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ORIGINAL RESEARCH

# Clinical Effect of Platelet-Rich Fibrin Combined with BIO-GENE Artificial Bone Meal in Bone Defects After Jaw Cyst Surgery

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**Purpose:** To compare the clinical repair effects of leaving the defect empty and using Platelet-Rich Fibrin (PRF) combined with BIO-GENE artificial bone powder in patients with bone defects 6 months after jaw cystectomy.

**Patients and Methods:** From June 2021 to June 2022, 70 patients who were admitted to the Department of Stomatology, Affiliated Hospital of Yanbian University, and were diagnosed with jaw cysts postoperatively were selected. All of the patients were divided into two groups according to random method, among which 35 patients who underwent cystectomy alone were recorded as group A, which served as blank control; 35 patients who underwent cystectomy and PRF combined with BIO-GENE artificial bone meal repaired bone defects during the same period were recorded as group B. 3D Slicer 5.0.3 software was used to reconstruct Cone Beam Computed Tomography (CBCT) after operation. In this study, the preoperative and postoperative CBCT data of the patients were analyzed using 3D Slicer 5.0.3 software in DICOM format to calculate the cleft volume before surgery and the newly formed bone volume after surgery. The osteogenesis rate was measured based on these calculations.The bone formation percentage in the bone defect area was recorded at 6 months, and the clinical curative effects of the two groups were compared.

**Results:** After 6 months of surgery, the patients showed varying degrees of restoration in the jaw cyst area.The osteogenesis rate at 6 months in group A was 76.06±13.38%, while group B had a rate of 92.87±5.72%.The CBCT values in group B were higher than those in group A at 6 months post-surgery ($P<0.05$), $t=-6.84$.Group A and Group B showed a statistically significant difference.

**Conclusion:** Compared with simple cystectomy, PRF combined with BIO-GENE artificial bone powder has a better effect on the speed of bone repair after cystectomy within 6 months and provides more favorable effects for the repair of postoperative dentition defects, and provides support to repair teeth after defects such as dental implants.

**Keywords:** PRF, bone transplantation, jaw cysts, bone regeneration

## Introduction

Various methods have been explored to treat intrabony periodontal defects, such as bone grafts (BG), guided tissue regeneration, and growth factors. These regenerative modalities aim to restore and repair the periodontal tissues affected by the defects.[1]

BIO-GENE is an allogeneic bone composed mainly of inorganic bone mineral components. It retains the three-dimensional grid structure of natural bone tissue and exhibits good cytocompatibility and bone conduction. It facilitates the adhesion, growth, and gene expression of bone cells.Over time, this product is finally completely replaced by crawling, and after bone healing, it permanently becomes the bone tissue of the human body. Among platelet concentrates, Platelet-rich fibrin (PRF) is a type of second-generation blood autologous preparation, which initially described by Choukroun et al.[2] During the PRF preparation process, a gel-like matrix is formed. This matrix contains a high concentration of non-activated and functional platelets. These platelets are embedded within a fibrin matrix,[2,3] which prevents the PRF rapid decomposition after application and allows for the gradual release of growth factors. This promotes the growth of new angiogenesis and

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supports the growth and differentiation of bone cells[4,5] Accelerating the healing process of transplanted bone or bone substitutes would be beneficial for patients. Platelet-rich plasma (PRP) has shown promise in this regard, although its use remains controversial.[6–21] Recent histological studies showed that the combination of PRF and BG yields greater benefits during bone healing compared to BG alone in maxillary sinus augmentation.[22] In terms of treatment, there are a variety of options available for addressing the muscular aspects of postures-related temporomandibular disorders. (TMD), including physical therapy, relaxation techniques and muscle exercises.[23,24] Intra-articular injection of PRF after joint replacement has a better effect on temporomandibular joint osteoarthritis (TMJ-OA).[25] There is limited information on the use of PRF combined with artificial BG for treating infrabony defects. This study aimed to examine how PRF combined with artificial bone graft affects the recovery of jaw cysts after surgery. The study involved 70 patients who were carefully selected.

# Materials and Methods

## Research Object

This study ran from April 2021 to January 2023.A retrospective analysis was performed on patients with postoperative pathological diagnosis of jaw cyst at the Department of Stomatology of Yanbian University Hospital from June 2021 to January 2023.The patients were notified about the study protocol, including the benefits and risks, we get the patient's consent, and they provided written informed consent to participate (a parent or legal guardian of patients under 18 years of age provided informed consent).The study obtained approval from the ethics committee of affiliated hospital of Yanbian University where the research took place (Ethics: 2023204).The study complies with the Declaration of Helsinki.A total of 70 cases met the inclusion exclusion criteria. According to the random number method, it was divided into two groups, among which 35 cases of simple cystectomy were recorded as group A; At the same time,35 cases of PRF combined with BIO-GENE artificial bone meal implantation were recorded as group B.

Inclusion Criteria:

(1) The postoperative pathological findings were jaw cyst;

(2) Jaw cyst surgery for the first time;

(3) The patient's medical record data is completed and there are completed postoperative review records.

Exclusion Criteria:

(1) Patients with poor habits such as smoking and alcohol abuse that could affect postoperative bone healing;

(2) Patients with systemic diseases such as diabetes, hypertension, and heart disease;

(3) Patients with solid tumors such as ameloblastoma.

The study is a randomized clinical trial (RCT) with a 1:1 allocation ratio between two parallel arms.Additionally, the statistician who carried out the study analysis and the outcome analyst were both blinded.

Group A: patients range in age from 15 to 80 years, with an average of (33.34±11.25) years; There were 24 males and 11 females.

Group B: patients ranged in age from 17 to 73 years, with an average of (40.83±12.31) years; There were 20 cases in males and 15 cases in females.Age differences between two groups of patients have no statistical significance, $P>0.05$.

## Materials and Equipment

C-TECH Medical Centrifuge (Changsha High & New Technology Industrial Development Zone Xiangyi Centrifuge Instrument Co., Ltd, Changsha, China), 10mL sterile additive-free glass test tube, Bio-GENE bone meal (Beijing Kejian Biotechnology Co., Ltd, Beijing, China).(shown in Figure 1). Haio Dental Prosthetic Membrane (Yantai Zhenghai Biotechnology Co., Ltd, Yantai, China).

## Method

The observation group was treated with a combination of PRF and artificial bone meal.The PRF was prepared according to the protocol described by Choukroun et al.[2] Ten milliliters of blood were taken from each patient's foot vein on the day of operation.In a sterile glass test tube without any anticoagulant, blood was drawn.The obtained blood was then immediately centrifuged in a chilled centrifugal machine for 15 minutes at 1400 rpm.As a result of the differential

**Figure 1** Bone repair materials: BIO-GENE.

densities, the centrifugation process led to the separation of three distinct fractions. At the bottom, there was a layer of red blood cells, while on the surface, there was acellular plasma. In between these two layers, a clot of PRF was formed. The middle layer (PRF) was removed and put in a sterile dish after the topmost layer was pumped out using a sterile dropper.The transplant material was combined with this clot, as depicted in Figure 2.

The patient received cefuroxime, and the oral and periodontal regions were disinfected and draped before surgery, selects the location of the intraoral incision according to the site and size of the cyst, incises the mucoperiosteum, flips the mucoperiosteal flap, removes the bone wall to expose the cyst cavity, carefully peels off the cyst wall, removes the cyst wall as completely as possible, and completely removes the cyst. In Group A, the patients were treated with normal saline rinsing, hemostasis, biofilm covering, and suturing of the wound. In Group B, 2 units of BIO-GENE artificial bone meal were mixed with PRF and used to suture the mucosa of the operative area.

## Observation Indicators

### Percentage of Osteogenesis at Bone Defects

In this investigation, we used a 3-dimensional (3D) reconstructed Cone Beam Computed Tomography (CBCT) to quantify the volume of the bone defects, following the methodology of Feng et al.[26] Six months following surgery, the patient's CBCT was rebuilt using 3D Slicer 5.0.3 software.Using a CS 9300 3D unit (Carestream Dental LLC, Atlanta, GA, USA) with a field of view of 50mm×50mm and voxel size of 0.09mm for a period of 19.96s for a 180-degree rotation, the CBCT pictures were acquired.The software is used to draw and measure the cyst cavity and osteogenic volume, and calculate the percentage of osteogenesis at the bone defect. To avoid systematic error, all measurements were averaged three times by the same physician on the same computer.

Bone generation rate of artificial bone meal = (bone volume implanted at some time after surgery) ÷ (bone volume implanted immediately after surgery) × 100%

Bone generation rate without artificial bone meal = (immediate postoperative cyst volume - postoperative capsule volume) ÷ (immediate postoperative cystic volume) × 100%

## Statistical Analysis

The analysis of the data was carried out using the Statistical Package for Social Sciences (SPSS) v.23.0.0 software (IBM Corp, Armonk, NY, USA).To evaluate statistical significance, normalize the two sets of data and assess separately if they follow a normal distribution, and the independent-samples *T*-test was performed.Statistics were judged significant at $P<0.05$.

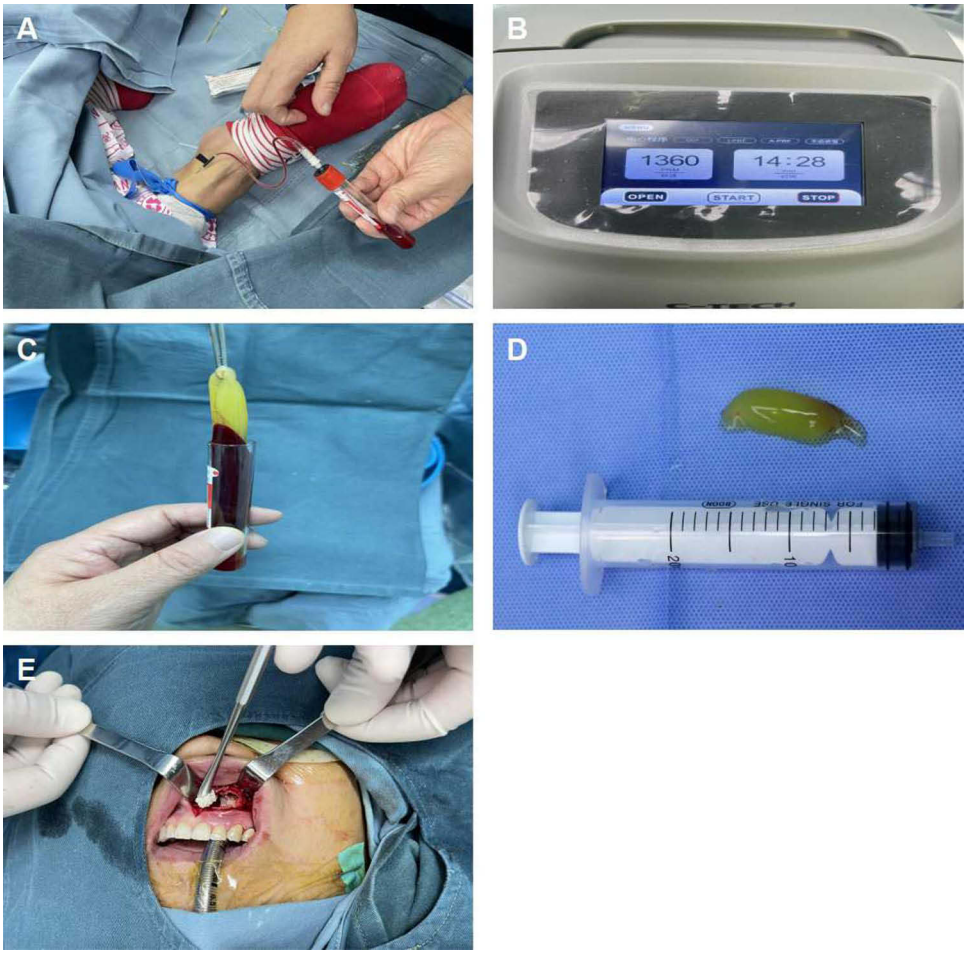


**Figure 2** Produced PRF. (**A**) Take foot venous blood. (**B**) Put the test tube into refrigerated centrifugal machine at 1400 for 15 min. (**C**) Prepared clot. (**D**) Prepared PRF. (**E**) Put 2 units of BIO-GENE artificial bone meal and PRF into the operative area.

## Results

In this study, 70 patients in total were enrolled using the comparative analysis of 3D reconstruction methodology. The CBCT scans and 3D reconstruction images taken six months following surgery for patients in groups A and B both revealed new bone development in the alveolar bone defect area and variable degrees of restoration of the patients' original jaw cyst area's fullness.The defect of the jawbone has been restored to varying degrees, and there is no clear boundary between the newly formed bone tissue and the surrounding original bone tissue.In terms of imaging density, as depicted in Figure 3, there appears to be no distinction from the typical bone tissue.Based on the reconstructed 3D image, the osteogenesis range was determined, as shown in Figure 4, and the osteogenic rate was calculated.The osteogenic rate data of the two components are shown in Table 1.The statistical analysis revealed that groups A and B's bone formation rates followed a normal distribution. Figure 5 displays the statistical results of bone rates in each group, The osteogenesis rate at 6 months in group A was 76.06±13.38%, while group B had a rate of 92.87±5.72%.The osteogenesis rate of the BIO-GENE+PRF group was found to be statistically significant at $P<0.05$ compared to the group that underwent cystectomy alone after jaw cyst surgery, supporting that the combination of BIO-GENE+PRF is effective for repairing bone defects after jaw cyst surgery, as shown in Table 2. The CBCT values in group B were higher than those in group A at 6 months post-surgery.The study had 70 patients in total. There were 24 males and 11 females in the group A, ranging in age from 19 to 52 (average 33.34±11.25 years).20 males and 15 females, aged 18 to 58 (mean 40.83±12.31 years), made up the B group.The variations in osteogenesis rates between group A and group B were not statistically significant.

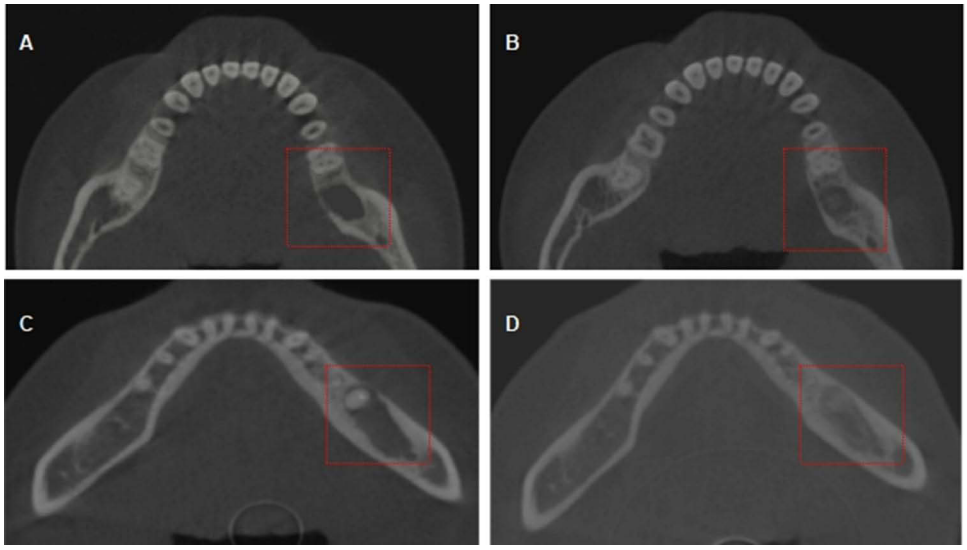


**Figure 3** Image performance. (**A**) Group A before surgery. (**B**) A group of six months after surgery. (**C**) Group B before surgery. (**D**) B group of six months after surgery.

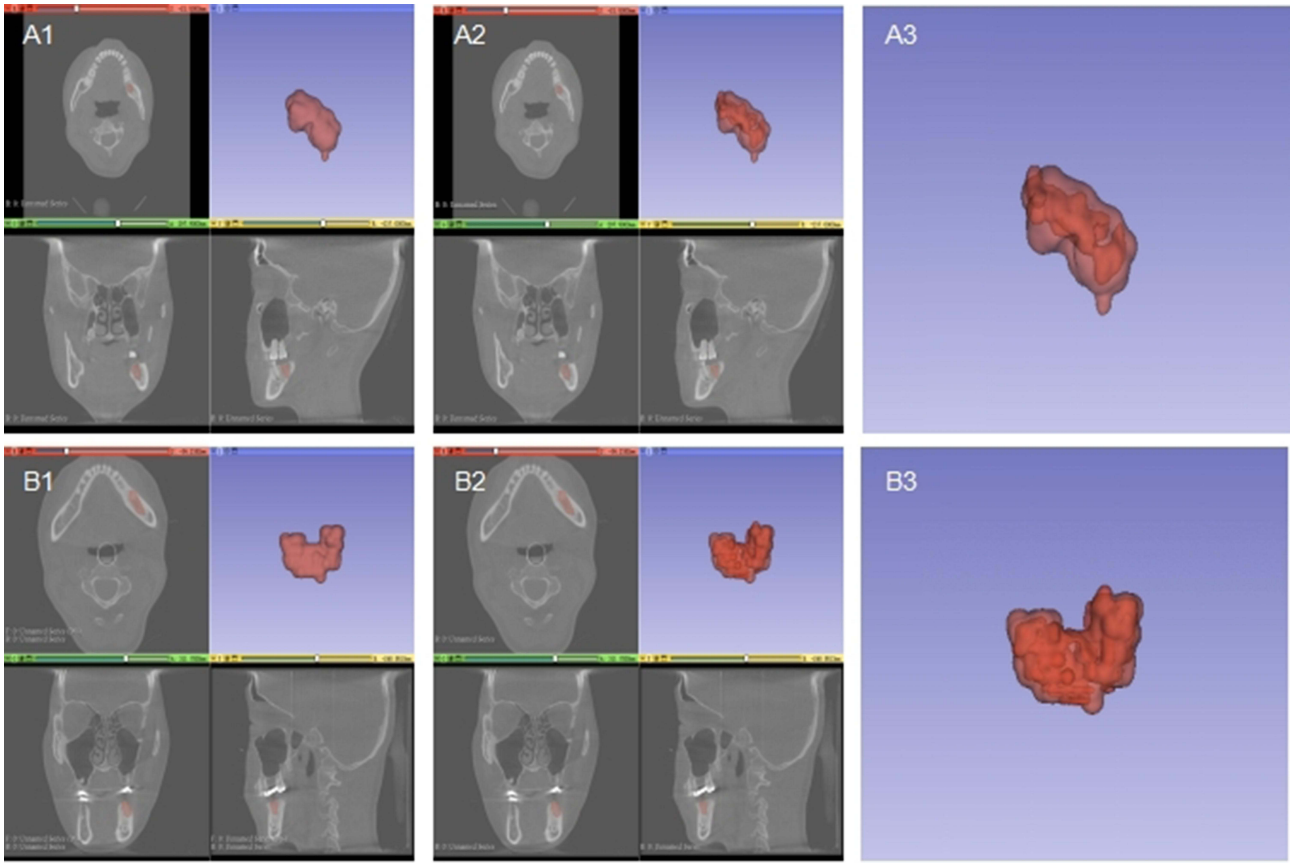


**Figure 4** Reconstructed 3D image. (A1) Group A had immediate 3D reconstruction of the capsule after surgery. (A2) In group A, the volume of the capsule immediately after surgery was overlapped with the area of bone formation 6 months later. (A3) In group A, the translucent red area is the volume of the cyst immediately after surgery, and the internal dark red area is the new bone at 6 months.(B1) Group B had immediate 3D reconstruction of the capsule after surgery. (B2) In group B, the volume of the capsule immediately after surgery was overlapped with the area of bone formation 6 months later. (B3) In group B, the translucent red area is the volume of the cyst immediately after surgery, and the internal dark red area is the new bone at 6 months.

**Table 1** The osteogenic rate data

| Postoperative Jaw Cyst Volume of Group A ($mm^3$) | Bone Defect Volume in Group A at Six Months After Surgery($mm^3$) | Composition Bone Rate of Group A | Postoperative Jaw Cyst Volume of GROUP B ($mm^3$) | Bone Defect Volume in Group B at Six Months After Surgery($mm^3$) | Composition Bone Rate of Group B |
|---|---|---|---|---|---|
| 1003.32 | 109.36 | 89.1 | 933.45 | 62.54 | 93.3 |
| 700.23 | 296.9 | 57.6 | 524.34 | 19.4 | 96.3 |
| 463.43 | 124.2 | 73.2 | 878.57 | 68.53 | 92.2 |
| 733.52 | 226.66 | 69.1 | 427.46 | 10.69 | 97.5 |
| 651.59 | 115.98 | 82.2 | 2011.53 | 130.75 | 93.5 |
| 1236.32 | 563.76 | 54.4 | 318.67 | 10.52 | 96.7 |
| 422.63 | 127.21 | 69.9 | 955.46 | 102.23 | 89.3 |
| 1023.53 | 231.31 | 77.4 | 1595.02 | 183.43 | 88.5 |
| 946.51 | 194.06 | 79.5 | 288.54 | 29.72 | 89.7 |
| 693.53 | 104.72 | 84.9 | 4067.33 | 406.73 | 90 |
| 594.56 | 99.89 | 83.2 | 759.95 | 43.55 | 94.4 |
| 843.56 | 256.44 | 69.6 | 549.92 | 36.84 | 93.3 |
| 1744.45 | 390.76 | 77.6 | 820.14 | 118.92 | 85.5 |
| 355.75 | 84.67 | 76.2 | 522.94 | 33.47 | 93.6 |
| 976.46 | 107.57 | 88.9 | 250.34 | 64.84 | 74.1 |
| 707.74 | 321.39 | 54.6 | 1552.82 | 178.58 | 88.5 |
| 623.94 | 90.16 | 85.5 | 834.52 | 27.54 | 96.7 |
| 1471.95 | 7.7 | 99.5 | 584.63 | 6.42 | 98.9 |
| 1499.96 | 20.51 | 98.6 | 905.73 | 75.46 | 91.7 |
| 712.91 | 477.57 | 33 | 1088.45 | 129.51 | 88.1 |
| 333.75 | 87.11 | 73.9 | 435.56 | 46.60 | 89.3 |
| 694.96 | 157.76 | 77.3 | 737.72 | 37.60 | 94.9 |
| 955.56 | 287.62 | 69.9 | 578.67 | 21.41 | 96.3 |
| 844.46 | 280.36 | 66.8 | 793.95 | 100.83 | 87.3 |
| 684.75 | 59.55 | 91.3 | 377.56 | 3.40 | 99.1 |
| 855.02 | 143.64 | 83.2 | 721.68 | 158.05 | 78.1 |
| 793.34 | 278.46 | 64.9 | 508.9 | 11.20 | 97.8 |
| 666.85 | 160.71 | 75.9 | 429.85 | 28.80 | 93.3 |
| 784.15 | 262.69 | 66.5 | 1320.65 | 38.30 | 97.1 |
| 663.43 | 163.87 | 75.3 | 550.37 | 6.05 | 98.9 |
| 772.82 | 174.66 | 77.4 | 1033.84 | 34.12 | 96.7 |

(*Continued*)

**Table 1** (Continued).

| Postoperative Jaw Cyst Volume of Group A ($mm^3$) | Bone Defect Volume in Group A at Six Months After Surgery($mm^3$) | Composition Bone Rate of Group A | Postoperative Jaw Cyst Volume of GROUP B ($mm^3$) | Bone Defect Volume in Group B at Six Months After Surgery($mm^3$) | Composition Bone Rate of Group B |
|---|---|---|---|---|---|
| 604.93 | 38.11 | 93.7 | 927.04 | 10.20 | 98.9 |
| 999.21 | 94.92 | 90.5 | 849.63 | 6.80 | 99.2 |
| 1703.48 | 387.17 | 77.8 | 790.52 | 20.55 | 97.4 |
| 639.30 | 168.78 | 73.6 | 947.48 | 52.11 | 94.5 |

## Discussion

In recent years, autologous PRF has been affirmed and clinically applied by doctors because it brings together high concentrations of growth factors that promote bone and soft tissue repair and regeneration, and has affinity and no immune rejection.[27] PRF can aid in the repair of the alveolar bone structure by promoting the growth and differentiation of homing stem cells.[27,28] Platelets, white blood cells, growth factors, and fibrin are all abundant in PRF.When the platelets are activated to release a large number of growth factors, fibrinogen slowly polymerizes under the action of physiological thrombin, chemically combines the released growth factors and platelets, and slowly releases internal growth factors again with fiber degradation during fiber matrix reconstruction, prolongs the action time of growth factors, increases the effect of promoting osteogenesis, and induces microvascular formation, plays an effective role in oral soft and hard tissue trauma and defect repair, and has a good immunomodulatory effect. PRF has been used in periodontal therapy, implant surgery, TMD, jaw cyst and other oral related treatment. Cross-infection and immune rejection are well avoided.[29] By using safe and effective bone grafting materials, the clinical efficacy of patients can be significantly improved.[30] Various graft materials and biomaterials, such as allografts[31] and autografts,[32] are utilized in treating bone defects.[33] The main focus of medical attention is the complicated process of bone repair.The synchronization of several

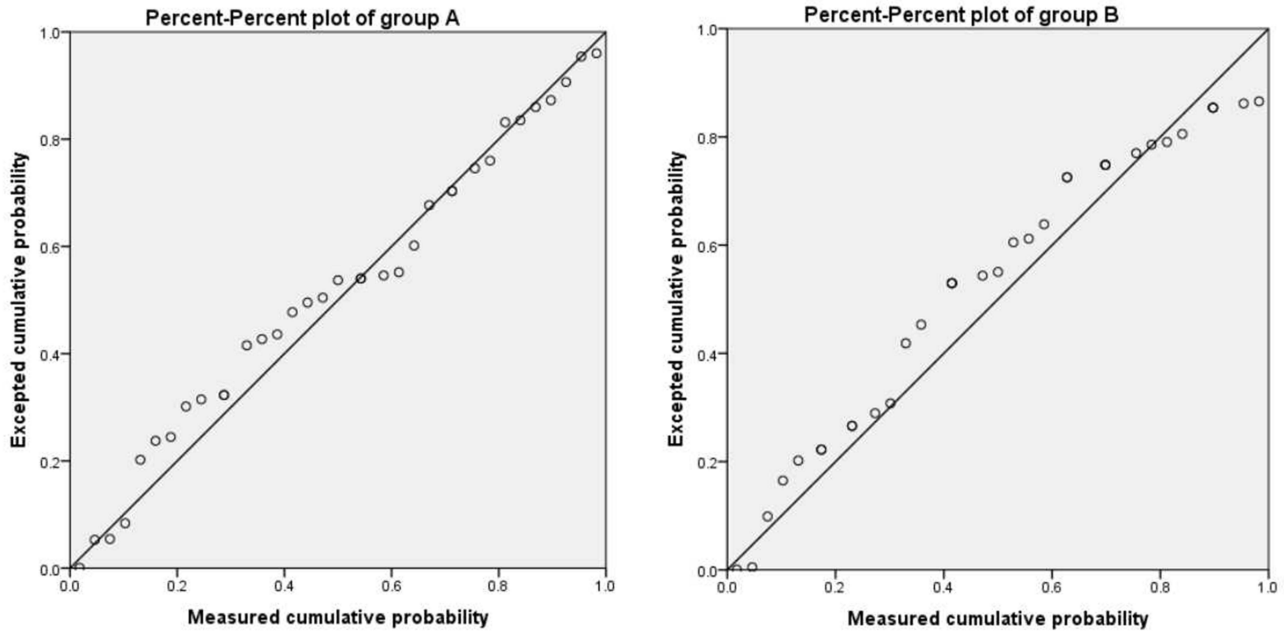


**Figure 5** Group A and B component bone rate data conform to a normal distribution.

**Table 2** (A) Independent-Samples T-test and (B) Group Statistics

| (A) Independent Samples Test | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Levene's Test for Equality of VARIANCES | | | | | | | | |
| | | F | Sig. | t | df | Sig. (2-Tailed) | Mean Difference | Std.Error Difference | 95% Confidence Interval of the Difference | |
| | | | | | | | | | Lower | Upper |
| Osteogenesis rate | Equal variances assumed | 10.323 | 0.002 | 6.838 | 68 | 0.000 | 16.81714 | 2.45944 | 11.90941 | 21.72487 |
| | Equal variances not assumed | | | 6.838 | 46.030 | 0.000 | 16.81714 | 2.45944 | 11.86664 | 21.76765 |
| (B) Group Statistics | | | | | | | | | | |
| | | Group | | N | Mean | | Std.Deviation | | Std.Error Mean | |
| Osteogenesis | | B | | 35 | 92.8743 | | 5.72047 | | 0.96694 | |

**Table 3** Abbreviations Used in the Text

| **Abbreviations Used in the Text** | |
|---|---|
| **Abbreviation** | **Full name** |
| PRF | Platelet-rich fibrin |
| CBCT | Cone Beam Computed Tomography |
| BG | Bone grafts |
| PRP | Platelet-rich plasma |
| TMD | Temporomandibular disorders. |
| TMJ-OA | Temporomandibular joint osteoarthritis |
| RCT | Randomized clinical trial |
| 3D | 3-dimensional |

cells and biological processes is essential for bone repair.[34] The data from the study mentioned supports the clinical efficacy of combining PRF with BIO-GENE artificial bone meal has better prognosis in the repair of bone defects following jaw cyst surgery. These findings align with those presented by Miron et al in 2021.[35] In simpler terms, some studies have shown that using PRF along with hydroxyapatite can provide significant benefits to patients. PRF has been found to have a positive effect on the cells responsible for bone formation in the alveolar bone and dental follicles. It promotes the growth of bone progenitor cells and enhances the differentiation of osteoblasts.[36]

Another study conducted on rats investigated the combination of PRF with a bone graft material called Bio-Oss. This study found a synergistic effect between PRF and Bio-Oss. Employing an autogenous graft and PRF combination was more successful than using an alternative different type of graft material, the difference was highly significant.[37]

The strengths of this study include having the same surgeon perform all surgeries, strict criteria for selecting patients, and the use of 3D reconstruction software for accurate evaluation of the rate of bone formation after grafting.Compared to earlier 2D evaluations, this is thought to be a more accurate predictor of bone healing.The limited sample size, the

varied nature of the flaws, and the short-term follow-up are some of the study's drawbacks.Histological evaluations of the postoperative healing process and the genuine nature of bone regeneration were not performed. Patient-related variables such to their age, sex, individual platelet counts, and biological particle sedimentation rates may also have had an impact on the quality of PRF generated.

## Conclusion

Within the study's limitations, we discovered that utilizing PRF in combination with BIO-GENE artificial bone meal after 6 months of jaw cyst surgery leads to a greater extent of osseous formation when compared to the control group. These findings suggest that the use of PRF combined with BIO-GENE artificial bone meal is a favorable choice for addressing bone defects following jaw cyst surgery, especially when rapid bone formation is prioritized in the short term.

## Abbreviations

Abbreviations used in the text are in Table 3.

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## Disclosure

The authors report no conflicts of interest in this work.

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