

Comparison of the Efficacy of Tricalcium Phosphate and Mineralized Plasmatic Matrix Graft for the Bone Defect in the Distal Second Molar Tooth After Surgery of the Lower Impacted Third Molar Tooth

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Article Info	ABSTRACT
Article History Received: 29.08.2023 Accepted: 20.02.2024 Published: 30.04.2024	Aim: After the extraction of mandibular horizontal and mesioangular teeth, a defect occurs in the distal part of the second molar. In this study, the effect of MPM on these defects was evaluated. Materials and methods: 36 patients randomly divided into 3 groups. The first group included MPM and PRF. The second group included B-tcp and PRF. In the 3rd group, the extraction socket was left empty. At preoperative and postoperative 6th months, periodontal pocket depth, gingival index and plaque index, and the distance between the enamel junction and crestal bone at the distal of the 2nd molar were measured by CBCT. 8 patients were removed for various reasons. 28 patients were evaluated. Results: Preoperative and postoperative periodontal pocket depths at the sixth month were 7.67 ± 1.58 mm and 4.67 ± 1.23 mm in the MPM group (p<0.001); 6.60±1.96 mm and 4.70±1.34 mm in the β-TCP group (p<0.001); 6.78±1.48 mm and 5.56±1.01 mm in the control group (p<0.023). Bone defects preoperatively and at six months postoperatively were 7.97 ± 1.04 mm and 3.59 ± 0.66 mm in the MPM group (p<0,001); 6.23 ± 1.37 mm and 2.90 ± 1.04 mm in the β-TCP group (p<0.001); 6.92±0.82 mm and 4.30±0.68 mm in the control group (p<0.001). Conclusion: MPM is an effective graft material to restore the periodontal health of the distal part of the second molar after impacted lower third molar surgery
Keywords: Tricalcium Phosphate, Platelet Rich Fibrin, Third Molar, Extraction of Tooth, Bone.	

Alt Gömülü Üçüncü Molar Dişin Çekimi Sonrası İkinci Moların Distalinde Oluşan Kemik Defektinde Trikalsiyum Fosfat ve Mineralize Plazmatik Matris Greftin Etkinliğinin Karşılaştırılması

Makale Bilgisi	ÖZET
Makale Geçmişi Geliş Tarihi: 29.08.2023 Kabul Tarihi: 20.02.2024 Yayın Tarihi: 30.04.2024	Amaç: Mandibular mesioangular ve horizontal dişlerin çekiminden sonra ikinci molar dişin distalinde defekt oluşmaktadır. Bu çalışmada bu defektlere MPM' in etkisi değerlendirildi. Materyal ve metod: 36 hasta rastgele 3 gruba ayrıldı. İlk grup MPM ve PRF içermekteydi. İkinci grup B-TCP ve PRF içermekteydi. Üçüncü grupta çekim soketi boş bırakıldı. Preoperatif ve postoperatif 6. ayda periodontal cep derinliği, dişeti indeksi, plak indeksi ve 2. moların distalindeki kemik ile mine bileşimi arasındaki mesafe KIBT ile ölçüldü. 8 hasta çeşitli sebeplerle çıkarıldı. 28 hasta değerlendirildi. Bulgular: Ameliyat öncesi ve sonrası altıncı ayda periodontal cep derinlikleri MPM grubunda 7,67 ± 1,58 mm ve 4,67 ± 1,23 mm (p<0,001); β-TCP grubunda 6,60±1,96 mm ve 4,70±1,34 mm (p<0,001); Kontrol grubunda 6,78±1,48 mm ve 5,56±1,01 mm (p<0,023). MPM grubunda ameliyat öncesi ve ameliyat sonrası altı ayda kemik defektleri 7,97 ± 1,04 mm ve 3,59 ± 0,66 mm idi (p<0,001); β-TCP grubunda 6,23 ± 1,37 mm ve 2,90 ± 1,04 mm(p<0,001); Kontrol grubunda 6,92±0,82 mm ve 4,30±0,68 mm (p<0,001) idi. Sonuç: MPM, gömülü alt üçüncü molar cerrahisi sonrasında ikinci molar dişin distal kısmının periodontal sağlığını yeniden sağlamada etkili bir greft materyalidir.
Anahtar Kelimeler: Trikalsiyum Fosfat, Trombositten Zengin Fibrin, Üçüncü Molar, Diş Çekimi, Kemik.	

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INTRODUCTION

There are several indications for the removal of impacted lower third molars, and one of them is the possibility that the impacted tooth may cause a bony defect on the distal aspect of the adjacent lower second molar.¹ This periodontal defect can develop due to the presence of the impacted third molar itself, as well as after its removal.² Especially people over the age of 26 with mesioangular or horizontally positioned third molars are more susceptible to such defects.³

To prevent periodontal problems caused by impacted third molars, various techniques such as different flap designs, guided tissue regeneration techniques, autografts, allografts and the use of platelet-rich fibrin (PRF) have been tried.⁴⁻⁷ Also some alloplasts including tricalcium phosphate (TCP), porous hydroxyapatite, bioactive glass or a combination of them have been used.⁴

One of the disadvantages of particulate grafts is that they cannot remain stable under masticatory forces.⁸ Recently, a biomaterial called mineralised plasmatic matrix (MPM) has been introduced. MPM is produced by mixing a plasma phase and a mineral phase. After centrifugation of the autologous blood, white blood cells (plasma phase) are removed and mixed with an autologous, alloplastic, allogeneic or xenogeneic bone graft (mineral phase). This produces a homogeneous, compact, stable, dense fibrin network and malleable graft material.⁹

Figure 1: Mesioangular and fully impacted lower third molars. The right tooth is fully impacted and its presence has already caused a severe defect on the distal aspect of the second molar.



Although there have been studies on the use of MPM in various oral surgical procedures, to our knowledge, there have not been sufficient studies on its efficacy after removal of impacted lower third molars. The aim of our study was to compare the efficacy of MPM and β -TCP on the defect that occurs on the distal aspect of the second molar after removal of the impacted lower third molars.

MATERIALS AND METHODS

This study received support from the Necmettin Erbakan University Scientific Research Projects. Ethical approval was obtained from the Ethics Committee of the Faculty of Dentistry at Necmettin Erbakan University.

Patient selection and study groups

Patients who applied for the removal of impacted lower molars between January 2018 and September 2018 were scanned. The inclusion criterias were:

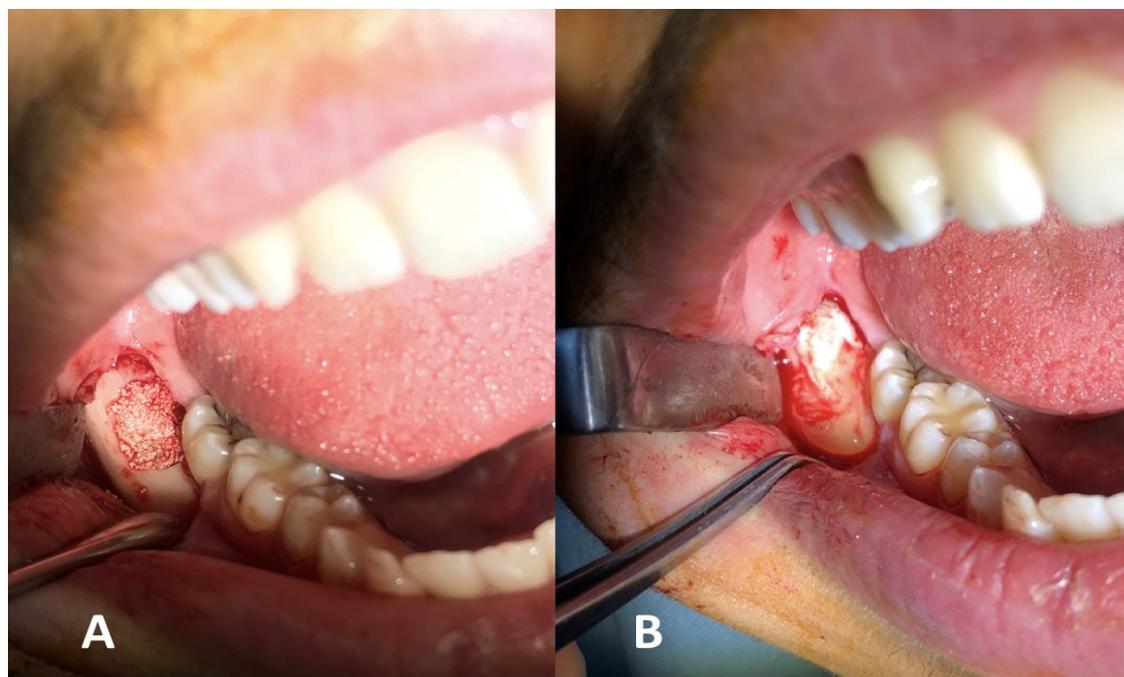
- The patient was over 18 years old
- Systemic status was ASA I or II
- The tooth was fully impacted
- The tooth was in a mesioangular or horizontal position
- Removal of the impacted third molar appeared to cause a severe periodontal defect on the distal aspect of the adjacent lower second molar (Figure 1).

Exclusion criterias were:

- The adjacent second molar had a crown restoration
- Poor oral hygiene
- Pregnant or breastfeeding women
- The patient has had or is having orthodontic treatment
- Smoking habit

A total of 36 patients (14 males and 22 females) aged between 18 and 38 years (mean age 24.39 ± 5.09 years) were eligible. Each patient had one impacted third molar included

Figure 2. A: Packing the MPM material into the aspiration port. B: Placement of the PRF membrane.



in the study. The patients were randomly divided into three groups:

- The MPM group (n=12): The extraction socket was filled with MPM containing β -TCP as the mineral phase and covered with a PRF membrane (Figure 2).
- The β -TCP group (n=12): The extraction socket was filled with β -TCP Alloplast only and covered with a PRF membrane.
- The control group (n=12): The aspiration port was left empty and allowed to fill with blood clot.

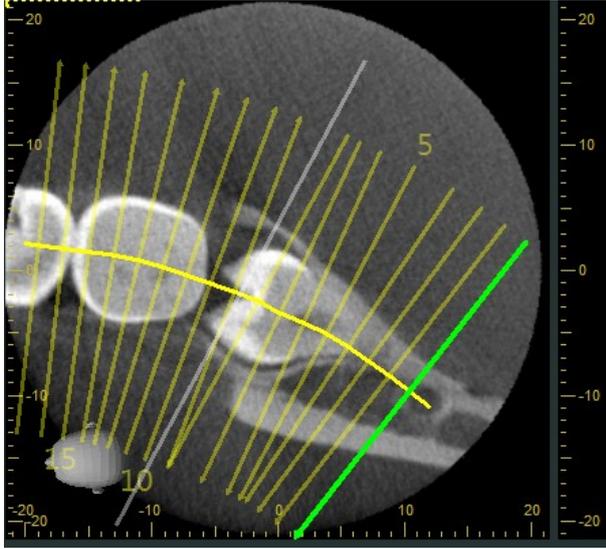
The following parameters were planned to be measured preoperatively (T_0) and in the sixth postoperative month (T_1):

- Periodontal parameters on the distal aspect of the adjacent second molar:
 - A Williams periodontal probe was used to measure the pocket depth on the distal aspect of the second molar, close to the central sulcus.
 - Gingival index.¹⁰
 - Plaque index.¹¹

- Measurement using cone beam computed tomography (CBCT) involves determining the distance between the enamel-cement junction and the crestal bone level on the distal side of the lower second molar. This measurement is taken in a tomographic slice that passes through the central sulcus of the tooth (Figure 3).

The null hypothesis was "There is no significant difference in the healing of the distal aspect of the adjacent lower second molar between grafting the extraction socket with β -TCP, MPM or leaving the socket to heal spontaneously".

Figure 3. Preoperative measurement of the bony defect on the distal aspect of the left lower second molar CBCT.



Preparation of the MPM

A dedicated MPM disposable kit (Matrices Plasmatiques Minéralisées, Kits de préparation, Atoll Implant, Toulouse, France) was used. It contained:

- Blood collection kit
- A 15mL syringe with a needle
- Four vacuette blood collection tubes
- Isotonic saline
- A special MPM tube
- Two graft containers: pink and yellow cups.

Before the surgery, we collected venous blood using four 9 mL Vacuette tubes that did not have any anticoagulant. After collection, the tubes were promptly placed in a centrifuge. (Ample Scientific Champion F-33, Norcross, Georgia, USA) and run at 2300 rpm for 15 minutes. This process separated the blood into two compartments: yellow plasma fluid at the top of the tube and red blood cells at the bottom. The yellow portion of each supernatant also contained platelets, which were withdrawn with a syringe and separated from the red blood cells. This plasma of about 2.5 mL was placed in a special MPM tube containing a clot activator and shaken by hand. It was then added to a sterile pink beaker containing 1 cc of wet β -TCP

bone graft (Suprabone Powder, BMT calsis, Ankara, Türkiye) with a particle size of 0.5-1 mm and immediately mixed with a curette for a few minutes or until the mineral phase began to aggregate in clumps. This produced a mouldable MPM graft material.

The yellow portions of the other two tubes, reserved for the production of the PRF membrane, were removed and added to the yellow beaker. The remaining liquid from the pink beaker was also added to the yellow beaker to speed up the formation of the PRF membrane. Within approximately five minutes, membrane-like PRF was formed with the conversion of fibrinogen to fibrin (Figure 4).

Figure 4. Mouldable MPM graft (left) and PRF membrane (right).



Surgical procedure

The impacted lower third molars were treated in the usual way under local anaesthetic. The tooth was extracted and the extraction

socket was irrigated with saline. Then, in the MPM group, the MPM graft was placed in the socket and covered with PRF membrane. In the β -TCP group, only the β -TCP particulate graft was placed and covered again with PRF membrane. In the control group, the extraction socket was left empty and allowed to fill with blood.

The surgical wound was closed with 3-0 silk sutures. Postoperative oral amoxicillin (500 mg, 3 \times 1), flurbiprofen (100 mg, 2 \times 1) and 0.12% chlorhexidine gluconate mouthwash were prescribed. Sutures were removed after one week.

Statistical analyses

SigmaPlot 12.5 (Systat Software Inc, San José, CA, USA) was used for statistical analyses. First, the Shapiro-Wilk test was performed to determine whether the data followed a normal distribution, and parametric or non-parametric tests were selected accordingly. Paired t-test was used for within-group comparisons and one-way ANOVA or Kruskal-Wallis test for between-group comparisons. When multiple comparisons revealed significant differences, the Tukey test was used after ANOVA and the Dunn test after Kruskal-Wallis. The Fisher exact test was used to compare infection rates between groups. The level of statistical significance was accepted as $p < .05$.

RESULTS

Eight patients were excluded from the study: One patient in the MPM group, two patients in the β -TCP group and three controls did not attend the follow-up visits. Two patients in the MPM group had a postoperative infection in the surgical area.

The remaining 28 patients were 18 women and 10 men. The mean age was 22.78 ± 2.28 in the MPM group, 23.1 ± 4.68 in the β -TCP group and 25.56 ± 5.08 in the control group ($p=.338$). T_0 values of periodontal pocket depth, periodontal and gingival indices were similar in all groups, but the alveolar bone defect was significantly deeper in the MPM group (Table 1).

Table 2 shows that pocket depth and bone defects decreased in all groups at six months.

Table 3 compares periodontal pocket depth and bone defect changes at six months.

At the six-month mark, there was a notable disparity in the periodontal pocket depth between the MPM group and the control group. However, there was no significant distinction observed between the MPM group and the β -TCP group, nor between the β -TCP group and the control group. There was a significant difference in the changes in bone defects between the MPM and control groups and between the MPM and β -TCP groups. The difference between the TCP and control groups was not significant (Table 4).

Table 1. Intergroup comparison of T_0 values.

	β -TCP Group (n=10)				Control group (n=9)				MPM Group (n=9)				P
	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max	
PPD	6.60	1.96	4.00	10.0	6.78	1.48	5.00	9.00	7.67	1.58	5.00	10.0	.365
BD	6.23	1.37	3.90	8.60	6.92	0.82	6.10	8.50	7.97	1.04	5.80	9.00	.009*
PI	1.00	0.67	0.00	2.00	0.89	0.60	0.00	2.00	0.67	0.71	0.00	2.00	.510
GI	1.40	0.69	0.00	2.00	1.22	0.67	0.00	2.00	1.33	0.50	1.00	2.00	.794

PPD: Periodontal pocket depth, BD: Bone defect, PI: Plaque index, GI: Gingival index *: Statistically significant difference

Table 2. Intragroup test results of periodontal pocket depth and bone defects.

		T ₀			T ₁			P
		Mean	Min	Max	Mean	Min	Max	
β-TCP Group	PPD	6.60	4.00	10.0	4.70	3.00	7.00	<.001*
	BD	6.23	3.90	8.60	2.90	1.10	4.20	<.001*
MPM Group	PPD	7.67	5.00	10.0	4.67	3.00	6.00	<.001*
	BD	7.97	5.80	9.00	3.58	2.60	4.30	<.001*
Control group	PPD	6.78	5.00	9.00	5.56	4.00	7.00	.023*
	BD	6.92	6.10	8.50	4.30	3.00	5.30	<.001*

PPD: Periodontal pocket depth, BD: Bone defect *: Statistically significant difference

Table 3. Intergroup comparison of the periodontal pocket depth and bone defect changes between T₀ and T₁.

	β-TCP group				Control group				MPM group				P
	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max	
PPD	1.90	0.74	1.00	3.00	1.22	1.30	0.00	4.00	3.00	1.12	1.00	4.00	.011*
BD	3.33	0.90	1.60	4.40	2.62	0.77	1.90	4.20	4.38	0.73	3.20	5.20	<.001*

PPD: Periodontal pocket depth, BD: Bone defect *: Statistically significant difference

Table 4. Amount of change in periodontal pocket depth and bone defect between T₀ and T₁.

	MPM vs Control		MPM vs β-TCP		β-TCP vs Control	
	Difference	P	Difference	P	Difference	P
PPD	1.78	<.05*	1.10	>.05	0.68	>.05
BD	1.76	<.001*	1.05	.024*	0.71	.158

PPD: Periodontal pocket depth, BD: Bone defect. *: Statistically significant difference

Postoperative infection was not observed in the β-TCP and control groups, but two patients in the MPM group had postoperative infection. The differences between the MPM and control groups and the MPM and β-TCP groups were not significant (p=.471 and p=.211 respectively).

DISCUSSION

After the removal of impacted lower third molars, there is a risk of experiencing crestal bone loss and developing deep periodontal pockets on the distal side of the neighboring second molar. Studies have shown that even two years post-surgery, 43.3% of patients may still have periodontal defects measuring 7mm or more on the second molar.^{12,13} Patient age,

angulation of the third molar, and extent of preoperative bone defect determine the risk.¹⁴ In our study, we excluded the factors that could influence the results, such as systemic diseases,¹⁵ prosthetic restorations,^{16,17} orthodontic treatment,¹⁸ smoking,¹⁹ and periodontal diseases. In addition, plaque, gingival index, age and type of defect^{3,12} were not statistically different between our groups.

Similar studies have been done previously using panoramic radiographs.³ However, in such cases the expected bone gain or loss is rather small. Magnification of panoramic radiographs and superimposition of hard tissues could affect the accuracy of measurements. Therefore, we preferred CBCT.

Researchers have proposed various techniques to prevent this residual defect, such as specific flap designs,^{5,20,21} root surface curettage and planing,²² regenerative periodontal treatment,^{23,24} guided tissue techniques, autografts, allografts, and PRF.⁴ In this study, we planned to evaluate the effectiveness of MPM. Autologous, allogeneic or xenogeneic bone can be used in MPM for the mineral phase.²⁵ In this study, we used β -TCP particulate graft. It is a biocompatible and osteoconductive material.²⁶ It does not contain growth factors but supports osteoblast proliferation and mesenchymal cell differentiation. There are studies using it in combination with blood products to increase its effectiveness, particularly in sinus lift surgery.²⁷

MPM is prepared by first collecting blood in empty tubes containing no anticoagulant or clot activator. After centrifugation, the upper layers of the tube contain fibrinogen, platelets and monocytes. This liquid phase is added to the bone graft material. When this plasma comes into contact with the calcium in the bone graft, the fibrinogen is converted into a fibrin network. This is an important property because it allows us to create a homogeneous composition containing bone graft, fibrin network, growth factors and cells. Moheb *et al.*²⁵ showed high cellular activity and formation of woven bone in the defects where MPM had been applied, but when a mixture of bone graft and PRF was used, only granulation tissue developed. They explained this by the stabilisation of the MPM graft.

Our results showed that while pocket depth decreased in all groups, the smallest gains were observed in the control group and the largest gains were observed in the MPM group. There was a significant difference in pocket depth between the MPM and control groups, but not between the other groups.

The depth of the periodontal pocket may not always correspond to the crestal bone level. Therefore, we measured both pocket depth and alveolar bone height. In all groups, the bone

defect on the distal side of the second molar decreased significantly. We observed the smallest increase in the control group and the largest increase in the MPM group. While there was a significant difference between the MPM group and the β -TCP group, the β -TCP and control groups were not significantly different. This suggests that the blood products in MPM may be effective in healing the extraction socket.

In an animal study in which the regeneration effect of mineralized plasmatic matrix was evaluated by creating 6mm critical defects in 6 male sheep, 5 defects were created in each animal. 4 of them were filled with MPM. 1 was left empty as a control group. Animals were killed at third and six weeks. Samples were evaluated histologically. New bone formation was significantly higher in the MPM group than in the control group.²⁸

In another study examined the effect of PRF efficacy on bone density after extraction, mandibular molars were extracted bilaterally. PRF was applied to the study group while the socket was left empty in the control group. Bone density was significantly higher in the PRF group when evaluated on radiographs.²⁹

In addition to all the graft materials, the use of dentin grafts for socket filling has become an increasingly popular treatment. In a study reporting the use of autologous dentin grafts in the prevention of periodontal defects after extraction of 3rd molars, the use of autologous dentin was evaluated in terms of the prevention of deep periodontal pocket formation distal to the mandibular 2nd molars. 10 patients were included in this split mouth study. 20 mandibular 3rd molar extractions were performed. The experimental areas were filled with dentin graft from the extracted 3rd molars, While the socket in the control group was left empty. At the 6-month follow-up, less pocket depth and more bone gain were found in the grafted areas. The study suggests that the graft obtained from the extracted 3rd molars may be useful in preventing periodontal defects distal to the 2nd molars.³⁰

It has been reported that periodontal bone defects should be at least 4 mm in order to compare regenerative techniques with controls.³¹ In other words, if the defect is less than 4 mm, it is not reasonable to compare any type of regenerative technique with a defect that is left to heal alone. In our study, all but one defect (3.90 mm) were deeper than this critical size.

Initially, there was a statistically significant difference between the bone defects of the MPM group (mean 7.97 ± 1.04 mm) and the β -TCP group (mean 6.23 ± 1.37 mm). It can be argued that there should have been no such variation, i.e. all groups should have been similar. This would of course be ideal, but the situation was unfavourable for the MPM group, which showed greater bone gains at the end. In the opposite scenario, where the β -TCP group had a deeper bone defect at the beginning, such a difference could be a more important problem. We think our situation is acceptable.

This study was not designed as a split-mouth study and this may be considered as a limitation. Compared with the current literature, our sample size is not insufficient, but to draw more valid conclusions, studies with larger sample sizes and longer follow-up are needed.

CONCLUSION

After surgery to remove impacted lower third molars, the bone defect and periodontal pocket on the distal aspect of the second molar will undergo partial healing, even without the use of regenerative techniques. However, the healing process can be further enhanced with the use of MPM, which is a simple and user-friendly method.

Ethical Approval

The required ethical approval for this study was received by Necmettin Erbakan University Non-Pharmaceutical and Medical Device ethics committee (2016/010).

Financial Support

No financial support was received from any institution or organization for this study.

Conflict of Interest

The authors deny any conflicts of interest related to this study

Author Contributions

Design: AK, BKI Data collection and processing: AK, BKI Analysis and interpretation: ŞD Literature review: ŞD Yazma: BKI, AK, ŞD

REFERENCES

1. Kindler S, Holtfreter B, Koppe T, Mksoud M, Lucas C, Seebauer C, et al. Third Molars And Periodontal Damage Of Second Molars In The General Population. *J Clin Periodontol.* 2018;45:1365-74.
2. Campbell JH. Second Molar Periodontal Health After Third Molar Surgery. *J Oral Maxillofac Surg.* 2017;75:662.
3. Krausz AA, Machtei EE, Peled M. Effects of lower third molar extraction on attachment level and alveolar bone height of the adjacent second molar. *Int J Oral Maxillofac Surg.* 2005;34:756-60.
4. Hassan KS, Marei HF, Alagl AS. Does grafting of third molar extraction sockets enhance periodontal measures in 30- to 35-year-old patients? *J Oral Maxillofac Surg.* 2012;70:757-64.
5. Alqahtani NA, Khaleelahmed S, Desai F. Evaluation of two flap designs on the mandibular second molar after third molar extractions. *J Oral Maxillofac Pathol.* 2017;21:317-8.
6. Ge J, Yang C, Zheng J, Hu Y. Autogenous bone grafting for treatment of osseous defect after impacted mandibular third molar extraction: A randomized controlled trial. *Clin Implant Dent Relat Res.* 2017;19:572–80.
7. Corinaldesi G, Lizio G, Badiali G, Morselli-Labate AM, Marchetti C. Treatment of intrabony defects after impacted mandibular third molar removal with bioabsorbable and non-resorbable membranes. *J Periodontol.* 2011;82:1404–13.
8. El M. The use of growth factors fibrin network

- to enhance architecture, mechanical and biological aspect of the graft particles. *Int J Prevent Clin Dent Res.* 2014;1:41-4.
9. El M. Growth factors and fibrin network to improve the particle bone grafting case report. *Int. J. Oral Care Res.* 2014;2:45-6.
 10. Loe H, Silness J. Periodontal disease in pregnancy, prevalence and severity. *Acta Odontol Scand.* 1963;21:533-51.
 11. Silness J, Loe H. Periodontal Disease in Pregnancy II. Correlation Between Oral Hygiene and Periodontal Condition, *Acta Odontologica Scandinavica.* 1964;22:121-35.
 12. Kugelberg CF, Ahlström U, Ericson S, Hugoson A, Kvint S. Periodontal healing after impacted lower third molar surgery in adolescents and adults. A prospective study. *Int J Oral Maxillofac Surg.* 1991;20:18-24.
 13. Kugelberg CF, Ahlström U, Ericson S, Hugoson A, Thilander H. The influence of anatomical, pathophysiological and other factors on periodontal healing after impacted lower third molar surgery. A multiple regression analysis. *J Clin Periodontol.* 1991;18:37-43.
 14. Kugelberg CF. Periodontal healing two and four years after impacted lower third molar surgery. A comparative retrospective study. *Int J Oral Maxillofac Surg.* 1990;19:341-5.
 15. Özçaka Ö, Becerik S, Bıçakçı N, Kiyak AH. Periodontal disease and systemic diseases in an older population. *Arch Gerontol Geriatr.* 2014;59:474-9.
 16. Dumitrescu AL, Okada M, Inagaki K. Periodontal-Restorative Interactions. In: *Etiology and Pathogenesis of Periodontal Disease.* 2010;49:491-516
 17. Kosyfaki P, del Pilar Pinilla Martín M, Strub JR. Relationship between crowns and the periodontium: a literature update. *Quintessence Int.* 2010;41:109-26.
 18. Gkantidis N, Christou P, Topouzelis N. The orthodontic-periodontic interrelationship in integrated treatment challenges: a systematic review. *J Oral Rehabil.* 2010 1;37:377-90.
 19. Tonetti MS, Pini-Prato G, Cortellini P. Effect of cigarette smoking on periodontal healing following GTR in infrabony defects. *J Clin Periodontol.* 2005;22:229-34.
 20. Rosa AL, Carneiro MG, Lavrador MA, Novaes AB Jr. Influence of flap design on periodontal healing of second molars after extraction of impacted mandibular third molars. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2002;93:404-7.
 21. Kirtiloğlu T, Bulut E, Sümer M, Cengiz I. Comparison of 2 flap designs in the periodontal healing of second molars after fully impacted mandibular third molar extractions. *J Oral Maxillofac Surg.* 2007;65:2206-10.
 22. Leung WK, Corbet EF, Kan KW, Lo ECM, Liu JKS. A regimen of systematic periodontal care after removal of impacted mandibular third molars manages periodontal pockets associated with the mandibular second molars. *J Clin Periodontol.* 2005;32:725-31.
 23. Lee CT, Hum L, Chen YW. The effect of regenerative periodontal therapy in preventing periodontal defects after the extraction of third molars: A systematic review and meta-analysis. *J Am Dent Assoc.* 2016;147:709-19.
 24. Camps-Font O, Caro-Bonfill C, Sánchez-Garcés MÁ, Gay-Escoda C. Periodontal Regenerative Therapy for Preventing Bone Defects Distal to Mandibular Second Molars After Surgical Removal of Impacted Third Molars: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. *J Oral Maxillofac Surg.* 2018;76:2482-514
 25. Moheb MEL, EL Moheb M, Al-Zarea B, Sghaireen MG, Toriya J, Mizohata A, et al. Mineralized Plasmatic Matrix to Enhance the Bone Grafting Technique. *J Hard Tissue Biol.* 2017;26:289-92.
 26. Kiliç SC, Güngörmüş M. Cone Beam Computed Tomography Assessment of Maxillary Sinus Floor Augmentation Using Beta-Tricalcium Phosphate Alone or in Combination with Platelet-Rich Plasma: A Randomized Clinical Trial. *Int J Oral Maxillofac Implants.* 2016;31:1367-75.
 27. Wiltfang J, Schlegel KA, Schultze-Mosgau S, Nkenke E, Zimmermann R, Kessler P. Sinus floor augmentation with beta-tricalciumphosphate (beta-TCP): does platelet-rich plasma promote its osseous integration and degradation? *Clin Oral Implants Res.*

- 2003;14:213–8.
28. Cakir S, Gultekin BA, Karabagli M, Yilmaz TE, Cakir E, Guzel EE, et al. Histological Evaluation of the Effects of Growth Factors in a Fibrin Network on Bone Regeneration. *J Craniofac Surg.* 2019;30:1078-84.
 29. Malhotra A, Kapur I, Das D, Sharma A, Gupta M, Kumar M. Comparative evaluation of bone regeneration with platelet-rich fibrin in mandibular third molar extraction socket: A randomized split-mouth study. *Natl J Maxillofac Surg.* 2020;11:241-7.
 30. Mazzucchi G, Lollobrigida M, Lamazza L, Serafini G, Di Nardo D, Testarelli L, et al. Autologous Dentin Graft after Impacted Mandibular Third Molar Extraction to Prevent Periodontal Pocket Formation-A Split-Mouth Pilot Study. *Materials .* 2022;15;15.
 31. Laurell L, Gottlow J, Zybutz M, Persson R. Treatment of intrabony defects by different surgical procedures. A literature review. *J Periodontol.* 1998;69:303-13.