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UPDATE ON KEY FACTORS FOR ACHIEVING OSSEOINTEGRATION

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ABSTRACT

During the past two decades, dental implants have been used extensively to achieve osseointergration for prosthetic rehabilitation of edentulism. For this, a surgical procedure is performed on patient to insert a foreign material i.e implant into the bone, after which a poorly organized woven bone is formed at the interface, thus having a relatively low inherent strength. After a period of 3 to 6 months, woven bone is replaced by lamellar bone which possess adequate strength for load bearing. This bone healing process is known as osseointegration. This process of osseointegration depends not only on implant related factors such as material, shape, topography and surface chemistry but also mechanical loading, surgical technique and patient variables such as bone quality and quantity. There are many materials and techniques present today to increase the rate of clinical success of implants but the ultimate long term success of an implant is dependent upon the efforts of both the patient and dentist in maintaining the health of the periimplant tissues. The purpose of this review is to enlight various factors that have significant affect on osseointegration.

KEYWORDS: *Osseointegration, Factors Affecting Osseointegration, Implant Bone Interface.*

INTRODUCTION

The long term success of any implant system depends on the biocompatibility of the materials used and the condition of the tissue bed before and at the time of installation.[14] An initially healthy tissue may be easily transformed into a necrotic state if a surgical technique with minimal tissue violence is used. Branemark et. al showed that if all of these factors are controlled, load-bearing osseointegrated dental implants are possible and a predictable long term functioning of such implants can be achieved routinely.[1]

Even if osseointegrated implants have been documented to result in excellent long-term results, this does not necessarily imply that every implant system claimed to be dependent on osseointegration will result in an acceptable clinical outcome. On the contrary, there are several reasons for primary as well as secondary failure of osseointegration. These failures may be attributed to an inadequate control of the different factors known to be important for the establishment of a reliable, long-term osseous anchorage of an implanted device. These factors are:[1]

1. Implant biocompatibility
2. Design characteristics
3. Surface characteristics
4. The state of the host bed
5. The surgical technique and
6. The loading conditions
7. Biomechanical Considerations

There is a need to control these factors more or less simultaneously to achieve the desirable goal of a direct bone anchorage.

Implant Biocompatibility

Response of bone to different implant material is the principal factor on which an implant material is selected as suitable or unsuitable for osseointegration.

Bone tissue may react in different ways when an implant is inserted. If the implanted material is incompatible e.g. copper, a thick connective tissue capsule is formed around the implant and rapid rejection will occur. More compatible materials may be anchored in the bone without an interposed connective tissue layer. Mature haversian bone is found only at some distance from the metal surface. The absence of well oriented bone does indicate, however, that the material is not fully accepted and that rejection may occur with time due to corrosive or other toxic effects of the materials used. Ordered haversian bone in the interface all around the implant is a clear indication of tissue acceptance.[2] An invitro study by Gould et al. revealed the formation of hemidesmosomes on titanium surfaces. The formation of hemidesmosomes is a clear indication that the soft tissues of the oral cavity accept titanium oxide as being tissue compatible.

The Branemark fixture is made of commercially pure titanium which is Ti: 99.75%, O: 0.10%, Fe: 0.05%, N: 0.03%, C: 0.01% and others: 0.06%. When the titanium fixture comes into contact with the atmosphere, an oxide layer immediately forms 50-100 Angstroms thick. When the fixture has healed properly into the bone, the oxide layer is surrounded by a glycoprotein layer, then a calcified layer approximately 100 Angstroms thick. Prior to insertion of the fixture into the bone, the surface of the titanium fixture must be kept sterile and contact with any other metal or protein substance should be strictly avoided. With respect to metals, commercially pure (c.p) titanium, niobium and possibly tantalum are known to be most well accepted in bone tissue**.** The unique biocompatibility of titanium may be explained on the basis of the tightly adherent oxide layer which immediately forms on the metal surface. Hence, titanium implants have excellent resistance to corrosion and load bearing capacity. The mechanical properties of Titanium alloy are superior to cp Titanium.[3]

Other metals:
- Niobium, tantalum
- Cobalt chrome molybdenum alloys
- Stainless steels
- Ceramics - calcium phosphate hydroxyapatite (HA) and various types of aluminium oxid
- Polymers

Whereas the load bearing capacity of c.p. titanium is sufficiently documented in the case of oral implants, there is less known about niobium in this aspect. Other metals such as different cobalt-chrome-molybdenum alloys and stainless steels have demonstrated less good take in the bone bed, but it is uncertain if this is valid for every possible such alloy and if it is biocompatibility effect alone that is responsible for their less satisfactory incorporation into bone, compared with c.p. titanium. A significantly impaired interfacial bone formation compared to c.p. titanium has been found with titanium-6 aluminium-4 vanadium alloy, probably dependent on a less good biocompatibility of the alloy. One concern with metal alloys is that one alloy component may leak out in concentrations high enough to cause local or systemic side effects.[4]

Another material which could used as implant material is polymers. for eg:
- Ultra high molecular weight polyurethane.
- Poly amide fibers.
- Poly methyl methacrylate resin.
- Poly tetra fluoro ethylene.

It was hypothetized that their flexibility will minimize the micro movement of the periodontal ligament and will allow the connection between the natural teeth but they had inferior mechanical properties like:
- Lack of adhesion to living bone
- Adverse immunologic reactions have eliminated these materials as a coating layer.

Now the use is restricted for making shock absorbing components incorporated in o the superstructures supported by implants.

The interface created around titanium implants may resemble that seen around ceramic implants. The latter material also shows excellent biocompatibility, but it is brittle and may function less adequately if loaded in a complete fixed prosthesis over long periods of time. Ceramics can make up the entire implant or they can be applied in the form of coating. Various types of ceramic implant coatings, such as bioglass, hydroxyapatite or tricalcium phosphates, have been developed to create surfaces that are said to be well tolerated. Ceramics such as the calcium phosphate, hydroxyapatite (HA) and various types of aluminium oxides are proved to be biocompatible and due to insufficient documentation and very less clinical trials, they are less commonly used.[5]

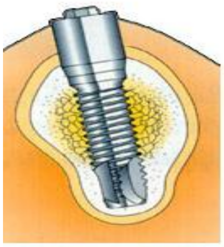
Grouping of hard tissue replacement materials according to their compatibility to bony tissue.[6]

Degree of Compatibility	Characteristics of Reactions of Bony Tissue	Materials
Biotolerant	Implants separated from adjacent bone by a soft tissue layer along most of the interface: distance osteogenesis	Stainless steels: CoCrMo and CoCrMoNi alloys
Bioinert	Direct contact to bony tissue: contact osteogenesis	Alumina ceramics, zirconia ceramics, titanium, tantalum, niobium, carbon.
Bioactive	Bonding to bony tissue: bonding osteogenesis	Calcium phosphate-containing glasses, glass-ceramics, ceramics, titanium (?)

Implant Design (Macro Structure)[7]

Threaded or screw design implants

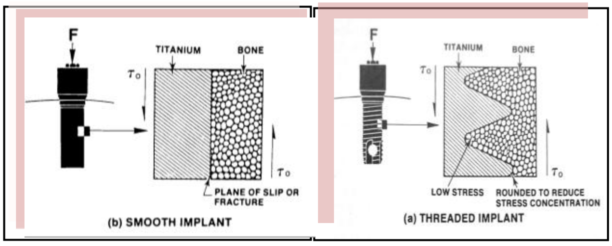
- Demonstrated to function for decades without clinical problems.
- Provide more functional area for stress distribution than the cylindrical implants.
- Minimal - <0.2 mm/year bone loss



Cylindrical implants

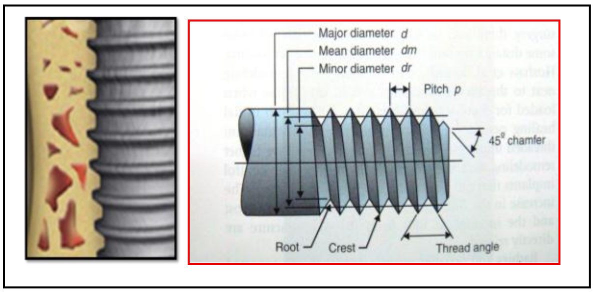
- These implants depend on coating or surface condition to provide microscopic retention and bonding to the bone.

Combination root forms have macroscopic features of cylinder and screw root forms.

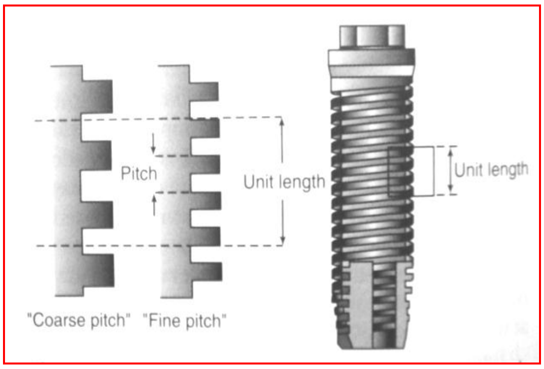


Threads on the implants improve initial stability, enlarge implant surface area and distribute stress favorably. Three geometric thread parameters are:

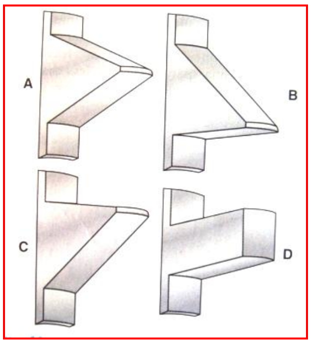
- Thread pitch
- Thread shape
- Thread depth



- Thread pitch is the distance between two adjacent thread crests. Decreased thread pitch increases the functional surface area. More the number of threads, more is the surface area.



- Thread depth is the distance between the major and minor diameter. Deep threads have more functional surface area but difficult to place whereas shallow threads are easy to place but have less functional surface area.
- Thread shape
  V-Shape
  Buttress
  Reverse buttress
  Square



There is at present, sufficient long-term documentation on threaded types of oral implants that have been demonstrated to function for decades without clinical problems. The threaded implants provide more functional area for stress distribution than the cylindrical implants. The design of the threads may also influence the long term osseointegration. For e.g. V-shaped thread transfer the vertical forces in an angulated path, may not be efficient in stress distribution as that of the square shaped threads. A wider diameter, more threads, deeper threads and surface structure that increase the initial bone contact percentage are of great benefit. Alterations in these are suggested according to Bone density.

It is known that where an implant fits tightly into its osteotomy site then osseointegration is more likely to occur. This is often referred to as primary stability, and where an implant body has this attribute when first placed, failure is less probable. This property is related to the quality of fit of the implant, its shape, bone morphology and density.

Implant Surface (Micro Structure, Surface Topography)[8]

A systematic review was performed on studies investigating the effects of implant surface roughness on bone response and implant fixation (MEDLINE from 1953 to 2003) and a positive relationship between bone-to-implant contact and surface roughness and it was found that surface characteristics affects success rate more in lower bone densities.

With respect to the surface topography there is clear documentation that most smooth surfaces do not result in an acceptable bone cell adhesion. Such implants do therefore end up as being anchored in soft tissue despite the material used. Clinical failure would be prone to occur. Some microirregularities seem to be necessary for a proper cellular adhesion even if the optimal surface topography remains to be described. But with a gradual increase of the surface topographical irregularities, problems due to an increased ionic leakage are prone to occur. With plasma sprayed titanium surfaces for instance, more than 1600 ppm titanium has been reported in implant adjacent haversian systems, probably resulting in an impairment of osteogenesis.

Another surface parameter is the energy state: where a high surface energy has been regarded as positive for implant take due to an improved cellular attachment. One practical way of increasing the surface energy is the use of glow discharge (plasma cleaning). However, published reports have not been able to confirm the superiority of artificially enhanced implant energy levels. One reason for this lack of confirmation of the surface energy hypothesis could be that the increased surface energy would disappear immediately when the implant makes in contact with the host tissues.

Many researchers recommended various procedures for improving the surface energy or surface characteristics of the implants to improve the osseointegration.[9]

METHODS

- Plasma sprayed titanium
- Plasma sprayed hydroxyapatite
- Sand blasting
- Sand blasting and acid attack
- Anodization
- Electrophoretic deposition
- Sol gel deposition (dip coating)
- Pulsed laser deposition

Stefini C.M. et al. (2000) recommended applying platelet derived growth factor and insulin like growth factors on the implant surface before placing into the cervical bed. According to their results, this method showed better wound healing and rapid integration.

Musthafa K. et al (2000) reported to sand blast the titanium implants with titanium oxide particles (45-90µ) to achieve higher rate of cell attachment.

Other authors like Lima Y.J. et al. (2001) and Orsini Z. et al. (2000) reported to perform acid etching of the titanium implants by hydrofluoric acid, aqueous nitric acid and sodium hydroxide to reduce the contact angle less than 10^0 for better cell attachment and utilization of 1% hydrofluoric acid + 30% nitric acid to clean the implant surface and to remove the alumina particles after sand blasting which improves the osseointegration.

Nishiguchi S. et al (2001) reported to provide alkali + heat treatment to improve the amount of bone bonding, i.e. 5 mol/lt NaOH at 60^0C for 24 hours and 600^0C for 1 hour (Dog study).

Rich and Harris presented some of the salient features of fibroblasts during healing i.e. Rugophalia: attracted towards rough surfaces, Haptotaxis: the directional cell movement that depends upon adhesive gradients on the substratum, Contact guidance : the tendency of the cells to be guided in their direction of locomotion by the shape of substratum. These properties denotes that the implant fixture with rough surface topography and more surface energy promotes faster and complete osseointegration.[10]

Role of surface coatings in osseointegration[11]

i. Titanium plasma spray

The titanium plasma spray (TPS) has been reported to increase the surface area of the bone to implant interface and acts similar to a three dimensional surface, which may stimulate adhesion osteogenesis. Although tremendous increase in total surface area occurs at microscopic level, the actual load bearing capability of the coating increases functional area by 25% to 30%, which is still substantial. The increased surface roughness may also improve the initial fixation of the implant, especially in softer bone.

ii. Hydroxyapatite coatings

Hydroxyapatite (HA) coatings have similar increase in surface roughness and increase in functional surface area as titanium plasma spray. A direct bond shown with HA-to-bone interface is greater than titanium to bone and even greater than TPS to bone. HA coatings have shown accelerated interfacial bone formation and maturation. The space or “gap’’ between the implant may affect the percentage of bone contact after healing. The gap healing may be enhanced by the HA coating. The corrosion rate of metal is also reduced, which is more significant for chrome cobalt alloys.

Clinical advantages of TPS or HA coatings

1. Increased surface area.
2. Increased roughness for initial stability
3. Stronger bone-to-implant interface.

Additional advantages of HA over TPS

1. Faster healing bone interface.
2. Increased gap healing between bone and HA
3. Stronger interface than TPS
4. Less corrosion of metal

Disadvantages of coatings

1. Flaking, cracking, or scaling upon insertion
2. Increased plaque retention when above the bone
3. Increased bacteria and nidus for infection when exposed
4. Complication of treatment of failing implants
5. Increased cost.

The HA or TPS coating, should not be the only system of load transfer to the bone. This is especially important when bone loss occurs, and the coating must be removed for repair of the implant. However, a coating may enhance an implant body design.

As a consequence, the decision to use a coating may be based more on the bone density than any other factor. D1 and D2 bone have the greatest strength and bone contact. There is also increased risk of material flaking from the implant during insertion. Rather than a coating, D1 and D2 implants benefit from a roughened surface, sound biomechanical design, and a minimum implant length of 10 to 11 mm. D3 bone is approximately 50% weaker than D2 bone. As a result the use of TPS can be considered in since increased initial fixation, increased bone contact, and greater strength of interface all supports its use. D4 bone has proven to be the one most at risk. Hence the benefits of HA are most required in this type of bone. Although it may have the greatest risk relative to bacteria, the benefits of gap healing, faster bone mineralization, and increased bone contact all favor HA. To minimize the crestal bone loss, larger diameter and an increased number of implants are also suggested in this very weak bone.

State of the Host Bed[12]

If available, the ideal host bed is healthy and with an adequate bone stock with adequate bone height, adequate bone width, adequate bone length and adequate bone density.

However, in the clinical reality, the host bed may suffer from previous irradiation, ridge height resorption and osteoporosis, to mention some undesirable states for implantation.

Previous irradiation need not be an absolute contraindication for the insertion of oral implants. However, it is preferable that some delay is allowed before an implant is inserted into a previously irradiated bed. Furthermore, some 10-15% poorer clinical results must be anticipated after a therapeutical dose of irradiation. The explanation for less satisfactory clinical outcome found in irradiated beds could be vascular damage, at least in part. One attempt to increase the healing conditions in a previously irradiated bed is by using hyperbaric oxygen, as a low oxygen tension definitely has negative effects on tissue repair. This is further verified by the finding that heavy smoking, causing among other things a local oral vasoconstriction, is one factor that will lower the expected outcome of an implantation procedure.

Other common clinical host bed problems involve osteoporosis and resorbed alveolar ridge. Such clinical states may constitute an indication for ridge augmentation with bone grafts. However, present clinical technique for bone grafting are under debate and it appears that 6-year success of oral implants in the 75% range is a realistic outcome after most such procedures. This figure is slightly alarming seen against the fact that, at least in the maxilla, 10-20% of an average edentulous population may be in need of a bone graft to improve the host bed and allow for the insertion of implants. On the contrary, if the bone quality and quantity in the maxilla is controlled, the expected outcome of an oral implantation procedure is similar to that of the mandible.

As stated by Branemark et al. and Misch, the bones with D1 and D2 bone densities shows good initial stability and better osseointegration. The bone densities D3 and D4 shows poor prognosis. Many authors have recommended to select suitable implants depending upon the quality and quantity of the available bone, i.e., HA coated or Ti plasma coated implants are better for D3 and D4 and conventional threaded implants for D1 and D2 bone qualities.

Surgical Considerations[13]

The main aim of the careful surgical preparation of the implant bed is to promote regenerative type of the bone healing rather than reparative type of the bone healing. If too violent a surgical technique is used, frictional heat will cause a temperature rise in the bone and the cells that should be responsible for bone repair will be destroyed. Bone tissue is more sensitive to heat than previously believed. In the past the critical temperature was regarded to be in the 56^{0}C range, as this temperature will cause denaturation of one of the bone enzymes, alkaline phosphatase. However, the critical time / temperature relationship for bone tissue necrosis is around 47^{0}C applied for one minute.[24] At a temperature of 50^{0}C applied for more than one minute we are coming close to a critical level where bone repair becomes severely and permanently disturbed.

Contamination of the implant site by organic and inorganic debris can prejudice the achievement of osseointegration. Material such as necrotic tissue, bacteria, chemical reagents and debris from drills can all be harmful in this respect.

Erickson R.A. recommended the importance of using well sharpened drills, slow drill speeds, using sharp drills, a graded series of drills (avoid making, for instance, a 4mm hole in one step) and adequate cooling by profuse irrigation. By using such a controlled technique it has been demonstrated in clinical studies that overheating may be totally avoided. The mechanical injury will of course remain and is quite sufficient to trigger a proper healing response. Erickson also recommended bone cutting speed of less than 2000 rpm and tapping at a speed of 15 rpm with irrigation.

Another surgical parameter of relevance is the power used at implant insertion. Too strong a hand will stimulate the resorption response. A moderate power at the screwing home of an implant is therefore recommended.

During the most critical steps in the surgical procedure, such as tapping the hole for the thread implant, Branemark advocates the use of an electrical machine (which works with adequate torque at low rotatory speeds). At drilling, the use of a rotatory speed of only 15-30 rpm together with adequate cooling procedures produces no heat-caused injuries.

Thus, at dental implant insertion, strict surgical routine ensuring minimal tissue violence is imperative for long term success. Careful and gentle tissue handling is essential during the entire surgical preparation, not only when cutting bone.

***Loading Conditions*[14]**

From histological investigations of animal as well as human implants we know that, irrespective of control of surgical trauma and other relevant parameters, the implant will, in the early remodeling phase, be surrounded by soft tissue. This means that some weeks after implant insertion it will be particularly sensitive to loading that results in movements, as movement will stimulate more soft tissue formation, leading eventually to a permanent soft tissue anchorage. In essence, the situation is similar to that of a fracture. Loading of an unstabilized fracture will result in soft tissue healing and poor function, whereas stabilization with plates or plaster of Paris will ensure a satisfying rigidity leading to bone healing of the fracture. The case of an implant is, in principle, very similar. Premature loading will lead to soft tissue anchorage and poor long-term function, whereas postponing the loading by using a two stage surgery will result in bone healing and positive long term function.

The length of time, loading should be avoided, is dependent on the implantation site as well as on the bone bed quality. Furthermore, there may be cases where an almost immediate loading would not disturb the bone healing response, but in general, loading must be controlled if osseointegration is to occur. Branemark with his controlled implant system advocated the use of a 3 month loading delay in the mandible and a 4-6 month delay in the healthy maxilla where the bone is, as a rule, more cancellous in character.

Furthermore, from a bone biologic point of view, a more suitable design would be to have the implant unloaded and then gradually increase the load. In the similar way Misch et al. recommended progressive loading criteria or staged loading and implant protective occlusion for better maturation of the bone surrounding the implants.

Recently, many authors are reporting the results of immediate loading of the endosseous implants. According to them the physiological loading of the healing implants promotes better osseointegration.

Sagara et al (1993) also showed evidence of osseointegration when titanium screw implants were immediately loaded with a unilateral prosthesis. Their findings showed that osseointegration did occur, although the immediately loaded implants exhibited less direct bone contact than with the delayed loading which were used as controls.

Salama et al (1995) reported on two patients in whom titanium root form implants were immediately loaded and successfully utilized to support provisional fixed restoration in the maxilla and mandible. Both the patients were followed from 37 to 40 months after implant placement and immediate loading. All implants osseointegrated and were restored with a fixed prosthesis.

Babbush and co-workers (1986) showed implant success rate of 88% to 97% over 5 to 13 years with immediate loading implants.

A connective tissue anchorage of dental implants is an indication of failure. The achievement of a solid bone anchorage for a dental implant can lead to predictable long term clinical results. This appears to depend on the control of the surgical trauma, the condition of the tissue bed, implant loading conditions and the biocompatibility of the materials used. In this manner a meticulous clinical approach can ensure a lasting and successful bone integration of an extracorporeal substitute.

Biomechanical Considerations[12-14]

Biomechanics is the scientific study of the load-force relationships of a biomaterial in the oral cavity.

Importance of Biomechanics in the Field of Dental Implants

- First, to know the loading (bite forces) exerted on the prosthesis.
- Secondly, to know the distribution of the applied forces to the implants and teeth supporting the prosthesis.
- Thirdly, the force on each implant must be delivered safely to the bony tissues which in turn depend on the shape and size of the implant.

- **Impact of implant stiffness on stress distribution**

Implants should be as stiff as possible from the biomechanical standpoint, and should have modulus of elasticity of atleast 100,000N/mm². The stiffness of an implant can also be increased by choosing an implant of larger diameter. If the diameter is increased by 30%, implant stiffness will be five times higher, and the stresses around the implant neck are thus reduced.The implant body design transmits the occlusal load to the bone. Threaded or finned dental implants impart a combination of all three force types (compressive, tensile and shear) at the interface under the action of a single occlusal load. Cylindrical implants are at highest risk for harmful shear loads under an occlusal load directed along the long axis of the implant body. As a result, cylinder implants require a coating to manage the shear stress at the interface through a more uniform bone attachment along the implant length. *Compressive forces should typically be dominant in implant prosthetic occlusion.*

- **Impact of implant shape on stress distribution**

The ***neck design*** in either implant system (i.e. root form & blade form) is particularly important in the consideration of implant geometry because the physiologic load is transmitted through the neck region to the implant body and the surrounding tissues. As the cross-sectional area of the neck decreases, the stress levels in the neck and the surrounding tissues increases. (stress= force/area.) The implant body must exhibit a macrogeometry suitable for force transfer to the surrounding tissues as well as for implantation into a bony site of a particular anatomic size.

- **Impact of implant surface on stress distribution**

Osteolytic loosening of an implant may result from selection of a biomechanically unfavorable implant shape.

This means that implant surface used for force transfer should be as large as possible. To minimize the compressive forces, the implant surface can be enlarged by:-

- Applying threads
- Plasma flame spray coating
- Surface roughening
- Acid etching

Another factor that influences the size of the surface area is the length of the implant.

In all these, the aim of biomechanical analysis is to foresee failure of any part of the system, including the prosthesis, the supporting implants and the biological tissue.

CONCLUSION

The term Osseointegration was coined by Dr Per Ingvar Branemark, Professor at the Institute for Applied Biotechnology, University of Goteborg, Sweden in the year 1985. It is defined as a direct bone deposition on implant surfaces at the light microscopic level. This functional unit able to transmit occlusal forces to the alveolar bone has also been described as functional ankylosis (Schroeder). Osseointegration, once looked upon with scepticism, is now considered as a frequently occurring, primitive foreign body reaction to an implanted material. Osseointegration mainly depends on the quality and quantity of the available bone. Various factors influence the process of osseointegration which include biocompatibility of the implant material, surface topography of the implant, the surgical protocol followed and on the loading of the implants. Systemic and local factors also influence osseointegration. Clinical results can be improved by using the newer materials, designs, surgical techniques and loading protocols by using evidence based approach.

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