Histologic and Histomorphometric Evaluation of Peri-implant Bone Subjected to Immediate Loading: An Experimental Study with *Macaca Fascicularis*

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Purpose: *Immediately loaded splinted implants can become osseointegrated when they are placed in the anterior part of the mandible. The concept of immediate loading has not been well examined in the posterior mandible. The aim of this study was to evaluate the hard tissue reactions around immediately loaded implants placed in the posterior mandible in the monkey model.* ***Materials and Methods:*** *Six adult M. fascicularis monkeys were used in this study. Thirty-six Ankylos implants (Degussa Dental, Hanau-Wolfgang, Germany) were placed after extraction of the second premolar, first, and second molar teeth and complete healing of the sockets. Control (C) group implants were placed and, after osseointegration, were loaded for 1 month using temporary acrylic resin prostheses and later for 2 months using splinted metal crowns. In the contralateral region of the mandible, test (T) group implants were placed and loaded immediately with the same sequence as carried out for the C implants. After sacrifice of the animals, specimens were examined histologically and evaluated histomorphometrically.* ***Results:*** *All implants were osseointegrated. Compact, cortical bone in contact with the implant surface without any gaps or connective tissue formation was demonstrated.* ***Discussion:*** *Histomorphometric findings of the bone-implant-contacts showed no significant differences between the T and C group implants. Peri-implant mineralized bone areas presented statistically significant differences and showed a higher density of bone between the threads of immediately loaded implants (P < .05).* ***Conclusions:*** *Immediately loaded splinted implants in the posterior mandible can become osseointegrated with a hard tissue peri-implant response similar to that of delayed loaded implants. Moreover, immediate loading seems to increase the ossification of the alveolar bone around endosseous implants.* (INT J ORAL MAXILLOFAC IMPLANTS 2002;17:44–51)

Key words: *bone, immediate loading, implant, monkey, posterior mandible*

A stress-free healing period is a prerequisite for successful implant placement according to the protocol of Brånemark and colleagues.[1] An early loading period may lead to fibrous tissue encapsulation instead of direct bone apposition.[2–4] Furthermore, necrotic bone at the interface immediately after implant placement is not capable of load-bearing and must be replaced by new bone.[1,4–5] When a controlled load is applied to the bone through the implant, bone remodels to an architecture related to the direction and magnitude of the load.[5] In addition, relevant studies have shown that the amount of micromotion may influence either positively or negatively the bone-implant anchorage.[6–8] Micromovements at the implant-bone interface immediately after implant placement are usually associated with implant failure, but osseointegration can still be achieved.[1]

The role of bone quality for successful implant placement has been extensively reported. In studies performed in the edentulous mandible, most

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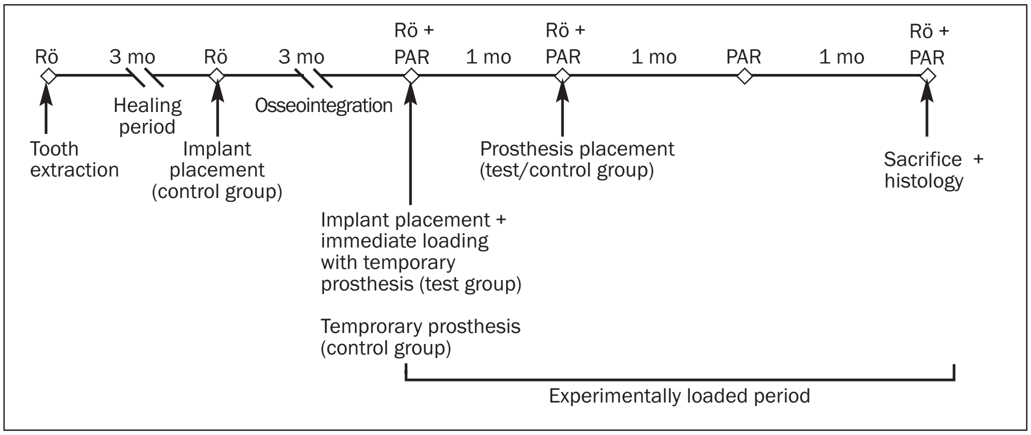

Fig 1 Experimental outline of the animal study.

implant failures occurred in posterior areas[9–12] because of inadequate bone quality with thick cortical bone (Class II) or loose cancellous bone (Class IV). In such cases delayed loading has been recommended.[13] Premature loading may also be clinically acceptable if certain requirements are met. The overall strategy of these requirements is control of interfacial movement between the implant and surrounding bone. Clinical studies,[14–30] as well as experimental studies with different animal models,[31–34] have demonstrated variable success rates for immediately loaded implants.

Most of the authors who recommend immediately loaded implants do so for the anterior mandible,[14,16,22,25,27] where bone quality is usually sufficient to achieve primary stability.

Some authors avoid bone tapping to provide better primary stability[19,21,24] or they have recommended the use of implant systems with good microinterlocking (surface) or macrointerlocking (screw design) properties for better primary anchorage.[14,16,22,25,30] Rough implant surfaces compared with smooth surfaces can demonstrate faster bone apposition.[35–38]

Adequate splinting, ie, immobilization of the implants immediately after surgery using bar-retained overdentures[14,16,22,25,30] or fixed prostheses,[21,24,26,27,29,39] is another requirement for immediately loaded implants.

Immediately loaded implants placed in good quality bone were able to obtain an increased stability clinically equivalent to implants using a standard protocol.[21,24] Even though this protocol has been extensively used in the human mandible, failures in the posterior part of the mandible have been reported.[19,24,26]

The aim of this study was to present histologic and histomorphometric observations in peri-implant hard tissues subjected to immediate loading of implants with a special designed progressive thread design in the posterior mandible of *Macaca fascicularis* monkeys.

MATERIALS AND METHODS

Six adult monkeys *(Macaca fascicularis)*, of both sexes, 7 to 12 years of age, and with a mean body weight of 5,738.45 (± 84.13) g were used in this study. The animals were housed individually in wire-bottomed cages and maintained on a commercial diet, which was supplemented daily with fresh fruits and water ad libitum. The experimental outline is illustrated in Fig 1 and provided 2 treatment groups for evaluation: 1-stage immediately loaded implants (T implants, test group) and 2-stage delayed loaded (after a healing period of 3 months) implants (C implants, control group). This study was approved by the Animal Ethic Committee of the University of Malaya-Kuala Lumpur, Malaysia (Ethics Ref No.: U1/10/6/96/TCG (R)-1) and supported financially by a Grant from the Ministry of Science, Technology, and Environment, Malaysia. Housing and feeding of the animals were performed according to standard animal care protocol of the Animal House, University of Malaya, Kuala Lumpur, Malaysia.

The second premolars, first and second molars of the animal mandibles were extracted with special care and the use of thin elevators to avoid trauma of the alveolar ridges. For that reason, hemisection of the molars was performed and the thin roots were removed without complication. After 3 months of healing, 3 Ankylos implants (Degussa Dental, Hanau-Wolfgang, Germany) with a length of 8.0 mm and a diameter of 3.5 mm were placed in 1 side of the mandible (2-stage implants).

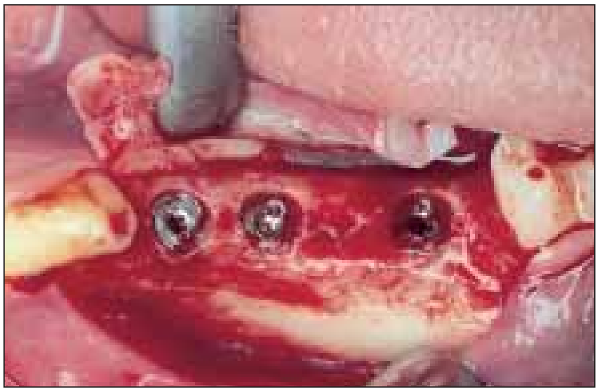

Fig 2a Implant placement in the edentulous alveolar ridge.

Fig 2b Suturing of the flap with silk suture material.

The special thread design of the Ankylos implant system is characteristic for the progressive, different shape of the threads provided from the coronal to the apical aspects. The implants were made from pure titanium (grade II), had a high-polished collar of 2.0 mm, and a sandblasted surface.

All surgery was performed under sterile conditions in an animal operation theater. For all surgical and oral hygiene procedures, the animals were sedated with an intramuscular injection using 4 to 6 mg/kg body weight of Titelamine hydrochloride (Zoletil 50, Virbac Laboratories, Carros, France).

Before implant placement, tooth debris and calculus involving the residual dentition were systematically removed. For implant placement, a mucoperiosteal flap was raised at the site of implantation to expose the bone area, and sockets were created using a special electric engine (KaVo IntraK-Boxes 947/948, KaVo, Leutkirch, Germany) and a handpiece (W&H, Bürmoos, Laufen, Germany) operated at a low speed no higher than 1,000 rpm/min, with low pressure on the cutting devices and continuous external saline irrigation. The surgical incision for mucoperiosteal flap elevation in the implant control group was made buccally so as to completely cover these implants with oral mucosa. For the T implants, the incision was made in the midline of the alveolar ridge crest.

The procedure for implant placement followed manufacturer recommendations for the Ankylos implant[40] into the threaded sockets until the screws were fully embedded into bone (Fig 2a). The flaps were readapted and sutured (Fig 2b) with 4–0 silk-suture material (Resorba, Nürnberg, Germany). Soft diet with bread and milk was given to the monkeys the first postoperative week and later fruits and nuts were included according to the standard feeding of the Animal House of the University of Malaya. The sutures were removed 10 days after surgery.

After a 3-month healing period, the C implants were exposed and abutments were placed. The abutments were specially fabricated by Degussa-Dental (Hanau-Wolfgang, Germany) for this study with a 1.0-mm sulcular rim and height of 2.5 mm. At the same time in the contralateral side of the mandible, 3 implants with their abutments were placed. Standardized periapical radiographs using customized resin bite blocks and Rinn Film Holders (Caulk Dentsply, Milford, DE) attached to a portable long cone X-ray machine (Porta X-1, Sanko X-ray, Osaka, Japan) were taken immediately after implant placement. Immediately after abutment connection, the 2 sides of the mandible were impressioned with a polyether impression material (Impregum, Espe, Seefeld, Germany) using customized trays. A record of occlusal intercuspal position was made using a vinyl siloxane registration paste (Regisil 2X Cartridge System, Caulk Dentsply, Milford, DE) for the fabrication of metal prostheses in the areas of the second premolar, first, and second molar. After the impression procedures, all of the implants (T and C groups) were loaded using customized acrylic resin (Trim, Harry Bosworth, Skokie, IL) provisional prostheses connecting all of the 3 implants on each side. The provisional restorations were screwed onto the abutments to allow easy removal of the prosthesis for evaluation of the clinical peri-implant condition. The implants were loaded with the provisional prostheses for a total period of 1 month. The prostheses had occlusal contacts in centric relation and no eccentric contacts were evident after verification using colored occlusal paper foil (GMH, Nurtingen, Germany).

Postoperatively, the animals were given antibiotics for 7 days (Amoxycillin 20%, Alfasan, Woerden, Holland) per intramuscular injection. The animals were inspected the first postoperative day and then weekly for general condition and for the detection of any wound dehiscence or infection. A systematic oral hygiene maintenance program was carried out using an electric toothbrush and dentifrice 3 times a week, supplemented by weekly rubber cup and pumice prophylaxis followed by an application of a 0.2% chlorhexidine gluconate gel (Chlorhodex, Colgate Oral Care, Australia) with cotton buds once a week throughout the period of the investigation. The oral hygiene procedures were performed under general anesthesia to maintain the periodontal tissues in a good condition with plaque accumulation kept to a minimum.

One month after placement of the provisional restorations, screw-retained metal prostheses that were waxed and cast from a nonprecious metal using a Ag-Pd alloy (Palliaq, Degussa-Dental, Hanau-Wolfgang, Germany) were placed on the implants. With the metal restorations, all implants were loaded for a further period of 2 months.

Three months after loading, all of the monkeys were sacrificed (according to the animal experimental guidelines of University of Malaya) by induction of a deep anesthesia followed by an intravenous overdose of sodium pentobarbital.

Histologic Processing of the Specimens

Specimens of the implants and surrounding tissues were removed en bloc from the mandibles of all of the animals. The samples were fixed by immersion in 4% buffered formalin solution for at least 72 hours and then dehydrated in ascending concentrations of ethanol, embedded in Technovit 7200 VCL resin (Kulzer, Wehrheim, Germany) and polymerized in a light polymerization unit (Exakt System, Exakt Apparatebbau, Norderstedt, Germany). The resin blocks were cut along the long axis of the implant in a mesiodistal direction with special thin-section equipment (Exakt-Cutting Grinding System, Exakt Apparatebbau, Norderstedt, Germany). The final ground sections had an initial thickness of 100 to 150 µm and then were ground and polished to a thickness of approximately about 10 µm according to the cutting-grinding technique described by Donath and Breuner.[41] During all procedures, care was taken to preserve the original implant-tissue interface. Finally, all of the sections were stained with 1% toluidine blue solution and examined by light microscopy.

Histomorphometric Analysis

Histomorphometric analyses were performed to get more information about the quality of the implant-tissue interface. The data were reported as percentage bone-to-implant contact (BIC) and percentage of total mineralized bone tissue within the threads (referred to as "bone area"). The bone-to-implant contact measurements were made for all threads in the total surface of each implant under 2.5× magnification and the bone area measurements under 10× magnification objective with a Leitz microscope (Zeiss, Photomicroscop II, Oberkochen, Germany) connected to an IBM PC, equipped with Videoplan computer software (Kontron Elektronik, Eching, Germany). For each implant, 6 measurements of the mineralized bone tissue (3 on the left and 3 on the right implant side) determined the bone areas within the threads.

Similar histomorphometric measurements at the hard tissue interface have been previously described as a quantitative method for the assessment of osseointegration and to describe better the quality of the interface.[42,43] For each monkey, mean values were calculated and expressed as a percentage for the 2 variables.

Statistical Analysis

Descriptive statistics were used to evaluate the histomorphometric findings. For the statistical analysis, the paired *t* test was used to evaluate the pairwise differences of the bone-implant contact (BIC) percentages and bone area-measurements between immediately and delayed loaded implants.

RESULTS

None of the specimens showed any signs of inflammation, such as redness or swelling, mobility of the implants, or mechanical damage of the superstructure at the end of the experimental periods. All implants were integrated with the bone after 3 months of loading as determined by clinical and radiographic examination. The healing after implant placement was without any complication.

Histologic Analysis

Immediately Loaded Implants. All implants were osseointegrated. No gaps or fibrous connective tissue were seen between the titanium surface and alveolar bone (Fig 3). For all of the implants, bone lamellae parallel to the threads were found between the threads (Fig 4a). In the crestal and middle part of the implants a higher deposition of new bone was observed. This bone could be differentiated from the older one by numerous lacunae with viable osteocytes seen in the newly formed woven bone (Fig 4b). At the apical part of the implants, only a few very thin bone trabeculae covered the metal

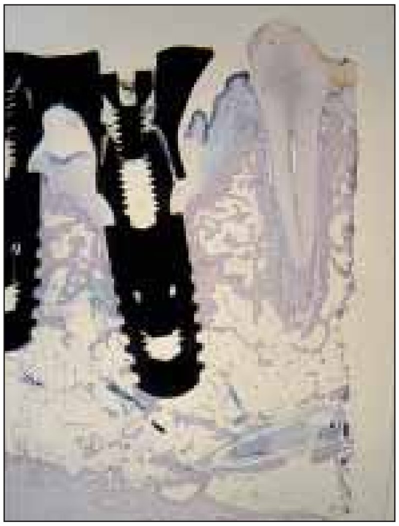

Fig 3 Immediately loaded implants showed no gaps or fibrous connective tissue between titanium surface and alveolar bone. In the crestal and middle part of the implants a higher deposition of new bone was found (original magnification: 1.25×).

surface of the implants in all of the animals. The marrow space of the cancellous bone was wide in these areas (Fig 4c).

Delayed Loaded Implants. All implants were osseointegrated. No resorption or any peri-implant inflammatory reactions were present. Fibrous connective tissue was not found between the titanium surface and the new bone. At the apical part of the implants, cancellous bone had decreased density in comparison with the bone localized around the cervical and middle parts of the implants (Fig 5).

Histomorphometric Analysis

The implant was used as a unit of observation. The number of samples was 18 in each group for statistical analysis. The Student *t* test for unpaired samples was used to evaluate the statistical significance of the differences in the percentage of bone-to-implant contacts (BIC) and bone areas between T and C implants.

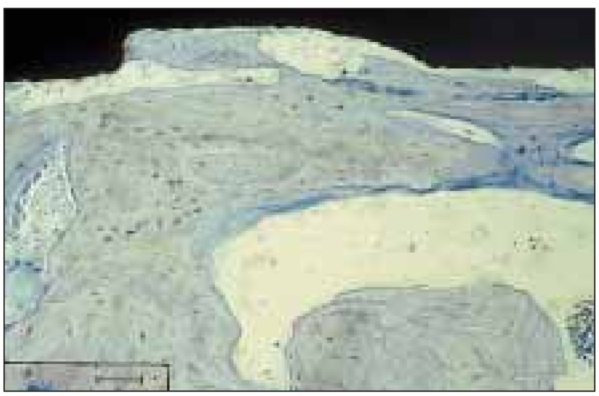

Fig 4a Well-differentiated newly formed bone in comparison to old bone in the interface of an immediately loaded implant. Bone lamellae parallel to the implant surface characterized the lamellar pattern (original magnification: 50×).

Fig 4b Newly formed bone with numerous viable osteocytes and numerous lacunae was found in close contact with the titanium surface of an immediately loaded implant (original magnification: 50×).

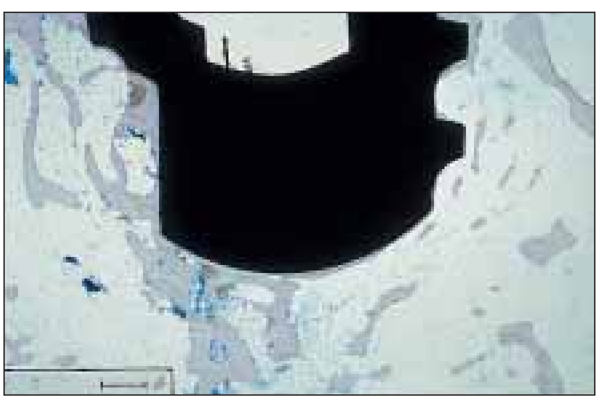

Fig 4c Demonstration of newly formed bone on the apical part of the immediately loaded implant. A few thin bone trabeculae were localized in contact with the implant surface (original magnification: 6.25×).

Fig 5 Osseointegrated control group implants without any fibrous connective tissue formation at the interface. In the apical part of the implants the cancellous bone had a decreased density in comparison with the surrounding bone in the cervical and middle part of the implants (original magnification: 1.56×).

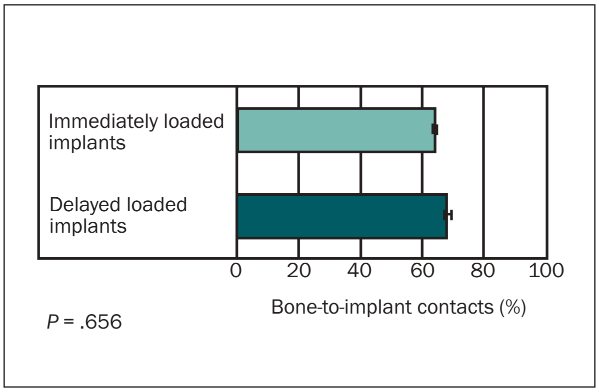

Fig 6 Percentage of the bone-to-implant-contacts (BIC) in the interface.

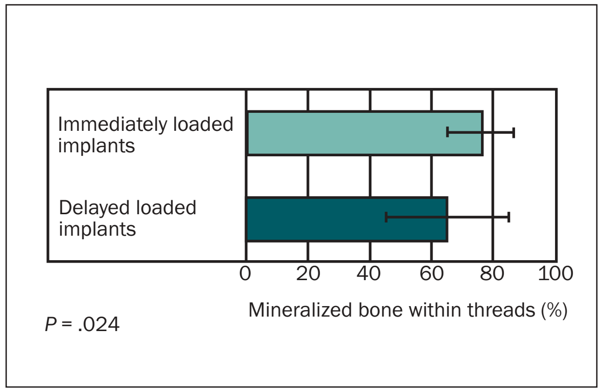

Fig 7 Percentages of the mineralized bone within the threads of the implant.

The mean values of BIC for the immediate loaded group was 64.25 (± 0.65)% and for the delayed loaded group 67.93 (± 1.60)%. BIC between test and control group implants (Fig 6) did not show any statistically significant differences ($P = .656$).

The bone area within the threads (Fig 7) had mean values for the test group 76.95 (± 11.35)% and for the control group 65.42 (± 19.88)%, respectively. These values showed statistical significant differences ($P < .05$).

DISCUSSION

Most definitions of osseointegration describe a direct contact between living bone and the implant at the light microscopic level.[2] The histologic findings of this study showed that immediately loaded implants with a special progressive thread design can become osseointegrated similar to delayed loaded implants in the posterior mandible of monkeys. No gaps or fibrous connective tissue were found between titanium surfaces and alveolar bone; instead, new bone formation with viable osteocytes was demonstrated in the newly formed woven bone.

To evaluate the bone-to-implant contact percentages, histomorphometric techniques have previously been extensively used.[42–45] In the present study, the percentage of BICs in the delayed loaded implants was about 68%. These observations are comparable with findings previously reported by Gotfredsen and associates,[46] who examined tissue reactions adjacent to submerged and nonsubmerged ITI implants also in monkeys. BICs were similar in the 2 implant groups and represented only about 48% of the interface. In contrast to these observations, Levy and coworkers[47] reported greater contacts in submerged implants placed in dogs.

The density of peri-implant bone in the threaded portion of submerged implants in the present study was about 65.4%. Abrahamsson and colleagues[48] showed in dogs that the bone density between the threads was 85.4% with the Astra system, 87.4% with the Brånemark system, and 88.4% with the ITI-Bonefit system. They concluded that these findings were not statistically significantly different.

In another study, when the BIC was measured around immediately loaded TPS-coated implants in monkeys, a mean level of 73.2% was reported.[34] The authors compared histologically and histomorphometrically the bone reactions around immediately and nonloaded implants. They reported a statistically significant difference between the 2 implant groups. As explanation of these findings, the authors suggested that the adequate splinting of immediately loaded implants, as well as the improved stability, was possibly related to the plasma-sprayed coating which contributed a sufficient degree of primary stability. This may decrease the micromotion at the interface and promote the stimulation of new bone formation. The Ankylos implant system which was used in the present study is comparable to the ITI system. Both systems have an internal seal between the implant and abutment and do not have any microgap.

It was not possible in the present study to observe any significant difference in the percentages of bone-implant contacts between the test and control groups. In contrast to this observation, there seemed to be a higher amount of mineralized bone within the threads around immediately loaded Ankylos implants. Cylindro-conical implant designs have been shown to provide sufficient bone ingrowth into the porous surface in 4 weeks.[49] The short integration period is perhaps related to the porosity because the surface state seems to play an important role on timing,[35] amount of integration,[38] and micromotion tolerance.[50–52]

Additional studies in monkeys have shown that the bone response and osseointegration is not dependent on the marginal fit of the supporting prosthesis.[53] According to the findings from the present study, there appears to be no clinical significance relating osseointegration and passivity of the prosthesis in immediately loaded implants. The sandblasted surface of the Ankylos implant system may positively influence bone integration under loading conditions because of its high porosity. Long-term references from human trials are necessary to support this hypothesis. Observations from the orthopedic literature showed that long-term immobilization of the long bones was associated with bone resorption.[54] A similar process is the phenomenon of "disuse atrophy" in the bone without loading.[55] New bone formation and active remodeling may be observed when the bone is mechanically stimulated.[56–57]

CONCLUSION

According to these observations and the findings presented in this limited study, peri-implant mineralized bone areas showed a higher density within the threads of immediately loaded implants. Immediately loaded splinted implants in the posterior mandible can become osseointegrated with a hard tissue peri-implant response similar to that of delayed loaded implants. Immediate loading may have the potential to increase ossification of the alveolar bone around endosseous dental implants.

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