Immediate Versus Delayed Loading of Dental Implants in the Maxillae of Minipigs: Follow-up of Implant Stability and Implant Failures

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Purpose: *To assess the course of the stability and the failure rate of dental implants placed in the partially edentulous maxillae of minipigs.* ***Materials and Methods:*** *Three months after tooth removal, implants were placed in 9 minipigs. Six implants (XiVE; Friadent, Mannheim, Germany) were placed on each side of the posterior maxilla after preparation of the implant sites either by an osteotome technique or with spiral drills. Implant stability was assessed by resonance frequency analysis (RFA) at the time of placement, at second-stage surgery (which took place after a healing periods of 1, 2, 3, 4, or 5 months), and after a loading period of 6 months.* ***Results:*** *Implant stability was significantly influenced by the healing period (*P = *.007). Implant stability decreased after 1 to 3 months of healing for both of the placement techniques and increased after a healing period of 4 months. After implant site preparation by an osteotome technique, 6 of 12 immediately loaded implants, 18 of 24 implants loaded after healing periods of 1 to 3 months, and 1 of 18 implants loaded after a healing period of 4 or 5 months were lost. After implant site preparation using spiral drills, 7 of 12 immediately loaded implants, 12 of 24 implants loaded after healing periods of 1 to 3 months, and 2 of 18 implants loaded after healing periods of 4 or 5 months were lost. Broad overlapping of confidence intervals for the number of implant failures revealed that there was no relevant difference between immediate and early functional loading for either of the 2 techniques.* ***Discussion and Conclusion:*** *Implant loading after healing periods of 1 to 3 months did not improve implant survival compared to immediate loading in the posterior maxillae of minipigs. Not until a healing period of 4 months was reached did implant stability begin to increase. Only when functional loading was started at this point in time was maximal implant survival achieved.* INT J ORAL MAXILLOFAC IMPLANTS 2005;20:39–47

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It has been claimed that the process of osseointegration requires 5 to 6 months on average before loading can be considered in the maxilla.[1] This principle of a delayed loading period was drawn from especially demanding clinical situations involving simultaneously: *(1)* patients with poor quality and quantity of bone, *(2)* implant designs that have since been improved, *(3)* surgical techniques that have since been improved, and *(4)* biomechanically demanding prostheses.[2] The long healing period was considered necessary to achieve the highest predictability possible when dental implants were introduced as standard therapy for masticatory rehabilitation. Implant therapy is now well established, and there is an increasing need for shorter rehabilitation times.[3] Immediate loading appears to increase patient satisfaction and avoids the difficulty of

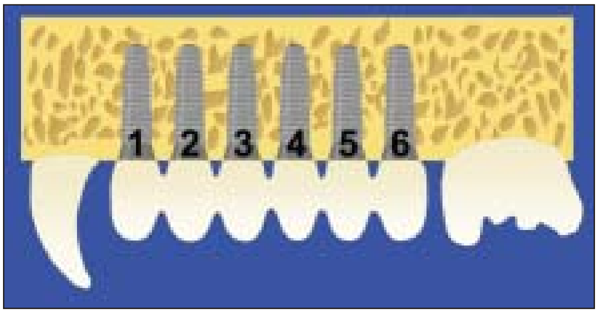


Fig 1 Schematic drawing of implants placed in the maxilla (most anterior implant = position 1; most posterior implant = position 6).

wearing a conventional denture during the healing phase.[4]

To date, there are insufficient data to determine a universally acceptable opinion on immediate loading in the maxilla. The clinical results are discordant; some authors have encountered high failure rates, while others have carried out this procedure successfully in edentulous and partially edentulous maxillae.[5–16]

Until now, neither clinical nor experimental studies have compared the effects of immediate and delayed loading of implants on their success. Therefore, it seemed reasonable to the authors to carry out these experiments on animals with a bone formation rate comparable to that of humans,[17] before the different approaches were applied as clinical procedures.

The aim of the present experimental study was to compare the stability of implants placed in the posterior maxilla of minipigs and loaded either immediately or after healing periods of up to 5 months. During a subsequent period of 6 months of functional loading, the influence of the different healing periods on the implant survival rates was assessed.

MATERIALS AND METHODS

The study protocol was approved by the Animal Care Committee of the Regional Government of Mittelfranken (Ansbach, Germany). The study population comprised 12 female Göttingen minipigs (Ellegaard Göttingen Minipigs, Dalmose, Denmark) between 18 and 21 months old and weighing 30 to 35 kg.

Removal of the teeth in the maxilla and implant placement were performed under sterile conditions and general anesthesia in a veterinary operating theater. The general anesthesia technique has been described in detail elsewhere.[18] Before removal of the teeth, bilateral impressions of the maxilla were made (Impregum Penta, ESPE Dental, Seefeld, Germany). The 3 premolars and the first molar were removed on each side. The wound closure was carried out with Vicryl 2-0 (Ethicon, Norderstedt, Germany). Plaster casts were generated and used to fabricate vacuum-formed templates for the prosthesis.

Implant placement was performed after a healing period of 3 months. Preoperatively, an antibiotic, a benzylpenicillin-dihydrostreptomycin combination (Tardomycel, BayerVital, Leverkusen, Germany) was administered subcutaneously (0.5 mL every 48 hours for 7 days). An analgesic was injected intramuscularly (buprenorphine, Temgesic, Boehringer Mannheim, Mannheim, Germany, 0.05 mg/kg body weight every 12 hours for 3 days). The mucosa was rinsed with 0.2% chlorhexidine gluconate (Doreperol, Dr Rentschler Arzneimittel, Laupheim, Germany).

After a crestal incision, a mucoperiosteal flap was reflected. One hundred eight implants were placed. Each hemimaxilla received 6 rough, cylindric, self-tapping screw-type implants 3.8 mm in diameter and 13 mm in length (XiVE, Friadent, Mannheim, Germany) (Fig 1). Following a randomization plan, in each pig, the implant sites in one half of the maxilla were sequentially enlarged to 3.8 mm in diameter by osteotomes. The sites in the other half were sequentially enlarged to 3.8 mm in diameter using pilot and spiral drills according to the standard protocol of the manufacturer (XiVE BoneCondenser and XiVE Surgical Tray, Friadent). To improve primary stability when the implant site was prepared by spiral drills, the final drill was inserted only 3 mm deep in the crestal bone to allow compression of the central trabecular bone by the implant.

A starting placement torque force of 10 Ncm was used. This force was increased by increments of 5 Ncm when rotation of the implant stopped because of friction with the jawbone. The implants were required to reach a placement torque of at least 15 Ncm. One implant did not reach a placement torque of 15 Ncm and therefore was replaced by an implant of 4.5 mm in diameter.

The implants were placed until only 1 mm of the coronal aspect remained uncovered by bone and the maximum torque value was documented (Fig 2). Subsequently, implant stability was assessed by resonance frequency analysis (RFA) in Hertz (Osstell/Integration Diagnostics, Göteborg, Sweden) (Fig 3). Wound closure was carried out with single resorbable Vicryl 2-0 sutures.

The implants were restored with fixed provisional prostheses immediately after placement or after healing periods of 1, 2, 3, 4, and 5 months, respectively. At second-stage surgery, implant stability was assessed again. Prefabricated temporary abutment crowns (Palavit G, Heraeus Kulzer, Wehrheim, Germany) were positioned on the temporary abutments. Fiber-reinforced strips (Fibrekor, Jeneric/Pentron, Wallingford,

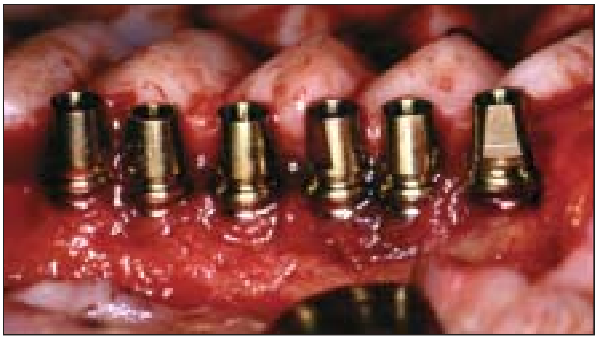
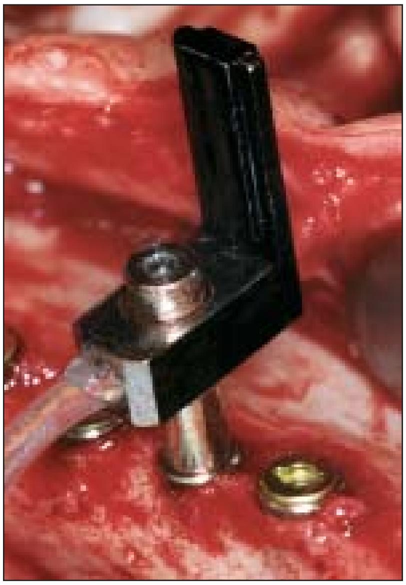


Fig 2 *(Above)* Implants immediately after placement.

Fig 3 *(Right)* Transducer for RFA mounted on an implant.



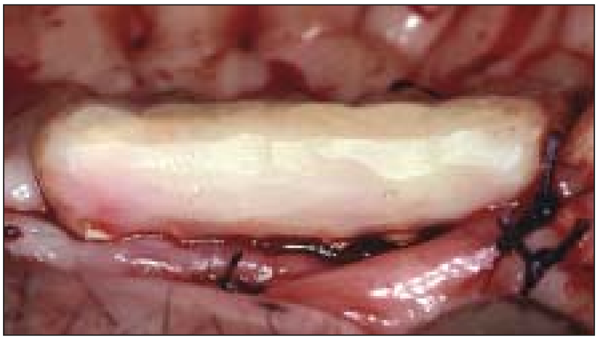


Fig 4a Provisional prosthesis immediately after placement.

Fig 4b Provisional prosthesis after 6 months of loading.

CT) were used to connect the temporary abutment caps. The vacuum-formed templates were filled with temporary acrylic resin (Protemp Garant, ESPE Dental, Seefeld, Germany) and positioned over the temporary abutment crowns. Copious saline irrigation was used to cool the resin during the polymerization period. Subsequently, the suprastructure was removed and contoured. The prostheses were luted with Havard cement (Richter & Hoffmann DentalGesellschaft, Berlin, Germany) (Fig 4a). Intraoral adjustments were made to eliminate any direct occlusal contact. This was verified with occlusal articulating paper (Hanel Folie, Hanel, Langenau, Germany).

After each surgical intervention, the diet of the animals was softened by soaking it with water for 7 days (Altromin 9020; Altromin, Lage, Germany). After the implants had been loaded, the animals were examined monthly. Lost implants were documented, and damaged provisional restorations were renewed if at least 3 implants were still in service. If only 1 or 2 implants were still in service, the animals were allowed to chew on the abutments.

After 6 months of functional loading, implant stability was assessed again using resonance frequency analysis (Fig 4b). Subsequently, the minipigs were sacrificed by inducing cardiac arrest with an intravenous injection of a 20% solution of pentobarbital.

Statistics

Because of the small case numbers, implants loaded after a healing period of 1, 2, or 3 months and implants loaded after 4 or 5 months were pooled into 2 groups. This grouping reflects the occurrence of implant failures. For description of the approximately normally distributed variables, mean values were given with standard deviations. Because of the intraindividual association between implant failures, the confidence intervals (CIs) of implant failure proportions are rough approximations of the CIs in the underlying population. To analyze the influence of preparation technique, healing period, and placement torque on implant stability adjusted for implant position and the individual animals, analyses of variance (ANOVAs) were performed. To evaluate

Fig 5 Implants placed by preparation of the implant sites with an osteotome technique showing a longitudinal fracture of the alveolar crest with gap formation.

Table 1 Distribution of the Placement Torque

Torque (Ncm)	Implant sites			
	Spiral drills		Osteotome technique	
	n	%	n	%
15	7	13.0	6	11.1
20	1	1.9	8	14.8
25	2	3.7	5	9.3
30	5	9.3	8	14.8
35	3	5.5	2	3.7
40	2	3.7	3	5.5
45	4	7.4	1	1.9
50	4	7.4	4	7.4
> 50	26	48.1	17	31.5
Total	54	100.0	54	100.0

the influence of preparation technique, healing period, placement torque, and implant stability on implant failure adjusted for implant position and the individual animals, generalized estimating equation (GEE) analyses were performed. P values ≤ .05 were considered significant. All calculations were done using SAS version 8.1 (SAS Institute, Cary, NC).

RESULTS

Three minipigs died after tooth removal. The remaining 9 animals recovered well after the first surgical intervention and implant placement. All gained weight throughout the healing periods. At the time of implant placement, the edentulous crests showed good bony regeneration. During preparation of the implant sites by an osteotome technique, longitudinal cracks along the alveolar crest occurred in 5 minipigs. The buccal aspect of the alveolar crest remained stable in all of these animals, although a gap was visible on the crest after implant placement (Fig 5). A total of 18 implants were in contact with gaps. In 1 animal, where a healing period of 2 months was planned, 1 implant placed by an osteotome technique showed mobility and did not withstand a reverse torque test with 10 Ncm, although it was not in contact with a gap. It was replaced by an implant 4.5 mm in diameter.

When the implants were placed in sites that were prepared by spiral drills, a placement torque value of > 50 Ncm was reached in more than 48% of cases. This was the case for only 31.5% of the implants placed using the osteotome technique (Table 1). The initial implant stability was significantly reduced when these implants were in contact with a gap in the crestal bone (P = .03). The course of implant stability was assessed by the RFA (Table 2). There was no significant correlation between initial implant stability and the technique used to prepare the implant site (P = .42), but there was a significant correlation between initial implant stability and healing period (P= .007) and between initial implant stability and placement torque (P < .001, Table 3). Implant stability decreased after 1 to 3 months of healing for both placement techniques and increased again after a healing period of 4 or 5 months (Table 2).

At the time of second-stage surgery, again the placement technique did not influence implant stability (P = 0.32, Table 3). After the fabrication of fixed provisional restorations, only in the group with a healing period of 1 to 3 months combined with an osteotome technique was an increase in implant stability seen after 6 months of loading. All other groups revealed a further decline of the implant stability (Table 2).

At the end of the loading period, implant stability showed a significant association with the preparation technique of the implant site (P = .007), but not with the healing period (P = .15) or placement torque (P = .12) (Table 3). After implant site preparation with an osteotome technique, higher RFA values were found than with the implant site preparation with spiral drills. Immediately loaded implants and implants loaded after a healing period of 4 or 5 months showed higher implant stability values than implants loaded after 1 to 3 months (Table 2).

The number of implant failures at second-stage surgery, after 1 month of loading, and after 2 months of loading are given in Table 4. After preparation of the implant sites by an osteotome technique, 2 implants were lost at second-stage surgery after a healing period of 1 month, 4 implants after a healing period of 3 months, and 1 implant after a healing period of 5 months. After 1 month of loading, 6 immediately loaded implants, 6 implants loaded after

Table 2 Distribution of Implant Stability (Resonance Frequency Analysis)

	Implant stability					
	Initial		Second-stage surgery		After 6 mo of loading	
Healing period (mo)	No. of implants	Mean ± SD (Hz)	No. of implants	Mean ± SD (Hz)	No. of implants	Mean ± SD (Hz)
Osteotome technique						
0	12	6,959.8 ± 293.9	–	–	6	6,641.2 ± 373.8
1 to 3	24	6,604.4 ± 243.3	18	6,313.5 ± 464.9	6	6,555.8 ± 460.4
4 or 5	18	6,991.3 ± 257.9	17	6,982.9 ± 305.2	17	6,674.8 ± 272.4
Spiral drill technique						
0	12	7,130.8 ± 166.3	–	–	5	6,624.0 ± 192.6
1 to 3	24	6,676.6 ± 273.2	22	6,544.9 ± 277.2	12	6,170.9 ± 484.4
4 or 5	18	6,935.5 ± 725.0	17	6,858.9 ± 414.1	16	6,484.9 ± 318.3

0 = immediate loading.

1 month, 2 implants loaded after 2 months, and 2 implants loaded after 3 months failed. After 2 months of loading, 2 implants that were allowed to heal for 3 months were no longer in place (Fig 6). At later examinations, no more implant failures had occurred with implant site preparation by an osteotome technique (Table 5). Gap formation in the crestal bone resulting from preparation of implant sites by an osteotome technique did not influence the number of implant failures in a significant way ($P = .90$).

Among sites where spiral drills were used for preparation of the implant sites, 1 implant allowed to heal for 2 months, 1 implant allowed to heal for 3 months, and 1 implant allowed to heal for 5 months had failed at the time of abutment connection. After 1 month of loading, 7 immediately loaded implants, 1 implant loaded at 1 month, 1 implant loaded at 2 months, 1 implant loaded at 3 months, and 1 implant loaded at 4 months were lost. At the follow-up examination after 2 months of loading, 1 implant that had healed for 2 months was lost (Fig 6). Subsequently, no more implant failures occurred. A total of 25 implants were lost with the osteotome technique, while 21 implants were lost after preparation of the implant sites by spiral drills (Table 5). For both preparation techniques, the broad overlapping of the CIs for the number of implant failures for immediate loading and a healing period of 1 to 3 months revealed that there was no relevant difference between immediate and early loading.

The rate of implant failures after 1 month of loading was significantly associated with the healing period ($P < .001$) and the RFA assessed at second-stage surgery ($P = .01$, Table 6). Again, the implant failure rate after 2 months of loading was significantly associated with the healing period ($P < .001$), but not with the RFA values assessed at second-stage surgery ($P = .02$, Table 7).

Table 3 Analysis of Influence of Placement Technique, Placement Torque, and Healing Period on Implant Stability

	P (ANOVA)		
Covariates	RFA at implant placement	RFA at stage-2 surgery	RFA after 6 mo of loading
Placement technique	.42	.32	.007
Healing period of 4 or 5 mo vs 0 to 3 mo	.007	.001	.15
Placement torque	< .0001	.001	.12

Table 4 Distribution of Implant Failures

	No. of implant failures		
Healing period (mo)	At second-stage surgery (loading)	After 1 mo	After 2 mo
Osteotome technique			
0 (immediate loading)	–	6	0
1	2	6	0
2	0	2	0
3	4	2	2
4	0	0	0
5	1	0	0
Spiral drill technique			
0 (immediate loading)	–	7	0
1	0	3	0
2	1	3	1
3	1	3	0
4	0	1	0
5	1	0	0

0 = immediate loading.

In 3 maxillary halves where the implant sites had been prepared with spiral drills and the implants were loaded immediately, after a healing period of 2 months, and after a healing period of 3 months,

Table 5 Distribution of Implant Failures

Healing period (mo)	Total no. of implants placed	Cumulative no. of failed implants (%; 95% CI)	Cumulative no. of surviving implants (%; 95% CI)	No. of implant failures at second-stage surgery	No. of implant failures after 1 mo	No. of implant failures after 2 mo
Osteotome technique						
0	12	6 (50; 21–79)	6 (50; 21–79)	–	6	0
1 to 3	24	18 (75; 58–93)	5 (21; 7–42)	6	10	3
4 to 5	18	1 (6; 0–27)	17 (94; 73–100)	1	0	0
Spiral drill technique						
0	12	7 (58; 28–85)	5 (42; 15–72)	–	7	0
1 to 3	24	12 (50; 29–71)	12 (50; 29–71)	2	9	1
4 to 5	18	2 (11; 1–35)	16 (89; 65–99)	1	1	0

0 = immediate loading; CI = confidence interval.

Table 6 Analysis of the Influence of Placement Technique, Placement Torque, Implant Stability (RFA), and Healing Period on Implant Failures After 1 Mo of Loading

Parameter	*P*	Odds ratio	Odds ratio 95% CI
Placement technique	.91	1.14	0.110–11.48
Placement torque	.10	0.85	0.690–1.030
RFA at implant placement	.89	1.000	0.999–1.002
RFA at second-stage surgery	.01	1.003	1.001–1.004
Healing period of 4 to 5 mo vs 0 to 3 mo	< .001	0.016	0.004–0.075

Table 7 Analysis of the Influence of Placement Technique, Placement Torque, Implant Stability (RFA), and Healing Period on Implant Failures After 2 Mo of Loading

Parameter	*P*	Odds ratio	Odds ratio 95% CI
Placement technique	.81	1.32	0.130–13.32
Placement torque	.81	0.98	0.810–1.180
RFA at implant placement	.59	1.000	0.999–1.002
RFA at second-stage surgery	.02	1.002	1.000–1.003
Healing period of 4 to 5 mo vs 0 to 3 mo	< .001	0.016	0.004–0.069

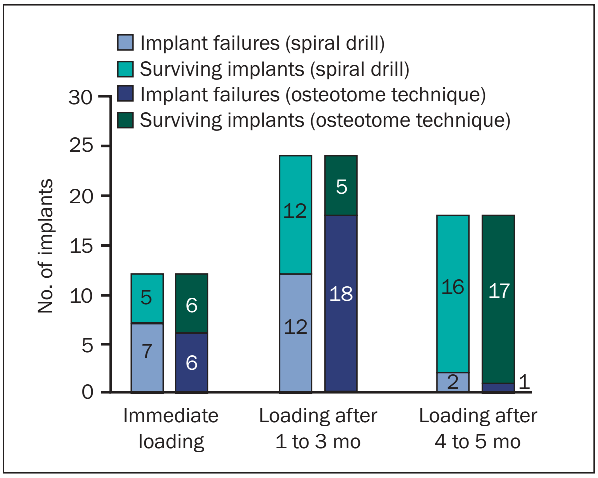


Fig 6 Distribution of implant failures after 6 months of loading.

respectively, only 2 implants in each case survived the first month of loading. After preparation of the implant site by an osteotome technique in 1 maxillary half, only 1 implant survived 2 months of loading after a healing period of 2 months. In another maxillary half, only 2 implants were in place at the time of second-stage surgery after a healing period of 3 months. According to the treatment protocol these implants did not receive new prostheses. The animals were allowed to chew on the abutments. During the second month of loading 1 additional implant was lost of the 2 implants that were placed after implant site preparation by spiral drills and were subjected to an unloaded healing period of 2 months. Both of the remaining implants where the implant site had been prepared by an osteotome technique and which were allowed to heal for 3 months were lost during the second month of loading. The remaining free-standing implants survived the complete follow-up period.

DISCUSSION

The high levels of predictability in implant therapy have encouraged re-evaluation of the traditional Brånemark System implant protocol of 5 to 6 months of unloaded healing in the maxilla.[1,19–21] Although immediate loading of implants placed in the maxilla has been carried out successfully in clinical studies, it is still considered problematic. Randomized controlled patient trials are not available. Different studies have been carried out on selected patients. However, immediate functional loading in the maxilla is an interesting subject, and only limited basic research has been conducted in experimental animal trials comparing immediate to delayed loading.[22–24]

Unfortunately, the animals used in previous studies have shown metabolic rates of bone at least 2 times higher than that of humans.[25] A very cautious approach must be used in the extrapolation of animal results to a human situation.[14,24] The Göttingen minipig model was chosen because it has a bone formation rate equal to that of humans.[18] It was the aim of the study to follow the stability of implants loaded immediately or using a delayed-placement protocol during the healing period and for 6 months of loading.

One of the main prerequisites for immediate loading is sufficient initial implant stability. In the maxilla, immediate provisionalization has been suggested when optimal primary stability is reflected by a placement torque greater than 32 Ncm.[26] Others have preferred even higher placement torque values (eg, > 40 Ncm).[5] The results of the present study revealed that there is no simple relationship between placement torque and implant failure. Torque value was not a reliable predictor of implant survival during the follow-up period. A correlation to implant failure was found only after 2 months of functional loading. Low torque values were not inevitably followed by implant failure; high torque values (> 50 Ncm) did not always lead to implant survival. Placement torque values exceeding a certain threshold may induce microfractures or even pressure necrosis and lead to implant failure.[27]

It has been claimed that implant placement by an osteotome technique not only improves primary stability but leads to accelerated bone healing compared to conventional implant placement with spiral drills in trabecular bone, as can be found in the human posterior maxilla.[28] However, in the maxillae of minipigs there were no statistically significant differences between sites prepared using an osteotome technique and those prepared with spiral drills. Slightly more implants were lost after preparation of the implant sites by an osteotome technique than by spiral drills. Longitudinal cracks and gap formation were observed at the alveolar crests after implant placement at sites where the osteotome technique was used. This finding may reflect the fact that the posterior maxilla of the minipig exhibits an amount of cortical crestal bone that is critical for implant placement with an osteotome technique. However, although a significantly reduced initial implant stability was found in the affected implants compared to implants placed in sites prepared by an osteotome technique without crack formation, there was no statistically significant difference concerning the number of lost implants between the 2 groups.

High predictability of immediately loaded implants splinted with fixed provisional restorations has been shown in previous reports.[16,18,21,29,30] This seems to indicate that these prostheses can help confine occlusal forces applied to the healing bone-implant interface to a physiologic range. However, most of these studies have addressed the mandible or were carried out on human maxillae. It has been said that micromotion between 28 and 100 μm has no adverse effect on osseointegration.[21,31,32] Unfortunately, the loading forces in experimental animal trials are poorly controlled and not comparable to a human situation.[33,34] Damage to provisional prostheses occurred frequently in the present study. The implants lost their splinting stabilization for a certain time interval until they were repaired during the follow-up examinations. It is well known that exposure to parafunctional forces can interrupt the course of osseointegration and increase the risk of implant failure.[35] According to the study protocol, prostheses were not renewed when only 2 implants remained in 1 maxilla. Interestingly, it could be shown that after an initial splinted period of 1 month, 2 immediately loaded implants were able to survive occlusal loading in a freestanding situation during the remaining follow-up period.

Because of the configuration of minipig maxillae, the implants had to be placed along a straight line. This configuration may be less favorable than cross-arch stabilization, which counteracts bending by lateral forces.[6,36] Cross-arch stabilization can regularly be achieved in the edentulous human maxilla. As unfavorable stresses are reduced and the distribution of occlusal masticatory forces is optimized, it is reasonable to assume that cross-arch stabilization leads to a significantly reduced failure rate in the human situation compared to the experimental animal study.

The course of implant stability, with decreasing values assessed by RFA during the early healing phase, reflected the implant failures that occurred. Implant stability values were high immediately after implant placement, but they decreased during the first 3 months of the healing period. As a consequence, a comparable number of implants in the 0-to-3-months'-loading group, independent of the implant site preparation technique. After a healing period of 4 or 5 months, only a minimal number of implants failed, while the RFA values finally began to increase. Although previous studies have shown favorable results for implants loaded after 6 and 8 weeks in the human maxilla, the present experimental study revealed that during the course of osseointegration, the first 3 months after placement appear to be the vulnerable phase for implant failure when unrestricted functional loading is initiated.[37,38] Clinically, it seems that loading delayed for 6 to 8 weeks is not always advantageous compared to immediate loading in the maxilla, because both healing intervals require special precautions to restrict occlusal loading to a level that does not interrupt osseointegration. A maximum safety margin is only achieved after a healing interval of 4 months. After this healing period, unrestricted functional loading of the implants is possible with minimal potential for implant failure.

CONCLUSION

This experimental animal trial showed that implant stability in the posterior maxillae of minipigs was reduced during the first 3 months of the healing period and was correlated to a high rate of implant failure when functional loading was initiated at this time. Loading after 1 to 3 months and immediate loading led to comparable numbers of implant failures, independent of the implant site preparation technique. Therefore, loading delayed for up to 3 months does not seem to be a feasible alternative to immediate loading in the posterior maxilla. Not until a healing period of 4 months had been reached did implant stability begin to increase. Maximal implant survival could be achieved when functional loading began after 4 months of healing.

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