Factors Affecting Osseointegration of Dental Implants: A Review

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Abstract

This literature review aimed to collect data about factors that can affect osseointegration. A comprehensive literature review can help identify the latest research findings on the subject, which can aid in the development of new approaches and strategies to optimize osseointegration and enhance the long-term stability and functionality of dental implants. To identify relevant literature an electronic search was performed using the term osseointegration and dental implant on PubMed Central. Titles and abstracts were screened and articles that fulfilled the inclusion criteria were selected for full-text reading. A review of selected articles enabled us to enlist various factors which have significant effects on osseointegration either by enhancing or inhibiting it.

Based on the review literature, each of these factors can affect the success of the implant in its own way, and therefore, careful attention to detail and proper planning is necessary to minimize the risk of complications and maximize the success rate. By understanding and optimizing these factors, dentists can provide their patients with the best possible outcomes for implant treatment.

Review (J Int Dent Med Res 2023; 16(3): 1272-1279)

Keywords: Osseointegration, Bone and implant, Factors of osseointegration, Implant-Bone surface.

Received date: 06 May 2023. **Accept date:** 27 July 2023

Introduction

Dental implants have certainly revolutionized the field of dentistry, providing a predictable and successful means of replacing missing teeth with a stable and functional solution. The discovery of osseointegration and its application to dental implants has opened new avenues for oral rehabilitation and improved quality of life for many patients. With the development of new implant designs, materials, and techniques, the success rate of dental implants has continued to increase, making them a reliable and long-lasting solution for tooth replacement.[1]

Osseointegration is a biological process in which the bone tissue directly attaches to the surface of the implant without the presence of fibrous tissue at the bone-implant interface. This process involves a complex interplay between the biomaterial properties of the implant, the biocompatibility of the material, and the mechanical environment in which the implant is placed. The end result is a stable and long-lasting anchorage of the implant in the bone, which allows for the functional restoration of missing teeth or other craniofacial structures.[2] Identifying specific biological markers that characterize pathological responses resulting in fibrosis and failure could help diagnose and monitor implant failures. Understanding the cellular and molecular mechanisms of osseointegration could also lead to the development of new treatment strategies to prevent implant failure.

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MECHANISM OF OSSEOINTEGRATION

Direct bone healing is a biological process that occurs in response to a lesion of the pre-existing bone matrix, and osseointegration follows a similar process that is divided into three stages: incorporation by woven bone formation, adaptation of bone mass to load through lamellar and parallel-fibered bone deposition, and adaptation of bone structure to load through bone remodeling.[3] Understanding the concepts of biology, physiology, anatomy, surgery, and tissue regeneration is necessary to fully understand the micro-mechanisms involved in osseointegration. Once activated, osseointegration follows a common, biologically determined program that is subdivided into 3 stages.[4,5,6]

- Incorporation by woven bone formation;
- Adaptation of bone mass to load (lamellar and parallel fibred bone deposition);
- Adaptation of bone structure to load (bone remodelling).

1. Incorporation by woven bone formation

Woven bone formation is the first stage of osseointegration and it typically occurs within the first 4-6 weeks after surgery. the newly formed woven bone provides a foundation for further bone remodeling and the gradual replacement of the woven bone with lamellar bone. The formation of woven bone is a critical stage in the process of osseointegration, as it provides initial stability and anchorage for the implant. However, complete osseointegration requires the subsequent replacement of woven bone with mature lamellar bone, which has a higher mineral density and a more organized collagen structure. This process can take several months to complete, and it is influenced by various factors, including implant design, surface characteristics, and loading conditions.[4,5,6]

2. Adaptation of bone mass to load (deposition of parallel fibered and lamellar bone)

Once the woven bone has formed, it is remodeled into a more organized, mature type of bone tissue known as lamellar bone.

• Lamellar bone is characterized by a parallel alignment of its collagen fibers, a higher mineral density, and a lower number of osteocytes than woven bone.

• Lamellar bone is able to withstand higher mechanical loads than woven bone and is therefore deposited in areas of the bone-implant interface that are subject to higher stress.

• Parallel fibred bone is another type of bone tissue that is formed during this stage. It is characterized by collagen fibers that are parallel to the bone surface, allowing for efficient load transfer between the implant and the bone.

• Adaptation of bone mass to load occurs between 6-12 weeks after surgery.[4,5,6]

3. Adaptation of bone structure to load (bone remodelling and modelling)

Once the bone mass has adapted to load, it undergoes further remodeling in response to ongoing mechanical stress.

• Bone remodeling involves the resorption of bone tissue in areas of low stress and the deposition of new bone tissue in areas of high stress.

• This ongoing process of bone remodeling allows the bone to maintain its structural integrity and adapt to changing mechanical demands.

• Bone remodeling can continue for years after osseointegration has been achieved.[4,5,6]

Overall, osseointegration is a complex process involving the formation of woven bone, the adaptation of bone mass to load, and the adaptation of bone structure to load. This process is essential for the long-term success of dental implants and requires a thorough understanding of the biological and mechanical factors involved.

FACTORS AFFECTING OSSEOINTEGRATION

During the second stage of osseointegration, adaptation of bone mass to load, the woven bone is gradually replaced by more organized and mechanically stronger lamellar bone, which is oriented parallel to the direction of load. This process is known as bone remodeling and can take several months to complete. The process of osseointegration is influenced by multiple factors and a thorough understanding of these factors is essential for achieving successful implant integration.

The successful outcome of any implant procedure is dependent on the interrelationship of the following[7]

1. Biocompatibility of the implant material: The material of the implant should be biocompatible, meaning that it does not elicit an adverse immune response or toxic reaction when it comes in contact with living tissue. Materials commonly used for dental implants include titanium, zirconia, and ceramic.
2. Macroscopic and microscopic nature of the implant surface: The surface of the implant should be designed to promote osseointegration by providing adequate roughness, porosity, and chemical properties for cell attachment and proliferation. Surface treatments such as sandblasting, acid etching, and plasma spraying are commonly used to modify the surface of the implant.
3. The status of the implant bed in both a health

(non-infected) and a morphologic (bone quality) context: The implant bed should be free from infection, inflammation, or any other condition that may impair the healing process. The quality and quantity of the bone in the implant site are also important factors that influence the success of the implant.

4. The surgical technique: The implant should be placed in the correct position and orientation, with adequate primary stability and avoidance of any damage to the surrounding structures. Proper surgical technique can minimize the risk of implant failure and promote osseointegration.
5. The undisturbed healing phase: The implant needs a sufficient time period for osseointegration to occur without any disturbance. This typically takes 3 to 6 months for the lower jaw and 6 to 9 months for the upper jaw.
6. The subsequent prosthetic design and long-term loading phase: The prosthetic design should provide functional and aesthetic restoration, with proper occlusion and distribution of forces. Long-term loading should be gradual and monitored to avoid excessive stress on the implant-bone interface, which can cause implant failure or bone loss around the implant.

The various factors affecting osseointegration can be categorized as:
According to LeGeros and Craig[8]

I. Biomaterial
II. Biomechanical
III. Biologic

Biomaterial Factors

In addition to the material itself, the surface characteristics of the implant also play a crucial role in promoting osseointegration. The implant surface can be modified to increase its roughness or porosity, which enhances its ability to integrate with bone tissue. This can be achieved through various techniques such as sandblasting, acid etching, or plasma spraying. The degree of surface roughness required for optimal osseointegration may vary depending on the type of implant and the bone quality of the patient.

It is also important to note that the surgical technique used during implant placement can greatly affect the outcome of osseointegration. Proper implant placement with adequate primary stability is critical for promoting bone formation and integration. If the implant is placed with inadequate primary stability or in a location with poor bone quality, it may not integrate properly and could result in implant failure. Additionally, any damage to the surrounding bone or soft tissue during surgery can also negatively impact osseointegration.

Biomechanical Factors

The Branemark implant system is a two-stage surgical procedure that involves the placement of a titanium implant into the jawbone during the first stage, followed by a period of osseointegration. During the second stage, a prosthesis is attached to the implant to restore function to the missing tooth or teeth. The success of this system is largely due to the extensive research and documentation by Dr. Per-Ingvar Branemark, who first discovered osseointegration in the 1950s. The Branemark system has a high success rate and has been widely adopted as the gold standard for implant dentistry.

Biologic Factors

Patient factors such as systemic diseases, medication use, smoking, poor oral hygiene, and inadequate bone quantity or quality can increase the risk of implant failure. In addition, inadequate surgical technique, implant design or material, and prosthesis loading can also contribute to implant failure. It is important for dental professionals to carefully assess and address all potential risk factors before proceeding with implant treatment to minimize the risk of failure.

According to the effect on osseointegration[9]

I. Enhancing factors
II. Inhibiting factors

Enhancing Factors

The factors that promote osseointegration include implant-related factors, the status of the host bone bed and its intrinsic healing potential, mechanical stability and loading conditions applied on the implant, use of adjuvant treatments such as bone grafting, osteogenic biological coatings, biophysical stimulation, and pharmacological agents such as simvastatin and bisphosphonates.

Implant-related factors such as implant design and chemical composition, topography of the implant surface, material, shape, length, diameter, implant surface treatment, and coatings can affect the osseointegration process by influencing the interaction between the implant and the host tissue. For example, surface topography can influence the adhesion, proliferation, and differentiation of cells on the implant surface, while coatings and treatments can affect the surface energy and wettability of the implant.

The status of the host bone bed and its intrinsic healing potential are also crucial factors for osseointegration. The quality and quantity of the bone tissue, the presence of systemic diseases, and the patient's age can affect the osseointegration process.

Mechanical stability and loading conditions applied on the implant are important for the success of osseointegration. Excessive mechanical stress can lead to implant failure, while appropriate loading can stimulate bone remodeling and enhance osseointegration.

Adjuvant treatments such as bone grafting, osteogenic biological coatings, and biophysical stimulation can also promote osseointegration by enhancing bone formation and remodeling.

Pharmacological agents such as simvastatin and bisphosphonates can also affect the osseointegration process by modulating bone metabolism and promoting bone formation.

Inhibiting Factors

Factors that can inhibit osseointegration include:

Excessive implant mobility and micromotion: excessive movement of the implant can interfere with the formation of new bone tissue around the implant.

Inappropriate porosity of the porous coating of the implant: if the porosity of the implant's porous coating is not suitable, it can prevent bone ingrowth and limit the implant's stability.

Radiation therapy: radiation therapy can damage bone tissue and impair the ability of bone to regenerate, thus inhibiting osseointegration.

Pharmacological agents: certain medications such as cyclosporin A, methotrexate, and cis-platinum, as well as anticoagulants such as warfarin and low molecular weight heparins, and non-steroidal anti-inflammatory drugs, especially selective COX-2 inhibitors, can inhibit bone healing and osseointegration.

Patient-related factors: certain patient-related factors such as osteoporosis, rheumatoid arthritis, advanced age, nutritional deficiency, smoking, and renal insufficiency can compromise bone quality and quantity, thereby inhibiting osseointegration.

Biocompatibility

The biocompatibility of dental implant materials is a crucial factor to consider because it determines the success or failure of the implant. The factors you mentioned - chemical composition, mechanical properties, electrical charge, and surface features - all play a role in determining the biocompatibility of a material.[10] Chemical composition refers to the elements and compounds that make up the material. Certain materials may cause adverse reactions or toxic effects when they come into contact with bodily fluids or tissues. Therefore, it is essential to choose materials that are inert and non-toxic to the body. Mechanical properties refer to the ability of a material to withstand stress and deformation. Dental implants are subjected to significant mechanical stresses, and materials with high strength and toughness are preferred. If the implant material is too brittle, it may fail or fracture under the stresses of normal use.[10]

Electrical charge is another important factor to consider. Materials with an electrical charge can interact with the surrounding tissues and cells, potentially causing inflammation or other adverse reactions. It is essential to choose materials with a neutral or slightly negative charge to minimize these effects. Finally, surface features such as roughness or smoothness can also influence the biocompatibility of a material. A rough surface can promote better integration with surrounding tissues, while a smooth surface may be less likely to cause irritation or inflammation.[11] Overall, the biocompatibility of dental implant materials is evaluated by studying the reaction between the implant and the bone (Table 1). This involves assessing the implant's ability to integrate with the surrounding bone tissue and avoid adverse reactions such as inflammation or infection.

Titanium is the most widely used material for implants. Other materials have been proposed as well, including various ceramics, polymers, and composites, but titanium remains the most widely used due to its excellent biocompatibility and mechanical properties. Additionally, the oxide layer on its surface allows for improved osseointegration, which is essential for the success of implant procedures.[10,11]

DEGREE OF COMPATIBILITY	CHARACTERISTIC OF REACTIONS OF BONY TISSUE	MATERIALS
Bio-tolerant	Implant separated from adjacent bone by a soft tissue layer along most of the interface *Distant osteogenesis*	• Stainless steels polymers • Co-Cr-Mo • Co-Cr-Mo Ni alloys
Bio-inert	Direct contact to bony tissue *Contact Osteogenesis*	Ceramics - Aluminum oxide, zirconium oxide titanium, tantalum niobium, carbon.
Bio-active	Bonding to bony tissue *Bonding Osteogenesis* (Bio-integration)	Ceramics - Glass ceramic, calcium phosphate containing glasses (hydroxyapatite)

Table 1. The reaction between the implant and the bone.

Ceramics are a type of substance made by compressing and heating inorganic, non-metallic, and non-polymeric materials. These materials can be classified as metallic oxides or other compounds. Oxide ceramics have been used to make surgical implants due to their resistance to biodegradation, strength, physical attributes like color, low thermal and electrical conduction, and varying elastic properties. Despite these advantages, the ceramics' low ductility and brittleness have posed some limitations in certain cases[11,12]

Zirconia, or ZrO2, is a type of ceramic material that is commonly used in implantology due to its biocompatibility, tooth-like color, and superior mechanical properties compared to alumina. ZrO2 implants are highly resistant to corrosion, flexion, and fracture, and are biocompatible, bioinert, and radiopaque. They can be used to make entire implants or coatings and have a similar contact with bone and soft tissue as titanium implants, with a thicker proteoglycan layer at the interface.[11.12]

On the other hand, Polyetheretherketone (PEEK) is an organic synthetic polymeric material that was developed in 1978. It belongs to the poly-aryl-ether-ketone polymer family and has good chemical resistance, high mechanical properties, and biocompatibility. PEEK is used as an implant superstructure, abutment, and implant fixture in areas where esthetics is a major concern, as it has a tooth-colored appearance. PEEK has a Young's modulus similar to that of cortical bone, which reduces stress shielding compared to titanium materials. To enhance its osseoconductive properties, PEEK can be coated and blended with bioactive particles, and various modifications have been made to improve its surface characteristics and biocompatibility.[13]

Wettability

The level of contact between a dental implant surface and its surrounding environment is influenced by the surface wettability, as illustrated in Figure 10.1. Surfaces that are highly hydrophilic are generally preferred over hydrophobic ones due to their better interactions with biological fluids, cells, and tissues. If a liquid can completely spread and cover a surface, it indicates that the material has high surface energy, is biocompatible, and hydrophilic. To clarify, it's actually surface free energy that is thought to play a role in osseointegration. Materials with high surface free energy can more easily adsorb proteins and other biomolecules, providing more favorable sites for cell attachment and promoting osseointegration. Typically, materials with a surface free energy within the range of 20 to 30 mJ/m² exhibit low adhesion, while materials with surface free energy above this range tend to show better outcomes for osseointegration. However, it's important to note that surface free energy is just one of many factors that can influence osseointegration, and the optimal surface characteristics for promoting osseointegration may vary depending on the specific material and application.[11]

INFLUENCE OF BONE

In theory, when considering implants with identical dimensions, the selection of surface finishing should be based on the type of bone that the implant will be placed in. Misch suggests that bone density can be classified and correlated with Hounsfield units.[3]

D1 bone is composed of dense cortical and trabecular bone. During surgery, there is typically little bleeding in D1 bone, indicating lower vascularization. Since it is harder than other types of bone, extra care should be taken when preparing the implant insertion site to prevent overheating. Localized heating can help prevent initial necrosis, which may be prolonged by ischemia caused by the implant compressing the bone walls and maintaining the contact area of bone in a compressed state. Implants with a length of 10 mm are typically suitable for use in D1 bone. The type of bone where the implant will be placed is an important consideration for achieving successful osseointegration. D1 and D2 bones are considered to be favorable for implant placement, while D3 and D4 bones are more challenging due to their lower mechanical strength and density. For D3 and D4 bone, implants with a treated surface area are recommended to improve the implant's initial stability and osseointegration. Larger implants with a larger diameter are also recommended for D4 bone. Careful surgical technique is necessary to avoid damaging the fragile bone during implant placement. (Table 2)

BONE QUALITY	HOUNSFIELD UNITS	DESCRIPTION	Typical anatomic location
D1	>1250	Dense cortical	Anterior mandible
D2	850-1250	Porous cortical and coarse trabecular	Anterior mandible Posterior mandible Anterior maxilla
D3	350-850	Porous cortical (thin) and fine	Anterior maxilla Posterior maxilla Posterior mandible
D4	150-350	Fine trabecular	Posterior maxilla

Table 2. Surgical technique is necessary to avoid damaging the fragile bone.

Surface characteristics of implants

The appropriate surface characteristics of implant surfaces are crucial for successful osseointegration. Roughened surfaces, including macro-textured and micro-textured surfaces, are generally more favorable for osseointegration compared to smooth surfaces. The surface roughness promotes direct osteoblast attachment and proliferation, enlarges the implant area in contact with the host bone, and promotes platelets and monocytes adhesion. Surface roughness also promotes both distance and contact osteogenesis. Moderate surface roughness is better for peri-implant bone growth than smoother or rougher surfaces. Moreover, a pore size above 80 micrometers is associated with improved bone ingrowth. The surface chemistry of implant coatings, such as ceramic-coated surfaces, also plays an important role in promoting osseointegration.[12]

Implant bone bed

In addition to proper cooling during implant bed preparation, the use of proper implant placement techniques can also impact osseointegration. For example, precise implant placement with a minimal gap between the implant and the surrounding bone can improve initial stability and reduce micromotion, which can inhibit osseointegration. The use of bone grafting materials or growth factors can also improve the quality and quantity of bone at the implant site, leading to improved osseointegration. Proper soft tissue management during implant placement is also important. Adequate soft tissue coverage can help prevent bacterial contamination and provide a favorable environment for wound healing. In addition, proper flap design and tension-free closure can reduce the risk of soft tissue dehiscence and promote proper wound healing.[3]

Finally, post-operative care and follow-up are crucial to the success of osseointegration. Proper oral hygiene, including regular brushing and flossing, can help prevent peri-implantitis and ensure long-term stability of the implant. Regular follow-up appointments with the dentist or periodontist can help detect any potential issues early and address them before they become more serious problems

Primary stability

In addition to implant design and surgical technique, bone quality and quantity are also important factors that affect primary stability. Poor bone quality or insufficient bone density may compromise primary stability, leading to implant failure. In cases where there is inadequate bone quantity or quality, bone grafting or other augmentation procedures may be necessary to improve the implant site before placement.[14]

Implant diameter and length also play a role in achieving primary stability. A larger diameter implant can provide better initial anchorage and resistance to lateral forces. A longer implant can engage a greater amount of bone, increasing the surface area of contact and improving primary stability.[15]

To achieve primary stability, the implant must be placed in the correct position and orientation within the bone bed. Accurate implant placement can be facilitated with the use of surgical guides or navigation systems. Proper insertion torque is also important, as over-tightening can lead to mechanical damage to the bone and under-tightening can compromise primary stability.[16]

In summary, achieving primary stability is crucial for successful osseointegration of dental implants. It depends on various factors such as bone quality and quantity, implant design, surgical technique, and accurate placement. Careful consideration of these factors can help ensure optimal outcomes for implant placement.[17]

MICROMOTION

Micro-motion at the bone-implant interface can affect the success of osseointegration. Some level of micro-motion is actually beneficial, as it stimulates bone formation. However, excessive micro-motion can lead to fibrosis and bone resorption at the interface, which can compromise the implant's stability and long-term success. The threshold for harmful levels of micro-motion is typically between 50 and 150 μm, with larger magnitudes of micromotion associated with a higher risk of implant failure. Factors that can affect the amount of micromotion at the interface include the design and surface characteristics of the implant, the surgical technique used, and the loading conditions placed on the implant.[18]

Bone-implant gap

An optimal gap size between the implant body and host bone is important for optimal osseointegration. An appropriate area between the implant and host bone enables the migration of osteogenic cells from the bone marrow towards the implant surface, which promotes rapid and extensive osteogenesis. However, when bone is in tight contact with the implant surface, poor bone formation or even bone resorption may occur. Conversely, gaps that exceed 500 μm can reduce the quality of newly formed bone and delay the rate of gap filling. Therefore, finding an appropriate balance between the implant body and host bone is crucial for optimal osseointegration.[20]

Growth factors

Several growth and differentiation factors have been used either alone or combined as bio coatings of conventional implants to accelerate and enhance the bone ingrowth and to strengthen implant fixation. Various techniques have been developed to modify the surface properties of implants to improve osseointegration. These techniques include acid etching, anodization, and plasma spraying, which alter the surface topography and create micro- and nano-scale roughness that enhances bone cell adhesion and proliferation. Surface modification can also involve the incorporation of bioactive molecules or peptides that promote cell adhesion and differentiation, such as bone morphogenetic proteins (BMPs) AND growth factors like platelet-derived growth factor (PDGF), insulin-like growth factor (IGF), and transforming growth factor-beta 1 (TGF,β-1). Other biological coatings that have been used to improve the osseointegration of titanium implants include collagen and other extracellular matrix proteins such as fibronectin and vitronectin.[21]

Conclusions

A successful outcome in implant dentistry depends on a combination of various factors that influence the prognosis and long-term results of the procedure. These factors include not only 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. Each of these factors can affect the success of the implant in its own way, and therefore, careful attention to detail and proper planning is necessary to minimize the risk of complications and maximize the success rate. By understanding and optimizing these factors, dentists can provide their patients with the best possible outcomes for implant treatment.

Declaration of Interest

The authors report no conflict of interest.

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