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A BRIEF REVIEW: OSSEOINTEGRATION

Dr. Shruti Dabi[1], Dr. Kuldeep Tiwari[2] , Dr. Ashpreet Kaur[3], Dr. Astha Doshi [4]
Private Practice[1,2] (Rajasthan University of Health Science)[1,2,3,4], Senior Lecturer[3,4]
[1]Private Practice, Ajmer (Rajasthan) (BDS, MDS in Periodontology & Oral Implantology),
[2]Private Practice, Bharatpur (Rajasthan) (BDS, MS in Oral Implantology),
[3]Senior Lecturer, Department of Periodontics, Geetanjali Dental and Research Institute, Eklingpura Udaipur (Rajasthan),
[4]Senior Lecturer, Department of Public Health Dentistry, Darshan Dental College and Hospital, Loyara, Udaipur (Rajasthan)

Corresponding Author:
Dr. Shruti Dabi
(BDS, MDS)

ABSTRACT

Termed osseointegration meaning "a direct functional and structural connection between living bone and the surface of a load carrying implant". This review aims to discuss the basic process, mechanism, theories, interaction, mechanism to evaluate & to enhance osseointegration for success of implant treatment.

Keywords: Osseointegration, Fibroosseous interaction, Functional ankylosis

INTRODUCTION

Albrektsson *et al*. (1981) suggested that osseointegration was "a direct functional and structural connection between living bone and the surface of a load carrying implant". Zarb and Albrektsson (1991) who proposed that "a process whereby clinically asymptomatic rigid fixation of alloplastic materials is achieved and maintained in bone during functional loading" was osseointegration. Acc to GPT- The apparent direct attachment or connection of osseous tissue to an inert, alloplastic material without intervening connective tissue". Schroeder *et al*. (1976, 1981, 1995) used the term *"functional ankylosis"* to describe the rigid fixation of the implant to the jaw bone, and stated that "new bone is laid down directly upon the implant surface, provided that the rules for atraumatic implant placement are followed and the implant exhibits primary stability".

OSTEOPRESERVATION (STALLARD R.E) Tissue integration around healed functioning endosteal dental implant in which the prime load bearing tissue at the interface is a periimplant ligament composed of osteostimulatory collagen.

PERIOSTEAL INTEGRATION Tissue integration around a healed functioning subperiosteal implant in which the load bearing tissue is the sheath of dense collagenous tissue constituting the outer layer of periosteum.

HISTORICAL ASPECT

The concept of Osseointegration based on research that began by ***Dr. Per-Ingvar Branemark in 1952***. He wanted to observe the microcirculation of both soft and hard tissues under various phases of injuries. He implanted titanium optic chamber into rabbit's fibula and carried the investigation with microscopic (essentially made of titanium) & when he tried to remove the titanium chamber, he found that bone was normally adhered to the metal.

PROCESS OF OSSEOINTEGRATION

Custom-made implants (made of c.p. titanium) in the shape of a solid screw and configured with a rough surface topography were utilized (Fig. 1). In the implant device, the distance between two consecutive profiles of the pitch (i.e., the threads in a vertical cross-section) were 1.25 mm. A 0.4-mm deep U-shaped circumferential trough had been prepared within the thread region during manufacturing (Fig. 2). The tip of the pitch was left untouched. Following the installation of the non-cutting device (Fig 3), the pitch was engaged in the hard tissue walls prepared by the cutting/ tapping device. This provided initial or primary fixation of the device. The void between the pitch and the body of the implant established a geometrically well-defined wound chamber (Fig.4). Biopsies were performed to provide healing periods extending from 2 hours following implant insertion to 12 weeks of healing. The biopsy specimens were prepared for ground sectioning as well as for decalcified sectioning.

Fig 1- Custom-made implants

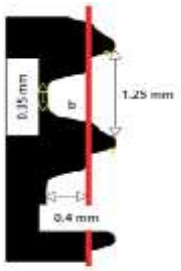


Fig 2 -Drawing illustrating the Dimensions of the wound chamber

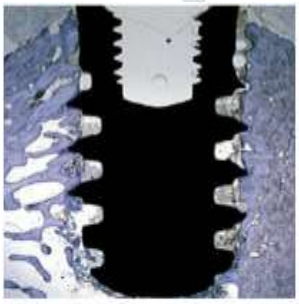


Fig 3- Ground section showing the implant and adjacent tissues immediately after implant installation. The pitch region is engaged in the hard tissue walls. The void between two consecutive pitch profiles include the wound chamber

Fig 4 -Detail of Fig.3. The wound chamber was filled with blood and a coagulum has formed.

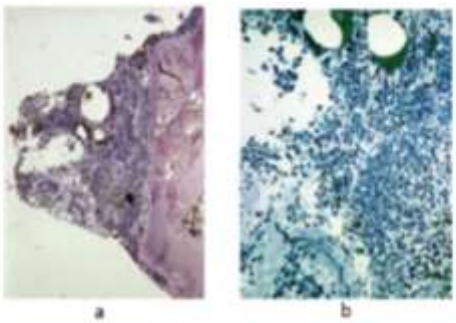
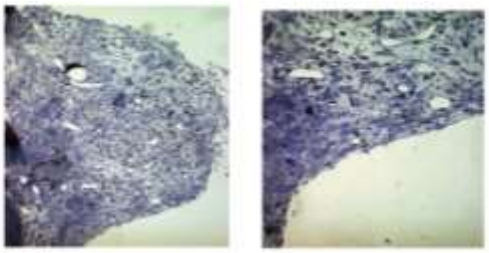


Fig 5 -Wound chamber 2 hours after implant installation. Decalcified sections.
(a) The wound chamber is filled with blood.
(b) Erythrocytes, neutrophils and macrophages are trapped in a fibrin

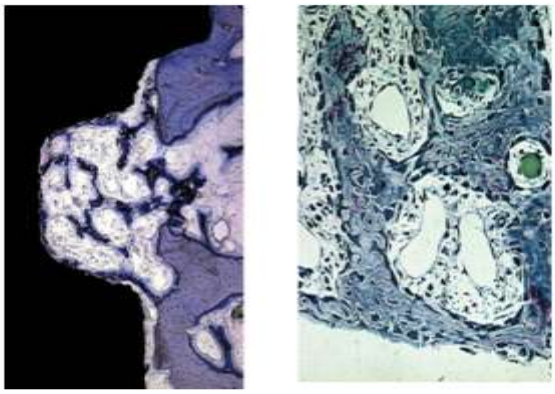
The wound chamber: Figure 4 illustrates a cross section (ground section) of an implant with surrounding soft and hard tissues from a biopsy specimen sampled 2 hours after installation of the metal device. The peripheral portions of the pitch were in contact with the invaginations of the track prepared by the tap in the cortical bone. The wound chambers (Fig. 5a) were occupied with a blood clot in which erythrocytes, neutrophils, and monocytes/ macrophages occurred in a network of fibrin (Fig. 5b). The leukocytes were apparently engaged in the wound cleansing process.

Fibroplasia: Figure 6a illustrates a device with surrounding tissues after 4 days of healing. The coagulum had in part been replaced with granulation tissue that contained numerous mesenchymal cells, matrix components, and newly formed vascular structures (angiogenesis) (Fig. 6b). A *provisional connective tissue (matrix)* had been established.



a b

Fig 6-Wound chamber after 4 days of healing (decalcified sections).
(a) Most portions of the wound chamber are occupied by granulation tissue (fibroplasia).
(b) In some areas of the chamber, provisional connective tissue

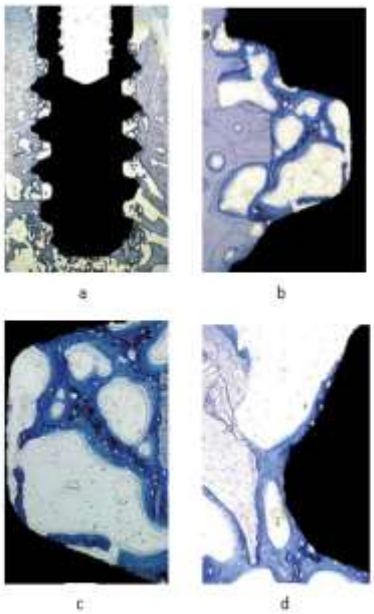


a b

Fig 7-(a) Ground section representing 1 week of healing. Note the presence of newly formed woven bone in the wound chamber. (b) Decalcified section. The woven bone is in direct contact with the implant surface.

Bone modeling: After 1 week of healing, the provisional connective tissue in the wound chambers was rich in vascular structures and contained numerous mesenchymal cells (Fig 7a). The number of remaining inflammatory cells was relatively small. In several compartments of the chamber, a cell-rich immature bone (woven bone) was seen in the provisional connective tissue that surrounded the blood vessels. Woven bone formation occurred in the center of the chamber as well as in discrete locations that apparently were in direct contact with the surface of the titanium device (Fig. 7b). This was considered to represent the very first phase of osseointegration; contact between the implant surface and newly formed woven bone.

After 2 weeks of healing, woven bone formation appeared to be pronounced in all compartments, apical as well as lateral, surrounding the implant (Fig.8a). Large areas of woven bone were found in the bone marrow regions "apical" of the implant. In the wound chamber, portions of the newly formed woven bone apparently extended from the old bone into the provisional connective tissue (Fig.8b) and had in many regions reached the surface of the titanium device. At this interval, most of the implant surface was occupied by newly formed bone and a more comprehensive and mature osseointegration had been established (Fig. 8c). In the pitch regions, there were signs of ongoing new bone formation (Fig. 8d). Thus, area of the recipient site located lateral to the device, that were in direct contact with the host bone immediately following installation surgery and provided initial fixation for the implant, had undergone resorption and were also involved in new bone formation after 2 weeks of healing.



a b c d

Fig 8- Ground sections showing, in various magnifications, the tissues in the wound chamber after 2 weeks of healing.
(a) Darker stained woven bone is observed in the apical area of the metal device.
(b–d) Most portions of the implant surface are coated with bone.

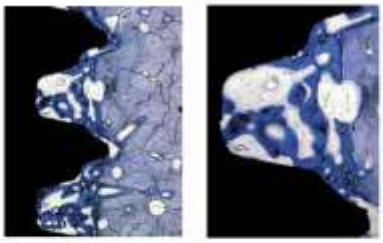


Fig 9- Ground sections representing 4 weeks of healing.
(a) Newly formed bone (dark blue) extends from the "old" bone into the wound chamber.
(b) Appositional growth. Note the presence of primary osteons.

At 4 weeks (Fig.9a), the newly formed mineralized bone extended from the cut bone surface into the chamber and a continuous layer of cell-rich, woven bone covered most of the titanium wall of the chamber. The central portion of the chamber was filled with a primary spongiosa (Fig.9b), rich in vascular structures and a multitude of mesenchymal cells

Remodeling: After 6–12 weeks of healing, most of the wound chambers were filled with mineralized bone (Fig. 5-19). Bone tissue, including primary and secondary osteons, could be seen in the newly formed tissue and in the mineralized bone that made contact with the implant surface. Bone marrow that contained blood vessels, adipocytes, and mesenchymal cells was observed to surround the trabeculae of mineralized bone.

Fig 10-Ground section representing 12 weeks of healing. The woven bone is being replaced with lamellar bone and marrow. Note the formation of secondary osteons.

MECHANISM OF OSSEOINTEGRATION

PHASE	TIME	SPECIFIC OCCURRENCE
INFLAMMATORY PHASE	DAY1-10	1. Adsorption of plasma protein 2. Platelet aggregation & activation 3. Clotting cascade activation cytokine release 4. Specific cellular inflammatory response 5. Macrophage mediated inflammation
PROLIFERATIVE PHASE	DAY 3-42 	1. Neovascularization (Differentiation , proliferation & activation of cell) 2. Production of immature C.T. matrix.
MATURATION PHASE	AFTER DAY 28	Remodeling (immature bone matrix with resorption & deposition & response to implant loading.

THEORIES OF OSSEOINTEGRATION

1 FIBRO-OSSEOUS INTEGRATION

It is presence of connective tissue between the implant and bone. In 1986, the American Academy of Implants Dentistry (AAID) defined fibrous integration as "tissue-to-implant contact with healthy dense collagenous tissue between the implant and bone". In this, soft tissue (cells/fiber) are interposed b/w 2 surfaces. This encapsulation of implant with C.T. occur more quickly than actual osseointegration. ***1980 Dr. Charles Weiss,*** proposed concept of fibroosseous integration. He stated that there is a fibroosseous ligament formed between implant & bone.

a) This ligament can be considered as equivalent to periodontal ligament found in gomphosis (Periimplant ligament with osteogenic effect & fibroosseous integration.) Therefore, implant can load immediately.

b) Fibroosseous integration is superior to osseointegration for mos

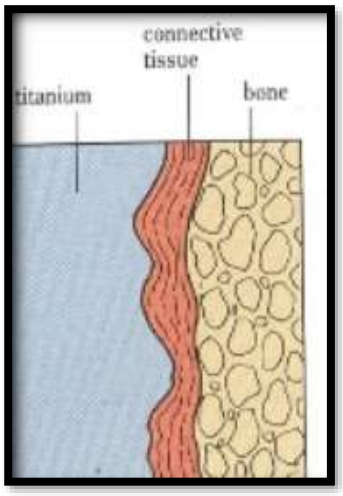


Fig 11 -Fibro-osseous integration

FAILURE OF FIBRO-OSSEOUS THEORY

According the theory, pseudo-periimplant Fibrous membrane gave a cushion effect and acted as similar as periodontal membrane in natural dentition.

A. No real evidence to suggest that these fibers functioned in the mode of periodontal ligament and when in function the forces are not transmitted through the fibers as seen in natural dentition. Therefore, remodeling was not expected to occur in fibrous integration.
B. Forces applied resulted in widening fibrous encapsulation, inflammatory reactions, and gradual bone resorption there by leading to failure.
C. Initial success may show, but long-term lead to failure due to collagen fibers (growing parallel to implant rather than directly into contact like natural).

2. OSSEOINTEGRATION

Meffert et al, (1987) redefined and subdivided the term osseointegration into "adaptive osseointegration" and "biointegration". "Adaptive osseointegration" is the osseous tissue approximating the surface of implant without apparent soft tissue interface at the light microscopic level and "Biointegration" is the Direct biochemical bone surface attachment confirmed at the electron microscopic level.

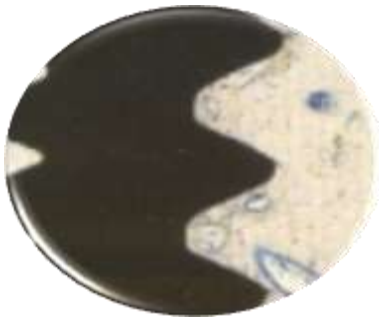


Fig 12- Osseointegration

de Lange & de Putter (1992), proposed 2 ways of implant anchorage or retention: -

1. MECHANICAL RETENTION - Can be achieved in cases where implant material is a metal.
Eg- Commercially pure titanium & titanium alloys. These cases, topological feature like vents, slots, dimples, thread (screw) etc. aid in retention of implant. There is no chemical bonding & retention depends on surface area i.e., greater surface area, greater is contact.

2. BIOACTIVE RETENTION- Can be achieved in cases where implant is coated with bioactive material such as hydroxyapatite. The bioactive material stimulates bone formation leading to a physio –chemical bond. Implant is ankylosed with the bone.

FACTOR AFFECTING

PATIENT RELATED FACTOR

1. Age
2. Gender
3. Metabolic disease
4. Rheumatic disorder
5. Smoking

LOCAL FACTOR

1. Status of host bone bed & its intrinsic healing potential.
2. Improper implant placement & inappropriate surgical procedure.

OTHER

1. Inappropriate porosity of porous coating of implant radiation therapy.
2. Pharmacological agents such as cyclosporine a, methotrexate & cis-platinum
3. Implant Biomaterial (Biocompatibility)
4. Implant Biomechanics
5. Implant Design
6. Implant Taper
7. Implant Width
8. Crest module design
9. Implant Surface Topography (Surface roughness)
10. Implant Surface Modifications
11. Contamination
12. Heat Production

INTERACTIONS

A) Implant epithelium interface (Biological seal)
During healing process, gingival shrinkage can be observed around neck of implant. During establishment of transmucosal attachment, soft tissue heals & re-organize itself acc. to new environment. During early phase of healing gingival tissue appears to shrink. This is due to longitudinal arrangement of major collagen fiber groups that amplifies the process of collagen

fibril contraction (part of collagen maturation) in vertical direction. Junctional epithelium around tooth (trigeminal ganglion= fiber contain neuropeptide, calcitonin gene related peptide & substance –P). (Similar periimplant) Periimplant epithelium is denser as compared to other parts of epithelium. Nerve fiber terminate close to peri-implant epithelium. Implant surface interface between epithelial cell = hemidesmosomes & basal lamina. Epithelial cell lining the implant surface = flattened, undifferentiated epithelial cells with few organelles such as mitochondria & endoplasmic reticulum.

B) Bone –Connective tissue interface

Connective tissue zone (close to implant) = scar tissue that is poor in vascular structures. Connective tissue (immediately next to implant surface) = absence of blood vessel & abundant fibroblast which are interposed between thin collagen fibers. Connective tissue at (distance from implant) has higher fiber content than that of gingiva around teeth.

Moon et al (1999) in dog experiment confirmed. Result showed 2 types of attachment.

1= Did not consist of any blood vessel with presence of fibroblast that aligned parallel to vertical axis (implant body).

2= Few fibroblast, high collagen fiber & vascular nerve structure (collagen fiber=85%, vasculature=3%, fibroblast=11%).

Collagen fibers are arranged parallel to titanium surface in implant as compared to natural tooth (perpendicular). Roughness of implant no bearing on adherence of soft tissue.

C) Bone-Implant Interface

A direct contact between living bone and implant".

Light microscopic level (100X) = Close adaptation of the regularly organized bone next to the Ti implants. Scanning electron microscopic level = Parallel alignment of the lamellae of Haversian system of the bone next to the Ti implants. No connective tissue or dead space at the interface. Ultramicroscopic (500 to 1000X) level= Amorphous coat of glycoproteins on the implants to which the collagen fibers are arranged at right angles and are partly embedded into the glycoprotein layer. Strength of the interface between bone & implant increases soon after implant placement (0–12 weeks). This strength may relate to the amount of bone surrounding the implant surfaces. Other factor that affects the strength of the interface = biophysical stimulation & time allowed for healing. Studies have shown measurable, increases in bone implant interactions take place for at least 3 years.

D) Bone –tissue Response

CONTACT OSTEOGENESIS=Bone 1st forms on implant surface. Osteogenesis proceed from implant to host bone. (The direct migration of bone-building cells through the clot matrix to the implant surface.)

Fig 13- Contact osteogenesis

DISTANCE OSTEOGENESIS Bone 1st form on surface of host bone & progressive towards implant surface. (Gradual process of bone healing inward from the edge of the osteotomy toward the implant). Implant surface play important role in osteogenesis. Experimental studies have shown, rough surface implant microtopography enhance osteoconduction & contact osteogenesis. On other hand, distance osteogenesis can be expected with polished surface & cortical host bone. Bone does not grow directly on the implant surface.

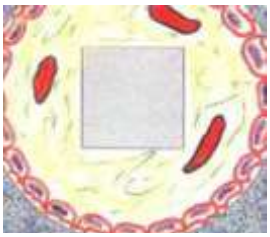


Fig 14- Distance Osteogenesis

METHODS OF EVALUATION OF OSSEOINTEGRATION

A- IMPLANT STABILITY

1. INVASIVE/DESTRUCTIVE METHODS:
   a) Histomorphometric analysis -This is obtained by calculating the peri-implant bone quantity and bone-implant contact (BIC) from a dyed specimen of the implant and peri-implant bone. Accurate measurement is an advantage, but due to the invasive & destructive procedure, it is not appropriate for long-term studies. It is used in the nonclinical studies and experiments & assessed at pre-, intra and post-surgical time points.
   b) Tensional test- It was earlier measured by detaching the implant plate from the supporting bone. Later modified by Branemark by applying the lateral load to the implant fixture. However, they also addressed the difficulties of translating the test results to any area independent mechanical properties.
   c) Push-out/pull-out test- Investigates the healing capabilities at the bone implant interface. It measures interfacial shear strength by applying load parallel to the implant-bone interface. Push-out/pull-out test, a cylinder-type implant is placed transcortically or intramedullary in bone structures & then removed by applying a force parallel to the interface. The maximum load capability (or failure load) is defined as the maximum force on the force displacement plot, and the interfacial stiffness is visualized as the slope of a tangent approximately at the linear region of the force displacement curve before breakpoint.

Fig 15- Push out / pull out test

   d) Removal torque analysis-Removal torque analysis implant is considered stable if the reverse or unscrewing torque was >20 Ncm. Disadvantage = at the time of abutment connection implant surface in the process of osseointegration may fracture under the applied torque stress. Reverse torque assessment; pull-out and push-out techniques are generally used only in preclinical applications and may be of value as research techniques. The clinical usage of destructive tests is limited due to ethical concerns associated with invasive nature of these methodologies.

2. NONINVASIVE/NONDESTRUCTIVE METHODS: -
   a) Cutting torque resistance analysis-This was developed by Johansson and Strid. Later improved by Friberg et al. The amount of unit volume of bone removed by current fed electric motor & is measured by controlling the hand pressure during drilling at low speed. Determines areas of low-density bone & quantifies bone hardness during implant osteotomy at the time of implant placement (implant failures was seen in jaws with advanced resorption & poor bone quality).

      Limitation
      I. Does not give any information on bone quality until the osteotomy site is prepared.
      II. Cannot identify the lower "critical" limit of cutting torque value (i.e., the value at which the implant would be at risk).
   b) Insertion torque measurement-Measure the bone quality. Used for independent stability measurement, but it may also act as variable, affecting implant stability. Mechanical parameter affects the implant design & bone quality at the implant site. Cannot assess the secondary stability by new bone formation & remodel around the implant. Hence,

it cannot collect longitudinal data to assess implant stability change after placement. Increase (insertion torque) = increase (primary stability).

c) Reverse torque test- Proposed by Roberts et al.& developed by Johansson and Albrektsson. Use to assess the secondary stability of the implant. Implants that rotate when reverse torque is applied indicate that BIC could be destroyed. Further, it cannot quantify the degree of osseointegration as threshold limits vary among patients, implant material, bone quality and quantity. The studies showed, the stress of the applied torque responsible for the failure. Not measure lateral stability that is a useful indicator for successful treatment outcome

d) Seating torque test- Like insertion torque, the final seating torque gives some information about the primary stability of the implant when the implant reaches its final apico-occlusal position.

e) Modal analysis /Vibration Analysis-Measures the natural frequency or displacement signal of a system in resonance, which is initiated by external steady-state waves or a transient impulse force. It can be performed in two models: Theoretical & Experimental.

f) Percussion test-Test is based upon vibrational-acoustic science and impact response theory. The clinical judgment on osseointegration is based on the sound heard upon percussion with a metallic instrument. A clearly ringing "crystal" sound indicates successful osseointegration, whereas a "dull" sound may indicate no osseointegration. However, this method heavily relies on the clinician's experience level and subjective belief. So, it cannot be used experimentally as a standardized testing method.

g) Pulsed oscillation waveform (Kanek)-Analyze mechanical vibrational characteristics of the implant-bone interface using forced excitation of a steady-state wave. POWF is based on estimation of frequency and amplitude of the vibration of the implant induced by a small pulsed force. This system consists of an acoustoelectric driver (AED), acoustoelectric receiver (AER), pulse generator and oscilloscope. Both the AED and AER consist of a piezoelectric element and a puncture needle. A multifrequency pulsed force of about 1 kHz is applied to an implant by lightly touching it with two fine needles connected with piezoelectric elements. Resonance and vibration generated from the bone-implant interface of an excited implant are picked up and displayed on an oscilloscope screen. It is used for in vitro and experimental studies. An in vitro study showed that the sensitivity of the POWF test depended on load directions and position.

h) Periotest- Quantifies the mobility of an implant by measuring the reaction of the peri-implant tissues to a defined impact load. Introduced by Schulte to perform measurements of the damping characteristics of the periodontal ligament, thus assessing the mobility of natural tooth. They are used as an electro-magnetically driven and electronically controlled tapping metallic rod in a handpiece. Periotest value range from −8 (low mobility) to +50 (high mobility). Can measure the bone density at the time of implant placement and postsurgical placement of the implant. Response to a striking or "barking" is measured by a small accelerometer incorporated into the head. Reliability of this method is questionable because of poor sensitivity, susceptibility to many variables.

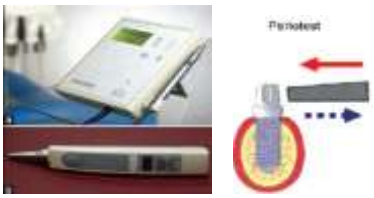


Fig 16- Periotest

i) Resonance frequency analysis-It was suggested by Meredith in 1998. Noninvasive diagnostic method that measures implant stability and bone density at various time points using vibration and a principle of structural analysis. Utilizes small L-shaped transducer that is tightened to the implant or abutment by a screw. Transducer comprises of two ceramic elements, one of which is vibrated by a sinusoidal signal (5–15 kHz) while the other serves as a receptor. Transducer is screwed directly to the implant body and shakes the implant at a constant input and amplitude, starting at a low frequency

and increasing in pitch until the implant resonates. High frequency resonance indicates stronger bone-implant interface. Provides baseline reading for future comparison and postsurgical placement of the implant. Widely used for clinically assessing osseointegration, as well as for prognostic evaluation. Most recent version of RFA = wireless gadget. A metal rod is attached to the implant with a screw connection. Rod has a small magnet attached to its top that is stimulated by magnetic impulses from a handheld electronic device. Rod mounted on the implant has two fundamental resonance frequencies; it vibrates in two directions, perpendicular to each other. One of the vibrations is in the direction where the implant is most stable and the other is in the direction where the implant is least stable. Currently, two RFA machines are in clinical use: Osstell® (integration diagnostics) and Implomates® (Bio TechOne).

Fig 17- Resonance frequency analysis

B-NEWER METHODS UNDER RESEARCH

a) Implatest conventional impulse testing
b) Electro-mechanical impedance method
c) Micro motion detecting device
d) Highly nonlinear solitary waves method

RIGID FIXATION

Absence of observed clinical mobility. A healthy implant moves less than **73microns** = zero clinical mobility. The goal for root form implants should be rigid fixation.

Scale	Description
0	Absence of clinical mobility with 500 g in any direction
1	Slight detectable horizontal movement
2	Moderate visible horizontal mobility up to 0.5 mm
3	Severe horizontal movement greater than 0.5 mm
4	Visible moderate to severe horizontal and any visible vertical movement

MISCH'S CLINICAL IMPLANT MOBILITY SCALE

THE SUCCESS CRITERIA Acc to (ALBERKTSSON ET AL):-

Commonly accepted criteria for the assessment of implant success were proposed by Albrektsson and colleagues (Albrektsson *et al*., 1986). Individual unattached implant showed immobile (clinically). Radiographic evaluation should not show any evidence of radiolucency. Vertical bone loss around fixtures should be less than 0.2mm per year after first year of implant loading. Implant should not show any signs of pain, infection, neuropathies, paresthesia, violation of mandible canals and sinus drainage. Success rate of 85% at the end of 5 year and 80% at the end of 10years**.** Over the past three decades, implant success has been assessed by survival rates, continuous prosthesis stability, radiographic bone loss, and absence of infection in the peri-implant soft tissues (Albrektsson *et al*., 1986; Smith and Zarb, 1989; Buser *et al*., 1990; Albrektsson and Zarb, 1998; Misch *et al*., 2008; Annibali *et al*., 2009).

ENHANCE OSSEOINTEGRATION-

1. Use of computer aided radiographic treatment planning & surgical guide fabrication using advanced computer aided design/computer aided manufacturing software.
2. Implant surfaces with hydrophilic properties that promote osteoconduction of new bone growth.
3. Use of recombinant human growth factors on the implant surface or as a part of the placement.
4. Surface chemistry modifications to accelerate bone growth (fluoride modified titanium oxide surface).

CONCLUSION

Thorough understanding and application of factors affecting the osseointegration and biological process of osseointegration in clinical practice is the key factor for success.

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