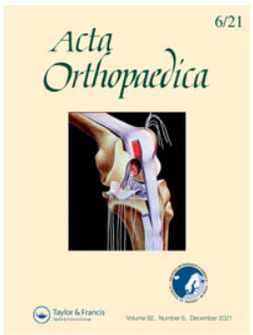

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OSSEOINTEGRATED TITANIUM IMPLANTS

Requirements for Ensuring a Long-Lasting, Direct Bone-to-Implant Anchorage in Man

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A total of 2895 threaded, cylindrical titanium implants have been inserted into the mandible or the maxilla and 124 similar implants have been installed in the tibial, temporal or iliac bones in man for various bone restorative procedures. The titanium screws were implanted without the use of cement, using a meticulous technique aiming at osseointegration – a direct contact between living bone and implant. Thirty-eight stable and integrated screws were removed for various reasons from 18 patients. The interface zone between bone and implant was investigated using X-rays, SEM, TEM and histology. The SEM study showed a very close spatial relationship between titanium and bone. The pattern of the anchorage of collagen filaments to titanium appeared to be similar to that of Sharpey's fibres to bone. No wear products were seen in the bone or soft tissues in spite of implant loading times up to 90 months. The soft tissues were also closely adhered to the titanium implant, thereby forming a biological seal, preventing microorganism infiltration along the implant. The implants in many cases had been allowed to permanently penetrate the gingiva and skin. This caused no adverse tissue effects. An intact bone-implant interface was analyzed by TEM, revealing a direct bone-to-implant interface contact also at the electron microscopic level, thereby suggesting the possibility of a direct chemical bonding between bone and titanium.

It is concluded that the technique of osseointegration is a reliable type of cement-free bone anchorage for permanent prosthetic tissue substitutes. At present, this technique is being tried in clinical joint reconstruction. In order to achieve and to maintain such a direct contact between living bone and implant, threaded, unalloyed titanium screws of defined finish and geometry were inserted using a delicate surgical technique and were allowed to heal *in situ*, without loading, for a period of at least 3–4 months.

Key words: bone-implant interface; osseointegration; electron-microscopic studies; clinical material; titanium; tibia; os ilium; os temporale; maxilla; mandibula

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Clinical background

Today's methods for permanent bone implantation frequently involve the use of bone cement. The problems associated with bone cement are several and have recently been reviewed by Linder (1980). There are, today, an increasing number of investigations being carried out with cement-free implants. Such implants are commonly used in the upper extremely (Salzer et al. 1979), but also, for example, in hip or knee joint prostheses (Judet et al. 1978, Ring 1978, Ritter et al. 1979). Both the cemented (Linder 1976, Anderson & Green 1980) and many of the cement-free implants, as for example the Judet prosthesis (Plenk et al. 1980), or the Madreporique hip prosthesis (Lord et al. 1979) are

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completely surrounded by a thin layer of connective tissue proper. Living bone tissue is as a rule not present at the cemented implant interface. An interface layer consisting of soft tissues is regarded by many authorities (Cook 1967, Southam et al. 1970, Linder & Lundskog 1975) as less desirable, resulting eventually in implant loss in many cases. In this context the difference between cemented and many cement-free implants may be considered as small.

The present paper is concerned with the possibility of an entirely different type of cement-free implantation – osseointegration. The idea is to endeavour to achieve a direct contact between *living* bone and implant, hoping in this way to improve the long-term function of the prosthetic device. This report is an attempt at a review of the osseointegration method. The total number of implants inserted at the Gothenburg Clinic since 1965 using this method amounts to about 3000, the majority of which were installed into mandibular or maxillar implantation sites, but there were several inserted into the tibial, temporal or iliac bones (Brånemark et al. 1970, Brånemark et al. 1977, Adell et al. 1981, Lindström et al. 1981, Tjellström et al. 1981a,b). The future of osseointegrated implants lies in the possibility of applying the method in joint reconstruction. A clinical investigation aiming at replacement of metacarpophalangeal joints, using the method described in the present paper, has already been started. Time will show if the clinical advantages of osseointegration for permanent bone anchorage can lead to an improved situation also in the field of joint replacements, in the same way as it has in the treatment of edentulous jaws.

Theoretical background

The interface zone between bone and implant has been the concern of a vast number of recent publications. *Osseointegration* means a direct – on the light microscopic level – contact between living bone and implant. Many different opinions on the possibility of achieving and maintaining osseointegration have been published. Collins (1954) stated that "Although histologically inert, an implanted object never becomes incorporated into the bone". Later Southam et al. (1970) concluded "When any metallic appliance is implanted in bone, a layer of fibrous tissue will always develop around the applicance which subsequently will never be as secure in the bone as it was at the time it was implanted".

Some authors believe that a direct contact between implant and bone is possible only if the implant is a ceramic, not if it is a metal (Jacobs 1976, 1977, Muster & Champy 1978). Jacobs (1977) reported that a direct bone-to-implant contact is achievable provided no metal is in direct contact with the bone. Osseointegration is, according to Jacobs, possible only with ceramic implants or with coated metal implants.

A majority of reports, particularly those published in the last 5 years, are of the opinion that it is also possible to obtain osseointegration with various types of metals such as e.g. *stainless steel* (Linder & Lundskog 1975), *vitallium* (Klawitter & Weinstein 1974, Linder & Lundskog 1975, Weiss 1977), *tantalum* (Grundschober et al. 1980) and *titanium* (Brånemark et al. 1969, 1977, Linder & Lundskog 1975, Karagianes et al. 1976, Schroeder et al. 1976, Juillerat & Küffer 1977). It should in this context be remembered that the surface of titanium becomes instantaneously coated with an oxide layer except under high vacuum and some equivalent conditions. Accordingly no metal or metal compounds are directly exposed to the surrounding tissues in a titanium implant. The oxide layer is built up of a combination of TiO, TiO_2, Ti_2O_3 and Ti_3O_4, the stable oxide coating of about 100 Å thickness preventing a direct contact between bone and metal. This means in fact that titanium as an implant material may be regarded as a ceramic, not as a metal. The importance of this fact for the establishment of lasting osseointegration should not be disregarded although more knowledge has to be gained to get a more definite understanding of the bonding between titanium and bone.

Cook (1967) argued that a direct bone-to-implant contact is a *sine qua non* for long-term implant function. This statement has been questioned, particularly where jaw bone implants used as anchorage for dental bridges are concerned. The goal for the surgeon should instead be to create a connective tissue sheath – a "periodontal

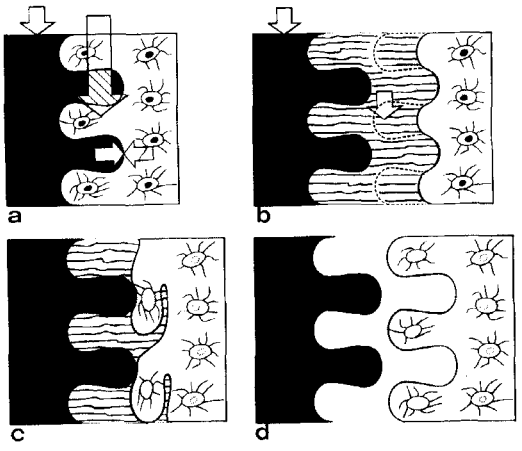


Figure 1. Schematical representation of the different interface types.
a. Living bone in immediate contact with the implant; osseointegration. Theoretically this type of implant anchorage is superior to the others and the only one in which the long-term fate in the individual case is predictable.
b. Living bone, interposed soft tissue layer and implant. This type of implant anchorage with time – sometimes several years – will lead to implant loss in spite of the bone being vital.
c. Dead bone partly in direct contact with the implant. This anchorage, although not able to withstand the same heavy loading as osseointegration, may function for years. The main disadvantage apart from its limited capacity to take load is the risk for ultimate bone resorption leading immediately to implant loss.
d. Interface zone of bone cement always leads to bone death in the cement border zone. The dead bone is usually replaced with connective tissue resulting in similar conditions as those described under b.

membrane" or a "pseudo-parodontium" around the implant (Linkow & Chercheve 1970, Linkow et al. 1973, Babbush 1973, Babbush & Staikoff 1974). Brunski et al. (1979) in a recent report reviewed the various opinions on the bone-implant interface and the authors concluded that the question of whether osseointegration is a necessity for long-term implant function cannot as yet be answered with certainty. Actually, not even avascular, dead bone at the interface zone necessarily leads to immediate implant loss. Dead bone may function, although not optimally, as an implant stabilizer in the same way as a dead bone graft may function as a framework even over periods of several years. The long-term fate of such an implant is, however, dubious and maximal load capacity is limited (Figure 1). Furthermore, possible late revascularization inevitably would lead to bone resorption and subsequent implant failure (Albrektsson 1979).

Aims of the present investigation

The purpose of this paper is an attempt at

1. An ultrastructural analysis of long-term functioning osseointegrated implants in man.
2. Requirements – based on experiences gained from 400 patients treated with osseointegrated implants inserted into various bones and followed for up to 15 years – for establishing long-lasting implant function in human bone tissue.

MATERIALS AND METHODS

The material consists of implants removed from three different bones (Figure 2).

Group I. In 400 patients reported elsewhere (Adell et al. 1980) titanium implants – fixtures – were inserted into edentulous jaws. The fixtures are carefully manufactured titanium[24] screws, which using a technique ensuring minimal tissue violence (Lindström et al. 1981) have been inserted into the jaw bone and later used as anchorage for dental bridges (Brånemark et al.

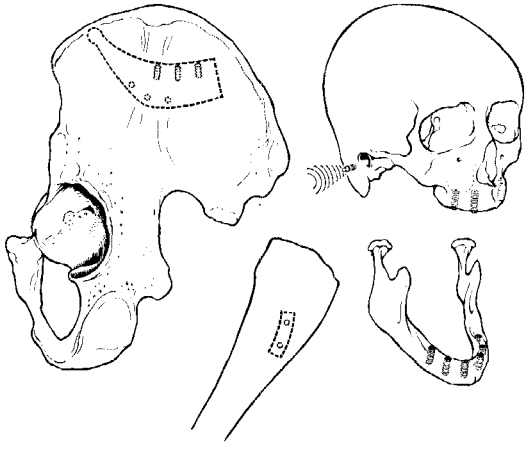


Figure 2. The material of the present paper consists of implants inserted into the jaw bones, the temporal bone and the iliac and tibial bones of man.

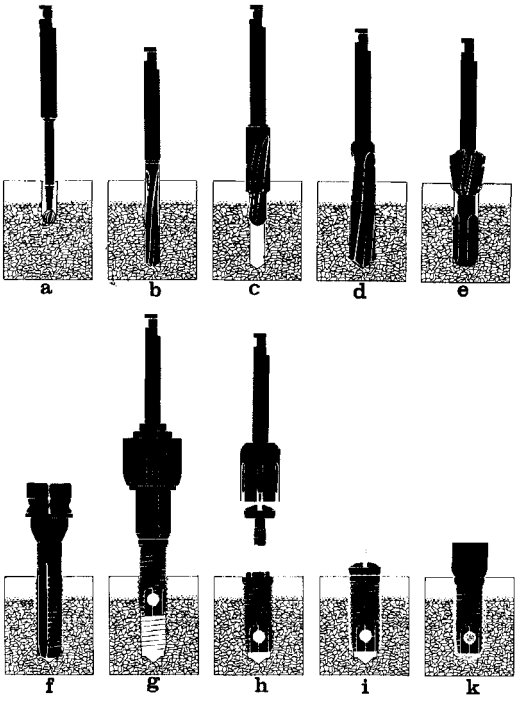


Figure 3. The surgical technique to ensure osseointegration includes using series of drills (a–d), a counter-sink (e) and a tap (f) before the implant is carefully inserted (g). Steps a–f are performed under generous saline irrigation. A cover screw is installed into the central hole of the fixture (h). After a defined healing period of several months (i) the cover screw is removed and replaced with an abutment (k) which if necessary can penetrate the skin for e.g. prosthesis attachment.

1977). Altogether 10 implants were removed from 3 patients for reasons mentioned below. The material of group I consists of these 10 implants.

Group II. In another experimental investigation (Tjellström et al. 1978a,b) 2 titanium screws were inserted into the upper tibial metaphysis of each one of 11 patients in order to stabilize a titanium mould for a preformed ossicular bone graft. At a predetermined time, 6 months after insertion, these 22 screws were removed using the technique described below and constituted the group II material together with 2 similar screws removed from the iliac bone (Brånemark et al. 1975).

Table 1. Survey of removed, stable titanium implants

	Sex and age of patient	Number or removed screws	Months in bone site	Implantation site	Reasons for removal
Group I:					
K J	f 60	7	30	Maxilla	Psychiatric
E Ö	m 68	1	42	Mandibula	Impl. fracture
B S	m 65	2	90	Maxilla	" "
Group II:					
A A	f 26	2	5	proximal tibia	Surgical*
S K	f 36	2	5	"	"
E L	f 40	2	5	"	"
Å N	m 32	2	5	"	"
H F	m 24	2	5	"	"
S L	f 43	2	6	"	"
K O	m 41	2	6	"	"
J O	m 31	2	6	"	"
K R	m 46	2	6	"	"
H K	m 24	2	6	"	"
G L	f 43	2	6	"	"
A H	f 41	2	6	"	"
R B	f 37	2	12	iliac crest	"
Group III:					
A H	m 41	1	12	temporal bone	Otological
I J	f 61	1	18	"	"

* These screws were functioning as anchorage for a preformed bone graft and were removed after a pre-determined interval.

Group III. Titanium screws were inserted into the temporal bone of 15 patients to function as bone anchorage for an external hearing aid. Two of these screws from 2 different patients had to be removed because of problems not associated with the bone integration.

The principal screw designs and mode of insertion are schematically explained in Figure 3 and did not significantly differ between groups I, II and III.

All 38 implants (Table 1) were at the time of removal roentgenologically bone integrated (Figure 4) and were quite stable as judged by the surgeon. The implants were cut out with a trephine under generous saline irrigation, leaving a continuous, intact bone cover around them (Figure 5). This bone cover was impossible to remove from the fixtures without the use of sharp instruments.

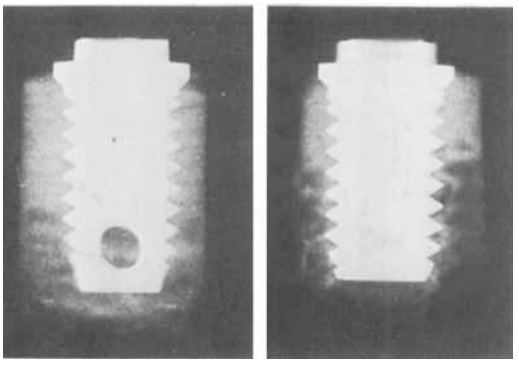


Figure 4. X-rays of removed tibial fixtures. An X-ray alone does not give conclusive evidence of osseointegration due to the poor resolution level.

Analysis of the clinical material

The extracted implants were immediately after removal fixed in cacodylate-buffered 3 per cent glutaraldehyde overnight. After removal of loose bone and blood clots by a jet stream of cacodylate buffer the fixtures with surrounding tissues were dehydrated by a graded series of ethanol, dried in a critical point equipment, coated with gold by sputtering and examined in a scanning electron microscope (Jeol JSM-35, Jeol 100-CX).

Parts of the specimens were, after dehydration, embedded in Epoxy (Spurr's medium, Spurr 1962) which was heat polymerized. These specimens were examined in a stereomicroscope and suitable parts prepared for thin sectioning in a LKB ultramicrotome. Sections from the border area between bone and titanium were cut with a diamond knife and double contrasted with uranyl and lead and then prepared for subsequent examination by light microscopy.

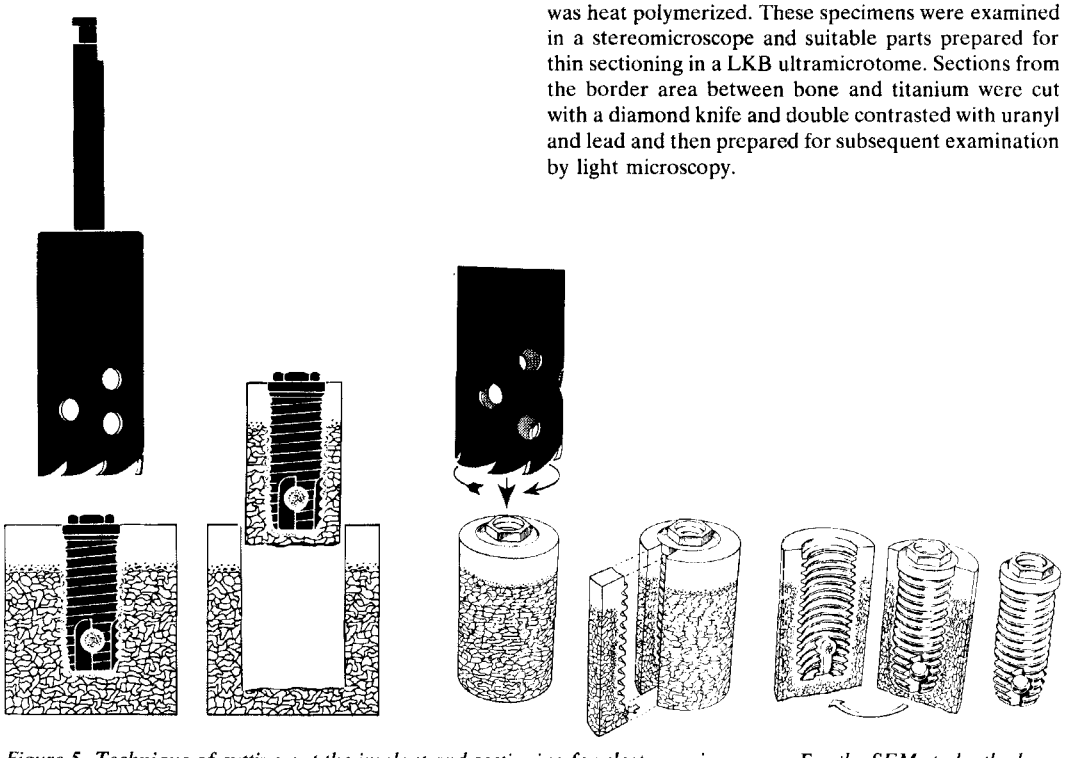


Figure 5. Technique of cutting out the implant and sectioning for electron microscopy. For the SEM study, the bone surrounding the titanium implant was divided in the manner shown and split into one bony and one bone-titanium part. The interface zone was then studied by SEM subject to conventional methodological treatment. In the TEM study a diamond knife was used to cut obliquely through the bone and implant without previous splitting. In this way it was possible to study the intact interface zone in the electron microscope.

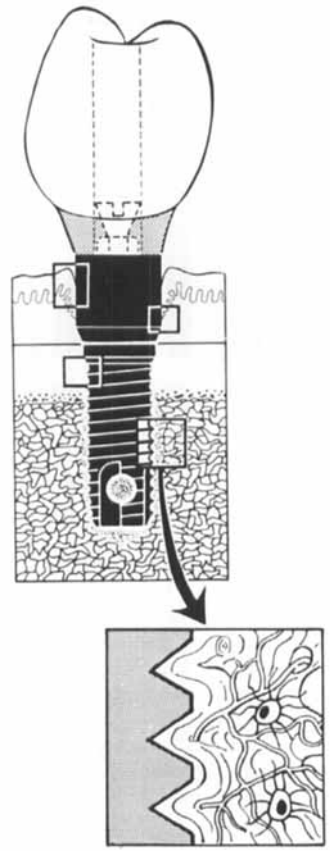


Figure 6. A titanium implant of group I in situ. Samples were secured from the interface zone between implant and marrow, and cortical bone and soft tissues, respectively. In addition, where groups I and III implants were concerned, gingiva or skin penetration sites were examined.

The possible occurrence of titanium in the bone parts of the specimens was considered. Analysis was performed by using EDAX energy-dispersive X-ray equipment in a Jeol JSM-35 scanning electron microscope.

Samples of skin or gingiva from the implant penetration site were examined; also examined were samples from the soft and hard tissues adjacent to the implant and from the bone marrow-implant interface (Figure 6).

RESULTS

Those parts of the implants of group I that penetrated the gingiva were covered with epithelium in all cases. This epithelial layer consisted of gingiva covering underlying connective tissue which was strongly adherent to all examined implants. The same was true for the bone which consisted of variable proportions of compact and cancellous type, the latter containing marrow cells. Groups II and III implants were also covered with a strongly adherent connective tissue layer.

When examining the specimens in the scanning electron microscope, imprints of the gingival

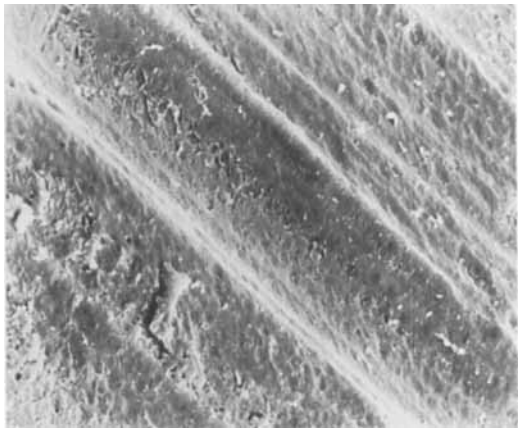


Figure 7. The border zone between the gingival layer and the titanium of a group I implant, at the place where the abutment penetrates the mucous membrane. Densely packed reticular cells are seen. For detail see Figure 8. 1000×

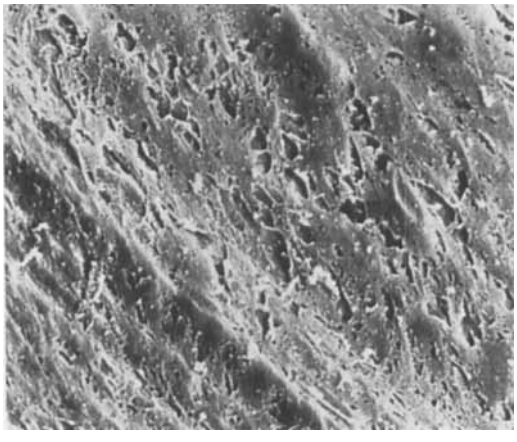


Figure 8. Detail of Figure 7. Gingival cells in a star-like pattern, densely packed on the titanium surface. There is a very sparse intercellular space. The cells adhere directly to the titanium surface, separated from it by only a thin layer of ground substance. 2000×.

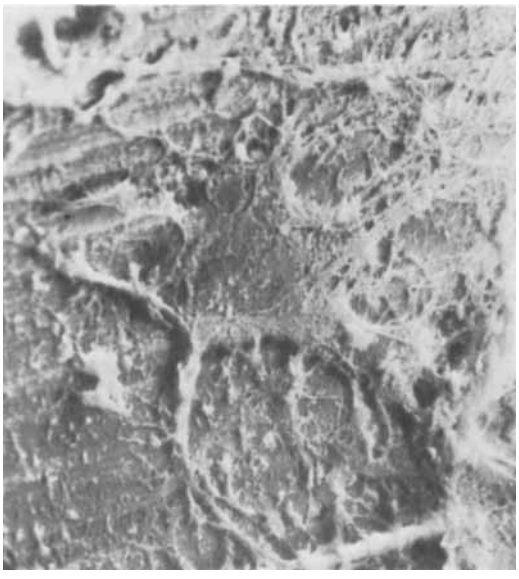
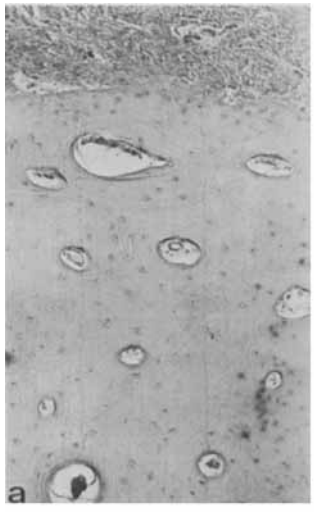


Figure 9. A multipolar connective tissue cell partly covered by collagenous filaments and ground substance. The cellular processes seem to adhere directly to the titanium surface. 20,000×.

epithelial cells could still be seen on the upper part of the group I implants (Figures 7, 8). The epithelial cells were of normal shape and size resembling the gingival cells found in the vicinity of the implant. In groups I, II and III the polygonal epithelial cells were of roughly uniform size and shape. They were separated by a limited intercellular space, lacking fibres, but containing small amounts of an amorphous coating. The actual border area between the cell and the implant consisted of ground substance, i.e. amorphous material, through which the contours of the titanium implant could be seen (Figure 9). The amorphous material was shown to attract lanthanum and Alcian blue, further evidence indicating that the border layer consisted of glycoproteins. There were no white blood cells nor any other types of inflammatory cells infiltrating the border area of the soft tissues.

The patterns of ridges, excavations and other surface irregularities of the implants found when examining the removed screws were in all cases similar to those found in examinations of other screws performed before insertion. No signs of corrosion were noticed on removed implants. No wear products from the implants could be found in the soft tissues.

The bone covering the implants was shown to be of a dense lamellar type, forming well-organized concentric lamellae (Figure 10). The collagenous fibres of the bone were tightly adhered to the titanium surface (Figure 11). The thick collagenous fibrils became split into thin filaments when approaching the actual surface of the implant (Figures 12, 13). These fibrils were



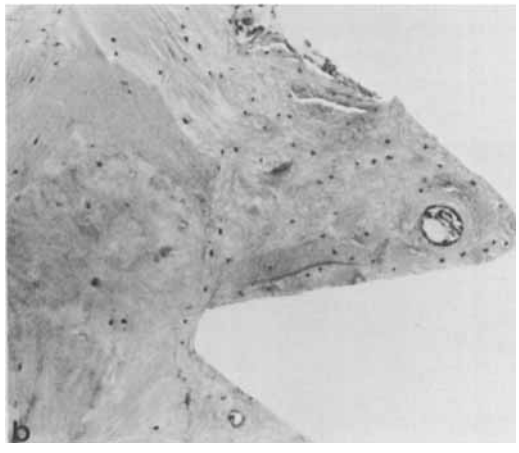


Figure 10. (a) Histological section of part of the bone covering a group II implant. Note well organized concentric lamellae.
(b) Histological section showing the bone tissue well remodelled to the screw thread pattern. The lacunae all contain osteocyte nuclei which, however, alone would not be sufficient evidence of living bone.

embedded in the amorphous or granular material formed by the proteoglycans, thus establishing a layer directly covering the titanium oxide. Cell processes from both connective tissue cells and osteogenic cells could further be seen on the titanium surface only separated from it by the ground substance layer (Figure 14). The thickness of the latter was of the order of up to a few hundred Å, i.e. at about the resolution limit of the microscopes used.

Examining the part of the implant that had been most deeply located it was quite apparent that the bone in this region was more cancellous and contained blood cells and bone marrow (Figure 15). Also in these areas, cells and cellular processes could be seen on the actual surface of the titanium (Figure 16), only separated from it by an amorphous coating of proteoglycans. Collagenous filaments adhering to the titanium surface could be seen among the cells. There were no signs of toxic reactions in either the cells or in the surrounding ground substance.

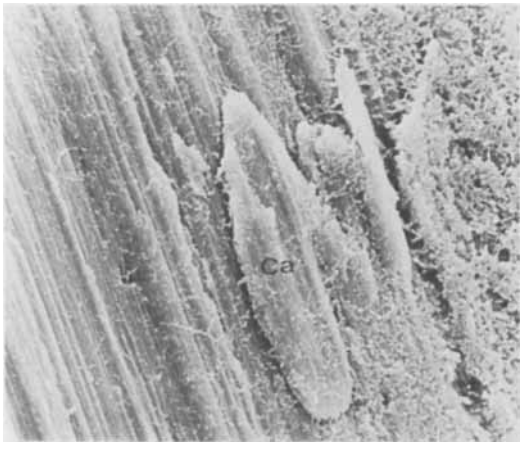


Figure 11. A group II implant showing bone tissue adjacent to the titanium surface. The ground substance seems to be tightly adhered to the titanium. 2000×. Ca = *Calcified tissue.*

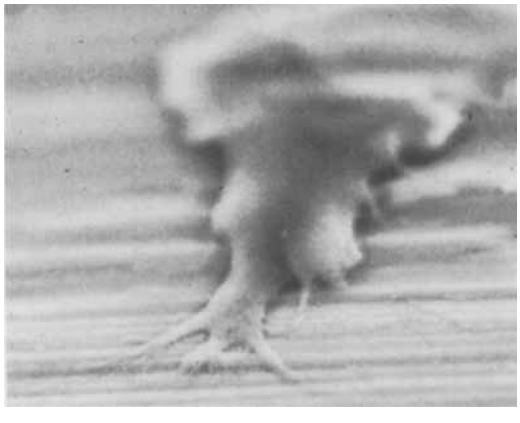


Figure 12. Fibroblast processes immediately attached to the surface of a temporal (group III) titanium screw. 10,000×. For detail see Figure 13.

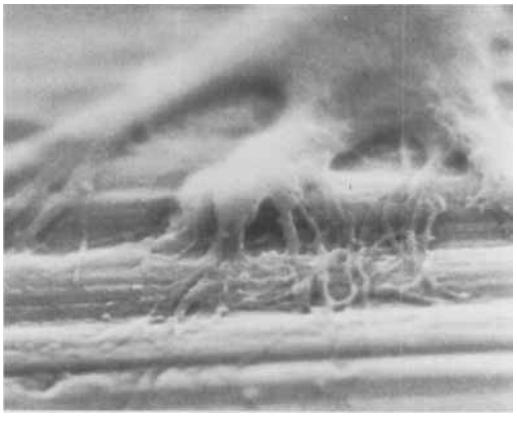


Figure 13. Detail of Figure 12. Note the exact congruence between the cellular processes and the titanium surface irregularities. 20,000×.

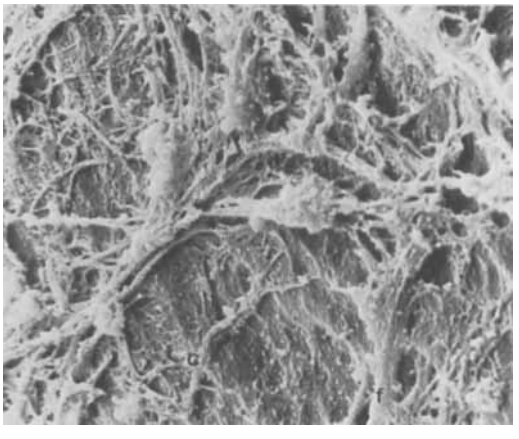


Figure 14. The surface of the titanium screw – at the border zone between cortical bone and marrow – can be seen partly covered by fibroblast processes (f), collagenous threads (c) in a 3-D network and ground substance, the latter partly of membraneous and partly of granular type. 3,600×.

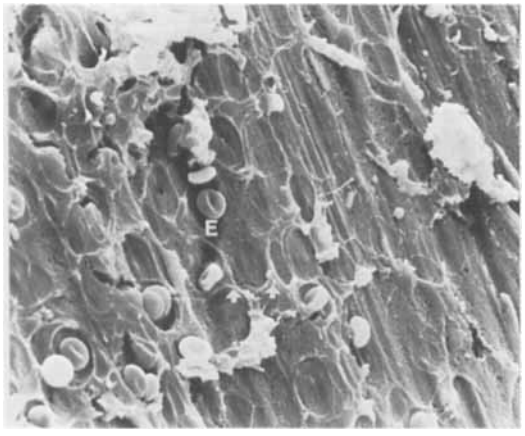


Figure 15. A titanium screw covered by the intercellular substance of bone marrow cells. The titanium structure can be clearly seen, indicating that the space between the cellular layer and the oxide is very thin. Arrows indicate ground substance pattern. E = Erythrocyte. 1000×.

When examining the bone split off from the fixtures, no traces of titanium could be observed within the detection limit of the equipment used.

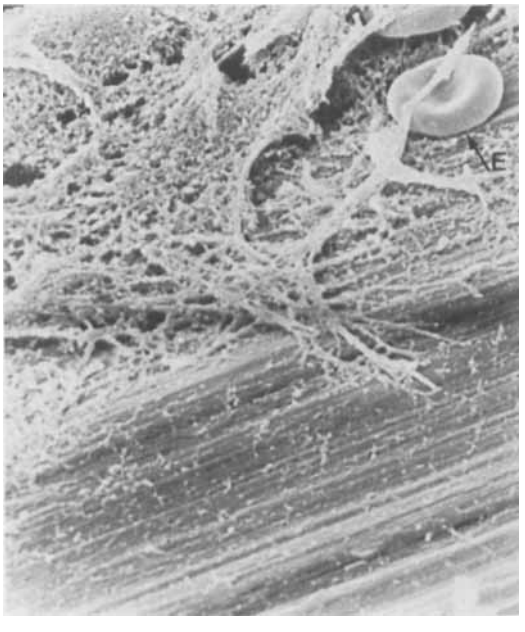


Figure 16. A fibroblast with multiple filaments, one of them covering an erythrocyte (= E). Judging by the filament depression on the red cell body, the erythrocyte must have been trapped in this position before removal of the titanium fixture. 3000×.

Titanium wear products could thus not be verified in spite of an implantation time for different screws varying between 6 and 90 months.

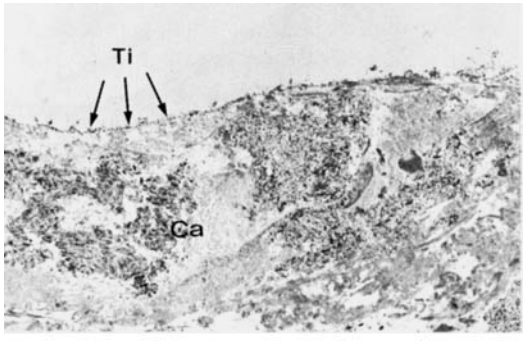
In a group I implant that had been removed after 90 months *in situ*, during which time it was clinically and roentgenologically stable, it was possible to cut through the implant and surrounding bone without disturbing the bone-implant connection. TEM-pictures of the intact bone-implant interface were obtained (Figure 17). These pictures revealed a direct contact between the bone and the implant also on the electron-microscopic level.

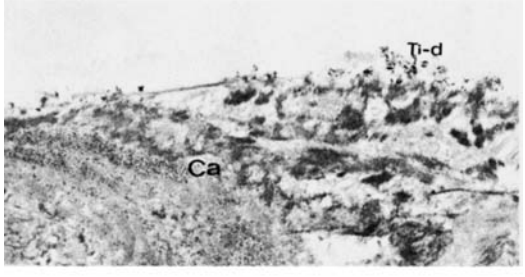
DISCUSSION

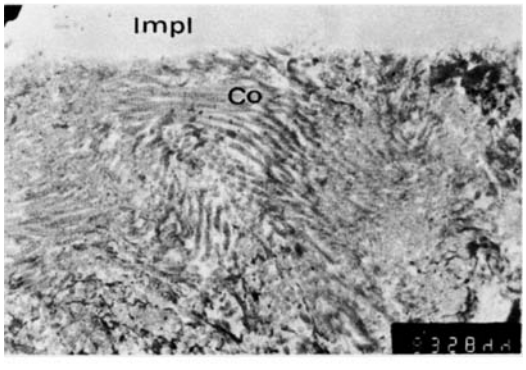
Implications of the findings in the present study

The scanning electron microscopic studies demonstrate a very close topographical relation between the implant and the bone. Collagenous filaments approaching from the bone could be seen adhering to the actual surface of the implant. The mechanism of the anchorage of the collagen filaments appeared to be of the same type as for the attachment of Sharpey's fibres to bone, i.e. gluing by the amorphous coating formed by the ground substance. This close relationship between the implant and the bone tissue forms the morphological substrate for the good mechanical stability achieved in the clinical series. The oxide layer formed on the surface of the titanium implants apparently reduces the risks of corrosion, reflected by the similarities in the surfaces of the implanted screws and those kept for reference without being implanted. This conclusion is further supported by the lack of toxic reactions in the studied cells bordering the implant. Furthermore, there were no signs of microorganism infiltration, nor of inflammatory cells in the soft tissues, also confirming the ability of these cells to adhere closely to the implant thereby forming a biological seal.

The jaw implants had to penetrate the gingiva to function as support for a dental bridge and the temporal implants pierced the skin to allow attachment of an external hearing aid. The skin penetration caused no adverse soft tissue effects, the reason for this being the inertness of the







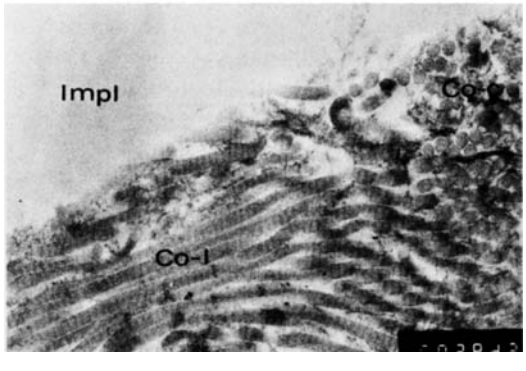


Figure 17. TEM picture of a group I implant removed after 30 months in situ. The sectioning has been performed without previous separation of the bone from the implant, i.e. the intact border zone can be directly studied.
a. Interface-zone between a titanium jaw implant (Ti) and calcified tissue (Ca). Observe the close relation between the hard tissue and the implant. 2,600×.
b. Border zone between implant and calcified tissue (Ca). Titanium deposits (Ti-d) – verified by EDAX – in surface irregularities of the implant are seen as black spots immediately adjacent to the hard tissues. 3,600×.
c. Collagen filaments (Co) from the region between bone and marrow. The technique used makes sectioning possible within a microns distance of the actual surface of the titanium. Impl = Former situation of Implant. 8,300×.
d. Detail of c. Collagen filaments are seen passing along the implant surface. This picture indicates the possibilities of a direct chemical bonding between tissue and titanium. Co-c = Collagen filaments cross-sectioned, Co-l = Collagen filaments longitudinally sectioned, Impl = former situation of Implant. 20,000×.

titanium fixtures and the prevention of free skin movements around the implant (Brånemark & Albrektsson 1981).

In the present material there were no signs of a connective tissue layer between the bone and the implant. The structural organisation implied that the implants did not induce any inflammatory reaction with formation of interposed scar tissue but allowed integration of the titanium screw with the adhering tissues. Grundshober et al. (1980) examined 4 tantalum and 2 titanium threaded, endosseous dental implants which had been inserted in man for 8–12 years. The authors found a direct bone-to-implant contact without encapsulating soft tissues.

TEM analysis of the intact bone-implant interface has not, according to our knowledge, previously been published. The finding of a direct bone-to-implant contact not only at the light microscopic but also at the electron-microscopic level provides interesting information and, in fact, further stresses the possibility of a direct chemical bonding between bone and titanium oxide, as suggested already by Emnéus (1967, personal communication). Theoretically, such a direct bonding would be possible in a bone-ceramic interface which bone-titanium consti-

tutes but be unlikely when metals such as stainless steel or alloys such as vitallium are implanted.

General comments on osseointegration of implants

Referring to the statements above, the discussion on osseointegration will be centred around titanium implants. Also other ceramic implants may be capable of a direct bone contact similar to that of titanium. The long-term results of other ceramic implants are, however, in spite of recent reports (Ferraro 1979, Salzer et al. 1979) still uncertain and the possible clinical use of them is as yet an open question (Willert 1976 cited by Swanson & Freeman 1977).

Schroeder et al. (1978) evaluated loaded titanium implants in the monkey and found osseointegration still present when the experiment was terminated at 16 months after implant insertion. The largest clinical material (as yet published) with a long-term follow-up of osseointegrated jaw bone implants was recently summarized by Adell et al. (1981). Adell et al. reported a complete survey of 400 patients treated with 2775 threaded, cylindrical titanium implants. Using refined methods for implant installation in edentulous jaws, based upon 15 years of clinical experience, the 5-year "survival rate" of functioning jaw bridges in Adell's material is approaching 100 per cent in the lower jaw and 95 per cent in the upper jaw. The same figures for individual fixtures are 91 and 82 per cent, respectively. The group I electron microscopic evaluations on the bone-implant interface found in the present paper are based on patients included in the study of Adell et al.

Apart from the jaw bone implants the present authors have examined 24 tibial bone, 2 iliac bone and 2 temporal bone screws (Tjellström et al. 1978a,b 1981a,b). Based upon the results, of these studies the question referred to in the introduction part of the present paper – whether osseointegration is possible and desirable for the long-term function of bone implants – must be answered in the affirmative. A direct bone anchorage can be achieved and maintained for an indefinite time, no matter if the jaw, tibial, iliac or temporal bones are the implantation sites. Loss of anchorage over a 5-year interval has, in the complete material, been less than 10 per cent. Connective tissue-anchored implants as tried, for example, in dental restorative surgery do not function as adequately. "The technique of connective tissue anchorage which purports to imitate the natural situation in which the tooth is anchored by means of periodontium does not succeed in practice, since the required tissue differentiation cannot be achieved" (Brånemark et al. 1977).

Pre-requisites for osseointegration

The establishment of osseointegration is according to our experience dependent on the following parameters: 1. Implant material; 2. Implant design; 3. Implant finish 4. Status of the bone; 5. Surgical technique; 6. Implant loading conditions. Even if the individual importance of each one of these factors is difficult to evaluate with certainty, it is important to discuss them in the light of personal experiences supplemented by comments from the literature.

1. Implant material

The implant should be manufactured from a tissue-tolerant material capable of withstanding the loads at the implantation site and having great resistance to corrosion. Choosing between the frequently used implant materials such as, for example, stainless steel, vitallium or titanium, which have all been shown to be at least initially implantable with a direct bone contact, led the present authors to prefer titanium based on several reports (Emnéus 1967, Emnéus & Berg 1967, Emnéus & Gudmundsson 1967) as well as personal observations.

Clarke & Hickmann (1953) testing metal reactions in equine serum determined the "Anodic Back e.m.f." (= ABE), a parameter bearing a close correlation to known corrosion resistance. Titanium was found the least corrosive material in the test, having an ABE-value more than five times higher than, for example, vitallium and seven times higher than stainless steel. Hille (1966) summarized his opinion about titanium as

an implant material claiming that titanium; 1) Shows an adequate resistance to corrosive forces of the body environment; 2) Induces a tolerable reaction in the host tissue and 3) Has the necessary strength, ductility and endurance limit.

Titanium was reported as having a low toxicity compared with stellite and steel in a biological test (Laing et al. 1967). Brettle (1970) concluded that titanium is probably the most inert material so far used for implant fabrication. Solar et al. (1979) presented an *in vitro* study of titanium in Ringer's solution at 37°C with different measures being taken to imitate the *in vivo* conditions. The findings of that study showed that titanium should tolerate exposure to physiological chloride solutions at body temperature for an indefinite time without corrosion.

To the knowledge of the present authors non-alloyed titanium is the only metal that has been shown to establish a direct bone-to-implant contact and to maintain such a direct connection, in man, for periods of more than 10 years. Possible lasting osseointegration with other materials is yet to be demonstrated in a consecutive patient material of adequate duration, i.e. at least 5 years follow-up time.

It should, of course, be remembered that non-alloyed titanium; even if it is an optimal implant material, has certain disadvantages when used for gliding surfaces in joint implants because of the very high friction between titanium surfaces in contact. This leads to galling (McQuillian & McQuillian 1956) and wear products (Amstutz 1973).

Tantalum and niobium are other materials which combine excellent mechanical properties and bioinertness (Schider et al. 1980). More clinical experience is, however, necessary before an accurate evaluation of these metals as implant material can be made.

2. *Implant design*

The importance of exact fit between bone and implant is stressed by several authors (Linkow & Chercheve 1970, Giro 1974, Griss et al. 1975). Osseointegration is more easily achieved with cylindrical, threaded implants which are inserted so as to create maximal contact between bone and implant (Predecki et al. 1972). In an *in vitro* comparison between conical, natural tooth and cylindrical geometrical implant configuration the latter was shown to minimize the high stresses both in the implant and in the mandibular model tested (Atmaram et al. 1979). The screw-design minimizes early implant movements (Ledermann 1979) that should be avoided (Uhthoff 1973, Cameron et al. 1973, Schatzker et al. 1975). "A screw provides an increased surface area for interaction between implant and tissue and is viewed, in this context, as a variant of the surface-porous implant system (Homsy et al. 1973).

3. *Implant finish*

Cellular contact, theoretically, could be dependent on the implant surface. The importance of this parameter is, however, difficult to evaluate at present. Baumhammers et al. (1971) compared smooth and sandblasted material and found the larger surface area of the latter to be beneficial for connective tissue cell attachment. In implants inserted according to Brånemark et al. (1977) very smooth surfaces have been avoided and instead somewhat rougher surface finish types have been tried. The data to support this preference are, however, only empirical. Some authors such as Swanson & Freeman (1977) do not believe the surface finish to be of any major importance for implant function.

In theory there are numerous ways of treating the implant surface to experimentally increase the bone-bonding capacity. Such methods include e.g. anodisation or collagenisation of the implant surface, ideas which at present are being investigated by several groups (Kasemo, Larsson, Lundström 1980, personal communication).

A technique of coating a metal substrate with a thin layer of glass – bioglass – has been described by Busceni & Hench (1976). Bioglass is supposed to admit a firm bone-to-implant fixation due to a consecutive series of chemical reactions occurring in the interface zone. This may increase the implant-to-bone bonding strength although a recent report concerning bioglass found its attachment to bone at 12 weeks to be less strong than a control porous specimen (Ducheyne et al. 1979).

4. Status of the bone

A healthy bone tissue is, of course, essential for proper osseointegration. Whether the implant is inserted into a cortical or a primarily cancellous bed is, however, of less importance for later success as there is a strong tendency for "corticalization" of spongy bone around metal implants (Breine & Brånemark 1980). In extreme cases of bone resorption, not uncommonly seen in the edentulous jaw, there is a need for a bone graft. In the jaw region where conventional bone grafts are frequently resorbed, a preformed bone graft is recommended based on several experimental and clinical reports (Brånemark et al. 1969, 1975, 1977, Adell 1974, Albrektsson et al. 1978, Lindström et al. 1981, Breine & Brånemark 1980). Titanium fixtures have, in fact, been inserted in the *donor* area in preformed bone grafts to later, after grafting, be used as support for dental bridges in the host bone (Lindström et al. 1981).

5. Surgical technique

A delicate surgical technique is essential to ensure osseointegration (Brånemark et al. 1977, Albrektsson et al. 1978, Ledermann 1979). The principles of "minimal tissue violence" are literally of vital importance for the bone surgeon. Recommendations to control the surgical trauma summarized by Lindström et al. (1981) include factors such as constant cooling during surgical procedures (Thompson 1958, Moss 1964, Costich et al. 1964, Jacobs & Ray 1972, Matthews & Hirsch 1972, Hughes & Jordan 1973, Jacobs et al. 1976, Krause 1977, Fister & Gross 1980), adequate drill geometry (Jacobs & Ray 1972, Matthews & Hirsch 1972, Jacobs et al. 1976, Hobkirk & Rusiniak 1977), adequate drill speed (Thompson 1958, Pallan 1960, Jacobs et al. 1976, Jacobs 1977) and careful tapping for the screws (Hughes & Jordan 1973).

6. Implant loading conditions

Osseointegration only occurs in perfectly stable situations. Due to the surgical trauma a necrotic border zone inevitably arises immediately adjacent to the implant no matter what precautions are taken at implant insertion. This dead bone should be remodelled before implant loading is allowed. Actually, osseointegration can be safely and predictably achieved only if the implant is allowed this defined healing time. In rabbits, known for rapid bone regeneration, 6 weeks may be an appropriate healing time whereas in man 3–4 months is necessary (Albrektsson et al. 1978). Perhaps the most important reason for the occurrence of the connective tissue sheath generally seen around different types of implants is the immediate loading allowed (Armitage et al. 1971, Driskell 1973, Nixon 1975). Another way of preventing osseointegration, as shown by Brunski et al. (1979), is to attach jaw bone implants to adjacent functioning teeth. The natural tooth is surrounded by a periodontal membrane that allows minor movements which makes a natural tooth a less suitable fixation for an implant needing optimal stabilization. Minor movements inhibit osteogenesis (Schatzker et al. 1975) and loading should not be allowed until the screw threads are filled with callus (Uhthoff 1973).

Possible future applications for osseointegrated implants

Conventional cemented implants for treating hip joint disorders show, in various materials, a complication rate of 10–20 per cent but still function well enough to be regarded as a clinical routine (Charnley 1973). It should, however, be remembered that the clinical materials presented comprise mostly patients over 60 years of age. Furthermore, cemented implants in the upper extremity show a greater percentage of loosening (Hagert 1980, personal communication). Gliding finger prostheses (Swanson 1973) have produced adverse tissue reactions, in many cases resulting in a progressive restriction of movements (Hagert 1975). Theoretically, osseointegrated implants, as shown in an experimental work (Brånemark et al. 1970) may considerably improve the success rates when used as support for bridging segmental defects with or without reconstruction of joints. Before a safe evaluation of the future role of osseointegrated joint replacements can be

made more knowledge ought to be gained about the true nature of the bond between bone and titanium implants and there should be a careful long-term follow-up of the results of the ongoing clinical osseointegrated joint reconstructions.

CONCLUSIONS

1. Osseointegration – a direct bone-to-implant connection – can be permanently achieved in man.
2. The basic mechanisms explaining the true nature of the bone-to-titanium bonding are, as yet, incompletely investigated.
3. Evidence for the occurrence of direct contact between titanium and bone now exists on the electron microscopic level.
4. To guarantee osseointegration, threaded, unalloyed titanium implants of defined finish and geometry should be used. They should be inserted using a delicate surgical technique and be allowed to heal *in situ* without loading for a period of at least 3–4 months.

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