# FIFTEEN-YEAR ASSESSMENT OF COMBINED REGENERATIVE THERAPIES WITH GUIDED TISSUE REGENERATION, BONE GRAFTS, AND PLATELET-RICH PLASMA FOR VERTICAL BONE REGENERATION: A SYSTEMATIC REVIEW

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## ABSTRACT

**Aim of the study** Every day in their practice, dentists are introduced to new, modern biological materials. Some of these materials have managed to overcome some of the shortcomings of those used to date and are becoming commercially available as an alternative regenerative option. Others, however, are disappearing very quickly due to their unremarkable effectiveness. At the same time as these biomaterial developments, new regenerative approaches are continually being proposed to provide predictable, post-operative results. The purpose of this systematic review is to summarize which methods involving various combinations of guided tissue regeneration (GTR), bone grafts and platelet-rich plasma (PRP) have been most preferred in the treatment of vertical bone defects. **Materials and methods.** Web of Science, Scopus and PubMed were the electronic databases that were screened for publications related to the topic of this study for the period from 1 January 2010 to 1 January 2025.) **Results** Twenty-three studies were included in this systematic review. It presents a summary of the most preferred surgical approaches combining guided tissue regeneration, bone grafts and platelet-rich plasma in the treatment of vertical bone defects and analyses their efficacy according to well-defined investigated parameters - probing depth, clinical level of attachment and bone filling. **Conclusions** It became clear that the most used combination method among the sought after is the one in which bone-repair materials and platelet-rich plasma are jointly applied. It would be good for future studies to pay more attention to other combined techniques including guided tissue regeneration, bone grafts and platelet-rich plasma to conclude whether they would be alternative methods in regenerative periodontal therapy.

**Key words:** Bone grafts, Combined regenerative therapy, Guided tissue regeneration, Intrabony periodontal defects, Platelet rich plasma, Regenerative periodontal therapy

## INTRODUCTION

Alveolar bone defects can be a result of traumatic, neoplastic, or infectious processes and sometimes their regeneration is extremely challenging [1-4]. To address the needs for abundant, biocompatible materials with improved mechanical and biological properties, novel materials and techniques have been constantly introduced. Their safety and effectiveness has been first validated by preclinical studies using clinical, radiological, histological and histomorphometric evaluation [5- 7].

Globally, periodontal disease is one of the most prevalent conditions and at the same time the most neglected. If timely measures are not taken to eliminate or minimize the effects of periodontopathogenic microorganisms, the prognosis, diagnosis and treatment of affected teeth are dramatically complicated [8].

In many clinical situations, problems related to periodontal structures can be solved by non-surgical periodontal therapy [9-11].

In the presence of a vertical bone defect, the progression and deepening of periodontitis develops very rapidly [12, 13].


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For more than 50 years, research has been conducted to achieve the complete regeneration of the periodontium, including hard components (cementum and alveolar bone) and soft components (periodontal ligament). Today, certain surgical techniques involving guided tissue regeneration (GTR), bone grafts and growth factors are approved for use [14, 15]. Their sole application has limited indications and the results they lead to in most cases are not satisfactory [16-18].

Nowadays, platelet-rich plasma (PRP) is increasingly used in various fields of medicine and dentistry [19-22]. This autogenous material has become a proven alternative source of growth factors that are fundamental to the success of regenerative procedures in periodontology [19, 23- 26].

Regenerative periodontal procedures that combine PRP-sourced growth factors with other proven regenerative materials, such as barrier membranes and bone-repair materials, have synergistic potential for comprehensive periodontal regeneration [17, 20, 27]. The combined regenerative methods to be studied in this systematic review are presented in Figure 1.

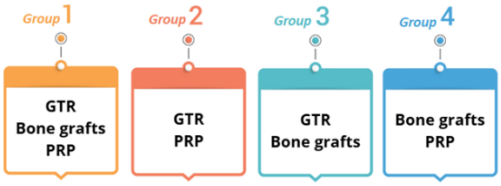


**Figure 1. Investigated combined methods`**

This systematic review aims to identify which of these four combined methods has been most preferred in the treatment of vertical bone defects over the past 15 years and to assess and compare their effectiveness by examining the parameters of probing depth, clinical attachment level and bone fill.

## MATHERIALS AND METHODS

This study is registered in the international prospective register of systematic reviews (PROSPERO, ID: CRD42025645989).

### 1. Eligibility Criteria

The systematic review included only clinical trials (randomized and non-randomized), and case reports for the last 15 years (from 1.01.2010 to 1.01.2025) containing the predefined keywords.

### 2. Information Sources

The conduct of this systematic review is in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [28].

A comprehensive search for papers across multiple online databases (Web of Science, Scopus, and PubMed) was performed on 2 February 2025.

### 3. Search Strategy

Only full-text clinical trials and case reports published in English were included in the study. The electronic search approach included an advanced search through the chosen databases:

- • In the Web of Science database, the formula including the following keywords was applied and 203 publications matching the criteria were found:

((((((((((TS=(Regenerative periodontal therapy)) AND TS=(Intrabony periodontal defects)) AND TS=(Combined regenerative therapy)) OR TS=(Guided tissue regeneration)) AND TS=(Bone grafts)) AND TS=(Platelet rich plasma)) OR TS=(Guided tissue regeneration)) AND TS=(Platelet rich plasma)) OR TS=(Guided tissue regeneration)) AND TS=(Bone grafts)) OR TS=(Bone grafts)) AND TS=(Platelet rich plasma)

- In the Scopus database, the formula including the following keywords was applied and 434 publications matching the criteria were found:


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( ALL ( regenerative AND periodontal AND therapy ) AND ALL ( intrabony AND periodontal AND defects ) AND ALL ( combined AND regenerative AND therapy ) OR ALL ( guided AND tissue AND regeneration ) AND ALL ( bone AND grafts ) AND ALL ( platelet AND rich AND plasma ) OR ALL ( guided AND tissue AND regeneration ) AND ALL ( platelet AND rich AND plasma ) OR ALL ( guided AND tissue AND regeneration ) AND ALL ( bone AND grafts ) OR ALL ( bone AND grafts ) AND ALL ( platelet AND rich AND plasma ) )

- In the PubMed database, the formula including the following keywords was applied and 161 publications matching the criteria were found:

((((((((((Regenerative periodontal therapy) AND (Intrabony periodontal defects)) AND (Combined regenerative therapy)) OR (Guided tissue regeneration)) AND (Bone grafts)) AND (Platelet rich plasma)) OR (Guided tissue regeneration)) AND (Platelet rich plasma)) OR (Guided tissue regeneration)) AND (Bone grafts)) OR (Bone grafts)) AND (Platelet rich plasma)

**4. Study Selection and Data Collection Process**

All publications were identified, reviewed and analysed for eligibility in this systematic review by three independent reviewers. Article titles, author collective, year of publication and DOI-number were exported from the Web of Science, Scopus and PubMed electronic databases to an MS Excel spreadsheet. After alphabetical ordering, duplicate articles were removed. Publications not found in full-text and those not written in English were also eliminated. Discrepancies among the reviewers were settled through conversation until an agreement was achieved.

## RESULTS AND DISCUSSIONS

The initial number of publications found related to the subject of the systematic review was 798. Subsequently, 110 duplicates were removed. This brings the number of articles to be analysed and assessed for eligibility by the three independent reviewers to 688. Of these, 26 studies were eligible, but 3 were not found in full-text. Finally, 23 clinical studies and case reports that met all eligibility criteria were included in this systematic review. A PRISMA flow diagram visualizing everything described above is presented in Figure 2.

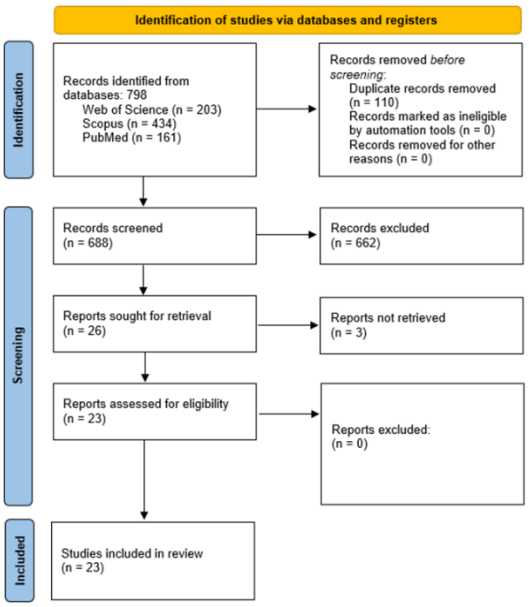


**Figure 2. PRISMA flow diagram**

Table 1 shows all included publications, the combined regenerative methodology they investigated and their results that are relevant to this systematic review.


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| | Study | Study type | Studied combined regenerative method | Bone defects | Number of bone defects | Follow-up period | Mean reduced PPD, mm | Mean CAL gain, mm | Bone sounding, mm |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Sharma et al., 2025 [29] | Randomized Clinical Trial | Allograft, PRP | Intrabony periodontal defects | 15 | 9 months | 4.00 | 3.00 | present, no data |
| 2 | Parihar et al., 2024 [17] | Non-randomized Clinical Trial | Alloplast, PRP | Intrabony periodontal defects | 10 | 6 months | 1.64 | 2.21 | 3.38 |
| 3 | Siddeshappa et al., 2023 [16] | Randomized Clinical Trial | GTR, Alloplast | Intrabony periodontal defects | 10 | 9 months | 5.50 | 5.50 | 4.30 |
| 4 | Satpathy et al., 2023 [30] | Randomized Clinical Trial | Alloplast, PRP | Intrabony periodontal defects | 10 | 6 months | 3.42 | 2.24 | not studied |
| 5 | Liu et al., 2021 [31] | Randomized Clinical Trial | GTR, Xenograft | Intrabony periodontal defects | 14 | 12 months | 6.10 | 4.00 | 4.52 |
| 6 | Tarquini, 2020 [32] | Non-randomized Clinical Trial | GTR, Bone grafts | Intrabony periodontal defects | 22 | 12 months | 5.10 | 4.70 | not studied |
| 7 | Agarwal et al., 2016 [33] | Randomized Clinical Trial | Allograft, PRP | Intrabony periodontal defects | 10 | 12 months | 4.88 | 4.26 | 3.24 |
| 8 | Thakkalapati et al., 2015 [34] | Case Reports | Allograft, PRP | Intrabony periodontal defects | 1 | 6 months | 5.60 | 5.10 | 5.00 |
| 9 | Kukreja et al., 2014 [35] | Randomized Clinical Trial | Allograft, PRP | Intrabony periodontal defects | 10 | 6 months | 4.10 | 3.54 | 2.50 |
| 10 | Pinipe et al., 2014 [36] | Randomized Clinical Trial | Alloplast, PRP | Intrabony periodontal defects | 10 | 6 months | 2.50 | 2.60 | not studied |
| 11 | Agarwal and Gupta, 2014 [37] | Randomized Clinical Trial | Allograft, PRP | Intrabony periodontal defects | 24 | 12 months | 3.65 | 3.15 | 3.02 |
| 12 | Kher et al., 2013 [38] | Randomized Clinical Trial | GTR, Allograft | Intrabony periodontal defects | 10 | 6 months | 4.06 | 3.00 | 2.40 |
| 13 | Döri et al., 2013 [39] | Randomized Clinical Trial | Bone grafts , PRP and EMD | Intrabony periodontal defects | 12 | 12 months | 5.50 | 4.50 | not studied |
| 14 | Hassan et al., 2012 [40] | Randomized Clinical Trial | Autograft, PRP | Intrabony periodontal defects | 12 | 12 months | 4.97 | 3.81 | 1.32 |
| 15 | Ozdemir and Okte, 2012 [41] | Randomized Clinical Trial | Alloplast, PRP | Intrabony periodontal defects | 14 | 6 months | 3.00 | 2.50 | present, no data |
| 16 | Guruprasad et al., 2012 [42] | Case Reports | Alloplast, PRP | Intrabony periodontal defects | 1 | 12 months | 5.00 | 5.00 | present, no data |
| 17 | Rodrigues et al., 2011 [43] | Randomized Clinical Trial | Alloplast, PRP | Intrabony periodontal defects | 10 | 9 months | 4.33 | 4.11 | 2.50 |
| 18 | Saini et al., 2011 [44] | Randomized Clinical Trial | Alloplast, PRP | Intrabony periodontal defects | 20 | 12 months | 3.55 | 3.20 | 3.20 |
| 19 | Kaushick et al., 2011 [45] | Randomized Clinical Trial | Alloplast, PRP | Intrabony periodontal defects | 10 | 6 months | 4.30 | 4.40 | 3.00 |
| 20 | Yilmaz et al., 2011 [46] | Non-randomized Clinical Trial | Xenograft, PRP | Intrabony periodontal defects | 40 | 12 months | 3.87 | 2.51 | 2.11 |
| 21 | Kaur et al., 2010 [47] | Randomized Clinical Trial | Alloplast, PRP | Intrabony periodontal defects | 10 | 6 months | 3.40 | 4.30 | 3.50 |
| 22 | Yilmaz et al., 2010 [48] | Non-randomized Clinical Trial | Xenograft, PRP | Intrabony periodontal defects | 57 | 12 months | 4.63 | 4.06 | 3.67 |
| 23 | Markou et al., 2010 [49] | Case Reports | Allograft, PRP | Intrabony periodontal defects | 3 | 6 months | 2.56 | 2.00 | present, no data |

Table 1. Studied publication and parameters

Risk of bias assessment of the included studies was performed, based on the type of study [50-52] (Figure 3, 4 and 5).

| Study | D1 | D2 | D3 | D4 | D5 | D6 | D7 | Overall |
|---|---|---|---|---|---|---|---|---|
| Parihar et al., 2024 | Y | PY | Y | Y | Y | Y | Y | Some concerns |
| Tarquini, 2021 | Y | Y | Y | Y | Y | Y | Y | Low |
| Yilmaz et al., 2011 | Y | Y | PY | PY | Y | Y | Y | Some concerns |
| Yilmaz et al., 2010 | Y | PY | Y | Y | Y | Y | Y | Some concerns |

**ROBINS-I V2 assessment tool*

D1: Risk of bias due to confounding
D2: Risk of bias in classification of interventions
D3: Risk of bias in selection of participants into the study (or into the analysis)
D4: Risk of bias due to deviations from intended interventions
D5: Risk of bias due to missing data

Figure 3. Risk of bias assessment with ROBINS v2 tool for non-andomized clinical trials


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| Study | D1 | D2 | D3 | D4 | D5 | D6 | D7 | D7 | Overall |
|---|---|---|---|---|---|---|---|---|---|
| Sharma et al., 2025 | Y | PY | PN | PY | PN | Y | Y | Y | Low |
| Siddeshappa et al., 2023 | Y | PY | PN | PY | PN | Y | Y | PY | Some concerns |
| Satpathy et al., 2023 | Y | PY | PN | PY | PY | PY | Y | PN | Some concerns |
| Liu, 2021 | Y | Y | N | PN | N | Y | Y | Y | Low |
| Agarwal et al., 2016 | Y | PY | PN | PY | N | Y | Y | Y | Low |
| Kukreja et al., 2014 | Y | Y | N | PY | PY | Y | Y | PY | Some concerns |
| Pinipe et al., 2014 | Y | PY | PN | PY | N | Y | Y | Y | Low |
| Agarwal and Gupta, 2014 | Y | Y | N | PY | N | PY | Y | PY | Low |
| Kher et al., 2013 | Y | PY | PN | PY | N | Y | Y | Y | Low |
| Döri et al., 2013 | Y | Y | N | N | N | Y | Y | Y | Low |
| Hassan et al., 2012 | Y | PY | PN | PY | PN | Y | Y | PN | Some concerns |
| Ozdemir and Okte, 2012 | Y | Y | PN | PY | PN | Y | Y | PY | Low |
| Rodrigues et al., 2011 | Y | PY | PN | PY | PN | Y | Y | PY | Low |
| Saini et al., 2011 | Y | Y | N | N | N | Y | Y | Y | Low |
| Kaushick et al., 2011 | Y | PY | PN | PY | PN | Y | Y | PN | Some concerns |
| Kaur et al., 2010 | Y | PY | PN | PY | N | Y | Y | Y | Low |

**RoB 2 assessment tool*

D1: Was the allocation sequence random?
D2: Was the allocation sequence concealed until participants were enrolled and assigned to interventions?
D3: Did baseline differences between intervention groups suggest a problem with the randomization process?
D4: Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?
D5: Were there failures in implementing the intervention that could have affected the outcome?
D6: Was an appropriate analysis used to estimate the effect of assignment to intervention?
D7: Were data for this outcome available for all, or nearly all, participants randomized?
D8: Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were

Figure 4. Risk of bias assessment with ROB2 tool for randomized clinical trials

| Study | D1 | D2 | D3 | D4 | D5 | D6 | D7 | D8 | Overall |
|---|---|---|---|---|---|---|---|---|---|
| Thakkalapati et al., 2015 | N | Y | Y | Y | Y | Y | Y | Y | Low |
| Guruprasad et al., 2012 | Y | Y | Y | Y | Y | Y | Y | Y | Low |
| Markou et al., 2010 | Y | Y | Y | Y | Y | Y | Y | Y | Low |

**JBI CRITICAL APPRAISAL CHECKLIST FOR CASE REPORTS*

D1: Were patient's demographic characteristics clearly described?
D2: Was the patient's history clearly described and presented as a timeline?
D3: Was the current clincal condition of the patient clearly described?
D4: Were diagnostic tests or assessment methods and the results clearly described?
D5: Was the intervention(s) or treatment procedure(s) clearly described?
D6: Was the post-intervention clinical condition clearly described?
D7: Were adverse events (harms) or unanticipated events identified and described?
D8: Does the case report provide takeaway lessons?

Figure 5. JBI's critical appraisal checklist for case reports

The distribution of articles by the years in which they were published and by publication type is presented in Figures 6 and 7.

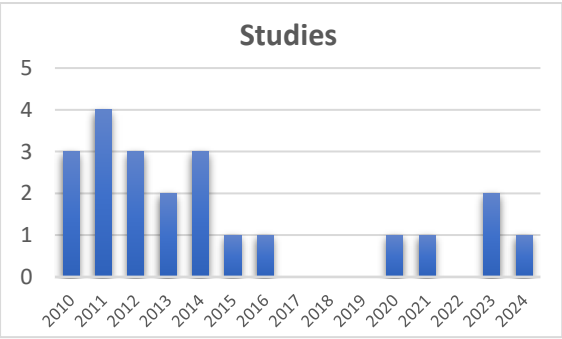


Figure 6. Distribution of articles by publication year

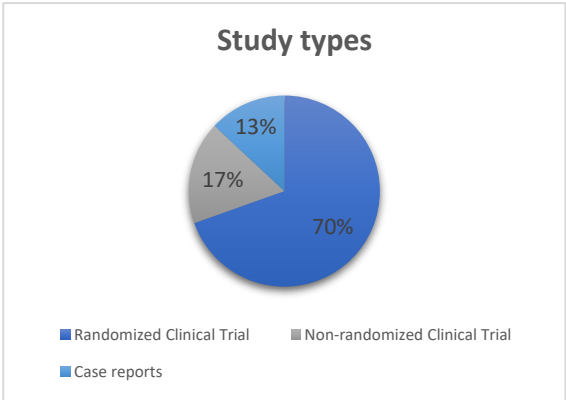


Figure 7. Types of articles studied

It became clear that for the last 15 years, the most preferred combination method in the treatment of vertical bone defects was #4,


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including the synergistic effect of bone repair materials and PRP (19 studies). Four studies were found investigating the results of applied combination method #3 (GTR, Bone grafts). No data were identified in the literature from 2010 to 2025 on studies investigating combined methods #1 (GTR, Bone grafts, PRP) and #2 (GTR, PRP) (Figure 8).

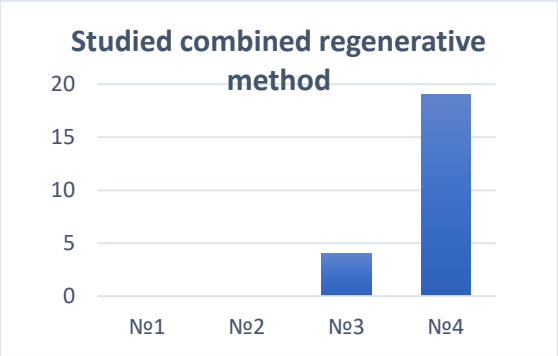



Figure 8. Distribution of articles by applied combined regenerative method

From the 19 studies found and compared that investigated the additive effect of bone-repair materials and PRP (#4 combined method), it is clear that their results according to the parameters investigated – probing pocket depth (PPD), clinical level of attachment (CAL), and bone fill differ. The reason for this may lie in the fact that different types of bone repair material were used in the different studies (Figure 9).

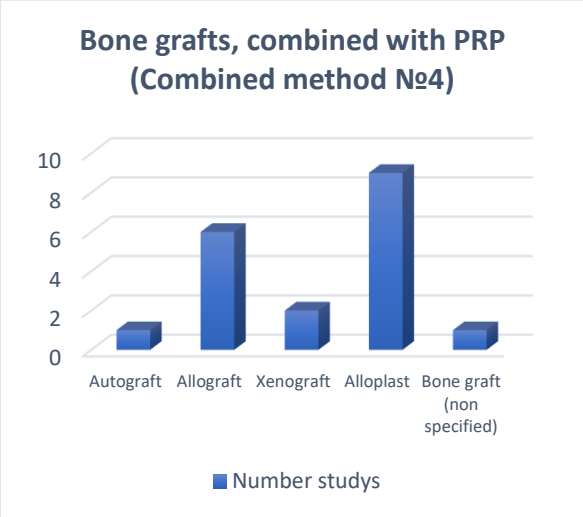
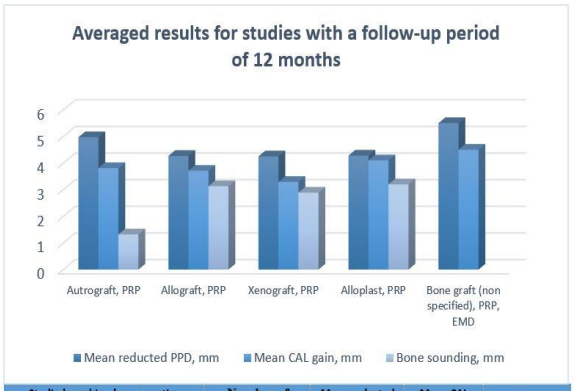


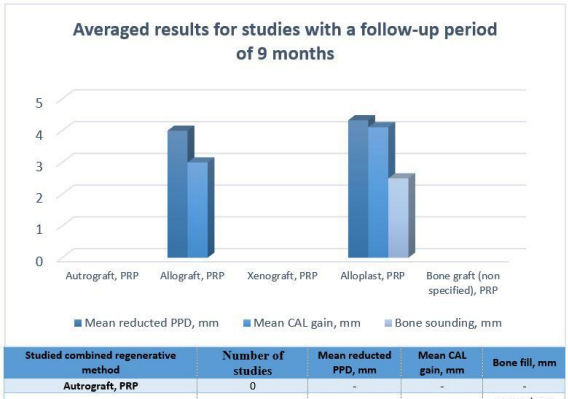

Figure 9. Types of Bone grafts used in combination with PRP, in method No.4

The following figures present the averaged values of reduction of PPD, CAL gain and achieved bone fill in the combined method #4 using different bone graft materials - autograft, allograft, xenograft, allograft or bone grafts (non-specified). For maximum objectivity, the studies were divided according to the follow-up period - 12 months (Figure 10), 9 months (Figure 11) and 6 months (Figure 12)




| Studied combined regenerative method | Number of studies | Mean reducted PPD, mm | Mean CAL gain, mm | Bone fill, mm |
|---|---|---|---|---|
| Autograft, PRP | 1 | 4.97 | 3.81 | 1.32 |
| Allograft, PRP | 2 | 4.27 | 3.71 | 3.13 |
| Xenograft, PRP | 2 | 4.25 | 3.29 | 2.89 |
| Alloplast, PRP | 2 | 4.28 | 4.1 | 3.2 |
| Bone graft (non specified), PRP, EMD | 1 | 5.5 | 4.5 | not studied |

Figure 10. Mean results for reduced PPD, CAL gain and achieved Bone fill, studies with a 12-month follow-up period




| Studied combined regenerative method | Number of studies | Mean reducted PPD, mm | Mean CAL gain, mm | Bone fill, mm |
|---|---|---|---|---|
| Autograft, PRP | 0 | - | - | - |
| Allograft, PRP | 2 | 4.00 | 3.00 | present, no data provided |
| Xenograft, PRP | 0 | - | - | - |
| Alloplast, PRP | 2 | 4.33 | 4.11 | 2.50 |
| Bone graft (non specified), PRP, EMD | 0 | - | - | - |

Figure 11. Mean results for reduced PPD, CAL gain and achieved Bone fill, studies with a 9-month follow-up period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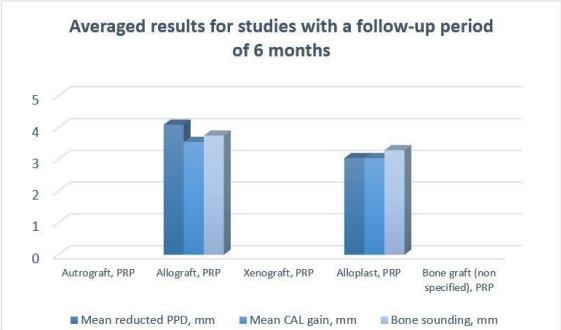


| Studied combined regenerative method | Number of studies | Mean reducted PPD, mm | Mean CAL gain, mm | Bone fill, mm |
|---|---|---|---|---|
| Autograft, PRP | 0 | - | - | - |
| Allograft, PRP | 3 | 4.09 | 3.55 | 3.75 |
| Xenograft, PRP | 0 | - | - | - |
| Alloplast, PRP | 6 | 3.04 | 3.04 | 3.29 |
| Bone graft (non specified), PRP, EMD | 0 | - | - | - |

Figure 12. Mean results for reduced PPD, CAL gain and achieved Bone fill, studies with a 6-month follow-up period

The studies with the combinations, the follow-up period and the results of the indicators - reduction of probing depth, gain of clinical level of attachment and bone filling of the defect in the applied combined method No. 3 - are presented in Table 2.

| Combined method №3 | No of studies | Follow-up period in months | Mean reduced PPD, mm | Mean CAL gain, mm | Bone fill, mm |
|---|---|---|---|---|---|
| **GTR, Autograft** | 0 | - | - | - | - |
| **GTR, Allograft** | 1 | 6 | 4.06 | 3.00 | 2.40 |
| **GTR, Xenograft** | 1 | 12 | 6.10 | 4.00 | 4.52 |
| **GTR, Alloplast** | 1 | 9 | 5.50 | 5.50 | 4.30 |
| **GTR, Bone grafts (non specified)** | 1 | 12 | 5.10 | 4.7 | not studied |

Vertical bone defects are associated with complicating the prognosis and treatment of damaged teeth [53]. Often, these cases are not responded to with nonsurgical periodontal therapy alone and clinicians need to make use of various regenerative approaches [14,27,53].

Modern biological materials used in various fields of medicine and dentistry play a major role in the success of regenerative procedures [1, 20, 54-58].

Today, the palette of regenerative possibilities is not at all small. Increasingly, so-called combined regenerative methods are being applied. These methods are characterised by the joint application of different regenerative methods, such as GTR, bone grafts or bioactive products, which would contribute to synergistic effectiveness and therefore better results [59]. There are many studies that clearly demonstrate the superior performance of combined methods compared to data from materials used alone [16, 17].

This systematic review included 23 articles that met all eligibility criteria. Studies investigating certain four types of combined regenerative methods used in the treatment of vertical bone defects were searched for the last 15 years.

It appears that among the combination methods sought, the most researched is the one in which both bone repair material and PRP are applied (#4). This is most likely due to the ability of bone-repair materials to secure and maintain the defect space, which is not more the capability of the PRP material [15]. At the same time, however, PRP material has a number of biological advantages over bone-repair materials [19, 21, 60]. For these reasons, it can be concluded that the combination of the two types of regenerative materials could lead to more reliable results [59].

A similar explanation would be used for the combined method No. 3, characterized by the simultaneous application of a barrier membrane and bone repair material [59].

According to their origin, bone-repair materials are divided into autogenous, allogeneic, xenogeneic, and alloplastic grafts [15, 61]. In the present work, it is clear that the most preferred combined methodology of


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group #4 is the one using alloplastic material with PRP, followed by the co-application of allogeneic graft and PRP.

From the data obtained, it was found that the combination of PRP with different types of bone repair material produced different results. Thus, after analyzing the studies investigating combination method No. 4 for a period of 12 months, it is clear that regarding the reduction of PPD, the best result was obtained with the combination of autogenous graft and PRP. In terms of CAL gain, the method with bone graft (non-specified), PRP and EMD was the first. In terms of bone filling, the combination of allogenic graft and PRP demonstrated the best result. Similarly, when evaluating the data from studies with a follow-up period of 9 and 6 months, different results were again observed. Consideration should be given to the fact that differences in results may be due not only to the type of bone graft material but also to the method of preparation of the PRP material in the different studies [62].

Lastly, the combined methods included in group #3 for the last 15 years are reviewed in Table 2. It can be clearly seen that each of them has been tracked for a different time period. It would therefore be biased to compare their results.

## CONCLUSIONS

1.Combined regenerative methods are the future of regenerative periodontal therapy. Through them, it is possible to overcome some of the disadvantages that characterize individually applied materials. Moreover, different combinations of biomaterials could contribute to additive, more effective results.

2.In the present systematic review, it is clear that the most used combination method among the four sought after is the one in which bone-repair materials and PRP are jointly applied. The results that were obtained among the studies followed up over a period of 6,9 and 12 months demonstrate the effectiveness of this method.

3.It would be good for future studies to pay more attention to other combined techniques including GTR, bone grafts and PRP to conclude whether they would be alternative methods in regenerative periodontal therapy.

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None

**Disclosure**
The author reports no conflicts of interest in this work.

## REFERENCES

1. Yotsova R, Peev S. Biological Properties and Medical Applications of Carbonate Apatite: A Systematic Review. Pharmaceutics. 2024; 16(2):291. https://doi.org/10.3390/pharmaceutics16020291
2. Yankov YG, Yotsova RV, Stoev L, Nikolaev NI, Dimanov S, Stoeva M. A Case Report of Mandibular Gingival Metastasis From Sigmoid Colon Adenocarcinoma With Phenotypical Transformation Into Neuroendocrine Carcinoma. Cureus. 2024 Jun 21;16(6):e62805. doi: 10.7759/cureus.62805.
3. Yankov YG, Dimanov S, Nikolaev NI, Stoev L, Yotsova RV, Stoeva M. Etiology and Demographic Distribution of Odontogenic Abscesses in the Maxillofacial Area in Patients Over 18 Years of Age: A Five-Year Retrospective Study. Cureus. 2024 Apr 30;16(4):e59334. doi: 10.7759/cureus.59334.
4. Dimanov SN, Stoev AL, Yotsova RV, Stoev LL, Yankov YG, Ruseva YR. A Rare Case of Cementoblastoma of the Second Right Maxillary Premolar in a 30-Year-Old Man. Cureus. 2024 Nov 15;16(11):e73737. doi: 10.7759/cureus.73737.
5. Peev S, Yotsova R, Parushev I. Histomorphometric Analysis of Osseointegrated Intraosseous Dental


DOI : 10.62610/RJOR.2025.2.17.11

Implants Using Undecalcified Specimens: A Scoping Review. Biomimetics (Basel). 2024 Nov 3;9(11):672. doi: 10.3390/biomimetics9110672.

6. Peev S, Parushev I, Yotsova R. A Modified Protocol for Staining of Undecalcified Bone Samples Using Toluidine Blue—A Histological Study in Rabbit Models. Applied Sciences. 2024; 14(1):461. https://doi.org/10.3390/app14010461
7. Yotsova R, Peev S, Ivanova N. Bone histomorphometry as a diagnostic tool. A review article. Scripta Scientifica Medicinae Dentalis. 2023; 9(1), 7-23. doi:http://dx.doi.org/10.14748/ssmd.v9i1.8602
8. Siddeshappa ST, Vemanaradhya GG, Sowmya NK. A clinical investigation to assess the regenerative potential of Biostite® (hydroxyapatite, type-I collagen and chondroitin-sulphate) with or without Paroguide® type-I collagen and chondroitin sulphate) membrane in the treatment of periodontal intrabony defects appraised with surgical re-entry and computer-assisted densitometric image analysis. J Indian Soc Periodontol. 2023;27(5):496-502. doi:10.4103/jisp.jisp_450_22
9. Wang Y, Xia Y, Qian J, Xie Y, Shu R, Lin Z. Native vs. ribosome-crosslinked collagen membranes for periodontal regeneration: A randomized clinical trial. J Periodontal Res. Published online July 4, 2024. doi:10.1111/jre.13321
10. Gerova-Vatsova T, Peev S, Yotsova R. THE RELATIONSHIP BETWEEN PERIODONTAL HEALTH AND FIXED PROSTETHIC RESTORA-TIONS. Journal of IMAB. 2023; 29(4), 4. doi:10.5272/jimab.2023294.5174
11. Gerova-Vatsova T. ORAL PYOGENIC GRANULOMA - MODERN TREATMENT APPROACHES. In: Joint Forum: 14-th SEEC & 34-th IMAB. Journal of IMAB - Annual Proceeding (Scientific Papers); 2024:40-43. doi:10.5272/jimab.2024v30Supplement2
12. Sanz M, Herrera D, Kebschull M, et al. Treatment of stage I-III periodontitis-The EFP S3 level clinical practice guideline [published correction appears in J Clin Periodontol. 2021 Jan;48(1):163. doi:10.1111/jcpe.13290
13. Gerova-Vatsova T. FLAP DESIGNS FOR PERIODONTAL REGENERATIVE THERAPY. In: Joint Forum: 14-th SEEC & 34-th IMAB. Journal of IMAB - Annual Proceeding (Scientific Papers); 2024:32-35. doi:10.5272/jimab.2024v30Supplement2
14. Gerova-Vatsova T. Initial clinical and cone-beam computed tomography (CBCT) outcomes of enamel matrix derivative-based regenerative therapy in vertical bone defects. Cureus. 2024;16(10), e72180. doi:10.7759/cureus.72180
15. Miteva M, Gerova T. Bone repair materials used in guided tissue regeneration-advantages and disadvantages. Int J Sci Res. 2019;8(10), 1490-94. doi: 10.21275/ART20202214.
16. Siddeshappa ST, Vemanaradhya GG, Sowmya NK. A clinical investigation to assess the regenerative potential of Biostite® (hydroxyapatite, type-I collagen and chondroitin-sulphate) with or without Paroguide® type-I collagen and chondroitin sulphate) membrane in the treatment of periodontal intrabony defects appraised with surgical re-entry and computer-assisted densitometric image analysis. J Indian Soc Periodontol. 2023;27(5):496-502. doi:10.4103/jisp.jisp_450_22
17. Parihar AS, Preethanath RS, Khan N, Mohapatra A, Reshma AP, Seshadri PR, Awinashe MV. Assessment of Platelet-Rich Plasma Alone and Platelet-Rich Plasma Combined with Bioactive Glass in the Management of Intrabony Defect. J Pharm Bioallied Sci. 2024 Feb;16(Suppl 1):S933-S935. doi: 10.4103/jpbs.jpbs_1100_23. Epub 2024 Feb 29. PMID: 38595565; PMCID: PMC11000911.
18. Iwata T, Yamato M, Ishikawa I, Ando T, Okano T. Tissue engineering in periodontal tissue. Anat Rec (Hoboken). 2014;297(1):16-25. doi:10.1002/ar.22812
19. Gerova-Vatsova T, Peev S. Application of platelet-rich plasma (PRP) for regeneration of vertical bone defects. Journal of IMAB–Annual Proceeding Scientific Papers. 2023;29(3), 5103-5107. doi:10.5272/jimab.2023293.5103
20. Gerova-Vatsova T. Beyond Bone Grafts: Exploring the Efficacy of Alternative Regenerative Therapies. Cureus. 2024;16(11), e73745. doi:10.7759/cureus.73745
21. Peev S, Atanasov D. Platelet-rich plasma–an accelerator of the secondary stability of immediate loaded implants. J IMAB. 2007;13(2):38-40.
22. Yotsova RV. Socket Preservation Using Dense Polytetrafluoroethylene Membranes and Platelet-Rich Plasma. Cureus. 2024 Oct 24;16(10):e72265. doi: 10.7759/cureus.72265.
23. Gerova-Vatsova T, Peev S. Application of autogenous platelet-rich plasma in periodontology. Scripta



DOI : 10.62610/RJOR.2025.2.17.11

Scientifica Medicinae Dentalis.2023; 9(1), 43-50. doi:10.14748/ssmd.v9i1.8753
24. Everts P, Onishi K, Jayaram P, Lana JF, Mautner K. Platelet-Rich Plasma: New Performance Understandings and Therapeutic Considerations in 2020. Int J Mol Sci. 2020;21(20):7794. Published 2020 Oct 21. doi:10.3390/ijms21207794
25. Egle K, Salma I, Dubnika A. From Blood to Regenerative Tissue: How Autologous Platelet-Rich Fibrin Can Be Combined with Other Materials to Ensure Controlled Drug and Growth Factor Release. Int J Mol Sci. 2021;22(21):11553. Published 2021 Oct 26. doi:10.3390/ijms222111553
26. Niemczyk W, Janik K, Żurek J, Skaba D, Wiench R. Platelet-Rich Plasma (PRP) and Injectable Platelet-Rich Fibrin (i-PRF) in the Non-Surgical Treatment of Periodontitis-A Systematic Review. Int J Mol Sci. 2024;25(12):6319. Published 2024 Jun 7. doi:10.3390/ijms25126319
27. Gerova-Vatsova T. Investigating the efficacy of regenerative therapy with autogenous platelet-rich plasma in vertical bone defects. Cureus.2024; 16(10), e72686. doi:10.7759/cureus.72686
28. Sarkis-Onofre R, Catalá-López F, Aromataris E, Lockwood C. How to properly use the PRISMA Statement. Systematic Reviews 10. 2021; 1-3.
29. Sharma S, Bhardwaj A, Kaur M. Comparative Analysis of Efficacy of Activated Platelet-rich Plasma along with Demineralized Freeze-dried Bone Allograft in Periodontal Intrabony Defects: A Pilot Study. World Journal of Dentistry. 2025;15(9):762-766. doi:10.5005/jp-journals-10015-2493
30. Satpathy S, Gupta J, Tenglikar P, et al. Evaluation of Bone Graft (Hydroxyapatite + Platelet-Rich Plasma) Alone and in Combination with Diode Laser in Management of Infrabony Defect. J Pharm Bioallied Sci. 2023;15(Suppl 2):S1230-S1232. doi:10.4103/jpbs.jpbs_151_23
31. Liu K, Huang Z, Chen Z, Han B, Ouyang X. Treatment of periodontal intrabony defects using bovine porous bone mineral and guided tissue regeneration with/without platelet-rich fibrin: A randomized controlled clinical trial. J Periodontol. 2021;92(11):1546-1553. doi:10.1002/JPER.20-0860
32. Tarquini G. Treatment of Intrabony Defects Using Equine-derived Bone Granules and Collagen Membranes: A Retrospective Study with a 13-year Follow-up. J Contemp Dent Pract. 2020;21(9):970-976. Published 2020 Sep 1.
33. Agarwal P, Chatterjee A, Gokhale S, Singh HP, Kandwal A. Evaluation of platelet-rich plasma alone or in combination with demineralized freeze dried bone allograft in treatment of periodontal infrabony defects: A comparative clinical trial. J Indian Soc Periodontol. 2016;20(1):42-47. doi:10.4103/0972-124X.170811
34. Thakkalapati P, R Chandran C, Ranganathan AT, Jain AR, Prabhakar P, Padmanaban S. Management of a One-wall Intrabony Osseous Defect with Combination of Platelet Rich Plasma and Demineralized Bone Matrix- a Two-year Follow up Case Report. J Dent (Shiraz). 2015 Sep;16(3):219-23. PMID: 26331153; PMCID: PMC4554316.
35. Kukreja BJ, Dodwad V, Kukreja P, Ahuja S, Mehra P. A comparative evaluation of platelet-rich plasma in combination with demineralized freeze-dried bone allograft and DFDBA alone in the treatment of periodontal intrabony defects: A clinicoradiographic study [retracted in: J Indian Soc Periodontol. 2014 Jul;18(4):425.]. J Indian Soc Periodontol. 2014;18(5):618-623. doi:10.4103/0972-124X.142457
36. Pinipe J, Mandalapu NB, Manchala SR, Mannem S, Gottumukkala NV, Koneru S. Comparative evaluation of clinical efficacy of β-tri calcium phosphate (Septodont-RTR)™ alone and in combination with platelet rich plasma for treatment of intrabony defects in chronic periodontitis. J Indian Soc Periodontol. 2014;18(3):346-351. doi:10.4103/0972-124X.134573
37. Agarwal A, Gupta ND. Platelet-rich plasma combined with decalcified freeze-dried bone allograft for the treatment of noncontained human intrabony periodontal defects: a randomized controlled split-mouth study. Int J Periodontics Restorative Dent. 2014;34(5):705-711. doi:10.11607/prd.1766
38. Kher VK, Bhongade ML, Shori TD, Kolte AP, Dharamthok SB, Shrirao TS. A comparative evaluation of the effectiveness of guided tissue regeneration by using a collagen membrane with or without decalcified freeze-dried bone allograft in the treatment of infrabony defects: A clinical and radiographic study. J Indian Soc Periodontol. 2013;17(4):484-489. doi:10.4103/0972-124X.118321
39. Döri F, Arweiler N, Húszár T, Gera I, Miron RJ, Sculean A. Five-year results evaluating the effects of platelet-rich plasma on the healing of intrabony defects treated with enamel matrix derivative and natural bone mineral. J Periodontol. 2013;84(11):1546-1555. doi:10.1902/jop.2013.120501



DOI : 10.62610/RJOR.2025.2.17.11

40. Hassan KS, Alagl AS, Abdel-Hady A. Torus mandibularis bone chips combined with platelet rich plasma gel for treatment of intrabony osseous defects: clinical and radiographic evaluation. Int J Oral Maxillofac Surg. 2012;41(12):1519-1526. doi:10.1016/j.ijom.2012.02.009
41. Ozdemir B, Okte E. Treatment of intrabony defects with beta-tricalciumphosphate alone and in combination with platelet-rich plasma. J Biomed Mater Res B Appl Biomater. 2012;100(4):976-983. doi:10.1002/jbm.b.32660
42. Guruprasad CN, Pradeep AR, Agarwal E. Use of Platelet-Rich Plasma Combined With Hydroxyapatite in the Management of a Periodontal Endosseous Defect Associated With a Palato-Radicular Groove: A Case Report. Clin Adv Periodontics. 2012;2(1):28-33. doi:10.1902/cap.2011.110028
43. Rodrigues SV, Acharya AB, Thakur SL. An evaluation of platelet-rich plasma without thrombin activation with or without anorganic bone mineral in the treatment of human periodontal intrabony defects. Platelets. 2011;22(5):353-360. doi:10.3109/09537104.2011.552135
44. Saini N, Sikri P, Gupta H. Evaluation of the relative efficacy of autologous platelet-rich plasma in combination with β-tricalcium phosphate alloplast versus an alloplast alone in the treatment of human periodontal infrabony defects: a clinical and radiological study. Indian J Dent Res. 2011;22(1):107-115. doi:10.4103/0970-9290.80008
45. Kaushick BT, Jayakumar ND, Padmalatha O, Varghese S. Treatment of human periodontal infrabony defects with hydroxyapatite + β tricalcium phosphate bone graft alone and in combination with platelet rich plasma: a randomized clinical trial. Indian J Dent Res. 2011;22(4):505-510. doi:10.4103/0970-9290.90278
46. Yilmaz S, Kabadayi C, Ipci SD, Cakar G, Kuru B. Treatment of intrabony periodontal defects with platelet-rich plasma versus platelet-poor plasma combined with a bovine-derived xenograft: a controlled clinical trial. J Periodontol. 2011;82(6):837-844. doi:10.1902/jop.2010.100503
47. Kaur M, Ramakrishnan T, Amblavanan N, Emmadi Pamela. Effect of platelet-rich plasma and bioactive glass in the treatment of intrabony defects - a split-mouth study in humans. Brazilian Journal of Oral Sciences. 2010; 9(2), 106-114. https://doi.org/10.20396/bjos.v9i2.8641885
48. Yilmaz S, Cakar G, Ipci SD, Kuru B, Yildirim B. Regenerative treatment with platelet-rich plasma combined with a bovine-derived xenograft in smokers and non-smokers: 12-month clinical and radiographic results. J Clin Periodontol. 2010;37(1):80-87. doi:10.1111/j.1600-051X.2009.01509.x
49. Markou N, Pepelassi E, Kotsovilis S, Vrotsos I, Vavouraki H, Stamatakis HC. The use of platelet-rich plasma combined with demineralized freeze-dried bone allograft in the treatment of periodontal endosseous defects: a report of two clinical cases. J Am Dent Assoc. 2010;141(8):967-978. doi:10.14219/jada.archive.2010.0310
50. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. Published 2019 Aug 28. doi:10.1136/bmj.l4898
51. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016;355:i4919. Published 2016 Oct 12. doi:10.1136/bmj.i4919
52. "Moola S, Munn Z, Tufanaru C, et al. Chapter 7: Systematic reviews of etiology and risk. In: Aromataris E, Munn Z (Editors). Joanna Briggs Institute Reviewer's Manual. The Joanna Briggs Institute, 2017."
53. Gerova-Vatsova T. Treatment approach to generalized severe periodontitis with the potential for additional tooth loss: a case report. Cureus. 2024; 16(11), e73336. doi:10.7759/cureus.73336
54. Yotsova RV, Papanchev GY, Ali M, Gerova-Vatsova T. Open Barrier Membrane Technique for the Treatment of Oroantral Communications: Two Case Reports. Cureus. 2024;16(7):e63854. Published 2024 Jul 4. doi:10.7759/cureus.63854
55. Yotsova R. Socket Sealing Using Free Gingival Grafts: A Randomized Controlled Trial. Dentistry Journal. 2025; 13(1):24. https://doi.org/10.3390/dj13010024
56. Gerova-Vatsova T. The efficacy of collagen barrier membranes in regenerating vertical bone defects: a clinical and cone beam computed tomography (CBCT) assessment. Cureus. 2024;16(10), e72550. doi:10.7759/cureus.72550
57. Parushev I, Gerova-Vatsova T. Methods for obtaining synthetic carbonate apatite for bone



DOI : 10.62610/RJOR.2025.2.17.11

regeneration: A review. Scripta Scientifica Medicinae Dentalis. 2025; 11(1). doi:http://dx.doi.org/10.14748/ssmd.v11i1.9879

58. Yotsova R. MANAGEMENT OF AN OROANTRAL COMMUNICATION USING A NONRESORBABLE PTFE MEMBRANE (OPEN BARRIER MEMBRANE TECHNIQUE).In: Joint Forum: 14-th SEEC & 34-th IMAB. Journal of IMAB - Annual Proceeding (Scientific Papers); 2024:36-39. doi:10.5272/jimab.2024v30Supplement2
59. Cortellini P, Tonetti MS. Clinical concepts for regenerative therapy in intrabony defects. Periodontol 2000. 2015;68(1):282-307. doi:10.1111/prd.12048
60. Prokurat M, Grudnik K, Niemczyk W, et al. Platelet-Rich Plasma - a remedy present in every human being. History, functioning, and the benefits of therapy using it. Pol Merkur Lekarski. 2024;52(2):240-245. doi:10.36740/Merkur202402114
61. Rogova VV, Peev S, Yotsova R, Gerova-Vatsova T, Parushev I. Histomorphometric Assessment of Non-Decalcified Plastic-Embedded Specimens for Evaluation of Bone Regeneration Using Bone Substitute Materials-A Systematic Review. Materials (Basel). 2024 Dec 30;18(1):119. doi: 10.3390/ma18010119.
62. Weibrich G, Kleis WK, Hafner G, Hitzler WE, Wagner W. Comparison of platelet, leukocyte, and growth factor levels in point-of-care platelet-enriched plasma, prepared using a modified Curasan kit, with preparations received from a local blood bank. Clin Oral Implants Res. 2003;14(3):357-362. doi:10.1034/j.1600-0501.2003.00810.x



DOI : 10.62610/RJOR.2025.2.17.11