Osseointegration
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Abstract
Nowadays dental implants have become an important part of patient management, and the treatment of choice in many dental reconstructive cases. The history of implant, its composition, different materials used for its manufacturing is still in a dilemma. This article describes titanium its historical background, different types of implants used before. Per Ingvar Brånemark was the first person who introduced the concept osseointegration. The aim of this paper is to make the clinician aware of the implant designs, materials for predictable success for rehabilitation of many clinical situations.

Keywords
Implants, osseointegration, titanium

Introduction
The goal of recent dentistry is to restore patients to normal function, speech esthetics, contour, comfort, health whether by removing caries from a tooth or replacing several teeth. What makes implant dentistry unique is the ability to achieve this goal, regardless of the disease, atrophy, or injury of the stomatognathic system.[1] However, the more teeth a patient is missing, the more challenging this task becomes. As a result of continued research, diagnostic tools, treatment planning, implant designs, materials and techniques, predictable success is now a reality for the rehabilitation of many challenging clinical situations.[1] Throughout the history of dentistry, clinicians and patients have struggled with options for replacing missing teeth. Treatment options have evolved from acrylic dentures to metal framework, removable partial dentures to fixed partial dentures. Recently, titanium implants have joined the armamentarium of restorative density. The successful replacement of lost natural teeth by means of tissue integrated implants represents a major advance in clinical treatment.[3]

They are used to replace missing teeth by anchoring the prosthesis to the mandible (or) maxilla. The prosthesis may be a single crown (or) on entire denture.[3] The success of titanium implants is based on the principle osseointegration. The discovery of osseointegration has been one of the most significant scientific breakthrough in dentistry. The term osseointegration was coined by Branemark in 1977, during his research on microcirculation in the bone repair mechanism.[4-5]

The proceedings of the, recent research conference in this area of “osseointegration, from molecule to man,” documents the strength of the key components of science and health that have contributed to the success of osseointegration. This requires undisturbed healing of differentiated tissues toward the fixture with neo – and revascularization occurring according to basic biologic principles, thus achieving restitution and integrum.[6]

Historical Background
Discovery of titanium

The element we now call Titanium was first identified by a Cornish cleric, the Revd. William Gregor (1761-1817) [Figure 1] in 1790, based on a sample from Tregon well mill, in lizard peninsula, Corn wall in Germany. Gregor originally called the new element as “menaccine or menaccanite,” but later in 1795, Klaproth working in Germany identified an element which he named “titanium.” He subsequently discovered that this was the same element as Gregor had originally discovered in 1791 and graciously acknowledged that Gregor was the true discoverer of the element. However, it was the name “titanium,” which subsequently became accepted for the element.[7-13]
Geo chemistry of titanium

Basic characteristics
Element: Titanium
Atomic number: 22
Atomic mass: 47.9

The geological characteristics of titanium:
1. It is very widespread, typically occurring at 1-2% (expressed as TiO₂) in many different kinds basic and ultrabasic igneous rocks such as dolerite, anorthosite, and gabbro.
2. It is very stable and immobile, which are easily brought into solution and transported from one geological environment to another.
3. The most familiar Ti-containing minerals are: Rutile (TiO₂) a reddish brown material with a specific gravity of 4.2-4.4, and Ilmenite (Fe, TiO₃) a black mineral with S.G of 4.5-5.0. anatase (TiO₂) is another significant titanium mineral.
4. Extremely reactive metals forms a tenacious oxide layer that contribute to its electrochemical passivity.
5. 9th most abundant element in earth’s crust.
6. Van Arkel refined the Ti ore in 1925. Krol developed commercial extraction procedures in 1930’s.
7. The atomic structure of Ti 1s², 2s², 2p⁶, 3s², 3p⁶, 3d², 4s².
8. The lightly held 3d2 and 4s2 electrons are responsible for the metal biocompatibility
9. Pure Ti exists as a hexagonal closed-packed atomic structure a(a-phase) up to 882°C.
10. About 882°C, the structure is body-centered cubic (b-phase).
11. Ti melts at 1665°C/1671°C.

The purified grains of TiO₂ are very white due to its high refractive index causing intense light scattering. The resulting white pigment is used in paint, paper, plastics, etc. The remainder is mainly used for metal production, for example in aerospace and medicine, where the special characteristics of high strength, especially at elevated temperatures, and resistance to corrosion is found advantageous-about 6% of weight of a modern airliner is titanium.

Osseointegration

Definition of osseointegration

According to Skalak and Branemark
The term osseointegration may be defined from various viewpoints and with respect to several scientific scales of interest.

From the viewpoint of the patient
A fixture is osseointegrated if it provided a stable and apparently immobile support of prosthesis under functional loads, without pain, inflammation, or loosening.

From the viewpoint of macroscopic and microscopic biology and medicine
Osseointegration of a fixture in bone is defined as the close apposition of reformed and new bone in congruency with the fixtures, including surface irregularities so that, at the light microscopic level, there is no interposition fibrous tissue and that a direct functional and structural connection is established, capable of carrying normal physiological loads without excessive deformation and without initiating rejection mechanisms.

From macroscopic, biomechanical point of view
A fixture is osseointegrated if there is no progressive relative motion between the surrounding living bone and marrow under functional levels and types of loading for the entire life of the patient.

Dorland’s illustrated Medical Dictionary 28th Edition
Os-seo-in-te-gra-tion is direct anchorage of an implant by the formation of bony tissue around the implant without the growth of fibrous tissue at the bone-implant interface.

An alternative definition has appeared in the literature
Osseointegration is defined as a direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant. Creation, and maintenance of osseointegration, therefore, depends on the understanding of the tissue’s healing, repair, and remodeling capacities.

In 1981, six factors were regarded as important to control for a reliable bone anchorage i.e. hardware implant biocompatibility, design and surface condition and various clinical conditions for the establishment of osseointegration.

To achieve an osseointegrated titanium with high predictability the implant;
1. Must be inserted with low trauma surgical techniques avoid over-heating of bone during the preparation of a precise recipient site.
2. Must be placed with initial stability
3. Should not be functionally loaded during the healing period of 3-6 months.

Extra oral application of titanium fixtures has been used since 1976 which included anchorage for craniofacial prostheses including ear, eye, and nose.
Osseointegration has also been applied to long bones in the reconstruction of damaged or diseased joints, osseointegrated fixtures have been used as an anchorage for a joint prosthesis in metacarpophalangeal joints.[5]

Concept of Osseointegration

The concept of osseointegration is based on research that began in 1952 with microscopic studies in situ of bone marrow in rabbit’s fibula. This investigation was carried out with a vital microscopic technique based on extremely gentle surgical preparation which consisted of grinding down the covering bone to a thickness of 10 μm. With the aid of specially developed microscopes unstained bone and bone marrow could be studied in vivo and in situ by transillumination at the resolution capacity of the light microscope. Blood circulation in the marrow was easily observed through the very thin bone layer. These intra vital studies revealed the intimate connection between marrow and bone tissue compartments.[4,5] With the aim of complete restitutio ad integrum at reconstructive surgical procedures traumatic factors detrimental to the healing process were further identified in differentiated tissue such as relative ischemia, local tissue temperature, and use of topically applied drugs (e.g. sodium fluorides, steroids, ENT drugs, and wound disinfectants). Titanium seemed to have better mechanical and surface characteristics for implantation in a biologic environment. These studies, in the early 1960’s indicated the possibility of establishing true osseointegration in bone tissue, because the optical chambers used could not be removed from the surrounding bone once they had healed. The titanium framework had become completely incorporated in the bone, and the mineralized tissue completely congruent with the micro-regularities of the titanium surface.[6]

Mechanisms of Osseointegration

The mechanisms by which endosseous Implants become integrated in the bone can be subdivided into three separate phenomena.[14-18]

They are:
1. Osteoconduction
2. De novo bone formation

Osteoconduction

A more complex environment characterizes the perimplant healing site since this will be occupied, transiently by blood. This begs the question: What is the role does implant surface design play in osteoinduction? In contrast, the implant surface will provide sufficient anchorage of the fibrin to withstand detachment during cell migration and thus maintain a migratory pathway for the differentiating osteogenic cells to reach the implant surface. Thus, the ability of an implant surface to retain fibrin attachment during this wound contraction phase of healing is critical in determining if the migrating cells will reach the former fibrin retraction. Those cells that differentiate before reaching the implant surface will synthesize bone matrix that will not be in contact with the implant surface. However, other cells will reach the implant surface before attaining the stage of differentiation at which matrix secretion is initiated. In the latter case, these cells will then be available to synthesize de novo bone on the implant surface itself. In so doing, they also stop migrating. Other cells still in the migratory mode will gain the contiguous implant surface and secrete bone. The histologic result will present itself as the apparent spreading of bone over the implant surface.[15,17,18]

Thus, the phenomenon of osteoconduction relies on the migration of differentiating osteogenic cells to the implant surface. Implant design can have a profound influence on osteoconduction by maintaining the anchorage of the temporary scaffold through which these cells reach the implant surface. It can be predicted that roughened surfaces would promote osteoconduction by both increasing available surface area for fibrin attachment and by providing surface features with which fibrin could become entangled. In addition, the chemistry of some implant surfaces may increase both the adsorption and retention of macromolecular species from the biologic milieu, and thus potentiate osteoconduction. This would provide a mechanistic explanation for the overwhelming evidence of accelerated early bone healing around calcium phosphate based implant materials.[15,17,18]

Distance and Contact Osteogenesis

The terms distance and contact osteogenesis were first described, by Osborn and Newesley in 1980 and refer to the general relationship between forming bone and the surface of an implanted material. While their classification was linked to different implant material types. Rather than the biologic mechanisms underlying their histologic observations, it still provides one of the most useful starting points in understanding the mechanisms of endosseous integration. Their terms describe essentially two distinctly different phenomena by which bone can become juxtaposed to an implant surface. In the first, distance osteogenesis, new bone is formed on the surface of bone in the implants site. Similar to normal oppositional bone growth, the existent bone surfaces provide a population of osteogenic cells that lay down the new matrix, which as osteogenesis continues, encroaches on the implant itself. Thus an essential observation here is that new bone is not forming on the implant itself, but rather that the implant becomes surrounded by bone.[15,17,18]

In the second phenomenon, contact osteogenesis, new bone forms first on the implant surface, since a prior, no bone was present on the surface of the implant upon implantation. The implant surface must become colonized by a population of osteogenic cells before initiation of bone matrix formation. This occurs, too at remodeling sites where an old bone surface is populated with osteogenic cells before new bone can be laid down. The common factor in these cases is that we are
De Novo Bone Formation

As mentioned above, the work of Oshorn and Newsley is particularly important in understanding contact osteogenesis. However, their work omitted a critical step that being the formation of the earlier mineralized matrix by differentiating osteogenic cells before they become mature polarized osteoblasts. This is the very stage which in normal bone remodeling sites; the osteogenic population secretes an initial matrix that provides the interface for old bone and new bone. Interestingly this interface was first described 123 years ago by a German histologist von Ebner, who coined the term “kittlinien” or cement lines, to describe the mineralized interfacial matrix laid down between old bone and new bone. Despite this early description of these prominent histologic features in bone, the cement line interface eluded both structural and compositional characterization, as well as an explanation of its cellular provenance until 1991 when, using in vitro methods, the formation of this matrix could be described by differentiating osteogenic cells in culture.[15,17,18]

This de novo bone formation cascade is a four stage process. Differentiating osteogenic cells initially secrete a collagen free organic matrix that provides nucleation sites for calcium phosphate mineralization. There are two noncollagenous bone protein, osteopontin, and bone sialoprotein, in this initial organic phase, but no collagen. Importantly, in the implant context it should be emphasized that the substratum does not act as an epitactic nucleoid in this biologic mineralization phenomenon. Calcium phosphate crystal growth follows nucleation and concomitant with crystal growth at the developing interface; there will be the initiation of collagen fiber assembly. Finally, calcification of the collagen fibers or in the inter-fiber compartment. Thus in this process of de novo bone formation, the collagen compartment of bone will be separated from the underlying substratum by a collagen free calcified tissue layer containing noncollagenous bone proteins.

This layer is approximately 0.5 mm thick, as are cement lines that form the interface between old and new bone at several sites.[15,17,18]

Bone Bonding

However, since the pioneering work of Hench, two classes of endosseous implants have been identified bone bonding and nonbonding; while metals such as titanium are nonbonding and calcium phosphate materials are considered bone-bonding.

The mechanism for the bone bonding phenomenon is generally accepted to be a chemical interaction that results in collagen from the bony compartment interdigitating with the chemically active surface of the implant. Clearly, in the case of de novo bone formation, this mechanism is inconceivable since the first extracellular matrix elaborated by bone cells at the implant surface is collagen free. As cement lines are found on both nonbonding and bonding biomaterials, then a reevaluation of the phenomenon of bone bonding is essential, the degree to which the cement line matrix can be visualized on the bone bonding materials will be a function of their chemical surface reactivity. In each case bonding of the de novo bone will occur by the fusion, or micromechanical interlocking, of the biologic cement line matrix with the surface reactive layer of the substratum. The creation, either during materials processing or post implantation due to surface reactivity of a micro topographically complex surface is essential for all bone bonding materials.[15,17,18]

Dense calcium phosphates are osteoconductive, but not bone bonding, while substrates of identical chemistry were rendered bone bonding by the introduction of micron-scale surface micro porosity. In other areas where connective tissue collagen is in contact with the implant, it will become encrusted in the surface reaction layer of so-called “bioactive” materials to produce the ultrastructural appearance of collagen interdigitation. This has been shown to be the case both in bony and soft tissue healing compartments, in addition to nonmineralizing bone cell cultures. While the metals are considered nonbonding materials, it has been shown that simple chemical treatments can render their surfaces bone bonding. The explanation of this change in biologic response has been based on chemical, rather than physical bonding.[15,17,18]

Bone Remodeling

Bone remodeling is of particularly critical importance in the long-term stability of the transcortical portion of an endosseous implant since the cortical bone will necrose as a result of the surgical trauma to the tissue. This has been demonstrated by Roberts to extend up to 1 mm away from the implant surface and addressed experimentally by Bruns and by Hoshaw et al. However, two important points should be made. First, during this long-term phase of peri-implant healing, it is only through
those remodeling osteons that actually implinge on the implant surface that de novo bone formation will occur at these specific sites on the transcortical option of the implant will be occupied by old, dead bone or connective tissue space created by peri-implant necrosis and lysis of bone tissue. Second, although trabecular remodeling also occurs, this is not vital to implant stability. However, the resorption as a result of this biologic activity occurs.[13,17,18]

Composition/Biomaterials of Dental Implants

The biomaterials or the composition of dental implants can be divided basically into 3 major categories. They are component of:

1. Metals and metal alloys
2. Ceramics and carbon
3. Polymers and composites.

In general the dental implant biomaterials are devices that extend from the bone to the oral cavity across the protective epithelial zones. Hence, these materials should have the property of biocompatibility.[19,20]

Metals and Alloys

The major groups of implantable materials in dentistry are:

- Titanium and alloys
- Cobalt chromium alloys
- Austenitic Fe-Cr-Ni-Mo steels
- Other metals and alloys.

Titanium and titanium-6 - aluminum-4 vanadium

Titanium was been used in dentistry for over 30 years. It is a highly reactive metal which rapidly absorbs oxygen and water. In the air, Ti is covered with a dense passive oxide layer, which protects the metal against corrosion. The nature of this layer confers biocompatibility of Ti. It is closer to those of bone which it overweighs when compared to stainless steels or Co-Cr alloys. It is sufficiently strong for use in major-load-bearing conditions, and it remains the material of choice for dental implants. There are two types of titanium implant biomaterials commercially pure (CP) Ti and Ti alloy. However, manufacturers use six different Ti-based biomaterials to fabricate dental implants. These include four grades of CP Ti and two Ti alloys.[13,20]

Cobalt Chromium - Molybdenum Based Alloy

Co-cr-mo based alloys are the most often used alloys in a cast and annealed metallurgic condition. This helps in the fabrication of subperiosteal frames, which are used as custom designs. The elemental composition of this alloy includes cobalt, chromium and molybdenum as the major elements. Cobalt provides the continuous phase for basic properties; secondary phases based on cobalt, chromium, molybdenum, nickel, and carbon provide strength (4 times that of compact bone), ductility and surface abrasion resistance. Chromium acts as corrosion resistance through the oxide surface, while molybdenum provides strength and bulk corrosion resistance. Nickel has been identified as biocorrosion product.[20-31]

The surgical stainless steel alloys. (e.g. 316 L carbon) have a long history of use for orthopedic and dental implant devices. These are High-strength and high ductility alloys. The ramus blade, ramus frame, stabilizer pins (old) and some mucosal inert systems have been made from the iron-based alloy.

This alloy is most subject to crevice and pitting biocorrosion. The iron-based alloys have galvanic potentials and corrosion characteristics that could result in biocorrosion and galvanic coupling if interconnected with titanium, cobalt, zirconium, or carbon implant biomaterials. Clearly, the mechanical properties and cost characteristics of this alloy offer advantages to clinical application. More recently, devices made from tungsten, hafnium and zirconium are used.[20]

Gold, platinum, and palladium are metals of relatively low strength and are used for certain implant designs. These are most often used in upper arch considering the cost per unit weight and the weight-per-unit volume (density). Gold because of its properties such as availability, ductility, nobility it is continued to be used as a surgical implant material. For example, the Bosker endosteal staple design represents the use of this alloy system.[20]

Ceramics

Ceramics are nonpolymeric nonmetallic, inorganic, materials manufactured by compacting and sintering at elevated temperature. They can be divided into metallic oxides or other compounds. These compounds are subjected to steam sterilization, results in a measurable decrease in strength, which treated with chemical solutions may leave residues and rough
surface on contact. This forms layer on the implant surface. Dry heat sterilization within a clean and dry atmosphere is recommended for most ceramics.

The properties such as chemical biocompatibility improved strength and toughness capabilities of zirconia; sapphire continue to make them excellent candidates for dental implants.[20-31]

Bioactive and Biodegradable Ceramics (Based on Calcium Phosphates)

The calcium phosphate (CaPO₄) ceramics are used in various clinical applications, dental reconstructive surgeries which include a wide range of implant types. The coatings of CaPO₄ ceramics on metallic surfaces using flame or plasma spraying (or other techniques) increased rapidly with great demand, with an overall intent of improving implant surface biocompatibility profiles and implants longevities.[14]

Carbon compounds are often classified as ceramics because to their chemical inertness and absence of ductility. However, they are conductors of heat and electricity. However, a combination of design, material, and application limitations resulted in a significant number of clinical failures and the subsequent withdrawal of this device from clinical use.[20,25,27]

Polymers and Composites

The use of synthetic polymers and composites continues to expand for biomaterial applications. The more inert polymeric biomaterials include polytetrafluoroethylene (PTFE), polyethylene terephthalate, polymethyl methacrylate, ultrahigh molecular weight polyethylene, polypropylene, polysulfone, and polydimethylsiloxane, or silicone rubber. In general, the polymers have lower strengths and elastic moduli and higher elongations to fracture compared with other classes of biomaterials. They are thermal and electrical insulators, and when constituted as a high molecular weight system without plasticizers, they are relatively resistant to biodegradation. Compared with bone, most polymers have lower elastic moduli with magnitudes closer to soft tissues.[20]

Polymers have been fabricated to porous and solid forms for tissue attachment, replacement, and augmentation and at coatings for force transfer to soft tissue and hard tissue regions. Most uses have been for internal force distribution connectors for osseointegrated implants where the connector is intended to better simulate biomechanical conditions for normal tooth functions. The indication for PTFE has grown exponentially in the last decade because of the development of membranes for guided tissue regeneration techniques. However, PTFE has a low resistance to contact abrasion and wear phenomena.

Combinations of polymers and other categories of synthetic biomaterials continue to be introduced. Several of the most inert polymers have been combined with particular or fibers of carbon, aluminum oxide, hydroxyapatite, and glass ceramics. Some are porous, whereas others are constituted as solid composite structural forms.

Excellent biocompatibility, Long-term experience, composite structure, and physical properties are much altered to suit the clinical application make polymers and composites excellent candidates for biomaterial applications for the implant biomaterial structure, compatibility to surrounding tissues when placed.[20]

References
