BONE REPAIRING BY
AUTOGENOUS GRAFTS -
evaluation and literature review

reparação óssea por
enxertos autógenos -
avaliação e revista da literatura

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ABSTRACT

For aesthetic correction and function, use of grafts, may be considered of autogenous, allogeneic, xenogenic or alloplastic origin. However, they can have differentiated mechanism acting through osteogenesis, osteoconduction and osteoinduction. Autogenous grafts or autografts are from the same individual, playing the role of osteogenesis, osteoinduction and osteoconduction. However, there are differences in results obtained in literature among researchers, as well as their properties and mechanism of incorporation. Objective of this study was to evaluate current stage of autogenous grafts and, what factors influence its incorporation.

RESUMO

Utilização de enxertos, para correção estética e função podem ser considerados de origem autógena, alógena, xenógena ou aloplástica. Contudo podem ter ação de mecanismo diferenciado, atuando através osteogênese, osteocondução e osteoindução. Enxertos autógenos ou auto enxertos são de mesmo indivíduo, desempenhando papel de osteogênese, osteoindução e osteocondução. Porém há divergências nos resultados obtidos na literatura entre pesquisadores, quanto suas propriedades e mecanismo de incorporação. Objetivo deste trabalho foi avaliar estágio dos enxertos autógenos e, quais fatores que influenciam sua incorporação.

Uniterms: Bone repairing; Autogenous grafts; Grafts.
Unitermos: Reparação óssea; Enxerto autógeno; Enxerto.
Osteocytes are cells that share similar lineage of osteoblasts, being highly differentiated by activity of alkaline phosphatase, lodging inside the matrix being mobile, multinucleated, giant, extensively branched cells formed by fusion of monocytes and its function is to reabsorb bone tissue (JUNQUEIRA; CARNEIRO, 1995). When large bone loss occurs, whether surgical or pathological, it is essential to use grafts for aesthetic and functional correction (MARZOLA, 2008).

As for mechanism of action, implant materials and bone grafts, can act by three different mechanisms (MISCH; DIETSCH, 1993): Osteogenesis, which refers to organic material capable of bone formation directly from osteoblasts; Osteoinduction, in which all material is capable of inducing transformation of undifferentiated mesenchymal cells into osteoblasts or chondroblasts, thus increasing growth or being able to form bone where it is not expected. This mechanism has been recognized as dependent on several factors, which include specific proteins (BMP morphogenetic bone protein), primarily located in cortical bone (URIST 1965). Osteoconduction, occurs when material, often inorganic, allowing bone apposition on preexisting bone, requiring presence of bone and differentiated mesenchymal cells. Osteoconductive material under soft tissue will not produce bone neoformation.

Grafts are classified as Autogenous grafts or autografts, when tissue is transferred from one position to another, of same individual, thus not provoking immune reaction, and may be bone, cortical or medullary when transplanted. Allogeneic, homogenous or homograft grafts grafted tissues between individuals of same species with non-identical genes, such as fresh, frozen, lyophilized (FDBA), demineralized and lyophilized (DFDBA) bone. Xenografts, heterografts or heterologues, grafts performed between individuals of different species, and here is bovine bone. Alloplastic, foreign body, inert, used for tissue implantation, such as calcium phosphate, hydroxyapatite, bioceramic, and other types (COSTA; VEINSTEIN (1994).

Graft with autogenous bone in host can generate local response of formation of new tissue. Extracting from bone tissue products that in absence of bone, could produce the same effect were called "morphogenetic bone proteins". Microscopic features of neoformed bone, in front of filling of the bone defect with autogenous graft show rapid repair, in stage of maturation (URIST, 1965).

Presence of neoformed bone replacing autogenous grafts are positive elements that better meet biological requirements, seeming to be preferred for indication and application without risks of preoperative sequelae (NISHIO et al., 2000). Currently, new interdisciplinary field has
emerged in use of autogenous bone grafting techniques, called human bioengineering (NIMNI, 1997).

Great search of this subject has aroused interest in new studies in present time, and this work intends to look for current stage of autogenous grafts, besides factors that could influence its incorporation. It is justified by evaluation and updating of literature.

**LITERATURE REVIEW**

Demineralized bone matrix was implanted in muscle tissue in rabbit leg, noting that after three weeks there was formation of ectopic bone tissue. Concluded that bone matrix contained some element capable of self-induction, bone morphogenetic protein "Bone Morphogenetic Protein" (BMP) (MARZOLA, 2008). Since this time we have been working on isolation of this factor, which in reality are several inductive factors, that is, several bone morphogenetic proteins (URIST, 1965).

Implants were tested made with different materials in vertebral musculature and femurs of 400 white rabbits, checking for presence of various degrees of inflammation, and intensity of reaction altered second implant used. Tissue reaction could be microscopically differentiated into two zones, first, collection of cells adjacent to implant formed pseudomembrane. Second area there was intense necrosed tissue reaction, cell free between pseudomembrane and implant. Titanium induced formation of thin pseudomembrane at bone-tissue interface as well as thin layer of fibrosis. Authors predicted good results of this material when implanted in humans (LAING; FERGUSON Jr.; HODGE, 1967).

Experimental results with membranous bone grafts maintain volume and viability with greater extension than in endochondral grafts, and may be related to more rapid vascularization of membranous bone. Microscopically quantified vascularization patterns showed that in 3 days, membranous grafts of bone evolved, demonstrating blood vessels in soft tissue and host, with little vascularization was seen in endochondral graft. On the 7th day, 2.5 blood vessels were identified incorporating membranous grafts, while an average of 0.6 blood vessels in endochondral grafts. On 14th day, there were average of 20 more vessels in membranous grafts, compared to 1.8 for their endochondral counterparts. At 21 days, endochondral grafts demonstrated central avascular areas noted in membranous grafts. Membrane grafts in rabbits are vascularized faster than endochondral grafts, and this factor maintains greater volume in experimental membranous grafts (KUSIAK; ZINS; WHITAKER, 1985).
Clinical outcomes of bone graft procedures depend on many factors, including the type and methods of fixation, site and host status. Autogenous bone, due to its exceptional regenerative structural capacity, is one most frequently transplanted in humans, being routinely used to repair skeletal defects caused by trauma, neoplasms and infection. However, this could happen, since there was possibility of retention of viable cells, revascularization of graft and, not probability of disease transmission (GOLDBERG, STEVENSON, 1987).

Principle was performed to perform bone regeneration based on hypothesis that different tissue components have varying rates of migration in wound area during healing after three weeks and all animals showed complete healing after six weeks. Little or no sign of healing was evident on the control side even after 22-week observation period (DAHLIN et al., 1988).

In present study, it was reported that in some faults there were particles incorporated with new viable bone at six months, and in others, however, particles were not noticed (BOWERS et al., 1989).

Advantages of use of autogenous bone as grafting material have been described and it is believed that because it has osteocompetent cells and all growth factors inherent to bone repair, this tissue should be of choice in apposition grafts common to maxillary and mandibular reconstructions (MARX, 1993). Another study was carried out where they presented clinical and microscopic data showing repair capacity inherent to autogenous bone. Author based his finding on large number of cases of maxillary and mandibular reconstruction of patients who had resections caused by neoplasias (MARX, 1994).

New ways have been described in craniofacial reconstruction in ancient post-traumatic defects or in craniotomy failures in fresh donor regions, as well as in congenital malformations, as in the Apert and Crouzon syndromes, as described. Stratified implants with BMPs induced early bone formation and were still rigid enough to serve as anchoring element on and between blocks of autogenous bone in cell reconstructions in forehead. Reconstructed areas became clinically sound after few months. In mid-term observations with more than one year, complete consolidation of all implants without signs of resorption was consistently the end result of this type of reconstruction (SAILER; KOLB, 1994).

Osseointegration predicts success of variety of dental implant procedures, however, one must consider modification of osseointegration process through knowledge of physiology, bone formation metabolism, and surgical repair (KOKA; VANCE; MAZE, 1995).
Repair process of open wounds caused in dorsal region was studied, noting through clinical, biometric and microscopic evaluations that wounds treated with Laser Radius revealed acceleration in repair process, with high vascular and fibroblast proliferation. All this, besides demonstrating well developed connective tissue and, rich in collagen fibers (GARCIA; CARVALHO; OLIVEIRA, 1995).

Residual particles of DFDBA, involved by viable bone were noted, with alveolus healed thirteen months after grafting, concluding that DFDBA particles must remain in grafted sites for long periods and that such particles affect nature or extent of regenerative response (BECKER et al., 1996).

Due to lack of research on DFDBA matrix targeting or residual particle effect on graft defects, these two conditions were examined microscopically, observing that 72% of defects exhibited residual DFDBA particles. These particles were incorporated with new viable bone, and significant amount of new insertion or attachment apparatus was also noted (REYNOLDS; BOWERS, 1996).

Recent advances in molecular biology of BMPs have shown bone tissue engineering stage framework, in addition to including periodontium. Bone derived from BMPs with collagen matrix, have induced regeneration of cementum and alveolar bone (RIPAMONTI; REDDI, 1997). Fibroblast Growth Factors (FGF) are mitogenic for endothelial cells with resulting increase in vascularization and, consequently, increased nutrient supply for local bone repair. When FGF are combined with high-level TGF-β-dependent dosage synergistic increases in DNA synthesis (STEFANI et al., 1997).

Behavior of lyophilized and demineralized homologous bone (Pacific Coast Dental Freeze-Dried Bone Products) was evaluated through its implantation in bone defects created in dog tibiae. Study comprised two standard bone defects in each tibia, one filled with clot and the other with demineralized lyophilized bone. Animals were sacrificed at 60, 90, 120 and 150 days, and results allowed to observe the formation of dense bone trabeculae with concentric disposition around grafts and slow reabsorption of the grafted material. It can be concluded that grafted material is biocompatible, not causing irritation to adjacent tissues, being bio-absorbable, bioinert/bioactive and therefore osteoconductive, causing delay in process (PASTORI, 1998).

Use of platelet-rich plasma as safe solution for use of growth factors in bone grafts has been shown to demonstrate clinical use of PRP factors associated with demineralized bone grafts and bone growth was much higher than that found in controls (MARX; CARLSON; EICHSTAEDT, 1998).
It was also verified that bone tissue possesses great regenerative potential with the condition of completely restoring it original structure and functions. However, in some situations, bone failures are not repairable by themselves. Moreover, they classified bone grafts as their origin in autogenous, allogeneic, xenogeneic and alloplastic (LINDHEN et al., 1999).

Significant increase was also observed in the repairs when PRP was used, and positive results were found in both bone and soft tissue repairs, both with mandibular grafts and with composites for replacement bone grafts in maxillary sinus elevation or in other surgeries (GARG, 1999).

Experimental study was carried out in three adult dogs to verify osteogenesis, osteoinduction and osteoconduction, using intra- and extra-buccal grafts with autogenous bone. Bone formation with all materials was more complete in extra-buccal than in buccal fields, demonstrating importance of surgical bed in grafting procedures (STUANI, 2000).

Successful dental implant therapy is related to amount of bone remaining and is not always found. There is no consensus for use of these materials, with high success rate for all. When it is smaller than 3 mm, pure autogenous bone becomes essential, besides which, allogeneic grafts are reabsorbed very slowly, forming bone of poor quality (KATO, 2000).

Microscopic study of bone repair of defects in rat mandibles was performed and, results showed bone neoformation at margin of failure after 3 days, as well as around some bone scurfs. In final period of observation, at 28 days, there was no complete bone failure completion (ALMEIDA et al., 2000).

Magnification was observed with respect to active form of vitamin D, which has immuno-modulatory effects on population of lymphocytes, macrophages and natural cytotoxic cells and, moreover, on production and action of cytokines both in vivo and in vitro. These effects are observed in experimental models of autoimmune diseases through clinical and microscopic improvement of lesions in neoplasias, where there is reduction in volume of solid tumors and in transplants, with increase in survival of grafts, making vitamin D possible immunosuppressive for future clinical use (BERTOLINI; TZANNO-MARTINS, 2000).

First clinical reports on bone regeneration of two human recombinant bone morphogenetic proteins (rhBMPs), BMP-2 and BMP-7 have been verified and described, as well as conditions that modulate BMP-dependent osteoinduction. All this was discussed and could provide clues as to how BMP performance used as bone graft substitute in humans could be improved (GROENEVELD; BURGER, 2000).
Research for an ideal bone substitute was performed for more than 20 years, being autologous bone considered best material for grafting, besides this potential to retain vital cells, being replaced by the host, not producing an immunological reaction. Bone morphogenetic proteins isolated from human and bovine cortical bone are responsible for mechanism of ectopic bone induction (CAMELO, 2001).

Analyzed quantitatively and qualitatively, repair pattern of autogenous bone graft in block with or without PTFE-e membrane. Results regarding periods of observation showed that bone loss occurs during repair period, initial graft area decreased over time. Bone graft in block was partially reabsorbed over time, while bone graft in block covered by PTFE-e membrane, showed additional bone neoformation. Therefore, association of the PTFE-e membrane to autogenous bone graft in block gave better results (JARDINI, 2001).

Jaws reconstruction is unique compared to other bones because of different demands of these structures on function. Unlike the long bones of body, reconstructed jaw should withstand shear forces rather than compressive forces and be able to withstand dental implants and prostheses rather than weight produced. Results allowed the authors to conclude that bone growth factors are fundamental to repair of bone grafts and its use has many advantages, including reduction of time necessary for formation of new bone, as well as increase of trabecular obtained in repair. Platelet rich plasma obtained by simplified protocol proposed by authors is important and safe aid in maxillary graft surgeries (LEMO; ROSSI JR; PÍPCIO, 2002).

Regeneration guided bone is performed routinely in surgical clinic, but membranes used to prevent invagination of soft tissues into interior of bone cavity, do not have optical characteristics to be used in procedures associated with laser therapy. Comparative microscopic study was performed showing increase in velocity of primary bone regeneration, showing greater formation of immature/osteoid bone tissue, as well as better quality in organization of granulation tissue. This fact suggests biostimulation in guided bone regeneration using optical membranes conjugated with Low Power Laser Therapy (TLBP), but encouraging results were verified demonstrating that membrane used allowed laser to act in biostimulation process (SALGADO, 2002).

Revascularization of autogenous bone graft in block, associated or not with PTFE-e membrane was analyzed, verifying if there was difference between groups. It was concluded that both groups showed revascularization of autogenous bone graft, being vascular origin limited to bed in the ME group, whereas group E received vessels from bed and surrounding connective
tissue. Revascularization occurred earlier in E group than in ME group, being more intense and extensive in all experimental periods (AZEM, 2002).

Incorporation of critically-sized irradiated fresh frozen membranous allogeneic bone grafts into rabbit calvarial defects was investigated. Neovascularization, bone marrow regeneration and bone neoformation were evident in grafts although revitalization of graft in its entirety was incomplete after 12 months. It has been shown that intramembranous grafts of irradiated fresh frozen bone were well incorporated into defects of rabbit calvaries (SHAND et al., 2002).

Experimental study in animals evaluating method for mandibular reconstruction was performed, being covered with original cortical framework and filled with particulate autogenous bone graft removed from iliac crest. To accelerate bone healing, platelet rich plasma (PRP) was agglutinated with particulate bone grafting in 14 goats. All had expected healing and, osteosynthesis plates and screws supported immediate loading for periods ranging from 3 weeks to 3 months. PRP use appeared to improve bone healing considerably (FENNIS; STOELINGA; JANSEN, 2002).

Literature review was carried out to investigate available information on potential of growth factors in skeletal reconstruction of maxillofacial area. In postnatal skeletal regeneration, PDGF plays an important role in inducing undifferentiated mesenchymal cell proliferation. IGFs play important roles in overall growth and maintenance of body’s skeleton. Effect of local application only of IGFs on craniofacial skeletal defects has not yet shown exclusive potential for improvement of bone regeneration at reported dosages (SCHILEPHAKE, 2002).

Combination of IGF-I with PDGF has been effective in promoting bone regeneration in dentoalveolar defects around implants or after periodontal bone loss. TGF-β alone in skeletal reconstruction appears to be associated with uncertain results. Presence of specific cells is required for enhancement of bone formation by TGF-β. It has biphasic effect, which suppresses proliferation and osteoblastic differentiation at high concentrations. BMPs, BMP2, BMP4 and BMP7 in particular, appear to be more effective growth factors in terms of osteogenesis and in repair of bone defects. Efficacy of BMPs for failure repair is very dependent on type of carrier, having been subject to unknown factors in clinical studies on its reliability providing ambiguous results (SCHILEPHAKE, 2002).

Recent studies have documented success of fusion being increased, generated by bone morphogenetic proteins compared to autogenous graft for posterolateral spinal arthrodesis. Radiographic differences in fusion maturation between treatment groups were evident as early as the 4-
week interval, continuing throughout the 24-week period. Osteogenic Protein-1 treatments demonstrated an accelerated rate of radiographic fusion within four weeks, stabilizing after 8 weeks (22% autogenic, 88% autogenic/rhOP-1 and 66% rhOP-1) (CUNNINGHAM et al., 2002).

In contrast, "gold standard" treatments with autogenous grafts reached maximum of 50% fusion in 6-month interval. Biomechanical test indicated lower level of movement range for axial rotation and flexion-extension in both rhOP-1 and allogeneic treatments, respectively, at 8 and 12-week intervals, respectively (P <0.05) (CUNNINGHAM et al., 2002).

Histomorphometric analysis showed no difference in posterolateral trabecular bone area (mm2) between three treatments (p>0.05) and, microscopically, no significant changes were noted. More distinctive finding in this study works with mechanisms of posterolateral ossification. Based on plane and polarized light microscopy, induction and bone development for rhOP-1 treatments, with or without autogenous graft, resulted from intramembranous ossification, whereas autogenous osseointegration process was only given by endochondral formation. At 24-week interval, no discernible difference in trabecular histomorphology was evident based on different mechanisms of ossification. Increased speed mechanism and incidence of fusion using growth factors (rhOP-1) was outlined by comprehensive study of preferential intramembranous ossification (CUNNINGHAM et al., 2002).

Long-term functional properties of regenerated bone induced by recombinant human morphogenetic protein-2 in segmented bone defects of primate jaws were evaluated. Formation and quality of the new bone were evaluated radiographically and microscopically at the periods of 15 and 30 weeks after surgery and, 4 and 24 weeks after masticatory force, with fully regenerated mandibles with rhBMP-2. Excellent remodeling and consolidation of new bone were observed after loading and this study demonstrated that new bone induced by rhBMP-2 in large segmented defects was maintained and was in place for at least 1 year. Regeneration induced by rhBMP-2 holds promise future therapy, and may be alternative treatment for autogenous bone grafts for implantology and reconstructive surgery (MARUKAWA et al., 2002).

Experimental models have been developed to investigate effects of mechanical stimulation on cells, but none of existing devices can simulate micromovements at mechanical-cellular interface with varying amplitudes and loads. Osteoblasts are sensitive to mechanical stimuli, so that to study bone-implant interface it would be important to quantify their reaction in situation, mimicking this mechanical alteration found at interface. Developed device
could be used to simulate different mechanical situations (PIOLETTI et al., 2003).

Due to increasing use of human homologous grafts, allografts, in reconstructive surgeries, there is need for complete knowledge of biomechanical and microscopic features. They do not need viable cells for their use, therefore, cryopreservation is useful method for storing allografts in tissue banks, not making their future use in orthopedic surgery impossible (BAPTISTA, 2003).

Bone tissue has great regenerative potential with the ability to completely restore its structure and original functions. There are situations in which bone defects cannot be repaired without grafts, those cases where it is necessary to use grafts, for correct treatment and good prognosis. Results suggest deficiencies in demineralization and/or withdrawal of antigenic potentials during biomaterial production. It can be concluded that particle size did not influence the evolution of the repair process of bone defects, acting only as filling substances, and that implanted material should be improved in quality control in production line, since it may represent good alternative for Bone grafts (CARNEIRO, 2003).

Bovine bone substitute (Bio-Oss) was compared to autogenous bone with respect to its value as material for maxillary sinus augmentation, with no healing problems observed. Microscopically, after 90 days, graft volume showed reduction of 14.6 ± 4.4% in group with Bio-Oss and of 3.8 ± 2.5% in group with autogenous bone. Contact bone-implant was 52.16 ± 13.15% in Bio-Oss group and 60.21 ± 11.46% in group with autogenous bone. At 180 days, group with Bio-Oss showed bone growth within substitute, whereas in group with autologous bone differentiation of original bone cannot be seen anymore. Volume reduction was 16.5 ± 8.67% in group with Bio-Oss and of 39.8 ± 16.14% in group with autogenous bone. Contact bone-implant was 63.43 ± 19.56% in group with Bio-Oss and 42.22 ± 12.80% in group with autogenous bone. Results indicated that due to non-resorptive properties of Bio-Oss bone substitute, regeneration of defects is possible. It was also demonstrated that bone substitute seemed to be permanent implant, and volume of grafted area by autogenous bone decreased during period of observation (SCHLEGEL et al., 2003).

Use of autogenous bone grafts could be considered as best choice to be made for reconstructive surgery. In periodontal literature, bone clot use was suggested in the late 1960s and results show that if adequate care is taken to avoid contamination by saliva during surgical procedure, this method of autogenous bone collection may prove useful in situations where small amounts of bone are needed (BLAY; TUNCHEL; SENDYK, 2003).
Progress has been reported in understanding the role of bone morphogenetic proteins BMPs in dental and craniofacial development, demonstrating stem cells in dental pulp. Accumulated knowledge on frameworks of biomaterials prepared ground for tissue engineering and regenerative therapy of craniofacial complex. In addition, recent approval by the US Food and Drug Administration (FDA, Rockville, MD, USA) of recombinant human BMPs to accelerate bone fusion in slow healing fractures indicates that this family of proteins may be very useful in design of regenerative treatments in applications dental implants. In short term, these advances are likely to be applied to endodontics or periodontal surgery and, ultimately, to facilitate approaches to regenerate all teeth for use in dental restoration (NAKASHIMA; REDDI, 2003).

Mandibular syphysis is preferred as donor site for relatively small bone grafts required for autogenous grafting procedure. Observation pertinent to cortical and trabecular bones, aid in determining the depth of osteotomy. These results provide useful information on graft removed from mandibular symphysis for placement of dental implants. These results will allow volume of cortical plate of mandibular symphysis region, its adequate size, depth and location to be predicted when removing the graft from graft (PARK, 2004).

We investigated two groups of biomaterials widely used in surgical procedures for bone regeneration in dentistry, autogenous and xenogene grafts. Insufficient bone volume is major condition for long-term instability of osseointegrated implants. Thanks to numerous surgical procedures and intense research, the possibility of rebuilding bone is now much more predictable than in past. This has given the clinician more solutions to handle complex situations and, in the last decade, demand for regenerative surgery for functional and aesthetic reasons has increased. Autogenous bone graft is considered as gold standard material for any regenerative procedures, due to its main properties being osteogenic, osteoinductive and osteoconductive. Autogenous bone can be collected from two different sites, intra and extra-buccal. Intra-buccal donor sites may be symphysis of mandible, mandibular branch and maxillary tuberosity. Extra buccal donor sites are iliac crest, tibia, and skull. Xenogenic bone graft is graft removed from donors of other species. These natural materials, thanks to their physical-chemical characteristics similar to those of human bone, show great osteoconductive properties (SIMION; FONTANA, 2004).

Benefit of platelet-rich plasma (PRP) in maxillary sinus graft was evaluated when compared to recombination of human bone morphogenetic protein-7 (rhBMP-7). No inflammatory reaction was observed on any
microscopic slide and on individual animals. Increased bone apposition in vicinity of host bone in presence of PRP was clearly detected, however, osseointegration of implants was not better at these sites.

Type of dental implant was surrounded by connective tissue in all cases treated with PRP. In contrast, bone marrow was observed throughout whole breast increased in presence of rhBMP-7, and implant was surrounded with neoformed bone in all cases. Mean bone in contact with implant using rhBMP-7 was 45.8% and 5.7% under PRP (p = 0.002). Mean weight of newly formed mineralized bone in area of increase using rhBMP-7 was 8.3 mm while PRP side was 3.6 mm (p = 0.013). Using PRP, mean area of neoformed bone increased (51.3%) when compared to rhBMP-7, however, difference was not statistically significant (p = 0.081). In conclusion, under selected experimental conditions use of rhBMP-7 obtained superior results with regard to osseointegration of dental implants and weight of neoformed bone compared to PRP use (ROLDAN et al., 2004).

Comparative study of devitalized bovine bone, porous coral hydroxyapatite, castor oil polyurethane, and autogenous bone graft were performed in 6x10mm bone defect repair in rabbits femurs. Implant of devitalized bovine bone induces slower guided tissue repair when compared to the autogenous bone graft and to the implants of porous hydroxyapatite of coral and castor polyurethane (FIGUEIREDO et al., 2004).

Surface roughness modulates osseointegration of orthopedic and dental titanium implants. High surface roughnesses are currently obtained by bombarding implant surfaces with abrasive particles of silicon or aluminum oxide. This process may cause cytotoxic silicon or aluminum ions to be released into peri-implant tissue. In order to generate rough and biocompatible titanium surface, an innovative bombardment process was developed using calcium phosphate (BCP) particles.

X-ray photoelectrochemical spectroscopy indicated tractions of calcium and phosphorus and, relatively less aluminum on the surface with BCP. Scanning electron microscopy and mitochondrial activity measurement (MTS) showed that MC3T3-E1 osteoblastic cells were viable in contact with BCP surface. In addition, results indicated that MC3T3-E1 osteoblastic cells expressed activity for alkaline phosphatase, retaining their response to BMP-2 bone morphogenetic protein. Overall results clearly indicate that this calcium phosphate blasting technique increases roughness of titanium implants, providing non-cytotoxic surface for osteoblasts in rats (CITEAU et al., 2005).
DISCUSSION

Osteogenic properties are unique characteristics referring to organic materials or to autogenous grafts, capable of stimulating bone growth, originating from cells transferred from within the graft. Neoform bone is processed directly from osteoblasts. In the first three days after graft installation, intense cellular activity begins, when capillaries can be seen penetrating the graft, due to the angiogenesis process. PDGF stimulates mitogenesis of cells in medullary canal transferred together with graft, initiating angiogenesis of capillary complex within the graft by induction of mitosis in endothelial cells (KUSIAK; ZINS; WHITAKER, 1985).

Bone tissue has great regenerative potential with condition of completely restoring its structure and original functions, however in some situations, bone defects are not repairable by themselves (LINDHEN et al., 1999). To reduce this deficiency, plausible hypothesis would be the use of autogenous or homogenous grafts. Disclassified and lyophilized bone induces differentiation of host mesenchymal cells into osteoblasts, stimulating bone neoformation. Bone induction becomes possible because demineralization exposes BMP-inducing proteins present in organic matrix of bone tissue (GOLDBERG; STEVENSON, 1987).

Comparing results obtained parameters were not observed. No acceleration of process was found, but rather delay, probably due to methodology used, where xenogenic model was used and because they are much larger particles than used (PASTORI, 1998 and MARZOLA, 2008).

Filling of periodontal defects with DFDBA reported that in some defects there were particles incorporated with new viable bone at six months and in others, however, particles were not noticed (BOWERS et al., 1989). Bone tissue has great regenerative potential with the ability to completely restore its structure and original functions. Concluded that particle size did not influence evolution of reparative process of bone defects, acting only as filling substances (CARNEIRO, 2003 and MARZOLA, 2008).

Residual particles of DFDBA, involved by viable bone, were observed with healed alveolus thirteen months after grafting, concluding that DFDBA particles must remain in grafted sites for long periods and that such particles affect nature or extent of regenerative response (BECKER et al., 1996).

Residual particles were observed in experimental wells of 150 days after grafting, incorporated into viable bone, with results similar to
those found in mentioned studies (PASTORI, 1998). However, it was not confirmed that permanence of these particles is related to size of studied ones. REYNOLDS; BOWERS (1996) found that 72% of defects exhibited residual particles of DFDBA and were incorporated with new viable bone.

For many years, bone grafts have been used in orthopedics to assist in repair of damaged bone, and autogenous grafts have been used in treatment of dental implants. Bone induction is in fact several sequential steps in cascade and key steps are chemotaxis, mitosis and differentiation. In this context, chemotaxis is directed migration of cells in response to chemical gradient of signals released from demineralized and insoluble bone matrix which is predominantly composed of type I collagen. This fibrocartin binding plasma, which in turn predominates collagen, fibrin and heparin. After 3 days mesenchymal cells attack the collagen and proliferative matrix as indicated by autoradiography. Differentiation of chondroblasts is evidenced at 5 days and chondrocytes at 7 days. Cartilage appears at 9 days and concomitantly vascular invasion with osteoblast differentiation. Alkaline phosphatase is maximal in 10 to 12 days, meaning bone formation. Osteocalcin carboxyglutamic acid from bone containing glycoproteins (BGP) increases in 28 days correlating with bone remodeling (MARKS; GARG, 1999).

Live cells transplanted essentially into the spongy region of graft during osteogenesis continue to exist in first three to four days by means of blood supply to recipient area. Osteoblastic cells present in bone trabeculae are able to assume proliferation and neoformation of bone tissue. This phase occurs in initial four weeks, in proportional ratio that transplanted bone cells die in recipient bed (GARG, 1999).

Tissue engineering of alveolar bone using therapeutic gene may offer potential to enhance release of promoter molecules such as morphogenetic proteins (BMPs) at graft sites. Cortical bone is primary source of these morphogenetic proteins. This phase begins after six weeks of transplantation and lasts at most six months. BMPs are members of superfamilies of growth factors being powerful controllers of cartilage formation, and bone during regeneration. It has been proven in several experiments that BMPs extracted from bone can produce cell differentiation, organization of bone tissue with intense vascularization, formation of cartilage and complete bone remodeling with formation of structures and renewal of calcified tissue. Later, genetic sequences and proteins responsible for these events were identified. This discovery was made through the analysis of amino acid sequence of carefully purified inducer proteins and reverse mapping of genetic localization of these sequences (URIST, 1965).
Thus, from the 1980s, each protein present in bone extracts was tested separately for its effectiveness as osteoinductive agent. It was therefore determined that BMPs are part of large family of growth factors, known as (TGF transforming growth factor), and are set of at least 18 different proteins with varied biological composition and effect. Generally these proteins are dimeric (from BMP-2 to BMP-8), with spatial structure and amino acid sequence similar to TGF-beta. Each chain contains disulfide bonds linking one chain to another. Bone growth factors are fundamental in graft repair. Use of these growth factors has many advantages, including reducing the time required for new bone formation as well as increasing trabeculation obtained in repair. Repair process of bone grafts depends on several factors, namely quality of donated tissue, vascularization of recipient area, immobilization of graft and efficiency of repair mechanisms. Among these factors, efficiency of repair mechanisms is independent of surgical technique or local surgical conditions being entirely dependent on patient (http://www.bmp.com.br/bmpmain/historia1.asp, 2004).

In 1980s, large research laboratories sought to investigate possibility of using chemical mediators in modulation of bone graft repair process. Many growth factors were identified, isolated, and tested for their ability to initiate bone growth. Growth factors act on osteoprogenitor cells differentiating them and aiding work of cells present in preexisting bone. Thus, in major bone defects where remaining bone cells are not sufficient to induce repair, growth factors play key role. Growth factors are biological mediators that regulate important cellular events in tissue repair, including cell proliferation, differentiation, chemotaxis, and matrix formation (SCHILEPHAKE, 2002).

Many in vivo and in vitro studies have evaluated effects of these polypeptides on bone formation, which include PDGF, TGF, (FGF), IGF, and BMPs. These factors are produced by several cells among them, platelets, fibroblasts, osteoblasts, chondroblasts and other mesenchymal cells (LYNCH et al., 1991). TGF-β stimulates pre-osteoblast and osteoclast mitogenesis to increase number of these cells, as well as promotes their differentiation into mature and functional osteoblasts. To support capillary invagination, TGF-β influences osteoblasts and fibroblasts to deposit bone and collagen matrix, respectively. IGF, in turn, acts on endosteal osteoblasts, which limit trabeculae of spongy grafted bone. From 5th to the 7th day, through PDGF chemotaxis mechanism (along with the oxygen gradient) it attracts macrophages to grafted area. From then on regenerative processes will be stimulated by macrophages derived growth factors (MDF). Autocrine auto-
stimulation response is maintained by cells of spinal canal that continue to secrete TGF-β and IGF (MARX, CARLSON; EICHSTAEDT, 1998).

Bone growth factors (BGFs) are produced either by bone cells or hematological cells and their effects may be autocrine, i.e., where cells of site and BGF producing cells are same, or paracrine, where cells of site are different but close to cells that produce BGF. Platelet-derived growth factors (PDGFs) are dimers, molecules containing two A and B chains, each resulting from separate genes. PDGF are presented in one of their three isoforms which are combinations of two chains: either as PDGF-AA or PDGF-BB homodimers or as PDGF-AB heterodimers. Former is associated with platelets and subsequently wound repair and, it is known that osteoblasts are capable of producing PDGF but of PDGF-A chain. Of three forms PDGF-BB is most active in terms of bone cells, producing a very large increase in replication of cells of calvary model. In enriched cultures of osteoblasts derived from fetal calvaria, PDGF-BB is approximately eight times more mitogenic than PDGF-AA and three times more than PDGF-AB. Although increased, collagen synthesis is reported in bone and bone culture after exposure to PDGF (KOKA; VANCE; MAZE, 1995).

Platelet-derived growth factors have been associated with stimulation and acceleration of soft and hard tissue healing, representing new biotechnology. Its ability to modulate regenerative processes has been described by several authors in field of orthopedics, bucomaxillofacial and implantodontics. Because quantity and quality of bone are fundamental in these areas, platelet-derived growth factors appear as coadjuvant therapeutic mechanism, which may make it possible to reduce surgeries to remove bone grafts and thereby decrease postoperative morbidity. Platelet growth factors stimulate different phases of differentiation and proliferation of osteoblast. Release of growth factors at site of bone lesion leads to increase of cells involved with bone lineage, neovascularization and inhibition of osteoclastic action. This set of actions determines favorable balance of bone formation (LEMOS, ROSSI JR., PÍPICO, 2002).

It is not very clear mechanism of action of BMPs in endochondral bone hindering their understanding. However, certain properties and effects of BMPs have been identified and may explain their ability to osteoinduce. Perhaps greatest discovery of effect of BMP is its ability to induce differentiation of osteoblastic mesenchymal cells and osteoprogenitous condroncys. Other growth factors either increase mitogenesis or affect cell function of differentiated cells that do not influence cell differentiation (GROENEVELD; BURGER, 2000).
In present study, expression of tumor cells in bone marrow and proliferation of mesenchymal cells in bone marrow, we present review of results on use of data in this paper. It was verified that after 3 days, graft was diffused, observing the presence of vascular shoots from the bed, and these vascular shoots were observed in more discreet way. After 7 days, revascularization occurred from vessels originating from the bed and surrounding connective tissue penetrating entire periphery of graft, whereas in membrane group only vessels from the bed reached the graft. On 14th day, group E (autogenous bone graft) showed penetration of vessels at the periphery of graft, reaching variable extensions inside graft. In ME group (autogenous bone graft associated with PTFE-e membrane), vascular penetration was observed in graft near perforation areas, at borders and at bed-graft interface. At 21 days, vascular penetration could be observed in both groups, E and ME, although presence of vessels in practically the entire extent of the graft was observed in group E, whereas in ME group, this vascular penetration was mainly noticed in regions close to drilling (AZEM, 2002).

Implantology literature offers promising but limited set of information that track use of bone growth factors. Research on dogs shows that clinical use of PDGF-B in combination with IGF-I increases bone regeneration around implant. Seven days after installing screw, treated implants had large percentage of bone filling peri-implant spaces and, higher percentage of bone at implant contact than untreated implants. At 21 days the percentage of bone obturating the peri-implant space was even more significantly increased in relation to control (MARX, 1993; MARX, 1994). These researches are in agreement with results found, when two factors work very well combined (SCHILEPHAKE, 2002).

To understand how platelet rich plasma (PRP) affects bone regeneration, regeneration sequence should be made clearly. Platelets are fragments responsible for hemostasis and, by initiation of regeneration of traumatized tissue. During autogenous graft procedure platelets become entangled in degranulated graft during time it releases two growth factors PDGF and TGF-β. PDGF binds endothelial cells to initiate capillary invagination and TGF-β that binds osteoblasts and stem cells to initiate mitosis by stimulating production of osteocytes. Increased oxygen gradient between graft and adjacent tissue activates macrophage chemotaxis which in turn stimulates macrophages to secrete macrophage-derived angiogenesis factor (MDAF) and macrophage-derived growth factor (MDGF). Within graft, platelets become entangled in clot degranulation and, after few hours of graft placement, release platelet-derived growth factor (PDGF). Thus, inherent
wound properties (particularly the oxygen gradient and PDGF) promptly initiate angiogenesis of adjacent capillaries and, mitogenesis of transferred osteocompetent cells (STEFANI et al., 1997). In addition, there was significant improvement in healing with use of PRP (MARX; CARLSON; EICHSTAEDT, 1998; GARG, 1999; FENNIS, STOELINGA, JANSEN, 2002; LEMOS, ROSSI JR.; PÍPICO, 2002 and MARZOLA, 2008).

First, macrophages are adhered to graft site by increasing oxygen gradient, and then histiocytes, macrophages, foreign body giant cells, and inflammatory cells of connective tissue are stimulated by degradation of dead matrix products to grow and repopulate area of decalcified graft bone (BERTOLINI; TZANNO-MARTINS, 2000).

While cleaning the region, adsorption of plasma transudates during inflammatory process, forming layer of 2 to 5 nm in first minutes of contact occurs rapidly on surface of the implant. In this plasma layer, growth factors that influence chemotaxis of cells specific for repair survive. Although there is ongoing debate about nature of proper implant adhesion, there is no doubt that at some stage cells are attracted and adhere to implant to form integration tissue. Adhesion of cells to surface of implant is complex subject because there are three distinct types of cells involved, epithelium, connective tissue and bone tissue (BRUNETTE et al., 1988 and MARZOLA, 2008).

CONCLUSIONS

Based on the works presented it can be concluded that:

1. Bone repair through autogenous grafts showed to be biocompatible material, not provoking irritation to adjacent tissues, suggesting, therefore, to be of low antigenicity.

2. Autogenous grafts or autografts are of the same individual, playing the role of osteogenesis, osteoinduction and osteoconduction and, according to authors consulted.

3. Autogenous grafting due to its exceptional regenerative structural capacity, allows retention of viable cells, revascularization, absence of disease transmission and, therefore, no risk of postoperative sequelae.

4. Autogenous grafts show better bone quality after complete incorporation.
5. Intramembranous grafts are better than endochondral grafts.
6. Cortical autologous grafts have a higher protein load.
7. Use of growth factors has many advantages, such as reducing the time required for new bone formation, as well as increased trabeculation obtained in the repair.
8. Use of PRP stimulates graft consolidation and mineralization in half the time with 15% to 30% effective gain in bone density.

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* According of the ABNT norms and modified by Dentistry Review - ATO.