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Osseointegration of bone implants

A review of an alternative mode of fixation

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The body's way of reacting to a nontolerated foreign material is to shield off the alien substance from the tissue through the formation of an enveloping fibrous layer, which is generally poorly vascularized. In fact, in soft tissue, it has been suggested (Laing et al. 1967) that the thickness of this fibrous coat is inversely related to the degree of tissue acceptance of the implanted material. In bone tissue, also, a soft tissue encapsulation of a foreign material is an indication that it is regarded as nonself rather than self (Albrektsson 1986), assuming that other implantation factors that may result in fibrous tissue formation are being controlled. Thus, the ideal biomaterial would be the one that is truly integrated into the body where all types of shielding-off reactions are absent.

It is not surprising that cement-anchored bone implants will become largely or totally anchored in fibrous tissue, some of the reasons for this tissue reaction being the exothermic and monomer releasing reactions during curing of the cement (Linder 1976), as well as long-term adverse reactions of tissue to the hardened fixative (Albrektsson 1984, Pedersen et al, 1983, Lintner 1983). However, also around currently used cementless joint components, there is, generally, evidence of an interfacial soft-tissue reaction, even if a biomaterial of a presumed excellent biocompatibility is being used. In such cases the soft-tissue encapsulation may be related, for instance, to the surgical trauma or the loading pattern of the implant – two parameters each which, if inadequately controlled, may prevent the desired bone healing and instead stimulate the formation of low differentiated scar tissue around the foreign device. Once such a soft-tissue reaction has become manifest, the situation is similar to that of a case of pseudarthrosis: spontaneously occurring later bone repair is unlikely.

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The osseointegration concept

Brånemark et al. (1969) were first to report of bone tissue growing in what appeared to be direct contact with a metallic implant. Later, Brånemark et al. (1977) coined the term *osseointegration* to describe this phenomenon. However, osseointegration was more a concept than a precisely defined biological term. The idea of any type of direct bone-metal contact without intervening soft-tissue layers was not at all accepted in the 1970s; on the contrary, it was regarded as inevitable with some type of fibrous encapsulation of metallic materials (Southam and Selwyn 1970). However, Brånemark, did not only present histologic evidence of a direct bone anchorage of titanium implants, he also developed an oral implant that gave excellent clinical results in sharp contrast to previously used fibrous tissue-anchored dental devices. To date, the Brånemark oral implant is the only dental implant that has received recognition by the American Dental Association, and osseointegration has become a well-known concept among those working in the field of dental materials. Brånemark (1985) suggested the following definition of osseointegration: *A direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant.*

From a practical viewpoint, this definition of osseointegration, unfortunately, results in more questions than answers where a given implant is concerned. For example, Draenert and Ruediger (1978) and Linder and Hansson (1983) have

convincingly shown that cemented joint implants may have zones in direct contact with bone, free of fibrous tissue. At least from a structural viewpoint, this would fulfill the definition of osseointegration. Nevertheless, it seems obvious that to call the implant osseointegrated must signify that a considerable proportion of that same implant is in direct contact with bone, and cemented implants have only been demonstrated as being spottily associated with bone. Until recently, however, no attempts have been made to define what minimal proportion of an implant must be in a direct contact with bone for the term osseointegration to be justified. Further, on what resolution level is the direct structural connection measured and how is it possible to measure if a true functional connection exists or not? Steinemann et al. (1986) have suggested a mechanical definition of osseointegration that may be said to include a functional parameter: Osseointegration is an implant anchorage with resistance to shear forces, as well as to tensile forces (Figure 1). Robert Baier (personal communication) has gone a step further and suggested that the true osseointegrated implant is the one that is so well anchored in the bone that attempts to implant removal will result in bone fracture rather than in fractures through the interface. There is, to date, no studies known to us that indicate that any current clinically used oral or orthopedic implant may become osseointegrated based on this strict definition, even if Galante (1985) has claimed that strength of fixation of the bone-implant bond in their experimental titanium implants may approach the strength of the surrounding bone.

Osseointegration from a structural and biomechanical viewpoint

Johansson and Albrektsson (1987) studied the interrelationship between the degree of contact with bone and necessary removal forces for unscrewing threaded titanium implants that earlier had been inserted in the rabbit tibial metaphysis (Figure 2). Irrespective of a gentle surgical technique, the interface during the first month consisted of soft tissue and low removal torques of the order of 10–15 Ncm were found (Figure 3). With increasing times of implantation, the implant-surrounding bone became gradually more mature and dense, and greater removal torques were required to unscrew the implants. One year after implantation, the average removal torque was 88 Ncm and 90 to 95 per cent of the intracortically localized implant part was found to have a direct metal-bone contact, whereas the remaining intramedullary part of the implant only showed a bony

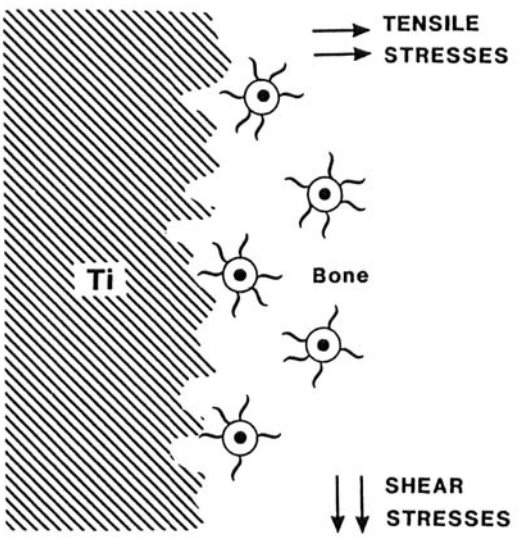

Figure 1. Shear and tensile stresses that act over the implant-bone interface. Resistance to both of these stress types is found with the osseointegrated implant according to Steinemann.

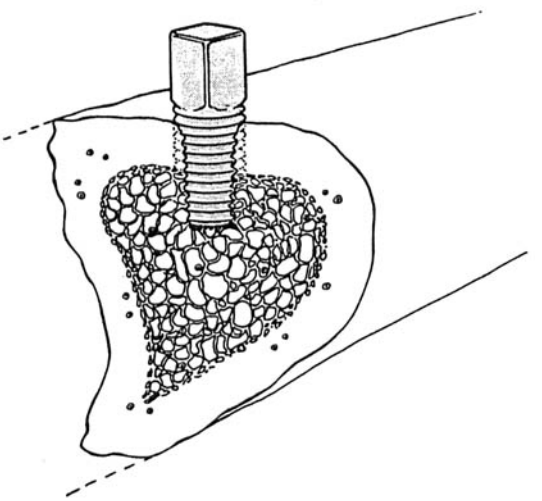

Figure 2. A solid, square-headed c.p. titanium screw used for investigations of removal force and for histomorphologic investigations of metalic implants.

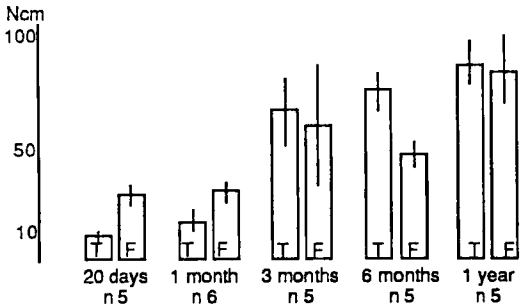

Figure 3. The torque necessary to remove tibial and femoral implants is about 15–25 Ncm at 20 days and 85–90 Ncm 1 year after surgery.

contact in about 50 per cent of the surface area. As previously demonstrated by Strid (1985), there is a tendency to bone condensation around an inserted titanium implant, and a fairly dense bone structure may often develop around loaded titanium devices at sites where only sparse bone trabeculae were observed prior to surgery. Based on these and previous findings (Albrektsson 1985), it seems reasonable to relate the structural definition of osseointegration to the loaded implant that has an average surface contact with bone of minimally 50 per cent and at the cortical passage of the order of 90 per cent. This figure is close to that observed by Harris et al. (1983), who found bony ingrowth in half of the porous surface of metallic acetabular cups in dogs. The resolution level required to judge if direct bone-implant contact exists is on the micron scale, and thus the analyses should be based on light-microscopic investigations. Radiographs with a maximum resolution capacity of 0.1 mm are not sufficient for diagnosis of osseointegration.

As shown in the study by Johansson and Albrektsson (1987), there is an obvious quantitative interfacial alteration with more bone directly bordering the implant with increasing implantation time (Figure 4). In theory, this gradual increase of interfacial bone would be sufficient to explain the gradually higher removal torques observed. However, an additional effect of a simultaneous qualitative interfacial reaction cannot be overlooked. Kasemo (1983), Parsegian (1983), and Albrektsson et al. (1983) have discussed the possibility of a gradually developing physico-chemical interaction between living bone tissue and the titanium oxide that inevitably covers a titanium implant. Van der Waals forces, as well as true chemical ionic bindings, have been suggested as acting upon the osseointegrated interface. Steinemann et al. (1986) investigated the capacity of the osseointegrated interface to withstand pure shear and tensile forces. They postulated that any resistance to pure tensile forces would indicate some sort of chemical bond acting over the interface, whereas resistance to shear forces could be biomechanically explained, i.e., mere bone ingrowth in a rough titanium surface could carry shear stresses even in the absence of any bonding mechanism. Interestingly enough, Steinemann et al. (1986) did find evidence of resistance to pure tensile stresses, which in their experimental model were found to develop initially 100 days or more after implantation. The resistance of tensile stress was of the magnitude of 4 N/mm^2 which is equivalent to the strength of trabecular bone. This is the first experimental indication known to us that some kind of chemical interaction may become established over the titanium-bone interface. Investigations of the material side of the interface have revealed that the oxide layer on implanted titanium devices does not seem to be static: There was a continuous growth of the oxide layer up to a thickness of 1,000–2,000 Å, observed after 7 years of clinical implantations, in contrast to nonimplanted titanium devices that retained an oxide layer of roughly 60 Å (McQueen et al. 1982). This interesting topic of possible interactions over the titanium-tissue interface is further discussed in a recently published excellent overview (Kasemo and Lausmaa 1986).

Factors that influence the interfacial reaction to an implant

There are several factors determining the interfacial response to a foreign material including the 1) biocompatibility, 2) design and 3) surface of the implant, 4) the status of the host bed, 5) the surgical technique used at insertion, and 6) the loading conditions applied afterwards (Albrektsson et al. 1981) (Figure 5).

1. *Material biocompatibility.* In a series of experiments, Albrektsson et al. (1982, 1985, 1986, 1987) have demonstrated that it is possible to osseoin-

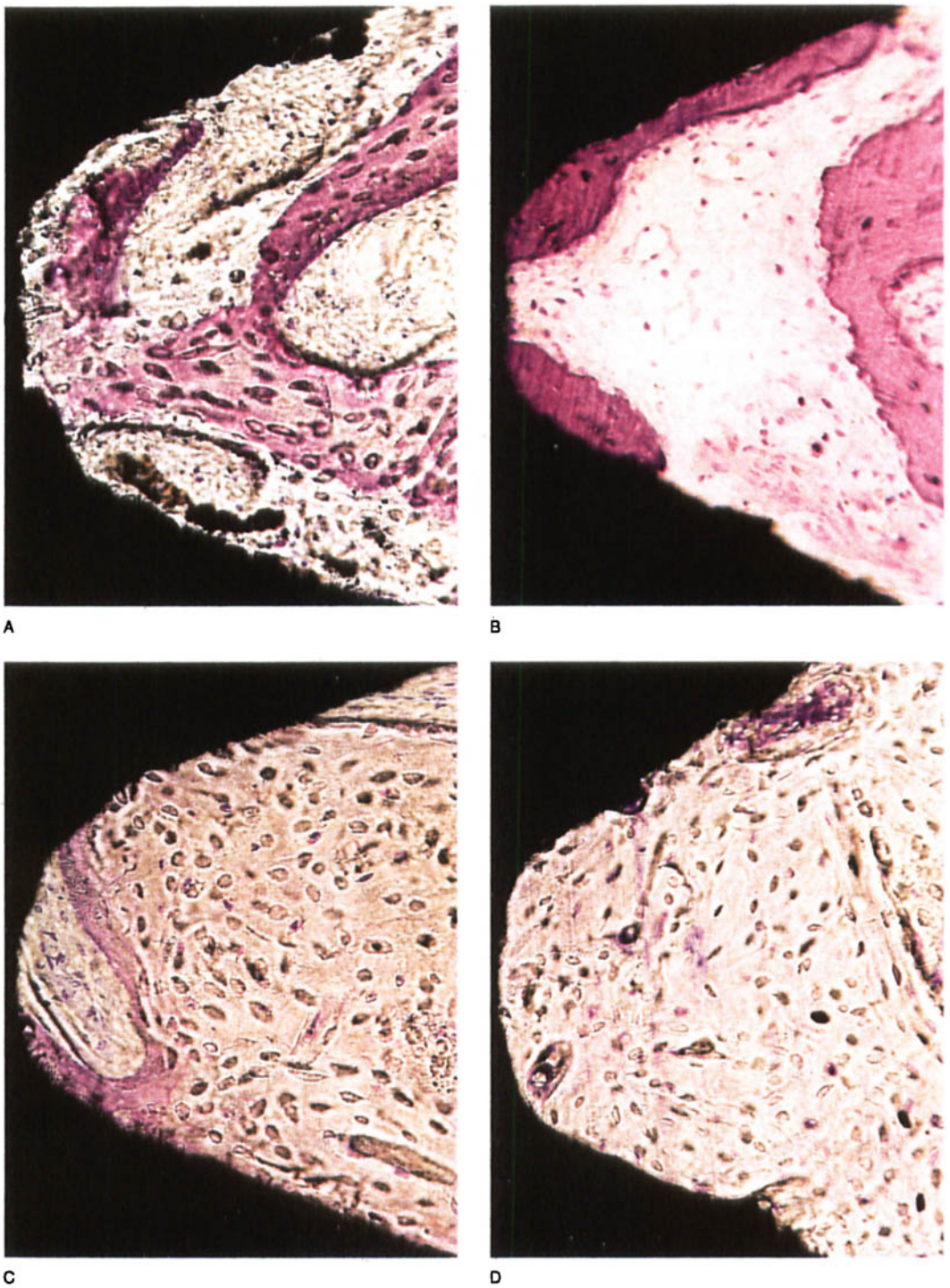

Figure 4. Integration of titanium screws in the rabbit metaphysis.
A. One month after implant insertion, there is very little bone in the interfacial region.
B. There is a variable amount of interfacial bone present in the interface 3 months after surgery; in some cases most of the threads at the cortical passage were filled out with bone; whereas in the case demonstrated in this figure, there was mostly soft tissue in the threads.
C. Six months after surgery, there is, with a relatively small interindividual variability, good bone filling in the threads at the cortical passage.
D. One year after surgery, there is, on an average, a bone-implant interfacial contact at the cortical passage of 90–95 per cent in tibial and femoral implants.

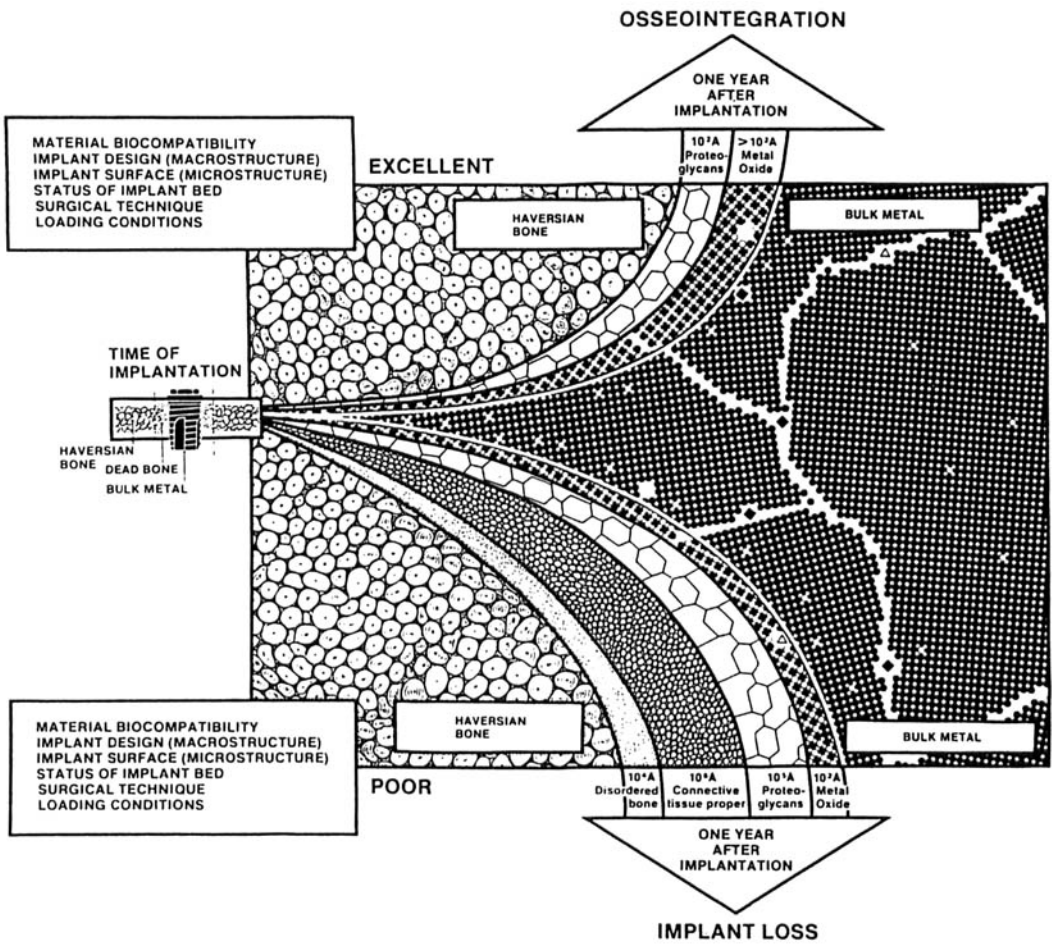

Figure 5. Whether an implant will become osseointegrated or not is dependent on the more or less simultaneous control of several parameters, such as material biocompatibility, implant design and surface, status of the implant bed, the surgical technique, and the loading conditions.

tegrate c.p. titanium, zirconium, and niobium metals, whereas it was not possible to establish soft-tissue/cellular-free interfaces around gold or stainless steel. However, Linder and Lundskog (1975) did show experimental indications of an established direct bone-metal interface of stainless steel experimental implants. These different results may be attributed to either the fact that there was no sectioning technique permitting investigations of intact bone-metal specimens in 1975 and that, thereby, hypothetically, a possible thin soft-tissue layer may have become lost in the sectioning procedure in the experiment by Linder and Lundskog (1975) or to the use of slightly different grades of stainless steels. Nevertheless, because of corrosion (Oron and Alter 1984), it is today generally agreed that stainless steel is not an ideal biomaterial, and even if it would be initially possible to establish a primary direct bone-stainless steel interface, it seems unlikely that this osseointegration will last indefinitely.

Titanium-6aluminum-4vanadium alloy was found by Albrektsson and Jacobsson (1987) to cause adverse tissue reactions in the interface in contrast to c.p. titanium, i.e., the metal that has been found to cause the most natural tissue reaction of those metals tested so far (Albrektsson 1986). Woodman et al. (1984) investigated the leakage of titanium and aluminum from implants inserted for up to 8 years in the baboon femur. Titanium levels became elevated in the lungs of the animal, but reached a plateau phase after 3 years. There was no evidence of titanium toxicity (Figure 6). Aluminum leaked out continuously

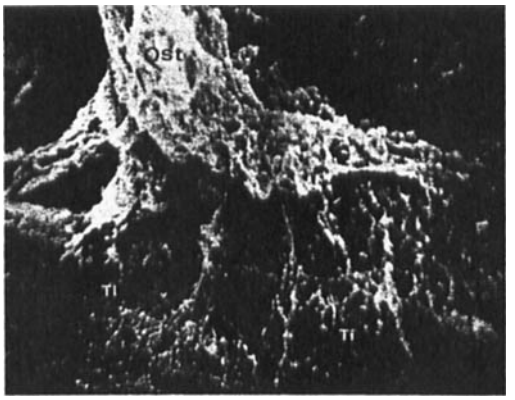

Figure 6. The excellent tissue biocompatibility of c.p. titanium is indicated by this osteoblast with numerous processes attaching to the irregular implant surface.

without a tendency to reach any plateau level that may be regarded alarming, especially relevant since it has been demonstrated that increased levels of aluminum are associated with Alzheimer's disease (King et al. 1981). However, whether leaking aluminum from implants actually will ever reach hazardous levels is not known.

Hydroxiapatites and tetracalcium phosphates have a great degree of tissue acceptance (Jarcho 1986), and some evidence has been presented that may indicate that these materials are more rapidly incorporated in bone than is c.p. titanium (Gerner et al. 1987). However, examinations of interfacial tissue reactions at the ultrastructural level have revealed very similar tissue reactions to hydroxiapatites and c.p. titanium (Albrektsson and Albrektsson 1987). Moreover, hydroxiapatite is brittle, and its use in orthopedic surgery seems limited to coatings on metal stems that may suffer the "side-effect" of subsequent loosening of the coating from the stem.

2. *Implant design.* Threaded implants have a good initial resistance to shear stress if inserted with a proper technique. However, in implants that were loaded early, it has recently been demonstrated that porous, slightly conical implants became more rapidly invaded by bone than did screw-shaped implants (Mariatopoulos et al. 1986). Probably both designs may become osseointegrated, even if, as summarized by Carlsson and Linder (1986), several reports on porous implant have demonstrated only a partial bony ingrowth or a fibrous tissue lining of the bone within the pores. Other designs, such as T-plates and irregular cylindrical implants, were found by Carlsson et al. (1986) to become less well anchored in bone than screws.

3. *The implant surface.* The implant surface is important for osseointegration from various aspects. Implants with minor surface irregularities become better anchored to bone than identical smooth implants (Skalak 1983, Röstlund et al. 1987). Surface energy has been defined (Hench and Ethridge 1982) as a measure of the extent to which bonds are unsatisfied at the surface of a metal. A high surface energy is preferable when compared with a low surface energy because the former state would result in an improved cellular attachment (Baier et al. 1984). The surface energy of any implant depends on the technique of manufacturing, as well as on the cleaning and handling of the implant afterwards. The surface state of the implant seems to be most important for its later take in the tissue, although this important topic has been insufficiently investigated. The interested reader is referred to the works of Baier et al. (1984, 1986) and to the review by Kasemo and Lausmaa (1986).

4. *State of the host bed.* A noninfected bone bed seems to be imperative for proper osseointegration. Previous irradiation is not an absolute contraindication. Clinical reports of craniofacial implants inserted in previously irradiated beds seem to point to 1–5 year success rates, 5–10 per cent poorer than those achieved with similar implants, but inserted in nonirradiated beds (Jacobsson et al. 1987, Albrektsson et al. 1987). Where osteoporosis is concerned, this state is no contraindication for insertion of osseointegrated implants provided there is enough bone stock available for anchorage.

5. *Surgical technique.* Conventional surgery, even if cooling is applied, may result in interfacial temperatures of 89° C (Eriksson et al. 1984). Such a high temperature will result in a permanent destruction that will not heal as bone, but as low differentiated scar tissue (Eriksson 1984). By avoiding high drill speeds, using sharp drills combined with cooling and a gradually increased drill size (instead of penetrating the bone in one

surgical sequence), Eriksson and Adell (1986) demonstrated that it is possible to cut through bone without inducing an interfacial temperature that exceeded the body temperature. The importance of another surgical parameter, the fit between implant and implant bed, has been pointed out by Harris et al. (1982) and Carlsson et al. (1987). The latter authors found that an implant-bone gap of 0.35 mm or more was not bridged by cortical bone in a stable rabbit implant model.

6. *Loading conditions.* Several authors have demonstrated that premature loading will stimulate the formation of fibrous tissue instead of the desired interfacial bone formation (Uhthoff 1973, Schatzker et al. 1975, Cameron et al. 1973). Brånemark et al. (1977) used a two-stage surgical technique as one way to ensure primary stability that seems necessary to avoid soft-tissue formation (Galante 1985).

Experimental and clinical ways to determine osseointegration

To date, there is only one way to show that osseointegration of a given implant has occurred: To study histologic sections of that same implant and demonstrate a cortical bone-implant contact of minimally 90 per cent. It is also important that the intact bone-foreign material interface is analyzed: viz., light microscopy of sections where the implant has been removed before analysis is not adequate, because it is uncertain what tissue layer may have been removed together with the implant. The technique of cutting metallic implants in situ in bone tissue permitting studies at the resolution level of 10 microns or better has been developed only during the last decade. This means that most evidence of osseointegration published as late as in the 1970s suffers from some uncertainty because a proper technique for analysis of intact bone/metal specimens was not generally available at the time.

Various types of push/pull-out tests would, at least theoretically, be used for identification of osseointegration, based on the assumption that the interface would be at least as strong as the surrounding bone tissue. Again, evidence is lacking that such strong bonds exist over the interface. Surely, the experimental design of "osseointegration tests" must take the implant design into consideration: it is, for instance, not sufficient to pull out a screw, because the design of the screw may result in bone breakage irrespective of the fact that there may be no bonds acting over the interface.

Techniques that permit examinations of the material-bone interface at the ultrastructural level are of a specific interest. Such different techniques in which the true interfacial structures can be studied with the electron microscope have been presented by Albrektsson et al. (1982), Linder (1985), and Thomsen and Ericson (1985). Presumably, it may be possible to relate different interfacial phenomena to tissue integration when the tissue reactions are studied at the ultrastructural level instead of with low-power light microscopy. An initially osseointegrated implant may later, at least theoretically, lose its bone-implant contact because of the effects of corrosion. Such an event may be preceded by an adverse tissue reaction detectable only on the electron-microscopic level. TEM observations of the interfacial reaction around bone implants have been reported by Albrektsson et al. (1982) and Linder et al. (1983). C.p. titanium has been demonstrated to be directly bordered by hydroxiapatite crystals at the resolution level of the electron microscope, i.e., 30–50 Å (Hansson et al. 1983). Collagen filaments have been regularly observed at a distance of only 200–400 Å from the titanium, and collagen threads a few thousand Å away from the interface (Albrektsson 1986). This is the most natural tissue behavior described with any metallic implant material (Figure 7).

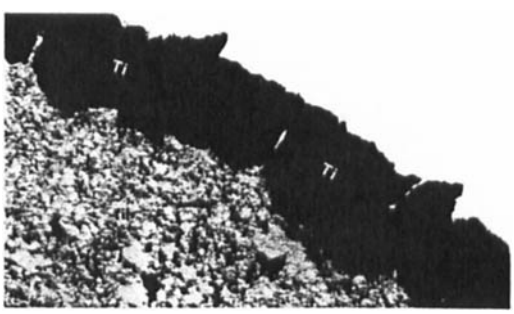

Figure 7. In experimental studies, collagen filaments (fil) are observed in close proximity (200–400 Å) to the titanium (Ti) surface, again an indication of an excellent biocompatibility of c.p. titanium.

It is clear from the above discussion that it is impossible to state with certainty that a clinical implant is osseointegrated. However, the state of nonintegration may sometimes be clearly identifiable, for instance, with radiography, revealing radiolucent zones around the implanted device. Strid (1985) has described a radiographic technique including computer-assisted density analyses of the interfacial tissues. This technique has been used to analyze oral implants, as well as metacarpophalangeal joint implants; and it does increase the quality of the interfacial diagnosis, although not to the point that the osseointegrated state can be unequivocally proven. Where certain implants, such as oral ones, are concerned, a clinical stability test may be used. Implant instability evoked with a manual test is a definite indication of the same implant being nonintegrated (Figure 8), but unfortunately stability with this type of testing does not provide evidence that proper osseointegration has occurred. "Sound tests" involving striking the implant with a metallic instrument and listening to the emitted sound waves have been clinically used as another indication of osseointegration, although there is no published evidence of typical sound diagrams for osseointegrated implants in contrast to nonintegrated ones.

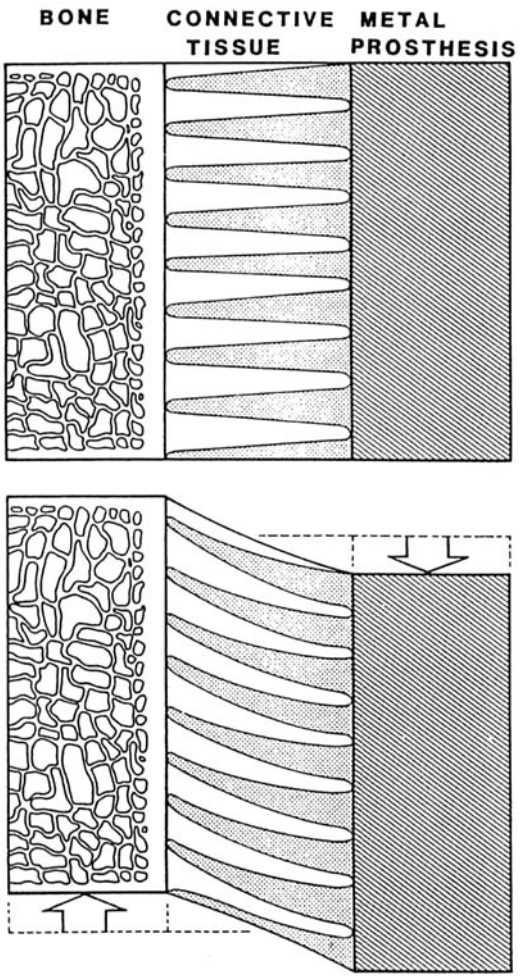

Figure 8. When loaded, an implant shielded off from the bone by a connective tissue layer will move relative to the tissue, whereas the osseointegrated implant moves with the bone leading to improved capacity for load bearing.

Clinical experience of osseointegrated implants

The best known clinical example of the successful use of osseointegrated implants is the oral implant developed by Brånemark. To date, more than 50,000 c.p. titanium screws have been inserted worldwide, with mandibular clinical success rates of 95 per cent or more during a follow-up period of 5 years (Adell et al. 1987, Albrektsson et al. 1987). The long-term clinical material of the outcome of the same implant (Adell et al. 1981, 1987) seems to indicate that nearly all mandibular implant failures occur within the first year of implantation and that failures occurring later are unlikely. This is a most interesting observation and is in contrast to the finding with currently used joint arthroplasties, which generally show an increased failure rate with time. There is histologic evidence available that these oral implants are verily osseointegrated. The same is true for craniofacial implants used for anchorage of facial epistheses or external hearing aids with the same technique (Tjellström et al. 1981). The 5-year clinical success rates with these titanium implants have also been in the range of 95–99 per cent (Albrektsson et al. 1987). Other bone sites where osseointegration has been experimentally and clinically verified include the tibia (Carlsson et al. 1986) and the iliac crest (Lindström et al. 1981). In the case of metacarpophalangeal joint arthroplasties, one paper presenting 3–5 year data of reconstructions aimed at osseointegration has recently been published (Hagert et al. 1986), but it is uncertain whether the described implants actually achieved integration as defined here. Attempts to use the osseointegration technique to

repair the distal radioulnar joint seem to have failed, and osseointegrated reconstruction of the ankle joint is still in a very preliminary clinical trial stage. There is experimental evidence of osseointegration in the case of canine knee joint arthroplasty (Carlsson et al. 1986), but it is still uncertain whether it will be possible to use such implants in human reconstructions.

Concluding remarks

The osseointegration principle is based on tissue cooperation (Brånemark 1985) in contrast to most currently used techniques for implantation. It is our conviction that a cemented joint arthroplasty, irrespective of the type of cement used or the cementation technique can never become ideal. The cemented implant works not because of the tissue compatibility of the fixative, but because of the restricted loading of the devices – true for the senior patient from whom we have the best clinical experience of this type of anchorage. However, in the case of arthroplasties, we have to date little evidence of the possibility to base reconstructions on any type of osseointegrated technique, for currently used cementless joint replacements are generally anchored in fibrous tissue, not in bone (Lord et al. 1979, Albrektsson and Albrektsson 1987). In fact, some authors (Walker et al. 1984) have even advocated that such a zone of fibrous tissue is beneficial because it may play a role in rendering stresses of the trabeculae tolerable. Instead, we concur with Hedley et al. (1982) who saw this fibrous tissue layer as potentially progressing if subjected to movement, thereby leading to clinical loosening and prosthetic failures.

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