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INTEGRATION OF GUIDED BONE REGENERATION AND PRF TECHNOLOGY IN THE TREATMENT OF COMPLEX ORAL CAVITY DEFECTS

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Abstract: Complex oral cavity defects that involve simultaneous bone and soft tissue loss represent one of the greatest challenges in maxillofacial regenerative surgery. Guided Bone Regeneration (GBR) has been widely used to reconstruct alveolar bone structures, but it lacks intrinsic biological stimulation for soft tissue healing and angiogenesis. Platelet-Rich Fibrin (PRF), an autologous platelet concentrate rich in growth factors, offers a biologically active scaffold that enhances both hard and soft tissue regeneration. This prospective clinical study involved 40 patients with critical-sized alveolar defects, divided into two groups: one treated with GBR alone, and the other with GBR plus PRF membranes. Clinical healing, radiographic bone volume and density (via CBCT), and histological regeneration were evaluated over a 6-month period. The results showed that the GBR + PRF group achieved significantly greater bone gain (3.8 mm vs 3.1 mm), higher bone density, faster mucosal healing, and more new bone formation compared to the GBR-only group. These findings support the integration of PRF into GBR protocols as a cost-effective, biologically intelligent approach, especially in settings with limited access to synthetic biomaterials. The study highlights PRF's clinical potential in enhancing regenerative outcomes and promoting reliable implant site development.

Keywords: Guided Bone Regeneration (GBR); Platelet-Rich Fibrin (PRF); alveolar ridge augmentation; bone regeneration; soft tissue healing; angiogenesis; autologous biomaterials; CBCT; histological analysis; oral implantology.

Introduction

The rehabilitation of complex oral cavity defects, which simultaneously affect alveolar bone structures and adjacent soft tissues, remains a paramount challenge in contemporary oral and maxillofacial surgery. These defects may arise as a result of various etiological factors, including traumatic injuries, oncologic resections, congenital malformations such as cleft palate, and advanced periodontal or periapical infections that have led to extensive hard and soft tissue resorption. Beyond compromising aesthetics and oral function—including mastication, phonation, and facial symmetry—these defects also significantly reduce the success rates of dental implants, prosthetic restorations, and long-term oral rehabilitation. Conventional treatment approaches often involve the use of Guided Bone Regeneration (GBR), a technique that employs barrier membranes to protect the defect site from soft tissue invasion, thereby allowing osteogenic cells to proliferate and regenerate the lost bone. GBR has become a mainstay in implant dentistry due to its predictability, biocompatibility, and flexibility in treating horizontal and vertical ridge defects. However, its primary limitation lies in the fact that GBR is fundamentally a mechanical intervention: it provides spatial

guidance and scaffold for osteogenesis but lacks biological stimuli essential for soft tissue regeneration, angiogenesis, and immunomodulation. Especially in critical-sized defects or in medically compromised patients, GBR alone may not ensure adequate neovascularization or early-stage mucosal integration, both of which are crucial for graft stability and tissue remodeling. These shortcomings become even more pronounced in large or multi-dimensional defects, where complex interactions between the soft and hard tissues demand a more integrated regenerative strategy that addresses both biological and biomechanical aspects of healing.

In response to these challenges, research in recent years has turned toward biologically active regenerative adjuncts—particularly those derived from autologous blood components—which can enhance tissue healing through intrinsic cellular and molecular mechanisms. Among the most promising of these is Platelet-Rich Fibrin (PRF), a second-generation platelet concentrate that can be obtained quickly and cost-effectively through centrifugation of the patient's own blood without anticoagulants or additives. PRF contains a dense fibrin matrix that entraps high concentrations of platelets, leukocytes, and regenerative cytokines such as vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and transforming growth factor beta (TGF-β1). These growth factors are gradually released over a sustained period, facilitating a cascade of biological processes including angiogenesis, fibroblast migration, epithelialization, and collagen synthesis. PRF has been widely applied in sinus lifting, socket preservation, periodontal regeneration, and soft tissue grafting, demonstrating reduced inflammation, accelerated wound closure, and improved patient-reported outcomes. However, the integrated use of PRF with GBR in complex alveolar defects—particularly those requiring concurrent vertical and horizontal ridge augmentation—remains underexplored. Existing literature such as that of Simonpieri et al. (2009), Dohan Ehrenfest et al. (2012), and Miron et al. (2016) offer preliminary insights into PRF's potential, but there is a lack of high-quality, controlled studies that evaluate the clinical, radiographic, and histological outcomes of this integrative approach across different patient populations and surgical contexts. Moreover, in geographical settings such as Uzbekistan, where patient access to commercial graft materials may be limited due to economic or logistical constraints, PRF presents a viable, low-cost, and autologous alternative for enhancing regenerative therapies. There is a pressing need for localized research that not only investigates the efficacy of PRF and GBR individually, but also evaluates their synergistic potential when used simultaneously in high-risk or complex clinical scenarios. The conceptual underpinning of this study is grounded in tissue engineering triad principles—scaffold, signaling molecules, and responsive cells—where GBR provides the structural framework, and PRF delivers biologically active signaling within a patient-specific matrix.

The theoretical basis for this research draws upon several interrelated models: Wolff's Law, which explains bone remodeling in response to mechanical load; the "diamond concept" of bone regeneration, which emphasizes the simultaneous presence of osteogenic cells, scaffold, signaling molecules, and mechanical stability; and the biopsychosocial model of patient healing, which incorporates immune compatibility, patient experience, and cost-efficiency. Previous studies have frequently isolated the effects of GBR or PRF but have failed to explore their dynamic interactions, particularly in multidimensional oral defects requiring comprehensive tissue recovery. Therefore, this study aims to fill that gap by conducting a prospective, comparative clinical trial evaluating the combined use of PRF and GBR in patients presenting with critical-sized alveolar ridge defects. The objectives are threefold: (1) to determine whether PRF accelerates mucosal healing and reduces membrane exposure; (2) to evaluate whether PRF improves bone volume gain and mineral density when combined with GBR; and (3) to assess histological quality of bone regeneration and angiogenesis at the microscopic level. The novelty of this study lies not only in the integrated biological-mechanical approach but also in its implementation within the Central Asian clinical context, contributing valuable evidence for regional practitioners and policymakers. The expected outcomes include faster soft tissue healing, enhanced bone quality, improved implant bed preparation, and reduced postoperative complications—making this approach especially relevant for patients with limited systemic healing capacity

or access to commercial graft materials. The findings may offer a cost-effective, biologically intelligent alternative to conventional GBR and set the foundation for future protocols incorporating autologous biomaterials into advanced oral regenerative medicine.

Methodology

This prospective clinical study aimed to assess the regenerative efficacy of combining Guided Bone Regeneration (GBR) and Platelet-Rich Fibrin (PRF) in the treatment of complex alveolar defects. The study involved 40 patients (aged 25–65) with horizontal or vertical ridge deficiencies greater than 4 mm. Patients were randomly assigned into two groups:

- Control Group (n=20): GBR using xenograft bone + collagen membrane
- Test Group (n=20): GBR + collagen membrane + autologous PRF membranes

PRF was prepared using Choukroun's protocol: 20 mL of venous blood was centrifuged at 2700 rpm for 12 minutes, and fibrin clots were pressed into membranes and applied during surgery. All patients underwent standard GBR with full-thickness flap elevation and tension-free closure. In the PRF group, membranes were layered over the graft and under the flap.

Outcome assessment included:

1. CBCT analysis (baseline, 3 months, 6 months) to measure bone width and density.
2. Clinical observation of wound healing, membrane exposure, and inflammation at weeks 1–8.
3. Histological evaluation in 10 patients per group at 6 months using trephine core biopsies.

Statistical analysis was performed with SPSS v27.0. Data were compared using t-tests and chi-square analysis, with $p < 0.05$ considered statistically significant.

Results

This clinical trial evaluated and compared the outcomes of two treatment protocols: Guided Bone Regeneration (GBR) alone, and GBR combined with autologous Platelet-Rich Fibrin (PRF) in patients presenting with complex alveolar defects. All 40 patients completed the 6-month study without severe postoperative complications such as infection, wound dehiscence, or implant failure. Early wound healing was uneventful in both groups, but the quality and speed of tissue regeneration varied significantly depending on the use of PRF. Postoperative follow-up at weeks 1, 2, 4, and 8 showed noticeable clinical advantages in the PRF group, including more stable graft containment, better flap adaptation, and reduced signs of inflammation. Patient-reported outcomes (pain, swelling, satisfaction) were also subjectively better among those receiving PRF, though not formally quantified in this study.

Radiological assessments performed through Cone Beam Computed Tomography (CBCT) demonstrated that patients in the PRF group achieved superior hard tissue regeneration compared to the control group. As detailed in Table 1, horizontal bone gain in the PRF group averaged 3.8 ± 0.4 mm, significantly greater than 3.1 ± 0.5 mm in the control group ($p < 0.01$). This indicates more effective space maintenance and cellular osteogenic activity in the PRF-treated defects. Moreover, bone density, measured in Hounsfield Units (HU), was markedly higher in the PRF group (895 HU) compared to the control group (810 HU, $p < 0.05$), suggesting a denser, more mineralized bone structure. These radiographic parameters collectively suggest that the integration of PRF not only accelerates bone formation but also enhances the quality and maturity of the regenerated bone.

Table 1. Radiographic and Clinical Comparison at 6 Months

Parameter	Control Group	PRF Group	*p*-value
Bone Volume Gain (mm)	3.1 ± 0.5	3.8 ± 0.4	< 0.01
Bone Density (HU)	810 ± 55	895 ± 60	< 0.05
Soft Tissue Healing Time (days)	25 ± 3.2	17 ± 2.5	< 0.05
Membrane Exposure (cases)	3	1	–

Soft tissue healing also significantly improved in the PRF group. The average time for complete mucosal closure was 17 ± 2.5 days, while the control group required 25 ± 3.2 days ($p < 0.05$), confirming the soft-tissue regenerative benefits of PRF's growth factor release. Additionally, the rate of membrane exposure—a known complication that compromises graft stability—was lower in the PRF group (1 patient) than in the control group (3 patients), indicating better vascularization, inflammation control, and soft tissue sealing. These findings reinforce that PRF not only benefits the underlying bone but also plays a key role in promoting flap healing and long-term wound stability.

Histological analyses, performed on biopsy samples from 10 patients in each group during implant placement at the 6-month point, further substantiated these observations. The amount of new bone formation was considerably higher in the PRF group (48.5% ± 5.2) compared to the control group (40.1% ± 6.0, $p < 0.01$), as outlined in Table 2. Moreover, PRF-treated samples displayed more intense osteoblastic activity (mean score 4.1 ± 0.3 vs 3.2 ± 0.4), indicating enhanced cellular turnover and bone remodeling. Neovascularization, although evaluated qualitatively, appeared more robust in the PRF group, evidenced by denser capillary networks and fewer inflammatory infiltrates under microscopy. The presence of residual graft particles was also less frequent in PRF-treated biopsies, which suggests a more efficient remodeling and graft resorption process.

Table 2. Histological Comparison at 6 Months

Parameter	Control Group	PRF Group	*p*-value
New Bone Formation (%)	40.1 ± 6.0	48.5 ± 5.2	< 0.01
Osteoblastic Activity (Score: 1–5)	3.2 ± 0.4	4.1 ± 0.3	< 0.01
Neovascularization (qualitative)	Moderate	High	Descriptive

These findings collectively demonstrate that the integration of PRF into GBR protocols significantly enhances the regenerative process in both hard and soft tissues. From radiographic and clinical perspectives, the PRF group not only showed more bone volume and faster mucosal closure, but also higher bone density and reduced complications. Histological outcomes confirmed the biological mechanisms underlying these improvements—namely, PRF's contribution to osteoblast activation and early vascular formation. The statistical significance of the results supports the hypothesis that PRF enhances both the quality and speed of tissue regeneration when used in conjunction with standard GBR techniques. These improvements could translate into better implant success rates, shorter treatment timelines, and higher patient satisfaction in complex reconstructive dental procedures.

Discussion

The outcomes of this clinical trial provide robust evidence supporting the hypothesis that the integration of Platelet-Rich Fibrin (PRF) into Guided Bone Regeneration (GBR) protocols leads to significantly enhanced regenerative outcomes in complex oral defects. The quantitative data collected across radiographic, clinical, and histological domains consistently demonstrated superior performance of the PRF-assisted group. Specifically, patients in the PRF group exhibited a statistically significant increase in bone volume and mineral density at 6 months postoperatively, as well as more favorable soft tissue healing dynamics, including accelerated mucosal closure and reduced membrane exposure. These findings are not merely

incremental; they represent a critical shift from passive, mechanically focused bone augmentation strategies toward an active, biologically driven regeneration model. Unlike conventional GBR that relies solely on barrier membranes and bone fillers to support osteogenesis, PRF introduces autologous biological factors that trigger and sustain cellular responses crucial for both hard and soft tissue regeneration. The dense fibrin matrix of PRF functions not only as a physical scaffold but also as a reservoir for the gradual release of growth factors such as PDGF, TGF-β, and VEGF. These factors play integral roles in stimulating angiogenesis, promoting fibroblast migration, enhancing collagen deposition, and accelerating osteoblastic differentiation. The histological evidence from this study confirms these mechanisms: PRF-treated biopsy specimens showed denser and more organized bone trabeculae, heightened osteoblastic activity, and a more vascularized microenvironment compared to GBR alone. This suggests that PRF contributes not only to the quantity but also to the quality of the regenerated tissue, thereby enhancing the biological readiness of the site for subsequent implant placement.

Furthermore, these findings carry significant theoretical, clinical, and regional relevance. Theoretically, the results validate the tissue engineering triad—scaffold, signaling molecules, and responsive cells—and affirm the “diamond concept” of bone regeneration, which emphasizes the need for osteoconductive matrix, osteoinductive signals, cellular activity, and mechanical stability for optimal regeneration. The synergy observed between PRF and GBR in this study supports this model, showing that a dual-modality approach leveraging both mechanical space maintenance and biological stimulation can overcome the limitations of either approach when used in isolation. From a clinical perspective, the advantages of PRF are manifold: it is autologous, inexpensive, easy to prepare chairside, and does not require external additives or bioengineering facilities. These characteristics make it especially valuable in resource-limited settings like Uzbekistan, where access to synthetic growth factors (e.g., BMPs) or advanced tissue products is restricted. Moreover, the use of PRF reduces reliance on non-autologous materials, thereby minimizing immunologic risks and improving patient acceptance. The reduced complication rate (membrane exposure, inflammation) and improved biological outcomes suggest that the GBR+PRF combination may be particularly beneficial in elderly patients, smokers, or individuals with systemic conditions where soft tissue healing is typically delayed. Despite these promising outcomes, the study acknowledges certain limitations, including a relatively small sample size and the short-term duration of observation. Longer follow-up is essential to evaluate the long-term implant survival rate, volumetric stability of the regenerated bone, and peri-implant tissue health. Furthermore, advanced techniques such as immunohistochemical staining, ELISA-based growth factor quantification, and molecular imaging could provide deeper insight into the precise biological mechanisms influenced by PRF. Future studies may also explore the integration of PRF with various membrane types (collagen, PTFE, cross-linked), combinations with stem cells or bioactive ceramics, and the use of PRF in vertical augmentation procedures or immediate implant placement protocols.

Conclusion

This clinical investigation has demonstrated that the combined application of Platelet-Rich Fibrin (PRF) and Guided Bone Regeneration (GBR) offers a superior regenerative strategy for the treatment of complex oral cavity defects. Through a systematic comparison of clinical, radiographic, and histological outcomes, the study revealed that the GBR + PRF protocol significantly enhances bone volume gain, mineral density, soft tissue healing, and new bone formation, while simultaneously reducing postoperative complications such as membrane exposure. These improvements are attributed to PRF's role as a biologically active scaffold that promotes angiogenesis, cellular differentiation, and tissue integration through the sustained release of autologous growth factors.

The results validate the conceptual framework of combining mechanical and biological regenerative elements and highlight the clinical value of PRF as an accessible, cost-effective adjunct to conventional GBR, particularly in resource-constrained settings. In countries like Uzbekistan, where access to synthetic

graft materials may be limited, the use of autologous PRF can significantly improve the quality and predictability of implant-based oral rehabilitation. Despite the positive outcomes, further research with larger cohorts, longer follow-up periods, and molecular analysis is necessary to confirm these findings and expand the clinical applications of PRF. Nonetheless, this study provides strong preliminary evidence supporting the integration of PRF into standard GBR protocols and lays the foundation for biologically enhanced, patient-centered regenerative dentistry.

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