MedNEXT
Journal of Medical an Health Sciences

REVIEW ARTICLE

DOI: 10.54448/mdnt25S214

Major randomized clinical studies on the use of Bio-Oss® with fibrin-rich plasma in the activation of microRNAs for bone augmentation and dental implant: a systematic review

Bruna Grance Lopes[1*], Pedro Lucas Frazão Ferreira[1], Alvaro José Cicareli[1], Fábio Alarcon Idalgo[1]

[1] UNORTE - University Center of Northern São Paulo, Dentistry Department – Implant Dentistry, São José do Rio Preto, São Paulo, Brazil.

*Corresponding author: Bruna Grance Lopes.
UNORTE - University Center of Northern São Paulo,
Dentistry Department – Implant Dentistry, São José do
Rio Preto, São Paulo, Brazil.
E-mail: brunagrance@hotmail.com
DOI: https://doi.org/10.54448/mdnt25S214
Received: 01-27-2025; Revised: 04-04-2025; Accepted: 04-27-2025; Published: 04-30-2025; MedNEXT-id: e25S214

Editor: Dr. Tanisha Mishra, MBBS.

Abstract

Introduction: In the context of bone elevation and dental implants, there are several clinical studies with increasing expectations to establish treatment guidelines. In this aspect, Bio-Oss® is composed of inorganic bovine bone and is widely used in several bone regeneration procedures in oral surgery for dental implants. It was investigated miRNAs whose expression was significantly modified in an osteoblast-like cell line (MG63) cultured with Bio-Oss®, as well as in the presence of fibrin-rich plasma. **Objective:** It was analyzing the main randomized clinical studies of the use of Bio-Oss® with fibrinrich plasma in the activation of microRNAs for bone augmentation and dental implant. **Methods:** The systematic review rules of the PRISMA Platform were followed. The search was conducted from June to July 2024 in the Web of Science, Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** A total of 133 articles were found. 25 articles were fully evaluated and 11 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 25 studies with a high risk of bias and 20 that did not meet GRADE and AMSTAR-2. Most studies presented homogeneity in their results, with X^2=89.4%>50%. According to the aim of this study on bone regeneration processes with the use of biomaterials and the main molecular and cellular constituents for subsequent dental implantation, it was found that the search for a solution to large bone defects guided the studies for regeneration therapy tissue or bone regeneration. Bio-Oss® is composed of an organic bovine bone and has been widely used in various bone regeneration procedures. The upregulated miRNAs were mir-423, mir-492, mir-191, mir-23a, mir-377, mir-494, mir-214, mir-193b, mir-320), and 4 downregulated miRNAs (mir-27a, mir-24, mir-188, let-7c) were identified for translational regulation in an osteoblast-like cell line (MG63) exposed to Bio-Oss®. However, MiR-214 was positively correlated with osteonecrosis and upregulated in cells exposed to Bio-Oss®. Also, the main filler biomaterials can be fibrin-rich plasma (FRP), Bio-Oss®. However, it is necessary to understand the chemical, physical, and biological processes of both the biological material and the biological niche of the host. Crossing compatible information between microenvironments allows cell recognition and signaling cascades for neovascularization, regeneration, and bone filling for successful posterior dental implants.

Keywords: Dental implants. Bio-Oss®. Fibrin-rich plasma. MicroRNAs. Bone augmentation.

Introduction

In the context of bone elevation and dental implants, there are several clinical studies with increasing expectations to establish treatment

guidelines. In this regard, Bio-Oss®, composed of inorganic bovine bone, is widely used in several bone regeneration procedures in oral surgery for dental implants [1-5]. Using miRNA microarrays containing 329 probes designed from human miRNA sequences, miRNAs whose expression was significantly modified in an osteoblast-like cell line (MG-63) cultured with Bio-Oss® were investigated. In this sense, three upregulated miRNAs (mir-337, mir200b, mir-377) and 4 downregulated miRNAs (mir-130a, mir-214, mir-27a, mir-93) were identified [6]. With the increasing modernization of implant dentistry, we have immediate implants as the procedure with the highest probability of success among the rehabilitation treatments of the oral cavity, using osseointegrated implants [6]. Immediate implants are those installed soon after the extraction of compromised roots or teeth, using the remaining alveolus for implant placement, minimizing trauma, and optimizing treatment [7-13].

Furthermore, platelet concentrates have been proposed as regenerative materials in tissue regeneration procedures. Among the platelet concentrates proposed in the literature, there are PRP (platelet-rich plasma) and FRP (fibrin-rich plasma) which act as autogenous platelet aggregates with osteoinductive properties. These biomaterials, due to their low morbidity and possible regenerative potential, have been indicated for use in combination with other biomaterials or even alone. FRP is a second-generation

concentrate, that is, no anticoagulant is used for its acquisition. The patient's blood, after being collected, is subjected to a specific centrifugation force, and thus, the figured elements are separated according to their density. From then on, the part corresponding to the red blood cells is discarded and the resulting platelet concentrate is used for regenerative purposes. Leukocytes and platelets synthesize and release a variety of cytokines and growth factors that act on chemotaxis, angiogenesis, cell differentiation, and inhibition [8-10].

Besides, xenografts are bone minerals derived from animals algae, and corals. The organic component is removed to eliminate the risk of immunogenic responses or disease transmission. Animal derivatives are the most used in guided bone regeneration (GBR), especially deproteinized sterilized bovine medullary bone, which has been extensively researched and demonstrated to have similarities with human medullary bone [11]. Deproteinized sterilized bovine medullary bone is an excellent osteoconductor, providing a favorable framework for bone formation. Its slow resorption contributes a lot to maintaining the graft volume. It has good wettability and a good surface contact angle, favoring contact with the blood clot. Elevations of the floor of the maxillary sinus performed using exclusively deproteinized sterilized bovine medullary bone demonstrate good osteoconductive capacity and excellent biological integration, which facilitates bone neoformation. A study with deproteinized sterilized bovine medullary bone used alone or mixed with autogenous bone at different percentages in maxillary sinus floor elevation demonstrated bone formation similar to that of autogenous bone after 9 months [11].

The most used xenograft in guided bone regeneration procedures is deproteinized bovine bone mineral, commercially known as Bio-Oss®, it is the most researched product in regenerative dentistry worldwide. It is a bone of bovine origin processed to produce natural bone minerals without organic elements [5,7]. After thermal and chemical treatments, the inorganic phase of bovine bone consists mainly of hydroxyapatite (HA) which retains the porous architecture. The excellent osteoconductive properties of Bio-Oss® lead to predictable and efficient bone regeneration, Bio-Oss® particles become an integral part of the newly formed bone structure and conserve its volume in the long term [8].

Due to its 'great' resemblance to the human bone, the Bio Oss® is 'incorporated' into the 'natural' process of shaping and reshaping. The highly porous structure of the Bio Oss® offers much space for the formation of blood vessels (angiogenesis) and the deposit of neoformed bone (osteogenesis) [5,7]. The microstructure of the surface of Bio-Oss® supports the 'excellent growth' of osteoblasts, which are 'responsible' for 'bone' formation. In this way, the Bio Oss® particles become an integral part of the structure of the new bone in formation and the low speed of conversion into proper bone (remodeled) from Bio-Oss®, stabilizes the structure and allows the volume of the graft to maintain over long term. These biofunctional processes make Bio-Oss® unique [7,8].

Although the results do not seem to confirm that FRP is better than other biomaterials, it is suggested that its use can result in a decrease in the total healing time, around 104 days, and improve the handling of the graft material. Furthermore, the use of FRP associated with Bio-Oss® seems to illustrate high success rates with minimal costs, which can reduce the amount of bone graft needed to fill the sinus cavity, reducing procedure costs [14].

Therefore, the present study aimed to analyze the main randomized clinical studies on the use of Bio-Oss® with fibrin-rich plasma in the activation of microRNAs for bone augmentation and dental implant.

Methods

Study Design

This study followed the international systematic review model, following the PRISMA (preferred reporting items for systematic reviews and meta-analysis) rules. Available at: http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1. It was accessed on: 07/17/2024. The AMSTAR-2 (Assessing the methodological quality of systematic reviews) methodological quality standards were also followed. Available at: https://amstar.ca/. It was accessed on: 07/17/2024.

Data Sources and Search Strategy

The literature search process was carried out from June to July 2024 and developed based on Web of Science, Scopus, PubMed, Lilacs, Ebsco, Scielo, and Google Scholar, covering scientific articles from various periods to the present day. The descriptors (DeCS / MeSH Terms. Available on: https://decs.bvsalud.org/) were used: "Dental implants. Bio-Oss®. Fibrin-rich plasma. MicroRNAs. Bone augmentation", and using the Boolean "and" between MeSH terms and "or" between historical findings.

Study Quality and Risk of Bias

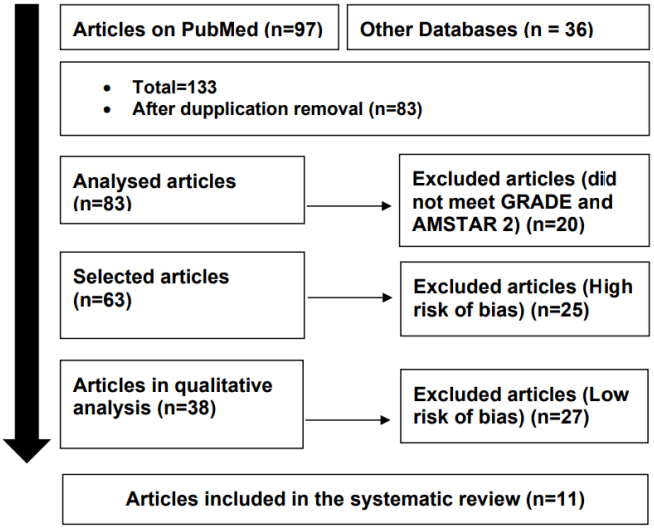
The quality was classified as high, moderate, low, or very low regarding the risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident emphasis was on systematic review articles or meta-analysis of randomized clinical trials, followed by randomized clinical trials. Low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument by analyzing the Funnel Plot graph (Sample size versus Effect size), using Cohen's d test.

Results and Discussion

Summary of Findings

A total of 133 articles were found that were submitted to eligibility analysis, and 11 final articles were selected from the total of 25 to compose the results of this systematic review. The studies listed were of medium to high quality (Figure 1), considering the level of scientific evidence of studies such as meta-analysis, consensus, randomized clinical, prospective, and observational. Biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies presented homogeneity in their results, with X^2=89.4%>50%. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 25 studies with a high risk of bias and 20 studies that did not meet GRADE and AMSTAR-2.

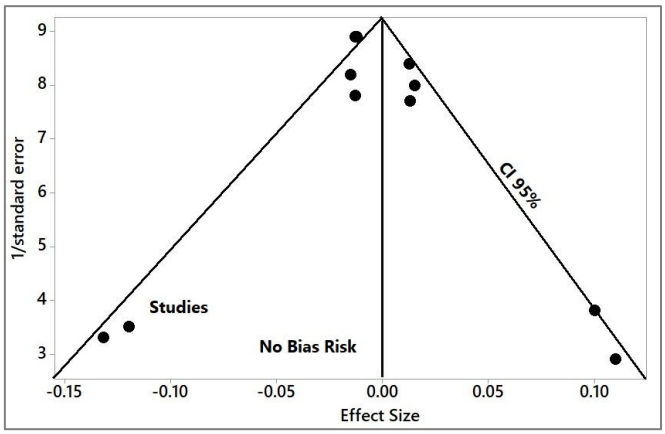
Figure 1. Flowchart showing the article selection process.



Source: Own Authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using Cohen's Test (d). Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph had a symmetrical behavior, not suggesting a significant risk of bias, both among studies with small sample sizes (lower precision) at the base of the graph and in studies with large sample sizes at the top.

Figure 2. The symmetrical funnel plot does not suggest a risk of bias among the studies with small sample sizes, which are shown at the bottom of the graph. High confidence and high recommendation studies are shown above the graph (n=11 studies).



Source: Own Authorship.

Major Clinical Finding

Bio-Oss® is composed of an organic bovine bone and has been widely used in various bone regeneration

procedures during oral surgery. MicroRNAs (miRNAs) represent a class of small, functional, non-coding RNAs of 19 to 23 nucleotides that regulate the transcription of messenger RNAs (mRNAs) into proteins. A study used the miRNA microarray technique to investigate the regulation of translation in an osteoblast-like cell line (MG63) exposed to Bio-Oss®. Nine upregulated miRNAs (mir-423, mir-492, mir-191, mir-23a, mir-377, mir-494, mir-214, mir-193b, mir-320) and 4 downregulated miRNAs (mir-27a, mir-24, mir-188, let-7c) were identified. Since each miRNA regulates 100 mRNAs, only mRNAs related to bone formation were analyzed. The vast majority of detected mRNAs are downregulated [15].

Also, miRNA expression was significantly modified in cells cultured with Bio-Oss®, and MiR-214 was positively correlated with osteonecrosis. Furthermore, miR-214 was upregulated in cells exposed to Bio-Oss®. Histological and histomorphometric data showed that bone formation was significantly increased in the experimental groups Bio-Oss® and bone marrow mesenchymal stem cells treated with antagomiR-214 compared to other groups [16].

In this scenario, normal bone formation and tissue repair involve coordinated interaction between bone-forming cells and biological signals. The main force in this process is the osteoblasts and their precursors [17]. Osteoblasts can produce new bones along with biomaterials and can initiate the release of biological signals that guide bone formation and remodeling [18]. These biological signals attract bone-forming cells to the recipient site. Growth factors and other proteins are some biological signs that may be involved in bone neoformation and tissue remodeling. Furthermore, through chemotaxis, there is migration of bone-forming cells to the application area, as the stimulation of cell migration occurs in response to chemical stimuli [19].

In this sense, monocytes, macrophages, and endothelial cells contribute to bone remodeling, either through contact with osteogenic cells or through the release of soluble factors such as cytokines and GF [19]. In the skeletal system, TNF-α stimulates bone and cartilage resorption and inhibits collagen and proteoglycan synthesis. IL-1 induces the expression of a wide variety of cytokines. LIF and IL-6 are two of these molecules that are known to stimulate the differentiation of mesenchymal progenitor cells into the osteoblastic lineage, they are also potent anti-apoptotic agents for osteoblasts. In bone, the main sources of IL-6 are osteoblasts and not osteoclasts. Prostaglandin E2 (PGE2) is also directly related to the expression of the cytokine IL-6 [20,21].

For the success of the dental implant practice, osseointegration is essential. However, it is a complex process with many factors interfering in the formation and maintenance of bone tissue around the implant, such as topography and surface roughness, biocompatibility, and loading conditions. In addition, a healthy, compatible host bone layer that allows for primary stability is needed [22-25]. Dental implants are being used more and more due to their high success rates. However, a large number of patients do not have sufficient minimum bone conditions for the installation of implants, therefore, previous bone reconstructive surgery is necessary. Dentists must master the knowledge in the healing process of post-extraction alveoli, to provide a correct planning of cases [1,24,25].

In this sense, after extraction, the repair process occurs in the inner region of the alveolus, together with the formation of a clot rich in cells and growth factors, promoting neoformation, bone remodeling, and soft tissue epithelialization. During this process, the alveolar ridge undergoes relevant changes, both in height and in thickness, which influence the possibility of installing the implants. Thus, the optimized processes of implantology and biomaterials allow the installation of implants in areas of thin bone thickness, width, and height, with simpler surgeries and greater success rate and patient comfort [25].

The lack of bone in the alveolar crests has been a major problem in the functional aesthetic recovery of patients who have suffered dentoalveolar trauma, traumatic tooth extractions, congenital tooth loss, and maxillary and mandibular pathologies. To fill large bone defects, the development of bone regeneration improves the epithelial barriers for the bone graft, favoring greater predictability in alveolar and peri-implant reconstructions and presenting a good prognosis. In this sense, filling biomaterials can be FRP, Bio-Oss®, hydroxyapatite, lyophilized and ground demineralized bone marrow, autogenous bone, which is considered the gold standard, among others [24,25].

Thus, FRP as an autologous biomaterial for use in oral and maxillofacial surgery has the majority of leukocytes, platelets, and growth factors, forming a fibrin matrix, with a three-dimensional architecture. The Bio-Oss® biomaterial, as it is biodegradable, biocompatible, non-toxic, and has low immunogenicity and biostimulation, can act in the regeneration of bone tissue, as it establishes, with adenomatous mesenchymal stem cells, the appropriate biological niche for bone growth and, thus, allowing the dental implant as effectively as possible [5,7,8].

Conclusion

According to the aim of this study on bone regeneration processes with the use of biomaterials and

the main molecular and cellular constituents for subsequent dental implantation, it was found that the search for a solution to large bone defects guided the studies for regeneration therapy tissue or bone regeneration. Bio-Oss® is composed of an organic bovine bone and has been widely used in various bone regeneration procedures. The upregulated miRNAs were mir-423, mir-492, mir-191, mir-23a, mir-377, mir-494, mir-214, mir-193b, mir-320), and 4 downregulated miRNAs (mir-27a, mir-24, mir-188, let-7c) were identified for translational regulation in an osteoblast-like cell line (MG63) exposed to Bio-Oss®. However, MiR-214 was positively correlated with osteonecrosis and upregulated in cells exposed to Bio-Oss®. Also, the main filler biomaterials can be fibrin-rich plasma (FRP), Bio-Oss®. However, it is necessary to understand the chemical, physical, and biological processes of both the biological material and the biological niche of the host. Crossing compatible information between microenvironments allows cell recognition and signaling cascades for neovascularization and regeneration and bone filling for successful posterior dental implants.

CRediT

Author contributions **Conceptualization**- Bruna Grance Lopes, Pedro Lucas Frazão Ferreira, Alvaro José Cicareli, Fábio Alarcon Idalgo; **Data curation -** Bruna Grance Lopes, Pedro Lucas Frazão Ferreira; **Formal Analysis -** Bruna Grance Lopes, Fábio Alarcon Idalgo; **Investigation -** Bruna Grance Lopes, Pedro Lucas Frazão Ferreira, Alvaro José Cicareli, Fábio Alarcon Idalgo; **Methodology -** Bruna Grance Lopes, Pedro Lucas Frazão Ferreira; **Project administration -** Bruna Grance Lopes, Pedro Lucas Frazão Ferreira; **Supervision-**Alvaro José Cicareli, Fábio Alarcon Idalgo; **Writing - original draft -** Bruna Grance Lopes, Pedro Lucas Frazão Ferreira, Alvaro José Cicareli, Fábio Alarcon Idalgo; **Writing-review & editing-** Bruna Grance Lopes, Pedro Lucas Frazão Ferreira, Alvaro José Cicareli, Fábio Alarcon Idalgo.

Acknowledgment

Not applicable.

Ethical Approval

Not applicable.

Informed Consent

Not applicable.

Funding

Not applicable.

Data Sharing Statement

No additional data are available.

Conflict of Interest

The authors declare no conflict of interest.

Similarity Check

It was applied by Ithenticate@.

Application of Artificial Intelligence (AI)

Not applicable.

Peer Review Process

It was performed.

References

1. Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJJ, Mouhyi J, et al. Platelet-rich-fibrin (PRF); A second generation concentrate. Part I: Tecnological concepts and evolution. Oral Sugery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology. 2006; 101 (3): e 37- e 44.
2. Nícoli LG, Pigossi SC, Araújo RFdSB, Marcantonio C, Marcantonio E, Marcantonio JRE. Multidisciplinary approach to oral rehabilitation with dental implants after gunshot injury. A clinical report. The Journal of Prothestic Dentistry. 2018; 119 (3): 329 – 33.
3. Jeong SM, Lee CU, Son JS, Oh JH, Fang Y, Choi BH. Simultaneous sinus lift and implantation using platelet-rich-fibrin as sole grafting material. J. Craniomaxillofac Surgery. 2014; 42 (6): 990 – 4.
4. Tajima N, Ohba S, Sawase T, Asahima I. Evaluation of sinus floor augmentation with simultaneous implant placement using platelet-rich-fibrin as sole grafting material. Int J Oral Maxillofac Implants 2013;28(1):77- 83.
5. Xuan F, Lee CU, Son JS, Jeong SM, Choi BH. A comparative study of the regenerative effect of sinus bone grafting with platelet-rich fibrin-mixed Bio-Oss® and commercial fibrin-mixed Bio-Oss®: an experimental study. J Craniomaxillofac Surg. 2014 Jun;42(4):e47-50. Doi: 10.1016/j.jcms.2013.05.029.
6. Annalisa P, Furio P, Ilaria Z, Anna A, Luca S,

Marcella M, Marzia A, Elena M, Carinci F. Anorganic bovine bone and a silicate-based synthetic bone activate different microRNAs. J Oral Sci. 2008 Sep;50(3):301-7. doi: 10.2334/josnusd.50.301.

7. Moreira AC, Silva JR, Samico RP, Nishioka GNM, Nishioka RS. Application of Bio-Oss in tissue regenerative treatment prior to implant installation: literature review. Braz Dent Sci. 22(2), 2019.
8. Li P, Zhu H, Huang D. Autogenous DDM versus Bio-Oss granules in GBR for immediate implantation in periodontal postextraction sites: A prospective clinical study. Clin Implant Dent Relat Res. 2018 Dec;20(6):923-928. doi: 10.1111/cid.12667. Epub 2018 Sep 19.
9. Costa JBZ, Silva F, Dultra CA, Souza LF, Santos MCNE. Uso de membranas biológicas para regeneração óssea guiada em implantodontia – uma revisão de literatura - Revista Bahiana de Odontologia. 2016 Mar;7(1):14-21.
10. Saghiri MA, Asatourian A, Garcia-Godoy F, Sheibani N. The role of angiogenesis in implant dentistry part II: The effect of bone-grafting and barrier membrane materials on angiogenesis. Med Oral Patol Oral Cir Bucal (2016), [doi:10.4317/medoral.21200].
11. Mesimäki K, Lindroos B, Törnwall J, Mauno J, Lindqvist C, Kontio R, Miettinen S, Suuronen R: Novel maxillary reconstruction with ectopic bone formation by GMP adipose stem cells. Int J Oral Maxillofac Surg 2009, 38 : 201-209.
12. Zotarelli Filho IJ, Frascino LF, Greco OT, Araujo JDD, Bilaqui A, Kassis EN, Ardito RV and Bonilla-Rodriguez GO. Chitosan-collagen scaffolds can regulate the biological activities of adipose mesenchymal stem cells for tissue engineering. J Regen Med Tissue Eng. 2013; 2:12. http://dx.doi.org/10.7243/2050-1218-2-12.
13. Egido-Moreno S, Valls-Roca-Umbert J, Céspedes-Sánchez JM, López-López J, Velasco-Ortega E. Clinical Efficacy of Mesenchymal Stem Cells in Bone Regeneration in Oral Implantology. Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2021 Jan 21;18(3):894. doi: 10.3390/ijerph18030894.
14. You JS, Kim SG, Oh, J.S., Kim, J.S. Effects of Platelet-Derived Material (Platelet-Rich Fibrin) on Bone Regeneration. Implant Dent. 2019 Mar 8 [doi: 10.1097/ID.0000000000000877.
15. Palmieri A, Pezzetti F, Brunelli G, Martinelli M, Lo Muzio L, Scarano A, Scapoli L, Arlotti M, Guerzoni L, Carinci F. Anorganic bovine bone (Bio-Oss) regulates miRNA of osteoblast-like cells. Int J Periodontics Restorative Dent. 2010 Feb;30(1):83-7.
16. Wang Y, He R, Yang A, Guo R, Liu J, Liang G, Sheng D, Zhong L. Role of miR-214 in biomaterial transplantation therapy for osteonecrosis. Biomed Mater Eng. 2022;33(5):351-364. doi: 10.3233/BME-211296.
17. Starch-Jensen T, Aludden H, Hallman M, Dahlin C, Christensen AE, Mordenfeld A. A systematic review and meta-analysis of long-term studies (five or more years) assessing maxillary sinus floor augmentation. Int J Oral Maxillofac Surg. 2018 Jan;47(1):103-116. doi: 10.1016/j.ijom.2017.05.001. Epub 2017 May 22.
18. Strauss FJ, Stähli A, Gruber R. The use of platelet-rich fibrin to enhance the outcomes of implant therapy: A systematic review. Clin Oral Implants Res. 2018 Oct;29 Suppl 18:6-19. doi: 10.1111/clr.13275.
19. Wu IH, Bakhshalian N, Galaustian R, Naini RB, Min S, Freire M, Zadeh HH. Retrospective Analysis of the Outcome of Ridge Preservation with Anorganic Bovine Bone Mineral: Marginal Bone Level at Implants Placed Following Healing of Grafted Extraction Sockets. Int J Periodontics Restorative Dent. 2019 Jan/Feb;39(1):131-140. doi: 10.11607/prd.3308.
20. Zhang Y, Tangl S, Huber CD, Lin Y, Qiu L, Raush-Fan X. Effects of Choukroun's platelet-rich-fibrin on bone regeneration in combination with deproteinized bovine bone mineral in maxillary sinus augmentation: a histological and histomorphometric study. J Craniomaxillofac Surg. 2012; 40 (4): 321 -8.
21. Zhou, J., Li, X., Sun, X., Qi, M., Chi, M., Yin, L., Zhou, Y. Bone regeneration around immediate placed implant of molar teeth with autologous platelet-rich fibrin: Two case reports. Medicine (Baltimore). 2018 Nov;97(44):e13058. doi: 10.1097/MD.0000000000013058.
22. Momen-Heravi F, Peters SM, Garfinkle L, Kang P. Acellular Dermal Matrix as a Barrier for Guided Bone Regeneration of Dehiscence Defects Around Dental Implants: A Clinical and Histological Report. Implant Dent. 2018 Aug;27(4):521-524 [doi: 10.1097/ID.0000000000000796].
23. Nizam N, Eren G, Akcali A, Donos N. Maxillary sinus augmentation with leukocyte and platelet-rich fibrin and deproteinized bovine bone mineral: A split-mouth histological and histomorphometric study. Clin Oral Implants Res. 2018 Jan;29(1):67-75 [doi: 10.1111/clr.13044. Epub 2017 Aug 8].

24. Pichotano EC, De Molon RS, Freitas De Paula LG, De Souza RV, Marcantonio E JR, Zandim-Barcelos DL. Early Placement of Dental Implants in Maxillary Sinus Grafted With Leukocyte and Platelet-Rich Fibrin and Deproteinized Bovine Bone Mineral. J Oral Implantol. 2018 Jun;44(3):199-206. doi: 10.1563/aaid-joi-D-17-00220. Epub 2018 Feb 19.
25. Tatullo M, Marrelli M, Cassetta M, Pacifici A, Stefanelli LV, Scacco S, Dipalma G, Pacifici L, Inchingolo F. Platelet Rich Fibrin (P.R.F.) in reconstructive surgery of atrophied maxillary bones: clinical and histological evaluations. Int J Med Sci. 2012;9(10):872-80 [doi: 10.7150/ijms.5119. Epub 2012 Nov 7].