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College of Dentistry

Osseointegration in dental implants

A project submitted to
the College of Dentistry, University of Baghdad, Department of prosthetic dentistry in partial fulfillment for requirement to award the degree of
B.D.S

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Dedication

To my heart family who stand with me at every step and never let me alone till this moment of my life and have the most role in my success, they gave me the power to stay strong and never fall down.

To my parents, I want to tell them that I did it, I promise them that I will make them proud of me, thank you for all you have done throughout my life, you raised me, protected me and taught me all what I know.

To my all friends thank you for being by my side today and always. Finally, to my supervisor who encourage me to keep going on in my graduation project.

Mohammed Salah

Certification of the supervisor

This is to certify that the organization and the preparation of this had been made by graduate student **Mohamed Salah Hadi** under my supervision in the College of Dentistry, University of Baghdad in partial fulfillment of the requirement for the 5th grade.

Signature:

Lec. Mustafa Mahdi

The supervisor

Acknowledgment

In the beginning, I thank "God" who gave me opportunity, ability, energy, spirit and patience to complete this project work.

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Introduction

A dental implant is one of the treatments to replace missing teeth. Their use in the treatment of complete and partial edentulism has become an integral treatment modality in dentistry. Dental implants have a number of advantages over conventional fixed partial denture. A high success rate (above 97% for 10 years) and a decreased risk of caries and endodontic problems of adjacent teeth with improved maintenance of bone in edentulous site and decreased sensitivity of adjacent teeth **(Oral Maxillofac Surg, et al, 2018).**

A dental implant is a structure made of alloplastic materials implanted into the oral tissues beneath the mucosa and periosteum and within or through the bone to provide retention and support for a fixed or removable dental prosthesis. The most common type of dental implant is endosseous comprising a discrete, single implant unit (screw or cylinder shaped are the most typical forms) placed within a drilled space within dentoalveolar or basal bone. Commercially pure titanium or titanium alloy are the common constituents of dental implants. However, alternative materials include ceramics such as aluminium oxide and other alloys (gold and nickelechromeevanadium) **(Buser D, Sennerby L, De Bruyn H. et al, 2017).**

Implant dentistry the second oldest dental profession; exodontia (oral surgery) is the oldest. Around 600 AD, the Mayan population used pieces of shells as implants to replace mandibular teeth. In 1809, J. Maggiolo inserted a gold implant tube into a fresh extraction site. In 1930, the Strock brothers used Vitallium screws to replace missing teeth. A post-type endosseous implant was developed by Formiggini (the father of modern implantology) and Zepponi in the 1940s. The subperiosteal implant was developed in the 1940s by Dahl in Sweden. In 1946 Strock designed a two-stage screw implant that was insertedwithout a permucosal post. The abutment post and individual crown

were added after this implant completely healed. The desired implant interface at this time was described as ankylosis. In 1967, Dr. Linkow introduced blade implants, now recognized as endosseous implants. Dental implants became a scientific cornerstone after the serendipitous invention of Dr. Branemark who helped in the evolution of the concept of osseointegration (direct, rigid attachment of the implant to the bone without any intervening tissue in between two implants) **(Nevins M. et al, 2014).**

Pre-Ingvar Brånemark

Through his initial observations on osseointegration, Branemark showed that titanium implants could become permanently incorporated within bone that is, the living bone could become so fused with the titanium oxide layer of the implant that the two could not be separated without fracture. It occurred to this investigator that such integration of titanium screws and bone might be useful for supporting dental prostheses on a long term basis **(Brånemark PI. et al, 1959).**

Aims of Review

This review focussed on the osseointegration of dental implant and the factors that affecting the osseointegration and the methods that help to enhance it.

Review of literature

Modern dental implantology began almost half a century ago. A review current literature shows great evolution not only on implant design and surgical techniques, but also on the classification of clinical success, failure and different surface treatments **(Bartlett et al,2007).**

Branemark coined the term 'osseointegration', which defines success and failure of dental implants. Osseointegration was originally defined at the light microscopic level as "a direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant **(Branemark Pi et al, 1977).**

From this discovery in experiments focused on observing the micromovements of bone, through its laboratory development and initial application in the dental sciences, osseointegration has become a realized phenomenon of importance. Currently, an implant is considered as osseointegrated when there is no progressive relative movement between the implant and the bone with which it has direct contact **(Branemark PI et al, 1983).**

The conventional protocol proposed by Branemark for treatment with dental implants establishes that implant procedures should be carried out in two phases. In the first, the 'surgical phase', the alveolus is prepared and the implant is installed. Furthermore, during the 'prosthetic phase' the prosthesis is molded, prepared and inserted. A 3-month interval between the surgical and prosthetic phase is recommended to allow proper healing of mandibular implants, whereas a 6-month interval is required for maxillary implants. **(Branemark PI et al, 1985).**

1-1- Osseointegration of dental implant

Defined as a direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant, is critical for implant stability, and is considered a prerequisite for implant loading and long-term clinical success of endosseous dental implants.

Osseointegration of titanium implant surfaces is dependent upon both physical and chemical properties **(Sul et al., 2005).** This structural and functional union of the implant with living bone is strongly influenced by the surface properties of the titanium implant. As titanium and its alloys cannot directly bond with living bone, modification of the implant surface has been proposed as a method for enhancing osseointegration. Scientific research works to assess the influence of implant surface properties on bone healing have identified several factors which are important for osseointegration. The surface characteristics of implant which influence the speed and strength of osseointegration include surface chemistry, topography, wettability, charge, surface energy, crystal structureand crystallinity, roughness, chemical potential, strain hardening, the presence of impurities, thickness of titanium oxide layer, and the presence of metal and non-metal composites. Among these, wettability and free surface energy of an implant surface are considered to be very crucial. The influence of physical properties such as surface topography and roughness on osseointegration have translated to shorter healing times from implant placement to restoration **(Cochran et al., 2002).** The biologic basis underlying these clinical improvements continues to be explored **(Kim et al., 2005).**

Osseointegration can occur only if the cells adhere to the bio-material surface. At this phase, reorganization of the cytoskeleton and information exchange between cells and the extracellular matrix at the cell-biomaterial interface occur, generating gene activation and specific tissue remodeling (fig 1). Both the morphology and roughness of the biomaterial's surface have an influence on

cell proliferation and differentiation, extracellular matrix synthesis, local factor production and even cell morphology. Adhesion of osteoblasts onto implant surfaces is not enough to ensure osseointegration; it is necessary for cells to receive signals inducing them to proliferate. For example, coating the titanium surface with bone morphogenic protein-2 induces osteoblastic cell division after adhesion. The presence of fibronectin during the interaction between these cells and the implant surface, or the presence of protein, increases the cell division of human osteoblasts. **(Carlos Nelson Elias and Luiz Meirelles., 2010).**

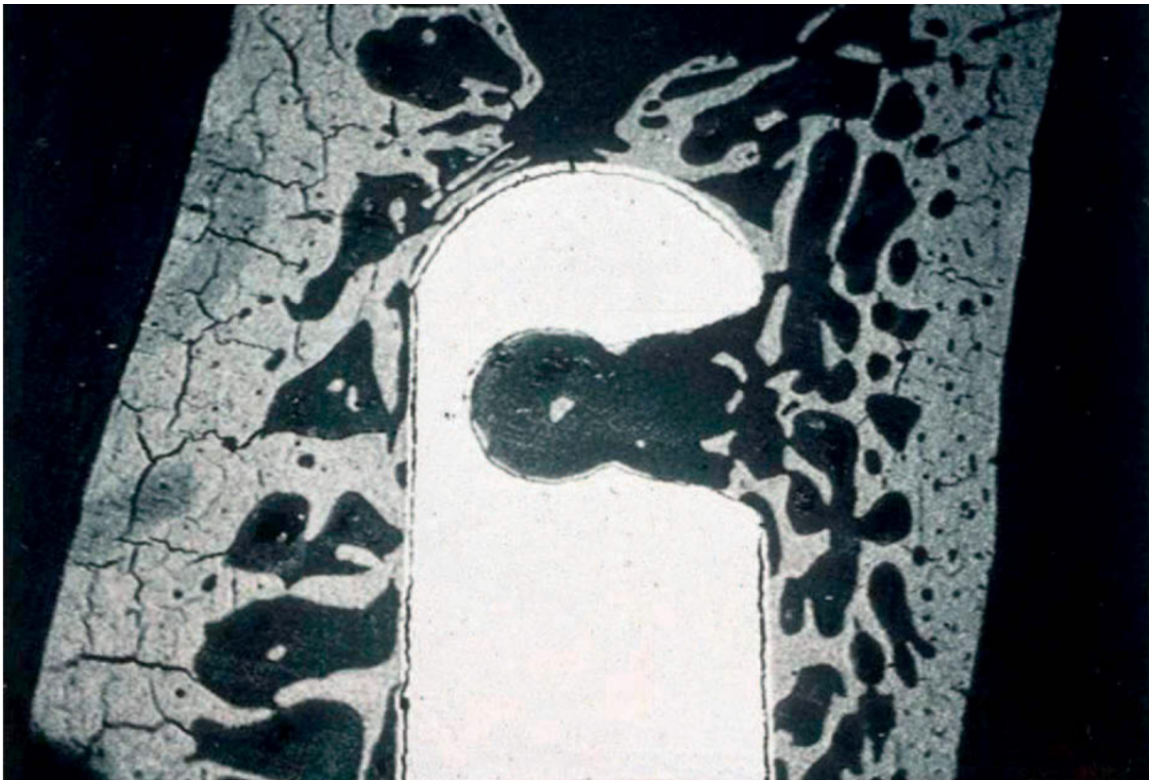

Figure 1: Bone grows from host bone out to the surface of the implant and then along the implant surface. (Dental implant Chapter 16 Bone Biology, osseointegration, and Bone Grafting).

Silva and Menezes cited that the success in the integration of biomaterial implants depends on responses such as cell attachment and cell adhesion **(Silva FC& Menezes GC et al.,2014).**

1-1-1 Interaction between cells and the surface of the dental implants

Since surface properties of biomaterials are important parameters influencing cellular reactions towards artificial materials, the properties of dental implant surfaces are extremely important in influencing the healing process leading to osseointegration and ultimate clinical success of the implant. Surface morphology modulates the response of cells to a dental implant, and surfaces with defined microstructures may be useful for enhancement of the stable anchorage **(Elias and Meirelles, 2010).**

Surface chemistry involves adhesion of proteins, bacteria, and cells on implants. Wettability and surface energy influence the adsorption of proteins, and increase adhesion of osteoblasts on the implant surface. The cell behaviour on hydrophilic surface is completely different from that on a hydrophobic one. A hydrophilic surface is better for blood coagulation Not than a hydrophobic surface. The expressions of bone-specific differentiation factors for osteoblasts are higher on hydrophilic surfaces. Consequently, dental implants manufacturers have developed high hydrophilic and rough implant surfaces which in turn exhibited better osseointegration than implants with smooth surfaces **(Boyan BD et al, 1996).**

Wound healing involves a highly orchestrated sequence of events which is triggered by tissue injury involving soluble mediators, blood cells, extracellular matrix and parenchymal cells. Ultimately, it culminates in either partial or complete regeneration or repair. Fracture healing in bone occurs in four phases which include inflammation, soft and hard callus formation, and remodelling. Following a fracture, blood coagulation and hematoma formation takes place. This is followed by inflammation.

Various chemical mediators such as thrombin and growth factors released by activated leukocytes and platelets in the hematoma serve as chemotactic signals to many cell types which play an important role in bone healing. Unlike soft tissue healing, bone healing does not lead to scarring. Instead it leads to restoration of the bony tissue. During successful implantation, insertion of metal implants into cortical bone eventually leads to complete healing. Following implant placement, unlike in fracture healing, implants extend into and persist in the marrow spaces and this may have a bearing on the healing process. Although implant healing must to some extent adjust to the presence of the implant, ultimately, sound bony tissues will be completely restored during wound healing. This adjustment involves imbedding the implant surface in a layer of bone, continuous with the original bone. Wound healing around a dental implant placed into a prepared osteotomy follows three stages of repair- Initial formation of a blood clot occurs through a biochemical activation followed by a cellular activation and finally a cellular response which will lead for new bone formation (fig 2) **(Stanford and Schneider, 2004).**

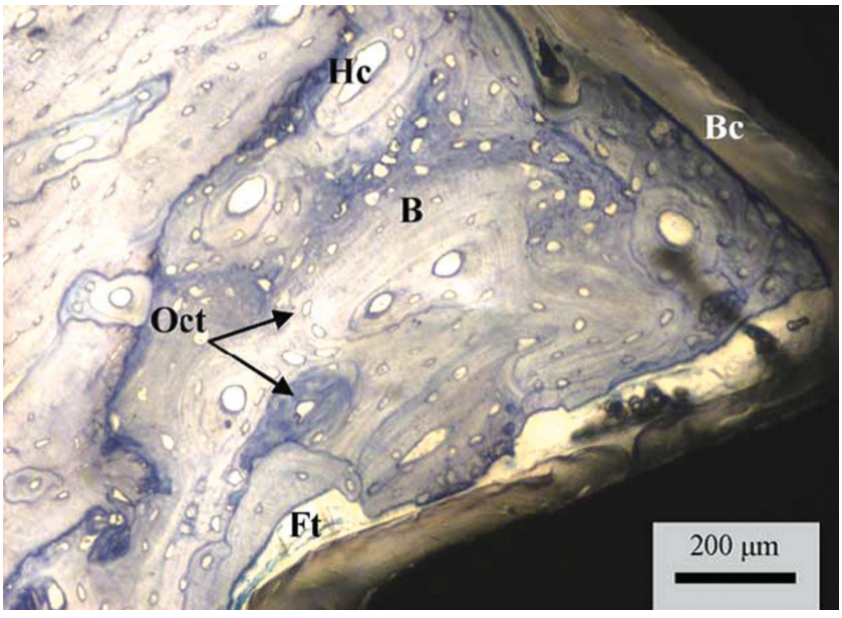

Figure 2: Photomicrograph taken by a light microscope at a high magnification. Newly formed bone (B) in direct contact with the implant, osteocytes (Oct) cells, Haversian canal (Hc) and some fibrous tissues (Ft). The biomimetic coating (Bc) can be observed in the implant's surface. (Reprinted from Publication: Materials Science and Engineering C, 24, ECS Rigo, AO Boschi, M Yoshimoto, S Allegrini Jr, B Konig Jr, MJ Carbonari, "Evaluation

1-1-2- Factor affect osseointegration

Albrektsson & Branemark highlighted six factors that are especially important for the establishment of reliable osseointegration: **(Albrektsson T. et al., 1981).**

1-1-2-1-implant material

Various metals, ceramics, and biostable polymers have been used to achieve osseointegration. The major metal types have included: cobalt chromium, tantalum, stainless steel, zirconium and commercial pure titanium and its alloys.

The elemental metal titanium was first discovered in England by William Gregor in 1790, but in 1795 Klaproth gave it the name of titanium.

Now, titanium has been widely advocated as the most biocompatible material for promoting osseointegration, due to its excellent mechanical properties, combination of low density, high strength to weight ratio, resistance to corrosion and its ability to develop an oxide layer on the surface (comprised of a dioxide chemical structure, TiO2) (fig 3). The presence of this oxide film that forms spontaneously in the passivation or repassivation process is a major criterion for the excellent biocompatibility and corrosion resistance of titanium and its alloys. The bone is both mechanically and chemically bind to the surface of titanium has been known to facilitate durable osseointegration and long-term implant survivorship **(Tummler HP, Thull R, Schaldach M. et al).**

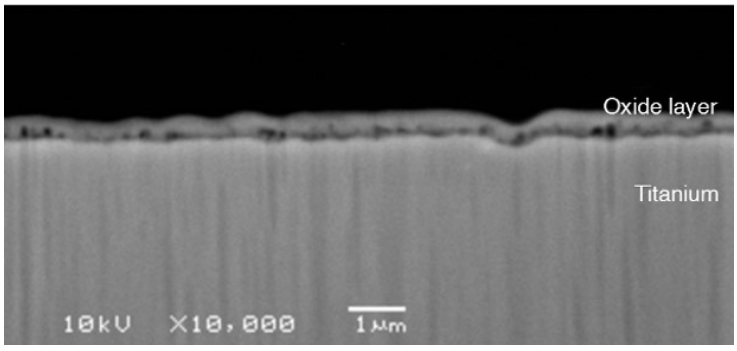

Figure 3: The cross section photograph of the anodic oxidation of titanium by an electron microscope. https://ebinadk.com/en/tech/titan-youkyokusanka/

Light, strong and totally biocompatible, titanium is one of the few materials that naturally match the requirements for implantation in the human body. Among all titanium and its alloys, the mainly used materials in biomedical field are the commercially pure titanium (cp Ti, grade 2) and Ti-6A1-4V (grade 5) alloy. **(Aaron RK, Herr HM, Ciombor DM, et al. 2006).**

They are widely used as hard tissue replacements in artificial bones, joints and dental implants. As a hard tissue replacement, the low elastic modulus of titanium and its alloys is generally viewed as a biomechanical advantage because the smaller elastic modulus can result in smaller stress shielding. The fundamental drawback of titanium and its alloys which limits wider use of these materials include their poor fretting fatigue resistance and poor tribological properties, because of its low hardness. Their poor tribological behavior is characterized by high coefficient of friction, severe adhesive wear with a strong tendency to seizing and low abrasion resistance. Titanium tends to undergo severe wear when it is rubbed between itself or between other materials.

A variety of chemical reactions occur on the surface of a surgically implanted alloy. The metallic components of the alloy are oxidized to their ionic forms and dissolved oxygen is reduced to hydroxide ions. **(Virginia Sáenz de Viteri and Elena Fuentes, 2013).**

1-1-2-2-implant design

Implant design refers to the three-dimensional structure of an implantwith all the components and features that characterize it (fig 4). It has been reported that the implant design is a vital parameter for attaining primary stability Studies have demonstrated a relationship between implant design and osseointegration. The growth of the bone occurs preferentially on the elevated or the protruded extensions on an implant surface, such as the ridges, crests, and edges of

threads. Moreover, the shape of the implant is also an essential determinant as it governs the surface area available for the transfer of stresses and the primary implant stability.

Figure 4: Dental implant bodies may be categorized by their design as cylinder type (top row), screw type (middle row), press fit (bottom row), or a combination of features (upper row, far right). Scientific Rationale for Dental Implant Design, https://Pocket dentistry.com

A threaded implant offers greater functional surface area than the smooth-sided cylindrical or tapering implants, as it can be rigidly fixated, thereby limiting the microenvironment during wound healing. Smooth-sided implants need an additional surface treatment, and the taper, when incorporated, reduces the surface area available for osseointegration **(C. E. Misch. et al 2015).**

Tapered implants were later introduced to enhance aesthetics and assist implant placement between adjacent natural teeth. The hypothesis behind using tapered

implants was to provide a degree of compression of the cortical bone in an implant site with inadequate bone, while the cylindrical wide body implants increase the risk of labial bone perforation especially in thin alveolar ridges due to presence of buccal concavities, whereas the decrease in diameter of the tapered implants toward the apical region accommodates for the labial concavity.

Studies have shown that implant design with grooves oriented 60° (downwards) to the long axis of the implant attracts higher densities of osteocytes in the peri-implant area assist in reducing distributing stress and reducing the extent of bone loss following the implant installation. **(C. E. Misch. et al 2008).**

1-1-2-3-surface morphology

Screw thread type (triangular, squared, trapezoidal, rounded, microscrew and grooved), roughness, porosity, topography, and surface energy all contribute to the host response to a titanium implant placed in apposition with cortical and/or cancellous bone. It is well observed that the implant surface morphology directly influences osteoblast and osteoclast attachment and metabolism. The implantation is most effective when using porous implants (50–400 μm) with roughened surfaces, where ingrowth and interdigitation of the newly formed bone into the porous structure stabilizes the interface (Figure 2). As stated by Boyan et al, implant surfaces should have a 4–7 μm layer of roughness to ensure proper osteoblast cuboid morphology, an essential characteristic for assuring the osseointegration . Osteoblasts seated on roughened surfaces have demonstrated increased proliferation **(Kieswetter K, Schwartz Z, Dean DD, Boyan BD. et al 1996).**

1-1-2-4-status of the bone

The significance of bone density and its association with implantdentistry has existed for more than two decades. Bone quality and quantity is referred to the amount and the topography of the cortical and cancellous bone in which the recipient site is drilled. A poor bone quantity and quality have been indicated as the main risk factors for implant failure as it may be associated with excessive bone resorption and impairment in the healing process compared with higher density bone (**Jaffin RA,Berman CLand and Herrmann I, Lekholm U, Holm S, Kultje C.).**

Clinical studies have reported dental implants in the mandible to have higher survival rates compared to those in the maxilla, especially for the posterior maxilla. In the posterior maxilla, there is commonly thinner cortical bone combined with thicker trabecular bone compared to the mandible **(Turkyilmaz et al).** Studies of the Branemark System over the last 20 years have shown a 10% higher implant failure rate in soft maxillary bone in comparison to the dense bone of the mandible **(Rasmussen et al, 1992).**

Surgical techniques, such as bone condensing, undersizing the osteotomy, improve the bone density and increase the primary (mechanical) stability **(Fawad Javed., et al).**

Misch Bone Density Classification (fig 5) **(Misch CE et al,1999)**

DI: Dense cortical bone.

D2: Thick dense to porous cortical bone on crest & coarse trabecular bone within.

D3: Thin porous cortical bone on the crest and fine trabecular bone within.

D4: Fine trabecular bone

DS: Immature, non-mineralized bone.

Figure 5 : Bone densities ,(A) D1 bone is dense cortical bone and is the highest in the density, (B) D2 bone is coarse trabecular bone surrounded by thick porous cortical bone, (C) D3 bone is fine trabecular bone surrounded by thin porous cortical bone, and (D) D4 bone is fine trabecular bone with almost no cortical bone (bone density according to misch, https:// pocket dentistry.com

1-1-2-5-surgical technique

The proper instrumentation and operative techniques help to minimize disturbance to the localized vascular network during osseointegration procedures, However, the critical time/temperature relationship for bone tissue necrosis is around 47 °C applied for 1 min. Uncontrolled thermal or mechanical factors (reaming, rasping, or drilling) used to ensure proper implant “fit and fill” or fixation may damage the host bone’s ability to remodel. Insertion of the dental implant into the host bone results in a localized region of necrotic tissue **(Ling RS. et al 1985).**

While it has been generally agreed upon that this amount of necrotic bone should be reduced during the initial implantation, Albrektsson et al have speculated that a minor region of dead bone may act as an early implant stabilizer during the preliminary phase of bone remodeling and may even be beneficial for anchoring osseointegrated implants in situ. In order to prevent premature implant failure, primary implant stability must occur immediately to

eliminate micromotion at the bone-implant site and to also prevent fibrous tissue formation. Gaps in excess of 50–150 μm between the implant surface texture and host bone may lead to fibrous tissue without skeletal attachment **(Albrektsson T, Brånemark PI, Hansson HA, Lindström J. et al 1986).**

Trauma to the host bone tissue during surgery may also accelerate local bone turnover. This has been termed the "regional acceleratory phenomenon" (RAP), which was first defined by Frost, using noxious stimuli, and then by Bloebaum et al. The RAP may occur for two reasons: the first being that placement of an intramedullary implant alters the dynamic strains to the host bone tissue. Depending on the "fit and fill," the implant may result in high concentrations of localized stress or "stress shielding;, second, the surgical procedure itself disrupts the blood supply to the endosteal wall (which results in a local tissue response to reestablish bone vascularity) thus causing an increase in cortical bone porosity. This increased vascular network is optimal for bone remodeling but will impact overall strength. Knowledge of the RAP is vital for the success of OI implants. In dentistry, increasing the severity of the RAP has been reported to accelerate the rate of orthodontic tooth movement **(Bloebaum RD, Willie BM, Mitchell BS, Hofmann AA. et al 2007).**

1-1-2-6- loading conditions

One of the challenges with the osseointegrated implant is to prevent the micromotion during the early phases of healing and allowing the bone to form a strong bone-implant interlock **(Meyer U, Joos U, Mythili J, et al. 2004).** if this is not achieved, a fibrous tissue interface (Figure 4) may form and prevent the primary stability. As noted above, limiting the initial forces on an osseointegrated implant has been based on the principle that stress must be exerted gradually to promote firm skeletal attachment since under or

overloading may compromise the integrity of the host bone **(Hofmann AA, Bachus KN, Bloebaum RD. et al 1993).**

To prevent mechanical loosening at the bone-implant construct, the procedures for dental applications initially have required periods of restricted load-bearing, to avert overloading. However, the dental literature now indicates that immediate implant loading may not compromise the integrity of the bone-implant interface or prevent osseointegration if micromotion is controlled with properly designed implants. However, key design elements must be considered and include the implant neck design, screw shape, abutment design, during the oral implant design **(Hofmann AA, Bachus KN, Bloebaum RD. et al 2009).**

1-1-2-7-implant Bed

A healthy implant host site is required. However, in the clinical reality; the host bed may have suffered from previous irradiation and osteoporosis, to mention some undesirable states for implantation. Previous irradiation is not an absolute contraindication for the insertion of oral implants. However, it is preferable that some delay is allowed before an implant is inserted into a previously irradiated bed. Furthermore, some 10-15 % poorer clinical results must be anticipated after a therapeutically dose of irradiation. Because of vascular damage, at least in part. One attempt to increase the healing conditions in a previously irradiated bed is by using hyperbaric oxygen, as a low oxygen tension definitely has negative effects on tissue repair **(Smith RA, Berger R, DodsonTB. et al 1992).**

Smoking has been reported to yield significantly lower success rates with oral implants. The mechanism behind this lowered success is unknown, but vasoconstriction may play a role **(Murray CG, Herson J, DalyTE, Zimmerman S. et al 1980).**

Other common clinical host bed problems involve osteoporosis and resorbed alveolar ridges. Such clinical states may constitute an indication for ridge augmentation with bone grafts. In jaws with insufficient bone volume for implant installation, a grafting technique has been recommended in order to increase the amount of hard tissues. To create more alveolar bone without grafting, a new surgical technique was tested, relying on the biologic principle of guided tissue regeneration. It is of great value in situations with insufficient alveolar bone volume **(Misch CM, Misch CE. et al 1995).**

1-1-3-Enhancement of osseointegration

Several techniques to enhance the implant surface have been proposed to improve the success rate of oral rehabilitation with osseointegrated implants **(Elias CN et al, 2008).**

However, osseointegration in many cases can occur between 3-6 months But to shorter this healing period roughness and coating technique can made on dental implant **(Cochran et al., 2002)** , Initially, one could expect that increasing the surface area of the implant should result in more sites for cell attachment, facilitating tissue growth and improving mechanical stability. However, this is not a general rule and may vary depending on the cell type. Fibroblasts avoid rough surfaces and accumulate on smooth ones. On the other hand, macrophages exhibit rugophilia, that is, they prefer rough surfaces, whereas epithelial cells are more attracted to rough surfaces than to smooth ones. Osteoblastic cells adhere to rough surfaces more easily, a finding also observed in commercially available implants with chemically treated surfaces **(Thull Ret al,2002).**Chemical composition of the surface has an influence on the secondary stability and reactivity of the implant.

Schneider et al. reported the effect of surface chemistry on the cell behavior of osteoblasts using a variety of cell cultures and animal models **(Schneider GB et al,2004).**Recently, many works have been carried out on surface treated commercial titanium implants to enhance the osseointegration function By increasing the surface roughness, an increase in the osseointegration rate and the biomechanical fixation of titanium implants have been observed. The implant modifications can be achieved either by additive or subtractive methods. The additive methods employed the treatment in which other materials are added to the surface, either superficial or integrated, categorized into coating and impregnation, respectively. While impregnation implies that the material/chemical agent is fully integrated into the titanium core, such as calcium phosphate crystals within Ti02 layer or incorporation of fluoride ions to surface, the coating on the other hand is addition of material/agent of various thicknesses superficially on the surface of core material. The coating techniques can include titanium plasma spraying (TPS), plasma sprayed hydroxyapatite (HA) coating, alumina coating, and biomimetic calcium phosphate (CaP) coating**.(Seunghan Oh,2015).**

1-1-3-1-Modification of Microtopography (mechanical surface treatment)

Microtopography is linked to microroughness on a micrometer scale (1-100 um) and is modified by manufacturing techniques like machining, acid-etching, anodization, sandblasting, grit-blasting, and different coating procedures. Commonly used scientific parameters to describe the surface roughness are the 2-dimensional (profile roughness average) and the 3-dimensional (area roughness average). The majority of dental implants on the market have a moderate rough surface of 1-2 um.

According to Albrektsson and Wennerberg, by this range seems to provide an optimal degree of roughness to promote osseointegration. Pits, grooves, and protrusions characterize the microtopography and set the stage for biological responses at the bone-to-implant interface. The modifications of microtopography contribute to an increase in surface area **(Shinji Kuroda el at 2016).**

1-1-3-1-1-Plasma spray treatment

A titanium plasma-spraying (TPS) method has been used for producing rough implant surfaces (Fig.6) This method consists in injecting titanium powders into a plasma torch at high temperature. The titanium particles are projected on to the surface of the implants where they condense and fuse together, forming a film about 30m thick. The thickness must reach 40-50 m to be uniform. The resulting TPS coating has an average roughness of around 7 m, which increases the surface area of the implant.

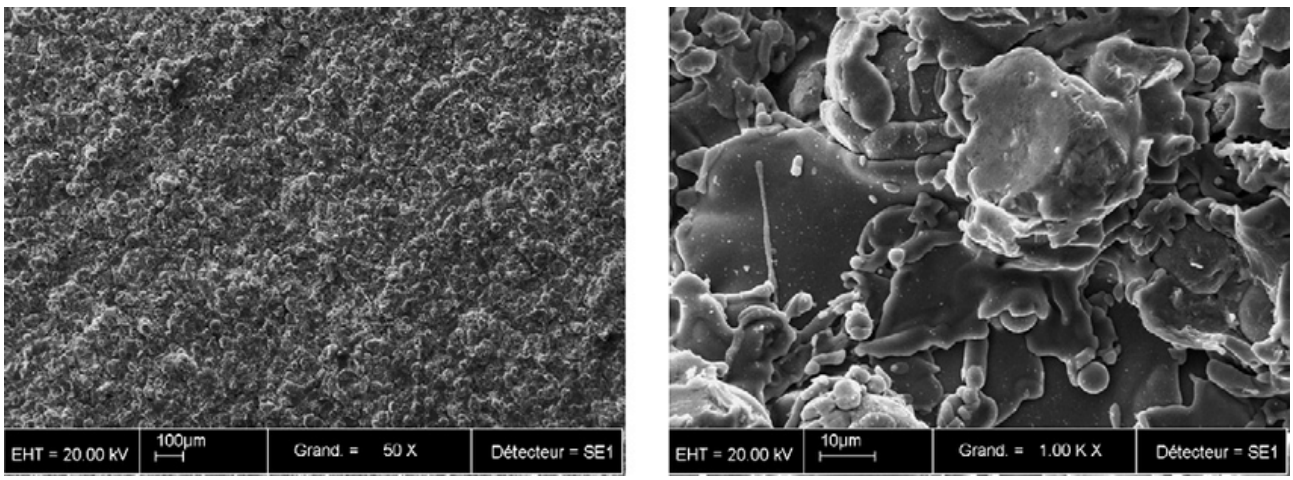

Figure 6: SEM micrographs of a titanium plasma-sprayed (TPS) surface (Courtesy of Cam Implants BV, The Netherlands).

It has been shown that this three-dimensional topography increased the tensile strength at the bone/implant interface. In this preclinical study using minipigs, the bone/implant interface formed faster with a TPS surface than with smooth surface implants presenting an average roughness of 0.2 m. However, particles of titanium have sometimes been found in the bone adjacent to these implants. The presence of metallic wear particles from endosseous implants in the liver, spleen, small aggregates of macrophages and even in the para-aortic lymph nodes have also been reported. Metal ions released from implants may be the product of dissolution, fretting and wear, and may be a source of Cancers due to their potentially harmful local and systemic carcinogenic effects.

However, the local and systemic adverse effects of the release of titanium ions have not been universally recognized. In a clinical study comparing SLA and TPS implant surfaces, no clinical difference was observed between these two surfaces. In a pre-clinical model, the percentage of bone/implant contact was found to be inferior for the TPS surface than for plasma-sprayed hydroxyapatite-coated implants. Nowadays, there is a consensus on the clinical advantages of implanting moderately rough surfaced implants (in the micrometric range) rather than using rough plasma-sprayed implant surfaces. **(Pierre Layrolle et al, 2007).**

1-1-3-1-2-Laser ablasion

The process of selectively remove material fromsurface of dental implant by irradiating it with laser ablastion the main problem of surface treatment is the contamination of the surface during the roughening procedure (fig.7). Using laser techniques for roughening the implants surface, contamination is avoided, because the laser enables implant surface treatment without direct contact, and an easier control of the micro-topography is achieved. Laser irradiation has here

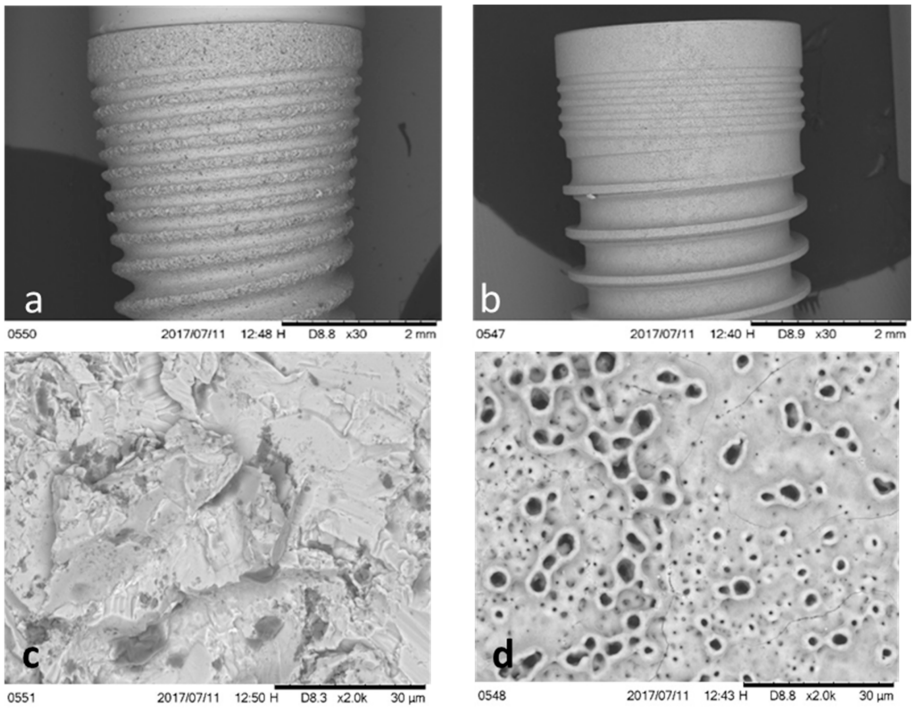

Figure 7: Scanning Electronic Microscope images of the two different implants tested: (**a**) dental implant sandblasted and acid-etched surface (SA); (**b**) dental implants with oxidized surface (OS); (**c**) surface of SA dental implants; (**d**) surface of OS dental implants.

been demonstrated to be a suitable, clean and easy method to improve bon response. A tendency to more bone formation was found for the laser treated implants compared t control implants. It can be due to the formation of TiN on the surface that improves biocompatibility **(M Marticorena 2007,et al).**

1-1-3-1-3-Acid Etching

In acid etching, the use of acids on metal surfaces is not only to clean the surface but also to modify the roughness. A strong acid like hydrofluoric (HF), nitric (HNO3), and sulphuric (H2S04) or a combination of these acids is commonly used in this technique. Acid etched surfaces had increased cell adhesion and bone formation, thus enhancing the osseointegration **(J. I. Rosales-Leal, et al 2010).** Due to its dissolution ability HF has been used for etching restorative ceramic materials in order to increase the bonding surface

for luting agents. The significance of this technique also renders the substrate with homogeneous roughening regardless of the sizes and shapes.

The roughness of titanium is one of the of the factors that helps in determining the stability of bone formation and resorption at the interface of bone implants. Alla et al. reported that a nanotopography that allows bone ingrowth via acid etching on an implant may improve the roughness. Previous study has reported that the rate of etching depends on the type and concentration of the acid, However, the suitability of these acids in etching was not determined as they required further tests particularly on the bone implant contact and torque removal. Titanium samples etched by H2SO4 with differentconcentrations demonstrated an increase in surface roughness **(Y. Iwaya,et al 2008).**

Concentrated H2O4 has been proven as an effective solution to roughen the surfaces particularly for biological applications.

1-1-3-1-4-Blasting ceramic particles

Another approach for roughening the Titanium surface consists in blasting (also called grit-blasting or sand-blasting) the implants with hard ceramic particles. The highly roughened implants have been shown to favor mechanical anchorage and primary fixation to bone. The abrasive ceramic particles are projected against the target material under high pressure. Thus, for the blasting of biomedical materials, the particles should be chemically stable, biocompatible, and should not hamper the osseointegration of the Titanium implants. Usually, Alumina (A1203), Titania (TiO2), or hydroxyapatite particles are applied for blasting treatments. The desired roughness can be set up by the particle size **(Ivanoff CJ, Hallgren C, Widmark G, Sennerby L, Wennerberg A. et al, 2001).**

1. Alumina is frequently used as a blasting material and produces surface roughness varying with the granulometry of the blasting media. However, the blasting material is often embedded into the implant surface and residue remains even after ultrasonic cleaning, acid passivation, and sterilization. Alumina is insoluble in acid and is thus hard to remove from the Titanium surface. In some cases, these particles have been released into the surrounding tissues and have interfered with the osseointegration of the implants. Moreover, this chemical heterogeneity of the implant surface may decrease the excellent corrosion resistance of Titanium in a physiological environment.

2. Titanium oxide is also used for blasting Titanium dental implants. An experimental study using microimplants in humans has shown a significant improvement for bone-to- implant contact (BIC) for the TiO2 blasted in comparison with machined surface implants. Other experimental studies confirmed the increase in BIC for Titanium-blasted surfaces. Furthermore, some authors have reported high clinical success rates for Titanium-blasted implants, up to 10 years after implantation.

3. A third possibility for roughening Titanium dental implants consists in using a biocompatible, osteoconductive, and resorbable blasting material. Calcium phosphates such as hydroxyapatite, B-tricalcium phosphate, and mixtures have been considered useful blasting materials. These materials are resorbable, leading to a clean, textured, pure Titanium surface **(Aparicio C, Gil FJ, Fonseca C, Barbosa M, Planell JA. et al, 2005).**

Experimental studies have demonstrated a higher bone-to-implant contact with these surfaces, when compared to machined surfaces and a BIC contact similar to that observed with other blasting surfaces when osseointegration is achieved.

Sub-micro and nano-porous surfaces, preferred to highly roughened one, can be produced by Etching and Anodization. These surfaces promote protein

adsorbtion, osteoblastic cell adhesion, and the rate of bone tissue healing in the peri-implant region **(Askeland DRP et al,2006).**

1-1-3-2-coating surface treatment

1-1-3-2-1-hydroxyapatite coating material

HA is one of the most biocompatible material ,HA enhance bone healing adjacent to the implant and a popular surface modification on dental implants (fig.8). HA coatings have the advantage of increasing surface area, decreasing

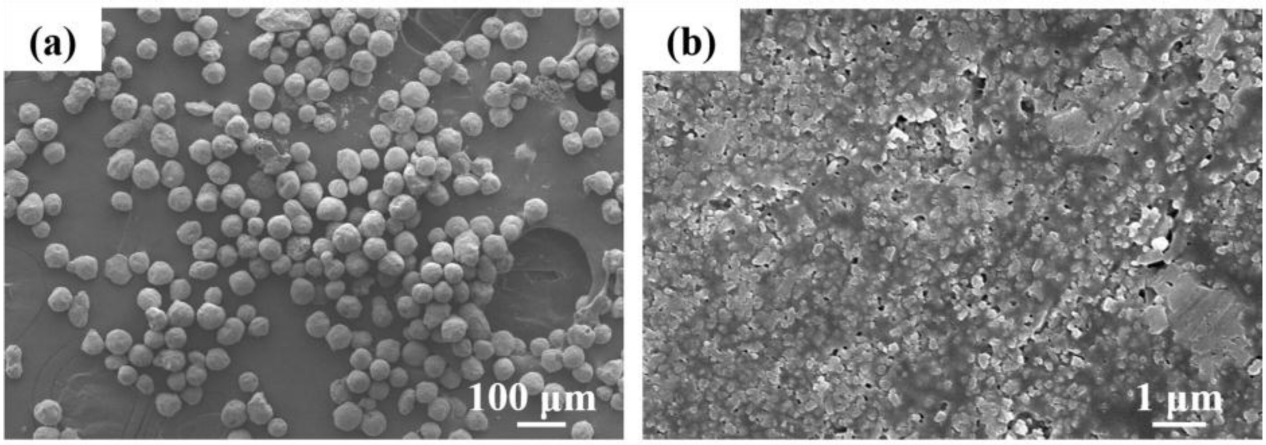

Figure 8: Hydroxyapatite (HA) powder morphology: (a) surface morphology; (b) cross-section morphology.

corrosion rates, and accelerating bone formation via faster osteoblast differentiation. Other advantages of HA include the more organized bone pattern and higher degree of mineralization at the interface, as well as increased bone penetration (which improves fixation). The bone bonding capabilities of HA make it a very desirable surface and probably the most reliable surface up to date. Due to their brittle nature, HA and fluorapatite cannot be used as implants in load-bearing applications **(Narayanan R, Seshadri SK, Kwon TY, Kim KH. et al 2008).** Therefore, load-bearing implants have been coated with HA and fluorapatite. The objectives of employing apatitic coatings are to cause

an earlier stabilization of the implants in the surrounding bone and to eliminate the use of polymethylmethacrylate bone cement around hip prostheses. Numerous methods of depositing HA on metallic implants have been reported. The current deposition process for commercial dental and orthopedic implants is plasma spraying or arc plasma spraying. Plasma spraying of HA usually takes place under normal atmospheric conditions, as opposed to the plasma spraying of some metallic powders during which a vacuum or an inert atmosphere is used to minimize oxidation. It has been reported that plasma spraying of HA results in coatings with a thickness greater than 30 um. This is a thermal spraying process that utilizes a gas stream to carry HA powders, which are then passed through an electrical plasma produced by a low-voltage, high-current electrical discharge **(Yang Y, Dennison D, Ong JL. et al 2005).** The composition of the carrier gas may be pure argon or a hotter plasma that is produced by a small addition of hydrogen or other gases. With all other coating parameters remaining unchanged, a gas composition of 90% argon and 10% hydrogen results in a significantly hotter plasma than the use of 100% argon. The semi-molten HA powders are sprayed onto the titanium substrate, where they solidify. Advantages of plasma spraying include a rapid deposition rate and sufficiently low cost. However, problems cited with the plasma-sprayed coatings include variation in bond strength between the coatings and the metallic substrates, alterations in HA structure due to the coating process, and poor adhesion between the coatings and metallic substrates. As in the case of the adhesion between the plasma-sprayed coatings and the metallic substrates, the nature of the substrate plays an important role. The bonding of the plasma-sprayed HA coatings appears to be entirely mechanical in nature. Evidence has been presented that a highly roughed substrate surface exhibits a higher bond strength when compared with a smooth substrate surface **(Joo LOng and Daniel Chan. et al, 2000).**

1-1-3-2-2-Carbon coatings:

carbon coatings as a type of implant coating material. Thin car bon film with a chemical composition of Ti0.500.3C0.2 has been used to coat TI implants. Carbon-coated implants were reported to give a good and stable chemical inertia between the carbon coating and the etching agent used. The carbon coatings were also found to be hemocompatible, histocompatible, bio stable, and chemically stable in vitro and in vivo.

The corrosion resistance of the carbon coating could be improved by plasma immersion ion implantation and deposition or by direct carbon bonding. The surface properties together with the biologic properties were found to be improved by carbon plasma immersion ion implantation and deposition. **(Oshida Y, et al).** The direct carbon bonding actually allows for osteoblast adhesion and proliferation at the surface of the nickel-titanium (NiTi) shape memory alloy. Even though this seems to be a promising form of implant coating, not much long-term data could be found and most studies focused on other more innovative materials.

1-1-3-2-3- Bioactive glass and bioactive ceramics:

Bioactive glasses and ceramics also have been proposed as good, innovative surface coatings for dental implants due to their glass properties, which would help obtain better implant osseointegration and reduced prosthetic corrosion in the body fluids. The thermal expansion coefficients of the bioactive glass es and ceramics are usually much larger than those of Ti oxide. This thermal expansion can be reducedby increasing the silicon dioxide (SiO2) content of the bioglass. On the other hand if the SiO2, content is increased the bioactivity of the glass

coating is reduced significantly. The main disadvantage of these coatings is the limitation of use in load-bearing areas. Bioactive glass is actually a family of glass compositions that allow bonding to the peri-implant tissues within a short span of time. In a recent study, a reactive plasma spray bioactive glass coating was used to demonstrate the behavior of this type of surface coat ing in load-bearing situations. It was concluded that a coating material can only be considered functional if it satisfies the following two criteria:

Able to withstand the load-bearing forces imposed on them while maintaining a strong bond with the implant surface to be totally functional. In vitro results showed that the bioactive glass satisfied both criteria even after a couple of months of load-bearing analyses. It was also demonstrated that the silicate glasses have to have a weight percentage higher than 60% so as to be able to withstand corrosion and thermal expansion of the coating. Silica contents above 60% weight would delaminate and crack. This can be circumvented by partial substitutions of calcium oxide (CaO) by magnesium oxide (MgO) and Na:O by potassium oxide (KO) in the bioglass composition to match the thermal expansion between the coatings and that of Ti-based alloys **(Lobez, estbana Set al,2003)** bioactive glasses were applied as a coating on Ti dental implants by an enameling technique with HA coatings acting as a control. Overall results showed that the bioactive glass coatings were as equally successful as HA coatings in achieving osseointegration and bioactivity. **(Maria xuereb, et al. 2015).**

1-1-3-3-Technique of coating:

1-1-3-3-1- plasma spattering technique:

Plasma-spraying is the most widely used technique for the commercial application of HA coatings to prosthetic implants. Even though it is the most

widely used technique due to the tight adhesion between the implant surface and the coating, studies have shown that the coating is prone to adhesion failure and cracking.Others have evaluated the elevated temperatures required during the coating process, which can cause detrimental effects on the prosthesis, including an alteration in the crystalline structure, the formation of a highly crystalline HA surface, and an eventual debonding of the coating." Plasma sprayed HA coating, which results in a minimal phase decomposition and high crystallinity without affecting the adhesive bond strength of the coating material, has been proposed. It was also found that disintegration of the surface coating occurred; this was mainly due to the excessive dissolution of the HA layer with amorphous Ca,(PO)2 formation and cracking of the coating.

The modulus of elasticity, stress, and strain; bonding strength; and microstructural analysis of such a coated implant were investigated in the presence of Hank's salt solution and also without being immersed in solution. It was concluded that all of the factors investigated deteriorated on insertion into the solution. This was mainly caused by the degraded co- hesive bonding in the coating material due to an in creased porosity.

From this, one may conclude that even though HA gives a promising bond with the Ti implant, the long-term properties of the material can alter from the initial ideal bonding to the eventual degradation of the cohesion **(Nikolia.etal.,2015).**

1-1-3-3-2-Hydrocoating techniques:

This is another way to coat Ti implants with an HA layer. Several hydro coating techniques have been proposed. These in clude cathode electrolysis, electrophoresis, and the thermal substrate technique. Because the latter two are single-step coating techniques, the HA is applied directly to the surface from solution. Hydroprocessing is used to coat complex-shaped substrates. This is

used in such cases where high temperatures cannot be used but at the same time the collagen content and mass has to be studied closely **(Jossete camilleri, et al. 2015).**

1-1-3-3-3-Nanoscale technology:

In a study by Jiang et al, HA particles were charged as they were expelled from a powder spray gun while being exposed to an electrostatic field. The latter guided the charged particles toward the Ti to form a uniform coating. The coated Ti was then sintered in a microwave furnace.

Nanoscale technology was found to give several benefits, include ing improved adhesion with decreased chances of delamination, increased surface areas for osseointegration, and improved implant-tissue integration to gether with a resulting chemistry mimicking that of natural osseous tissue. This showed that this innovative technology can overcome the problems arising with other mentioned coating methods, thus improv ing the properties of the prosthesis. **(Attard, et al. 2015).**

1-1-3-3-4-Two process stage technique:

Two-stage process. This process involves micro arc oxidation of Ti forming Ti films followed by UV light illumination of the films in simulated body fluids. This technique was then further developed and improved into the sol-gel technique. This more innovative method resulted in a coating having a good homogenous composition, low crystallization temperature, and fine grain size. HA and fluor-HA films were deposited on a Ti substrate using the sol-gel technique.

Various fluoride concentrations were in corporated into the HA structure during the sol phase preparation. The coating rate of dissolution decreased with increasing fluoride concentrations. As expected, pure Ti implants gave less expression levels when compared to the activity present between the alkaline phosphatase and the apatite coatings **(Attard, et al. 2015).**

1-1-4-Assessment of Osseointegration

Continuous and reliable monitoring of the status of osseointegration is recommended for the success of implants. Implant stability, more specifically the secondary implant stability, reflects the quality of osseointegration. Microscopic or histological analysis has been the standard methodology for assessing osseointegration status for centuries; however, due to its invasiveness, other methods such as radiographic, cutting torque resistance, reverse torque, and model analyses are now being used.

1-1-4-1- Histomorphometric Assessment:

Histological assessment provides an in depth knowledge of the bone quality around the implant, contact percentage between bone and implant, type of bone formed, and morphological characteristics of the osteocytes, such as size, orientation, and alignment to the bone lamellae, number and density, proximation to blood vessels, and lacunocanalicular interconnectivity between neighboring and distant osteocytes (fig.9).

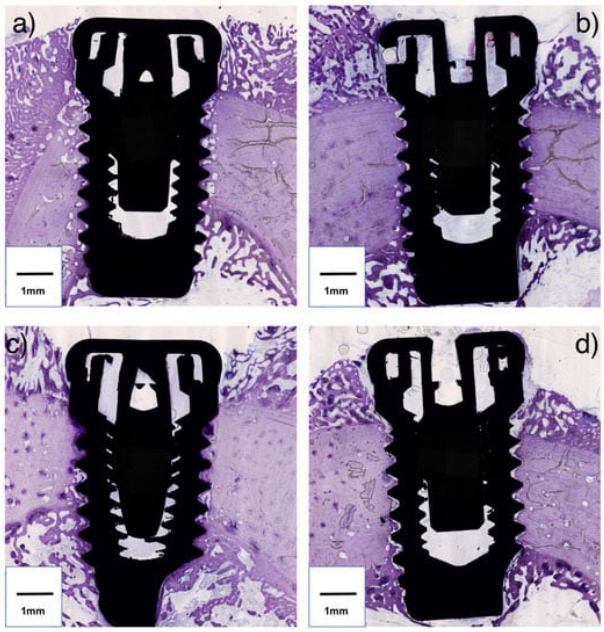

Figure 9: Histologic sections of the implant and peri-implant bone (original magnification 20×). Representations of group A, B, C, and D are depicted in (**a**), (**b**), (**c**), and (**d**), respectively. https://doi.org/10.1111/j.1600-0501.2011.02306.x.

However, due to the invasiveness of the analysis, it is reserved for nonclinical studies or experiments **(F. A. Shah, P. Stenlund, A. Martinelli, P. Thomsen, and A. Palmquist, et al 2016).**

1-1-4-2- Radiographic Assessment:

Radiographic visualization through the routinely used techniques is a noninvasive way to assess osseointegration by radiographical points (fig.10). The evaluation of the osseointegration is by using a digital orthopantomogram and cone-beam computed tomography (CBCT).

The osseointegration was found to be 0.03 mm at the apical portion of implants and 0.04 mm at the crestal bone height on digital orthopantomogram and 0.01 mm at the apical portion on CBCT after three months of implant placement.

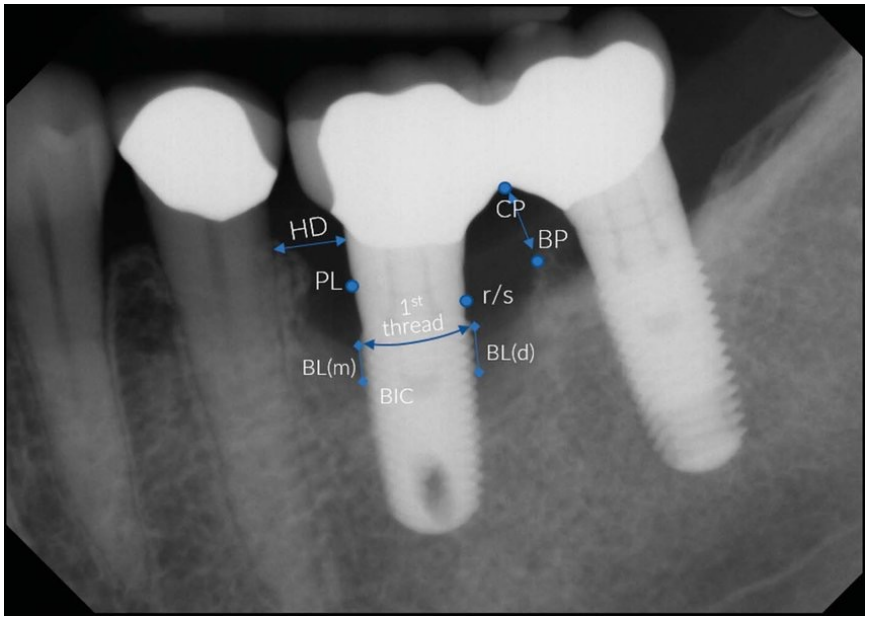

Figure 10: Radiographic points, Schematic drawing showing the selected reference points. PL, r/s, and first radiographic BIC were identified. HD represents horizontal distance between the adjacent tooth and PL, and BL-1st TD (m) and BL-1st TD (d) represent vertical distance between BL and the first implant thread at mesial (BL (m)) and distal (BL (d)) implant surfaces at the most recent follow-up appointment respectively. PL indicates implant platform; r/s, rough/smooth implant border; BIC, bone-implant contact. https://jkamprs.springeropen.com/articles/10.1186/s40902-020-00258-3.

They suggested that both orthopantomogram and CBCT are efficient at assessing osseointegration.

Although computed tomography lures a clinician as a better technique for evaluating the same, one must restrict its use to the point of benefit with the lowest radiation doses. It is essential to differentiate between the bone formed by contact and distant osteogenesis. At times, failure may occur due to poor bone to implant contact despite large amounts of bone in the implant threads **(A.Chopra,A.A.Mhapuskar,S.Marathe,S.U.Nisa,S.Thopte, and R. Saddiwal. et al, 2016).**

This differentiation is difficult on routine radiographs, and in fact, even the highly sophisticated ex vivo X-ray microcomputed tomography cannot resolve

the first few millimeters around the implant surface. We can use of synchrotron radiation X-ray microimaging to evaluate osseointegration. They used unmonochromatic synchrotron radiation to study the bone-to-implant interface and compared the yielded image quality with microcomputed tomography images and conventional dental radiographs, focusing the evaluation mainly on the osseous contact at the bone-to-implant interfaces. They unveiled that the synchrotron radiation imaging technique provided finer details of the osseous contact. Thus, they expected this technique to bring an enormously positive influence on the studies on the evaluation of osseointegration **(A. Palmquist, F. A. Shah, L. Emanuelsson, O. Omar, and F. Suska. et al, 2017).**

1-1-4-3- Clinical Assessment:

The tests used in clinical practice are either invasive or noninvasive.

1-1-4-3-1- The tensional test:

Which involves detaching the implant plate from the supporting bone, was one of the invasive tests used in the past. Later, Branemark tested osseointegration by applying lateral load to the implant fixture. Similarly, the push or pull out test, which assesses strength and stiffness at the bone-implant interface by applying a load parallel to the interface, is only applicable to nonthreaded cylindrical implants and is technique dependent **(S. Meenakshi, N. Raghunath, S. N. Raju, S. Srividya, and P. N. Indira. et al, 2013).**

1-1-4-3-2-The reverse torque test:

To assess secondary stability, may rotate the implants and destroy the bone-implant interface when torque is applied.

Furthermore, due to varying threshold limits among patients, implant material, and bone quality and quantity, the test cannot quantify the degree of osseointegration. Recently, the focus has shifted to noninvasive methods that now outnumber the invasive ones. These noninvasive methods can be enlisted from the simplest one, involving the perception of a surgeon acquired by the cutting resistance and seating torque during implant placement. However, this typically measures the primary stability of the implant, not reflecting the real picture of osseointegration at the healing stages **(T. Albrektsson, P. I. Brånemark, H. A. Hansson, and J. Lindström. et al, 1981).**

1-1-4-3-3- The insertion torque values:

Can be used to assess the quality of bone in various parts of the jaw during implant placement, but they cannot evaluate the secondary stability provided by the new peri implant bone formation and remodeling **(T. Irinakis and C. Wiebe. et al, 2009).**

1-1-4-3-4- The percussion test:

A simpler test, using a metallic instrument, based upon the science of vibration, acoustics, and impact response, can evaluate osseointegration, with the “crystal-like” clear sound indicative of successful osseointegration and a dull sound expressive of otherwise. However, it is a subjective method and cannot be standardized. An advanced technique using the forced excitation of steady state waves that helped examine the mechanical vibrations at the bone

implant interface displayed on an oscilloscope screen **(D. Bayarchimeg, H. Namgoong, B. K. Kim. et al, 2013).**

1-1-4-3-5- The resonance frequency analysis:

Measures bone densities at different time points using vibrations and the principle of structural analysis. The implant is shattered at a constant amplitude by an amplifier vibrated by a sinusoidal signal (5-15kHz). A high frequency resonance indicates a strong bone implant interface. This method has been widely used to assess osseointegration in clinical settings. The Osstell (electronic technology resonance frequency analysis) and Osstell mentor are advanced versions of this technique (magnetic technology resonance frequency analysis) **(C. Aparicio, N. P. Lang, and B. Rangert, et al, 2006).**

1-1-5- Failure of osseointegration

Osseointegration may be failed due infection or over loading of implant. In case of infection, Infections within 3 months are considered as early postoperative infection, while delayed (or subacute) infection occurs after 3-24 months and late infection more than 24 months later **(Montanaro et al., 2011; Zimmerli, 2014).**

Bacterial colonization on dental implants may not lead to ultimate implant failure; however, prolonged exposures may generate host tissue inflammatory reaction. There are two major types of dental implant infection: peri-implant mucositis and peri-implantitis **(Norowski PA, Bumgardner JD. et al 2009).**

The peri-implant mucositis is defined as a reversible inflammatory reaction in soft tissues surrounding the dental implant, peri-implantitis is considered to be an inflammatory reaction with the loss of supporting bone surrounding an implant. Pontoriero et al studied the clinical and microbiological response to the development of experimental gingivitis and experimental peri-implant mucositis and concluded that there were no significant differences found between them.The treatment option for peri-implant mucositis largely is based upon the management of plaque control, where surface debridement constitutes the basic element for treatment **(Pontoriero R, Tonelli MP, Carnevale G, Mombelli A. et al 1994)**

Peri-implantitis has an overall incidence rate of 12%–43%. If the early stages of peri-implantitis persist, implant–bone integration may be compromised, and subsequently, the implant will be lost **(Albrektsson T, Isidor F. et al 2011).**

Presently, no single pathogen has been closely associated with infection of any implant system. however, the microbial floras of failing implants have been associated with the pathogens of periodontitis. Several reports cited that these implants were colonized with putative periodontal pathogens, including *Peptostreptococcus micros*, *Fusobacterium* spp., enteric gram-negative rods, and yeast. Moreover, the frequency of peri-implantitis in patients with a history of periodontitis has been reported to be four to fivefold higher than that of individuals with no histology of periodontitis, thereby indicating a closer tie between both types of infections **(Klinge B, Hultin M, Berglundh T. et al 2005).**

After operation, patients need systemic antibiotic treatment to prevent infections, but the rising antibiotic resistance of bacteria can make the existing antibiotics noneffective **(Park et al., 2019).** Also, the concentration of antibiotics in the focus site is insufficient, resulting in the rapid proliferation

and secretion of extracellular polymers to form a biofilm after some pathogens gather and adhere to the implant surface **(Gristina and Costerton, 1985).**

A review of the treatment used for peri-implantitis has revealed that surgical removal of the lesion followed by cleaning of the affected implant with hydrogen peroxide, chlorhexidine, citric acid, tetracycline, lasers, etc, and a systemic antibiotic therapy are effective methods **(Pye AD, Lockhart DEA, Dawson MP, Murray CA, Smith AJ. et al 2009).**

Revised criteria for implant success **(Gross KA et al, 1997).**

1. Individual unattached implant is immobile when tested clinically.

2. No evidence of peri implant radiolucency is present as assessed on an undistorted radiograph.

3. Mean vertical bone loss is less than 0.2 mm after 1st year of service.

4. No persistent pain, discomfort or infection.

5. A success rate of 85% at the end of a 5-year observation period and 80% at the end of a 10 years period are minimal levels of success.

Conclusion

I.Osseointegration" is a multifactorial entity. It is because of the attention to training, research & clinical studies that osseointegration has now become an accepted part of the treatment regime in many countries worldwide and no longer regarded as the last resort when all else has failed but often as a treatment of choice.

II. Various processes exist to treat the surface of commercially available implants. Most of these surfaces have been analyzed by in vivo and in vitro studies, showing high clinical success rates. However, the methodologies used to prepare these surfaces are mostly empirical, requiring a great number of assays. Moreover, the tests are not standardized and this makes it difficult to compare the results.

III. The dental implant surface treatment influences the way cells adhere to the surface, which influences differentiation, proliferation and formation of extracellular matrix.

IV. Topographic characteristics, roughness, energy and chemical composition modify cell growth and change cell function at the initial stages of osseointegration.

V. Further studies are needed to improve and describe the interaction between cells and implant surfaces, as well as to assess the influence of different parameters involved, such as proteins, bone formation stimuli and individual therapy, for compromised patients.

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