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REVIEW ARTICLE



Some aspects of bone remodeling around dental implants

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ABSTRACT

Considering that success of dental implants is not only related to osseointegration, but also with their survival rates, the aim of this study was to perform a literature review about bone remodeling around osseointegrated implants. A detailed search strategy was used for this, and articles published between the years 1930 and 2012 were selected. The rare data found in the literature demonstrated that implants are osseointegrated 30 days after their placement. However, active bone remodeling with osteoclasts and osteoblasts working in synchrony continues to occur. Therefore, after osseointegration, the initially formed bone, which presents characteristics of spongy bone, is gradually resorbed and replaced by compact bone after 90 days. Furthermore, other portions of bone tissue a little more distant from the interface, which establish direct contact with the implant, are also damaged during the drilling process, and therefore, they also need to be remodeled. Among the rare studies found in the literature about bone remodeling after osseointegration, there were no verified studies on the possible influence of implant surface treatments on bone remodeling that occurs after osseointegration. Only studies involving implants with machined surfaces have been conducted up to now.

KEYWORDS

Dental implants, Bone remodeling, Osteoclast, Osteoblast.

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INTRODUCTION

Bone, a type of connective tissue, presents cells, and in spite of being mineralized, it is constantly renewed by the bone remodeling process. This process is characterized by bone resorption by osteoclasts, followed by bone formation by osteoblasts.⁽¹⁾ Several studies have demonstrated the relevance of bone remodeling to tissue responses that guarantee osseointegration,⁽²⁻⁶⁾ which is defined as the direct structural and functional connection between the organized vital bone and the surface of a titanium implant, capable of receiving functional loads.⁽⁷⁻⁹⁾

The success of implants is associated first with their osseointegration, and later on with their survival rate; that is to say, their long term permanence in function. Although there are several studies involving osseointegration of dental and/or orthopedic implants, the majority of the investigations have elucidated the tissue responses that constitute the initial process of bone-implant integration.^(2,10-14)

Considering that the remodeling process is continuous, it may be of relevance not only to osseointegration, but also to the longevity of dental implants. Therefore, the purpose of this study was to conduct a review of the literature with a view of elucidating the events associated with bone remodeling after the osseointegration of implants. In addition, it was also performed a search to data regarding a possible influence of treatments for modifying implant surfaces on these same events.

MATERIALS AND METHODS

In order to conduct this literature review, a detailed search strategy was used in various data bases, between the years 1930 and 2012. The following descriptors were used: "Osseointegrated Implant", "Bone remodeling", "Osteoclast", "Osteoblast" and "Surface treatments". The inclusion criteria were systematic reviews, meta-analyses, conventional reviews of the literature, controlled and randomized case studies, non-randomized clinical cases and articles of opinion, with an approach to the above-mentioned uniterms. Studies that were not written in the Portuguese and English languages were excluded. After critical analysis of the bibliography surveyed, the suitable articles were selected. The data obtained were carefully analyzed and correlated for discussion of the results pointed out in the literature.

LITERATURE REVIEW

Considerations about bone tissue and bone remodeling

Bone, a connective tissue, has cells, and in spite of presenting the particularity of being mineralized, it is constantly renewed by the bone remodeling process.⁽¹⁾ In clinical terms, the rate of bone remodeling, also denominated bone turnover, is the period necessary for new bone to replace the existent bone, guaranteeing adaptation of the neoformed bone to its microenvironment.⁽¹⁵⁾ Microscopically, bone remodeling consist in bone resorption by osteoclasts, followed by bone formation by osteoblasts^(16,17) (Fig. 1). Both cells may be characterized by morphological and biochemical aspects. Osteoclasts, formed by the fusion of mononucleated cells of the hematopoietic lineage,^(18,19) are multinucleated giant cells that degrade the mineralized bone matrix. They are located in excavations on the bone surface, denominated Howship lacunae.^(18,20,21) In their cytoplasm, osteoclasts present the enzyme acid phosphatase, which may be distinguished from the other isoenzymes because it is resistant to inhibition by tartaric acid, thus denominated tartrate resistant acid phosphatase (TRAP).^(4,29) In addition to TRAP, the osteoclasts also synthesize other enzymes, such as metalloproteinase-9 (MMP-9) and cathepsin K.⁽²²⁾

On the other hand, the osteoblasts, cells originating from precursors of mesenchymal origin, are mononucleated, smaller in size than osteoclasts and related to the production and mineralization of bone tissue matrix. They are disposed in a continuous layer on the surface of the bone matrix. Osteoblasts and pre-osteoblasts exhibit high levels of alkaline phosphatase enzyme (ALP) on the surface of their cytoplasmic membranes which, when released, contribute to the initiation of mineralization and progressive growth of hydroxyapatite crystals. In the initial process of bone tissue formation, after the osteoblasts have secreted the first layer of organic matrix, they appear to assume an important role in its mineralization. From the osteoblasts adjacent to the recently synthesized organic bone matrix, small vesicles emerge. ALP belongs to a family of enzymes that hydrolyze phosphate ions, supplying them to the interior of the vesicles. An increase in the concentration of calcium ions inside these vesicles also occurs, probably through the phospholipids in their membranes. Thus a supersaturation of phosphate and calcium occurs, resulting in the precipitation of phosphate and calcium inside the vesicles. Afterwards, there is vesicle membranes rupture and mineralization spreads throughout the matrix. This process is characteristic of the sites

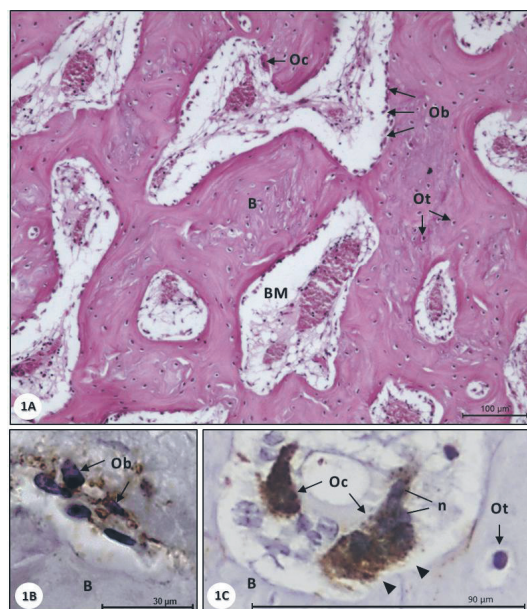


Figure 1. Light micrographs of portions of tibiae which were surrounding the implants. (1A) Several bone trabeculae (B) and bone marrow regions (BM) are observed. Osteoblasts (Ob) and osteoclasts (Oc) are located on bone surface, whereas osteocytes (Ot) are located inside the bone matrix (B). H&E. Bar: 100µm. (1B) Osteoblasts (Ob), located on bone surface (B), show alkaline phosphatase (ALP)-positive cytoplasm (brown-yellow color). Immunohistochemistry for detection of ALP (osteoblast marker) counterstained with Hematoxylin. Bar: 30µm. (1C) Giant multinucleated osteoclasts (Oc) exhibiting intense TRAP-positivity in the cytoplasm (brown color) are observed. n: nuclei. Ot: osteocytes. Arrowheads: Howship lacunae. Immunohistochemistry for detection of TRAP (osteoclast marker) counterstained with Hematoxylin. Bar: 90µm.

in which bone tissue formation and mineralization is occurring. Thus, ALP contributes to the beginning of mineralization and progressive growth of hydroxyapatite crystals of bone matrix.^(21,23) In this context of tissue renewal, the periosteum may be included, because it is an important source of osteogenic cells. It is made up of two layers: An external layer of fibrous connective tissue, in which there are few cells and vessels, and an internal layer, that has osteoprogenitor mesenchymal stem cells, and a vast network of blood vessels in direct contact with the bone.^(2,24)

As bone matrix is produced, some osteoblasts become trapped within its lacunae, and begin to exhibit cytoplasmic extensions, which are found inside the bone canaliculi. These extensions go toward to the extensions of adjacent osteocytes, and in the direction of other cells. Then, gap junctions which allow intercellular communications are established between osteocytes/osteocytes and osteocytes/other bone cells. The junctional communications enable even the osteocytes located in the deepest regions of bone to respond to systemic changes, and modifications on the bone surface. Therefore, osteocytes constitute a complex network that interconnects the bone surface with the most internal portions, and are responsible for the maintenance and vitality of the bone matrix.^(21,23) In addition, the osteocytes are considered essential for bone remodeling, and it has been demonstrated that apoptosis of this cell appears to stimulate the resorptive activity of osteoclasts.⁽²⁵⁾ Osteoclasts are responsible for the phagocytosis of these osteocytes, thereby avoid triggering an inflammatory process within bone tissue.⁽²⁶⁻²⁸⁾

Osseointegration and bone remodeling around osseointegrated implants

In the 1960s, the Swedish orthopedist Branemark and his collaborators discovered, by chance, the occurrence of bone integration with titanium, denominated osseointegration. Thus, osseointegration consists of the clinically asymptomatic, rigid fixation of alloplastic materials, maintained during functional loads.⁽⁷⁾

In rats, osseointegration is acquired around 1 month after implants placement,⁽³⁾ and is characterized by the coverage of the implant threads by the adjacent bone tissue, in addition to the presence of insignificant inflammation and absence of fibrous tissue.^(3,5,12) A suitable model for this type of study was introduced in 1998, using the rat maxilla for observation of the tissues responsible for titanium implantation from 1 to 30 days after insertion of the implant. In this study, it was observed that the appearance of neoformed bone tissue occurred on the fifth day after implant placement, and covered the entire implant 30 days after osseointegration. However,

concomitant with osseointegration, damaged bone was observed, exhibiting lacunae of empty osteocytes, or osteocytes with a picnotic appearance between the pre-existent and neoformed bone around the implants.^(3,5,12) Considering that the remodeling process is continuous, it may be of relevance with respect not only to osseointegration, but also to the longevity of dental implants, the purpose of this study was to conduct a review of the literature with a view to elucidating the events associated with bone remodeling after the osseointegration of implants. In addition, it was performed a search to investigate the existence of data regarding a possible influence of treatments for modifying implant surfaces on these same events. A long term study investigating the response of bone tissue presents around osseointegrated machined titanium implants was performed in rats by Haga et al.⁽²⁹⁾ These authors showed by means of active bone remodeling, with osteoclasts and osteoblasts working in synchrony, the spongy bone initially formed around the implant is gradually resorbed and completely replaced by compact bone at the end of 90 days. The morphological and biochemical alterations associated with the bone remodeling process, which occur around machined implants from 1 to 3.5 months after osseointegration are illustrated in Fig. 2.⁽²⁹⁾

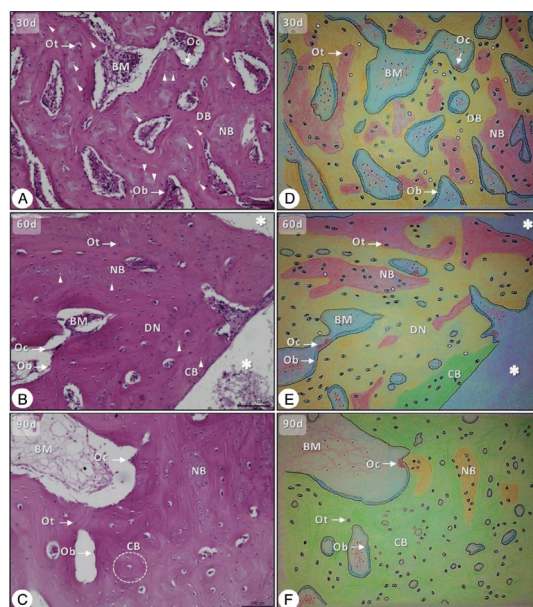


Figure 2. Light micrographs showing morphological changes in the surrounding bone around implants at 1, 2 and 3 months after osseointegration (2A–2C). Bar: 100µm. The schematic representation of each light micrograph summarizes the main histological events in the replacement of the injured bone by newly formed bone (2D–2F). (2A, 2D): One month (30 days) after implant osseointegration, woven bone and bone marrow regions (BM) are observed in the light micrograph. Many osteoblasts (Ob) and osteoclasts (Oc) are located on bone surface. It can be found many regions of newly formed bone (NB), which are represented in pink color in the scheme. Inside the bone matrix, several osteocytes (Ot) are observed. However, empty osteocyte lacunae are still observed (white color), mainly in the regions of damaged bone (DB), in yellow color. (2B, 2E): Two months (60 days) post-osseointegration, the woven bone seems to reduce in volume when compared with 1-month period. Moreover, the woven bone previously in contact with the implant is being replaced by cortical.

One month after implant placement

Osseointegration is observed in all the surfaces of the implants.^(3,29) There is a thin layer of neoformed bone on the implant surface. However, a part of this surface is shown not to be in contact with the neoformed bone. In these areas, medullary spaces containing small blood capillaries are shown to be in contact with the implant surface. The neoformed bone contains osteocytic lacunae exhibiting intact osteocytes. In the region of pre-existent bone, a cement line is easily identified beyond the empty osteocytic lacunae. The double staining of TRAP and ALP enzymes for the detection of osteoclasts and osteoblasts, respectively, show positivity for both cells on the neoformed bone surface. ALP-positive osteoblasts are found close to the area occupied by TRAP-positive osteoclasts, suggesting the occurrence of synchrony and equivalence of the activity of these cells, and therefore, of bone remodeling.⁽²⁹⁾

From 1.5 to 2.5 months after the implant placement

The formation of bone tissue proceeds in the direction of the damaged

bone containing empty osteocytic lacunae, resulting in a reduction in it. Almost the entire implant surface is covered by neoformed bone. The portion of neoformed bone exhibits characteristics of spongy bone. Some empty osteocytic lacunae remain, however, the area containing this type of structure is shown to be smaller. There is the presence of an evident cement line between the pre-existent bone (containing empty osteocytic lacunae) and the neoformed bone. A lower number of ALP-positive osteoblasts and TRAP-positive osteoclasts are observed. In addition, both cell types present reduced volumes, suggesting less cell activity.⁽²⁹⁾

Three months after the implant placement

The area of pre-existent bone has been replaced by neoformed bone containing intact osteocytes. The neoformed bone presents the morphological characteristics of compact bone. There are only some capillaries found between the implant and neoformed bone. ALP-positive osteoblasts and TRAP-positive osteoclasts are rarely observed around the implants, except in the bone marrow regions.

In the period comprised between 3 and 3.5 months after acquisition of osseointegration, minimal morphological and biochemical changes are related, such as for example, a slight increase in neoformed bone thickness (with its corticalization proceeding for up to 12 months after osseointegration).

The distribution and density of ALP-positive osteoblasts and TRAP-positive osteoclasts, and the distance between the cementing lines are identical to those observed in the period of 3 months after implant placement. Once again it is important to emphasize that the neoformed bone undergoes gradual changes from spongy to compact bone due to its continuous remodeling. However, it exhibits the same biological properties as intact bone after osseointegration is acquired.⁽²⁹⁾

Implant surface treatments and bone remodeling after acquisition of osseointegration

Commercially pure titanium (cpTi), biocompatible material, shows no biological properties of osteoinduction or osteogenesis. For this reason, various surface treatments of titanium implants have been proposed, and carefully investigated. These studies have allowed observing that the process of osseointegration is favored by surface treatments, not only by showing the speed up of the complete osseointegration, but also by showing the favoring of the process where bone quality and quantity are not suitable^(30,47). The biological logic of these treatments is to make this microenvironment as similar as possible to the bone microenvironment. For this purpose, the implant surfaces provided have been mimicking the morphology and composition of the constituents of bone tissue itself.
(30,31,47)

The process of changing the cpTi surface may be performed by the techniques of subtraction, particle adhesion or by association of both.⁽³¹⁾

The treatments of subtraction consist of removal of portions of the implant surface. An example of subtraction treatment is irradiation of the implant surface with a LASER beam. This process results in an increase in resistance to corrosion and biocompatibility of titanium, due to its oxidation and subsequent formation of oxides and nitrides.⁽³²⁾ Moreover, irradiation with LASER joins advantages characteristics, such as non-contamination of the surface and a high degree of reproducibility of this technique, which produces a complex and homogeneous surface morphology, with a high degree of purity, thus favoring osseointegration and increasing the removal torque.^(30,32-34) In addition to these techniques, treatments with acids either associated with airborne, particle abrasion with titanium oxide – TiO₂ or aluminum oxide – Al₂O₃,⁽³⁵⁾ or not, are also forms of subtraction techniques.

As opposed to subtraction treatments, addition treatments consist of the addition of substances to the implant surface, such as, for example, the incorporation of ceramics such as hydroxyapatite (HA) [Ca₁₀(PO₄)₆(OH)₂].⁽³⁶⁾ It has been shown that coating implant surfaces with calcium phosphate accelerates osseointegration, especially under conditions of a limited quantity and quality of bone tissue.^(37,38) This may be owing to the fact that HA helps to establish an early chemical bond, and consequently, a strong physical chemical interaction with bone in the initial stages of osseointegration. On the implant surface, a layer of apatite hydroxycarbonate is formed, which is chemically and structurally equivalent to the mineral phase of bone, thus a biochemical bond occurs between the implant surface and bone by means of bone matrix deposition on the HA surface. This physical chemical interaction between the collagen of bone and HA of the implant is denominated biointegration. Moreover, greater bone tissue formation is observed around implants coated with HA, than in cpTi implants.⁽³⁹⁾

When materials such as HA, considered bioactive, are in contact with the live tissue, they undergo superficial dissolution induced by cell activity, releasing calcium and phosphorous ions into the extracellular matrix. These ions are incorporated into the microcrystals of HA of the

bone; that is to say, bone matrix is deposited on the HA surface, leading to biointegration.⁽⁴⁰⁾ Furthermore, HA is commonly used for coating metal implants, due to the mechanical advantages of metals added to the excellent biocompatibility and bioactivity of HA. This association (cpTi and HA) provides an increase in the strength of the interface with bone tissue.^(30,41-43) Methods of chemical deposition of HA have been studied to improve the bond of the coating to the implant surface. Among these, there is emphasis on the biomimetic method, which mimics the body's biological process of hard tissue formation and consists of immersion of the substrate to be coated in a synthetic solution denominated simulated body fluid solution (SBF)⁽³⁶⁾ and was performed by Queiroz et al.⁽³⁰⁾ SBF has chemical composition, temperature and pH that simulate blood plasma.

The implant surface treatment methods may also be classified according to the topographic characteristics they give implants. Implant surface topography varies according to the method by which it is obtained; that is to say, by means of macro, micro or nanotechnology.^(14,30,34,44)

By implant surface treatments greater implant surface roughness may be obtained. Roughness represents a micro or nanomorphological structural modification that provides an increase in the area of contact between the bone and implant.⁽⁶⁾ It is possible to distinguish between macroroughness (100µm to millimeters), microroughness (100nm–100µm) e nanoroughness (less than 100nm).⁽³¹⁾ Each type of topography has a specific influence on the mechanisms involved in osseointegration. For example, accumulation and organization of the blood clot on the rough surface create an important physical phenomenon for osteogenesis, such as greater adhesion, proliferation and expression of osteoblast differentiation markers. This leads to an increase in the bone-implant bond strength, and consequently, to success of therapy with implants in the long term.⁽⁴⁵⁻⁴⁷⁾ Clinical proof of the positive influence of surface treatments on osseointegration is the higher torque required for removal of implants with rough surfaces, when compared with those that have smooth surfaces.^(11,48)

The cpTi implants modified on a nanometric scale by LASER beam with HA deposition by the biomimetic method, with and without afterwards receiving heat treatment in an oven at 600°C, favor osseointegration in the periods of evaluation of 30 and 60 days after implant placement in rabbit tibias. Moreover, the surface containing HA that did not undergo heat treatment presented greater biological activity, reducing the time of osseointegration. This latter result is probably associated with the lower degree of crystallinity of hydroxyapatite, which therefore becomes more soluble and similar to biological hydroxyapatite.⁽³⁰⁾

In general, the goal of surface treatments is to reduce the time of loading after surgery; accelerate bone growth and maturation to allow immediate loading; increase primary stability; guarantee the success of implants when they are placed in regions that present bone with lower quality and quantity; obtain bone growth directly on the implant surface; obtain the largest possible area of osseointegration; obtain bone-implant contact without the interposition of amorphous protein layers; attract mesenchymal, pre-osteoblastic and osteoblastic cells, in addition to proteins with specific binding to osteogenic cells.^(9,44,49,50)

The success of osseointegration, and the maintenance of implants is dependent on adequate rates of bone remodeling.^(44,51) However, up to the present time, we have not found any studies in the literature, which investigate a possible differential effect of these surface treatments of implants on the bone remodeling that occurs after the acquisition of osseointegration.

DISCUSSION

Osseointegration is described as an effective interaction between bone tissue and the implant surface.⁽⁷⁻⁹⁾ However, damaged bone tissue, with empty osteocytic lacunae, resulting from cutting of the bone for implant placement, remains in the microenvironment around the implant, even after its osseointegration.⁽²⁹⁾ In the literature, studies with respect to bone remodeling around implants that have already become osseointegrated are rare. Of the articles selected for this review, only one study directly analyzed the events involving renewal of bone tissue in the microenvironment around the implant after osseointegration, in the absence of loads, in an animal model (rats).⁽²⁹⁾ This study was conducted on the basis of the results obtained by Fuji et al.⁽³⁾ who demonstrated that this type of investigation could be conducted in animal models (rats) 30 days after the placement of a conventional implant with a machined surface, which was shown to be almost completely covered by bone tissue.

Haga et al.⁽²⁹⁾ observed that one month after osseointegration, there was still bone tissue around the implant, presenting empty or picnotic osteocytic lacunae. By means of balanced bone remodeling, in which bone

resorption by TRAP-positive osteoclasts and bone neof ormation by ALP-positive osteoblasts are synchronic and equivalent, the damaged bone is remodeled in a gradual manner and disappears completely 3 months after implantation. Initially, there is replacement of the pre-existent bone, damaged by cutting,⁽⁵²⁾ by spongy bone, and of this, by compact bone, thus improving the bone quality.⁽²⁹⁾ These data clearly demonstrated that continual bone remodeling, even after osseointegration is essential for the survival and success of dental implants in the long term.

It is important to emphasize that the studies investigating events associated with bone remodeling after the acquisition of osseointegration, mentioned in this review of the literature, were conducted in the absence of loads.⁽²⁹⁾ In the presence of loading and depending on the value of the load applied, modifications occur in the bone tissue located around the implant, which must have its structure adequately adapted to receive the forces applied.⁽⁵³⁾ Furthermore it requires continuous remodeling to replace the regions damaged by fatigue, in order to prevent the occurrence of fractures and loss of the implant.^(4,6,54) Therefore, there are higher bone remodeling rates in implants submitted to the action of loads.⁽⁶⁾

In spite of the large number of studies on the topographical, physical and chemical changes on implant surfaces,^(14,30,34) up to the present

time, we have found no articles in the literature, which have investigated a possible differential effect of these surface treatments on the bone remodeling that occurs after osseointegration has been established.

CONCLUSIONS

It is reasonable to suggest, for example, that bioactive surfaces may continue to be active in the long term, stimulating the bone cells and leading to a higher degree of tissue turnover. On the other hand, it is also possible that the properties obtained by means of the surface treatments may influence osseointegration only, seeing that at this time the bone cells have greater access to the treated surface.

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FUNADESP/UNIARA.

CONFLICT OF INTEREST

No conflicts of interest have been declared.

References

- Raisz LG, Rodan GA. Embryology and cellular biology of bone. In: Avioli LV, Krane SM, editors. Metabolic bone disease and clinically related disorders. 3rd ed. New York: Academic Press; 1998. p. 1-22.
- Ham AW. Histological study of de early phases of bone repair. J Bone Joint Surg. 1930;12:827-44.
- Fujii N, Kusakari H, Maeda T. A histological study on tissue responses to titanium implantation in rat maxilla: the process of epithelial regeneration and bone reaction. J Periodontol. 1998;69:485-95.
- Minkin C, Marinho VC. Role of the osteoclast at the bone-implant interface. Adv Dent Res. 1999;13:49-56.
- Futami T, Fujii N, Ohnishi H, Taguchi N, Kusakari H, Ohshima H, et al. Tissue response to titanium implants in the rat maxilla: ultrastructural and histochemical observations of the bone-titanium interface. J Periodontol. 2000;71: 287-98.
- Degidi M, Scarano A, Piattelli M, Perotti V, Piattelli A. Bone remodeling in immediately loaded and unloaded titanium dental implants: a histologic and histomorphometric study in humans. J Oral Implantol. 2005;31:18-24.
- Branemark PI, Adell R, Breine U, Hansson BO, Lindström J, Ohlsson A. Intraosseous anchorage of dental prostheses. I. Experimental studies. Scand J Plast Reconstr Surg. 1969;3:81-100.
- Albrektsson T, Branemark PI, Hansson HA, Lindström J. Osseointegrated titanium implants. Requirements for ensuring a long-lasting, direct bone-to-implant anchorage in man. Acta Orthop Scand. 1981;52:155-70.
- Zarb GA, Albrektsson T. Osseointegration - a réquiem for the periodontal ligament? Int J Periodontics Restorative Dent. 1991;11:88-91.
- Buser D. Influence of surfaces characteristics on bone integration of titanium implants. J Biomed Mater Res. 1991;25:889-902.
- Sykaras N, Lacopino AM, Marker VA, Triplett RG, Woody RD. Implants, materials, designs and surfaces topographies: their effect on osseointegration. A literature review. Int J Oral Maxillofac Implants. 2000;15:675-90.
- Shirakura M, Fujii N, Ohnishi H, Taguchi Y, Ohshima H, Nomura S, et al. Tissue response to titanium implantation in the rat maxilla, with special reference to the effects of surface conditions on bone formation. Clin Oral Implants Res. 2003;14: 687-96.
- Braga FJC, Marques RFC, Filho EA, Guastaldi AC. Surface modification of Ti dental implants by Nd:YVO laser irradiation. Appl Surf Sci. 2007;253:9203-98.
- Wennerberg A, Albrektsson T. Effects of titanium surfaces topography of bone integration: a systematic review. Clin Oral Implants Res. 2009;20:172-84.
- Misch CE, Bidez MW, Sharawy M. A bioengineered implant for a predetermined bone cellular response to loading forces. A literature review and case reports. J Periodontol. 2001;72: 1276-86.
- Faloni AP, Cerri PS. Mecanismos celulares e moleculares do estrógeno na reabsorção óssea. Rev Odontol UNESP. 2007;36:181-8.
- Klika V, Marsik F. A thermodynamic model of bone remodelling: the influence of dynamic loading together with biochemical control. J Musculoskelet Neuronal Interact. 2010;10: 220-30.
- De Vries TJ, Schoenmaker T, Hooibrink B, Leenen PJ, Everts V. Myeloid blasts are the mouse bone marrow cells prone to differentiate into osteoclasts. J Leukoc Biol. 2009;85: 919-27.
- De Souza Faloni APS, Schoenmaker T, Azari A, Katchburian E, Cerri PS, de Vries TJ, et al. Jaw and long bone marrows have a different osteoclastogenic potential. Calcif Tissue Int. 2011;88:63-74.
- Faloni AP, Sasso-Cerri E, Rocha FR, Katchburian E, Cerri PS. Structural and functional changes in the alveolar bone osteoclasts of estrogen-treated rats. J Anat. 2012;220:77-85.
- Katchburian E, Arana V. Histologia e embriologia oral. Texto-atlas-Correlações clínicas. 3rd ed. Rio de Janeiro: Guanabara Koogan; 2012.
- Parikka V, Lehenkari P, Sassi ML, Halleen J, Risteli J, Härkönen P, et al. Estrogen reduces the depth of resorption pits by disturbing the organic bone matrix degradation activity of mature osteoclasts. Endocrinology. 2001;142:5371-8.
- Katchburian E, Cerri PS. Formação e destruição óssea. In: Cardoso RJA, Gonçalves EAN, editors. Periodontia, Cirurgia para Implantes, Cirurgia, Anestesiologia. 1st ed. São Paulo: Artes Médicas; 2002. p. 437-45.
- Wlodarski KH. Normal and heterotropic periosteum. Clin Orthop Related Res. 1988 Apr;(241):265-277.
- Gu G, Mulari M, Peng Z, Hentunen TA, Väänänen HK. Death of osteocytes turns off the inhibition of osteoclasts and triggers local bone resorption. Biochem Biophys Res Commun. 2005;335:1095-101.
- Elmardi AS, Katchburian MV, Katchburian E. Electron microscopy of developing calvaria reveals images that suggest that osteoclasts engulf and destroy osteocytes during bone resorption. Calcif Tissue Int. 1990;46:239-45.
- Boabaid F, Cerri PS, Katchburian E. Apoptotic bone cells may be engulfed by osteoclasts during alveolar bone resorption in young rats. Tissue Cell. 2001;33:318-25.
- Cerri PS, Boabaid F, Katchburian E. Combined TUNEL and TRAP methods suggest that apoptotic bone cells are inside vacuoles of alveolar bone osteoclasts in young rats. J Periodontol Res. 2003;38:223-6.
- Haga M, Fujii N, Nozawa-Inoue K, Nomura S, Oda K, Uoshima K, et al. Detailed process of bone remodeling after achievement of osseointegration in a rat implantation model. Anat Rec. 2009;292:38-47.
- Queiroz TP, Souza FA, Guastaldi AC, Margonar R, Garcia-Júnior IR, Hochuli-Vieira E. Commercially pure titanium implants with surfaces modified by LASER beam with and without chemical deposition of apatite. Biomechanical and topographical analysis in rabbits. Clin Oral Implants Res. 2013;24: 896-903.
- Campos PSS, Faloni APS, Margonar R, Faeda RS, de Souza Rastelli AN, Marcantonio E, et al. Aspectos biológico-celulares da osseointegração baseados nas superfícies de implantes. Implant News. 2012;9:168-79.
- György E, Pérez Del Pino A, Serra P, Morenza JL. Chemical composition of domeshaped structures grown on titanium by multi-pulse Nd:YAG laser irradiation. Appl Surf Sci. 2004;222:415-22.
- Cho SA, Jung SK. A removal torque of the laser-treated titanium implants in rabbit tibia. Biomaterials. 2003;24:4859-63.
- Faeda RS, Tavares HS, Sartori R, Guastaldi AC, Marcantonio E Jr. Evaluation of titanium implants with surface modification by LASER beam. Biomechanical study in rabbit tibias. Braz Oral Res. 2009;23:137-43.
- Braga FJC, Marques RFC, Filho EA, Guastaldi AC. Surface modification of Ti dental implants by Nd:YVO laser irradiation. Appl Surf Sci. 2007;253:9203-8.
- Aparecida AH, Fook MVL, Santos ML, Guastaldi AC. Influência dos íons K⁺ e Mg²⁺ na obtenção de apatitas biomiméticas. Ecl Quím. 2005;30:13-8.
- Hayakawa T, Yoshinari M, Nemoto K, Wolke JG, Jansen JA. Effect of surface roughness and calcium phosphate coating on the implant/bone response. Clin Oral Implants Res. 2000;11:296-304.
- Park EK, Lee YE, Choi JY, Oh SH, Shin HI, Kim KH, et al. Cellular biocompatibility and stimulatory effects of calcium metaphosphate on osteoblastic differentiation of human bone marrow derived stromal cells. Biomaterials. 2004;25: 3403-11.
- Meirelles L, Currie F, Jacobsson M, Albrektsson T, Wennerberg A. The effect of chemical and nanotopographical modifications on the early stages of osseointegration. Int J Oral Maxillofac Implants. 2008;23:641-7.
- Albrektsson T, Wennerberg A. Oral implant surfaces: Part 1 - Review focusing on topography and chemical properties of different surfaces and in vivo responses to them. Int J Prosthodont. 2004;17:536-43.
- Macdonald DE, Betts F, Stranick M, Doty S, Boskey AL. Physicochemical study of plasma-sprayed hydroxyapatite-coated implants in humans. J Biomed Mater Res. 2001;54: 480-90.
- Lee IS, Kim DH, Kim HE, Jung YC, Han CH. Biological performance of calcium phosphate films formed on commercially pure Ti by electron-beam evaporation. Biomaterials. 2002;23:609-15.
- Abe Y, Kokubo T, Yamamuro T. Apatite coating on ceramics, metals and polymers utilizing a biological process. J Mater Sci Mater Med. 1990;1:233-8.
- Sisti K, Guastaldi A, Brochado Antonioli A, Aydos RD, Guastaldi AC, Queiroz TP, et al. Surface and biomechanical study of titanium implants modified by laser with and without hydroxyapatite coating, in rabbits. J Oral Implantol. 2012;38: 231-7.
- Klokkevold PR, Johnson P, Dadgostari S, Caputo A, Davies JE, Nishimura RD. Early endosseous integration enhanced by dual acid etching of titanium a torque removal study in rabbit. Clin Oral Implant Res. 2001;12:350-7.

46. Trisi P, Lazzara R, Rebaudi A, Rao W, Testori T, Porter SS. Bone-implant contact on machined and dual acid-etched surfaces after 2 months of healing in the human maxilla. *J Periodontol*. 2003;74:945-56.
47. Wennerberg A, Albrektsson T. Structural influence from calcium phosphate coatings and its possible effect on enhanced bone integration. *Acta Odontol Scand*. 2009;67:333-40.
48. Wennerberg A, Albrektsson T, Anderson B, Krol JJ. A histomorphometric and removal torque study of screw-shaped titanium implants with three different surfaces topographies. *Clin Oral Implant Res*. 1995;6:24-30.
49. Schroeder A, van der Zypen E, Stich H, Sutter F. The reactions of bone, connective tissue, and epithelium to endosteal implants with titanium-sprayed surfaces. *J Maxillofac Surg*. 1981;9:15-25.
50. Abrahamsson I, Berglundh T, Linder E, Lang NP, Lindhe J. Early bone formation adjacent to rough and turned endosseous implant surfaces. An experimental study in the dog. *Clin Oral Implants Res*. 2004;15:381-92.
51. Tavares MG, de Oliveira PT, Nanci A, Hawthorne AC, Rosa AL, Xavier SP. Treatment of a commercial, machined surface titanium implant with H₂SO₄/H₂O₂ enhances contact osteogenesis. *Clin Oral Implants Res*. 2007;18: 452-8.
52. Queiroz TP, Souza FA, Okamoto R, Margonar R, Pereira-Filho VA, Garcia Júnior IR, et al. Evaluation of immediate bone-cell viability and of drill wear after implant osteotomies: immunohistochemistry and scanning electron microscopy analysis. *J Oral Maxillofac Surg*. 2008;66:1233-40.
53. Wiskott HW, Cugnoni J, Scherrer SS, Ammann P, Botsis J, Belser UC. Bone reactions to controlled loading of endosseous implants: a pilot study. *Clin Oral Implants Res*. 2008;19:1093-102.
54. Garetto LP, Chen J, Parr AJ, Roberts WE. Remodeling dynamics of bone supporting rigidly fixed titanium implants: a histomorphometric comparison in four species including humans. *Implant Dent*. 1995;4:235-43.