Using synthetic biomaterial to fill peri-implant defects (gap) in immediate implants

Abstract / Osseointegrated implant placement requires proper bone volume, however, tooth extraction requires different standards of bone resorption and bone remodeling. Alveolar ridge resorption has been considered an inevitable consequence of tooth extraction and may be a significant issue for Implantodontics. Despite immediate implant placement, the edentulous site of the alveolar process undergoes substantial bone remodeling, with reduction in the dimensions of the alveolar crest after tooth extraction. After implant placement in a fresh extraction site, a gap is often formed between the ridge and the implant surface. With a view to overcoming this issue and to favor bone formation within the gap, several grafting procedures have been employed in association or not with barrier membranes as well as several types of bone substitutes. In this context, this article aims at conducting a literature review to discuss the use of synthetic biomaterial to fill the gaps that form around implants placed in fresh sockets. Nevertheless, no biomaterial available to date provides the desirable properties. Additionally, residual bone volume must be assessed before tooth extraction in order to allow the dental surgeon to employ different techniques with a view to preserving the alveolar bone.
/ Keywords / Dental implants. Bone transplant. Biocompatible material.

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How to cite this article: Colet D, Neiss FA, Conci RA, Griza GL. Using synthetic biomaterial to fill peri-implant defects (gap) in immediate implants. Dental Press Implantol. 2013 Oct-Dec;7(4):98-105.

Submitted: August 18, 2013 - **Revised and accepted:** November 25, 2013

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The authors inform they have no associative, commercial, intellectual property or financial interests representing a conflict of interest in products and companies described in this article.

INTRODUCTION

Physiological hard and soft tissue loss after tooth extraction often causes bone deformities in the alveolar ridge, which, as a result, hinders ideal implant placement as well as esthetics and speech.[1]

The search for esthetic as well as predictable functional results yielded within a shorter period of time; a better understanding of repair processes established around implants; and the development of new implant designs and surfaces allowed new surgical techniques to be developed and favor immediate implant placement after extraction in fresh sockets. This procedure has been recommended as a therapeutic protocol aiming at reducing bone resorption after extraction. It is considered an inexorable technique that reduces treatment time and costs.[2] On the other hand, it has the disadvantage of forming a gap around the implant as a result of morphological differences between the implant and the dimensions of the post-extraction socket, which is of greater diameter in comparison to the implant. Furthermore, the extraction socket is not usually round-shaped, as the implant to be placed normally is.[3] According to Botticelli et al,[4] the space formed between the implant and the bone or adjacent soft tissue is known as gap. Experimental studies report that a large gap favors the formation of connective tissue between the coronal portion of the implant and the peri-implant bone tissue. On the other hand, little gaps between the implant and the bone are normally filled with neoformed bone, with or without bone graft or biological barriers. Modifying the implant shape and filling the gaps with bone substitutes can solve the issue of gap formation.[3] In this context, the use of bone graft prevents potential changes in fresh socket morphology, thus keeping its dimensions. Preserving the amount of gingival tissue is another important factor, given that successful immediate implant placement is also associated with complete implant coverage.

Autograft is still considered as the gold standard of graft procedures, however, the search for the ideal grafting material that reduces or eliminates the need for a donor site led to advances in researches on the theme. For this reason, several bone substitutes have become increasingly popular. They include alogenous, heterogeneous and alloplastic material used alone or in combination with bone. In this context, this article aims at conducting a literature review to discuss the use of synthetic biomaterial to fill the gaps that form around implants placed in fresh sockets.

LITERATURE REVIEW

Extraction socket healing relies on a series of factors, including blood clot formation, which is replaced by bone tissue while the alveolar walls undergo resorption and are gradually remodeled.[5] The major reactions affecting the alveolar process occur within the first 3 months after tooth extraction and lead to bone resorption, especially in the buccal-lingual direction. Studies conducted with animals assessed the changes in the dimensions of the ridge crest after tooth extraction. The remodeling process is described in two phases: During the first phase, bone is remodeled and replaced by recently-formed bone tissue, which reduces the vertical ridge. In the second phase, the buccal surface of the alveolar crest is remodeled and causes horizontal volume reduction as well as additional vertical volume reduction.[1] Residual alveolar process remodeling is progressive and chronic, and results in atrophy and reduction in the residual crest. As a result of tooth extraction and lack of support, bone is resorpted and formed into a smooth contour, causing bone structures to become thinner.[6] Bone loss after extraction is quick during the first 6 months. It is followed by gradual bone remodeling as well as remodeling of the remaining bone, which reduces alveolar bone height in 40% and thickness in 60% within the first 6 months.[7] Bone loss is more severe in the vestibular direction of the alveolar process, in comparison to the buccal/palatal direction.[8]

Initially, it was suggested that implant placement in fresh extraction sockets could prevent bone remodelling.[9] Other authors state the hypothesis that implant placement cannot be associated with alveolar crest remodeling, given that buccal-lingual thickness normally reduced within 4-6 months after extraction, regardless of implant placement.[10] Another study assessing a potential association between immediate implant placement and bone remodeling revealed that implant placement in fresh extraction sockets caused significant changes in height and thickness of the buccal-lingual walls.[6] Even though the cause of bone loss around immediately placed implants is not clear, many studies have highlighted the role the following factors play: socket positioning, buccal alveolar crest thickness, gap between the implant and the alveolar wall, and implant surface notopography.[11,12,13]

After implant is placed in a fresh extraction site, a gap is often formed between the ridge and the implant surface. With a view to overcoming this issue and to favor bone formation within the gap, several graft procedures have been employed in association or not with barrier membranes. Additionally, it has also been suggested that hard tissue healing depends on the size of the defect, as well as on the properties, the technique and the material used.[4] Small bone peri-implant defects can be completely repaired without employing guided bone regeneration (GBR) procedures, given that gaps greater than 2 mm must be filled.[14]

Another research assessing immediate implant placement focuses on the influence of the type of implant surface treatment over peri-implant bone healing. Treated-surface implants were compared with machined-surface implants placed in sockets of dog's mandibles with gaps ranging from 1 to 1.5 mm. The study revealed better filling of bone defect as well as greater implant-bone contact for treated-surface implants.[15]

The search for material that eliminate the need for a donor site led to advances in research on biomaterial and, during the last few years, to the development of several bone substitutes. Bone substitutes or biomaterial are natural or synthetic material used in humans or animals as substitutes of all types of tissue or body functions. However, their biocompatibility has not been fully proved, for this reason, their use is restricted.[16] Biocompatibility is the ability of biomaterial to exert a desired function during therapy without inducing undesired local or systemic effects, but producing more beneficial cell and tissue response and optimizing the relevant clinical responses of the given therapy.[17] Thus, biomaterial are biocompatible when they are inserted into the bone cavity and, after bone repair, remain incorporated to the neoformed bone. Furthermore, they are biocompatible because they act for a given purpose and, even though they are not incorporated by the organism, they do not cause any injuries and are not toxic.

Biomaterial are important additional products that aid tissue regeneration. For this reason, they are key for Dentistry, given that their chemotactic action can speed up or order bone repair process. They fill the bone bed with a sponge-like structure that forms a porous area that induces the formation of osteoblasts which, later on, will form bone tissue.[18] At present, due to technological advances in biomaterial associated with advances in biological knowledge on bone tissue, it is possible to selectively influence bone formation and, as a consequence, control the quality and quantity of bone inside oral structures. Nevertheless, researches on the ideal implant material used to replace autograft remain as a daunting challenge in modern Dentistry. There is a wide variety of biomaterial, synthetic or biological, available on the market. They vary in the size of their particles and are classified according to their mechanism of action: osteoconduction, osteoinduction or osteogenesis.[19]

Biomaterial are primary used to recruit cell populations, carry growth factors, attract, stimulate and favor the growth of specific cells, and provide cell and tissue growth structures that allow biomaterial to interact as well as promote homeostasis and integration with regenerated tissues.[18]

In the case of peri-implant gap filling, particulate biomaterial are confined within the bone walls, and demineralized or mineralized material, bioactive glass and particulate autogenous bone can be used. Autograft is considered a gold standard procedure due to its potential of osteogenesis, osteoinduction and osteoconduction; however, its increased morbidity leads clinicians and researchers to search for alternative biomaterial. The grafting biomaterial available on the market have different physical and chemical properties: particle size; porosity; crystallinity and chemical composition, all of which affect the *in vivo* behavior of these material. It is essential that clinicians know the physical and chemical characteristics of biomaterial available on the market, so as to choose the best material for a given application. According to the aforementioned characteristics, biomaterial must present biocompatibility; osteoconductivity; surface area that provides proper revascularization for the receiving site; high porosity that allows the material to be completely incorporated by the new bone; and mild resorption that allows bone remodeling over time. Furthermore, biomaterial must also have physical and chemical characteristics that are ideal for bone regeneration, namely: particle size between 0.25 and 1.00 mm, porous particles and low crystallinity.[20]

With a view to developing new biomaterial that aim at enhancing bone healing, some researchers have focused their studies on synthetic graft. Among them, biphasic calcium phosphate (BCP) has been increasingly used as a bone substitute in Orthopedics as well as for buccal and maxillofacial purposes.[21] Biphasic calcium phosphate is chemically similar to human bone and it consists of a combination of hydroxyapatite (HA) and tricalcium phosphate (TCP), i.e., it is a two-phase matter. TCP dissolution offers the basic material for calcium and phosphate ions, which sets off a mineralization process. At the same time, HA also keeps the framework for osteoblasts adhesion and new bone formation, which favors volume maintenance necessary against excessive resorption. Histological evaluations revealed that biphasic calcium phosphate promotes osteoblastic activity and induces osteogenesis. Thus, the Havers system and a remodeling process were observed after 12 weeks. In comparison to other grafting material, TCP revealed significantly greater osteogenic capacity, and seems to be as safe and efficient as autograft.[22] As a consequence, when grafted in bone defects, biphasic calcium phosphate (BCP) proves to be biocompatible, bioactive and osteoconductive.[23]

Hydroxyapatite (HA) is another synthetic material used to fill gaps. Chemically speaking, HA crystals are the main components of bone mineral phase. It is a calcium and phosphate –based matter gleaned from natural sources, such as coral reefs, as well as by means of synthetic methods. HA is currently available on the market as resorbable and non-resorbable particulate or block material. Resorbable hydroxyapatite is more widely used in maxillofacial reconstruction. Its porous structure — low density, with less organized crystals in comparison to non-resorbable hydroxyapatite — and the presence of secondary substances allow dissolution in physiological means, however, at very slow rates. HA is a biocompatible, osteoconductive matter with bioactive surface that allows chemical interaction between its surface and the receiving bone. It has been widely researched for orthopedic and dental purposes for more than 20 years.[24,25]

Bioactive glass (BG), also known as bioglass, was first developed in the early 70s as ceramic biomaterial capable of establishing direct adhesion to bone tissue. Its particles vary between 300 and 355 μm and consist of a mixture of oxides, in which silicone oxide, calcium and phosphate are predominant.[30] When bioglass is grafted, its surface interacts with body fluids, promoting alkaline ions exchange as well as deposition of a surface calcium and phosphate layer that chemically bonds to the tissue. The outer layer gradually dissolves and reveals an inner silica gel layer that is absorbed by macrophages. Its particles progressively excavate, which allows bone deposition to occur inside and outside the framework of particles that are reabsorbed and replaced by neoformed bone. Studies using BG for bone reconstruction yield results that vary from complete bone neoformation, with excavated granules filled with neoformed bone tissue; to results in which the material is wrapped up by fibrous tissue of low bone formation rate.[22]

Beta tricalcium phosphate (β-TCP) is a ceramic resorbable biomaterial that differs from hydroxyapatite in terms of the calcium/phosphate ratio. The main clinical characteristic that differs β-TCP from HA is the solubility of the former in a physiological environment. Differently from HA and bioactive glass, β-TCP is easily and quickly reabsorbed by the chemical dissolution produced by osteoclasts. Similarly to HA, β-TCP resorption is determined not only by the solubility of its components, but also by the morphology of its crystal as well as by its porosity. The main disadvantage of β-TCP is its lack of predictability regarding maintenance of bone volume after resorption. Many studies demonstrate that the material is quickly reabsorbed and replaced by a variable amount of bone tissue. Such discrepancy has not been fully explained, but it is believed that accelerated resorption contributes to loss of neoformed bone. With a view to decreasing biomaterial resorption rate, biphasic substances with β-TCP + HA have been developed. In this association, HA, which has lower solubility in comparison to β-TCP, acts to keep grafting material volume, while β-TCP is reabsorbed and replaced by neoformed bone.[26]

DISCUSSION

Remodeled alveolar process can hinder prosthetic therapy performed with conventional or implant-supported prostheses. This fact highlights the importance of preserving the alveolar process of which most important esthetic objectives are maintenance or improvement of buccal and interproximal gingival contour and interproximal papilla height. Soft tissue color, consistency and contour are key factors that influence the esthetic results

yielded by this type of procedure. In short, alveolar process preservation minimizes residual crest resorption, provides maintenance of crest volume after extraction, allows ideal implant placement in terms of bone and gingival tissue, minimizes or eliminates the need for grafting procedures during implant placement and avoids hard and soft tissues loss, all of which provide the patient with the best esthetic results possible.[1]

Alveolar ridge remodeling after extraction follows a time-dependent standard procedure, with alveolar crest resorption and remodeling. The longer the time interval after extraction, the greater the resorption. To maintain proper bone height and achieve rehabilitation within a shorter period of time, immediate implant placement is recommended. The literature discloses positive results yielded by this procedure without further complications. Experimental studies reveal that gap formation between the implant and the socket is inevitable even if the difference between them is not greater than 2 mm.[27] After extraction, vertical and horizontal bone loss occur regardless of immediate implant loading. Since the technique is used to replace lost teeth in the anterior maxilla, where esthetic results are of paramount importance, buccal wall resorption may negatively affect esthetic results.[28] For this reason, graft placement inside the residual gap between the implant and the buccal bone wall is recommended. If a gap forms between the implant and the socket, bone bridge formation may be incomplete or delayed, which hinders osseointegration. Experimental studies conducted with animals confirm such hypothesis.[28] The use of regenerative material prevents connective and epithelial tissue cells from migrating, thus favoring bone regeneration. The use of regenerative material is recommended when residual bone defect is greater than 1-2 mm of horizontal space between the implant surface and the buccal wall.[29] Nevertheless, this value has not been conclusively proved. For this reason, some studies suggest that residual bone defect satisfactorily heal without bone regeneration procedures or grafting material.[29]

The study conducted by Barone[13] confirms that dimensional alterations occur in the alveolar crest even after implants are placed in fresh extraction sockets, regardless of regenerative procedures and peri-implant, marginal lacunae being completely filled 3 months after bone formation. Nevertheless, bone resorption was observed in grafted sockets, especially on the buccal side, and, in that case, the regenerative procedure may have limited alveolar bone remodeling.

Biomaterial are natural or synthetic material used to treat, enhance or restore the function of injured or lost biological tissues. They are classified according to their origin, mechanism of action and physiological behavior. Ideally, they must not cause any physical harm to the receiving tissue, must be pharmacologically inert, must not cause allergic or foreign body-type reactions, and must be enough to fill the bone defect. Furthermore, biomaterial must present proper biomechanical, biological, physical and chemical properties.[30]

Ideal grafting material must not cause reduction in bone volume after extraction, and must remain *in situ* until bone formation is completely achieved. Bone substitutes must allow osteogenesis onset and must function as a bed for cell penetration, thus favoring bone formation. Several grafting osteoinductive and/or osteoconductive material, including autogenous, allogeneic, xenograft and alloplastic bone, were used in the attempt to preserve the alveolar crest. Should the alveolar bone walls be undamaged, only osteoconductive grafting material can be used, which eliminates the need for barrier membranes. Conversely, should the alveolar bone walls be damaged, regenerative techniques, osteoinductive grafting material and/or barrier membranes must be used.[1]

Osteogenesis, osteoinduction and osteoconduction are mechanisms by means of which bone substitutes act in contact with the organism. Osteogenesis is the formation and development of bone tissue. Osteogenic grafting material is gleaned from tissue involved with bone growth and repair. Osteoinduction is the process by which osteogenesis is induced. It is an active process that represents the ability of graft to induce bone formation in the receptor tissue. Osteoconduction occurs when a physical matrix functions as a framework for the formation of new bone. It is a passive process that represents the ability of graft to allow invasion of blood and cells from the receptor site. It basically relies on the number and size of canals going through the graft. All bone substitutes have at least three mechanisms of action.[31]

According to Araújo et al,[32] biomaterial must meet the following criteria in order to be used as grafting material: 1. Ability to form bone by cell proliferation of transplanted osteoblasts or cell osteoconduction over the graft surface; 2. Ability to form bone by osteoinduction of recruited mesenchymal cells; 3. Ability to remodel immature bone in mature lamellar bone; 4. Maintenance of mature bone without loss of function; 5. Ability to promote implant stabilization after implants are concurrently placed with graft; 6. Have low infection risk; 7. Be effective; 8. Have a high safety level.

Autograft remains as the "gold standard" of biomaterial due to its osteoinductive, osteoconductive and osteogenic properties as well as for being immunologically inert and, as a result, allowing bone formation. Nevertheless, potential accidents (paresthesia, infections, etc.) associated with the techniques employed to harvest autogenous bone have encouraged the search for a substitute. In this context, allogeneic, xenograft and alloplastic material play an important role in aiding or promoting bone tissue reconstruction.[18] Choosing an appropriate bone substitute basically depends on its purpose and detailed understanding of the biological mechanisms established around it. Particulate bone substitute is used to fill alveolar and sinus cavities or small bone defects with at least three remaining bone walls that provide stability.[18] Unlike block graft, in which stability is provided by the use of screws, particulate bone substitute needs at least three remaining bone walls or a framework that provide stability and keep the osteoconductive properties of this type of material.[16]

With a view to optimizing osseointegration in critical-sized lacunae, several bone substitutes have been used to stimulate bone growth. This type of material present osteoconductive properties and function as a framework for cell adhesion and proliferation, which favors gap filling.[23,33] Additionally, different types of biomaterial have been used in association with implants, thus yielding successful results.[34]

No biomaterial available to date provides the following desirable properties: biocompatibility; previsibility; clinical application; absence of intra-operative risks or sequelae; and patient's acceptance. Xenograft material, such as inorganic bovine bone, as well as alloplastic material, such as synthetic hydroxyapatite, are bone substitutes that favor bone repair as a result of high osteoconduction. Thus, this type of material has been recommended in cases of periodontal repair, maxillary sinus lifting and socket filling.[35]

Recovery of crack defects depends on the implant surface and on the size of the bone defect. Osseointegration of implants placed in gap sites is influenced by the characteristics of the implant surface. For instance, calcium phosphate-coated implants yield more favorable bone response. Studies focusing on the healing process of bone defects of different dimensions reveal that healing was strongly impaired in bigger bone defects.[3]

Circumferential defects heal without the use of regenerative therapy, provided that buccal bone is undamaged and the defect is not critical-sized. Lacunae with width not greater than 1-1.25 mm and depth not greater than 5 mm around rough implant surfaces are better filled and have less marginal bone resorption than machined implant surfaces. Nevertheless, cases in which buccal bone is removed or the defect is greater than 1.25 mm require additional regenerative therapy. A wide variety of regenerative therapies are used to treat circumferential defects. The use of barrier membrane as bone substitute yielded the most favorable results.[3]

It is worth noting that the aforementioned biomaterial are used in very specific cases, within the limitations of such cases and without demanding unreal biological outcomes such as bone neoformation as a result of biomaterial use. Bone neoformation is a biological process happening solely as a result of osteblastic activity. The quality of neoformed bone tissue in the presence of biomaterial (bone substitutes)is not uniform and depends on the following: (1) material; (2) material origin; (3) clinical conditions of the receptor site; (4) indications and surgical technique.[19]

The material constitutive, structural, physicochemical, degradation surface, absorption and resorption properties are responsible for the bioconductive and bioinductive abilities of biomaterial. The aforementioned concepts are the basis of current and future researches, and aid professionals in the attempt to choose among different products available on the market. Thus, the clinical use

of any type of biomaterial must be essentially based on previous research which include scientific evaluation, *in vivo* laboratory trials and longitudinal clinical studies conducted with humans.[18]

Choosing the most appropriate biomaterial depends on whether or not it exerts the desired functions of filling, regeneration or both. One should consider the material osteoconductive and osteoinductive properties, as well as its provenance (homogenous or allogeneic, heterogeneous or xenograft, or synthetic). Resorption time, whether slow or quick, must also be taken into account. Bone substitutes must provide stability and protection achieved by the use of barrier membranes, in addition to avoiding contamination that hinders bone repair.[18]

CONCLUSIONS

Tooth extraction requires different standard procedures of bone resorption and bone remodeling. Thus, residual bone volume must be assessed before extraction in order to allow the dental surgeon to employ different techniques with a view to preserving the alveolar bone. Nevertheless, clinical assessment of critical-sized bone defect (> 2 mm) remains limited and, for this reason, no biomaterial has provided all the ideal properties.

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