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Dog model for study of supracrestal bone apposition around partially inserted implants

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Abstract: A dog model for study of supracrestal bone growth around partially inserted implants is described. The mandibular premolar teeth (P_1, P_2, P_3 and P_4) were extracted on both sides of the mandible in four dogs. At a surgical exposure 12 weeks later, two 10 mm titanium implants were partially inserted on each side, 15 mm apart, in the areas of the P_1 and the P_3 so that five threads protruded from the bone crest. A titanium mesh was fastened to the coronal aspect of the two fixtures and covered with an ePTFE membrane. Thus, a space for potential bone formation was created between the two implants. The surgical flaps were coronally positioned and secured with vertical mattress sutures. After 12 weeks of healing, biopsy specimens were retrieved and examined histologically. In three of the four dogs under study, the partially inserted implants had integrated and the intended large wound spaces had been created around the noninserted parts of the implants. However, bone was not formed around the protruding implants. Accordingly, this experimental model may prove useful for future studies on the use of various procedures that hypothetically may enhance bone formation.

For several years, implants have been used in the treatment of partially and totally edentulous jaws (Adell et al. 1981, 1990; Albrektsson et al. 1988; see review by van Steenberghe et al. 1999). However, in areas of limited alveolar bone height, installation of implants may not be possible. Such areas include the maxillary premolar and molar region where only a thin bony wall may separate the maxillary sinus from the oral cavity, and the corresponding mandibular region with its mandibular nerve canal. Surgical methods such as sinus inlay grafts are used to overcome this problem in the maxilla (Hirsch & Ericsson 1991; Loukota et al. 1992). In the mandibular premolar and molar region, mandibular nerve transposition may be used. These techniques involve risk of morbidity, such as long-term mental nerve damage (Rosenquist 1994). Autogenous bone grafts from the hip may also be used to increase the height of the alveolar ridge (Keller & Tolman 1992; Nyström et al. 1993; Schliephake et al. 1994). However, this procedure involves additional surgery and increased discomfort to the patient.

Another approach to remedy the problem with insufficient alveolar bone is to partially insert the implants in the available bone, followed by bone augmentation procedures in order to cover and support noninserted implant threads. However, few studies have been conducted to evaluate this possibility. In dogs, Jovanovic et al. (1995) demonstrated a mean supracrestal bone formation of 1.8 mm under titanium reinforced ePTFE membranes covering implants with two threads protruding above the alveolar crest. Renvert et al. (1996), also

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in dogs, found partial bone fill, using bone grafts placed under domes attached to implants, with six threads protruding from the surrounding bone level. In humans, Simion et al. (1994) obtained 3–4 mm vertical bone growth for implants protruding 4–7 mm from the bone crest and covered with titanium reinforced membranes. Tinti et al. (1996), using the same surgical model in humans but combined with autogenous bone grafts, reported up to 7 mm vertical ridge augmentation.

A dog model to evaluate techniques to obtain supracrestal bone growth around partially inserted implants might facilitate future research efforts. Therefore, this study was designed to develop such a model.

Material and methods

Animals and experimental procedures

Four young adult Labrador dogs were used. General anaesthesia was induced using thiopentone sodium and maintained with halothane. The mandibular premolar teeth (P_1, P_2, P_3 and P_4) were extracted on each side of the mandible. Any alveolar bone was not removed. The dogs were allowed to recover from the anaesthetic and then reinstalled in a kennel, where they were kept for 12 weeks.

Following the 12-week period, general anaesthesia was again provided as mentioned above. For each side of the mandible, buccal and lingual flaps were raised from the canine to the first molar using crestal incisions. Two implant sites, approximately 15 mm apart, were prepared in each side in the areas of the P_1 and the P_3 using a graded series of drills. Standard 10 mm Brånemark implants (Nobel Biocare Norden AB, Gothenburg, Sweden) were partially inserted so that five threads protruded from the bone crest (Fig. 1). A 0.3-mm-thick titanium mesh (Dynamic Titanium Mesh, Leibinger GmbH & Co., Freiburg, Germany) was fastened to the coronal aspect of the two fixtures on each side using the cover screws. The mesh bridged the distance between the implants and rested buccally and lingually on the alveolar ridge (Fig. 2). The space beneath the mesh was filled with peripheral, venous blood that had been set aside to coagulate prior to placement. The mesh was then covered with an ePTFE membrane, 0.1 mm thick with 0.1 μm pores (Surgical Membrane, W.L. Gore & Associates, Flagstaff, AZ, USA) in order to reduce any abrasive effect of the mesh on the overlying flap. The membrane was trimmed to coat the buccal and lingual borders of the titanium mesh and to form apron-like covers over the anterior and posterior terminations of the created wound space (Fig. 3). The buccal and lingual flaps were mobilised to a level near the lower border of the mandible. Horizontal releasing incisions were made through the periosteum. The flaps were coronally positioned and secured with vertical mattress and interrupted sutures (Fig. 4).

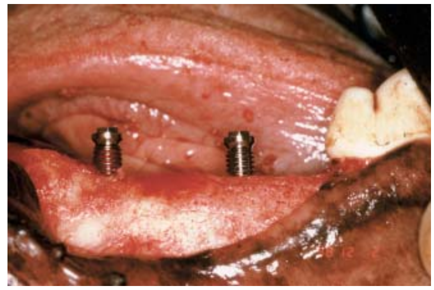

Fig. 1. Two 10 mm implants placed in the edentulous mandibular area, approximately 15 mm apart, with five threads protruding above the alveolar crest.

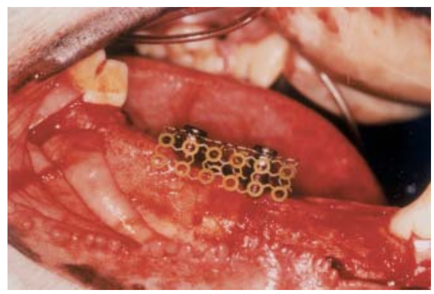

Fig. 2. A titanium mesh fastened to the fixtures with the cover screws. The mesh is resting on the alveolar ridge buccally and lingually.

Fig. 3. An ePTFE membrane covering the titanium mesh.

Fig. 4. Coronally positioned buccal and lingual flaps secured with vertical mattress and interrupted sutures.

Postoperatively, the animals were given amoxicillin intramuscularly to the dosage of 150 mg/10 kg body weight and thereafter maintained on amoxicillin tablets, 200 mg twice daily, for 4 days. The dogs were fed a soft diet and water *ad libitum*. Following a healing period of 12 weeks, the animals were sacrificed with an overdose of thiopentone sodium.

Preparation of specimens and histological analysis

Specimen blocks of the implants and the surrounding tissues were retrieved, immersed in 10% neutral buffered formaldehyde and processed for ground sectioning according to the method described by Donath & Breuner (1982) and Donath (1988). The blocks were dehydrated in increasing grades of ethanol and subsequently infiltrated and polymerised in Technovit 7200 VLC-resin (Kulzer, Friedrichsdorf, Germany). The blocks incorporating the two implants and bone were cut in one central section in the mesio-distal plane using a cutting-grinding unit (Exakt® Apparatebeau, Norderstedt, Hamburg, Germany). The 250-μm-thick sections obtained were further reduced by microgrinding and polishing to a final thickness of 10–20 μm. They were stained in toluidine blue mixed with pyronin G and analysed under a Leitz Aristoplan light microscope (Leitz, Wetzlar, Germany). Histomorphometry was performed using Leitz Microvid equipment connected to a computer, and included the following measurements for the mesial and distal surfaces of each implant:

1 The height of newly formed bone in mm in direct contact with the implant coronal to the 5th thread.
2 The percentage area of newly formed bone in a rectangular region extending

from the 1st to the 5th thread and 5 mm mesially/distally to the implant ('region of interest', approximately 15 mm^2, Fig. 5).

3 The percentage of bone in contact with the implant surface within each thread ('bone-to-metal contact'). Calculations were made for the three best consecutive threads in the crestal region of each implant (Johansson 1991), and for the parts coronal and apical to the 5th thread, respectively.
4 The percentage of bone area inside each thread. Calculations were made for the three best consecutive threads in the crestal region of each implant (Johansson 1991) (Fig. 6), and for the parts coronal and apical to the 5th thread, respectively.
5 'Mirror image' area: the percentage of bone in the outfolded thread area was calculated in the three best consecutive threads in the crestal region (Johansson 1991) (Fig. 6).

Calculations of means for each animal, followed by computation of group means and standard deviations were carried out for all measurements.

Fig. 5. Illustration of the histomorphometric method to calculate the percentage area of newly formed bone in the 'region of interest': newly formed bone (lower portion of rectangle) in an area extending from the 1st to the 5th thread (visible to the very left) and 5 mm mesially/distally to the implant.

Results

Healing was uneventful throughout the 12-week postoperative period. Membrane exposure did not occur in any of the four dogs under study. The distance between the pairs of implants forming the eight wound spaces was measured from radiographs and amounted to a mean of 14.6 mm (range 14–16 mm).

Qualitative microscopic observations (Fig. 7)

The overview of the sections showed the two implants, the mesh and the membrane underneath the oral mucosa. Out of the total of 16 implants, three implants had failed to integrate and were encapsulated in inflamed soft tissues coupled with evidence of resorption of adjacent bone (both implants on the right side and one implant on the left side of the same dog). This dog was excluded from the histomorphometric evaluation described below.

Newly formed bone in direct contact with the implant coronal to the 5th thread was not observed in any of the wound spaces. Between the mesh and the bone surface, pycnotic cells embedded in a lightly stained material, presumably tissue fluids, were seen. Closer to the bone surface a layer of richly vascularised granulation tissue with inflammatory cells was observed. The bone surface itself often showed osteoclasts indicating resorptive activity.

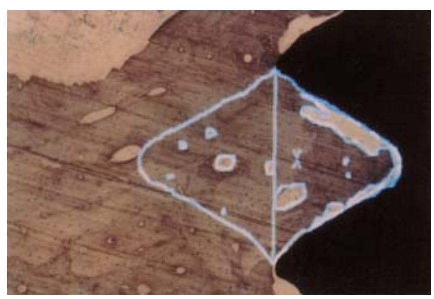

Fig. 6. Illustration of the histomorphometric methods to calculate: (i) the percentage of bone area inside each thread: calculated for the right triangular area between the peaks of the threads (labelled X); and (ii) the 'mirror image' bone area ratio: ratio between the percentage bone area inside each thread (right triangular area) and the percentage bone area in a mirror image region outside the same thread (left triangular area), expressed as a percentage.

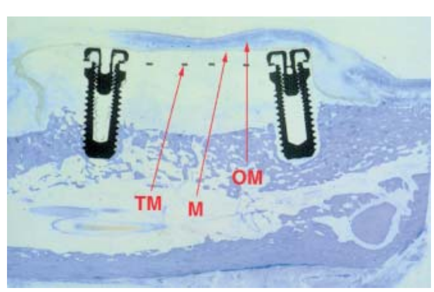

Fig. 7. Section showing the two implants in the left mandible of one dog (the dog excluded from histomorphometric evaluation). Only one of the implants show osseointegration (left) in this jaw quadrant. No bone has formed in the created wound space, which is filled with a lightly stained material, presumably tissue fluids. OM, oral mucosa; TM, titanium mesh; M, ePTFE membrane.

Histomorphometric results ($n = 3$)

Results for the measurements as listed under Material and methods were as follows:

1 Height of newly formed bone in direct contact with the implant coronal to the 5th thread: 0 mm.
2 Mean percentage of newly formed bone in the 'region of interest': 16 ± 16% (range 5–35%).
3 Mean 'bone-to-metal contact' percentages:

Three best consecutive threads in the crestal region: 30 ± 6% (range 23–34%)
All threads apical to the 5th thread: 22 ± 8% (range 13–28%).
All threads coronal to the 5th thread: 0%.

4 Mean percentage bone area inside the threads:
Three best consecutive threads in the crestal region: 73 ± 4% (range 69–77%).
All threads apical to the 5th thread: 60 ± 13% (range 45–69%).
All threads coronal to the 5th thread: 0%.
5 Mean 'mirror image' bone area ratio:
Apical to the 5th thread: 78 ± 11% (range 68–90%).
Coronal to the 5th thread: 0%.

Discussion

The present study was designed in order to develop a dog model to be used in the evaluation of techniques aimed at facilitating supracrestal bone growth around partially inserted implants. Two implants were placed approximately 15 mm apart. Five threads were left nonsubmerged coronal to the surrounding bone and a titanium mesh was attached to the implants and covered by an ePTFE membrane, creating a large space potentially allowing for new bone formation.

In one dog, three implants did not osseointegrate. It is possible that these implants were traumatically overloaded during the healing period. Isidor (1996, 1997) have demonstrated in monkeys that occlusal overload may lead to disintegration of implants. Several clinical studies have also indicated that overload may result in implant disintegration (Adell et al. 1981, 1986; Lindquist et al. 1988; Quirynen et al. 1992).

The concept of 'guided bone regeneration' using barrier membranes (Buser et al. 1990; Nyman et al. 1990) was applied in the dog model used. However, only occasional coronal growth of bone into the wound space was detected. This is contrary to previous findings by Jovanovic et al. (1995) in dogs and by Simion et al. (1994) in humans. This difference in results may partly be explained by the the large wound space, in the present study created coronal to a nonreduced alveolar crest. The discrepancy of results may also be due to the fact that perforations of the cortical bone facing the wound space were not performed.

Rompen et al. (1999) evaluated the influence of cortical perforations and peripheral blood fill of the wound space as potentially enhancing factors for bone formation. Wound chambers of minor size were created on the rat skull. Four approaches were studied: (1) cortical perforations alone; (2) peripheral blood fill alone; (3) combination of cortical perforations and peripheral blood fill; and (4) control. The authors observed that the combination of cortical perforations and blood fill resulted in the best bone formation.

The use of cortical perforations may be critical in large wound spaces as those used in the present dog model in order to ensure sufficient blood supply for organisation of a clot and subsequent migration of osteoblasts. The fact that most of the wound spaces in the present study were occupied by pycnotic cells embedded in a lightly stained material, presumably tissue fluids, may support the notion that clots placed under the membranes during surgery did not organise. The present model could therefore be used to study the importance of cortical penetrations for the healing events in large wound spaces.

Histomorphometric measurements both apical and coronal to the level of implant insertion (5th thread) were made and reported in the present study. Since there was no bone tissue in contact with the implants coronal to the 5th thread, the results presented for the apical portions, by themselves, might seem of limited interest. The apical results, however, demonstrate a number of parameters routinely used for evaluation of implant integration in bone (Johansson 1991; Gottlander 1994; Ivanoff 1999), and will be of significance in future studies on this dog model.

The histomorphometric results, as presented here, were combined for those aspects of the implants that were facing the centre of the wound space and for those aspects distant to the wound centre. In future studies, they should be presented separately, as the potentials for bone growth may be different due to the proximity of the ePTFE membrane to the distant aspects. This was illustrated in the present study by the results for bone fill in the 'area of interest'. When bone was observed in this area, this occurred primarily for the distant aspects.

In summary, in three of the four dogs under study, the partially inserted implants had integrated and the intended large wound spaces had been created around the noninserted parts of the implants. Bone was not formed around the protruding implants after a 12-week healing period. Accordingly, this experimental model may prove useful for future studies on the use of various procedures that hypothetically may enhance bone formation, particularly in view of the demanding nature of the model with a large wound space coronal to a nonreduced alveolar crest. We are currently undertaking a study using this dog model to evaluate the effect of bone morphogenetic protein.

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Résumé

Pour étudier la croissance osseuse suscrestale autour d'implants insérés partiellement, un modèle de chien est décrit. Les prémolaires inférieures (P1, P2, P3, P4) ont été bilatéralement avulsées chez quatre chiens. Lors d'une mise à nu chirurgicale douze semaines plus tard, deux implants en titane de 10 mm ont été partiellement insérés de chaque côté à 15 mm de distance dans les zones de P1 et P3 de telle manière que cinq filetages restaient à découvert. Une mèche en titane a été maintenue dans la partie coronaire des deux implants et recouverte par une membrane en téflon. Un espace pour la formation osseuse potentielle a donc été créé entre les deux implants. Les lambeaux chirurgicaux ont été repositionnés coronairement et consolidés par des sutures verticales en matelas. Après douze semaines de guérison, des biopsies ont été prélevées et examinées histologiquement. Chez trois des quatre chiens, les implants insérés partiellement s'étaient intégrés et des espaces de guérison intentionnellement larges avaient été créés autour des parties non-insérées des implants. Cependant, l'os ne s'était pas formé autour des implants partiellement découverts. Ce modèle expérimental peut être intéressant pour des études sur l'utilisation de différents processus pouvant théoriquement augmenter la formation osseuse.

Zusammenfassung

Es wird ein Hundemodell zur Untersuchung des suprakrestalen Knochenwachstums um teilweise versenkte Implantate beschrieben. Bei four Hunden wurden auf beiden Seiten im Unterkiefer die Prämolaren (P_1, P_2, P_3 und P_4) extrahiert. Bei der Wiedereröffnung 12 Wochen später wurden in der Gegend von P1 und P3 in einem Abstand von 15 mm zwei 10 mm Titanimplantate teilweise versenkt. Fünf Gewindegänge lagen oberhalb des Knochenkammes. Im koronalen Anteil der Implantate wurde ein Titannetz befestigt und mit einer ePTFE-Membran abgedeckt. So konnte ein Hohlraum für eine mögliche Knochenbildung zwischen den zwei Implantaten geschaffen werden. Die chirurgischen Lappen wurden koronal positioniert und mit vertikalen Matrazennähten gesichert. Nach einer Heilungszeit von 12 Wochen wurden Biopsieproben entnommen und histologisch untersucht. Bei three der four Hunde in der Studie waren die teilweise versenkten Implantate integriert und der gewünschte grosse Wundraum um die nicht versenkten Anteile der Implantate konnte gebildet werden. Jedoch konnte keine Knochenbildung um die nicht versenkten Implantatanteile festgestellt werden. Dieses experimentelle Modell könnte sich als nützlich für zukünftige Studien erweisen, welche die Anwendung von verschiedenen Verfahren zur Förderung einer Knochenbildung untersuchen.

Resumen

Se describe un modelo en perro para estudio del crecimiento de hueso supracrestal alrededor de implantes parcialmente insertados. Se extrajeron los premolares inferiores (P_1, P_2, P_3 y P_4) en ambos lados de la mandíbula en four perros. En una exposición quirúrgica 12 semanas mas tarde, se insertaron parcialmente en cada lado dos implantes de titanio, separados 15 mm, en las áreas de P1 y P3 de tal manera que protruyeran 5 roscas de la cresta ósea. Se fijó una malla de titanio al aspecto coronal de las dos fijaciones y se cubrió con una membrana de ePTFE. De este modo, se creó un espacio para la formación potencial de hueso entre los dos implantes. Los colgajos quirúrgicos se posicionaron coronalmente y se aseguraron con suturas de colchonero. Tras 12 semanas de cicatrización, se recogieron especímenes de biopsias y se examinaron histológicamente. En three de los four perros del estudio, los implantes insertados parcialmente se integraron y los amplios espacios que se crearon intencionalmente alrededor de las partes no insertadas de los implantes. De todos modos, el hueso no se formó alrededor de los implantes protruyentes. Por consiguiente, este modelo experimental puede resultar útil para futuros estudios en el uso de diferentes procedimientos que hipotéticamente puede incrementar la formación ósea.

要旨

犬のモデルにおいて、部分的に埋入したインプラント周囲の歯槽頂線上の骨成長について研究した。犬４匹の下顎両側前臼歯（Ｐ1，Ｐ2，Ｐ3，Ｐ4）を抜去した。１２週間後に外科的に局所を露出させて、各側に１５ｍｍ間隔でP1とP3の部位に長さ１０ｍｍのチタン製インプラント２本を、骨頂からネジ山５コが突出するように部分的に埋入した。２本のフィクスチャーの歯冠側はチタン・メッシュで固定し、ePTFEメンブレンで被覆した。このように、骨が成長するための空隙を２本のインプラントの間に作成した。歯肉弁は歯冠側に位置移動し、垂直マットレス縫合で閉じた。治癒１２週間後に生検標本を採取し、組織学的な検査を行った。４匹のうち３匹の犬において、部分的に埋入したインプラントは統合しており、インプラントの埋入されていない部分の周囲に意図的に大きな術創の空隙が作成された。しかし骨はインプラントの突出している部分の周囲には形成されなかった。従ってこの実験モデルは、骨形成を促進すると想定されている各種の術式に関して、将来の研究にとって有用であると思われる。

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