understood, even when implants are placed in a model with good fixation (primary stability measured by insertion torque) and a dense bone (type A/1 according to Lekholm and Zarb[18]).

The angular craterlike geometry of the alveolar defects (see Figure 4) has been reported in other animal studies with excessive nonaxial loads around osseointegrated implants: (1) in monkey[19,20] and dog[21] mandibles and (2) in rabbit tibiae[3] and mandible[22] following controlled pathological load application. Bone response to altered loading conditions is said to be dependent on the anatomical location[23] and implant inclination.

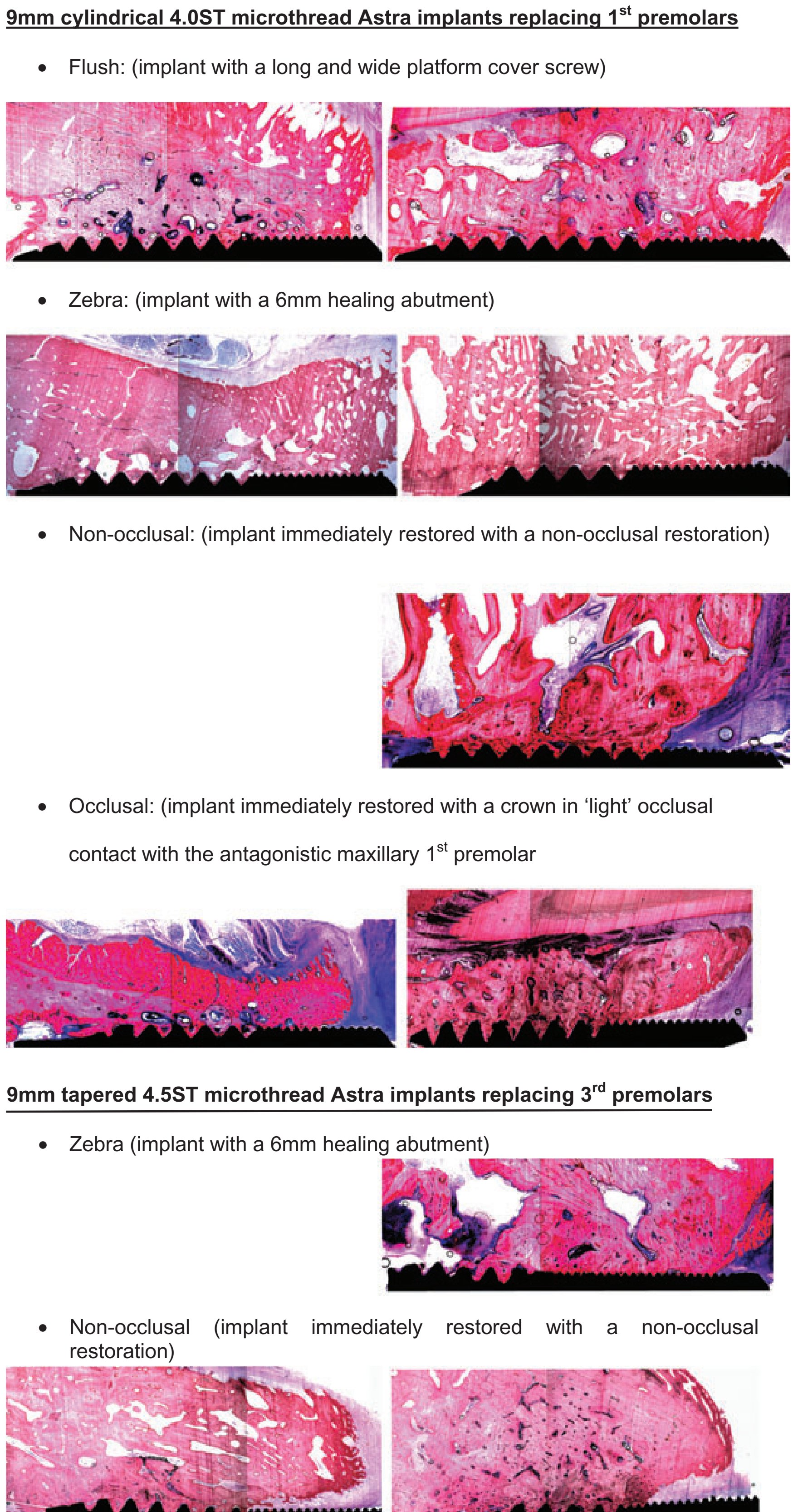

Figure 4 Histological sections in bucco-lingual (*left*) and mesio-distal (*right*) directions for both cylindrical (4.0ST) and tapered (4.5ST) implant pillars.

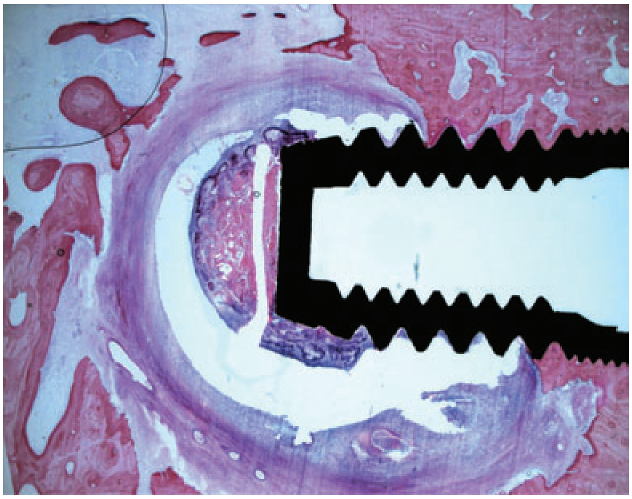

Figure 5 Connective tissue encapsulating the implant apical part of a tapered 4.5ST implant. This is more likely to occur either due to incomplete healing of the alveolar socket following the third premolar extraction or communication of the implant with the contents of the mandibular canal following preparation of the implant osteotomy site (residual alveolar height of less than 9 mm available).

Average bite force values of 560 N were measured during a chewing cycle in the Berkshire pig model in third premolar sites[24] and were considered responsible for the failure to establish a stable bone-implant interface. No effect of food hardness on implant failure pattern could be demonstrated as even numbers of implants failed in both groups of animals (six implants in the soft and six in the hard groups).[8]

Furthermore, the ability of the microthread Astra Tech AB implant (Mölndal, Sweden) to sustain high loads was demonstrated in three implants, restored with occlusal crowns, as these remained partly osseointegrated 10 weeks after placement in the first premolar sites following functional (occlusal) loading (see Figure 4). Moreover, this strong bone-implant interlock was confirmed with values of enhanced BIC (80–99%) with TiO_2 surface-blasted implants, which was in accordance with previous studies.[7,25]

However, a clear effect of the bite force stimulus on the enhancement of osseointegration with immediate

TABLE 1 Summary Statistics for All Histomorphometry Variables

Group		Bone-implant contact % mm^2	Epithelial ingrowth ratio	Inside thread bone mass (mm^2)	Outside thread bone mass (mm^2)
Flush	*n*	9	9	9	9
	Median	86.54	0.23	0.90	0.92
	Minimum	62.96	0.13	0.78	0.84
	Maximum	91.26	0.58	1.00	0.98
Zebra	*n*	9	9	9	9
	Median	85.79	0.16	0.85	0.86
	Minimum	51.61	0.05	0.72	0.81
	Maximum	91.24	0.31	0.94	0.97
Non occlusal	*n*	8	8	8	8
	Median	83.43	0.27	0.92	0.91
	Minimum	66.29	0.11	0.72	0.80
	Maximum	97.99	0.61	0.99	0.99
Occlusal	*n*	3	3	3	3
	Median	72.67	0.38	0.84	0.84
	Minimum	70.77	0.22	0.81	0.83
	Maximum	88.07	0.41	0.99	0.95
Total	*n*	29	29	29	29
	Median	85.79	0.22	0.90	0.90
	Minimum	51.61	0.05	0.72	0.80
	Maximum	97.99	0.61	1.00	0.99

TABLE 2 Results of Kruskal–Wallis Tests for Histomorphometry Variables

	Bone-implant contact %	Soft tissue ingrowth ratio	Bone mass inside thread	Bone mass outside thread	Difference in bone mass (ΔBM) inside-outside thread
Chi-square test statistic	0.820	7.122	2.240	2.895	
Degrees of freedom	3	3	3	3	3
p value	0.845	0.068	0.524	0.408	0.726
p value (excluding values for three occlusal implants)	0.846	0.085			0.975

loaded implants was not defined histomorphometrically. There was no statistically significant difference in bone mass values inside and outside the implant macrothreads for any of the four implant pillar groups at week 10 (see Figure 6C). Although someone would expect bone mass to be increased/decreased due to immediate loading inside the triangular areas adjacent to the macrothreads compared to the "mirror" areas outside the macrothreads, it seems that dense bone (with high BIC) may be insensitive to loading signals.[26] However, it should be emphasized that this study did not investigate any histological differences at earlier time intervals, that is, at 6 weeks, and might have missed any changes at the implant-bone interface presented earlier. In clinical terms, this could mean that "physiological loading" might have contributed in a "faster" healing response.

Interface strains exceeding the physiological tolerance threshold of bone (3,500 $\mu\varepsilon$) prior to osseointegration may also explain why bone loss is observed at the tip of the threads in histological analyses of implants[3]. Two implants were associated with apical bone loss (see Figure 5) and signs of inflammation probably due to initial communication with the mandibular canal during osteotomy site preparation. This bone loss is of no biomechanical etiology, and its rationale and management are discussed elsewhere.[27,28]

TABLE 3 Median Crestal Bone Loss Values in Millimeters for 9-mm Astra Tech AB Implants

	Median (mm)	Minimum (mm)	Maximum (mm)
Flush ($n = 9$)	2.07*	1.17	5.22
Zebra ($n = 9$)	1.42	0.45	2.79
Non occlusal ($n = 8$)	2.38	0.99	5.49
Occlusal ($n = 3$)	3.42	1.98	3.69

*There is a pattern of progressive crestal bone loss from implants with a zebra abutment toward implants with occlusal crowns. The overall high crestal bone loss values for the implants with a cover screw (flush) are related to the initially observed episodes of dehiscence for three of the implants.

Interestingly, single-stage nonsubmerged implants (cylindrical 4.0ST microthread, Universal System, Astra Tech AB, not currently commercially available), loaded with a fixed prosthesis after 6 months of healing, demonstrated much higher crestal bone loss of 1.80 mm than the average bone loss (0.2 mm) observed around the same implants following application of the two-stage submerged approach.[29] Possibly, the higher healing rate in the Berkshire pig model is responsible for this increased soft tissue ingrowth with nonsubmerged implants even with implants in the healing abutment group (average 1.45 mm bone loss) 10 weeks after placement.

By minimizing bone-implant interface micromotion with implant splinting, higher BIC (64.2%) was achieved with an immediately loaded Osseotite implant (3i Implant Innovations, Palm Beach, FL, USA), when compared with less contact (38.9%) with a submerged implant in the human maxilla (soft bone, type IV bone).[30] Once established, the osseointegrated interface can tolerate much more trauma and foreign influence than during its formation.[31] In contrast, similar BIC and bone mineral apposition rates were observed with both immediately loaded and unloaded splinted implants, placed in the mini-pig mandible (insertion torque at least 30 Ncm).[15]

In this animal study, average BIC values of 85% were observed around implants with a cover screw (flush), long healing abutment (zebra), and a composite restoration with no occlusal contact (nonocclusal) (see Figure 6A). However, lower BIC values of 70% were

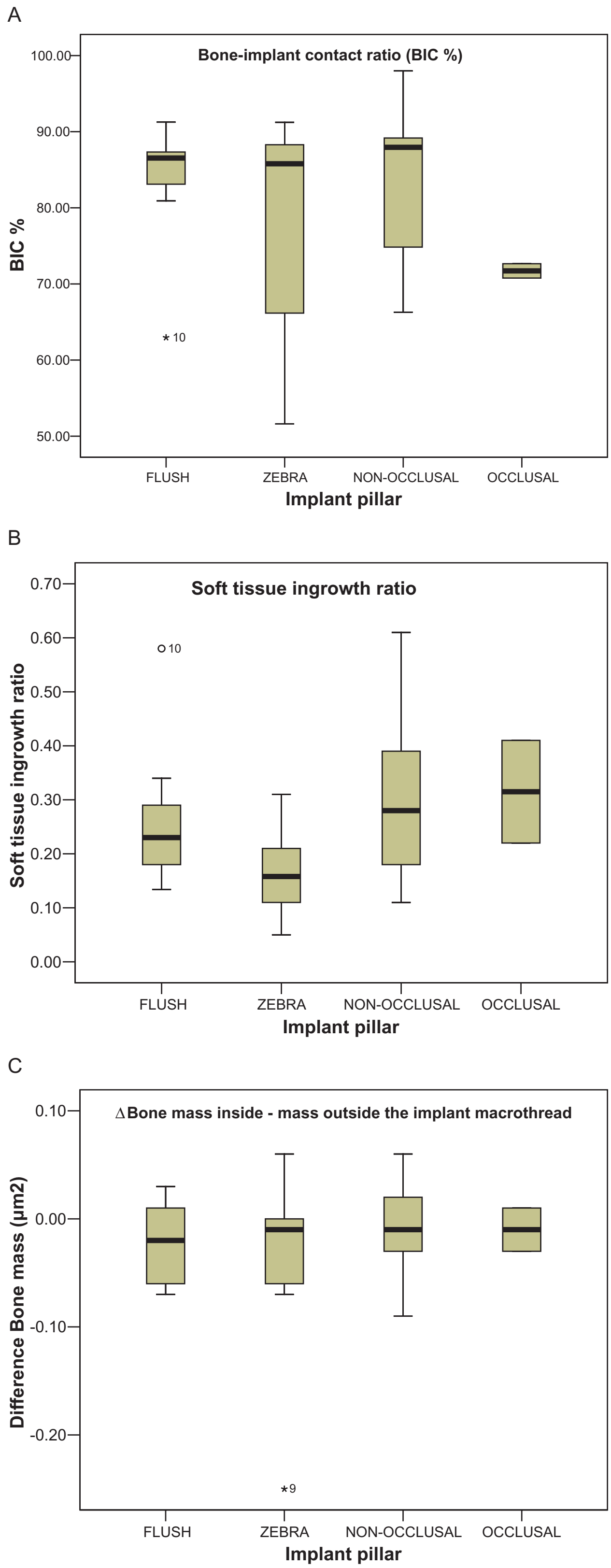

Figure 6 Box plots of the variables under investigation: (A) bone-implant contact (BIC), (B) epithelial downgrowth ratio, and (C) difference in bone mass (ΔBM) inside and outside the implant macrothreads for flush/healing abutment and nonocclusal and occlusal implants. No significant differences were observed.

observed around the three implants with occlusal restorations (see Figure 6A), which may indicate an influence of heavy/uncontrolled loading, although this is not possible to verify statistically.

The present study failed to show significant differences in histomorphometrical variables between implants under different masticatory environments, placed in dense bone (type A/1) for an observation period of 10 weeks. Cochran and colleagues[26] had shown similar findings with grit-blasted acid-etched implants, having initial high BIC levels (placement in dense bone in dog mandible), and confirmed that these BIC levels did not increase any more during functional loading.

When initial BIC values are low, that is, in the posterior maxilla, enhancement of early osseointegration can be influenced by application of controlled direct mechanical loading regimens of short duration.[32,33]

CONCLUSION

The data support allowing treatment protocols with immediate loading of implants provided high initial BIC is achieved.

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