UNIVERSIDADE DE SÃO PAULO
FACULDADE DE ODONTOLOGIA DE BAURU

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Pre-clinical and clinical studies of a novel porous biphasic calcium phosphate ceramic as alternative to repair bone defects

Estudos pré-clínico e clínico de uma nova cerâmica bifásica porosa de fosfato de cálcio como uma alternativa para o reparo de defeitos ósseos

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Tese constituída por artigos apresentada a Faculdade de Odontologia de Bauru da Universidade de São Paulo para obtenção do título de Doutor em Ciências no Programa de Ciências Odontológicas Aplicadas, na área de concentração Biologia Oral.

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“What we do in life, echoes to eternity”

— Gladiator (2000)

ABSTRACT

Objectives: We compared a novel porous biphasic calcium phosphate (pBCP) containing 70% HA and 30% β-TCP with autogenous bone (AB) regarding bone formation, graft granular size influence (0.7, 1.0 or 1.5 mm), physicochemical properties, and volumetric changes of the total grafted area as well its components (newly formed bone, graft particle stability and soft tissue). **Materials and methods:** Article 1 used a critical size defect in rats. Analyzes included XRD (X-ray diffraction), SEM (scanning electron microscope) and EDS (Energy-dispersive X-ray spectroscopy) *in vitro* and then histomorphometry of biopsies collected from rat skull. Article 2 used a bilateral MSFA by lateral wall surgery in 12 patients in a split-mouth design. Analyses of three-dimensional (3D) cone beam computed tomography (CBCT) scans at different periods (T0, T1 and T2), and of micro-CT scans and histological slides of graft core biopsies were performed. **Results:** In the preclinical approach, similar physicochemical characteristics among pBCPs with different granular sizes were found. Besides, osteopromotion regarding pBCP granular sizes of 0.7 and 1.0 were higher than AB. In the clinical approach, pCBP was similar to AB. However, in both approaches, the volume of the total grafted area and particles within the grafted area were more reduced for AB (45% and 37%, respectively, in article 1 and 31% and 33%, respectively, in Article 2). For pBCP these volumetric changes did not occur, except for 1.5 mm size group in the preclinical approach, which showed a significant reduction in the last period (24 weeks). **Conclusion**: pBCP70:30 physicochemical characteristics, such as slow resorption, creates a favorable microenvironment for bone formation that is directly influenced by the granule size. pBCP70:30 promotes greater preservation of the grafted volume than AB, thus being a good alternative for MSFA and bone regeneration procedures.

Keywords: Bone substitutes;Bone regeneration; Maxillary sinus; X-Ray Microtomography; Histology

RESUMO

Objetivos: Nós comparamos um novo fosfato de cálcio bifásico poroso (pBCP contendo 70% HA e 30% β-TCP com o osso autógeno (AB) quanto à formação óssea, influência do tamanho granular do enxerto (0,7, 1,0 ou 1,5 mm), propriedades físico-químicas e alterações volumétricas da área total enxertada, bem como seus componentes (osso recém-formado, estabilidade das partículas do enxerto e tecido mole). MATERIAIS E MÉTODOS: O artigo 1 usou um defeito de tamanho crítico em ratos. As análises *in vitro* incluíram XRD (difração de raios X), SEM (microscopia eletrônica de varredura) e EDS (espectroscopia de dispersão de energia por raios X) e depois análise histomorfometria de biópsias coletadas da calvária de ratos. O artigo 2 envolveu utilização do material para elevação bilateral de seio maxilar em 12 pacientes, em um desenho *split-mouth*. Análise de tomografia computadorizada tridimensional (3D) de feixe cônico (TCFC) em diferentes períodos (T0, T1 e T2), micro-CT *scans* e lâminas histológicas de biópsias do enxerto foram realizadas. Resultados: Na abordagem pré-clínica, foram encontradas características físico-químicas semelhantes entre os pBCPs com diferentes tamanhos granulares. Em adição, a osteopromoção, para os tamanhos granulares do pBCP de 0,7 e 1,0 mm foram maiores que para o AB. Na abordagem clínica, o pBCP foi semelhante ao AB. No entanto, em ambas as abordagens, o volume total da área enxertada e o volume das partículas dentro da área enxertada foram menores para o AB (45% e 37% respectivamente no artigo 1 e 31% e 33% respectivamente no Artigo 2). Para o pBCP mudanças volumétricas não ocorreram, exceto para o grupo tamanho 1,5 mm na abordagem pré-clínica, que mostrou uma redução significativa no último período (24 semanas). Conclusão: As características físico-químicas do pBCP, como a lenta reabsorção, criam um microambiente favorável para a formação óssea e isso é diretamente influenciado pelo tamanho dos grânulos. O pBCP70: 30 promove maior preservação do volume enxertado em comparação ao AB, sendo uma boa alternativa para o aumento do seio maxilar e para os procedimentos de regeneração óssea.

Palavras-Chave: Substituos ósseos; Regeneração óssea; Seio Maxilar; Microtomografia por Raio-X; Histologia

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1 INTRODUCTION

1 INTRODUCTION

Bone grafting aims to replace missing bone in complex areas where bone reposition or healing fails. It is achievable due to the bone tissue capacity to regenerate completely if sufficient space is provided into which it has to grow. In orthopedic and maxillofacial surgery fields, various types of biomaterials are being used for bone repair and regeneration procedures (Jordana *et al.*, 2017). The development and modification of these materials seek to improve the speed and quality of healing (Ebrahimi *et al.*, 2017), since in Dentistry, there are different clinical situations that need biomaterials with specific characteristics or properties.

Concerning bone grafting and substitute materials, for many years autogenous bone (AB) has been the first biomaterial of choice, since it has the three main properties of a bone grafting substitute including osteoconductivity, osteoinductivity and osteogenicity. Autogenous bone grafts, besides its unique natural three-dimensional structure and host cells, contain growth factors and promote the recruitment of new stem cells. Therefore, AB is currently the "gold standard" in bone grafting. These three main properties are determined by the chemical composition, cells and the physical structure of the biomaterials (Daculsi *et al.*, 2013). n case of AB, the amount of graft is very limited, the removal of intraoral bone increases the surgical time and the morbidity of the donor site, and it represents another potential local for postoperative pain and complications.

Due to these disadvantages, many bone substitutes have been developed in laboratory with materials from extracted humans, animals and synthetic sources. In Dentistry, bone grafts are used as fillers and scaffolds to facilitate bone formation during wound healing (Polo-Corrales *et al.*, 2014). The grafts should be bioresorbable and have no antigenic

properties. For example, bone allografts and xenografts are recognized by the recipient's immune system as foreign and will therefore be attacked in a process termed rejection (Shibuya and Jupiter, 2015). Additionally, the grafts should act as a mineral reservoir, which in turn induces new bone formation. Accordingly, there is a variety of bone substitutes classified by the origin or the type of material used on their production. It includes allografts, synthetic variants, xenografts, growth factors, alloplastic grafts, ceramic based grafts, polymer-based grafts and cell based grafts (Kumar *et al.*, 2013). Some of them have shown good rate of success and are widely accepted and supported by literature, however availability and cost could be still a disadvantage (Wang and Yeung, 2017).

Ceramic based-bone substitute grafts include calcium phosphate, calcium sulphate, and bioglass used alone or in combination. Most of the materials present a single phase then they are referred as monophasic, that is seen in hydroxyapatite (HA) bioceramics. Thus, terms such as biphasic and multiphasic are used for bioceramics having two or more compounds with similar physical properties (Dorozhkin, 2012). Tricalcium phosphate was originally presented as a single phasic material until it was found that it had 20% of HA and 80% of tricalcium phosphate TCP (Ebrahimi *et al.*, 2017). HA is a natural compound of the mineral phase of bone; therefore it has good biocompatibility and, additionally, it is more stable and has better mechanical properties than α- and β-TCP (Dorozhkin, 2012; Bouler *et al.*, 2017; Ebrahimi *et al.*, 2017). HA is most often combined with β-TCP because of its higher stability and lower solubility than α-TCP (Vereecke and Lemaître, 1990; Chow, 1991). Furthermore, β-TCP induces more bone formation in mesenchymal stromal cells than HA (Yuan *et al.*, 2010; Prins *et al.*, 2016). Indeed, the combination of HA with TCP is the most studied material among bone ceramics, since this combination forms a bioactive compound with good grafting properties. Efforts to obtain a bone substitute with favorable properties and suitable for MSFA are still being done. Attention has grown for BCPs scaffolds for having not only

osteoconductive but also osteoinductive properties, even when implanted heterotopically (Coathup *et al.*, 2012). In this respect, article 1 approaches the use of porous HA/TCP 70/30 in MSFA in patients compared to autogenous bone with a 6-month period of healing prior to implant placement.

BCPs may also show some drawbacks such as poor mechanical strength, lack of collagen or other organic compounds, presence of impurities, micro-scale grain size and non-homogenous particle size and shape. However, in the last years, several changes on the production parameters such as sintering temperature, sintering soaking time, pH and purity of the initial materials, have given rise to biomaterials with improved physicochemical properties regarding specific surface area, surface energy, surface charge, surface topography and roughness, grain size and porosity (Daculsi and Legeros, 2006; Zhang *et al.*, 2018). Porosity has called attention due to particular situations, as for example, it was reported that bone did not form in ceramics lacking microporosity, additionally, the osteoinduction potential seems to increase with their presence (Habibovic *et al.*, 2005; Hing *et al.*, 2005; Yuan *et al.*, 2010; Coathup *et al.*, 2012). The macroporosity also potentiates the osteoinductive capacity of microporous structures (Habibovic *et al.*, 2005; Coathup *et al.*, 2012). Recently, Wang et al. (2015) pointed out that porosity has a direct relation with the particle size. In this regard, different outcomes were obtained on the studies comparing particle size of bone ceramics in its efficiency on bone repair (Coathup *et al.*, 2013; Wang *et al.*, 2015) therefore an optimal mean size for BCP particles for clinical use is still inconclusive. It should be noted that in addition to the particle size, all physicochemical configurations of bone substitutes directly influence the host response to bone grafting (Chen *et al.*, 2015).

In an attempt to approach the role of the particle size of BCPs on the healing and regeneration of the bone defects, we performed a second preclinical and complementary

experimental research. The article 1 uses the critical size cranial defect model in rats to test different particle size of the porous HA/TCP-70/30. Few studies exist on the effect of BCP particle size on healing and regeneration of critical-size bone defects and the outcomes are diverse. We hypothesized that particle size variation may influence the bioactivity of the biomaterial as well as the host healing response.

Atrophy of the alveolar bone is aggravated by tooth loss in a chronic, progressive and irreversible way (Bodic *et al.*, 2005). Losing bone by pneumatization of the maxillary sinus is another condition that occurs with aging in both dentulous and edentulous individuals. However, it is more intense in cases of loss of two or more teeth and alveolar atrophy in the posterior region. In these cases, immediate implant placement or immediate bone grafting is indicated (Sharan and Madjar, 2008). For implant placement, host factors such as the residual amount of the bone, quality of the bone, patient's overall condition, local environment and anatomical variability can affect implant success (Martin *et al.*, 2009; Chrcanovic *et al.*, 2017). Therefore, rehabilitation of these patients by use of dental implants remains a challenge in Dentistry.

To overcome these issues, bone augmentation in posterior maxilla is performed with different surgical techniques and the most used are alveolar ridge augmentation and maxillary sinus floor augmentation. Alveolar ridge augmentation is less invasive and within its category are other techniques such as, guided bone regeneration (GBR), onlay/veneer grafting (OVG), combinations of onlay, veneer, interpositional inlay grafting (COG), distraction osteogenesis (DO), ridge splitting (RS), free and vascularized autografts for discontinuity defects (DD), mandibular interpositional grafting (MI), and socket preservation (SP) (Aghaloo and Moy, 2007; Mcallister and Haghighat, 2007). They show good rate of success, however alveolar bone augmentation by maxillary sinus floor augmentation is the most successful method

because it resolves vertical dimension's deficiency, which is the major challenge for implant placement (Aghaloo and Moy, 2007).

Maxillary sinus floor augmentation (MSFA) has begun in the 60`s, particularly, to obtain a correct maxillary ridge and ideal vertical dimensions for prothesis making (Boyne and James, 1980). After that time, sinus floor augmentation was used in combination with dental implants. Currently, there are two techniques to approach the sinus cavity, the transalveolar approach and the lateral window approach (Caldwell-Luc technique) (Mohan *et al.*, 2015). The choice mainly depends on the alveolar residual ridge height (RRH) (Pal *et al.*, 2012). The lateral window approach technique to be used in combination with autogenous bone graft was first described by Tatum and published by Boyne and James in 1980 (Boyne and James, 1980). In 1988, two clinical cases using autogenous bone harvested intraorally and placed within the sinus were reported. Six months later, the implants were placed (Wood and Moore, 1988). Since then, the maxillary sinus floor augmentation is being performed for grafting with the intention of returning the height and width of the bone with a high degree of success (Dongo *et al.*, 2018). The success comes from the fact that it is simple technique, allows ideal blood irrigation, makes it difficult surgical contamination and allows the possibility of grafting large quantities of bone substitutes with a favorable postoperative healing. In article 2, we investigate bone regeneration and its volumetric stability after MSFA of the atrophied maxilla treated with novel porous biphasic calcium phosphate (pBCP70:30) in comparison with AB.

Thus, the general approach of these two studies is to evaluate the performance of a new porous BCP termed as pBCP70/30 in animal and human models. In both studies, factors such as time of healing, new bone formation and bone stability are assessed. They are relevant issues for MSFA, implant placement and other grafting purposes. Still there is scarce knowledge regarding bone substitutes to be used during MSFA and other medical-dental

procedures. The outcomes provided in these studies are helpful and provide new strategies in the bone regeneration and reconstruction field.

3 DISCUSSION

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AB remains as the gold standard for bone regeneration (Sakkas *et al.*, 2017). In the present research, the porous HA/TCP-70/30 bone ceramic showed a bioactivity and bone formation similar to autogenous bone AB in the preclinical critical sized defect model in rats and maxillary sinus augmentation procedures in patients. Both approaches showed particular bone formation in different regions within the grafted area, highlighting the higher osteoconductive potential of this pBCP. Moreover, in the clinical approach, a good graft stability, i.e., low graft remodeling rate, during maxillary sinus augmentation and prior to dental implant placement, was observed in the short term. Physicochemical characteristics of both HA and β-TCP phases in the preclinical approach appeared stable among the different granular sizes of 0.7, 1.0 and 1.5 mm. All granular sizes showed more graft stability than AB in the long term (4-24 weeks). However, the 1.5 mm pBCP was less stable and less advantageous in promoting bone formation than other granule sizes. We found a similar performance of porous HA/TCP:7030 to AB as a bone substitute for bone regeneration in the preclinical critical size defect model and maxillary sinus floor augmentation procedure in patients.

According to our outcomes, bone formation promotion between AB and pBCP/70:30 appeared similar in the clinical approach in the short term. However, in the preclinical approach and long term, granular sizes of 0.7 and 1 mm promoted more bone formation than AB and 1.5 mm was equal to the latter. Additionally, differences in the quality of bone formation were clearly observed and most of these differences were related to the common properties of the biomaterial (osteoinductivity, osteoconductivity and osteogenenicity). This is seen in the host tissue response to the biomaterial used.

The outcomes of articles 1 and 2 are in agreement with the current literature (Vos *et al.*, 2009; Sakkas *et al.*, 2017; Chavda and Levin, 2018), considering AB as the gold standard for bone regeneration. At this point, AB displayed all the three main properties of a bone grafting substitute and it was evidenced by the presence of newly formed bone around AB particles in all regions within the grafted area. Although it could not be seen in the clinical approach (MSFA), because of its short-term design and the impossibility of harvesting more than one bone graft core biopsy, it was more evident in the preclinical approach in the long term (figure 5, 1st article). On the other hand, pBCP/70:30 showed to be more osteconductive than osteoinductive (Habibovic *et al.*, 2008; Tortamano *et al.*, 2012; Wang *et al.*, 2015). Thus, bone formation occurred around the BCP granule surfaces locally, but in a panoramic view, the bone was formed from the border toward the center of the defects and also from the duramater side toward the teguments (figure 5, 12st article). A previous study from our research group analyzed HA/TCP 70/30 implanted in mandibular critical size defects and within muscle bundles and reported new bone formation over their surface, pores and concavities (Santos *et al.*, 2018). While comparing granules size of this BCP, different microenvironments were stablished that may explain the differences in bone formation rate among the granular size groups. Thus, our outcomes support that bone formation rate is affected by pBCP granular variations. Besides, we also consider that proper physicochemical characterization of a biomaterial must be performed as an integral part of the *in vivo* testing studies (Ebrahimi *et al.*, 2017).

In some clinical situations, such as sinus augmentation (MSFA), graft volume stability is necessary (Kirmeier *et al.*, 2008; Kuhl *et al.*, 2015), which means that low resorption rate is desired in such cases. On this issue, AB showed to be less advantageous than pBCP/70:30, since its higher resorption rate led to graph volume diminution, which can affect the total volume needed for the implant placement. HA/TCP ratios are adjusted to obtain a proper

balance between the resorption time of the scaffold and the timing of new bone formation in specific clinical situations (Jensen *et al.*, 2009; Mangano *et al.*, 2015; Helder *et al.*, 2018). The low rate of pBCP/70:30 biodegradability is explained by the higher proportion of HA content versus β-TCP. Regarding this graft stability, in a mandibular defect model, AB graft can be comparable to BCP 20/80, whereas BCP 60/40 and BCP 80/20 rather equaled the known as ‘‘bone substitute control’’ DBBM xenograft (Jensen *et al.*, 2009). In MSFA procedure, BCP 60/40 showed an 84.32% graft volume maintenance until a short-term post-op of 6 months (Ohe *et al.*, 2016). Addition of AB to BCP 60/40 also increased its reabsorption rate from 15% to 18% after six months of MSFA (Kuhl *et al.*, 2015). Our clinical results pointed a significant higher grafted sinus volume maintenance by pBCP/70:30 (85%) vs AB (70%). However, AB resorption rate relies on the quality of the donor area. The cancellous AB from extraoral sites usually has a high resorption rate and leads to minimal bone formation (Block and Kent, 1997; Block *et al.*, 1998). In the preclinical approach, critical size defect model (Article 1), grafted volume reduction of AB reached 45% in the long term. On the other hand, the differences in granular size of pBCP/70:30 (0.7 mm, 1.0 mm and 1.5 mm) did not influence the total grafted volume maintenance, which was far higher than AB at 24 weeks. In spite of pBCP volume maintenance, 1.5-mm granules group showed significant graft volume reduction versus other granular size groups, indicating that there might not be a direct relationship between granular size stability and volume maintenance.

In bone substitutes studies, animal experimentation is a better approach than in vitro tests, and usage of animal models is often essential in extrapolating the experimental results and translating the information into a human clinical setting (Bigham-Sadegh and Oryan, 2015). Critical size defect in rats still represents a reliable preclinical model to analyze bone regeneration. Despite clinical studies are far more significant, sample size and other factors such as variability of individuals may represent a difficulty for them. In the clinical approach,

a self-controlled study design known as split-mouth study is preferred because it eliminates most of the sources of bias that occur in similar controlled studies (Al-Almaie *et al.*, 2017). Core biopsies are limited and represent a challenge in the clinical practice;, once performed they provide valuable data regarding other factors that influence MSFA than implant placement and survival (Kirmeier *et al.*, 2008).

In summary, pBCPs seem to be good substitutes to treat bone loss. Moreover, in Dentistry ceramic bone substitutes and autografts show more acceptance and preference among patients when compared to allografts and xenografts (Fernández *et al.*, 2015). Both preclinical and clinical approaches support that pBCP/70:30 having similar bioactivity to AB, while promoting bone formation and higher graft stability. Granular size points potential influence on the biomaterial performance, however this topic deserves further analyses in specific clinical conditions. For the clinical practice, to get a predictable MSFA outcome, precise measurement methods of the grafted area would be one of the important factors for successful implant treatment, because loss of graft height and width might compromise the future implants placement into the grafted maxilla (Ohe *et al.*, 2016). More studies are still necessary to get a more comprehensive panorama regarding graft stability and granular size influence on bone regeneration processes.

4 CONCLUSIONS

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In conclusion, this study demonstrated:

- The novel BCP evaluated in this study is a ceramic biphasic formatted by hydroxyapatite and β-TCP in a 70/30 ratio. This material contains several concavities and micropores on its surface, increasing surface area for bone deposition and a Ca/P ration of 1.8.
- The presence of concavities in pBCP surface creates a favorable microenvironment for bone formation, which is directly influenced by the granule size. Small and medium granule size of pBCP promoted higher bone gain than large size in an 8-mm critical bone defect in rat skull.
- In the preclinical model, although AB graft showed a higher bone gain at the shorter period (4 weeks), this gain was not maintained at longer periods (12 and 24 weeks), while the slow absorption of pBCP favored the bone ingrowth until 24 weeks at higher values than AB.
- Clinically, pBCP promoted a similar amount of bone formation and less loss of graft volume when compared to AB in patients undergoing MSFA procedures in the short term (six months).
- Thus, pBCP might be an efficient bone substitute to repair large bone defects and to promote bone augmentation, as an alternative to autologous bone.

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APPENDIXES

DECLARATION OF EXCLUSIVE USE OF THE ARTICLE IN THESIS

We hereby declare that we are aware of the article **"Porous biphasic calcium phosphate ceramic for maxillary sinus floor augmentation: a randomized controlled clinical trial with CBCT, micro-CT and histomorphometry studies"** will be included in the Thesis of the student **Ricardo Quirico Pinheiro Machado** and was not used and may not be used in other works of Graduate Programs at the Bauru School of Dentistry, University of São Paulo.

Bauru, November 21, 2018

Ricardo Quírico Pinheiro Machado
Author — Signature

Ever Mena Laura
Author — Signature

Tania Mary Cestari
Author — Signature

Gerson Francisco de Assis
Author — Signature

Rumio Taga
Author — Signature

Marilia Afonso Rabelo Buzalaf
Author — Signature

DECLARATION OF EXCLUSIVE USE OF THE ARTICLE IN THESIS

We hereby declare that we are aware of the article **"Influence of biphasic calcium phosphate particle size on the repair of cranial critical-size bone defects"** will be included in the Thesis of the student **Ricardo Quirico Pinheiro Machado** and was not used and may not be used in other works of Graduate Programs at the Bauru School of Dentistry, University of São Paulo.

Bauru, November 21, 2018

Ricardo Quirico Pinheiro Machado
Author — Signature

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ANNEXES

ANNEX

Approval of Ethical Committee

FACULDADE DE ODONTOLOGIA DE BAURU-USP

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Avaliação Histológica e Histomorfométrica de um procedimento de elevação de seio maxilar utilizando uma cerâmica bifásica porosa: estudo clínico randomizado com avaliação após 4 meses de cicatrização

Pesquisador: Ricardo Quírico Pinheiro Machado

Área Temática:

Versão: 3

CAAE: 03525812.1.0000.5417

Instituição Proponente: Faculdade de Odontologia de Bauru-USP

DADOS DO PARECER

Número do Parecer: 139.405

Data da Relatoria: 31/10/2012

Apresentação do Projeto:

Trata-se de um projeto de mestrado com o título "AVALIAÇÃO HISTOLÓGICA E HISTOMORFOMÉTRICA DE UM PROCEDIMENTO DE ELEVAÇÃO DO SEIO MAXILAR UTILIZANDO UMA CERÂMICA BIFÁSICA POROSA: ESTUDO CLÍNICO RANDOMIZADO COM AVALIAÇÃO APÓS 4 MESES DE CICATRIZAÇÃO" de

autoria de Ricardo Quírico Pinheiro Machado sob a orientação da Profa. Dra. Marilia Afonso Rabelo Buzalaf.Para tal serão recrutados 36 pacientes, com idade entre 18 e 75 anos, com altura de osso alveolar menor que 5 mm na região mais estreita entre a parede do seio maxilar e a crista alveolar. Os 36 sujeitos da pesquisa serão aleatoriamente alocados em 3 grupos de tratamento (12/grupo) neste estudo clínico randomizado. A diferença entre os grupos será o tipo de material a ser utilizado para a elevação do seio maxilar, a saber: cerâmica bifásica porosa (experimental, HA+βTCP,Baumer S.A.), cerâmica bifásica comercial (GENPHOS, HA+βTCP,Baumer S.A.)ou osso autógeno. Quatro meses após a cirurgia, a formação do novo osso será avaliada através de tomografia computadorizada,bem como análises histológicas e histomorfométricas dos sítios de biópsias obtidas através da colocação dos implantes.O pesquisador pretende recrutar seus pacientes entre as pessoas que recorrerem à clínica de implantodontia da Associação Brasileira de Cirurgiões Dentistas de Balneário Camboriú, Santa Catarina, nos anos de 2012 e 2013, para reabilitação protética unilateral de suas regiões maxilares parcialmente edentulas.

Endereço: DOUTOR OCTAVIO PINHEIRO BRISOLLA 75 QUADRA 9
Bairro: VILA NOVA CIDADE UNIVERSITARIA **CEP:** 17.012-901
UF: SP **Município:** BAURU
Telefone: (14)3235-8356 **Fax:** (14)3235-8356 **E-mail:** mferrari@fob.usp.br

FACULDADE DE ODONTOLOGIA DE BAURU-USP

Objetivo da Pesquisa:

Esta pesquisa tem por objetivo testar a hipótese nula de que a utilização de uma cerâmica bifásica porosa não terá efeito significativo na formação de novo osso 4 meses após a elevação da parede do seio maxilar, em comparação à cerâmica bifásica densa (GENPHOS, Baumer S.A.) e ao osso autógeno.

Avaliação dos Riscos e Benefícios:

Riscos: O estudo oferece certo risco ou desconforto aos participantes, uma vez que os procedimentos realizados serão cirúrgicos. Os riscos não devem ultrapassar uma normalidade dentro das cirurgias orais deste tipo. Pode-se esperar desconfortos pós operatórios, tais como: dor leve e moderada nos primeiros dias,abertura da sutura (pontos), sangramento moderado, edema (inchaço) localizado. Segundo o autor da pesquisa, todo voluntário terá o acompanhamento necessário no pré e pós operatório.

Benefícios: Segundo o autor da pesquisa, através dos resultados desta pesquisa, saber-se-á a quantidade e qualidade do novo osso formado, bem como a ausência ou não de inflamações teciduais. A coleta intrabucal de enxerto de osso autógeno pode levar à morbidade do sítio doador e prolongar o tempo cirúrgico, além de prover material de enxerto em quantidade limitada. Além disto, quando utilizado como um enxerto onlay, o osso

esponjoso autógeno de origem extrabucal sofre reabsorção, o que resulta em mínimo ganho ósseo. Com a utilização dos biomateriais pretende-se minimizar esta morbidade da regiao doadora e a quantidade do material para enxertia pode ser obtido tanto quanto necessário.

Comentários e Considerações sobre a Pesquisa:

Trata-se de um estudo clínico randomizado que irá testar a utilização de uma cerâmica bifásica porosa e se utilizará de 36 voluntários. Os voluntários não saberão o tipo de tratamento ao qual serão submetidos de modo que o estudo será conduzido de maneira triplo-cega. Todos os voluntários se submetrão a tomadas radiográficas, sofrerão intervenções cirúrgicas e alguns desconfortos. Sendo do conhecimento deles todos os

procedimentos a que serão submetidos, não existe problema ético que inviabilize a pesquisa.

Considerações sobre os Termos de apresentação obrigatória:

Todos os documentos e explicações solicitadas para análise desta pesquisa foram devidamente encaminhados pelos pesquisadores.

Recomendações:

Não há.

Conclusões ou Pendências e Lista de Inadequações:

Depois de exclarecidas todas as pendências, apresentados todos os documentos necessários para análise, com a devidas adequações, sou de parecer que o projeto possa ser aprovado.

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FACULDADE DE ODONTOLOGIA DE BAURU-USP

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

Considerações Finais a critério do CEP:

O CEP acata o parecer APROVADO emitido pelo relator.

Esse projeto foi considerado APROVADO. O CEP-FOB/USP exige a apresentação de relatórios anuais (parciais e finais), conforme o cronograma apresentado. Qualquer alteração na metodologia e/ou título e a inclusão ou exclusão de autores deverá ser prontamente comunicada. Lembramos que na apresentação do relatório final, deverão ser incluídos todos os TCLEs e/ou termos de doação de dentes devidamente assinados e rubricados.

BAURU, 06 de Novembro de 2012

Assinador por:
Maria Teresa Atta
(Coordenador)

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