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POTENTIAL USE OF MESENCHYMAL STEM CELLS AND BIO-OSS® IN SURGERY SKULL-MAXILLO-FACIAL: A REVIEW

[1,2]Elias Naim Kassis, [1,2,4*]Idiberto José Zotarelli Filho, [4]Marinônio Lopes Cornélio, [2]Álvaro José Cicarelli, [3]Luiz Fernando Frascino and [1,2]Taylane Soffener Berlanga de Araújo

[1]Unorp, University Center North Paulista, São José do Rio Preto, SP, Brazil
[2]Unipos, Post Graduate and Continuing Education, Street Ipiranga, 3460, São José do Rio Preto SP, Brazil
[3]Frascino Plastic Surgery, Street Antonio de Godoy, 3945, Redentora, São José do Rio Preto SP Brazil
[4]State University of São Paulo - IBILCE-UNESP, Rua Cristovão Colombo 2265, São José do RioPreto SP Brazil 15054-000

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ABSTRACT

The WHO (World report on road traffic injury prevention, 2002) predicts that by 2020 road accidents are the third leading cause of facial trauma in the world. Moreover, according to the Brazilian Association of organ transplantation, the number of bone transplants per million population reaches 450 (18,200 transplants). The lack of bone in the alveolar ridge has been a major problem in functional aesthetic recovery in patients who have suffered dentoalveolar trauma, traumatic dental extractions, dental congenital absence, disease involving the maxilla and mandibular. With the emergence of regenerative medicine, the use of stem cells and adult stem cells is a new therapeutic modality with various treatments. Experimentally, tissue regeneration compounds such as periodontal tissue was also demonstrated, showing that AMSC associated with platelet-rich plasma can regenerate alveolar bone, cementum and periodontal ligament eight weeks after implantation. Thus, biomaterials Bio Oss® (Geistlich), being biodegradable, biocompatible, nontoxic, and its low immunogenicity, can act in the regeneration of bone tissue, they establish with mesenchymal stem cells from adipose tissue proper biological niche (microenvironment favorable) for bone growth, both in animal studies and in human studies.

INTRODUCTION

According to the World Health Organization (WHO), in 1990 there were about 999 000 people in mountainous roads and highways, while in 2002 there were 1.1 million, ie an increase of 10% (Bezerra and Lenharo, 2002). This increase is attributed to underdeveloped and developing countries, according to World Report on Traffic Injury Prevention, 2002 In order to alert the world's population to the severity of the situation, the WHO (World report on traffic injury prevention, 2002) predicts that by 2020 road accidents are the third leading cause of facial trauma in the world (Calasans *et al*., 2011). Furthermore, according to the Brazilian Association of organ transplantation, the number of bone transplants per million population reaches 450 (18,200 transplants) in the State of São Paulo, 110 (4100 transplants) in the State of Paraná, and 30 (1,200 transplants) in the State of Rio de Janeiro, available in 5 Tissue Banks three States during the 10th quarter of 2012 (Fardin *et al*., 2010). The lack of alveolar bone has been a major problem in aesthetic functional recovery in patients who suffered dentoalveolar trauma, traumatic dental extractions, dental pathologies involving congenital absence of the jaws, and infections due to emotional consequences and the possibility of deformity and also the impact economical than they have on the National Health System (NHS) (Calasans *et al*., 2011 and Fardin *et al*., 2010). Bone loss can also occur due to periodontal disease, traumatic surgeries, or for physiological reasons due to lack of or inadequate function of the load flange prosthesis (Merkx *et al*., 2003). The trauma of the face region can affect both soft tissues (skin, muscles, nerves) and hard tissues (bones, teeth), for these injuries can affect the quality of life and health of the victim (Fontanari *et al*., 2007; Giannoudis *et al*., 2005 and Lima and Martorelli, 2008). With the emergence of

Correspondingauthor: Idiberto José Zotarelli Filho
State University of São Paulo - IBILCE-UNESP, Rua Cristovão Colombo 2265, São José do Rio Preto SP Brazil 15054-000.

regenerative medicine, the use of stem cells and adult stem cells is a new application with various treatments (Zuk *et al*., 2001 and Nardi and Meirelles, 2006). Adipose tissue has mesodermal origin and consists of populations of cells: mature adipocytes and adipose Stem Cell Derived (ADSC) vascular fraction comprising a heterogeneous fraction including preadipocyte, endothelial cells, smooth muscle cells, pericytes, fibroblasts, macrophages and ASC (adipose stem cell) (Zuk *et al*., 2001; Nardi and Meirelles, 2006 and Planat Bernard *et al*., 2004). The adipocytes are more than 90% of the volume of adipose tissue but less than 50% of the total number of cells (Rodriguez *et al*., 2003). Other cell types that can be extracted from the adipose tissue by enzymatic digestion with collagenase shows the distribution of about 35% ASC and 15% of endothelial cells (Zotarelli Filho *et al*., 2013).

For the ADSC minimally invasive procedures such as liposuction fat or resection may be performed for each and 1.0 g of fat, there are about 5,000 adipose stem cells, which is about 500 to 1,000 times the number of cells 1.0 g pluripotent present in the bone marrow (Zotarelli Filho *et al*., 2013). Because of this abundant number of cells, methods for the expansion of cells in culture systems, such as those made from bone marrow stem cells, or even management techniques iPSC and hESC become unnecessary for clinical use, it is known that the best treatment is with fresh and minimally manipulated biological materials, it is necessary to ensure safe treatment. Thus, ASCs are readily available for minimally manipulated implant way, however, there is need to investigate the genetic stability (Zotarelli Filho *et al*., 2013; Caplan and Buder, 2001 and Greco *et al*., 2013). Moreover, ASC are more resistant to ischemia and can keep operating for 72 hours. In studies comparing the production methods, it was found that only half the ASC obtained by excising tissue from lipoaspirate are present in the material (Gimble *et al*., 2013 and Gir *et al*., 2012). This is because a significant portion of these cells are located around the vessels was maintained in the area of the donor (Zago and Covas, 2006). Thus, it becomes imperative to obtain these vessels to increase the number of ADSC collected.

In clinical studies ADSC as the regeneration of periodontal tissues has been shown and ADSC showed that when associated with platelet-rich plasma can regenerate alveolar bone, cementum and periodontal ligament eight weeks after implantation (Mazzoneto, 2009 and Maiorana *et al*., 2003). In addition, there is a combined study of bone graft with fibrin glue, a biodegradable biomaterial and ADSC for reconstruction of large bone defects in the skull of a victim of seven years of trauma (Maiorana *et al*., 2003). In a few cases, ADSC complex allowed the regeneration of wounds, improving the resulting radiation fibrosis (Gimble *et al*., 2013). Other studies involve research on the safety and efficacy of ADSC for treating fistulae in patients with Crohn's disease, critical limb ischemia in diabetic patients, develop bone bioengineering and treatment of myocardial failure (Planat Bernard *et al*., 2004 and Locke *et al*., 2009).

Bone Tissue Engineering

Tissue engineering is a tool that allows by means of a suitable biological niche for any construction and regeneration of tissues and organs (Iwasaki *et al*., 2011 and Jin *et al*., 2004). Tissue engineering offers numerous benefits that meet the needs of injured tissue or to the regeneration process organ (Burg *et al*., 2000; Chen *et al*., 2010; Dumas *et al*., 2010 and Fu *et al*., 2010). Therefore, understanding the chemical, physical and biological processes of both organic materials as the biological niche in the host is necessary (Gorustovich *et al*., 2008; Marie, 2010 and Rahaman *et al*., 2011).The crossing of compatible information between microenvironments allows cascades of cell recognition and signaling to neovascularization (Fontanari *et al*., 2007 and Mizutani *et al*., 1990). Another advantage is minimally invasive surgery, or allows the use of surgical techniques that cause less risk to the patient (Lima and Martorelli, 2008 and Aubin and Liu, 1996). So biomaterial Bio Oss® (Geistlich), being biodegradable, biocompatible, nontoxic, and low immunogenicity, can act in the regeneration of bone tissue, they establish with mesenchymal stem cells from adipose tissue appropriate biological niche (microenvironment favorable) to bone growth in both animal studies and human studies beings (Figure 1) (Aubin and Liu, 1996; Liu *et al*., 2010 and Boccafoschi *et al*., 2005).

The maxillary sinus augmentation procedure has been well publicated and the long-term clinical survival (> 5 years) of implants placed, regardless of graft materials used, compares favorably to implants placed conventionally as reported in other systematic reviews (Hing, 2004; Rodriguez *et al*., 2005 and Mesimäki *et al*., 2009). Studies that met the inclusion criteria seemed to be comparable and yielded favorable results in supporting dental implants. However, alveolar ridge augmentation techniques do not have detailed documentation or long-term follow-up studies (Mesimäki *et al*., 2009; Chan and So, 2005; Langer and Vacanti, 1993; Khan *et al*., 2009 and Schmitt *et al*., 2013). The alveolar ridge augmentation procedures may be more technique and operator experience sensitive, and implant survival may be a function of residual bone supporting the dental implant rather than grafted bone (Schmitt *et al*., 2013). More in-depth, multicenter studies are required to provide further insight into augmentation procedures to support dental implant survival (Cordaro *et al*., 2008).

Then, clinical study realized by Schmitt et. al., 2013 (Schmitt *et al*., 2013) focused on a comparison of clinical and histological characteristics after sinus floor augmentation with Biphasic Calcium Phosphate (StraumannBoneCeramic®), anorganic bovine bone (Geistlich Bio-Oss®), mineralized cancellous bone allograft (Zimmer Puros®) or autologous bone. As results, ninety-four implants were placed in the augmented positions and 53 bone biopsies were taken and evaluated. The bone volume fraction of newly formed bone was measured as Table 1 (Schmitt *et al*., 2013). Another clinical study, forty-eight maxillary sinuses were treated in 37 patients. Lateral sinus augmentation was used with grafting using either Bio-Oss® (ABB) (control group; 23 sinuses) or Biphasic Calcium Phosphate (BCP) (test group; 25 sinuses). Histology showed close contact between new bone and graft particles for both groups, with no significant differences in the amount of mineralized bone, the bone-to-graft contact, remaining percentage of graft substitute material and more soft tissue components, as Table 2 (Cordaro *et al*., 2008).

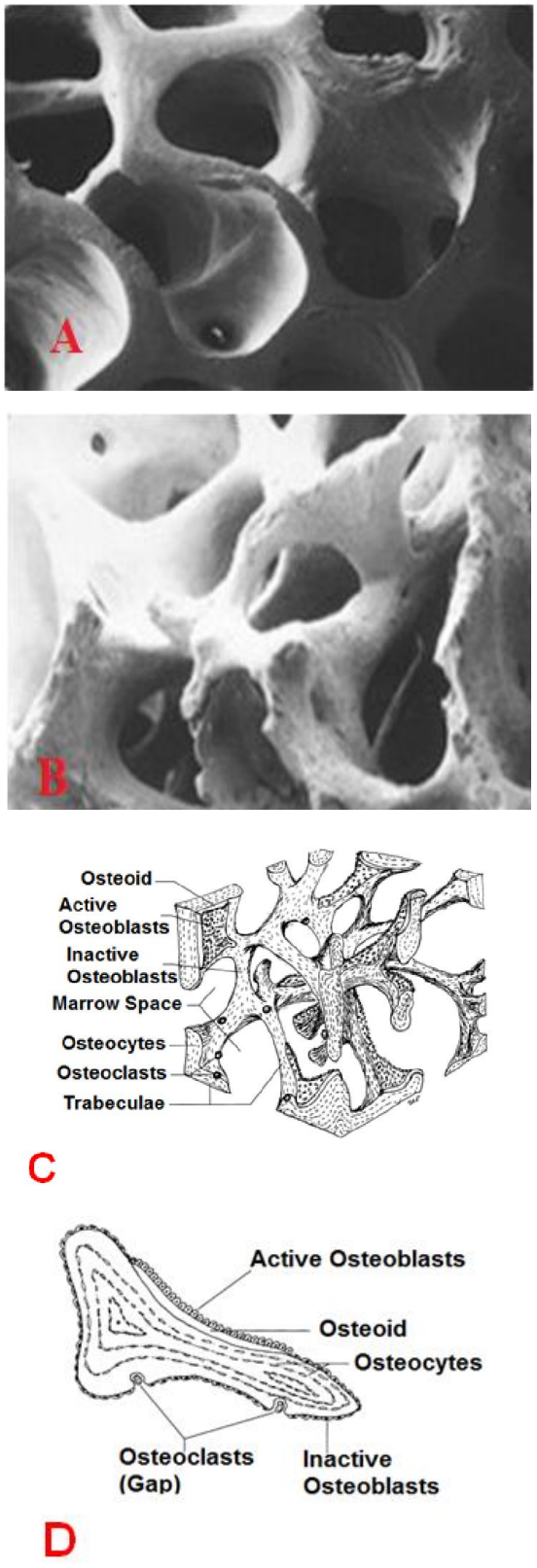

Figure 1. Due to its similarity to human bone (B, C and D), Bio-Oss ® (A) is integrated in the natural process modeling and remodeling. The highly porous structure of Bio Oss ® provides plenty of space for the proliferation of blood vessels (angiogenesis) and the formation of new bone (osteogenesis). The microstructure of the surface of Bio-Oss ® promotes optimal growth of osteoblasts responsible for bone formation. Thus, the particles of Bio-Oss ® become an integral part of the bone structure is that formation (Gorustovich et al., 2008)

Table 1. Relationship between the main biomaterials used for holding the maxillar graft and bone formation that each promoted (Schmitt *et al*., 2013)

MATERIALS	FORMED BONE (VOLUME)
Biphasic Calcium Phosphate (BCP)	30.28 ± 2.16 %
Anorganic Bovine Bone (Bio-Oss)	24.9 ± 5.67 %
Mineralized Cancellous Bone Allograft	35.41 ± 2.78 %
Autologous Bone	41.74 ± 2.10 %

Table 2. Relationship between the main biomaterials used for holding the maxillar graft and Mineralized Bone, Bone-to-Graft Contact and Remaining of graft that each promoted (Cordaro *et al*., 2008)

MATERIAL	MINERALIZED BONE	BONE-TO-GRAFT CONTACT	REMAINING OF GRAFT
Biphasic Calcium Phosphate (BCP)	21.6 ± 10.0 %	34.0 ± 14.0 %	26.6 ± 5.2 %
Bio-Oss® (ABB)	19.8 ± 7.9 %	48.2 ± 12.9 %	37.7 ± 8.2 %

As an example of polymeric biomaterials, chitosan has properties that can stimulate bone formation by presenting polycationic nature, stimulating the biological tissue and the release of cytokines for angiogenesis and osteogenesis. However, there are still many gaps in information about their biocompatibility and immunogenicity (Sollazzo *et al*., 2010). Also, for your application, you must crosslinking in its molecular structure and assign it to another biopolymer to impart greater flexibility to its structure (Berglundh and Lindhe, 1997).

Apart from chitosan, lactic acid, glycolic acid along with collagen, chitosan and N-succinyl-chitosan, observing adhesion, proliferation and differentiation of osteoblastic cells but not on no randomized multicenter clinical study of these elements study (Haas *et al*., 2002). However, these biomaterials have not been consolidated for full use, as there are still many gaps in information that can be answered by randomized multicenter studies (Valentini and Abensur, 1997; Piattelli *et al*., 1999 and Tadjoedin *et al*., 2003). Others biomaterials such as the Titanium knee and hip implants and poly (lactide-co-glycolide) - Both PLGA screws have experienced good success into differentiation of mesenchymal stem cells into osteoblasts and osteocytes. These materials, However, do not have the same mechanical properties to bone and as a result, cannot be used for long-term implants (Carvalho *et al*., 2004).

The challenge is to understand the science of biomaterials is multidisciplinary and its application requires adjustments to its processing, sterilization and structural changes to promote interaction with the tissue of interest (Carvalho *et al*., 2004; Hallman *et al*., 2001; Breyner *et al*., 2010 and Baldwin and Kiick, 2010). Thus, the bioengineered and cell therapy act together to regenerative medicine, facilitating and improving the biological conditions to accelerate tissue repair and regeneration, and thereby maintain tissue homeostasis course (Bauer and Muschler, 2000 and Delacure, 1994). This condition is maintained because the cells involved in the biological niche secrete growth factors for cell proliferation and differentiation and supramolecular structures that ensure the functional organization of tissue generated by means of

stereochemistry and its systemic integration (Hart *et al*., 1986; Mccarthy, 2003 and Misch, 2008).

Why the use of ADSC in Bone Engineering

The main types of stem cells are embryonic stem cells, iPSC, hESC and adult stem cells that can be umbilical cord, peripheral blood, bone marrow and other tissues such as adipose tissue (Sodek and Mckee, 2000). From a therapeutic standpoint, meaning its application in the regeneration of damaged tissues or tissue engineering, stem cells have various advantages and disadvantages (Solomon, 1991). Due to the practical difficulties of obtaining embryonic stem cells and considering the ethical and legal aspects, numerous researchers have conducted their studies with adult stem cells, particularly those derived from bone marrow stroma. Recent studies show that this cell population can be isolated from adipose tissue collected through liposuction (Tabit *et al*., 2012).

The ADSC have various advantages such as low cost, availability, and low immunogenicity compared with acellular fillers such as collagen, hyaluronic acid, chitosan and others (Tabit *et al*., 2012). When added to biomaterials as Bio-Oss its site of improved and more permanent implant survival, reaching several mechanisms including revascularization increased, the reduction of apoptosis and promotion of the differentiation of osteocytes for the regeneration of alveolar bone, increasing thickness of the jawbone (Khan *et al*., 2009 and Tran and Kahn, 2013).Moreover, the ADSC when cultured in the presence of bone releases cytokines osteopoiese undergo a process that involves the proliferation and maturation of primitive precursor cells to the formation of functional osteoblasts and bone cells originated ADSC this phenomenon is committed osteoprogenitor cells and pre-osteoblasts osteoblasts and osteocytes (Gimble *et al*., 2013 and Verfaille, 2004). Unlike osteoconductive materials, osteoinductive substances promote

bone formation in extra-skeletal sites. Also are members of the TGF-β family. TGF-β belongs to a family of multifunctional growth proves to be one of the mediators of normal cellular physiology, embryogenic tissue involved in a number of responses associated with inflammation and tissue repair factors (Gimble *et al*., 2013). Its main source is the bone extracellular matrix and platelet reservoir to the second polypeptide. TGF-β has an excellent performance in cellular activity, including control of proliferation and expression of different phenotypes of various types of specific cells in the skeleton, especially the precursor of mesenchymal stem cells to chondrocytes, osteoblasts and osteoclasts (Nardi and Meirelles, 2006 and Verfaille, 2004). The ADSC contains several types of cells, such as stem cells from adipose tissue endothelial cells and smooth muscle cells and their progenitors for preadipocytes. The adipose stem cells can secrete VEGF, HGF and IGF-1, which are pro-angiogenic, and pro-adipogenic effects antipoptóticos (Nardi and Meirelles, 2006 and Caplan and Buder, 2001). Furthermore, due to the abundance of progenitor cells in the vessels of ADSC also suggests that these cells are highly capable of enhancing neovascularization, such studies have shown that there is a significant relationship between fat cells and vascular system (Planat Bernard *et al*., 2004).These cells represent a heterogeneous population of microvascular endothelial cells, are a convenient source of multipotent cells and are not restrictive (Rodriguez *et al*., 2003 and Zotarelli *et al*., 2013). The ADSC have the advantages of self-renewal, immunomodulatory character multipotentiality, ease of isolation, purification, expansion "in vitro" as well as cryopreservation. Thus, ADSC must provide the minimum requirements adherent cells and the proliferation, differentiation into at least three cell lines (adipocytes, chondrocytes and osteocytes) and display panel with the surface markers typical of MSCs so that they can studies be used according to the recommendations of the International Society for Cellular Therapy (Nardi and Meirelles, 2006). In culture conditions, the adipose stem cells grow easily in monolayers, retain multipotentiality normally until the 10th passage and feature fibroblastoid morphology (elongated) (Nardi and Meirelles, 2006).

For immunophenotyping of CTMA series of markers (antibodies) positive CD9, CD10, CD13, CD29, CD44, CD49, CD54, CD55, CD59, CD73, CD90, CD105, CD106, CD144, CD146, CD166 and HLA-1 are necessary and one negative number for CD11, CD14, CD19, CD31, CD34, CD45, CD79 alpha, CD80, CD117, CD133, CD144, HLA-DR, and Stro-1 (Zuk *et al*., 2001 and Nardi and Meirelles, 2006). The ADSC secrete a cascade of cytokines and growth factors with paracrine, autocrine and endocrine activities such as colony stimulating factor macrophage (M-CSF), colony stimulating factor granulocyte-macrophage (GM-CSF), macrophages inflammatory protein (MIP-1α / CCL3) (12). These factors, when combined, may produce a series of local immune responses by stimulating angiogenesis and the induction of proliferation and differentiation of mesenchymal stem cells to the desired tissue (Zago and Covas, 2006 and Verfaille, 2004). Furthermore, the ADSC induces expression of proteins junction and increase microvessel integrity and nitric oxide (NO) by macrophages (Verfaille, 2004 and Volpon and Costa, 2000).

Indication of Bio-Oss for Bone Remodeling

Histological reports in the literature revealed that Bio-Oss ® particles were surrounded by mature, well organized and compact bone. Osteoblasts were observed in the bone directly overlay process on the particle (Schmitt *et al*., 2013). Thus, the bone was always in close contact with the particles, with no gaps interface. Furthermore, no inflammation was observed around the particles or on the bone interface. Previous studies have also shown the exact mechanism of how Bio-Oss ® acts on PB-hMSCs, changes in the expression of bone markers related genes (RUNX2, SPP1, SP7, COLIA1, COL3A1, BGLAP, ALPL and FOSL1) and mesenchymal-cell marker trunk (ENG) were investigated using real-time RT-PCR (Cordaro *et al*., 2008). Bio-Oss ® also modulates the expression of genes encoding extracellular matrix proteins such as collagen type 1 collagen alpha-1 (COL1A1) and type 3collagen alpha-1 (COL3A1), probably because this gene is activated in step late differentiation and is associated with the synthesis of extracellular matrix (Sollazzo *et al*., 2010). The normal bone formation and restore tissue involves coordinated bone forming cells and biological interaction of signals action

(Sollazzo *et al*., 2010). The main strength of this process are osteoblasts and their precursors, mesenchymal stem cells from adipose tissue. Osteoblasts can produce new bone, along with the biomaterial, which can initiate the release of biological signals that lead to remodeling and bone formation (Cordaro *et al*., 2008; Sollazzo *et al*., 2010; Berglundh and Lindhe, 1997 and Haas *et al*., 2002). These biological signals attract mesenchymal cells and other bone forming cells to the site of the receptor, stimulating the differentiation of mesenchymal cells into osteoblasts (Valentini and Abensur, 1997 and Piattelli *et al*., 1999). Growth factors and other proteins are some of the biological signs that may be involved in the formation of new bone and tissue remodeling (Figure 2) (Tadjoedin *et al*., 2003). In addition, chemotaxis, there is a migration of bone forming cells to the area of application for the stimulation of cell migration in response to chemical stimuli (Gorustovich *et al*., 2008 and Cordaro *et al*., 2008).

Figure 2. Schematic illustration of the main elements to promote bone regeneration and reconstruction biomaterial along with Bio-Oss maxillar in the area

Mesenchymal stem cells, PMG, osteoblasts bleeding bone, muscle and periosteum infiltrating the biomaterial in the graft area (Sollazzo *et al*., 2010). GMP binds to specific receptors on the surface of ADSC and promote differentiation of these bone-forming cells. Monocytes, macrophages, and endothelial cells contribute to bone remodeling or by contact with osteogenic cells or the release of soluble factors such as cytokines and GF (Valentini and Abensur, 1997 and Piattelli *et al*., 1999). Skeletal system, TNF-α stimulates bone resorption and cartilage and inhibits the synthesis of collagen and proteoglycans. IL-1 induces the expression of a variety of cytokines. LIF and IL-6 are two such molecules that are known to stimulate the differentiation of mesenchymal progenitor cells in the osteoblast lineage are also potent anti-apoptotic agents osteoblasts. In bone, the main sources of IL-6 are not the osteoblasts and osteoclasts. Prostaglandin E2 (PGE2) is also directly related to the expression of IL-6 (Sollazzo *et al*., 2010 and Volpon and Costa, 2000).

Conclusion

We conclude that among the various types of stem cells, ADSC stand out positively in the management, in the quantity and quality of their use with Bio-Oss biomaterial, providing appropriate biological conditions for reconstruction and bone formation, a more practical way and effective.

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Disclosure of potential conflicts of interest

The authors Indicate the potential Conflicts of Interest.

REFERENCES

Aubin, J. E. and Liu, F. 1996. The osteoblast lineage. in: bilizekian, j., raisz, l., and rodan, g., editors. principles of bone biology. sandiego, ca: academic press: 39-50.

Baldwin, A.D. and Kiick, K.L. 2010.Polysaccharide-modified synthetic polymeric biomaterials. *Biopolymers*; 94 :128–140.

Bauer, T.W. and Muschler, G.F. 2000. Bone graft materials. An overview of the basic science. *Clinorthop*, 371:10-27.

Berglundh, T. and Lindhe, J. 1997. Healing around implants placed in bone defects treated with bio-oss. an experimental study in the dog. *Clin Oral Implants Res*, april 8 (2) : 117-124.

Bezerra, F.J.B. and Lenharo, A. 2002. Advancedtherapy in clinicalimplantology. sãopaulo; Artes médicas.

Boccafoschi, F., Habermehl, J., Vesentini, S. and Mantovani, D. 2005. Biological performances of collagen-based scaffolds for vascular tissue engineering.*Biomaterials*; 26 (35) : 7410-7417.

Breyner, N.M., Hell, R.C. and Carvalho, L.R. 2010. Effect of three dimensional chitosan porous scaffold on the differentiation of mesenchymal stem cells into chondrocytes. cto; 191 : 119-28.

Burg, KJL., Porter, S. and Kellam, JF. 2000. Biomaterial developments for bone tissue engineering. *Biomaterials* 21:2347–2359. doi:10.1016/s0142-9612(00)00102-2.

Calasans, M.D., Fernandes, G.V.O. and Granjeiro, J.M. 2011. Preservação alveolar com enxertos após exodontias e previamente à instalação de implantes. Revistaimplant news, 6: 583-590.

Caplan, A.I. and Buder, S.P. 2001. Mesenchymal stem cells: building blocks for molecular medicine in the 21st century. *Trendsmol Med*; 7 : 259-64.

Carvalho, P. S. P., Ponzoni, D., Bassi, A.P.F. and Carvalho, M.C.A. 2004. Manutenção de volume do processo alveolar após exodontia com raspa de osso cortical autógeno. implantnews; 1 (1):53 – 58.

Carvalho, P.S.P. *et al*. 2004. Revisão e proposta de nomenclatura para os biomateriais. revistaimplantenews, 1(3) : 255-60.

Chan, B. P. and So, K. F. 2005. Photochemical crosslink improves the physicochemical properties of collagen scaffolds. *Journal Biomedical Materials Research*.part; 75 (3) : 689-701.

Chen, QZ., Quinn, JMW., Thouas, GA., Zhou, XA. and Komesaroff, PA. 2010. Bone-like elastomer-toughened scaffolds with degradability kinetics matching healing rates of injured bone. *Adv Eng Mater* 12: B642–B648. doi:10.1002/ adem.201080002.

Cordaro, L., Bosshardt, DD., Palattella, P., Rao, W., Serino, G. *et al*. 2008. Maxillary sinus grafting with Bio-Oss or Straumann Bone Ceramic: histomorphometric results from a randomized controlled multicenter clinical trial. *Clin Oral Implants Res*. Aug; 19(8):796-803. doi: 10.1111/ j.1600-0501.2008.01565.x.

Delacure, M.D. 1994. Physiology of bone healing and bone grafts. otolaryngolclin north am; 27 : 859-74.

Dumas, JE., Davis, T., Holt, GE., Yoshii, T., Perrien, DS., Nyman, JS., Boyce, T. and Guelcher, SA. 2010. Synthesis, characterization, and remodeling of weight-bearing allograft bone/polyurethane composites in the rabbit. *Acta Biomater*, 6:2394–2406. doi:10.1016/j.actbio.2010.01.030.

Fardin, A.C., *et al*. 2010. Enxerto ósseo em odontologia: revisão de literatura. innovimplant j, biomateresthet, são paulo, 5 (3): 48-52.

Fontanari, l. A., Manne, J.M. and Junior, W.T. 2007. Utilização de enxerto homógenos para reconstrução em áreas atróficas pré-implante: banco de ossos. revistaimplantnews, 5 (6) : 539-597.

Fu, Q., Rahaman, MN., Fu, H. and Liu, X. 2010. Silicate, borosilicate, and borate bioactive glass scaffolds with controllable degradation rate for bone tissue engineering applications. I. Preparation and in vitro degradation. *J Biomed Mater Res*, A 95A:164–171. doi:10.1002/ jbm.a.32824.

Giannoudis, P.V. *et al*. 2005. Bone substitutes: an update. injury, int. j. care injured, 36s, s20—s27. ed. Elsevier.

Gimble, J.M., Katz, A. J. and Bunnell, B.A. 2013. Adipose-derived stem cells for regenerative medicine. *Circ Res*; 100:1249-1260.

Gir, P., Brown, S.A., Oni, G., Kashefi, N. and Mojallal, A. 2012. Fat grafting: eveidence-based review on autologous fat harvesting, processing, reinjection and storage. *Plastreconstr Surg*., 130(1): 249-58.

Gorustovich, AA., Steimetz, T., Nielsen, FH. And Guglielmotti, MB. 2008. A histomorphometric study of alveolar bone modelling and remodelling in mice fed a boron-deficient diet. *Arch Oral Biol*, 53:677–682. doi:10.1016/j. archoralbio.2008.01.011.

Greco, O.T., Filho, I.J.Z., Bellini, M.F., Bilaqui, A. and Souza, A.S.J. 2013. Cardiomyopathy and cell therapy: ejection fraction improvement and cardiac muscle mass increasing, after a year of bone marrow stem cells transplantation, by magnetic resonance image. *J Stem Cell Res Ther* s6: 008. doi:10.4172/2157-7633.s6-008.

Haas, R., Baron, M., Donath, K., Zechner, W. and Watzek, G. 2002. Porous hydroxyapatite for grafting the maxillary sinus: a comparative histomorphometric study in sheep. intj oral maxillofac implants; may-jun;17(3):337-346.

Hallman, M., Cederlund, A., Lindskog, S., Lundgren, S. and Sennerby, L.A. 2001.Clinical histologic study of bovine hydroxyapatite in combination with autogenous bone and fibrin glue for maxillary sinus floor augmentation.results after 6 to 8 months of healing. *Clin Oral Implants Res*., apr; 12(2):135-143.

Hart, M.M., Campbell, E.D. and Kartub, M.G. 1986. Establishing a bone bank. *Aorn J*., 43:808-811.

Hing, K. A. 2004. Bone repair in the twenty-first century: biology, chemistry or engineering? Philos. *Trans. R. Soc. Lond. B. Biol Sci*., 362 (1825): 2821-2850.

Iwasaki, N., Kasahara, Y., Yamane, S., Igarashi, T., Minami, A. and Nisimura, SI. 2011. Chitosan-based hyaluronic acid hybrid polymer fibers as a scaffold biomaterial for cartilage tissue engineering. Polymers 3:100-113.

Jin, J., Song, M. and Hourston, DJ. 2004. Novel chitosan-based films cross-linked by Genipin with improved physical properties. Biomacromolecules 5:162-168 PubMed Abstract | Publisher Full Text.

Khan, F..Tare, R. S., Oreffo, R. O. C. and Bradley, M. 2009. Versatile biocompatible polymer hydrogels: scaffolds for cell growth. *Angew. Chem. Int*.; 48: 978 – 982.

Langer, R. and Vacanti, J.P. 1993. Tissue engineering.*Science*; 260: 920-926.

Lima, A. F. and Martorelli, 2008.Enxertos ósseos: características de alguns materiais. revista abo nacional, 16(3).

Liu, Y.,Clark, R. A. F., Huang, L. and Rafailovich, M. H. 2010. Hyaluronic acid-gelatin fibrous scaffold produced by electrospinning of their aqueous solution for tissue engineering applications. in advances inmaterial design for regenerative medicine, drug delivery and targeting/ imaging; 1140 :131-136.

Locke, M., Windsor, J. and Dunbar, P.R. 2009. Human adipose-derived stem cells: isolation, characterization and applications in surgery. *Anz J Surg*,79:235-244.

Maiorana, C., Sommariva, L., Brivio, P., Sigurtà, D. and Santoro, F. 2003. Maxillary sinus augmentation with anorganic bovine bone (bio-oss) and autologous platelet-rich plasma: preliminary clinical and histologic evaluations. *Int J Periodontics Restorative Dent* ; jun;23 (3) : 227-235.

Marie, PJ. 2010. The calcium-sensing receptor in bone cells: A potential therapeutic target in osteoporosis. Bone 46:571–576. doi:10.1016/j. bone.2009.07.082.

Mazzoneto, R. 2009. Reconstruções em implantodontia – protocolos clínicos para o sucesso e aprevisibilidade. ed. napoleão, 1ª edição. Nova Odessa – SP, Brasil.

Mccarthy, C. 2003. Dental implants and onlay bone grafts in the anterior maxilla: analysis of clinic outcome. *Int. J. Oral maxillofac. Implants, lombard*, 18 (2): 238-41.

Merkx, M.A., Maltha, J.C. and Stoelinga, P.J. 2003.Assessment of the value of anorganic bone additives in sinus floor augmentation: a review of clinical reports. *Int J Oral Maxillofacsurg*, feb; 32 (1): 1-6.

Mesimäki, K., Lindroos, B., Törnwall, J., Mauno, J. and Lindqvist, C. 2009. Novel maxillary reconstruction with ectopic bone formation by gmp adipose stem cells. *Int J Oral Maxillofacsurg*, 38: 201-209.

Misch, C.E. 2008. Implantes dentais contemporâneos. biomateriais utilizados em implantes dentaised. *Elsevier*, 3a. edição, 24 : 511-542.

Mizutani, A., Fujita, T., Watanabe, S., Sakakida, K. andOkada, Y. 1990. Experiments on antigenicity and osteogenicity in allotransplantes cancellous bone. *International orthop*.

Nardi, N.B. and Meirelles, S.L. 2006. Mesenchymal stem cells: isolation, in vitro expansion and characterization. hep; 174 : 249-82.

Piattelli, M., Favero, G.A., Scarano, A., Orsini, G. and Piattelli, A. 1999. Bone reactions to anorganic bovine bone (bio-oss) used in sinus augmentation procedures: a histologic long-term report of 20 cases in humans. *Intj Oral Maxillofac Implants*; nov-dec; 14(6):835-840.

Planat Bernard, V., Silvestre, J.S., Cousin, B., *et al*. 2004. Plasticity of human adipose lineage cells towards endothelial cells: physiological and therapeutic perspectives. *Circulation*; 109: 656 -63.

Rahaman, MN., Day, DE., Bal, BS., Fu, Q., Jung, SB., Bonewald, LF. and Tomsia, AP. 2011. Bioactive glass in tissue engineering. Acta Biomater 7:2355–2373. doi:10.1016/j.actbio.2011.03.016.

Rodriguez, A., Anastassov, G.E., Lee, H., Buchbinder, D. and Wettan, H. 2003. Maxillary sinus augmentation with deproteinated bovine bone and platelet rich plasma with simultaneous insertion of endosseous implants. *J Oral Maxillofacsurg*; feb; 61(2):157-163.

Rodriguez, A.M., Elabd, C., Amri, E.Z., Ailhaud, G. and Dani, C. 2005.The human adipose tissue is a source of amultipont stem cells. *Biochimie*; 87:125-128.

Schmitt, CM., Doering, H., Schmidt, T., Lutz, R., Neukam, FW. *et al*. 2013. Histological results after maxillary sinus augmentation with Straumann® Bone Ceramic, Bio-Oss®, Puros®, and autologous bone. A randomized controlled clinical trial. *Clin Oral Implants Res*.May;24(5):576-85. doi: 10.1111/j.1600-0501.2012.02431.x. Epub 2012 Feb 13.

Sodek, J. and Mckee, M.D. 2000.Molecular and cellular biology of alveolar bone.periodontology; 24:99-126.

Sollazzo, V., Annalisa Palmieri, Luca Scapoli, Marcella Martinelli, *et al*. 2010. Bio-Oss®acts on Stem cells derived from Peripheral Blood OMJ. 25, 26-31; doi:10.5001/ omj.2010.7

Solomon, L. 1991. Bone grafts. *J. Bone Joint Surg*. (br), 73-b: 706-7.

Tabit, C.J., Slack, G.C., Fan, k., Wan, D.C. and Bradley, J.P. 2012. Fat grafting versus adipose-derived stem cell therapy: distinguishing indications, techniques and outcomes. *Aestbeticplast Surg*. 36(3): 704-13.

Tadjoedin, E.S., Lange, G.L., Bronckers, A.L., Lyaruu, D.M. and Burger, E.H. 2003.Deproteinized cancellous bovine bone (bio-oss) as bone substitute for sinus floor elevation.a retrospective, histomorphometrical study of five cases. *Jclinperiodontal*; mar; 30 (3) : 261-270.

Tran, T.T. and Kahn, C.R. 2013. Transplantation of adipose tissue and stem cells: role in metabolism and disease. *Nat Rev Endocrinol* 6:195 213.

Valentini, P. and Abensur, D. 1997. Maxillary sinus floor elevation for implant placement with demineralized freeze-dried bone and bovine bone (bio-oss): a clinical study of 20 patients. *Int J Periodontics Restorative Dent*; jun; 17(3):232- 241.

Verfaille, C.M. 2004. "Adult" stem cells: tissue specific or not ?in: hasndbook of stem cells. vol 2. adult and fetal stem cells. pp 1-20, elsevier academic press, uk.

Volpon, J.B. and Costa, R.M.P. 2000.Ensaio mecânico e uso clínico do enxerto homógeno processado. revista brasileira de ortopedia, 35 : 219-224.

Zago, M.A. and Covas, D.T. 2006. Células-tronco: origens e propriedades. in: células-tronco: a nova fronteira da medicina. ed. m. zago e d. t. covas, pp. 3-20. editoraatheneu são paulo.

Zotarelli Filho, I.J., Frascino, L.F., Greco, O.T., Araujo, J.D.D., Bilaqui, A. *et al*. 2013. Chitosan-collagen scaffolds can regulate the biological activities of adipose mesenchymal stem cells for tissue engineering. *J Regen Med Tissue Eng*.; 2:12.http://dx.doi.org/10.7243/2050-1218-2-12.

Zuk, P.A., Zhu, M., Mizuno, H., Huang, J., Futrell, J.W. *et al*. 2001. Multilineage cells from human adipose tissue: implications for cell-based therapies. *Tissue eng*; 7(2): 211-28.

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