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**ORIGINAL ARTICLE**

# Long-term clinical results on the use of platelet concentrate in the treatment of intrabony periodontal defects

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**Abstract**

***Objective.*** The purpose of this clinical investigation was to evaluate long-term results obtained with the combination of platelet pellet (PP) plus bioabsorbable barrier membrane (BM) and to compare this outcome with the results obtained using bioactive glass (BG) graft material with a BM. ***Materials and methods.*** Using a split mouth design, 11 chronic periodontitis patients (power ≥ at least 80%) were randomly assigned to treatment with a combination of PP/GTR or BG/GTR in contra-lateral dentition areas. Clinical attachment level (CAL) as the primary outcome variable, calculated as the sum of probing pocket depth (PPD) and gingival recession, and radiological alveolar bone level were recorded at baseline, 6 months and 5 years. ***Results.*** There were no statistical differences between test and control defects at baseline. PPD reductions and CAL and radiological alveolar bone height gains were statistically significant between baseline and 6 months and between baseline and 5 years in both groups ($p < 0.01$). Six months results of frequency distribution showed that 82% of the defects attained ≥ 4 mm CAL gain in both groups, while 5 year results showed that 73% of the defects attained 2 mm ≤ CAL gain < 4 mm in the PP/BM group and 55% of the defects attained 2 mm ≤ CAL gain < 4 mm in the BG/BM group. All parameters evaluated showed no significant differences between 6 months and 5 years in both groups ($p > 0.05$). No statistically significant difference in any of the clinical parameters was observed at 6 months and 5 years between the groups ($p > 0.05$). ***Conclusions.*** The long-term efficacy of platelet concentrate combined with a barrier membrane is similar with the combination of bioactive glass graft material and barrier membrane, suggesting that results obtained with both treatment approaches can be maintained over a period of 5 years.

**Key Words:** *bone graft, guided tissue regeneration, long-term, platelet-rich plasma, randomized controlled trial*

## Introduction

Periodontitis, an oral infectious disease, is characterized by clinical attachment loss, alveolar bone resorption, periodontal pocketing and gingival inflammation [1]. The purpose of periodontal therapy is to control the infection and regenerate the tissues that have been lost due to destructive periodontal disease [2,3]. Although regeneration of the periodontium is the ultimate goal of periodontal therapy, complete regeneration is not a predictable healing outcome following traditional periodontal treatment [4]. A number of studies have demonstrated successful regeneration of periodontal tissues using regenerative periodontal therapies such as guided tissue regeneration (GTR), applications of enamel matrix derivative, platelet concentrates, various polypeptide growth factors and combinations of these therapies [5–10].

In recent years, there has been a growing interest in the use of platelet concentrates for the treatment of periodontal defects [11,12]. Platelet-rich plasma (PRP) is a volume of autologous plasma that has a higher platelet concentration than baseline [13]. It is known that the increased number of platelets deliver an increased number of polypeptide growth factors that modulate the wound healing response by binding to specific cell surface receptors in hard and soft tissues [14,15]. Platelets contain these growth factors in their alpha granules [16].

For the purpose of periodontal regeneration, platelet concentrate has generally been combined with graft materials (inorganic bovine bone, $\beta$-tricalcium phosphate, demineralized freeze-dried bovine bone, bioactive

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glass and hydroxyapatite) [12,17–19] and also additional GTR using porcine-derived collagen membranes, polylactic acid membranes, synthetic bioabsorbable membranes and expanded polytetrafluoroethylene membranes [20–28] in randomized clinical trials.

Meta-analysis of 10 randomized trials showed a significantly greater clinical attachment level (CAL) gain in the PRP-administered defects compared to control sites [11,17,18,22,24,26,29,30]. Data from this meta-analysis also suggest that combination of PRP and graft materials without GTR demonstrated a significant positive effect on periodontal intra-bony defects [11,12,17,18,30,31]. However, recent controlled clinical trials suggested that PRP failed to improve the results obtained with the combinations of bone graft materials/bioabsorbable and non-resorbable GTR membranes [22,24,26,27,29].

There is only one case series investigating the individual role of autologous platelet concentrate or GTR membrane in the treatment of intra-bony defects which suggested that platelet concentrate and GTR treatments led to similar improvements in clinical and radiographic parameters over a 52-week period [9]. Greater healing success in cementum formation after surgical therapies with both platelet pellet (PP, platelet concentrate with higher platelet content) and PP/GTR combination compared to the open flap debridement in class II furcation defects with regard to the histomorphometric findings were shown in our previous experimental study in dogs [10]. Moreover, both the combination of PP/GTR and synthetic bone grafting material/GTR treatments led to a significant pocket depth reduction, gain in clinical attachment and alveolar bone level after 6 months [23]. Despite these favorable clinical results with the use of platelet concentrates in periodontal regeneration, no studies are at present available evaluating the long-term results of this therapy.

The purpose of this clinical investigation was to report the long-term results of a randomized clinical trial comparing two regenerative approaches in the treatments for periodontal intra-bony defects based on combination therapy: PP covered with a bioabsorbable barrier membrane (BM) or bioactive glass (BG) grafting material covered with a BM.

## Materials and methods

The short-term results of this clinical trial were reported in a previous article [23], a randomized clinical trial of 6 months' duration using a split-mouth design, in which the experimental design and surgical protocol are described in detail.

### *Subject selection*

Briefly, 11 chronic periodontitis patients (five males and six females) with a mean age of 39.1 ± 7.4 years (range = 29–51 years) exhibiting radiographic evidence of bone loss and paired, similar vertical periodontal osseous defects in each of two contra-lateral quadrants were followed over 5 years.

All subjects were systemically healthy and non-smokers who completed the basic periodontal therapy and were willing to comply with the prescribed oral hygiene and periodontal recall regimen.

After receiving information on the study, the patients signed a consent form indicating their agreement to participate in the study. The study protocol and consent form were approved by the University Institutional Review Board.

### *Clinical and radiological measurements*

Clinical attachment level (CAL) as the primary outcome variable, calculated as the sum of probing pocket depth (PPD) and gingival recession, was measured at baseline, 6 months and 5 years [23]. The full-mouth plaque score (FMPS), full-mouth bleeding score (FMBS), site-specific plaque score and site-specific bleeding score were recorded for assessing subject compliance with the prescribed supportive therapy.

Radiological examinations were done at baseline, 6 months and 5 years. Radiological alveolar bone height was determined, as described previously [23].

### *Surgical procedure*

All periodontal surgical procedures were performed on an outpatient basis under aseptic conditions by two experienced periodontal clinicians under local anesthesia. The same clinician performed all surgical procedures (GCK) and the other assisted during the procedures (BOC). The paired intra-bony defects were randomly assigned to receive either PP/BM treatment or BG/BM treatment by a flip of a coin. Following buccal and lingual intra-crevicular incisions, mucoperiosteal flaps were raised. All granulation tissue was removed from the defects and the roots were thoroughly scaled and planed using hand and ultrasonic instruments. The surgical sites were rinsed with sterile saline.

PerioGlas (US Biomaterials Corp., Alachua, FL) was used as a bioactive glass graft material in the present study. PerioGlas was mixed with sterile saline to form a paste according to the manufacturer's instructions. At the time of application, PP was coagulated by adding 10% calcium chloride at a 1:10 ratio (v/v) [32].

All defects were completely filled by either PP or BG and care was taken not to overfill the defects. Atrisorb (Atrix Laboratories, Inc., Fort Collins, CO), an absorbable membrane made of polylactic acid, was used for GTR. Atrisorb was prepared according to the manufacturer's instructions and placed over the BG-grafted or PP-filled defect.

Table I. FMPS and FMBS at baseline, 6 months and 5 years.

| | Baseline | Post-operative 6-months | Post-operative 5-years |
|---|---|---|---|
| FMPS | 9.06 ± 0.53 | 10.25 ± 0.60[a] | 10.55 ± 0.63[ab] |
| FMBS | 12.57 ± 0.76 | 10.57 ± 0.76[a] | 10.85 ± 0.70[ab] |

Paired-samples *t*-test. Data are expressed as the mean ± standard deviation.
FMPS, Full-mouth plaque score; FMBS, Full-mouth bleeding score.
[a] Statistically significant difference from baseline ($p < 0.001$).
[b] No significant difference from post-operative 6-month ($p > 0.05$).

Table II. SSPS and SSBS at baseline, 6 months and 5 years.

| | Baseline | Post-operative 6-months | Post-operative 5-years | *p*-value[b] |
|---|---|---|---|---|
| SSPS[a] | | | | |
| PP/BM | 0.36 ± 0.50<br>0 (0–1) | 0.18 ± 0.40<br>0 (0–1) | 0.27 ± 0.47<br>0 (0–1) | 0.65 |
| BG/BM | 0.46 ± 0.52<br>0 (0–1) | 0.27 ± 0.47<br>0 (0–1) | 0.27 ± 0.47<br>0 (0–1) | 0.60 |
| SSBS[a] | | | | |
| PP/BM | 0.46 ± 0.52<br>0 (0–1) | 0.18 ± 0.40<br>0 (0–1) | 0.27 ± 0.47<br>0 (0–1) | 0.31 |
| BG/BM | 0.55 ± 0.52<br>1 (0–1) | 0.27 ± 0.47<br>0 (0–1) | 0.27 ± 0.47<br>0 (0–1) | 0.22 |

Data are expressed as the mean ± standard deviation and as the median (minimum–maximum).
PP, platelet pellet; BG, bioactive glass; BM, barrier membrane; SSPS, site-specific plaque score; SSBS, site-specific bleeding score.
[a] No significant difference between the groups ($p > 0.05$), Wilcoxon signed-rank non-parametric test.
[b] No significant difference among the groups ($p > 0.05$), Friedman test.

Flaps were replaced and secured by a 4–0 silk suture utilizing an interrupted suture technique to achieve primary closure.

### *Post-operative care*

Patients were prescribed a 0.2% chlorhexidine-gluconate mouth rinse to be used twice a day for 2 weeks. Silk sutures were removed 1 week after surgery. Subjects were then placed on a strict recall program every 3 months for 5 years. At each recall visit, all subjects received debridement as needed, together with reinforcement of their oral hygiene practices.

All clinical and radiological measurements were recorded at 6 months and 5 years. All measurements at 6 months were done by the same calibrated investigator (GA) who was blinded with respect to treatment modality. The measurements at 5 years were done by another calibrated and blinded investigator (FP) who was calibrated with the senior investigator (GA). A calibrated exercise was carried out to obtain acceptable intra- and inter-examiner reproducibility, as previously described by Cortellini et al. [33]. Briefly, intra-examiner reproducibility was evaluated as the standard deviation of the difference of triplicate measurements. All investigators reached the target of a standard deviation lower than 0.4 mm for attachment level. Inter-examiner variability was evaluated as the standard deviation of the difference from the gold standard represented by the senior investigator (GA). The computed value for attachment level was less than 0.4 mm for all clinicians.

### *Statistical analysis*

Statistical analysis was performed using a commercially available software program (SPSS 15.0, SPSS Inc., Chicago, IL). In the statistical analysis, only the recordings representing the deepest clinical site in each defect were used [2]. The Shapiro-Wilk test was used to investigate whether or not the data were normally distributed.

Intra-group comparisons were carried out using the Wilcoxon signed-rank and Friedman non-parametric tests to assess the differences between the baseline and 6-month and the 6-month and 5 year evaluations for two treatment modalities. Inter-group comparisons were also performed using Wilcoxon signed-rank and Mann-Whitney U non-parametric tests. The intra-group comparisons for FMPS and FMBS were carried out using paired-samples *t*-test. Significance was set at $p < 0.05$.

Power analysis indicated that 11 defects for each treatment modality would be sufficient to demonstrate statistical significance at the $p < 0.05$ level with a power of (at least) ≥ 80%.

## Results

### *Subject follow-up*

Eleven subjects with 22 intraosseous defect completed the study; there were four dropouts during the 5-year follow-up period. Eight two-wall and three three-wall defects (upper/lower teeth 6/5 and premolar/molar teeth 6/5) were treated with PP/BM, seven two-wall and four three-wall (upper/lower teeth 6/5 and premolar/molar 4/7) with BG/BM. The depth of the intra-bony component for the defects treated with PP/BM and BG/BM were 5.27 ± 0.90 mm and 5.09 ± 0.94 mm, respectively. An analysis of the defect characteristics at the baseline revealed no significant differences between the treatment modalities ($p > 0.05$).

The subjects demonstrated good plaque control with ≤ 10% plaque index at baseline. However, this level of plaque control was minimally deterioted throughout the study; the FMPS was 10.55% at 5 year evaluation. FMBS were diminished and remained stable throughout the study (Table I).

Site-specific plaque score and site-specific bleeding

Table III. Clinical and radiological findings of intraosseous defects (mm).

| | Baseline | Post-operative 6-months | Post-operative 5-years |
|---|---|---|---|
| CAL* | | | |
| PP/BM | 8.36 ± 1.50 | 4.18 ± 1.33 | 6.00 ± 1.27 |
| | 8 (6–12) | 4 (3–7)[a] | 6 (4–8)[ab] |
| BG/BM | 8.00 ± 1.55 | 3.55 ± 0.93 | 5.36 ± 0.81 |
| | 8 (6–10) | 3 (2–5)[a] | 5 (4–7)[ab] |
| PPD* | | | |
| PP/BM | 7.64 ± 0.92 | 3.27 ± 0.47 | 4.73 ± 0.79 |
| | 8 (6–9) | 3 (3–4)[a] | 5 (4–6)[ab] |
| BG/BM | 7.46 ± 1.29 | 2.73 ± 0.47 | 4.07 ± 0.63 |
| | 7 (6–10) | 3 (2–3)[a] | 4 (3–5)[ab] |
| REC* | | | |
| PP/BM | 0.73 ± 1.10 | 0.91 ± 1.45 | 1.27 ± 1.27 |
| | 0 (0–3) | 0 (0–4)[c] | 1 (0–4)[ab] |
| BG/BM | 0.55 ± 0.93 | 0.82 ± 1.08 | 1.36 ± 0.67 |
| | 0 (0–2) | 0 (0–3)[c] | 1 (1–3)[ab] |
| RABL* | | | |
| PP/BM | 8.73 ± 2.37 | 3.36 ± 1.63 | 5.27 ± 1.35 |
| | 8 (6–14) | 3 (1–6)[a] | 5 (3–7)[b] |
| BG/BM | 8.09 ± 2.55 | 3.18 ± 1.83 | 5.09 ± 1.70 |
| | 8 (3–12) | 3 (1–8)[a] | 5 (2–9)[b] |

Wilcoxon signed-rank non-parametric test.
Data are expressed as the mean ± standard deviation and as the median (minimum–maximum).
PP, platelet pellet; BG, bioactive glass; BM, barrier membrane; PPD, probing pocket depth; CAL, clinical attachment level; REC, Recession; RABH, radiological alveolar bone height.
* No significant difference between the groups ($p > 0.05$).
[a] Statistically significant difference from baseline ($p < 0.01$).
[b] No significant difference from post-operative 6-month ($p > 0.05$).
[c] No significant difference from baseline ($p > 0.05$).

score at 5 years were not statistically different from baseline scores ($p > 0.05$), as depicted in Table II.

*Main outcome measurements*

The changes in CAL, PPD, gingival recession and radiological alveolar bone height between the baseline, 6-month and 5-year evaluations are reported in Table III. Between baseline and 6 months, there was a mean PPD reduction of 4.36 ± 0.81 mm in PP/BM group and 4.73 ± 1.19 mm in BG/BM group. The mean gains in CAL and in radiological alveolar bone height during this evaluation period were 4.18 ± 0.75 mm and 5.36 ± 1.69 mm for the defects treated with PP/BM and 4.45 ± 1.29 mm and 4.91 ± 1.70 mm for the defects treated with BG/BM. At 5 years; PPD reductions and CAL and radiological alveolar bone height gains rebounded slightly in both groups. There was a mean PPD reduction of 2.91 ± 0.94 mm for the PP/BM group and 3.45 ± 0.93 mm for the BG/BM group and a mean CAL and radiological alveolar bone height gain of 2.36 ± 0.92 mm and 3.45 ± 1.81 mm for the defects treated with PP/BM and 2.64 ± 1.12 mm and 3.00 ± 1.48 mm for the defects treated with BG/BM. When intra-group differences were evaluated; these PPD reductions and CAL and radiological alveolar bone height gains were statistically significant between baseline and 6 months and between baseline and 5 years in both groups ($p < 0.01$). Although seven treated defects in group PP/BM and six treated defects in group BG/BM with respect to the CAL gain deteriorated after 5 years compared to the 6 months data, no significant differences were found between 6 months and 5 years in any of the parameters evaluated in both groups ($p > 0.05$) (Table IV). Also, no statistically significant difference in any of the clinical parameters was observed at 6 months and 5 years between the groups regarding to the inter-group comparisons ($p > 0.05$).

The distribution of the subjects in both groups according to CAL gain and PPD reduction at 6 months and 5 years is shown in Tables IV and V, respectively. The radiological images at baseline, 6 months, and 5 years are also shown in Figures 1 and 2.

## Discussion

The present study evaluated the long-term effect of PP/BM and BG/BM combinations in the treatment of intra-bony periodontal defects. This randomized clinical study used a split-mouth design, considering the subject as the experimental unit of analysis since each subject provided two intra-bony defects, one for PP/BM treatment and one for BG/BM treatment. No clinical and radiological differences in any of the investigated parameters were observed at all periods

Table IV. Frequency distribution of CAL gains ($n$ [%]).

| | CAL gain: Baseline–6 months | | | CAL gain: Baseline–5 years | | |
|---|---|---|---|---|---|---|
| | CAL gain < 2 mm | 2 mm ≤ CAL gain < 4 | CAL gain ≥ 4 mm | CAL gain < 2 mm | 2 mm ≤ CAL gain < 4 | CAL gain ≥ 4 mm |
| PP/BM | — | 2 (18%) | 9 (82%) | 1 (9%) | 8 (73%) | 2 (18%) |
| BG/BM | — | 2 (18%) | 9 (82%) | 2 (18%) | 6 (55%) | 3 (27%) |

PP, platelet pellet; BG, bioactive glass; BM, barrier membrane; CAL, clinical attachment level.

Table V. Frequency distribution of PPD reduction (*n* [%]).

| | PPD reduction: Baseline–6 months | | | PPD reduction: Baseline–5 years | | |
|---|---|---|---|---|---|---|
| | PPDr < 3 mm | 3 mm ≤ PPDr ≤ 5 | PPDr ≥ 6mm | PPDr < 3 mm | 3 mm ≤ PPDr ≤ 5 | PPDr ≥ 6mm |
| PP/BM | — | 10 (91%) | 1 (9%) | 4 (36%) | 7 (64%) | — |
| BG/BM | — | 9 (82%) | 2 (18%) | 2 (18%) | 9 (82%) | — |

PP, platelet pellet; BG, bioactive glass; BM, barrier membrane; PPD, probing pocket depth; PPDr, probing pocket depth reduction.

evaluated between the two treatment modalities. Our previous randomized clinical trial was planned to investigate whether platelet concentrate would have an effect similar to graft materials when used in conjunction with guided tissue regeneration membranes in periodontal regeneration. This is the first long-term report on the use of PP/BM combination in intra-bony periodontal defects for regeneration.

Our previous clinical report with 6-month period is the only study using combination of PP/BM in the treatment of intra-bony defects and comparing this treatment modality to BG/BM treatment. Data suggest that PP may be as effective as bioactive glass graft materials and may be used as graft materials for treating periodontal defects when combined with guided tissue regeneration. When these long-term results were taken into consideration, there is a positive correlation with the findings of our previous clinical study.

It is important to also consider that there was a small rebound in the periodontal parameters between 6 months and 5 years. There is a direct relationship between deterioration of the periodontal clinical parameters and the lack of subject compliance in fulfilling the required recall regimen and in maintaining adequate plaque-control practices [34]. Subject compliance is important, as erratic compliers required more periodontal re-treatment and had a greater risk for recurrent periodontitis, even if they had completed the treatment plan [35–37]. Erratic compliers (three subjects) were excluded from this long-term trial. One subject moved to another city and this study was completed with 11 subjects. There is evidence from long-term studies that compliance with a regular periodontal supportive care program and smoking are important prognostic factors in regenerative periodontal therapy [33,37–40]. All subjects were non-smokers and performed a prescribed oral hygiene and recall regimen in the present study. From a clinician's perspective, it is notable that a slight rebound in periodontal parameters can be negligible since there is no statistically significant difference in the values of clinical and radiological parameters between 6 months and 5 years.

The scientific literature clearly shows that most of the failures in regenerative therapy were explained with negative patient factors, sub-optimal use of surgical approaches and materials and insufficient clinical skill and experience of the surgeon [41–45]. To overcome the cited problems, similar vertical periodontal osseous defects in each of two contralateral quadrants were recruited in a carefully selected patient population and the experienced clinicians performed surgical procedures within a strict periodontal supportive care program in the present study.

The following conclusions can be drawn from the present study:

(1) Regenerative periodontal therapies (PP covered with a bioabsorbable barrier membrane and

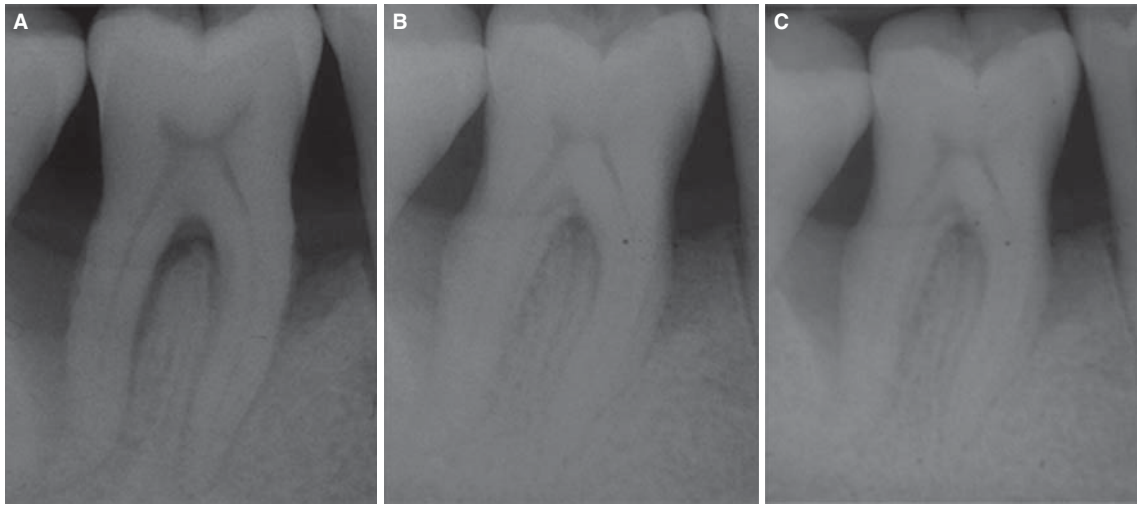


Figure 1. Radiographic appearances ofaosseous defect treated with PP/BM. (A) Baseline; (B) Post-operative 6-months; (C) Post-operative 5-years.

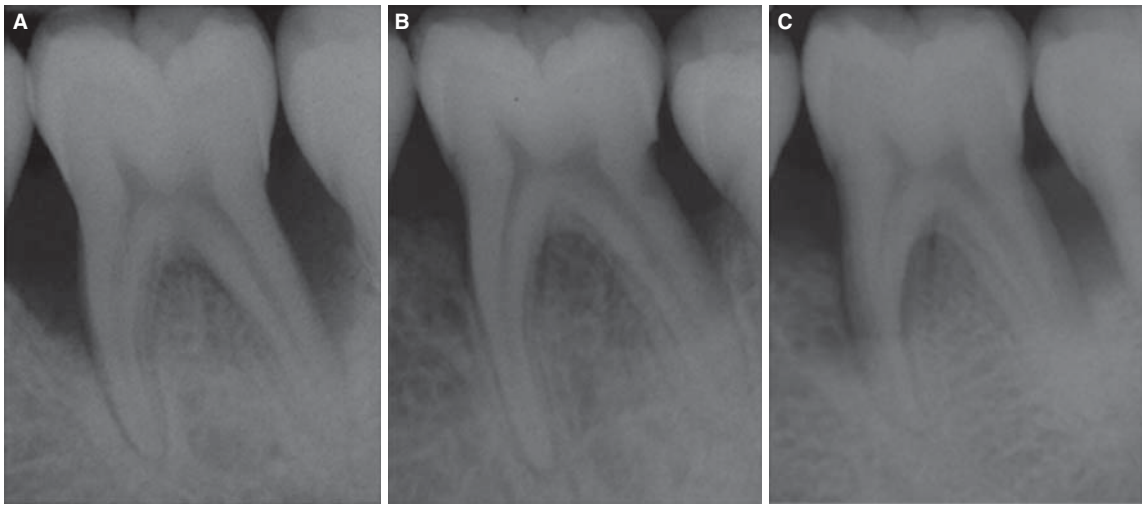


Figure 2. Radiographic appearances of an intraosseous defect treated with BG/BM. (A) Baseline; (B) Post-operative 6-months; (C) Post-operative 5-years.

bioactive glass grafting material covered with a bioabsorbable barrier membrane) resulted in favorable clinical healing in 11 subjects during the 5-year follow-up period.

(2) No clinical and radiological differences in any of the investigated parameters were observed at all periods evaluated between the two regenerative treatments.

(3) A slight worsening of periodontal parameters in 5 years can be negligible, since there is no statistically significant difference in the values of clinical and radiological parameters between 6 months and 5 years.

(4) The long-term efficacy of platelet concentrate combined with a barrier membrane is similar with the combination of bioactive glass graft material and barrier membrane, suggesting that the results obtained with both treatment approaches can be maintained over a period of 5 years.

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