

# Comparative Evaluation of the Efficacy of Platelet-rich Fibrin and Calcium Phosphosilicate Putty alone and in Combination in the Treatment of Intra-bony Defects: A Randomized Clinical and Radiographic Study

## Abstract

**Background:** Combination of platelet-rich fibrin (PRF) and bone substitutes for the treatment of intra-bony pockets is based on sound biologic rationale. The present study aimed to explore the clinical and radiographic effectiveness of autologous PRF and calcium phosphosilicate (CPS) putty alone and in combination in treatment of intra-bony defects. **Materials and Methods:** A total of 45 intra-bony defects were selected and randomly divided into three groups. In Group I, mucoperiosteal flap elevation followed by placement of PRF was done. In Group II, mucoperiosteal flap elevation followed by placement of CPS putty was done. In Group III, mucoperiosteal flap elevation followed by placement of PRF and CPS putty was done. Clinical parameters such as gingival index (GI), pocket depth (PD), clinical attachment level (CAL), gingival marginal position and radiographic parameters such as bone fill, changes in crestal bone level, and defect depth resolution were recorded at baseline and after 6 months postoperatively. **Results:** Statistically significant changes in GI, PD reduction, CAL gain, defect fill, and defect depth resolution from baseline to 6 months were seen in all the three groups ( $P < 0.05$ ). On intergroup comparison, no statistically significant changes were seen in all clinical parameters. However, the difference in defect fill and defect depth resolution between the Groups I and III and Group II and III was significant. **Conclusion:** Within limitations of study, combination of PRF and CPS putty showed a significant improvement in PD reduction, CAL gain, and bone fill.

**Keywords:** Bone graft, growth factors, intra-bony defect, periodontal regeneration

## Introduction

Conventional open flap debridement (OFD) falls short of regenerating tissues destroyed by the disease. A wide range of graft materials including autografts, allografts, xenografts, and synthetic materials has been used for the treatment of intra-bony defects.<sup>[1]</sup> Alloplasts are synthetic, inorganic, biocompatible, and bioactive bone graft substitutes which promote healing through osteoconduction. Alloplasts offer the advantages of unlimited quantity, no additional surgical site, and no potential for disease transmission.<sup>[2,3]</sup>

Bioactive glasses are one of the widely used alloplastic bone graft materials used in the treatment of intra-bony defects in humans.<sup>[4,5]</sup> Calcium phosphosilicate (CPS) putty (NovaBone Dental putty; NovaBone products, Alachua, FL) is a premixed composite of bioactive CPS particulate and an absorbable binder which is a

combination of polyethylene glycol (PEG) and glycerin. The volume of active ingredient is 70%, and the putty is delivered in ready-to-use state. PEG and glycerin are both water soluble and to be absorbed from the site in 3–5 days. The smaller CPS particles (32–125  $\mu\text{m}$ ) are more rapidly resorbed, providing the initial burst of Ca and P ions. Subsequently, the larger particles (90–710  $\mu\text{m}$ ) react, being more resistant to resorption, continues process of regeneration. Unlike other bone graft materials, putty form of NovaBone eliminates need for a membrane to stabilize the graft material. It also provides ease of handling the material.<sup>[6,7]</sup>

A different approach to periodontal regeneration is the use of polypeptide growth factors. These factors, abundant in alpha granules of platelets, may control the growth of cells and hence the number of cells available to produce a tissue. Platelet-rich fibrin (PRF) described by

Isha Agrawal,  
Sarath Chandran,  
Priyadarshini Nadig

Department of Periodontology  
and Implantology, M.P. Dental  
College and Hospital, Vadodara,  
Gujarat, India

### Address for correspondence:

Dr. Isha Agrawal,  
15, Sakar Bunglows,  
Nr Ward Office 6,  
Vadodara, Gujarat, India.  
E-mail: ishaden@yahoo.com

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Choukroun *et al.*<sup>[8]</sup> allows one to obtain fibrin membranes enriched with platelets and growth factors. Being autogenous in nature, with no artificial chemical agents involved, makes PRF a safe and inexpensive treatment modality. The physiologic fibrin matrix of PRF, obtained as the result of slow polymerization, has the ability to hold various growth factors and cytokines which are released at the wound site for a prolonged period. This unique structure may act as a vehicle for carrying cells that are essential for tissue regeneration.<sup>[9,10]</sup>

The purpose of present study is to evaluate periodontal regeneration in intrabony defects using PRF and CPS putty (NovaBone putty) alone and in combination.

## Materials and Methods

### Patient selection

A total of 45 patients with chronic periodontitis were selected from the Outpatient Department of Periodontics and Implantology, Manubhai Patel Dental College, Vadodara. After ethical and research approval, written consent was obtained from the participants of the study. Patients with the presence of clinical and radiographic evidence of three wall/two wall intrabony defects  $\geq 3$  mm deep along with interproximal probing depth  $\geq 5$  mm following Phase I therapy (scaling and root planing) were selected for study.

Patients with any systemic disease, patients who underwent periodontal surgery 1 year back, patients having insufficient platelet count, patients with coagulation defect or anticoagulation treatment, pregnant or lactating mothers, a smoker or an alcoholic patient, and those with unacceptable oral hygiene after the reevaluation of Phase I therapy were excluded from the study. In addition, teeth with furcation involvement or Miller grade II or greater mobility were also excluded.

### Presurgical therapy

A general assessment of selected participants was made through their history, clinical examination, and routine investigations. All participants were treated with the initial Phase I therapy involving oral hygiene instructions, scaling, and root planing. Following Phase I therapy, the participants were reevaluated after 6 weeks, and those fulfilling the selection criteria were finally taken up for the study.

Sites were randomly divided (lottery method) into three groups. In Group I, mucoperiosteal flap elevation followed by OFD and placement of PRF was done. In Group II, OFD followed by placement of NovaBone putty was done. In Group III, OFD followed by placement of PRF and NovaBone putty was done.

### Clinical and radiographic parameters

Gingival index (GI),<sup>[11]</sup> pocket depth (PD),<sup>[12]</sup> gingival marginal position, and clinical attachment level (CAL)<sup>[13]</sup> of the selected sites were recorded using customized acrylic occlusal stents at baseline before surgery and again recorded at 6 months postoperatively [Figure 1 - left side] [Figure 1 shows Group III site].

Standardized intraoral periapical radiographs with X-ray grid were taken using long cone paralleling technique and film holder [Figure 1 - right side]. Radiographic measurements were calculated from the radiographic image. The landmarks such as cemento-enamel junction (CEJ), alveolar crest (CD), and base of the defect (BD) were marked on the image of the radiograph. The distance from CEJ to the BD and from CEJ to the crest of the defect was measured by counting the number of the grid to nearest mm.<sup>[14]</sup>

The depth of the intrabony defect was calculated by subtracting the CEJ-CD from CEJ-BD.

The following radiographic parameters were recorded at baseline and 6 months postoperatively to evaluate the hard tissue response.

- $A_0$ : Distance from CEJ to BD (initial)
- $A_6$ : Distance from CEJ to BD (6 months' postsurgery)
- $B_0$ : Distance from CEJ to the CD (initial)
- $B_6$ : Distance from CEJ to the CD (6 months' postsurgery).

### Arithmetic determination

- $C_0$ : Distance from the CD to the BD ( $A_0 - B_0$ )
- $C_6$ : Distance from the CD to the BD ( $A_6 - B_6$ ).

### Amount of defect fill

It is defined as initial distance from the CEJ to BD – 6 months' postsurgery distance from CEJ to BD ( $A_0 - A_6$ ).



Figure 1: Pre- and post-operative measurement of clinical parameters (left side) and radiographic parameters (right side)

### Changes in the alveolar crest level

It is defined as initial distance from the CEJ to CD – 6 months' distance from the CEJ to CD ( $B_0$ - $B_6$ ).

### Defect depth resolution

It is defined as initial distance from the CD to the BD – 6 months' postsurgery initial distance from the CD to the BD ( $C_0$ - $C_6$ ).

### Preparation and application of platelet-rich fibrin

PRF was prepared by drawing intravenous blood from the antecubital fossa of the patient as per Choukroun's standard protocol.<sup>[8]</sup> The PRF clot/gel located in the middle of the tube soaked in a cellular plasma was removed with a tweezer and used as graft material at the experimental site.

### Surgical procedure

An intraoral antiseptis was performed with a 0.12% chlorhexidine digluconate rinse, and an iodine solution was used to carry out an extraoral antiseptis. After the administration of local anesthesia, 2% lignocaine hydrochloride with adrenaline (1:80,000), the crevicular and interdental incisions, and full-thickness mucoperiosteal flaps were reflected, taking care to retain the interdental papillary tissue as far as possible. Meticulous debridement and root planing was done Gracey curettes and Cumine scalars (Hu-Friedly).

Freshly prepared PRF gel or NovaBone putty was placed into the osseous defect with light pressure till it filled up to the most coronal level of osseous wall. For Group III, the defect was filled with PRF mixed along with NovaBone putty.

The mucoperiosteal flaps were repositioned and secured in place using nonabsorbable 4-0 silk sutures.

### Postoperative care

All patients received systemic antibiotic therapy (amoxicillin 500 mg thrice daily) for 7 days and analgesic therapy (ketorolac tromethamine 10 mg dispersible tablets twice daily) for 3 days to reduce discomfort and postoperative pain and edema. Sutures were removed 7 days following surgery.

### Postsurgical evaluation

Patients were examined weekly for 1 month after surgery and then at 3 and 6 months. Supragingival scaling and

reinforcement of oral hygiene instructions were provided at all appointments.

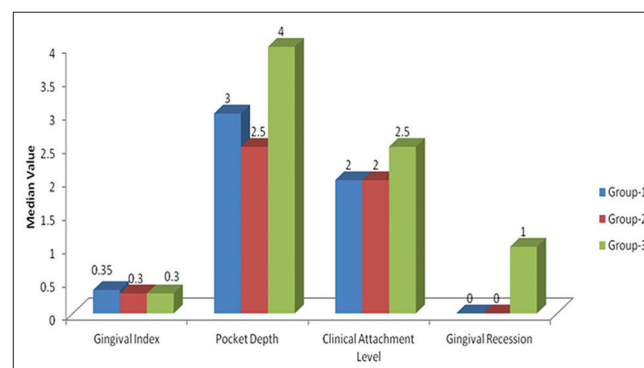
### Statistical analysis

For all the variables, descriptive data including median and interquartile ratio were calculated for each clinical and radiographic parameter at baseline and at 6 months. Wilcoxon Signed-Rank test was used to compare average value at baseline and 6 months for intragroup comparison whereas Mann-Whitney test is applied to compare average values between two groups and Kruskal-Wallis test between three groups for intergroup comparison.

### Results

A total 40 out of 45 defects completed the study while five defect site patients failed to return for the 6 months' recall. As a result, 14 defects were present in Group I (PRF), 12 were present in Group II (NovaBone), and 14 were present in Group III (PRF + NovaBone).

There was statistically significant reduction in GI, PD, and clinical attachment gain before and after surgical procedure in all the three groups [Table 1]. On comparison, three groups did not show statistical significant difference among themselves at all-time intervals [Table 2 and Graph 1]. There was statistically significant increase in gingival recession before and after surgical procedure in Group I and Group III [Table 1]. There was statistically significant difference between bone fill and bone defect resolution in all groups from baseline to 6 months [Table 3]. On comparison, the differences in bone fill and bone defect resolution between Group I and Group III and Group II and Group III were



Graph 1: Intergroup comparison of clinical parameters

Table 1: Clinical parameters at baseline and 6 months

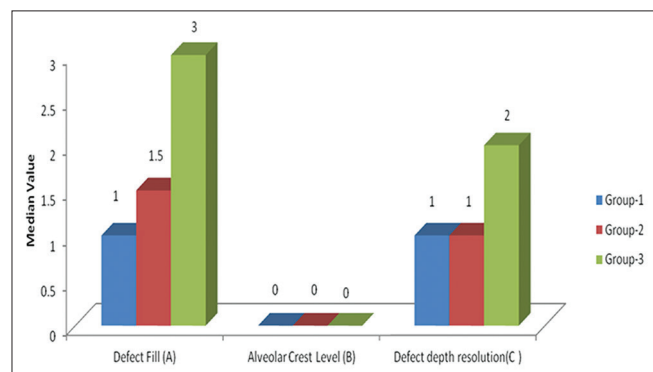
Clinical parameters	Median (IQR)						P		
	Group I		Group II		Group III		Group I	Group II	Group III
	Baseline	6 months	Baseline	6 months	Baseline	6 months			
GI	0.85 (0.30)	0.50 (0.40)	0.90 (0.18)	0.60 (0.15)	0.90 (0.13)	0.65 (0.20)	0.001	0.002	0.001
PD	7.00 (2.25)	3.50 (1.00)	6.50 (2.00)	3.00 (1.00)	9.00 (3.25)	4.50 (2.00)	0.001	0.002	0.001
CAL	7.00 (2.25)	5.00 (2.25)	7.00 (2.50)	4.50 (3.00)	9.00 (3.50)	6.00 (3.00)	0.001	0.002	0.001
GR	0.00 (2.00)	1.00 (3.00)	0.00 (0.075)	0.50 (1.00)	0.00 (1.00)	1.00 (1.00)	0.026	0.102	0.005

GI: Gingival index; PD: Pocket depth; CAL: Clinical attachment level; GR: Gingival recession; IQR: Interquartile ratio

statistical significant [Table 4 and Graph 2]. The difference in CD level at baseline and 6 months was not statistical significant in Group I and Group II. On comparison, the CD level between Group I and Group III and Group II and Group III was statistical significant [Table 4 and Graph 2].

### Discussion

The aim of periodontal therapy is to arrest and control the periodontal infection and ultimately to regenerate lost periodontal structures. The complete regeneration of the periodontium after periodontal treatment modalities has



Graph 2: Intergroup comparison of radiographical parameters

been difficult to achieve because of differences in healing abilities among periodontal tissues.<sup>[15]</sup> The present study evaluates the clinical efficacy of combination of NovaBone and PRF in the treatment of intrabony defects in patients with chronic periodontitis, and result shows a significant improvement in clinical and radiographic parameters.

Smoking, tobacco products, and systemic disease such as diabetes are important factors that were shown to significantly influence the outcomes of regenerative periodontal surgery. Because the present study excludes smokers and only includes patients who were able to maintain acceptable oral hygiene, it may be assumed that the careful patient selection was also responsible for the positive outcomes obtained in all groups.<sup>[16]</sup>

While one-wall intrabony defects are characterized by only one limited area for periodontal ligament (PDL) cell proliferation in the apical portions of the defect, angular defect border by at least two bony walls yields lateral sources for PDL cell proliferation and hence may heal in a more predictable way than one wall intrabony defects. Hence, in the present study, 3 wall/2 wall defects were included.<sup>[17]</sup>

Bioactive glass is widely used alloplast in periodontal therapy. However, they are granular in nature and unreliable

Table 2: Intergroup comparison of clinical parameters

Difference in clinical parameters	Median (IQR)			P		
	Group I	Group II	Group III	Group I versus Group II	Group I versus Group III	Group II versus Group III
GI	0.35 (0.23)	0.30 (0.10)	0.30 (0.23)	0.423	0.240	0.672
PD	3.00 (2.00)	2.50 (2.00)	4.00 (3.00)	0.559	0.260	0.140
CAL	2.00 (2.00)	2.00 (2.50)	2.50 (3.25)	0.915	0.450	0.579
GR	0.00 (1.25)	0.00 (0.75)	1.00 (1.00)	0.345	0.486	0.075

GI: Gingival index; PD: Pocket depth; CAL: Clinical attachment level; GR: Gingival recession; IQR: Interquartile ratio

Table 3: Radiographic parameters at baseline and 6 months

Radiographical parameters	Median (IQR)						P		
	Group I		Group II		Group III		Group I	Group II	Group III
	Baseline	6 months	Baseline	6 months	Baseline	6 months			
Defect fill (A)	5.50 (2.25)	4.00 (2.00)	7.00 (2.75)	4.00 (3.25)	7.00 (2.25)	4.50 (2.00)	0.001	0.002	0.001
Changes in alveolar crest level (B)	3.00 (1.25)	3.00 (1.50)	3.00 (0.75)	3.00 (1.00)	3.50 (2.00)	2.50 (2.00)	0.705	0.083	0.024
Changes in defect depth resolution (C)	3.00 (1.00)	3.00 (1.00)	3.00 (2.00)	1.00 (1.00)	4.00 (2.25)	2.00 (2.00)	0.001	0.002	0.001

IQR: Interquartile ratio

Table 4: Intergroup comparison of radiographical parameters

Difference in radiographical parameters	Median (IQR)			P		
	Group I	Group II	Group III	Group I versus Group II	Group I versus Group III	Group II versus Group III
Defect fill (A)	1.00 (1.00)	1.50 (1.00)	3.00 (2.00)	0.246	0.001	0.018
Changes in alveolar crest level (B)	0.00 (1.25)	0.00 (0.75)	0.00 (1.25)	0.213	0.037	0.233
Changes in defect depth resolution (C)	1.00 (1.00)	1.00 (1.00)	2.00 (1.00)	0.651	0.003	0.023

IQR: Interquartile ratio



as a scaffold matrix.<sup>[4,5]</sup> To overcome this limitation, in the present study, CPS putty was used which has excellent osteostimulative and osteoconductive property. It also has a transient hemostatic effect, encouraging clot stabilization and promotes healing. Putty does not adhere to the surgical gloves and instruments during manipulation.<sup>[7]</sup>

PRF consists of a fibrin matrix polymerized in a tetramolecular structure, the incorporation of platelets, leukocyte, and cytokines, and circulating stem cells.<sup>[18]</sup> PRF would be able to progressively release growth factors (such as transforming growth factor-1  $\beta$ , platelet-derived growth factor-AB, and vascular endothelial growth factor) and glycoproteins (such as thrombospondin-1).<sup>[19]</sup> In the present study, PRF group showed improvement in clinical and radiographic parameters which in accordance with clinical trials conducted by Sharma and Pradeep,<sup>[20]</sup> Thorat *et al.*,<sup>[21]</sup> and Bajaj *et al.*<sup>[22]</sup>

In CPS putty (NovaBone putty) treated sites, significant change in GI reduction, PD reduction and CAL gain, defect fill, and defect depth resolution was seen from baseline to 6 months. Similar results were observed in studies conducted by Chacko *et al.*,<sup>[23]</sup> Lovelace *et al.*,<sup>[24]</sup> Froum *et al.*,<sup>[25]</sup> and Shukla *et al.*<sup>[7]</sup> Mengel *et al.*<sup>[26]</sup> and Singh and Mehta<sup>[27]</sup> also reported that the sites treated with bioactive glass have shown statistically significant gain of attachment levels 6 months' postsurgery. This decrease in defect depth and attachment gain can be attributed to soft and hard tissue improvements following resolution of inflammation and osteogenic potential of CPS putty.

Till now, no study compared the combined use of both autologous PRF and NovaBone putty as graft materials in the treatment of human periodontal intrabony defects. Thus, a direct comparison with other studies was not possible. In the present study, significant change in GI, PD reduction, CAL gain, gingival recession, defect fill, crestal bone level changes, and defect depth resolution was seen from baseline to 6 months. Lakshmi P *et al.*<sup>[28]</sup> reported the combination of PRF and bioactive glass and showed significant difference in pocket depth reduction, CAL gain, and defect depth at the end of 9 months. In contrast, Shukla *et al.*<sup>[7]</sup> compared CPS putty with and without platelet-rich plasma (PRP) in infrabony defects and concluded that addition of PRP to CPS putty does not seem to provide any additive benefit.

In the present study, combination of PRF and NovaBone putty demonstrated more favorable radiographic results compared to PRF or NovaBone putty alone. The precise role played by PRF in the defect fill is difficult to determine but may be explained on the basis of tissue engineering. Bioactive glass in NovaBone can be considered a scaffold for delivery of growth factors in PRF. The negatively charged hydroxyl-carbonate apatite layer attracts proteins such as growth factors and fibrin which act like an organic glue attracting osteoblasts and

stem cells to the layer which differentiates to produce bone. Collagen attaches to the surface and embeds in the hydroxyl-carbonate apatite layer, and this, in turn, inhibits epithelial migration. The PDGF and TGF in PRF may work in promoting the growth and differentiation of periodontal and alveolar bone cells rapidly.<sup>[29,30]</sup>

Based on the results of our study, there was no difference when PRF and NovaBone putty were used alone. Hence, considering the cost-benefit ratio, PRF provides comparable regenerative therapy when compared to expensive alloplast materials such as NovaBone putty. NovaBone putty does not provide any clear cut additional benefit when used alone over PRF.

Certain limitations to the present study such as measurement of clinical parameters are subjective due to the absence of any objective measurable method. Due to ethical issues, re-entry of the surgical site was not possible; hence, the question whether the bone formed was a vital bone remains unanswered, and also, histological examination cannot be done to prove the evidence of clinical and radiological parameters.

## Conclusion

Within the limits of the present study, it can be concluded that the combination of CPS putty (NovaBone putty) and PRF though effective in improving the radiologic parameters did not enhance the clinical outcome of the therapy compared to the PRF or NovaBone putty alone. Furthermore, PRF showed comparable regenerative potential with CPS putty when used alone. Thus, considering cost-to-benefit ratio, PRF proved better option for regeneration decreasing the cost of regeneration therapy, and placement of PRF is also less technique sensitive. However, the findings of study cannot be directly extrapolated as an outcome of periodontal regeneration as these are not supported by histologic evidence. So further, long-term clinical trials with large samples along with histological examination are needed to evaluate the regenerative potential of PRF and CPS putty.

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## Conflicts of interest

There are no conflicts of interest.

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