Implant and Bone Augmentation Materials

A critical problem in dentistry is treating the edentulous patient. According to a survey by the World Health Organization, 26% of the US population older than 65 years is totally edentulous, and a substantial number of other patients are partially edentulous, having an average of 10 missing teeth[Au: Please reference.]. Although removable dentures and fixed partial dentures offer effective treatments for many edentulous patients, those who have lost substantial tooth-bearing portions of bone and cannot manage prostheses or masticate properly can improve their oral function through the use of dental implants.

The use of implants as a means of treating these patients has accelerated in the last two decades, and there are now more than 1 million dental implants in use in the United States. Dental implants are effective in providing long-term total and partial support for restorations. Despite the expanded use of implants, however, they are largely evaluated only on a qualitative level. To better understand and quantify the clinical effectiveness of dental implants, a greater understanding of the parameters governing the long-term success of this complex material/tissue aggregate is needed.

In this chapter, design considerations important to implant dentistry are presented. Following an overview of general concepts and indications for implant use, osseointegration is defined and discussed, methods of achieving osseointegration are presented, and parameters important to achieving implant success are reviewed, with a primary focus on biomaterials and biomechanical factors.

Indications for Dental Implant Use

The general requirement for dental implants is adequate bone to support the implant with the physiologic parameters of width, height, length, contour, and density. Note that the importance of these parameters varies, depending on the specific implant type (Table 23-1). Despite the "glamour" of the implant dentistry, a conservative treatment protocol must be stressed. Dental implants should not be the first treatment option considered. Unsatisfactory treatment with removable dentures or fixed partial dentures is often an important indication for implant use. A number of contraindications for implant use also exist (Box 23-1).

Box 23-1 Contraindications for dental implant use[1]

Unattainable prosthodontic reconstruction

Patient sensitivity to implant component(s)

Debilitating or uncontrolled disease

Pregnancy

Inadequate practitioner training

Conditions, diseases, or treatments that may compromise healing (ie, radiation therapy)

Poor patient motivation/hygiene

Perceived poor patient compliance

Unrealistic patient expectations

Table 23-1 Summary of dental implant types and indications for each[1]

IMPLANT TYPE	INDICATIONS
Endosseous	
Cylindrical	Adequate bone to support implant—width and height of primary concern Maxillary and mandibular arch locations Completely or partially edentulous patients
Blade	Adequate bone to support implant—width and length of primary concern Maxillary and mandibular arch locations Completely or partially edentulous patients
Ramus frame	Adequate anterior bone to support implant—width and height of primary concern Mandibular arch location Completely edentulous patients
Subperiosteal	
Complete	Atrophy of bone, but adequate and stable bone to support implant
Unilateral	Maxillary and mandibular arch locations
Circumferential	Completely and partially edentulous patients
Transoseous	
Staple	Adequate anterior bone to support implant—width and height of primary concern
Single pin	Anterior mandibular arch location
Multiple pin	Completely and partially edentulous patients

■ Types of Implants

Dental implants are classified into three categories (see Table 23-1, Fig 23-1).

1. *Endosseous implants* are embedded in mandibular or maxillary bone and project through the oral mucosa covering the edentulous ridge.
2. *Subperiosteal implants* rest on the surface of the bone beneath the periosteum.
3. *Transosseous implants* penetrate the inferior mandibular border and also project through the oral mucosa covering the edentulous ridge.

Root-form endosseous screw-threaded implants are the most common implants in clinical practice. This subclass of implants is the only one for which good long-term (eg, 10- to 15-year) clinical tracking of large patient populations is available. Success rates for implants placed in the mandible are approximately 95% at 5 years and greater than 85% at 15 years. For maxillary implants, success rates are approximately 85% to 90% at 5 years and 80% at 15 years. The clinician's expertise and surgical technique are more important than the specific implant and are the primary factors dictating clinical outcome.

■ Osseointegration

Unlike many biomaterials, which serve to replace as much of a tissue's natural structure and function as possible, dental implants do not restore function by mimicking the natural function of the periodontal ligament (Fig 23-2). Instead, **osseointegration**, or the direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant, is what should occur with a well-functioning implant. This definition was originally based on retrospective radiographic and light microscopic observations and has since been modified based on scanning and transmission electron microscopic observations. However, the general working def-
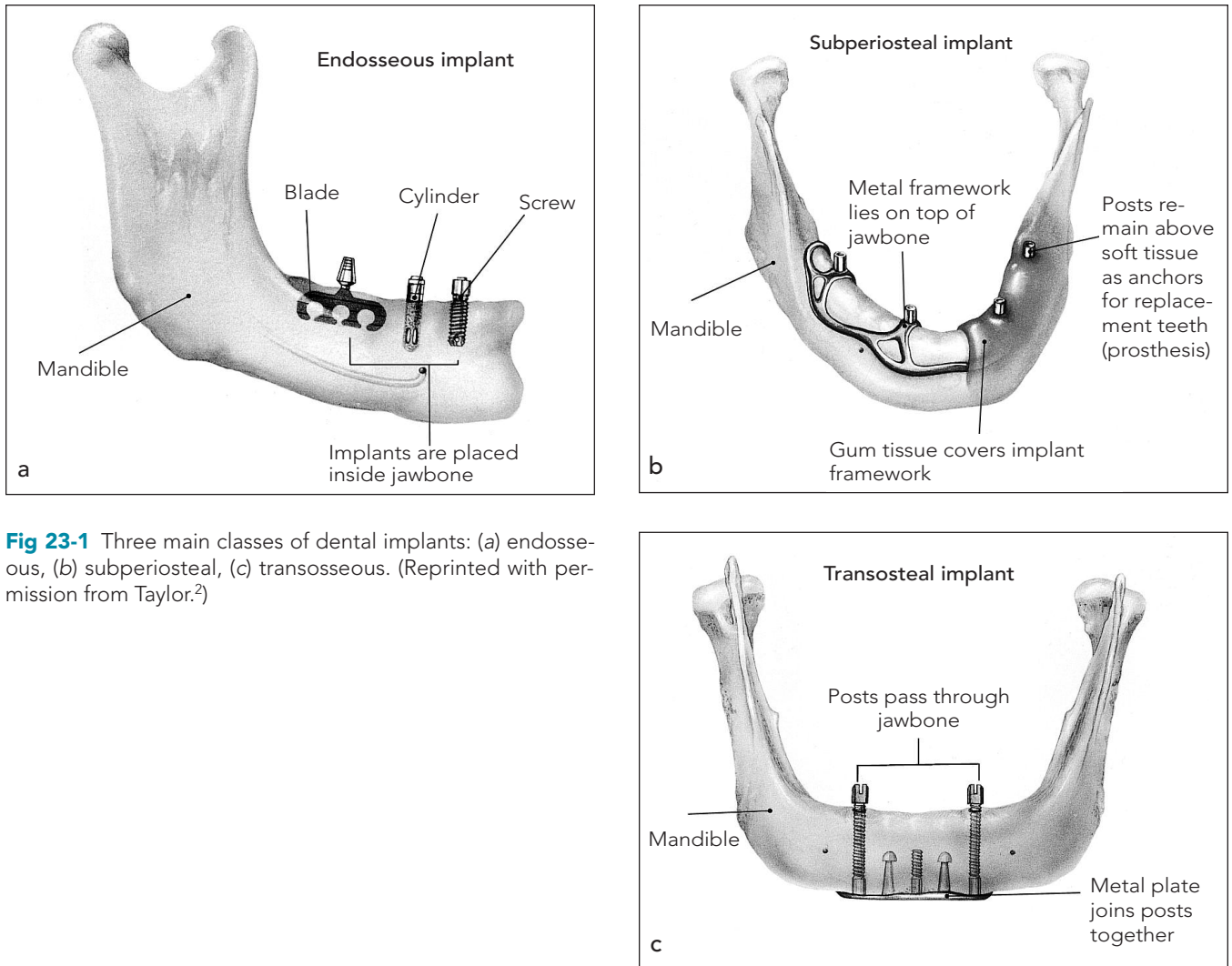
Fig 23-1 Three main classes of dental implants: (*a*) endosseous, (*b*) subperiosteal, (*c*) transosseous. (Reprinted with permission from Taylor.[2])

inition of osseointegration is fundamentally the same—the host bone responds in a safe, predictable, and versatile manner, to surgical placement of an implant in a sterile wound, with a healing cascade leading to interfacial osteogenesis and mechanical stability of the implant (Fig 23-3). In a well-functioning implant, interfacial osteogenesis and clinical stability are achieved (Fig 23-4a), and a stable marginal bone level is maintained. In comparison, poorly differentiated connective tissue adjacent to an implant leads to clinical mobility and implant failure (Fig 23-4b).

There are a multitude of interrelated clinical, biologic, and engineering factors that control the oral cavity's response and dictate the success of osseointegration.

Achieving and enhancing implant-tissue attachment

An implant must be capable of carrying occlusal stresses. In addition, stresses must be transferred to the adjacent bone. Not only must stresses be transferred across the implant-tissue interface, but they must be of a "correct" orientation and magnitude so that they mimic the normal physiologic stresses and allow tissue viability to be maintained. The ability to transmit stress from the implant to the adjacent bone is largely dependent on attaining interfacial fixation. Thus, the interface must stabilize in as short a time postoperatively as possible and remain stable for as long a time as possible.
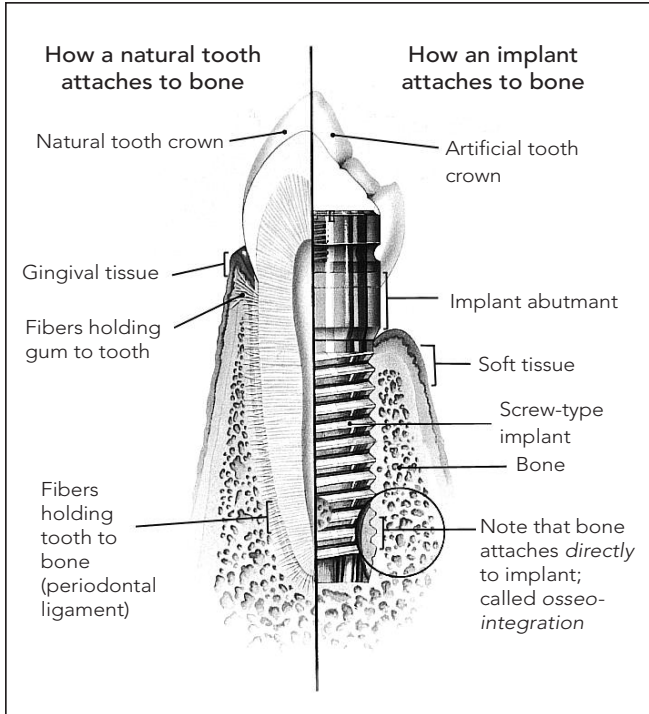
Fig 23-2 Schematic of natural tooth vs implant attachment to bone. (Reprinted with permission from Taylor.[2])
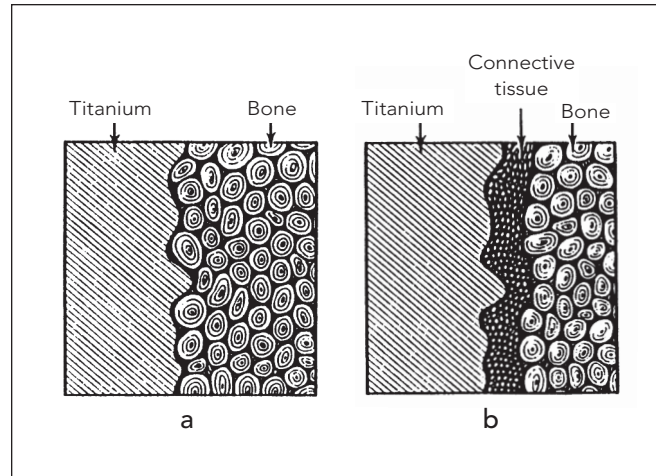

Fig 23-3 Schematic of localized sections of interfacial zone, showing (a) osseointegrated and (b) fibrous-integrated tissue adjacent to implant surface. Osseointegration is more likely with a greater implant stability, as excess tissue-implant–relative motion may result in fibrous-integrated tissue. **[Au: Edit OK?]**(Reprinted with permission from Brånemark et al.[3])
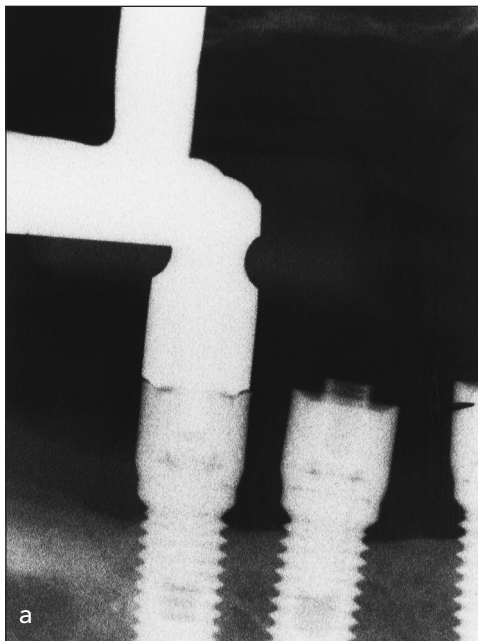

Fig 23-4 Radiographic example of (a) well-functioning and (b) failing dental implants. (a) A well-osseointegrated interfacial zone provides interfacial stability, whereas (b) a poorly differentiated interfacial connective tissue leads to mobility and implant failure.

Fig 23-5 Schematic of interfacial zone, showing constituents: bulk metal, metal oxide, proteoglycans, connective tissue, disordered and ordered bone, and relative proportions of each for good and poor osseointegration. (Reprinted with permission from Brånemark et al.[3])
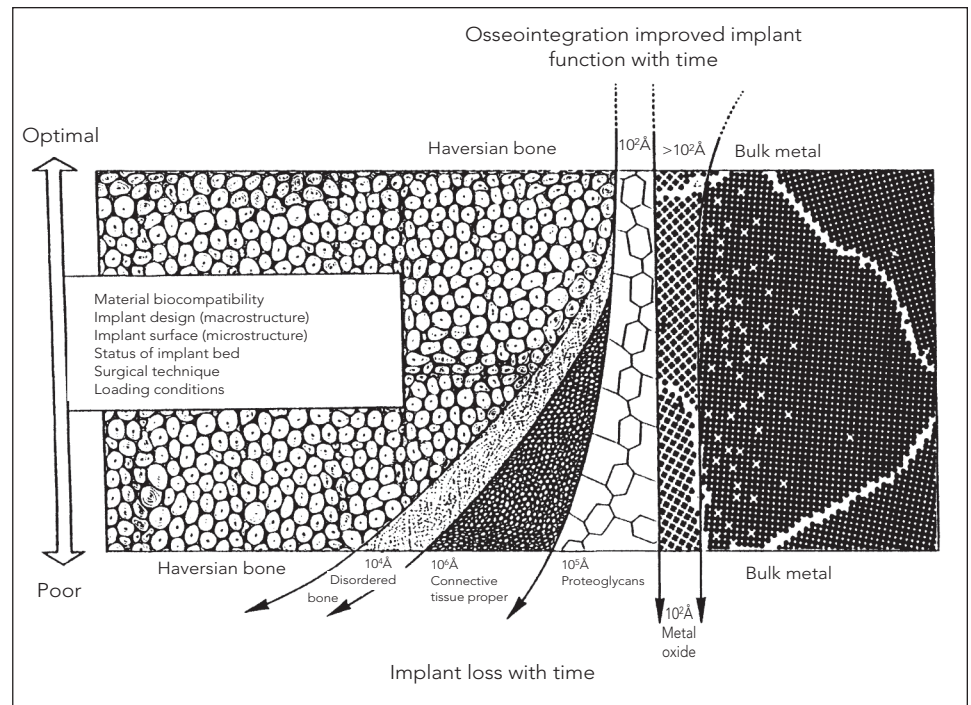
Developing an "optimal" implant that meets all of these objectives requires the integration of material, physical, chemical, mechanical, biologic, and economic factors. While all of these properties are important, they cannot all be optimized in a given design. Optimization of one property often detracts from another. Thus, in designing a dental implant and in choosing an implant for a specific clinical scenario, a ranking of requirements and objectives is necessary.

In an ideal situation, such as that achieved with commercially pure titanium (CPTi), calcified tissue can be observed within several hundred Angstroms of the implant surface. In Fig 23-5, a layer of proteoglycans 200 to 400 Å thick lies adjacent to the metal oxide, and collagen filaments can be observed about 200 Å from the surface. Less than optimal surgical techniques or implant surface chemistry and relative motion between the implant and tissue can lead to a thicker zone of proteoglycans, soft connective tissue, and disordered bone.

Because a stable interface must be developed before loading, it is desirable to accelerate tissue apposition to dental implant surfaces. Material developments that have been implemented in clinical practice include the use of surface-roughened implants and bioactive ceramic coatings. Other, more experimental techniques include electric stimulation, bone grafting, and recombinant growth factors. [Au: Are all these techniques still considered experimental?]

A variety of implant surface configurations can improve the cohesiveness of the implant-tissue interface, leading to increased transfer of occlusal loads to the adjacent tissue that minimizes relative motion between implant and tissue, fibrous integration, and ultimately loosening, thereby lengthening the service life of the implant. Metal implant surfaces may be smooth, textured, screw threaded, plasma sprayed, or porous coated. By far, the most common surface configuration is the screw-threaded dental implant. Osseointegration around screw-threaded implants occurs through tissue ongrowth, or direct apposition between tissue and the implant surface. Alternative methods of implant-tissue attachment, based on tissue ingrowth into roughened or three-dimensional surface layers, yield higher bone-metal shear strength than other types of fixation. Increased interfacial shear strength results in a better stress transfer from the implant to the surrounding bone, a more uniform stress distribution between the implant and bone, and lower stresses in the implant. In principle, the result of a stronger interfacial bond is decreased implant loosening.

A progression of surfaces from the lowest implant-tissue shear strength to the highest is as follows: smooth, textured, screw threaded, plasma sprayed, and porous.

Two factors must be stressed, though. First, different surface structures necessitate different osseointegration times. Second, surface roughening, particularly of titanium-based materials, results in reduced fatigue strength. Thus, improvements in implant-tissue attachment strength are often countered by a loss of structural strength and must be met with design compromises to avoid material failure.

◉ Criteria for Successful Implant Placement

Three aspects of an implant-tissue system are important in determining clinical success: *(1)* the implant material(s) and adjacent tissue(s), *(2)* the **interfacial zone** between the implant and tissue, and *(3)* the effect of the implant and its breakdown products on the local and systemic tissues. Although the interfacial zone is composed of a relatively thin (< 100 µm) layer consisting of heterogeneous metallic oxide, proteinacious layer and connective tissue, it has an effect on the maintenance of interfacial integrity. The integrity of the implant-tissue interface is also dependent on material, mechanical, chemical, surface, biologic, and local environmental factors, all of which change as functions of time in vivo. In addition, implant "success" is dependent on the patient's overall medical and dental status, the surgical techniques used, and the extent and time course of tissue healing. The focus of this section is on the biomaterial and biomechanical factors, summarized in Fig 23-6.

Surgical parameters

Adequate preparation of bone is critical for bone-cell survival, well-ordered connective tissue apposition close to an implant surface, the establishment of a reliable bone anchor, and long-term implant and tissue viability. Poor surgical technique or premature functional loading may result in an inability to achieve osseointegration, a fibrous adaptation, and an early implant failure. The standard clinical protocol therefore calls for a two-stage implant placement. The stage-one surgery involves the careful preparation of the implant site in a manner that minimizes trauma and optimizes healing and interfacial osteogenesis. Certain thermal limits should not be exceeded during surgery. If these temperatures are exceeded, thermal necrosis can occur, resulting in a thicker layer of soft tissue directly apposing the implant surface and jeopardizing osseointegration. Following the initial surgery, the im-

plants undergo a submerged healing in situ for 3 to 6 months. During this period, ordered, living bone, with the potential for ultimately carrying occlusal loads, develops within the interfacial zone. **[Au: What does the stage-two surgery involve?]**

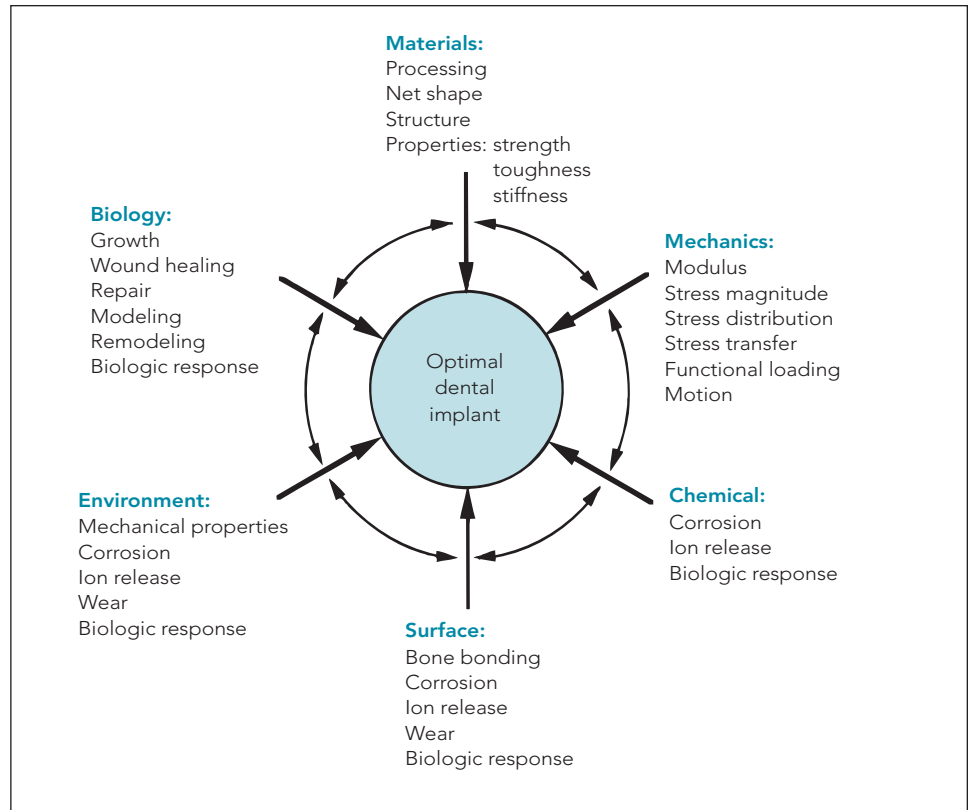## Surface chemistry and biologic response

Implant materials may corrode and/or wear, leading to the generation of micron- or submicron-sized debris that may elicit both local and systemic biologic responses. Metals are more susceptible to electrochemical degradation than ceramics. Therefore, a fundamental criterion for choosing a metallic implant material is that it elicits a minimal biologic response. **Titanium**-based materials are well tolerated by the body because of their passive oxide layers. The main elemental constituents as well as the minor alloying constituents can be tolerated by the body in trace amounts. However, larger amounts of metals usually cannot be tolerated. Therefore, minimizing mechanical and chemical breakdown of implant materials is a primary objective.

Local accumulation of material around an implant may include membrane-bound ions released due to wear or fatigue processes or insoluble reaction products. Excessive metal ion accumulation can lead to metallosis or tissue discoloration and also to reduced phagocytosis and cytoxicity.

Understanding implant surface chemistry is important to ensure that *(1)* implant materials must not adversely affect local tissues, organ systems, and organ functions, and *(2)* the in vivo environment must not degrade the implant and compromise its long-term function. The interfacial zone between an implant and the surrounding tissue is therefore the most important entity in defining the biologic response to the implant and the response of the implant to the body.

The success of any implant depends on its bulk and surface properties, the site of implantation, tissue trauma during surgery, and motion at the implant-tissue interface. The surface of a material is almost always different in chemical composition and morphology than the bulk material. These differences arise from the molecular arrangement, surface reactions, and contamination. Interface chemistry is therefore determined primarily by the properties of the metal oxide and not as much by the metal itself.

Fig 23-6 Schematic of interdependent engineering factors that affect the success of dental implants. (Reprinted with permission from Kohn.[4])

Materials:
Processing
Net shape
Structure
Properties: strength
toughness
stiffness

Biology:
Growth
Wound healing
Repair
Modeling
Remodeling
Biologic response

Mechanics:
Modulus
Stress magnitude
Stress distribution
Stress transfer
Functional loading
Motion

Optimal
dental
implant

Environment:
Mechanical properties
Corrosion
Ion release
Wear
Biologic response

Chemical:
Corrosion
Ion release
Biologic response

Surface:
Bone bonding
Corrosion
Ion release
Wear
Biologic response

Metallic oxides dictate the type of cellular and protein binding at the implant surface. Surface oxides are continually altered by the indiffusion of oxygen, hydroxide formation, and the outdiffusion of metallic ions. Thus, a single oxide stoichiometry does not exist. The surface potential may also play an important role in osseointegration. For example, oxides with high dielectric constants may inhibit the movement of cells to an implant surface. Last, the type and orientation of cells attaching to metal surfaces is influenced by the microscopic geometry of the substrate surface.

Mechanical parameters

Mechanical properties important in designing implant materials include stiffness, yield and ultimate strengths, fracture toughness, and fatigue strength. Stiffness, or modulus of elasticity, dictates, to a large extent, the ability of the implant to transmit stresses to the adjacent tissue and maintain tissue viability over time. Static and fatigue strengths obviously are important in minimizing material failures. Fracture toughness is a gauge of the energy needed to cause failure in the presence of a defect, and is a critical parameter in evaluating implants with surface contours that could serve as stress raisers.

Implants are subjected to axial, shear, bending, and torsional loads, so, in addition to the magnitude of the loading, directionality must also be considered. With the above-mentioned considerations and only a qualitative knowledge of "*stability*"—the maximum allowable displacement at an implant-tissue interface that will still result in osseointegration and bone maintenance—it must be stressed that the time at which an implant can begin to undergo loading is most likely implant- and location-specific and generally unknown.

Although rare, material failure of implants, generally by fatigue, does occur. Failure of implant structures or abutments should be not disregarded or viewed as isolated instances. Fatigue of implant materials is clinically important for several reasons. First, fatigue properties of implant materials should be accurately quantified so improvements in implant design may be achieved. Second, the stress distribution between an implant and surrounding bone tissue depends on the section size of the implant as well as the elastic moduli of both the implant and tissue. Therefore, use of a larger, stiffer implant to avoid mechanical failure may result in less stress transfer to the adjacent bone. Third, coated implants may undergo local fracture processes that do not necessarily compromise
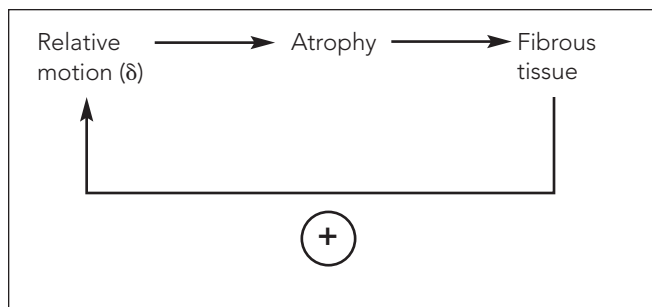
Fig 23-7 Schematic of positive feedback mechanisms leading to implant loosening. (Reprinted with permission from Kohn.[4])

the integrity of the implant but do compromise its functionality and ability to transmit stress to tissue.

Implant design

The design of dental implants is based on many interrelated factors, including the geometry of the implant, how this geometry affects mechanical properties, and the initial and long-term stability of the implant-tissue interface. There is no singularly agreed-on design criterion. Implants can be designed to maximize strength, interfacial stability, or load transfer, with each of these criteria requiring different material and interface properties. Two goals of any implant design are to maximize initial stability (ie, through implant design and surgical precision, create as tight a fit as possible at the time of surgery and accomplish osseointegration in as short a time as possible following implant placement) and minimize loosening (ie, maintain osseointegration for as long a time as possible following achievement of stability).

To ensure osseointegration and achieve the potential benefits of biologic fixation, the interface must be stable (ie, relative motion must be minimized) before loading and throughout the service life of the device. However, there is no quantitative definition of stability, only the qualitative understanding that excessive relative motion at the implant-tissue interface leads to bone atrophy and the formation of a fibrous tissue layer, further increasing motion (Fig 23-7).

Quantifying stresses and strains in implants, tissues, and implant-tissue interfaces is important for understanding mechanically mediated response mechanisms and for implant design. Implant and tissue geometry, elastic properties, loading, boundary conditions, interface conditions, and local stresses and strains are all important.

Biologic parameters and properties of tissue

Perhaps more important than the definition of osseointegration is the corollary that the creation and maintenance of osseointegration depends on the understanding of the tissue's healing, repair, and remodeling capacities. Dental implant design and function, therefore, are not only based on material considerations but also on the properties of the surrounding tissue.
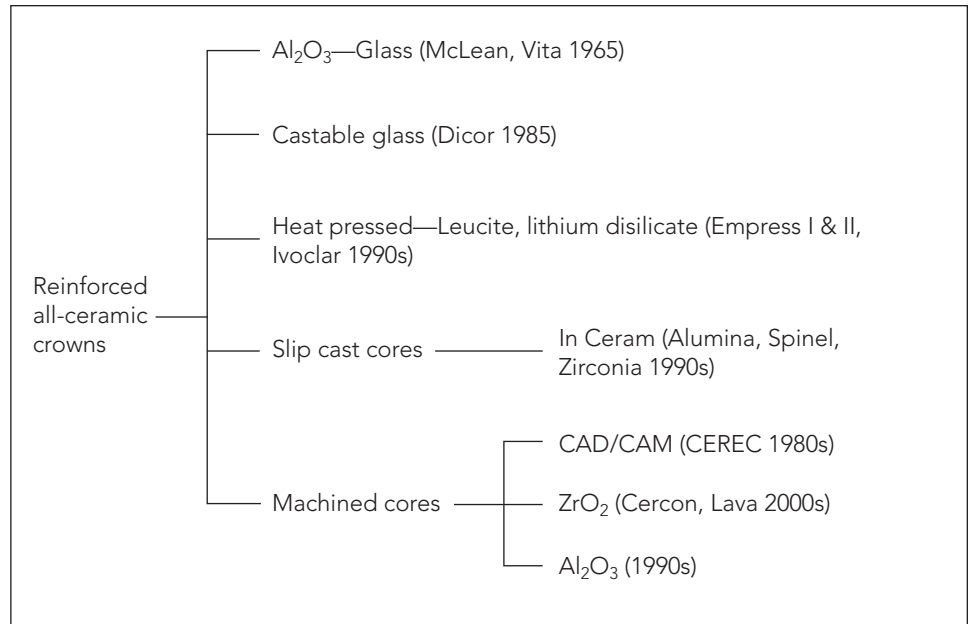
The microstructure of the mandible and maxilla is complex. For example, the basilar and alveolar bone of the mandible—which has no well-defined boundary between the two—is composed of secondary Haversian bone, regular and irregular primary lamellar bone, and plexiform lamellae of varying orientations. [AU: Edit OK?] The basilar bone forms the body of the mandible. Alveolar bone, formed in conjunction with tooth eruption, is a thin lamella that surrounds the tooth roots, attaches to the periodontal ligament fibers, and is surrounded by another layer of bone that supports the tooth sockets.

The material and mechanical properties of the mandible and maxilla are nonuniform and vary as functions of anatomic location, age, sex, and metabolic state. Variations in these properties are functions of variations in composition and microstructure. The understanding of synthetic materials at an atomic level holds true for tissue also. In biologic materials, it is necessary to understand mechanisms at the cellular and molecular levels. An understanding of regional properties will provide a better understanding of localized bone regeneration, repair, modeling, remodeling, and disease states and possibly facilitate the design of site-specific dental implants and bone augmentation materials.

◉ Materials Used in Dental Implants

Two classes of materials—metals and ceramics—are used in dental implants, either alone or in hybrid fashion (Fig 23-8). Metallic implant materials are largely titanium based, either CPTi or Ti-6Al-4V alloy. However, the synergistic relationship among processing, composition, structure, and properties of both the bulk metals and their surface oxides effectively leaves more than two metals. Processing conditions, such as casting, forging, and

Fig 23-8 Classification of dental implant materials.

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                                 ┌─── Al₂O₃—Glass (McLean, Vita 1965)

                                 ├─── Castable glass (Dicor 1985)

                                 ├─── Heat pressed—Leucite, lithium disilicate (Empress I & II,
                                 │    Ivoclar 1990s)
             Reinforced
             all-ceramic ────────┤
             crowns              ├─── Slip cast cores ───── In Ceram (Alumina, Spinel,
                                 │                          Zirconia 1990s)

                                 │                          ┌── CAD/CAM (CEREC 1980s)
                                 └─── Machined cores ────────┼── ZrO₂ (Cercon, Lava 2000s)
                                                             └── Al₂O₃ (1990s)
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machining of metal implants, densification of ceramics, deposition of ceramic and metal coatings onto metal implants, as well as cleaning and sterilization procedures, can all alter the microstructure, surface chemistry, and properties, primarily through temperature and pressure effects.

Metals

Metallic dental implants are almost exclusively titanium based. A good deal of the knowledge about titanium stems from the extensive aerospace and metallurgy literature. Many requirements of an aerospace component, primarily high strength and corrosion resistance, are characteristic properties needed in a dental implant. Thus, titanium has been called the "material of choice" in dentistry because of its strength and the minimal biologic response it elicits. The strength of titanium is due to its hexagonal close-packed crystal lattice and crystallographic orientation, whereas its biocompatibility (corrosion resistance) is attributed to its stable, passive oxide layer.

Titanium-based implants are in their passive state (ie, their oxide is stable) under typical physiologic conditions, and breakdown of passivity should not occur. Both CPTi and Ti-6Al-4V alloy possess excellent corrosion resistance for a full range of oxide states and pH levels. It is the coherent oxide layer and the fact that titanium repassivates almost instantaneously that renders titanium so corrosion resistant. However, even in its passive condition, titanium

is not "inert." The release of titanium ions that does occur results from chemical dissolution of titanium oxide. However, the low dissolution rate and relative nonreactivity of titanium dissolution products allow bone to thrive and therefore osseointegrate with titanium.

The Ti-6Al-4V alloy has a 60% greater strength than pure titanium, but it is more expensive. Both CPTi and Ti-6Al-4V alloy have complex, heterogeneous surface oxides. There may be differences in cell adhesion, and tissues may be in closer proximity to pure titanium surfaces than to alloy surfaces. However, there does not seem to be any difference in implant function between the two types of titanium.

The mechanical properties of titanium-based materials are well established. Microstructures with a small (< 20 µm) grain sizes have the highest fatigue strength (approximately 500 to 700 MPa). Surface roughening, whether through screw threading or deposition of coatings, results in a reduced fatigue strength compared with smooth-surfaced implants.

Ceramics

The initial rationale for using ceramics in dentistry was based on the relative biologic inertness of ceramics compared with metals. Ceramics are fully oxidized materials and therefore chemically stable. Thus, ceramics are less likely to elicit an adverse biologic response than metals, which only oxidize at their surface. Ceramics promote os-

seointegration by nature of their excellent osteoconductivity of host cells.

Three types of "inert" ceramics of interest are carbon, alumina (Al_2O_3), and zirconia (ZrO_2). Recently, a greater emphasis has been placed on bioactive and bioresorbable ceramics, materials that not only elicit normal tissue formation but may also form an intimate bond with bone tissue and even be replaced by tissue over time. While "inert" ceramics elicit a minimal tissue response, bioactive ceramics are partially soluble, enabling ion transfer and the formation of a direct bond between implant and bone. Bioresorbable or biodegradable ceramics have a higher degree of solubility than bioactive ceramics, gradually resorb and integrate into the surrounding tissue, and are used as bone augmentation materials. Bioactive ceramics are primarily used as scaffold materials or as coatings on more structurally sound metal substrates.

The concept of bioactivity was originally introduced with respect to bioactive glasses via the following hypothesis: The biocompatibility of an implant material is optimal if the material elicits the formation of normal tissues at its surface, and, in addition, if it establishes a contiguous interface capable of supporting the loads that normally occur at the site of implantation. Examples of these materials are bioactive glasses, glass ceramics, and **calcium phosphate ceramics**. Bioactive glasses and glass ceramics include bioglass, which is a synthesis of several glasses containing mixtures of silica, phosphate, calcia, and soda; Ceravital (E.Leitz Wetzlar), which has a different alkali oxide concentration from that of bioglass; and apatite-wollastonite glass ceramic, a glass ceramic containing crystalline oxyapatite and fluorapatite [$Ca_{10}(PO_4)6(O,F_2)$] and wollastonite (SiO_2-CaO) in a MgO-CaO-SiO_2 glassy matrix. The calcium phosphate ceramics can have varying calcium-to-phosphate ratios, depending on processing-induced physical and chemical changes. Among them, the apatite ceramics, one of which is **hydroxyapatite**, have been studied most and are the focus of this section.

The impetus for using synthetic hydroxyapatite as a biomaterial stems from the perceived advantage of using a material similar to the mineral phase in bone and teeth for replacing these materials. As such, better tissue bonding is expected. Additional advantages of bioactive ceramics include low thermal and electric conductivity, elastic properties similar to those of bone, control of degradation rates through control of material properties,

and the possibility of the ceramic functioning as a barrier to metallic corrosion products when it is coated onto a metal substrate.

However, processing-induced phase transformations provoke changes in dissolution rates and the different structures and compositions alter the biologic response. Given the range of chemical compositions available in bioactive ceramics and the fact that pure hydroxyapatite is rarely used, the broader term *calcium phosphate ceramics* (CPC) should be used in lieu of the more specific *hydroxyapatite*. Each CPC is defined by a unique set of chemical and physical properties.

Mixtures of hydroxyapatite, tricalcium phosphate, and tetracalcium phosphate may evolve as a result of plasma spraying and other processes used to deposit ceramics onto metals. Physical properties of importance to the clinical function of calcium phosphate ceramics include:
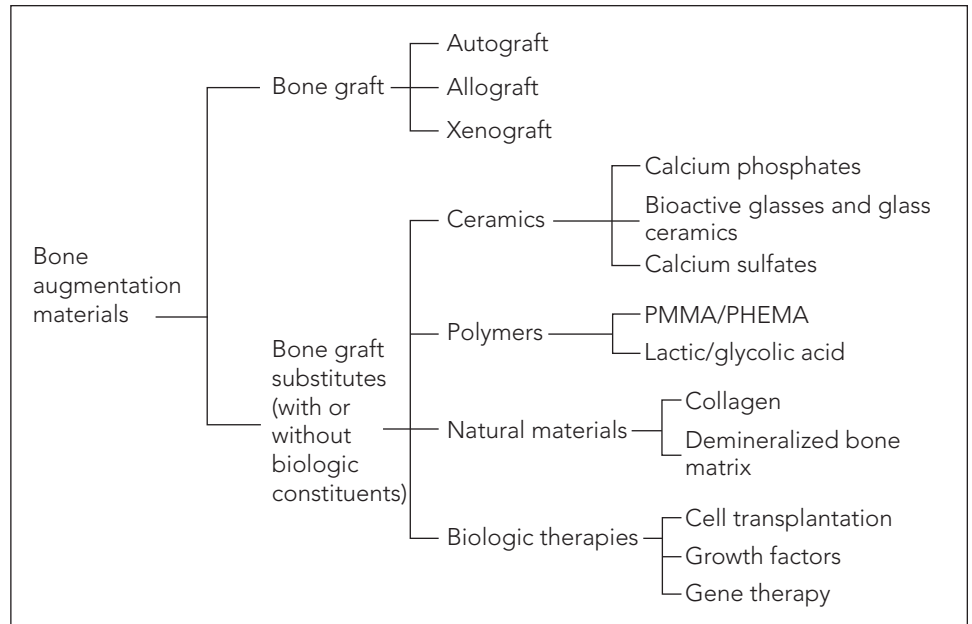
1. Powder particle size and shape
2. Pore size, shape, and distribution
3. Specific surface area
4. Phases present
5. Crystal structure and size
6. Grain size
7. Density
8. Coating thickness, hardness, and surface roughness

● Problems and Future Directions

Although there is no consensus regarding methods of evaluating dental implants and what parameters are most important, clinical evaluations have generally shown that dental implants are successful 5 years after placement in at least 75% of cases. Despite advances in materials synthesis and processing, surgical technique, and clinical protocols, clinical failures occur at rates of approximately 2% to 5% per year. Causes of failure and current problems with dental implants include:

1. Early loosening, stemming from a lack of initial osseointegration
2. Late loosening, or loss of osseointegration
3. Bone resorption
4. Infection
5. Fracture of the implant and/or abutment
6. Delamination of the coating from the bulk implant

Fig 23-9 Classification of bone augmentation materials.

Bone augmentation materials
- Bone graft
  - Autograft
  - Allograft
  - Xenograft
- Bone graft substitutes (with or without biologic constituents)
  - Ceramics
    - Calcium phosphates
    - Bioactive glasses and glass ceramics
    - Calcium sulfates
  - Polymers
    - PMMA/PHEMA
    - Lactic/glycolic acid
  - Natural materials
    - Collagen
    - Demineralized bone matrix
  - Biologic therapies
    - Cell transplantation
    - Growth factors
    - Gene therapy

The most common failure mechanism with endosseous implants is alveolar crest resorption, leading to progressive periodontal lesions, decreased areas of supporting tissues, and ultimately implant loosening. Aseptic failures are most often the cumulative result of more than one of the above-mentioned factors.

As a result of these clinical problems, basic and clinical research should focus on the complete characterization of materials, including bulk and surface properties, development of new materials, more engineering-based designs for both existing and new materials, quantification of stresses and stress transfer between implant and tissue, mechanical and biologic responses of tissues, and host response to implants.

Future materials

Although titanium and, to a lesser extent, ceramic and ceramic-coated implants have an excellent clinical record in implant dentistry, these materials are not necessarily end-stage materials. Continuing developments in the materials and biomedical fields can be expected in the next decade.

Because one of the long-term problems with dental implants is stress shielding, or mechanically mediated bone resorption, which is due in part to the elastic mismatch between metal and bone, polymer and composite implants that offer reduced moduli are being considered. The motivation for using composite materials for implants is based on several concepts. Composite materials can be very strong, because materials in fiber form exhibit strengths near the theoretical values. As a result, advanced composites can be as strong as metals and, in some cases, more flexible. The properties of composites can be more easily tailored than those of metals. A specific example is that of the modulus of composites, which can be tailored to be near that of bone.

◉ Augmentation Materials and Tissue Engineering

Persistent skeletal defects arising from trauma, infection, tumor resection, congenital malformations, and progressively deforming skeletal diseases are of significant clinical concern. The standard approach to repair skeletal defects is a bone graft, either an *autogenous bone graft* (graft from a patient's own body) or an *allogeneic bone graft* (graft from another person). While bone grafts are widely used and clinically successful, they have limitations and, in some cases, lack clinical predictability. For example, autogenous bone grafts can have failure rates as high as 30%, and there is concern about transmission of viruses with allogeneic bone grafts. Therefore, increased research into alternative substitute materials, such as ceramics, polymers, composites, bone derivatives, and natural materials is underway (Fig 23-9). Examples of dense and porous calcium phosphate ceramics are shown in
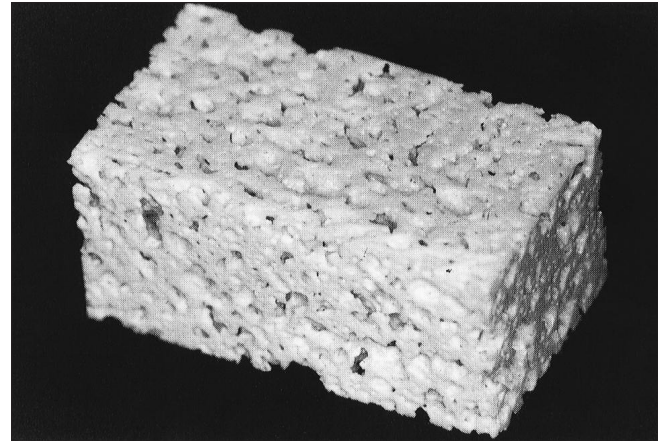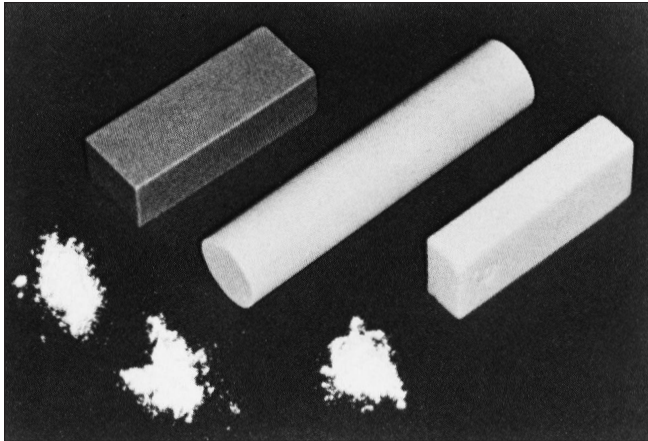
Fig 23-10 *(a)* Dense hydroxyapatite ceramic augmentation material with starting powders. (Reprinted with permission from Denissen et al.[5]) *(b)* Porous hydroxyapatite augmentation material, 44 × 18 × 16 mm; porosity = 45%. (Reprinted with permission from Osborn.[6])

Fig 23-11 Porous coralline hydroxyapatite ceramic augmentation material (Pro Osteon Implant 500, Interpore Cross International).

Figs 23-10 and 23-11. Many of these synthetic materials are designed to be permanently implanted. Most problems with synthetic materials manifest themselves at the biomaterial/tissue interface, in part because the tissue has the ability to functionally adapt, whereas the synthetic material does not. Therefore, despite the success of current treatments for skeletal defects, and the significant impact that man-made biomaterials have had on dentistry, combinations of synthetic materials and biologic constituents (eg, cells or growth factors), as well as more biologically interactive materials are being investigated.

The three primary application areas for augmentation materials in dentistry are intramucosal, endodontic, and bone-substitute materials. An ideal bone-substitute material for these clinical applications should be:

1. Biocompatible
2. Easy to fabricate, sterilize, and shape intraoperatively
3. **Osteoinductive**
4. **Osteoconductive**
5. Of sufficient mechanical integrity to support loads encountered at the implant site over a lengthy service life
6. Inexpensive

Regeneration of bone defects can be pursued by one or a combination of three general strategies: conduction, induction, and/or cell transplantation. In a conductive approach, a biomaterial provides an appropriate microenvironment for host cells to attach, grow, and function, ultimately leading to the formation of new bone within the material. Currently such materials are the most clinically prevalent. An inductive approach is more proactive in that biologic agents, typically growth factors, are introduced to induce the host cells to form new bone. Cell-based therapies may include not only the transplantation of differentiated and uncommitted cells, but also genetically manipulated cells, and can be used in combination with a supporting biomaterial (conductive) and also with inductive agents.

Stem cells from a number of sites, including bone marrow, perisoteum and muscle, have been pursued as

sources of cells capable of differentiating into bone, ultimately leading to bone regeneration. When transplanted under appropriate conditions, ex vivo expanded cells are capable of regenerating bone. This capacity has obvious clinical and commercial applications. However, results demonstrate large variability, implying that the nature of the microenvironment that cells are exposed to, including the biomaterial used for transplanting the cells, is a critical parameter.

Glossary

calcium phosphate ceramics A class of ceramics with varying calcium-to-phosphate ratios, which can form a direct bond with bone.

hydroxyapatite A specific form of calcium phosphate with a stoichiometry $Ca_{10}(PO_4)6(OH)_2$ and a Ca/P ratio of 1.67. Bone is a nonstoichiometric form of hydroxyapatite.

interfacial zone The thin zone at the surface of an implant, which includes the surface oxides, protein layers, and connective tissue.

osseointegration A direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant.

osteoconductive material A material that acts as a scaffold for new bone formation by providing an appropriate environment for attachment, proliferation, and function of osteoblasts or their progenitors, leading to formation new bone matrix.

osteoinductive material A material and/or biologic agent that causes the conversion of nonlineage committed cells preferentially to bone progenitor cells.

titanium The "material of choice" in dentistry, primarily because of its excellent biocompatibility (as a result of its stable oxide layer), mechanical properties, and its proven ability to achieve osseointegration in implant dentistry.

Discussion Questions

1. What are the properties (bulk and surface) of titanium that make it attractive for use as a dental implant?

2. What is/are the rationale(s) for using bioactive ceramics (eg, hydroxyapatite) as coatings on dental implants?

3. What is the importance of implant-tissue interfacial stability, and what are current methods of accelerating osseointegration such that the time between stage-one and stage-two implant surgery be reduced?

4. What are the physical, mechanical, and biologic parameters affecting the clinical success of dental implants?

Study Questions

(See appendix E for answers.)

1. What is osseointegration?

2. What materials are used for osseointegrated implants?

3. What factors dictate the effectiveness of osseointegration?

4. What parameters influence implant success?

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