 DOI: 10.21608/adjalexu.2024.282413.1497

# COMPARATIVE EVALUATION OF THE EFFECT OF TITANIUM PLATELET-RICH FIBRIN VERSUS HYALURONAN BIOACTIVE COATING ON OSSEOINTEGRATION OF DENTAL IMPLANTS IN ESTHETIC ZONE (RANDOMIZED CONTROLLED CLINICAL TRIAL)

Ahmad Bassam Zaaza[1*], Nevein Showkey Mohamed[1], Gaafar Nabil Ahmed El Halawani[1]

## ABSTRACT

**INTRODUCTION:** Osseo-integrated dental implants were traditionally load-free for up to six months while they healed. Patients usually feel dissatisfied with the long loading times. Several studies have been conducted to improve osseointegration, decrease loading time, and increase patient satisfaction.

**OBJECTIVES:** This study aimed to evaluate and compare both clinically and radiographically the effect of hyaluronic acid (HA) versus Titanium-Platelet Rich Fibrin (T-PRF) in enhancing osseointegration around anterior maxillary dental implants.

**MATERIALS AND METHODS:** Twelve patients with extracted maxillary anterior teeth treated using 16 implants allocated into two groups; the study group was treated using delayed implant placement with hyaluronic acid as a bioactive coating, and the control group was treated using delayed implant placement with Titanium-Platelet Rich Fibrin as a bioactive coating. The patients were clinically evaluated at immediate postoperative and three months for implant stability. They were also evaluated radiographically at immediate postoperative, three, and six months for peri-implant bone density and crestal bone loss.

**RESULTS:** There was no significant difference between the Hyaluronic acid group and the Titanium Platelet-Rich Fibrin groups regarding implant stability, crestal bone loss, and bone density.

**CONCLUSIONS:** According to the results of our study, it was concluded that Both HA and T-PRF are equally beneficial in enhancing implant stability, peri-implant bone formation, and osseointegration.

**KEYWORDS:** Implant bone contact, Implant Stability, Osseointegration, Hyaluronan, TPRF

**RUNNING TITLE:** Titanium Platelet-Rich Fibrin Versus Hyaluronic acid in dental implants.

---

1 -Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Alexandria University

***Corresponding author:***
ahmedzaaza1993@hotmail.com

## INTRODUCTION

A dental implant is a synthetic prosthesis surgically placed within the jawbone to support a fixed or removable prosthesis.

Dental implants are a highly advantageous solution for individuals with good overall oral health who have lost teeth due to various reasons such as periodontal disease, unsuccessful endodontic treatment, an injury, or other causes. Moreover, they are a viable option for treating edentulous patients (lacking natural teeth). They are known to significantly enhance denture retention, stability, and functional efficiency, ultimately leading to an improved quality of life.(1)

Nevertheless, patients frequently express discontent with the extended waiting periods for loading.(2) Therefore, shortening the healing period without compromising the success of the implant would greatly benefit patients. With this in mind, several trials have been conducted to expedite the loading time and enhance osseointegration, improving patient satisfaction.(3)

Many methods and biomaterials are applied to reduce the time required for bone to heal. Applying hyaluronic acid biomaterials coated dental implants is an ongoing investigation within this domain.(4,5) Hyaluronic acid, sodium hyaluronate or hyaluronan (HA), is a glycosaminoglycan characterized by its high molecular weight. It comprises repeating disaccharide units of D-glucuronic acid and N-acetylglucosamine, which are non-sulfated.(6,7)
Hyaluronic acid, a linear polymer found in nearly all body tissues and fluids, effectively conveys

mechanical and biological signals to neighboring cells and tissues.

When cells directly attach to HA through membrane receptors, this interaction leads to the transmission of biochemical signals and the strengthening of mechanical connections. Consequently, this process mediates adhesion and facilitates cellular movement.(8)

Hyaluronic acid is recognized to have an osteo-promotive action during bone regeneration.(9,10) Its significance stems from its active involvement in various biological processes linked to morphogenesis and tissue healing. It participates in these crucial processes and stands out due to its biocompatibility, biodegradability, and non-immunogenicity.

Over recent decades, hyaluronic acid has garnered significant interest as a potent biomaterial for tissue engineering. In bone healing, hyaluronic acid plays a pivotal role by promoting the differentiation of undifferentiated mesenchymal cells into osteoblastic cells. It achieves this through stimulating cell migration, facilitating cell adhesion, and encouraging cell proliferation, thereby contributing to the bone healing process.(11)

A new development known as T-PRF (Titanium Platelet-Rich Fibrin) has emerged recently. T-PRF involves the creation of fibrin enriched with thrombin, utilizing titanium tubes. This innovation is built on the concept that titanium tubes are notably more effective in promoting clotting factors than glass tubes, especially compared to the conventional Chouckroun's approach.(12,13) researchers have discovered that the clots formed in titanium tubes resemble those formed in glass tubes. Additionally, they observed that the co-aggregation induced by titanium was comparable to that seen with glass, indicating a similar clotting effect.(14)

Because of the use of titanium particles rather than silica particles to activate platelets, T-PRF has unique characteristics, including enhanced biocompatibility and longer resorption length..(15)
There is a lack of studies comparing hyaluronan and titanium-platelet-rich fibrin in implant placement, particularly in the anterior maxilla.(16) Consequently, this study aims to assess and compare the efficacy of hyaluronic acid and titanium-platelet-rich fibrin concerning peri-implant osseointegration and stability.

## MATERIALS AND METHODS

### MATERIALS

Materials included:
Hyaluronic acid 0.2% (Gengigel Dompé farmaceutici S.P.A., Milan, Italy)
Dental implant system (Dual Implant, Cairo, Egypt).
Osstell ISQ Monitor(Osstell AB, Gothenburg, Sweden) .
Centrifugal machine (Yuli Medical, Jiangsu, China).
Surgical sutures (Ghatwary Medical GMS, Egypt )
Titanium Tube (Tunalie especially manufactured titanium tubes, Turkey)

### METHODS

Twelve patients with extracted maxillary anterior teeth treated using 16 implants. They were recruited from the Outpatient Clinical of Alexandria University Teaching Hospital and in the Oral and Maxillofacial Surgery Department (OMFSD), Faculty of Dentistry, Alexandria University. They were allocated into two groups: the study group (7 patients: 8 implants) were treated using delayed implant placement with hyaluronic acid as a bioactive coating, and the control group (5 patients: 8 implants) were treated using delayed implant placement with Titanium-Platelet Rich Fibrin as a bioactive coating.
Inclusion criteria: The chosen patients must understand the proposed surgical procedure and offer their informed consent. The following inclusion criteria(17) were met by all patients: ages twenty to forty years and patients with extracted anterior maxillary teeth. Patients with bad oral hygiene, para functional habits, heavy smokers, and patients with relevant diseases affecting bone healing were excluded.
Pre-surgical phase
First history was obtained, including name, age, gender, occupation, address, phone number, patient's chief complaint, and medical in addition to the dental history, followed by clinical examination of dental and gingival condition. Moreover, CBCT scanning was performed before surgery to assess the ridge's height and width and for treatment planning. Furthermore, all patients underwent preoperative scaling and root planning and were given oral hygiene instructions.
Surgical procedure
The procedure was conducted using local anesthesia infiltration at the surgical site using 4% articaine with epinephrine 1:100,000 (Alexandria Co., Alexandria, Egypt). A mid-crestal incision with a Bard Parker blade no. 15 and reflection of the buccal mucoperiosteal flap with a periosteal elevator.

The drilling process was carried out according to the manufacturer's instructions until the appropriate size of the implant was achieved. Patients were allocated into two groups:
Group A received implants coated with hyaluronic acid of 0.2 % concentration. First, about 1ml of hyaluronic acid must be put in the implant vial and left for one hour till osteotomy is formed, then another 1ml of hyaluronic acid in the osteotomy site before implant placement.(18,19)

Group B received T-PRF-coated implants coated. The implant was treated by dipping in the titanium-platelet-rich fibrin just before insertion.(18,20) Wound closure was achieved using simple interrupted 30 silk sutures.

*The Titanium- platelet-rich fibrin preparation:*

A twenty-one gauge needle syringe was used to collect twenty ml of venous blood from the anti-cubital region by an experienced nurse before beginning the surgical procedure. Subsequently, they were moved to Grade IV titanium sterile tubes specifically constructed for this purpose without using any anticoagulant. Tubes centrifugation at 2,700 revolutions per minute for 12 minutes using a table centrifuge operating at room temperature. Following centrifugation, the T-PRF clot located in the center of the tube was extracted using sterile tweezers and separated from the red blood cell layer without using scissors. After preparation of T-PRF, it was compressed between two sterile glass slabs into PRF membrane, to be placed in the osteotomy before implant insertion.(21)

Postoperative phase

Postoperative instructions

Patients were instructed to rinse for ten days with warm, salty water. After their initial visit, patients were seen ten days later for suture removal.

Postoperative medications

Amoxicillin 875 mg Clavulanic acid 125 mg (GlaxoSmithKline, London, UK) every twelve hours for seven days. Diclofenac Potassium 50 mg (Novartis, Switzerland) every eight hours for five days, and Chymotrypsin 300 EAU (14u Katals) + Trypsin 300 EAU (5u Katals) (Amoun Pharmaceutical Company, Egypt) as an anti-inflammatory drug, was given one hour immediate postoperatively and continued every eight hours for three days.

Follow up phase

Clinical evaluation

Implant Stability: The patients were clinically monitored to assess the implant's stability right after the surgery and again three months later using Osstell.(22)

Radiographic evaluation

Crestal bone loss and bone density were measured immediately postoperative, three months, and six months postoperative.(23) Figure (3)

Crestal bone: The crestal bone loss was measured using the implant platform as a reference point. Two perpendicular lines were drawn from the platform to the first bone-implant contact, one on the mesial and distal aspects. The length of these lines was determined, and the mean value was calculated using OnDemand 3D software (Cybermed Inc., Seoul, South Korea).(24)

Bone Density: The OnDemand 3D software, developed by Cybermed Inc. in Seoul, South Korea, was utilized to assess the bone density surrounding the implant at various locations in the peri-implant bone near the interface between the implant and bone. The average bone density measurement was obtained using in-house field units (HU).(24) Figure (4)

Prosthetic Phase

The patient was referred to the prosthodontist for a fixed porcelain fused metal crown at three months postoperative.

**STATISTICAL ANALYSIS**

The collected data underwent statistical analysis and were subsequently shown in tables, graphs, and charts utilizing the IBM Statistical Package for Social Science (SPSS) software version 25.0.(25) The sample size was determined to identify disparities in crestal bone loss and peri-implant bone stability. Based on Lupi et al. (2019),(26) parameters including a power of 80% (β=0.20) to detect a standardized effect size of 1.814 in bone stability and a significance level of 5% (α error acceptable =0.05), it was determined that a minimum sample size of six patients per group (number of groups=2) is required. The whole sample size consisted of 16 patients.(27,28) After adjustment for a dropout rate of 10%, the sample size was increased to 8 patients per group (number of groups=2) (Total sample size=16 patients.(29) The sample size was calculated using GPower version 3.1.9.2.(30)

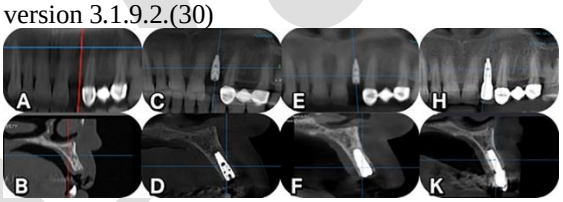


**Figure (3)** Tomographic sections of the Hyaluronic acid Group.

(A) Preoperative CBCT (Panoramic view) (B) Preoperative cone beam computed tomography (cross-sectional view) (C) CBCT (Panoramic view) immediately (D) CBCT (Cross-sectional view) immediately (E) CBCT (Panoramic view) after three months (F) CBCT (Cross-sectional view) after three months (H) CBCT (Panoramic view) after six months (K) CBCT (Cross-sectional view) after six months

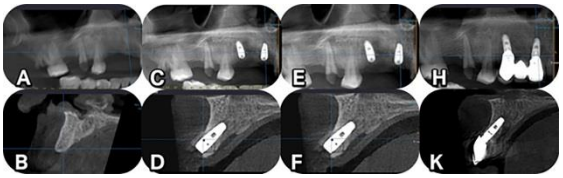


**Figure (4)** Tomographic sections of the Titanium Platelet-Rich Fibrin Group.

(A) Preoperative cone beam computed tomography (Panoramic view) (B) CBCT (cross-sectional view) (C) CBCT (Panoramic view) immediately (D) CBCT (Cross-sectional view) immediately (E) CBCT (Panoramic view) after three months (F) CBCT (Cross-sectional view) after three months (H) CBCT (Panoramic view) after six months (K) CBCT (Cross-sectional view) after six months

## RESULTS

This study included twelve patients (with sixteen implants) with extracted maxillary anterior teeth allocated to Two groups:

Hyaluronic acid group (study group): Seven patients (eight implants) were treated using delayed implant placement with hyaluronic acid as a bioactive coating. Figure (1)

Titanium platelet-rich fibrin group (comparison group): Five patients (eight implants) were treated using delayed implant placement with Titanium-Platelet Rich Fibrin as a bioactive coating. Figure (2)

Data are presented as median, 95% Confidence Interval (CI) of the median [[25$^{th}$-75$^{th}$ Percentile].

Clinical evaluation

Implant Stability: Table (1)

Immediate postoperative: in the Hyaluronic acid group, the median implant stability was 72.50, 95% CI of 63.00-72.00, and 25$^{th}$ Percentile – 75$^{th}$ Percentile of 63.50-70.50, in the Titanium Platelet-Rich Fibrin group, it was 68.00, 95% CI of the median of 68.00-75.00, and 25$^{th}$ Percentile – 75$^{th}$ Percentile of 67.50-71.50. Three months postoperative: in the Hyaluronic acid group, implant stability median was 72.00, 95% CI of 69.00-76.00, and 25$^{th}$ Percentile – 75$^{th}$ Percentile of 69.50-75.00, in the Titanium Platelet-Rich Fibrin group, it was 76.50, 95% CI of the median of 68.00-80.00, and 25$^{th}$ Percentile – 75$^{th}$ Percentile of 68.50-79.00. There was no statistically significant difference in the Implant stability between the two studied groups immediately and three months postoperative (($p$=.291, $p$=.527, respectively). Implant stability showed a statistically significant increase three months postoperative compared to immediately postoperative in the Hyaluronic acid and Titanium Platelet-Rich Fibrin groups ($p$= .011; $p$=.012; respectively).

Implant stability percentage change: In the Hyaluronic acid group the median was 7.41%, 95% CI of 4.69-9.52%, and 25$^{th}$ Percentile – 75$^{th}$ Percentile of 5.12-8.66%, while in the Titanium Platelet-Rich Fibrin group, it was 5.59%, 95% CI of the median of 1.49-14.71%, and 25$^{th}$ Percentile – 75$^{th}$ Percentile of a 2.08-13.24%. There was no statistically significant difference in the percentage change of implant stability between the two studied groups ($p$=.674).

Radiographic Evaluation

Crestal Bone Loss: Table (2)

Three months postoperative: in the Hyaluronic acid group, the median crestal bone loss was 0.61 mm, 95% CI of the median of 0.51-0.69 mm, and 25$^{th}$ Percentile – 75$^{th}$ Percentile of 0.52-0.67 mm, while in the Titanium Platelet-Rich Fibrin group, it was 0.66 mm, 95% CI of the median of 0.61-0.73 mm and 25$^{th}$ Percentile – 75$^{th}$ Percentile of 0.63-0.73 mm. Six months postoperative: in the Hyaluronic acid group, the median crestal bone loss was 0.70 mm, 95% CI of 0.64-0.76 mm, and 25$^{th}$ Percentile – 75$^{th}$ Percentile of 0.64-0.75 mm, while in the Titanium Platelet-Rich Fibrin, it was 0.74 mm, 95% CI of the median of 0.67-0.79 mm and 25$^{th}$ Percentile – 75$^{th}$ Percentile 0.69-0.79 mm. There was no statistically significant difference in crestal bone loss between the two studied groups at three and six months postoperative (($p$=.073, $p$=.244, respectively). The Crestal bone loss statistically significantly increased at six months postoperative compared with three months in the Hyaluronic acid group ($p$=.012) and the Titanium Platelet-Rich Fibrin group ($p$=.012).

Crestal bone loss percentage change: In the Hyaluronic acid group the median was 190.64%, 95% CI of the median of 70.04-240.49%, and 25$^{th}$ Percentile – 75$^{th}$ Percentile of 70.76-230.78%, while in the Titanium Platelet-Rich Fibrin group, it was 70.90%, 95% CI of 30.08-160.39%, and 25$^{th}$ Percentile – 75$^{th}$ Percentile of a 40.00-130.06%. There was no statistically significant difference in crestal bone loss percentage change between the two studied groups ($p$=.093).

Bone density: Table (3)

Immediately postoperative, the median radiological bone density (HU) in the Hyaluronic acid Group was 489.00, 95% CI of 488.00-685.00 and 25$^{th}$ Percentile – 75$^{th}$ Percentile of 482.50-607.48 HU, in the Titanium Platelet-Rich Fibrin Group it was 568.00%, 95% CI of the median of 512.34-656.00 and 25$^{th}$ Percentile – 75$^{th}$ Percentile of 512.67-655.00 HU.

Three months postoperative, the median radiological bone density in the Hyaluronic acid Group was 550.00, 95% CI of 534.00-710.00 and 25$^{th}$ Percentile – 75$^{th}$ Percentile of 534.50-649.00 HU, in the Titanium Platelet-Rich Fibrin Group, it was 665.50, 95% CI of 553.00-698.00 and 25$^{th}$ Percentile – 75$^{th}$ Percentile of 588.00-688.00 HU.

Six months postoperative, the median radiological bone density in the Hyaluronic acid Group was 639.50, 95% CI of 623.00-755.00 and 25$^{th}$ Percentile – 75$^{th}$ Percentile of 627.50-716.65 HU, in the Titanium Platelet-Rich Fibrin Group, it was 712.00%, 95% CI of 634.12-742.00 and 25$^{th}$ Percentile – 75$^{th}$ Percentile of 662.06-733.00 HU.

There was no statistically significant difference in the radiological Bone density between the two studied groups immediately after the operation, three months postoperatively, and six months postoperatively ($p$=.127, $p$=.227, $p$=.294; respectively).

Repeated measures analysis showed a statistically significant increase in the radiological bone density among the different measurement times in the Hyaluronic acid Group and the Titanium Platelet-Rich Fibrin Group ($p$<.001, $p$<.001; respectively).

Pairwise comparisons revealed that the radiological bone density was statistically significantly higher at six months compared to immediately postoperative in the Hyaluronic acid Group and the Titanium Platelet-Rich Fibrin Group ($p$<.001 and $p$<.001, respectively).

In the Hyaluronic acid Group (n=8), the median radiological bone density percentage change three months vs immediately postoperative was 9.87%, 95% CI of 5.84-14.35, and 25$^{th}$ Percentile – 75$^{th}$ Percentile of a 6.42-12.90%, in the Titanium Platelet-Rich Fibrin Group, it was 8.29, 95% CI of 6.40-21.44, and 25$^{th}$ Percentile – 75$^{th}$ Percentile of a 6.71-16.18%. There was no statistically significant difference in the radiological bone density percentage change three months vs immediately postoperative between the two studied groups ($p$=1.000).

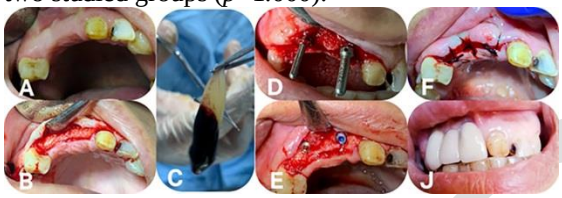


**Figure (1)** Titanium platelet-rich fibrin group (A) preoperative clinical (B) FLAB (C) T-PRF (D) parallelism check (E) implant with cover screw (F) suture (J) restoration


**Figure (2)** (A) preoperative clinical (B) FLAB (C) IMPLANT IN Hyaluronic acid (D) parallelism check (E) implant with cover screw (F) suture (J) restoration

## DISCUSSION

The current investigation found no statistically significant disparity in implant stability between the two groups. Furthermore, there was no statistically significant disparity in the percentage alteration of implant stability between the two examined groups. However, implant stability showed a statistically significant increase three months postoperatively compared to immediately postoperative in the Hyaluronic acid and T-PRF groups; this coincides with Kuzu and Ozdemir et al.(31) assessed the implant stability of peri-implant osseous defects treated with titanium prepared platelet-rich fibrin using resonance frequency analysis. They concluded that T-PRF exhibits a regenerative capacity nearly equivalent to autogenous grafts, as indicated by Osstell values. Additionally, they suggested that T-PRF might be employed as a standalone graft material.

Moreover, a study by Abhigna et al.(32) Assessed the impact of topically applying hyaluronic acid gel on the reduction of bone loss around dental implants and the maintenance of implant stability. The primary stability scores of the test and control groups did not exhibit any statistically significant differences. However, the secondary stability scores for the test were statistically significantly higher than the control group.

In our study, there was no statistically significant difference in the crestal bone loss and its percent change between the two groups at three and six months postoperative. However, the crestal bone loss statistically significantly increased at six months postoperative compared to three months in the Hyaluronic acid and Titanium Platelet-Rich Fibrin groups.

In line with our findings, Ustaoğlu et al.(33) conducted a study to assess the impact of T-PRF on Connective Tissue Graft on Peri-Implant bone and soft tissue thickening, as well as Keratinized Mucosa. There was no statistically significant occurrence of crestal bone loss in dental implants.

In their study, Abhigna et al.(32), studied the efficacy of locally applying hyaluronic acid gel to prevent bone loss around dental implants. They found that implants were inserted after injecting 1 mL of HA gel in the study group, whereas in the control group, implants were inserted without any HA gel injection. The average amount of bone loss at the crest was greater in the control group compared to the test group, and this difference was statistically significant.

The current investigation found no statistically significant disparity in radiographic bone density between the two groups immediately after the procedure and at three and six months postoperative. Nevertheless, there was a noteworthy and meaningful rise in radiographic bone density across several measurement periods in both the HA and T-PRF groups.

Our results match Guangshuai Zhang et al.(34), who found that the physical stability of curcumin-zein nanoparticles can be enhanced by using thiol-modified hyaluronic acid, which forms disulfide bonds with zein. However, the unstable physical adsorption between hyaluronic acid and zein may lead to poor physical stability. Hence, forming a covalent bond between HA and zein is a logical strategy to achieve enhanced physical stability.

Schultz et al. (2014)(35) conducted a study to examine the impact of coating dental implants with synthetic matrices made from collagen and sulfated hyaluronan on osseointegration. The study involved dental titanium implants coated with an artificial extracellular matrix (aECM) consisting of collagen type I and two different forms of low-sulfated hyaluronan derivatives. These coated implants were

then compared to commercially available pure titanium implants. The results showed no statistically significant differences between the two groups.

Moreover, three studies(36-38) have provided evidence supporting the efficacy of T-PRF in rectifying both hard and soft tissue deficiencies. The investigations used a sample of 100 participants who were 18 years old or older. These subjects received treatment with T-PRF for infra-bony deformities utilizing open flap debridement. In summary, the findings suggest that T-PRF is a more effective option than other platelet concentrates for enhancing both the physical and structural aspects of periodontal abnormalities.

## CONCLUSION

Our study determined that HA and T-PRF have equivalent benefits in improving implant stability, peri-implant bone growth, and osseointegration.

**CONFLICT OF INTEREST**

The authors had no conflict of interest.

**FUNDING**

No dedicated funding was obtained for this work.

## REFERENCES

1. Ravi Kumar C, Pratap K, Venkateswararao G. Dental Implants As An Option In Replacing Missing Teeth: A Patient Awareness Survey In Khammam, Andhra Pradesh. Indian Journal of Dental Sciences. 2011;3.
2. Tettamanti L, Andrisani C, Bassi MA, Vinci R, Silvestre-Rangil J, Tagliabue A. Immediate loading implants: review of the critical aspects. ORAL and Implantology. 2017;10:129-39.
3. Esposito M, Grusovin MG, Maghaireh H, Worthington HV. Interventions for replacing missing teeth: different times for loading dental implants. Cochrane Database of Systematic Reviews. 2013;2013:Cd003878.
4. R Hemeda A, A Mohamed M, A El Feke A. Evaluation of the stability of immediate placed dental maxillary implant in fresh extracted socket versus delayed placed implant. Al-Azhar Journal of Dental Science. 2018;21:533-8.
5. Cervino G, Meto A, Fiorillo L, Odorici A, Meto A, D'Amico C, et al. Surface treatment of the dental implant with hyaluronic acid: An overview of recent data. International Journal of Environmental Research and Public Health. 2021;18:4670.
6. Aslan M, Şimşek G, Dayi E. The effect of hyaluronic acid-supplemented bone graft in bone healing: experimental study in rabbits. Journal of biomaterials applications. 2006;20:209-20.
7. Schnabelrauch M, Scharnweber D, Schiller J. Sulfated glycosaminoglycans as promising artificial extracellular matrix components to improve the regeneration of tissues. Current medicinal chemistry. 2013;20:2501-23.
8. Wolf KJ, Kumar S. Hyaluronic acid: incorporating the bio into the material. ACS biomaterials science & engineering. 2019;5:3753-65.
9. Alcantara CEP, Castro MAA, Noronha MSd, Martins-Junior PA, Mendes RdM, Caliari MV, et al. Hyaluronic acid accelerates bone repair in human dental sockets: a randomized triple-blind clinical trial. Brazilian oral research. 2018;32:e84.
10. Bagnol R, Grijpma D, Eglin D, Moriarty T. The production and application of bacterial exopolysaccharides as biomaterials for bone regeneration. Carbohydrate polymers. 2022;291:119550.
11. Chen F-M, Liu X. Advancing biomaterials of human origin for tissue engineering. Progress in polymer science. 2016;53:86-168.
12. Lokwani BV, Gupta D, Agrawal RS, Mehta S, Nirmal NJ. The use of concentrated growth factor in dental implantology: A systematic review. The Journal of the Indian Prosthodontic Society. 2020;20:3.
13. Tunalı M, Özdemir H, Küçükodacı Z, Akman S, Yaprak E, Toker H, et al. A novel platelet concentrate: titanium-prepared platelet-rich fibrin. biomed research international. 2014;2014.
14. Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J, et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part I: technological concepts and evolution. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2006;101:e37-e44.
15. Ehrenfest DMD, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). Trends in biotechnology. 2009;27:158-67.
16. Sircar T. Comparing the Efficacy of Platelet Rich Fibrin Matrix (PRFM) and Titanium Platelet Rich Fibrin (T PRF) in Periodontal Intrabony Defects: Rajiv Gandhi University of Health Sciences (India); 2019.
17. Tsai C-F, Pan W-L, Pan Y-P, Chan C-P, Ju Y-R, Wang Y-M, et al. Comparison of 4 sinus augmentation techniques for implant placement with residual alveolar bone height≤ 3 mm. Medicine. 2020;99.
18. Clark D, Rajendran Y, Paydar S, Ho S, Cox D, Ryder M, et al. Advanced platelet-rich fibrin and freeze-dried bone allograft for ridge preservation: a randomized controlled clinical trial. Journal of periodontology. 2018;89:379-87.
19. Strauss FJ, Stähli A, Gruber R. The use of platelet-rich fibrin to enhance the outcomes of

implant therapy: a systematic review. Clinical oral implants research. 2018;29:6-19.
20. Miron RJ, Pinto NR, Quirynen M, Ghanaati S. Standardization of relative centrifugal forces in studies related to platelet-rich fibrin. Wiley Online Library; 2019. p. 817-20.
21. Dohan Ehrenfest DM, Pinto NR, Pereda A, Jiménez P, Corso MD, Kang B-S, et al. The impact of the centrifuge characteristics and centrifugation protocols on the cells, growth factors, and fibrin architecture of a leukocyte- and platelet-rich fibrin (L-PRF) clot and membrane. Platelets. 2018;29:171-84.
22. Karagah A, Tabrizi R, Mohammadhosseinzade P, Mirzadeh M, Tofangchiha M, Lajolo C, et al. Effect of Sinus Floor Augmentation with Platelet-Rich Fibrin Versus Allogeneic Bone Graft on Stability of One-Stage Dental Implants: A Split-Mouth Randomized Clinical Trial. International Journal of Environmental Research and Public Health. 2022;19:9569.
23. Gulec M, Tassoker M, Magat G, Lale B, Ozcan S, Orhan K. Three-dimensional volumetric analysis of the maxillary sinus: a cone-beam computed tomography study. Official journal of the Polish Anatomical Society. 2020;79:557-62.
24. Trisi P, Rao W. Bone classification: clinical-histomorphometric comparison. Clinical oral implants research. 1999;10:1-7.
25. IBM Corp. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.; Released 2017.
26. Lupi SM, Rodriguez y Baena A, Cassinelli C, Iviglia G, Tallarico M, Morra M, et al. Covalently-linked hyaluronan versus acid etched titanium dental implants: A crossover RCT in humans. International Journal of Molecular Sciences. 2019;20:763.
27. Charan J, Biswas T. How to calculate sample size for different study designs in medical research? Indian J Psychol Med. 2013;35:121-6.
28. Walters SJ, Jacques RM, dos Anjos Henriques-Cadby IB, Candlish J, Totton N, Xian MTS. Sample size estimation for randomised controlled trials with repeated assessment of patient-reported outcomes: what correlation between baseline and follow-up outcomes should we assume? Trials. 2019;20:1-16.
29. Pannucci CJ, Wilkins EG. Identifying and avoiding bias in research. PLASTIC AND RECONSTRUCTIVE.SURGERY. 2010;126:619-25.
30. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods. 2007;39:175-91.
31. Kuzu TE, Özdemir H. Evaluating the Implant Stability of Titanium Prepared Platelet Rich Fibrin Treated Periimplant Osseous Defects with Resonance Frequency Analysis. Cumhuriyet Dental Journal. 2016;19:154-65.
32. Abhigna P, Rao MR, Preethi PL, Sathish M, Anumolu SH, Chandini S, et al. Effect of local application of hyaluronic acid gel on marginal bone loss and stability of dental implants. Journal of Dental Implants. 2023;13:92-7.
33. Ustaoğlu G, Paksoy T, Gümüş KÇ. Titanium-prepared platelet-rich fibrin versus connective tissue graft on peri-implant soft tissue thickening and keratinized mucosa width: a randomized, controlled trial. Journal of Oral and Maxillofacial Surgery. 2020;78:1112-23.
34. Zhang G, Qin M, Guo M, Li M, Zhang D, Sun Y, et al. Thiol-modified hyaluronic acid improves the physical stability of curcumin-zein nanoparticles by forming disulfide bonds with zein. Food Chemistry. 2023;429:136858.
35. Schulz MC, Korn P, Stadlinger B, Range U, Möller S, Becher J, et al. Coating with artificial matrices from collagen and sulfated hyaluronan influences the osseointegration of dental implants. Journal of Materials Science: Materials in Medicine. 2014;25:247-58.
36. Gummaluri SS, Bhattacharya HS, Astekar M, Cheruvu S. Evaluation of titanium-prepared platelet-rich fibrin and leucocyte platelet-rich fibrin in the treatment of intra-bony defects: A randomized clinical trial. Journal of Dental Research, Dental Clinics, Dental Prospects. 2020;14:83.
37. Ustaoğlu G, Aydin ZU, Özelçi F. Comparison of GTR, T-PRF and open-flap debridement in the treatment of intrabony defects with endo-perio lesions: a randomized controlled trial. Medicina oral, patologia oral y cirugia bucal. 2020;25:e117.
38. Arabaci T, Albayrak M. Titanium-prepared platelet-rich fibrin provides advantages on periodontal healing: A randomized split-mouth clinical study. Journal of periodontology. 2018;89:255-64.