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Perspective article

Perspectives of the new horizon in bone regeneration with standardized, centrally manufactured freeze-dried platelet-rich plasma

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The use of autologous platelet concentrates (APCs) has become a cornerstone of regenerative dentistry. The transition from the first-generation platelet-rich plasma (PRP) to the second-generation platelet-rich fibrin (PRF) represents a significant advancement, providing fully autologous products with promising clinical outcomes.[1,2] Recently, the preparation of PRF has been modified as many flowable variants, such as liquid fibrinogen, with enhanced clinical application by enabling the creation of cohesive "sticky bone" for superior graft stability.[3]

Despite these advances, the lack of standardization remains a fundamental challenge. The biological efficacy of any chair-side APC preparation is subject to a host of variables that are difficult to control. Patient-related conditions, such as underlying systemic diseases, can alter platelet and leukocyte counts, while technical factors like centrifugation force and duration directly impact the final composition and fibrinogen concentration of the product.[4,5] In particular, the inability to consistently control platelet counts across preparations may lead to significant variations in the concentration of growth factors, thereby affecting the quality and reproducibility of each treatment. The delay of just a few minutes between blood draw and centrifugation could drastically alter the fibrin matrix structure and reduce the final dimensions of PRF membrane.[6] This inherent variability might hinder the ability to reliably predict clinical outcomes and complicates.[7] To address this long-standing issue, blood bag centrifugation system was developed to consistently isolate platelets, extract their growth factors, and lyophilize them for long-term storage. Therefore, a product termed "Platelet-Rich Plasma Plus (PRP+)" has been established to bring consistency to platelet-derived therapies.[8] It is uniformly prepared in a centralized laboratory (I Care YOU Biotech Co. Ltd., Taipei, Taiwan).[9] This contributes to the standardization of product quality, providing more consistent platelet counts and growth factor levels, thereby addressing the wide variation issues present in traditional PRP preparation protocols.

To offer a preliminary view of its potential, we recently applied this novel PRP+ in a clinical socket preservation approved by the ethical committee, Chung Shan Medical University Hospital (NO. CS1-22165). A 59-year-old healthy male required extraction of teeth 35 and 37 due to a failing

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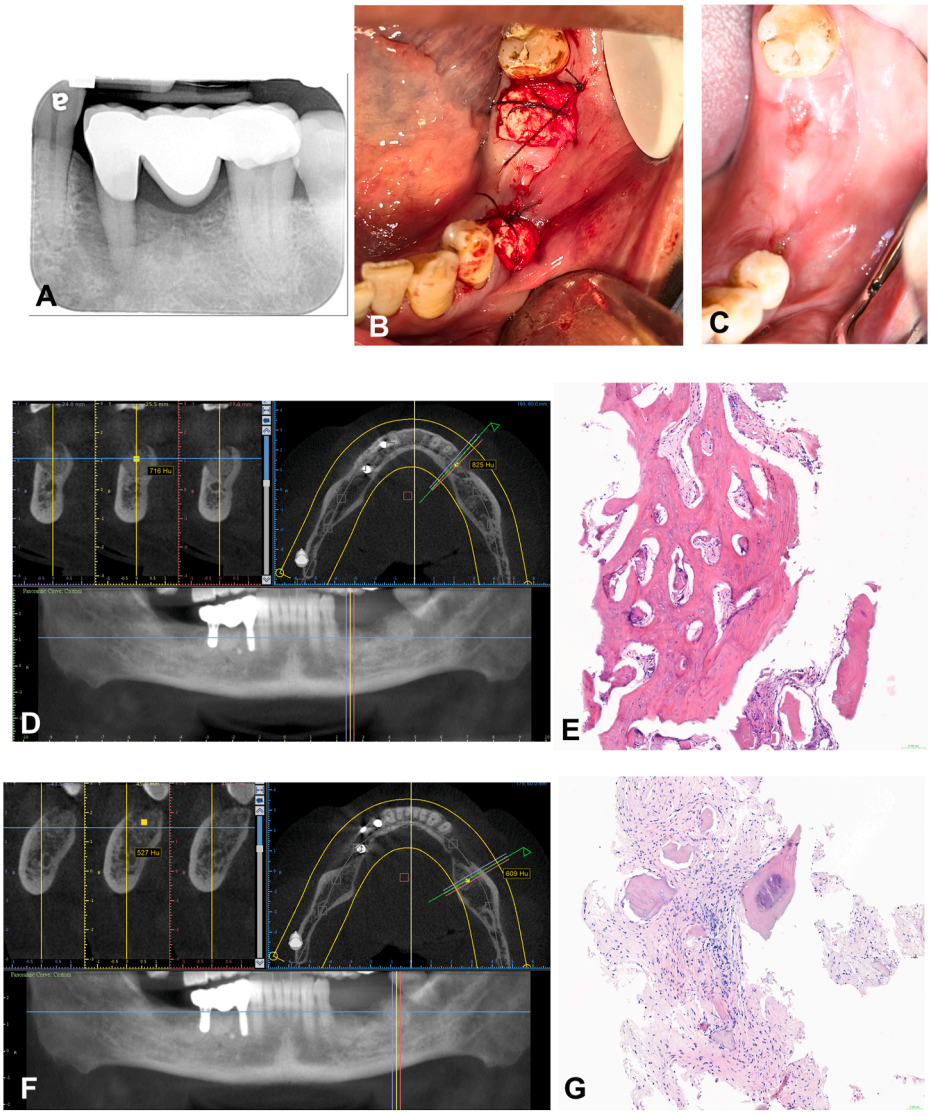

Figure 1 Clinical, radiographic, and histological comparison of socket preservation by using the PRP+ versus the liquid fibrinogen. (A) Initial periapical radiograph revealing significant bone loss around tooth 35 and caries beneath the prosthesis at tooth 37. (B) Immediate post-operative view after extraction and grafting with collagen plugs sutured over both tooth 35 PRP+ socket and tooth 37 liquid fibrinogen socket, respectively. (C) Clinical view after two weeks post-surgery revealed uneventful soft tissue healing. (D) Cone-beam computerized tomography (CBCT) scan after three months showing the grafted site of tooth 35 PRP+ socket with measured bone density ranging from 716 to 825 Hounsfield Units (HU). (E) Histological specimen from the tooth 35 PRP+ socket site at five months, showing well-organized, mature bone with Haversian canals (H&E stain, 200 × magnification). (F) CBCT scan after three months of the grafted site of tooth 37 liquid fibrinogen socket site, with measured bone density ranging from 527 to 609 HU. (G) Histological specimen from tooth 37 liquid fibrinogen socket site at five months, characterized by less mature bone and a higher proportion of fibrous connective tissue (H&E stain, 200 × magnification).

bridge and underlying pathology (Fig. 1A). Following atraumatic extractions, the tooth 37 socket was grafted with freshly prepared liquid fibrinogen, a flowable variant of PRF,[3] mixed with a demineralized freeze-dried bone allograft. The tooth 35 socket received the same allograft, but mixed with reconstituted PRP+ (I Care YOU Biotech Co. Ltd.). Collagen plugs (Teruplug, Olympus Terumo Biomaterials, Tokyo, Japan) were placed over both sites and sutured, respectively (Fig. 1B).

Both healing processes were uneventful, with no signs of infection or complications (Fig. 1C). Cone-beam computerized tomography scans at three months after operation revealed a notable difference in bone density. The Hounsfield units (HU) at tooth 35 PRP+ site ranged from 716 to 825 (Fig. 1D), while tooth 37 liquid fibrinogen site ranged from 527 to 609 (Fig. 1F). This semi-quantitative data hinted the superior bone formation in the tooth 35 PRP+ group. The most compelling evidence emerged at five months, when core biopsies were harvested during implant placement. Histological analysis showed high-quality, mature bone with well-formed Haversian canals at the tooth 35 PRP+ site (Fig. 1E). However, tooth 37 liquid

fibrinogen site contained significantly fibrous connective tissue and less mature bone (Fig. 1G). The histological outcome suggests that a standardized, acellular product can not only match but potentially exceed the regenerative capacity of its fresh, autologous counterpart in this application.

This case provided the compelling evidence supporting a new perspective in bone regeneration with the shift from variable, chair-side preparations to consistent, manufactured biologics. The preliminary finding is not merely the safety of PRP+, but also its ability to produce a histologically superior bone quality when compared directly to a traditional APC. This outcome can be attributed to the core advantages inherent in its design as following.

First, the standardized manufacturing process addresses the greatest weakness of autologous preparations. The quality of freshly prepared L-PRF or liquid fibrinogen is susceptible to numerous patient- and operator-dependent variables. In contrast, the PRP+ is produced in a centralized laboratory with a validated protocol, ensuring that each vial contains a consistent and therapeutically effective concentration of growth factors. The superior bone quality seen in this case serves as powerful in vivo evidence that this standardized growth factor cocktail effectively orchestrates high-quality tissue regeneration.

Second, the product's stability, achieved through lyophilization, fundamentally changes the clinical workflow. The ability for long-term storage at room temperature eliminates the need for in-office centrifuges and time-sensitive preparations. This "off-the-shelf" accessibility makes advanced regenerative techniques more predictable and efficient, democratizing their use beyond specialized centers. Published research confirms that freeze-dried PRP can maintain its bioactive substance levels for at least one year, ensuring that its clinical efficacy is not compromised by storage.[10] The PRP+ typically takes several weeks to produce. This means that the PRP+ cannot be immediately used to treat emergency. Although the ability to prepare PRP+ in advance benefits planned dental applications, the off-site manufacturing process precludes its use in scenarios that require immediate preparation.

With the limitation of this single clinical application, this case demonstrates that a standardized, acellular biologic can yield superior regenerative results compared to its autologous counterpart. The era of biologics like PRP+ moves us beyond hoping for a good outcome to planning for one, based on a product with a validated composition and predictable effects. Future works must validate these findings through studies with larger sample sizes and quantitative histomorphometry.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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References

1. Marx RE, Carlson ER, Eichstaedt RM, et al. Platelet-rich plasma: growth factor enhancement for bone grafts. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1998;85:638–46.
2. Su NY, Yang LC, Chang YC. Platelet-rich fibrin is the first-line treatment option for periodontal regeneration. *J Dent Sci* 2017;12:203–4.
3. Quirynen M, Siawasch S, Temmerman A, et al. Do autologous platelet concentrates (APCs) have a role in intra-oral bone regeneration? A critical review of clinical guidelines on decision-making process. *Periodontol* 2000 2023;93:254–69.
4. Sato A, Kawabata H, Aizawa H, et al. Distribution and quantification of activated platelets in platelet-rich fibrin matrices. *Platelets* 2020;33:110–5.
5. Goel A, Windsor L, Gregory R, Blanchard S, Hamada Y. Effects of platelet-rich fibrin on human gingival and periodontal ligament fibroblast proliferation from chronic periodontitis versus periodontally healthy subjects. *Clin Exp Dent Res* 2021;7:436–42.
6. Castro A, Andrade C, Li X, et al. Impact of g force and timing on the characteristics of platelet-rich fibrin matrices. *Sci Rep* 2021;11:6038.
7. Lee HM, Shen EC, Shen JT, et al. Tensile strength, growth factor content and proliferation activities for two platelet concentrates of platelet-rich fibrin and concentrated growth factor. *J Dent Sci* 2020;15:141–6.
8. Andia I, Perez-Valle A, Del Amo C, Maffulli N. Freeze-drying of platelet-rich plasma: the quest for standardization. *Int J Mol Sci* 2020;21:6904.
9. Weng HP, Cheng YY, Lee HL, et al. Enhanced platelet-rich plasma (ePRP) stimulates wound healing through effects on metabolic reprogramming in fibroblasts. *Int J Mol Sci* 2021;22:12263.
10. Nakajima R, Saita Y, Kobayashi Y, et al. Comparison of bioactive substances in novel-developed freeze-dried platelet-rich plasma (PRP) and activated normal PRP, and investigation of bioactive substance levels after long-term storage. *Regen Ther* 2024;27:200–6.