Flemming Isidor

Influence of forces on peri-implant bone

Authors' affiliation:
Flemming Isidor, Department of Prosthetic Dentistry, Faculty of Health Sciences, School of Dentistry, University of Aarhus, Aarhus, Denmark

Correspondence to:
Flemming Isidor
Department of Prosthetic Dentistry
Faculty of Health Sciences
School of Dentistry
University of Aarhus
Vennelyst Boulevard 9
DK-8000
Aarhus C
Denmark
Tel.: +45 8942 4082
Fax: +45 8619 5665
e-mail: flisidor@odont.au.dk

Key words: bone remodeling, bone resorption, dental implants, implant failure, mechanical stress, occlusal load.

Abstract: Occlusal forces affect an oral implant and the surrounding bone. According to bone physiology theories, bones carrying mechanical loads adapt their strength to the load applied on it by bone modeling/remodeling. This also applies to bone surrounding an oral implant. The response to an increased mechanical stress below a certain threshold will be a strengthening of the bone by increasing the bone density or apposition of bone. On the other hand, fatigue micro-damage resulting in bone resorption may be the result of mechanical stress beyond this threshold. In the present paper literature dealing with the relationship between forces on oral implants and the surrounding bone is reviewed. Randomized controlled as well as prospective cohorts studies were not found. Although the results are conflicting, animal experimental studies have shown that occlusal load might result in marginal bone loss around oral implants or complete loss of osseointegration. In clinical studies an association between the loading conditions and marginal bone loss around oral implants or complete loss of osseointegration has been stated, but a causative relationship has not been shown.

Occlusal forces affect the bone surrounding an oral implant. Mechanical stress can have both positive and negative consequences for bone tissue (Frost 2004) and, thereby, also for maintaining osseointegration of an oral implant.

After the first year of function, loss of marginal bone is small around most oral implants (Brånemark et al. 1977; Adell et al. 1981, 1986; Quirynen et al. 1991, 1992b; Isidor et al. 1999; Manz 2000), although a considerable loss can be observed at some implants (Brånemark et al. 1977; Adell et al. 1981; Cox & Zarb 1987; Block & Kent 1990; Malmqvist & Sennerby 1990; Naert et al. 1992; Quirynen et al. 1992a; Isidor et al. 1999; Carlsson et al. 2000; Fransson et al. 2005). Furthermore, it has been stated that the occlusal forces on an oral implant can result in loss of the marginal bone or complete loss of osseointegration even after a long time of service (Adell et al. 1981; Jemt et al. 1989; Naert et al. 2001a, 2001b).

An association between oral microbiota (plaque accumulation), peri-implant mucositis, loss of marginal bone (peri-implantitis), and subsequently loss of implants has also been described (for a review see Quirynen et al. 2002). With the exception of the consequences of mechanical load, peri-implantitis as well as other biologic factors causing loss of ossointegration (Esposito et al. 1998a, 1998b) will not be discussed in this paper.

It is difficult clinically to quantify the magnitude and direction of naturally occurring occlusal forces. Clinical indices concerning these and their impact on

To cite this article:
Isidor F. Influence of forces on peri-implant bone. *Clin. Oral Imp. Res.* **17** (Suppl. 2), 2006; 8–18

prostheses and oral implants are not available as they are for plaque accumulation and peri-implant mucositis (Mombelli et al. 1987). This makes it very difficult to correlate occlusal loading and implant failure. The occlusal forces may exceed the mechanical or biological load-bearing capacity of the osseointegrated oral implants or the prosthesis, causing either a mechanical failure or failure in the osseointegration. If this happens, the load can be classified as an 'overload' (Isidor 1999).

This review will mainly focus on the consequences loading has on the bone surrounding already osseointegrated oral implants.

Search strategy

A search in the PubMed database (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi) was performed initially with the terms oral implant/dental implant/implant (limited to dental journals) and load/overload/force and bone. None of the 607 papers revealed were randomized controlled clinical studies or prospective cohort studies in respect to evaluating the influence of controlled forces on peri-implant bone. Therefore, a expanded search including a hand search in the following journals was done *Archives of Oral Biology*, *Clinical Implant Dentistry & Related Research*, *Clinical Oral, Implants Research*, *European Journal of Oral Sciences*, *Implant Dentistry*, *International Journal of Oral & Maxillofacial Implants*, *International Journal of Periodontics & Restorative Dentistry*, *International Journal of Prosthodontics*, *International Journal of Oral and Maxillofacial Surgery*, *Journal of Clinical Periodontology*, *Journal of Dental Research*, *Journal of Dentistry*, *Journal of Oral Implantology*, *Journal of Oral Rehabilitation*, *Journal of Peridontology*, *Journal of Prosthetic Dentistry*, *Journal of Prosthodontics*, *Oral Surgery*, *Oral Medicine*, *Oral Pathology*, *Oral Radiology and Endodontics*, *Periodontology 2000*. This more extensive search failed to reveal any randomized controlled clinical studies or prospective cohort studies in respect of the evaluation of the influence of controlled forces on peri-implant bone. Furthermore, in the clinical studies the reporting of the loading conditions, e.g. bruxism , parafunctional habits, was retrospective or speculative in nature. As consequence, the mode of a narrative review was chosen. Part of the paper deals with a description of bone physiology theory, and another part with animal experimental studies and clinical studies addressing the possible effects of loading on bone surrounding oral implants.

Reactions of bone to mechanical stress

The bones of the maxilla and mandible, as well as other bones carrying mechanical loads, adapt their strength to the applied load (Frost 1992, 2004; Kannus et al. 1996; Lanyon & Skerry 2001). This continuous remodeling maintains the mechanical competence of the bone (Frost 2004). In the maxilla and mandible mechanical load is mainly a result of muscle forces. The mechanical stress on bone results in strain, i.e. a deformation of the bone. This is defined as the relative change in the length of the bone, i.e. either lengthening or shortening and is often expressed in microstrain, where 1000 microstrain corresponds to a deformation of 0.1%. The amount of strain is directly correlated to the stress applied to the bone, for instance through the loading of an oral implant. But the strain is also dependent on the mechanical properties of the bone (e.g., stiffness). This means that a given force may affect different bones or bone tissues differently, that is the same amount of stress can result in different amount of strain in bones with different properties.

Adaptation of bone to loading

Frost (1992) has proposed the hypothesis that bone cells respond to a local deformation of the bone produced by mechanical stress. The bone adapts to a certain strain – in a steady state. With slightly increased strain, the bone becomes mildly overloaded and compensates by forming more bone. If the strain goes beyond a threshold which exceeds the bone's capacity fatigue fracture can occur.

Typically a bone is believed to function within the strain range of approximately 50–1500 microstrain (Frost 2004). If the peak load on a bone results in strains of 1500–3000 microstrain a mild overload occurs. According to Frost's hypothesis (Frost 1992, 2004), this can result in mechanical fatigue damage, but remodeling normally repairs the damage and thus prevents it accumulating. Loads influencing the bone in this interval may even result in an osseous adaptation by formation of bone (reshaping and strengthening), presumably to reduce the future functional strain within the bone. Overloading the bone can increase the micro-damage (and the repair). Repeated stress on the bone resulting in deformations greater than 3000 microstrain increase the micro-damage. Such deformations can overwhelm the repair mechanism and result in a fatigue failure (Fig. 1). In comparison, normal bone fractures suddenly at forces causing a deformation of about 2.5% (25,000 microstrain).

In contrast, if the strain in the bone does not exceed 50–100 microstrain, disuse of the bone occurs and remodeling results in a net loss of bone. Thus, a moderate increase from the optimal functional strains induces an increase in bone mass that, if the loading remains constant, re-establishes new optimal strains. Conversely, where functional loading is reduced to a level where optimal strains are not achieved, bone loss occurs to adapt to the new demand (Frost 1992).

It is important to appreciate that in this theory it is not the actual load that is important but the effect of the load on the bone – the resulting strain in the bone. This also depends on the amount of bone tissue. According to Frost (2004) a load of 1–2 MPa (approximately equivalent to 0.1–0.2 kg/mm^2) results in 50–100 microstrain in cortical lamellar bone in healthy young adult mammals, and 60 MPa in 3000 microstrain. The level for sudden fracture is 25,000 microstrain and is obtained with a stress of 120 MPa. It has been suggested that there is not always a linear relationship between stress and bone failure, with one group reporting that a doubling of the stress that originally caused 2000 microstrain increased the microscopic fatigue damage in bone by 400 times (Pattin et al. 1996).

It has been shown that more dense bone surrounds mechanically loaded oral implants than non-loaded implants in monkeys (Piattelli et al. 1993, 1997, 1998). On the other hand, a higher bone-to-implant contact, but not increased bone density, was observed around implants in dogs after

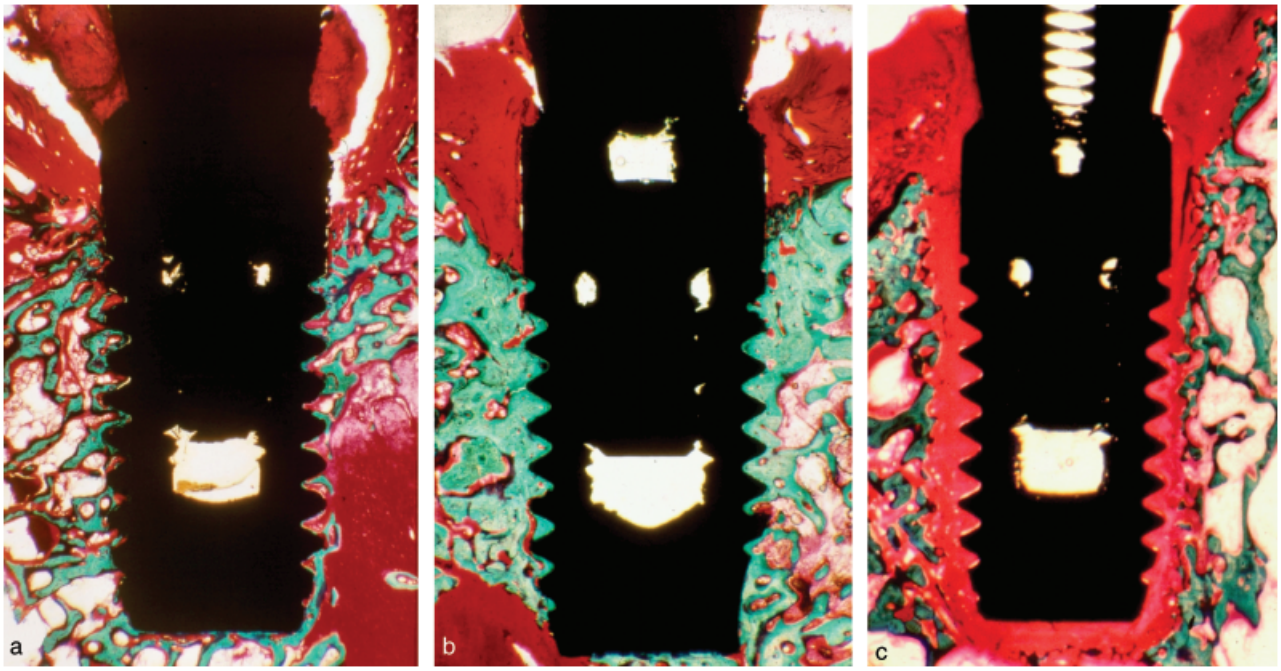

Fig. 1. Histologic sections of a non-loaded implant (a) and two excessively loaded implants (b and c). Mineralized bone is green and soft tissue is red. The marked difference in bone density between (a) and (b) may reflect that the bone adjacent to the excessively loaded implant (b) is adapted to the load. The bone adjacent to the excessively loaded implant (c) could not adapt to the load and the implant lost osseointegration completely. A zone of fibrous tissue is interposed between the implant and surrounding bone. The specimens are from the study of Isidor (1997b, 1998).

10 months of functional load (Berglundh et al. 2005). In a study by Melsen & Lang (2001) specially designed oral implants were inserted in monkeys and after healing subjected to well-defined continuous loading. None of the implants had lost osseointegration after 11 weeks of loading, but loading significantly influenced the turnover of the alveolar bone in the vicinity of the implants. Bone apposition was most frequently found when the calculated strain varied between 3400 and 6600 microstrain. On the other hand, when the strain exceeded 6700 microstrain the remodeling of the bone resulted in a net loss of bone. Together these studies support the theory that apposition of bone around an oral implant is the biological response to a mechanical stress below a certain threshold, whereas loss of marginal bone or complete loss of osseointegration may be the result of mechanical stress beyond this threshold.

In athletes, bony apposition has been observed as a result of increased loading (Jones et al. 1977) and bone loss as a result of decreased loading due to immobilization (Jaworski et al. 1980). Furthermore, fatigue fractures have been observed in athletes and special force trainees (Verma & Sherman 2001; Frost 2004).

There seem to be differences from person to person when it comes to bone strength, as a few individuals seem unusually prone to fatigue or traumatic fractures while others are unusually resistant to them (Frost 2004).

How aging might affect the stiffness of the bone is uncertain although the fracture strength may be lower. Therefore, the risk for fatigue fracture may also be increased in aged adults (Martin 1993; Diab et al. 2005).

It is not known how bone registers the strain and reacts on it. Osteocytes can respond to strain and it might be, although not known, these cells that regulate the respond to strain in bone (Frost 2004). At the cellular level the modeling of the bone occurs through the shift in balance between osteoclasts, which resorb the calcified matrix, and osteoblasts, which synthesize new bone matrix (Frost 1992). Furthermore bone modeling, as a result of mechanical loading, is predominantly achieved by differentiation of bone cells but also to some extent by recruitment and proliferation of osteoblast precursors (Pavlin & Gluhak-Heinrich 2001).

Mechanical load and bone healing

The strength of the bone increases from the beginning of loading after surgical exposure and up to 1 year after loading, both because the bone become more dense and because of an increase in mineral content (Roberts et al. 1987). Partially mineralized bone is weaker than fully mineralized bone. Furthermore, an organization of the surrounding bone is going on during the first year after implant insertion. Because of the trauma from placement of the implant the surrounding bone becomes necrotic and is replaced by woven bone. Several months later lamellar bone replaces the woven bone. The well organized and more mineralized lamellar bone is stronger than unorganized woven bone. The occlusal load in the first period after loading may, therefore, be sufficient to cause micro-damage in the bone surrounding the implant, even though a load of the same magnitude will not be sufficient to cause failure later after healing and adaptation of the bone.

To avoid high stress/strain in the surrounding bone in the adaptation period, it has been advocated to apply progressive

loading on oral implants (Misch et al. 1998). In a recent clinical study healed implants were progressively loaded by gradually increasing the height of the occlusal table from a state of infra-occlusion to full occlusion by adding acrylic resin to an acrylic crown (Appleton et al. 2005). Implants restored with a metal ceramic crown acted as controls. With digital image analysis and digital subtraction radiography, progressively loaded implants demonstrated less loss in marginal bone height than conventionally loaded implants. Furthermore, the progressively loaded implants showed over time a continuous increase in peri-implant bone density.

Immediate loading of oral implants

A slight load on healing bone shortens healing rather than prolong it. Strains in healing bone not exceeding mild overload might improve healing. On the other hand, in healing bone a load will more readily cause an overload and fracture than in normal bone (Frost 1992).

Both animal experiments (Duyck et al. 2005; Quinlan et al. 2005) and clinical studies (Bischof et al. 2004; Esposito et al. 2004; Attard & Zarb 2005; Degidi et al. 2005; Froum et al. 2005) have shown that immediately loaded oral implants acting as support for a prosthesis can osseointegrate providing that the forces and implant micro-motion can be controlled (Buchter et al. 2005; Duyck et al. 2006).

Load transfer between oral implants and surrounding bone

The stiffness of oral implants of titanium or its alloys is several times greater than that of cortical bone (Kitamura et al. 2004; Misch et al. 2005). When an oral implant is occlusally loaded, the stress will be transferred to the bone, with the highest stress in the most coronal portion of the supporting bone. This is a consequence of a general engineering principle stating that when two materials are in contact and the one is loaded, the stress will be highest where the materials have first contact. This has also been observed in simulated loaded implants in both photoelastic and 3D finite-element analyses (Rieger et al. 1990; Bidez & Misch 1992; Kitamura et al. 2004). Therefore, an increased strain in the bone resulting in an overload would also be most likely to happen first in this area.

Some marginal bone loss around oral implants during the first year of function has been a common observation. Many different causes for this phenomenon have been given, including the reflection of the periosteum during surgery, preparation of the implant bed, the level of the microgap between the abutment and implant body, bacterial invasion, the establishment of a biological width, the configuration of the coronal part of the implant, and also occlusal overload (Oh et al. 2002). A smooth collar at the most coronal part of an implant may transmit shear forces to the bone. Bone is strongest under compressive forces, weaker under tensile loads, and even weaker to in shear (Hoshaw et al. 1994; Misch et al. 2005). Therefore, even though osseointegration may be present at the smooth metal collar at the top of the implant during healing and before loading, the weaker shear interface in this region may result in an overload of the bone when the implant is loaded (Misch et al. 2005). This may be the explanation of why a bone loss corresponding at least to the length of the smooth collar or to the first thread has been found for various implant designs with varying length of the collar (Adell et al. 1981; Jemt et al. 1990; Hämmerle et al. 1996; Jung et al. 1996; Wiskott & Belser 1999; Ricci et al. 2004).

The design (e.g., screw type, cylindrical) and the surface configuration (e.g., configuration of threads and machined, sandblasted or plasma-sprayed surfaces) of an oral implant may effect the stress distribution in the bone and, thereby, also the strain in the bone–implant interface, as shown with computerized (Rieger et al. 1989) or photoelastic (French et al. 1989) stress analyses.

In an experimental study in baboons, the histological and histomorphometrical observations after 18 months of functional loading indicate that screw type implants have a higher 'bone-to-implant contact' than cylindrical implants. This was more pronounced in the maxilla than in the mandible (Watzak et al. 2005). Furthermore, a higher marginal bone level was observed around implants with a titanium plasma-sprayed surface compared with machined implants, and the amount of bone-to-implant contact as well as the density of the peri-implant bone were lower at the machined than at the titanium plasma-sprayed implants (Gotfredsen et al. 2001c).

The importance of the configuration of the implant was also observed in a clinical study by Zechner et al. (2004). Radiographic marginal bone loss was observed after 4 years of observation, even though there were no clinical findings of inflammation or exudation. The radiographic marginal bone loss was higher in implants with machined-surfaced V-threads than in implants with sandblasted/acid etched square threads. In a study by Quirynen et al. (1992a) a higher frequency of failures after loading was observed with standard (machined surface) implants than with self-tapping implants. On the other hand, no difference in marginal bone loss over time was observed between the two implant designs.

Static and cyclic loads on oral implants

Bone loss was observed around the necks of implants exposed to high cyclic axial tension but not around unloaded controls in a study with screw-type implants inserted in dog tibiae (Hoshaw et al. 1994). Similar results were also observed in a dog model by Duyck et al. (2001). Static and cyclic loads were applied to 10-mm-long implants installed bicortically in rabbit tibiae. The loading continued for 14 days. The histological picture was similar for controls and statically loaded implants. Dense cortical lamellar bone was present around the marginal and apical parts of these implants with no signs of bone loss. On the other hand, crater-shaped bone defects were observed in the marginal bone area around the cyclic loaded implants. This study shows that excessive cyclic loads can cause crater-like bone defects lateral to osseointegrated implants. In contrast, several studies where orthodontic forces have been applied have found apposition or increase in bone density rather than loss of bone surrounding an implant (Roberts et al. 1984; Wehrbein & Diedrich 1993; Asikainen et al. 1997; Akin-Nergiz et al. 1998).

In a series of experiments Gotfredsen et al. (2001a, 2001b, 2001c, 2002) studied the effect of static load created with expansion screws on implants inserted in dog mandibles. In none of the studies did implants fail because of the static load. In contrast, a structural adaptation of the peri-implant bone to this laterally directed load

occurred as the bone density and the mineralized bone-to-implant contact were higher adjacent to the laterally loaded implants than at non-loaded control sites (Gotfredsen et al. 2001b).

No failure of implants placed in baboon and rabbit tibias was observed after mounting prostheses with poor fit (Carr et al. 1996; Michaels et al. 1997). The mounting of a prosthetic reconstruction with poor fit results in a static load similar to that induced by orthodontic appliances.

Together these studies indicate that high cyclic loads have a more detrimental effect on the bone around an implant than static loads.

Axial and non-axial loads on oral implants

The length of the cantilever and the resultant stress on the nearest abutment are directly related (Duyck et al. 2000) due to a cantilever acting as a lever arm. In a study in dogs mainly axial loading and mainly non-axial loading conditions were created by mounting a bilaterally supported fixed partial prosthesis or a cantilever fixed partial prosthesis on two implants in the mandible (Barbier & Schepers 1997). At mainly axial loaded implants an histologically quiescent remodeling that gradually decreased from the coronal aspect to the apex of the implant was observed. Mainly non-axial loading resulted in more dynamic remodeling of the surrounding cortical and especially trabecular bone tissue. Furthermore, osteoclastic activity in some sites of the mainly non-axial loaded implants was observed. The authors interpreted this to mean that an experimental period longer than 7 weeks could have resulted in marginal bone loss. The view that a non-axial load is more detrimental to oral implants than an axial load is further supported by findings in studies using 3D finite-element analysis (Papavasiliou et al. 1996; Kitamura et al. 2005), where non-axial loads resulted in higher stress levels in the peri-implant bone than axial loads.

Load and progressive marginal bone loss

Clinical (Quirynen et al. 1992a) as well as experimental studies (Miyata et al. 1997, 1998, 2000) may indicate that occlusal overload can increase the incidence of marginal bone loss around oral implants.

Animal experimental studies

In a series of experiments Miyata et al. (1997, 1998, 2000) studied the influence of controlled increase of occlusal load (overload) on implants in monkeys. Crowns with or without premature occlusal contacts were placed on osseointegrated oral implants. After up to 4 weeks of increased occlusal load the implants with the surrounding tissues were removed and evaluated histologically. The results showed that the implants remained osseointegrated. The marginal bone levels for implants with crowns 100 μm 'high' and control implants without occlusal loading were similar for implants with no inflammation in the peri-implant tissues (Miyata et al. 1998). On the other hand, statistically significant marginal bone loss was observed when the superstructure was 180 μm too high. When the superstructures were created with 250 μm supra-occlusion up to three times more bone loss was observed than adjacent to control implants (Miyata et al. 2000). In conclusion, these experiments show that occlusal overload can result in marginal bone loss around oral implants with no inflammation in the peri-implant tissues.

Clinical studies

In several clinical studies marginal bone loss around oral implants has been associated with high occlusal stress on the implants (Lindquist et al. 1988; Jemt et al. 1989; Ahlqvist et al. 1990; Block & Kent 1990; Naert et al. 1992, 2001a; Quirynen et al. 1992a). For instance, Quirynen et al. (1992a) reported a correlation between overloading/parafunction and progressive marginal bone loss/implant loss in patients with complete fixed prostheses or overdentures. Naert et al. (1992) even suggested that occlusal overload is the most probable cause of implant and marginal bone loss after loading based on a study of 146 consecutive patients with 589 implants. On the other hand, in a study with 379 patients who had worn implant-supported restorations for many years, occlusal wear failed to have any statistical impact on the rate of annual vertical bone loss (Engel et al. 2001). Furthermore, when poor occlusion (according to common prosthodontic criteria) on mandibular implant-supported fixed prostheses was related to marginal peri-implant bone loss no correlation was observed (Wennerberg et al. 2001). In other words, results from some studies indicate an association between occlusal problems and an increased loss of marginal bone while others do not.

The length of the cantilever on fixed prostheses and the stress to the nearest abutment are directly related (Duyck et al. 2000). An increased marginal bone loss has been observed around the implant closest to a cantilever unit (Lindquist et al. 1988; Shackleton et al. 1994; Wyatt & Zarb 2002; Baron et al. 2005). This observation indicates that high stress on the supporting bone around implants may have negative consequences for the marginal bone level.

In a prospective human study, it was observed that the amount of radiographic marginal bone loss around implants was related to the density of bone as observed during surgery (Manz 1997). With more dense bone, less peri-implant bone loss was observed 6 months after prosthetic treatment. In contrast, the peri-implant bone loss from implant insertion to the surgery for implant exposure was similar for all bone qualities (Manz 2000). These observations can be interpreted to mean that the higher density of the bone had reduced the strain in the marginal bone when the implant became loaded and, thereby, may have reduced marginal bone loss in the adaptation phase.

Failing implants in six patients were divided into two groups based on whether clinical peri-implant infection was present or not. Histological evaluation of the peri-implant soft tissues around implants without clinical signs of infection showed healthy peri-implant mucosa without inflammation. The authors interpreted the results to mean that the marginal bone loss around these implants probably could be related to an occlusal overload (Sanz et al. 1991).

It is difficult clinically to quantify the magnitude or direction of naturally occurring occlusal forces, and even more to control or standardize these. Consequently, even though increased bone loss in areas of relatively high stress has been reported in some clinical studies, a causative relationship with overload has not been established.

Load and loss of osseointegration

In the field of orthopedics, aseptic loosening of non-cemented hip (Søballe et al. 1987) and knee (Foran et al. 2004) prostheses has been observed. It should be appreciated that this is a closed system without microbially induced inflammation. Concerning oral implants, both the results from experimental (Isidor 1996, 1997b) and clinical studies (Quirynen et al. 1992a; Fugazzotto 2001) have indicated that occlusal overload on oral implants can result in complete loss of osseointegration.

Animal experimental studies

In a study in monkeys (macaques) it has been demonstrated clinically, radiographically and histologically (Isidor 1996, 1997a, 1997b, 1998) that occlusal overload can result in loss of osseointegration of previously osseointegrated oral implants. The occlusal overload was created by mounting a fixed partial prosthesis on two implants in the lateral segment in each of four monkeys. The prosthesis was in supra-occlusal contact with an antagonizing metal splint and caused a lateral displacement of the mandible during occlusion, resulting in a lateral rather than an axial excessive occlusal load. The two implants retaining the prosthesis were brushed once a week and subgingival cleaning was performed once a month. Three other implants in each monkey were never cleaned, and additionally a cotton cord was placed passively around each of these to promote plaque accumulation. Five out of eight implants with an excessive occlusal load clinically lost osseointegration (increased mobility and peri-implant radiolucency) $4\frac{1}{2}$ months to $15\frac{1}{2}$ months after the occlusal overload was initiated. An additional implant exhibited questionable mobility and peri-implant radiolucency. The loaded implants in one monkey did not become mobile. Two of the mobile implants were lost in an attempt to demount the fixed prosthesis. All implants with plaque accumulation remained clinically osseointegrated as also observed histologically although marginal bone loss was observed. Furthermore, a dense inflammatory infiltrate in the supra-crestal connective tissue and osteoclastic activity at the bone crest was apparent adjacent to the implants with plaque accumulation. In contrast, only a moderate inflammatory infiltrate was observed in the supra-crestal peri-implant mucosa at implants with an occlusal overload. Of the six excessively occlusally loaded implants available for histological analysis, two implants (in one monkey) with manifest clinical and radiographic signs of having lost osseointegration had also histologically lost osseointegration completely. The bone crest was near the margin of the implants, but a narrow zone of fibrous connective tissue was interposed between the implant and the bone (Fig. 1). In another monkey, the two implants with manifest or possible clinical and radiographic signs of having lost osseointegration the bone crest was near the margin of the implant, but the implants were only osseointegrated in the apical half with only a minor proportion of the implant surface in contact with mineralized bone tissue. In these few areas with bone-to-implant contact, bone resorption was often observed. This study (Isidor 1996, 1997b) showed that occlusal overload on oral implants can result in complete or partial loss of osseointegration. Implants with plaque accumulation, on the other hand, may show signs of peri-implantitis with marginal bone loss.

In a study in dogs Heitz-Mayfield et al. (2004) did not observe loss of osseointegration or loss of marginal bone height around implants in supra-occlusion. In six dogs two titanium plasma-sprayed implants and two sandblasted, acid-etched implants were placed on each side of the mandible. In order to create excessive occlusal load, gold crowns with supra-occlusal contact with the opposing teeth were placed on implants on one side of the mandible. The implants in the other side were not loaded. Plaque control was performed throughout the experimental period. There were no statistically significant changes for any of the clinical and radiographic measurements from baseline to 8 months at the loaded and unloaded implants. Furthermore, the histological evaluation showed similar mean mineralized bone-to-implant contact in the control implants (73%) and in the test implants (74%). The authors concluded that in the presence of peri-implant mucosal health, a period of 8 months of excessive occlusal load on titanium implants did not result in loss of osseointegration or marginal bone loss when compared with non-loaded implants (Heitz-Mayfield et al. 2004). An explanation for the difference in outcome of this study and the study by Isidor (1996, 1997b) may be related to the animals used, i.e. dogs and monkeys, and the density of the bone surrounding the implant. In the study of Heitz-Mayfield et al. (2004) the bone density (the proportion of mineralized bone at a distance of 1 mm from the implant surface) was on average 69% and 79% for the two types of non-loaded implants, whereas it was only 38% for non-loaded implants in the study of Isidor (1997b). The excessive load causing loss of implants in the study of Isidor (1996, 1997b) had a lateral direction on the implants whereas, Heitz-Mayfield et al. (2004) stated that the load in their study was hyper-contact in centric occlusion. Non-axial loads are considered to create more stress in the peri-implant bone than axial loads (Papavasiliou et al. 1996; Kitamura et al. 2005). Furthermore, in the study of Isidor (1996) occlusal splints were used to ensure that the opposing teeth did not migrate or were intruded because of the occlusal load, as observed by Ogiso et al. (1994). In this study the occlusion was raised with a splint, resulting in an axial load on the implants. Intrusion of the opposing teeth was observed clinically and remodeling and thickening of the bone surrounding the loaded implants was observed histological.

Together these experimental studies (Ogiso et al. 1994; Isidor 1996; Heitz-Mayfield et al. 2004) indicate the importance of the experimental design for the resulting stress and strain in the peri-implant bone and, thereby, the biologic consequences of the load.

Animal experimental models – bone density and bite force

The mechanical properties of bone tissues from different mammals are presumably not markedly different (Frost 2004). For instance, the elastic properties of mandibular bone in macaques and humans are similar (Dechow & Hylander 2000). The bone mass, the amount of trabecular and cortical bone, may of cause differ considerably and, thereby, also whole-bone strength.

It has been shown that the maximal stimulated bite forces in monkeys, such as macaques, is in the range from 23 N

(Ström et al. 1994) to 140 N (Dechow & Carlson 1990), this is in contrast to the observed average maximal voluntary bite forces for normal woman/men of 383 N/547 N (Raadsheer et al. 2004), 442 N/512 N (Ikebe et al. 2005), and 678 N/1.019 N (Cosme et al. 2005). The bite force has been studied in dogs of varying size with a mean of 256 N but with a large variation (Lindner et al. 1995).

Due to the higher bite force an overload of the peri-implantat bone presumably is more likely to occur in humans than, for instance, in small monkeys.

Clinical studies

The results from several studies (Brånemark et al. 1977; Adell et al. 1981; Lindquist et al. 1988; Jemt et al. 1989; Ahlqvist et al. 1990; Block & Kent 1990; Rosenberg et al. 1991; Sanz et al. 1991; Naert et al. 1992, 2001b; Quirynen et al. 1992a; Tonetti & Schmid 1994; Buser et al. 1997; Ekfeldt et al. 1997, 2001; Fugazzotto 2001; Raghoebar et al. 2001) have suggested overloading as a important reason for oral implants to fail.

Quirynen et al. (1992a) studied the effect of overload on oral implants in 69 patients with one or two complete fixed prostheses and found that after the first year of loading loss of implants correlated well with the presence of overload due to a lack of anterior contact, the presence of parafunctional activity and full-fixed prostheses on osseointegrated implants in both jaws. Furthermore, more failures were observed with shorter implants. Other studies has also associated an increased rate of late failures with parafunction (Balshi et al. 1997; Balshi & Wolfinger 1997; Ekfeldt et al. 2001).

In a retrospective study of 1472 implants in the molar region Fugazzotto (2001) found that lone standing terminal abutment implants demonstrated the lowest success rate and the failures were often associated with untreated parafunction, e.g. eight of 11 late-failed implants in the second molar region of the mandible were placed in patients with a detectable parafunctional habit. The results of another study showed that oral implants were more likely to fail when used for posterior single-tooth replacements or removable prostheses rather than for complete fixed prostheses or overdentures (Moheng & Feryn 2005).

Histological findings from failed Brånemark implants inserted in humans have according to the authors indicated that the etiologic factor for the failure of eight of 10 examined implants was occlusal overload (Esposito et al. 2000). The implants judged to have failed due to excessive loading (radiolucent line around clinically mobile implants but no clinical inflammation), had peri-implant marginal tissues which displayed moderate inflammatory infiltrates located adjacent to and beneath the junctional epithelium, and a dense, fibrous tissue capsules with minimal inflammation surrounding the implants. In a previous study (Esposito et al. 1997), immuno-histochemical evaluation showed that implants with clinical signs of loss of osseointegration (peri-implant radiolucency and mobility) were characterized by a chronic inflammatory response of the surrounding tissues with macrophages as the predominant labeled cell type. The authors concluded, that these findings suggest that an on-going infection was unlikely to have been the etiological factor for the failure.

In a pair of comprehensive review papers, Esposito et al. (1998a, 1998b) have calculated the frequency of late implant failures from 19 different publications with Brånemark implants with a machined surface. Of the failures observed after more than 1 year of loading, occlusal overload was estimated to account for approximately 90% and peri-implantitis for 10% of the few late failures (4.6% of the inserted implants).

Bone density and oral implants

In many studies of various types of prostheses and implant designs, an increased rate of late failures has been observed for implants placed in areas considered to have low bone density, i.e. posteriorly or in the maxilla (Engquist et al. 1988; Jaffin & Berman 1991; Johns et al. 1992; Saadoun & LeGall 1992; Hutton et al. 1995; Jemt & Lekholm 1995; Jemt et al. 1996; Scurria et al. 1998; Ekfeldt et al. 2001; Becktor et al. 2002; Weng et al. 2003). This observation may serve as indirect evidence of an association between occlusal overload and failure of osseointegrated implants.

Titanium plasma-sprayed vs. machined implant surface

Loss of implants due to occlusal overload has more frequently been reported for implants with a machined surface only (Brånemark et al. 1977; Adell et al. 1981; Cox & Zarb 1987; Lindquist et al. 1988; Jemt et al. 1989; Ahlqvist et al. 1990; Sanz et al. 1991; Naert et al. 1992; Quirynen et al. 1992a; Ekfeldt et al. 1997, 2001; Fugazzotto 2001) than for implants with a rough, titanium plasma-sprayed surface (Buser et al. 1997; ten Bruggenkate et al. 1998; Fugazzotto 2001; Mericske-Stern et al. 2001; Ferrigno et al. 2002). However, a direct comparison between the implant surfaces is not valid from these clinical studies, since it is not only the surface roughness that change from one implant system to another but also the design (e.g., screw type, cylindrical) and the surface configuration (e.g., one or two piece; configuration of threads or even no threads) and this may effect the stress distribution in the bone surrounding an oral implant and, thereby, also the strain in the bone–implant–interface (French et al. 1989; Rieger et al. 1989).

It has been suggested that implants with a rough surface may have a reduced risk of failure from occlusal overload because of the increased surface area (Esposito et al. 1998a, 1998b). Furthermore, implants with a titanium plasma-sprayed surface have shown a better anchorage in the bone than implants with a machine-produced surface when a removal torque test has been applied (Gotfredsen et al. 1992; Carr et al. 1997). But, the effect of surface roughness of oral implants on the resistance to fatigue failures due to occlusal overload is not clarified.

Occlusal overload in combination with peri-implantitis

The combination of occlusal overload and peri-implantitis may theoretically intensify the effect of both the overload and the inflammation.

Miyata et al. (2000) showed histologically in monkeys that crowns with 100 μm supra-occlusion could result in increased bone loss with the presence of experimental peri-implantitis (Miyata et al. 1997) but not when the peri-implant tissues were without inflammation (Miyata et al. 1998). On the other hand, statistically significant marginal bone loss was observed when the superstructure was

180 μm or more too high at implants with the peri-implant tissue kept in an inflammation-free state (Miyata et al. 2000). In contrast, in a study in monkeys 'repetitive mechanical trauma' showed no effect on histological peri-implant bone loss either in healthy sites or in sites with experimental peri-implantitis (Hürzeler et al. 1998). On the other hand, significantly less height of supporting bone as a fraction of the total implant length was observed around implants with peri-implantitis compared with healthy implants. Similarly, static, lateral load created with expansion screws did not induce marginal bone loss around implants with mucositis nor did it increase the bone loss at implants with ligature-induced peri-implantitis in dogs (Gotfredsen et al. 2002).

Together these experiments indicate that at implants with peri-implantitis increased occlusal load may result more pronounced marginal bone loss while other type of high loads, e.g. static load, may not have this effect.

The consequence of occlusal overload in combination with peri-implantitis has not been demonstrated in humans. In can be speculated, that in the clinical situation the effect of occlusal overload may increase when bone resorption is already ongoing in the marginal area and, even more, the implant also has a reduced marginal bone level. The other way round, the lack of bone-to-implant contact in a bone defect caused by occlusal overload may favor epithelial downgrowth. After a while the bone defect may be infected with periopathogenic micro-organisms (Quirynen et al. 2002) which can contribute to further bone loss, and the defect may now be difficult to distinguish from a lesion caused solely by peri-implantitis.

Conclusions

In the available literature from clinical studies it is apparent that only few authors report possible reasons for implant failures. Furthermore, most clinical studies have only few patients included and, at the same time, only a small frequency of failed implants. Moreover, it is difficult clinically to quantify the magnitude and direction of naturally occurring occlusal forces. All together this makes it difficult to discover a possible correlation between occlusal forces (overload) and implant failures. Much of the knowledge in this field, therefore, is derived from a relatively small number of experimental animal studies, and it may be difficult to draw definitive conclusions. Bone tissue reacts to strain (i.e., deformation). Depending on the properties of the tissue, a given force may affect different bones or bone tissues differently, but mechanically loaded bones adapt to the load. If the strain in the bone surrounding an oral implant is in the 'mild overload' range (1500–3000 microstrain), apposition of bone seems to be the biological response. On the other hand, strain in the bone beyond this range will at some point result in fatigue fracture and bone resorption. Animal experimental studies have shown that occlusal load may result in increased marginal bone loss around oral implants. Furthermore, in clinical studies increased bone loss has been observed in areas of relatively high stress, but a causative relationship with overload, however, has not been established. Only one animal experimental study has shown that excessive occlusal load can cause complete loss of osseointegration. Although it has been stated in clinical studies, that occlusal forces may be associated with loss of oral implants, a causative relationship has never been convincingly demonstrated.

References

Adell, R., Lekholm, U., Rockler, B. & Brånemark, P.-I. (1981) A 15-year study of osseointegrated implants i the treatment of the edentulous jaw. *International Journal of Oral Surgery* **10**: 387–416.

Adell, R., Lekholm, U., Rockler, B., Brånemark, P.I., Lindhe, J., Eriksson, B. & Sbordone, L. (1986) Marginal tissue reactions at osseointegrated titanium fixtures (I). A 3-year longitudinal prospective study. *International Journal of Oral and Maxillofacacial Surgery* **15**: 39–52.

Ahlqvist, J., Borg, K., Gunne, J., Nilson, H., Olsson, M. & Åstrand, P. (1990) Osseointegrated implants in edentulous jaws: a 2-year longitudinal study. *International Journal of Oral & Maxillofacial Implants* **5**: 155–163.

Akin-Nergiz, N., Nergiz, I., Schulz, A., Arpak, N. & Niedermeier, W. (1998) Reactions of peri-implant tissues to continuous loading of osseointegrated implants. *American Journal of Orthodontics and Dentofacial Orthopedics* **114**: 292–298.

Appleton, R.S., Nummikoski, P.V., Pigno, M.A., Cronin, R.J. & Chung, K.H. (2005) A radiographic assessment of progressive loading on bone around single osseointegrated implants in the posterior maxilla. *Clinical Oral Implants Research* **16**: 161–167.

Asikainen, P., Klemetti, E., Vuillemin, T., Sutter, F., Rainio, V. & Kotilainen, R. (1997) Titanium implants and lateral forces. An experimental study with sheep. *Clinical Oral Implants Research* **8**: 465–468.

Attard, N.J. & Zarb, G.A. (2005) Immediate and early implant loading protocols: a literature review of clinical studies. *Journal of Prosthetic Dentistry* **94**: 242–258.

Balshi, T.J., Ekfeldt, A., Stenberg, T. & Vrielinck, L. (1997) Three-year evaluation of Brånemark implants connected to angulated abutments. *International Journal of Oral & Maxillofacial Implants* **12**: 52–58.

Balshi, T.J. & Wolfinger, G.J. (1997) Immediate loading of Brånemark implants in edentulous mandibles: a preliminary report. *Implant Dentistry* **6**: 83–88.

Barbier, L. & Schepers, E. (1997) Adaptive bone remodeling around oral implants under axial and nonaxial loading conditions in the dog mandible. *International Journal of Oral & Maxillofacial Implants* **12**: 215–223.

Baron, M., Haas, R., Baron, W. & Mailath-Pokorny, G. (2005) Peri-implant bone loss as a function of tooth-implant distance. *International Journal of Prosthodontics* **18**: 427–433.

Becktor, J.P., Eckert, S.E., Isaksson, S. & Keller, E.E. (2002) The influence of mandibular dentition on implant failures in bone-grafted edentulous maxillae. *International Journal of Oral & Maxillofacial Implants* **17**: 69–77.

Berglundh, T., Abrahamsson, I. & Lindhe, J. (2005) Bone reactions to longstanding functional load at implants: an experimental study in dogs. *Journal of Clinical Periodontology* **32**: 925–932.

Bidez, M.W. & Misch, C.E. (1992) Issues in bone mechanics related to oral implants. *Implant Dentistry* **1**: 289–294.

Bischof, M., Nedir, R., Szmukler-Moncler, S., Bernard, J.P. & Samson, J. (2004) Implant stability measurement of delayed and immediately loaded implants during healing. *Clinical Oral Implants Research* **15**: 529–539.

Block, M.S. & Kent, J.N. (1990) Factors associated with soft- and hard-tissue compromise of endosseous implants. *Journal of Oral and Maxillofacial Surgery* **48**: 1153–1160.

Brånemark, P.I., Hansson, B.O., Adell, R., Breine, U., Lindström, J., Hallen, O. & Ohman, A. (1977) Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. *Scandinavian Journal of Plastic & Reconstructive Surgery – Supplementum* **16**: 1–132.

Buchter, A., Wiechmann, D., Koerdt, S., Wiesmann, H.P., Piffko, J. & Meyer, U. (2005) Load-related implant reaction of mini-implants used for orthodontic anchorage. *Clinical Oral Implants Research* **16**: 473–479.

Buser, D., Mericske, S.R., Bernard, J.P., Behneke, A., Behneke, N., Hirt, H.P., Belser, U.C. & Lang, N.P. (1997) Long-term evaluation of non-submerged ITI implants. Part 1: 8-year life table analysis of a prospective multi-center study with 2359 implants. *Clinical Oral Implants Research* **8**: 161–172.

Carlsson, G.E., Lindquist, L.W. & Jemt, T. (2000) Long-term marginal periimplant bone loss in edentulous patients. *International Journal of Prosthodontics* **13**: 295–302.

Carr, A.B., Beals, D.W. & Larsen, P.E. (1997) Reverse-torque failure of screw-shaped implants in baboons after 6 months of healing. *International Journal of Oral & Maxillofacial Implants* **12**: 598–603.

Carr, A.B., Gerard, D.A. & Larsen, P.E. (1996) The response of bone in primates around unloaded dental implants supporting prostheses with different levels of fit. *Journal of Prosthetic Dentistry* **76**: 500–509.

Cosme, D.C., Baldisserotto, S.M., de Andrade Canabarro, S. & Shinkai, R.S. (2005) Bruxism and voluntary maximal bite force in young dentate adults. *International Journal of Prosthodontics* **18**: 328–332.

Cox, J.F. & Zarb, G.A. (1987) The longitudinal clinical efficacy of osseointegrated dental implants: a 3-year report. *International Journal of Oral & Maxillofacial Implants* **2**: 91–100.

Dechow, P.C. & Carlson, D.S. (1990) Occlusal force and craniofacial biomechanics during growth in rhesus monkeys. *American Journal of Physical Anthropology* **83**: 219–237.

Dechow, P.C. & Hylander, W.L. (2000) Elastic properties and masticatory bone stress in the macaque mandible. *American Journal of Physical Anthropology* **112**: 553–574.

Degidi, M., Scarano, A., Piattelli, M., Perrotti, V. & Piattelli, A. (2005) Bone remodeling in immediately loaded and unloaded titanium dental implants: a histologic and histomorphometric study in humans. *Journal of Oral Implantology* **31**: 18–24.

Diab, T., Sit, S., Kim, D., Rho, J. & Vashishth, D. (2005) Age-dependent fatigue behaviour of human cortical bone. *European Journal of Morphology* **42**: 53–59.

Duyck, J., Ronold, H.J., Van Oosterwyck, H., Naert, I., Vander Sloten, J. & Ellingsen, J.E. (2001) The influence of static and dynamic loading on marginal bone reactions around osseointegrated implants: an animal experimental study. *Clinical Oral Implants Research* **12**: 207–218.

Duyck, J., Vandamme, K., Geris, L., Van Oosterwyck, H., De Cooman, M., Vander Sloten, J., Puers, R. & Naert, I. (2006) The influence of micro-motion on the tissue differentiation around immediately loaded cylindrical turned titanium implants. *Archives of Oral Biology* **51**: 1–9.

Duyck, J., Van Oosterwyck, H., Vander Sloten, J., De Cooman, M., Puers, R. & Naert, I. (2000) Magnitude and distribution of occlusal forces on oral implants supporting fixed prostheses: an in vivo study. *Clinical Oral Implants Research* **11**: 465–475.

Duyck, J., Vrielinck, L., Lambrichts, I., Abe, Y., Schepers, S., Politis, C. & Naert, I. (2005) Biologic response of immediately versus delayed loaded implants supporting ill-fitting prostheses: an animal study. *Clinical Implant Dentistry and Related Research* **7**: 150–158.

Ekfeldt, A., Christiansson, U., Eriksson, T., Lindén, U., Lundqvist, S., Rundcrantz, T., Johansson, L.Å., Nilner, K. & Billström, C. (2001) A retrospective analysis of factors associated with multiple implant failures in maxillae. *Clinical Oral Implants Research* **12**: 462–467.

Ekfeldt, A., Johansson, L.Å. & Isaksson, S. (1997) Implant-supported overdenture therapy: a retrospective study. *International Journal of Prosthodontics* **10**: 366–374.

Engel, E., Gomez-Roman, G. & Axmann-Krcmar, D. (2001) Effect of occlusal wear on bone loss and Periotest value of dental implants. *International Journal of Prosthodontics* **14**: 444–450.

Engquist, B., Bergendal, T., Kallus, T. & Lindén, U. (1988) A retrospective multicenter evaluation of osseointegrated implants supporting overdentures. *International Journal of Oral & Maxillofacial Implants* **3**: 129–134.

Esposito, M., Hirsch, J.M., Lekholm, U. & Thomsen, P. (1998a) Biological factors contributing to failures of osseointegrated oral implants. (I). Success criteria and epidemiology. *European Journal of Oral Sciences* **106**: 527–551.

Esposito, M., Hirsch, J.M., Lekholm, U. & Thomsen, P. (1998b) Biological factors contributing to failures of osseointegrated oral implants. (II). Etiopathogenesis. *European Journal of Oral Sciences* **106**: 721–764.

Esposito, M., Thomsen, P., Ericson, L.E., Sennerby, L. & Lekholm, U. (2000) Histopathologic observations on late oral implant failures. *Clinical Implant Dentistry & Related Research* **2**: 18–32.

Esposito, M., Thomsen, P., Molne, J., Gretzer, C., Ericson, L.E. & Lekholm, U. (1997) Immunohistochemistry of soft tissues surrounding late failures of Brånemark implants. *Clinical Oral Implants Research* **8**: 352–366.

Esposito, M., Worthington, H.V. & Coulthard, P. (2004) Interventions for replacing missing teeth: different times for loading dental implants. *Cochrane Database of Systematic Reviews* CD003878.

Ferrigno, N., Laureti, M., Fanali, S. & Grippaudo, G. (2002) A long-term follow-up study of non-submerged ITI implants in the treatment of totally edentulous jaws. Part I: ten-year life table analysis of a prospective multicenter study with 1286 implants. *Clinical Oral Implants Research* **13**: 260–273.

Foran, J.R., Mont, M.A., Rajadhyaksha, A.D., Jones, L.C., Etienne, G. & Hungerford, D.S. (2004) Total knee arthroplasty in obese patients: a comparison with a matched control group. *Journal of Arthroplasty* **19**: 817–824.

Fransson, C., Lekholm, U., Jemt, T. & Berglundh, T. (2005) Prevalence of subjects with progressive bone loss at implants. *Clinical Oral Implants Research* **16**: 440–446.

French, A.A., Bowles, C.Q., Parham, P.L., Eick, J.D., Killoy, W.J. & Cobb, C.M. (1989) Comparison of peri-implant stresses transmitted by four commercially available osseointegrated implants. *International Journal of Periodontics & Restorative Dentistry* **9**: 221–230.

Frost, H.M. (1992) Perspectives: bone's mechanical usage windows. *Bone and Mineral* **19**: 257–271.

Frost, H.M. (2004) A 2003 update of bone physiology and Wolff's Law for clinicians. *Angle Orthodontist* **74**: 3–15.

Froum, S.J., Simon, H., Cho, S.C., Elian, N., Rohrer, M.D. & Tarnow, D.P. (2005) Histologic evaluation of bone-implant contact of immediately loaded transitional implants after 6 to 27 months. *International Journal of Oral & Maxillofacial Implants* **20**: 54–60.

Fugazzotto, P.A. (2001) A comparison of the success of root resected molars and molar position implants in function in a private practice: results of up to 15-plus years. *Journal of Peridontology* **72**: 1113–1123.

Gotfredsen, K., Berglundh, T. & Lindhe, J. (2001a) Bone reactions adjacent to titanium implants subjected to static load of different duration. A study in the dog (III). *Clinical Oral Implants Research* **12**: 552–558.

Gotfredsen, K., Berglundh, T. & Lindhe, J. (2001b) Bone reactions adjacent to titanium implants subjected to static load. A study in the dog (I). *Clinical Oral Implants Research* **12**: 1–8.

Gotfredsen, K., Berglundh, T. & Lindhe, J. (2001c) Bone reactions adjacent to titanium implants with different surface characteristics subjected to static load. A study in the dog (II). *Clinical Oral Implants Research* **12**: 196–201.

Gotfredsen, K., Berglundh, T. & Lindhe, J. (2002) Bone reactions at implants subjected to experimental peri-implantitis and static load. A study in the dog. *Journal of Clinical Periodontology* **29**: 144–151.

Gotfredsen, K., Nimb, L., Hjørting-Hansen, E., Jensen, J.S. & Holmen, A. (1992) Histomorphometric and removal torque analysis for TiO_2-blasted titanium implants. An experimental study on dogs. *Clinical Oral Implants Research* **3**: 77–84.

Hämmerle, C.H., Brägger, U., Burgin, W. & Lang, N.P. (1996) The effect of subcrestal placement of the polished surface of ITI implants on marginal soft and hard tissues. *Clinical Oral Implants Research* **7**: 111–119.

Heitz-Mayfield, L.J., Schmid, B., Weigel, C., Gerber, S., Bosshardt, D.D., Jonsson, J., Lang, N.P. & Jonsson, J. (2004) Does excessive occlusal load affect osseointegration? An experimental study in the dog. *Clinical Oral Implants Research* **15**: 259–268.

Hoshaw, S.J., Brunski, J.B. & Cochran, G.V.B. (1994) Mechanical loading of Brånemark implants affects interfacial bone modeling and remodeling. *International Journal of Oral & Maxillofacial Implants* **9**: 345–360.

Hürzeler, M.B., Quinones, C.R., Kohal, R.J., Rohde, M., Strub, J.R., Teuscher, U. & Caffesse, R.G. (1998) Changes in peri-implant tissues subjected to orthodontic forces and ligature breakdown in monkeys. *Journal of Peridontology* **69**: 396–404.

Hutton, J.E., Heath, M.R., Chai, J.Y., Harnett, J., Jemt, T., Johns, R.B., McKenna, S., McNamara, D.C., van Steenberghe, D., Taylor, R., Watson, R.M. & Herrmann, I. (1995) Factors related to success and failure rates at 3-year follow-up in a multicenter study of overdentures supported by Brånemark implants. *International Journal of Oral & Maxillofacial Implants* **10**: 33–42.

Ikebe, K., Nokubi, T., Morii, K., Kashiwagi, J. & Furuya, M. (2005) Association of bite force with ageing and occlusal support in older adults. *Journal of Dentistry* **33**: 131–137.

Isidor, F. (1996) Loss of osseointegration caused by occlusal load of oral implants. A clinical and radiographic study in monkeys. *Clinical Oral Implants Research* **7**: 143–152.

Isidor, F. (1997a) Clinical probing and radiographic assessment in relation to the histologic bone level at oral implants in monkeys. *Clinical Oral Implants Research* **8**: 255–264.

Isidor, F. (1997b) Histological evaluation of peri-implant bone at implants subjected to occlusal overload or plaque accumulation. *Clinical Oral Implants Research* **8**: 1–9.

Isidor, F. (1998) Mobility assessment with the Periotest system in relation to histologic findings of oral implants. *International Journal of Oral & Maxillofacial Implants* **13**: 377–383.

Isidor, F. (1999) Occlusal loading in implant dentistry. In: Lang, N.P., Karring, T. & Lindhe, J., eds. *Proceedings of the Third European Workshop on Periodontology – Implant Dentistry*, 358–375. Berlin: Quientessence Books.

Isidor, F., Brøndum, K., Hansen, H.J., Jensen, J. & Sindet-Pedersen, S. (1999) Outcome of treatment with implant-retained dental prostheses in patients with Sjogren syndrome. *International Journal of Oral & Maxillofacial Implants* **14**: 736–743.

Jaffin, R.A. & Berman, C.L. (1991) The excessive loss of Brånemark fixtures in type IV bone: a 5-year analysis. *Journal of Peridontology* **62**: 2–4.

Jaworski, Z.F., Liskova-Kiar, M. & Uhthoff, H.K. (1980) Effect of long-term immobilisation on the pattern of bone loss in older dogs. *Journal of Bone and Joint Surgery (Br)* **62-B**: 104–110.

Jemt, T., Chai, J., Harnett, J., Heath, M.R., Hutton, J.E., Johns, R.B., McKenna, S., McNamara, D.C., van Steenberghe, D., Taylor, R., Watson, R.M. & Herrmann, I. (1996) A 5-year prospective multicenter follow-up report on overdentures supported by osseointegrated implants. *International Journal of Oral & Maxillofacial Implants* **11**: 291–298.

Jemt, T. & Lekholm, U. (1995) Implant treatment in edentulous maxillae: a 5-year follow-up report on patients with different degrees of jaw resorption. *International Journal of Oral & Maxillofacial Implants* **10**: 303–311.

Jemt, T., Lekholm, U. & Adell, R. (1989) Osseointegrated implants in the treatment of partially edentulous patients: a preliminary study on 876 consecutively placed fixtures. *International Journal of Oral & Maxillofacial Implants* **4**: 211–217.

Jemt, T., Lekholm, U. & Gröndahl, K. (1990) 3-year. followup study of early single implant restorations ad modum Brånemark. *International Journal of Periodontics & Restorative Dentistry* **10**: 340–349.

Johns, R.B., Jemt, T., Heath, M.R., Hutton, J.E., McKenna, S., McNamara, D.C., van Steenberghe, D., Taylor, R., Watson, R.M. & Herrmann, I. (1992) A multicenter study of overdentures supported by Brånemark implants. *International Journal of Oral & Maxillofacial Implants* **7**: 513–522.

Jones, H.H., Priest, J.D., Hayes, W.C., Tichenor, C.C. & Nagel, D.A. (1977) Humeral hypertrophy in response to exercise. *Journal of Bone and Joint Surgery (Am)* **59**: 204–208.

Jung, Y.C., Han, C.H. & Lee, K.W. (1996) A 1-year radiographic evaluation of marginal bone around dental implants. *International Journal of Oral & Maxillofacial Implants* **11**: 811–818.

Kannus, P., Sievänen, H. & Vuori, I. (1996) Physical loading, exercise, and bone. *Bone* **18**: 1S–3S.

Kitamura, E., Stegaroiu, R., Nomura, S. & Miyakawa, O. (2004) Biomechanical aspects of marginal bone resorption around osseointegrated implants: considerations based on a three-dimensional finite element analysis. *Clinical Oral Implants Research* **15**: 401–412.

Kitamura, E., Stegaroiu, R., Nomura, S. & Miyakawa, O. (2005) Influence of marginal bone resorption on stress around an implant – a three-dimensional finite element analysis. *Journal of Oral Rehabilitation* **32**: 279–286.

Lanyon, L. & Skerry, T. (2001) Postmenopausal osteoporosis as a failure of bone's adaptation to functional loading: a hypothesis. *Journal of Bone and Mineral Research* **16**: 1937–1947.

Lindner, D.L., Marretta, S.M., Pijanowski, G.J., Johnson, A.L. & Smith, C.W. (1995) Measurement of bite force in dogs: a pilot study. *Journal of Veterinary Dentistry* **12**: 49–52.

Lindquist, L.W., Rockler, B. & Carlsson, G.E. (1988) Bone resorption around fixtures in edentulous patients treated with mandibular fixed tissue-integrated prostheses. *Journal of Prosthetic Dentistry* **59**: 59–63.

Malmqvist, J.P. & Sennerby, L. (1990) Clinical report on the success of 47 consecutively placed Core–Vent implants followed from 3 months to 4 years. *International Journal of Oral & Maxillofacial Implants* **5**: 53–60.

Manz, M.C. (1997) Radiographic assessment of peri-implant vertical bone loss: DICRG interim report No. 9. *International Journal of Oral and Maxillofacial Surgery* **55**: 62–71.

Manz, M.C. (2000) Factors associated with radiographic vertical bone loss around implants placed in a clinical study. *Annals of Periodontology* **5**: 137–151.

Martin, B. (1993) Aging and strength of bone as a structural material. *Calcified Tissue International* **53** (Suppl. 1): S34–S39.

Melsen, B. & Lang, N.P. (2001) Biological reactions of alveolar bone to orthodontic loading of oral implants. *Clinical Oral Implants Research* **12**: 144–152.

Mericske-Stern, R., Grutter, L., Rosch, R. & Mericske, E. (2001) Clinical evaluation and prosthetic complications of single tooth replacements by non-submerged implants. *Clinical Oral Implants Research* **12**: 309–318.

Michaels, G.C., Carr, A.B. & Larsen, P.E. (1997) Effect of prosthetic superstructure accuracy on the osteointegrated implant bone interface. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics* **83**: 198–205.

Misch, C.E., Hoar, J., Beck, G., Hazen, R. & Misch, C.M. (1998) A bone quality-based implant system: a preliminary report of stage I & stage II. *Implant Dentistry* **7**: 35–42.

Misch, C.E., Suzuki, J.B., Misch-Dietsh, F.M. & Bidez, M.W. (2005) A positive correlation between occlusal trauma and peri-implant bone loss: literature support. *Implant Dentistry* **14**: 108–116.

Miyata, T., Kobayashi, Y., Araki, H., Motomura, Y. & Shin, K. (1998) The influence of controlled occlusal overload on peri-implant tissue: a histologic study in monkeys. *International Journal of Oral & Maxillofacial Implants* **13**: 677–683.

Miyata, T., Kobayashi, Y., Araki, H., Ohto, T. & Shin, K. (2000) The influence of controlled occlusal overload on peri-implant tissue. Part 3: a histologic study in monkeys. *International Journal of Oral & Maxillofacial Implants* **15**: 425–431.

Miyata, T., Kobayashi, Y., Shin, K., Motomura, Y. & Araki, H. (1997) An experimental study of occlusal trauma to osseointegrated implants: Part 2. *Journal of the Japanese Society of Periodontology* **39**: 234–241.

Moheng, P. & Feryn, J.M. (2005) Clinical and biologic factors related to oral implant failure: a 2-year follow-up study. *Implant Dentistry* **14**: 281–288.

Mombelli, A., van Oosten, M.A., Schurch, E. Jr. & Land, N.P. (1987) The microbiota associated with successful or failing osseointegrated titanium implants. *Oral Microbiology and Immunology* **2**: 145–151.

Naert, I., Quirynen, M., van Steenberghe, D. & Darius, P. (1992) A study of 589 consecutive implants supporting complete fixed prostheses Part II: prosthetic aspects. *Journal of Prosthetic Dentistry* **68**: 949–956.

Naert, I.E., Duyck, J.A., Hosny, M.M., Quirynen, M. & van Steenberghe, D. (2001a) Freestanding and tooth-implant connected prostheses in the treatment of partially edentulous patients Part II: an up to 15-years radiographic evaluation. *Clinical Oral Implants Research* **12**: 245–251.

Naert, I.E., Duyck, J.A., Hosny, M.M. & van Steenberghe, D. (2001b) Freestanding and tooth-implant connected prostheses in the treatment of partially edentulous patients. Part I: an up to 15-years clinical evaluation. *Clinical Oral Implants Research* **12**: 237–244.

Ogiso, M., Tabata, T., Kuo, P.T. & Borgese, D. (1994) A histologic comparison of the functional loading capacity of an occluded dense apatite implant and the natural dentition. *Journal of Prosthetic Dentistry* **71**: 581–588.

Oh, T.J., Yoon, J., Misch, C.E. & Wang, H.L. (2002) The causes of early implant bone loss: myth or science? *Journal of Peridontology* **73**: 322–333.

Papavasiliou, G., Kamposiora, P., Bayne, S.C. & Felton, D.A. (1996) Three-dimensional finite element analysis of stress-distribution around single

tooth implants as a function of bony support, prosthesis type, and loading during function. *Journal of Prosthetic Dentistry* **76**: 633–640.

Pattin, C.A., Caler, W.E. & Carter, D.R. (1996) Cyclic mechanical property degradation during fatigue loading of cortical bone. *Journal of Biomechanics* **29**: 69–79.

Pavlin, D. & Gluhak-Heinrich, J. (2001) Effect of mechanical loading on periodontal cells. *Critical Reviews in Oral Biology and Medicine* **12**: 414–424.

Piattelli, A., Corigliano, M., Scarano, A., Costigliola, G. & Paolantonio, M. (1998) Immediate loading of titanium plasma-sprayed implants: an histologic analysis in monkeys. *Journal of Periodontology* **69**: 321–327.

Piattelli, A., Corigliano, M., Scarano, A. & Quaranta, M. (1997) Bone reactions to early occlusal loading of two-stage titanium plasma-sprayed implants: a pilot study in monkeys. *International Journal of Periodontics & Restorative Dentistry* **17**: 162–169.

Piattelli, A., Ruggeri, A., Franchi, M., Romasco, N. & Trisi, P. (1993) An histologic and histomorphometric study of bone reactions to unloaded and loaded non-submerged single implants in monkeys: a pilot study. *Journal of Oral Implantology* **19**: 314–320.

Quinlan, P., Nummikoski, P., Schenk, R., Cagna, D., Mellonig, J., Higginbottom, F., Lang, K., Buser, D. & Cochran, D. (2005) Immediate and early loading of SLA ITI single-tooth implants: an in vivo study. *International Journal of Oral & Maxillofacial Implants* **20**: 360–370.

Quirynen, M., De Soete, M. & van Steenberghe, D. (2002) Infectious risks for oral implants: a review of the literature. *Clinical Oral Implants Research* **13**: 1–19.

Quirynen, M., Naert, I. & van Steenberghe, D. (1992a) Fixture design and overload influence marginal bone loss and fixture success in the Brånemark system. *Clinical Oral Implants Research* **3**: 104–111.

Quirynen, M., Naert, I., van Steenberghe, D., Dekeyser, C. & Callens, A. (1992b) Periodontal aspects of osseointegrated fixtures supporting a partial bridge. An up to 6-years retrospective study. *Journal of Clinical Periodontology* **19**: 118–126.

Quirynen, M., Naert, I., van Steenberghe, D., Teerlinck, J., Dekeyser, C. & Theuniers, G. (1991) Periodontal aspects of osseointegrated fixtures supporting an overdenture. A 4-year retrospective study. *Journal of Clinical Periodontology* **18**: 719–728.

Raadsheer, M.C., Van Eijden, T.M., Van Ginkel, F.C. & Prahl-Andersen, B. (2004) Human jaw muscle strength and size in relation to limb muscle strength and size. *European Journal of Oral Sciences* **112**: 398–405.

Raghoebar, G.M., Timmenga, N.M., Reintsema, H., Stegenga, B. & Vissink, A. (2001) Maxillary bone grafting for insertion of endosseous implants: results after 12–124 months. *Clinical Oral Implants Research* **12**: 279–286.

Ricci, G., Aimetti, M., Stablum, W. & Guasti, A. (2004) Crestal bone resorption 5 years after implant loading: clinical and radiologic results with a 2-stage implant system. *International Journal of Oral & Maxillofacial Implants* **19**: 597–602.

Rieger, M.R., Fareed, K., Adams, W.K. & Tanquist, R.A. (1989) Bone stress distribution for three endosseous implants. *Journal of Prosthetic Dentistry* **61**: 223–228.

Rieger, M.R., Mayberry, M. & Brose, M.O. (1990) Finite element analysis of six endosseous implants. *Journal of Prosthetic Dentistry* **63**: 671–676.

Roberts, W.E., Smith, R.K., Zilberman, Y., Mozsary, P.G. & Smith, R.S. (1984) Osseous adaptation to continuous loading of rigid endosseous implants. *American Journal of Orthodontics* **86**: 95–111.

Roberts, W.E., Turley, P.K., Brezniak, N. & Fielder, P.J. (1987) Implants: bone physiology and metabolism. *Journal of the California Dental Association* **15**: 54–61.

Rosenberg, E.S., Torosian, J.P. & Slots, J. (1991) Microbial differences in 2 clinically distinct types of failures of osseointegrated implants. *Clinical Oral Implants Research* **2**: 135–144.

Saadoun, A.P. & LeGall, M.L. (1992) Clinical results and guidelines on steri-oss endosseous implants. *International Journal of Periodontics & Restorative Dentistry* **12**: 486–495.

Sanz, M., Alandez, J., Lazaro, P., Calvo, J.L., Quirynen, M. & van Steenberghe, D. (1991) Histopathologic characteristics of peri-implant soft tissues in Brånemark implants with 2 distinct clinical and radiological patterns. *Clinical Oral Implants Research* **2**: 128–134.

Scurria, M.S., Morgan, Z.V., Guckes, A.D., Li, S. & Koch, G. (1998) Prognostic variables associated with implant failure: a retrospective effectiveness study. *International Journal of Oral & Maxillofacial Implants* **13**: 400–406.

Shackleton, J.L., Carr, L., Slabbert, J.C. & Becker, P.J. (1994) Survival of fixed implant-supported prostheses related to cantilever lengths. *Journal of Prosthetic Dentistry* **71**: 23–26.

Søballe, K., Olsen, N.J., Ejsted, R., Christensen, F. & Luxhøj, T. (1987) Revision of the uncemented hip prosthesis. *Acta Orthopaedica Scandinavica* **58**: 630–633.

Ström, D., Holm, S. & Möller, A. (1994) Fatigue development during electrical stimulation in the masseter muscle of rhesus monkeys (*Macaca mulatta*). *Archives of Oral Biology* **39**: 417–423.

ten Bruggenkate, C.M., Asikainen, P., Foitzik, C., Krekeler, G. & Sutter, F. (1998) Short (6-mm) nonsubmerged dental implants: results of a multicenter clinical trial of 1 to 7 years. *International Journal of Oral & Maxillofacial Implants* **13**: 791–798.

Tonetti, M.S. & Schmid, J. (1994) Pathogenesis of implant failures. *Periodontology 2000* **4**: 127–138.

Verma, R.B. & Sherman, O. (2001) Athletic stress fractures: part I. History, epidemiology, physiology, risk factors, radiography, diagnosis, and treatment. *American Journal of Orthopedics* **30**: 798–806.

Watzak, G., Zechner, W., Ulm, C., Tangl, S., Tepper, G. & Watzek, G. (2005) Histologic and histomorphometric analysis of three types of dental implants following 18 months of occlusal loading: a preliminary study in baboons. *Clinical Oral Implants Research* **16**: 408–416.

Wehrbein, H. & Diedrich, P. (1993) Endosseous titanium implants during and after orthodontic load – an experimental study in the dog. *Clinical Oral Implants Research* **4**: 76–82.

Weng, D., Jacobson, Z., Tarnow, D., Hürzeler, M.B., Faehn, O., Sanavi, F., Barkvoll, P. & Stach, R.M. (2003) A prospective multicenter clinical trial of 3i machined-surface implants: results after 6 years of follow-up. *International Journal of Oral & Maxillofacial Implants* **18**: 417–423.

Wennerberg, A., Carlsson, G.E. & Jemt, T. (2001) Influence of occlusal factors on treatment outcome: a study of 109 consecutive patients with mandibular implant-supported fixed prostheses opposing maxillary complete dentures. *International Journal of Prosthodontics* **14**: 550–555.

Wiskott, H.W. & Belser, U.C. (1999) Lack of integration of smooth titanium surfaces: a working hypothesis based on strains generated in the surrounding bone. *Clinical Oral Implants Research* **10**: 429–444.

Wyatt, C.C. & Zarb, G.A. (2002) Bone level changes proximal to oral implants supporting fixed partial prostheses. *Clinical Oral Implants Research* **13**: 162–168.

Zechner, W., Trinkl, N., Watzak, G., Busenlechner, D., Tepper, G., Haas, R. & Watzek, G. (2004) Radiologic follow-up of peri-implant bone loss around machine-surfaced and rough-surfaced interforaminal implants in the mandible functionally loaded for 3 to 7 years. *International Journal of Oral & Maxillofacial Implants* **19**: 216–221.