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APPLICATION OF AUTOLOGOUS PLATELET CONCENTRATES (PRP/PRF) IN ACNE SCAR REDUCTION AND THEIR ROLE IN IMPROVING PATIENTS' PSYCHOSOCIAL QUALITY OF LIFE: A LITERATURE REVIEW

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ABSTRACT

Background: Atrophic acne scars represent a prevalent dermatological challenge with significant cosmetic and psychosocial implications. While autologous platelet concentrates (APCs), such as platelet-rich plasma (PRP), are widely used to promote tissue repair, single-modality approaches often yield sub-optimal structural reconstruction in deep scarring.
Objective: This review evaluates the biophysical mechanisms, release kinetics, and clinical efficacy of autologous platelet concentrates – specifically comparing classical PRP with advanced liquid platelet-rich fibrin (f-PRF/i-PRF) – both as monotherapy and within hybrid protocols combined with microneedling, subcision, and ablative fractional CO2 laser resurfacing.
Methods: A comprehensive synthesis of current preclinical and clinical literature was conducted, analyzing the impact of centrifugation physics (relative centrifugal force, rotor geometry, chemical additives) on cellular viability and the structural remodeling cascade.
Results: Liquid PRF modalities, prepared without exogenous anticoagulants, demonstrate superior biological kinetics compared to PRP, forming a three-dimensional bio-scaffold that enables sustained growth factor release (up to 10–14 days) and homogenous leukocyte migration. Clinical data unequivocally indicate that hybrid procedures outperform monotherapies. Synergizing physical interventions such as microneedling, CO2 laser resurfacing, or subcision with autologous cytokines markedly enhances neocollagenesis and extracellular matrix remodeling. Furthermore, combining APCs with physical modalities significantly reduces post-procedural erythema, edema, downtime, and the incidence of post-inflammatory hyperpigmentation.
Conclusion: Advanced platelet-rich fibrin matrices represent a therapeutic evolution over traditional PRP, particularly in preventing fibrous re-anchoring during subcision and providing extended paracrine signaling. Establishing standardized centrifugation protocols and objective evaluation metrics remains essential to fully optimize APC-driven regenerative therapy in dermatological surgery.

KEYWORDS

Platelet-Rich Plasma (PRP), Platelet-Rich Fibrin (PRF), Autologous Platelet Concentrates, Atrophic Acne Scars, Psychosocial Quality of Life (QoL), Aesthetic Dermatology

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1. Introduction

Acne vulgaris is a chronic inflammatory dermatosis affecting up to 9% of the global population and up to 85% of adolescents and young adults (aged 12 to 24 years). This widespread prevalence positions acne vulgaris as a leading diagnosis among dermatological conditions worldwide (Eichenfield et al., 2021).

The most distressing long-term complication of resolved inflammation is the formation of permanent facial atrophic acne scars, which affect nearly half of all patients. Beyond the physical destruction of cutaneous architecture, visible facial scarring induces a severe psychosocial burden frequently triggering body dysmorphic disorder (BDD), social anxiety, severe depression, and a profound decline in health-related quality of life (HRQoL).

While conventional resurfacing techniques often yield inconsistent results or prolonged downtime, modern interventional dermatology increasingly relies on autologous platelet concentrates – such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) – to accelerate tissue repair. The objective of this narrative literature review is to synthesize current evidence on the biological mechanisms, application protocols, and clinical efficacy of PRP/PRF (both as monotherapy and within hybrid protocols combined with microneedling, subcision, and fractional lasers), while evaluating their direct impact on improving patients' psychosocial well-being and quality of life.

1.1. Acne as a Global Public Health Issue: Prevalence and the Formation of Atrophic Scars as Permanent Dermatological Complications

Acne vulgaris is a chronic inflammatory disorder affecting the sebaceous glands and hair follicles. The clinical presentation of this dermatosis is characterized by a diverse array of lesions – ranging from primary comedones to inflammatory papules and pustules, culminating in deep nodulocystic lesions. These lesions demonstrate a symmetrical distribution, predominantly affecting anatomical regions with the highest density of sebaceous glands, with particular involvement of the facial area (Deng et al., 2024).

The etiopathogenesis of acne is multifactorial and sequential. Key pathomechanistic drivers include androgen-induced hyperactivity and hyperplasia of the sebaceous glands (seborrhea), altered keratinization of the follicular infundibulum (retention hyperkeratosis), and secondary bacterial colonization (predominantly by Cutibacterium acnes). These factors trigger a complex, immunologically mediated inflammatory response (Deng et al., 2024).

The most common and distressing complication of resolved inflammation is the development of permanent acne scars. It is estimated that this defect occurs in nearly half of all acne sufferers, exhibiting a strong predilection for socially visible areas such as the cheeks and other facial regions (Boen & Jacob, 2019).

Clinical classification categorizes these scars into three primary morphotypes: atrophic, hypertrophic, and keloids (Arora et al., 2024). Among these, atrophic scars are statistically predominant. Due to their destructive tissue architecture, they present a major aesthetic concern while causing a profound decline in patients' quality of life (Dreno et al., 2021; Gieler et al., 2015).

To objectively assess severity and standardize therapeutic strategies, numerous scoring systems have been introduced in the literature. Among these, the Goodman and Baron quantitative grading system remains the leading tool in clinical practice and research, parameterizing the severity of scarring based on morphology, lesion count, and the degree of tissue involvement (Goodman & Baron, 2006).

1.2. Psychosocial Burden of Atrophic Scars: Social Stigma, Anxiety, Body Dysmorphic Disorder (BDD), and Social Withdrawal

Psychosocial Burden and Social Stigma in the Context of Atrophic Scars

The facial localization of acne lesions generates profound and long-lasting psychosocial consequences that extend far beyond the bounds of a conventional cutaneous defect. From a psychodermatological perspective, the high prevalence of acne vulgaris among adolescents coincides with a critical stage of identity formation. The destruction of tissue integrity in this region significantly disrupts body image perception, inducing acute feelings of loneliness, alienation, and social withdrawal in affected patients (Gieler et al., 2015). This situation is dramatically exacerbated by the fact that nearly half of all patients (approximately 47%) develop permanent scarring as a result of the inflammatory process. Research demonstrates that chronic scarring induces not only somatic symptoms such as pain, persistent pruritus, or motor impairment but serves primarily as a source of permanent psychological crisis, exhibiting a distinct correlation with clinical depression and post-traumatic stress disorder (PTSD) (Bock et al., 2006; Brewin & Homer, 2018; Oh & Boo, 2017; Novintan et al., 2026; Van Loey & Van Son, 2003).

Chronic dermatoses affecting visible anatomical regions drastically diminish self-esteem, driving a fear of negative evaluation by others and leading to deep dissatisfaction with one's physical appearance (Dreno et al., 2021). This condition affects the majority of individuals, given that the most common manifestation of acne complications – atrophic scars – accounts for 80% to 90% of all reported cases (Aljefri et al., 2022). Even conservative estimates indicating that severe scarring directly impacts up to 14% of the acne-affected population highlight behavioral implications such as social isolation, body dysmorphic disorder, and occupational absenteeism as a major public health challenge (Eyuboglu et al., 2018).

The presence of permanent cutaneous damage in the facial region induces paralyzing self-consciousness in patients, impeding the formation and maintenance of interpersonal relationships, communication, and functioning within occupational structures (Brewin & Homer, 2018). A particularly notable methodological insight warrants emphasis: the degree of impairment in quality of life is primarily determined by the presence of the scar as a stigma itself, rather than solely by its clinical severity grade (Limongelli et al., 2017). The ubiquity of this concern is reflected in patient self-reports in surveys, up to 91% of respondents declared that even a minimal reduction in scar visibility is of paramount importance to them from a subjective standpoint, regardless of the initial lesion depth (Young & Hutchison, 2009). The effects of internalized stigma and functional limitations in patients with acne scars demonstrate striking similarities to the burdens experienced by individuals with severe keloids, hypertrophic scars, or burn scars (Brewin & Homer, 2018).

Analysis of Empirical Evidence: Findings from Cross-Sectional Studies

Key arguments in this domain are provided by recent observational studies. A multicenter cross-sectional study involving 175 patients with facial acne scars demonstrated a direct linear relationship between tissue pathology and affective disorders (Tunca et al., 2024). These findings align with reports by Tan et al. (2021), who diagnosed clinical symptoms of Body Dysmorphic Disorder (BDD) in 16.9% of a cohort comprising 723 adult patients with permanent scarring, as evaluated using the Dysmorphic Concern Questionnaire (DCQ) (with significantly higher scores among individuals with severe forms of scarring; mean: 8.04 for mild vs. 10.13 for severe, $P = 0.001$) (Tunca et al., 2024; Heah et al., 2025).

Another epidemiological study (median age: 26.9 years; 56% female), which parameterized the severity of scarring using the SCAR-S scale and assessed psychological well-being via the DLQI, HADS, and FASQoL questionnaires, provided the following data (Heah et al., 2025):

1. In the subgroup with severe and very severe scarring, as many as 69.2% of patients reported a critical reduction in quality of life (DLQI > 10).

2. A statistically significant correlation was confirmed between scar severity and the intensity of anxiety ($p = 0.009$) and depression ($p < 0.001$), along with a strong positive correlation between HADS and DLQI scores ($r = 0.602$, $p < 0.001$).

3. The mean global DLQoL score was 6.26. Subjective perception of scarring as a "very/extremely severe" problem was declared by 19.3% of patients with mild lesions, 20.1% with moderate lesions, and 34.0% with severe lesions ($p = 0.003$). Progression in the severity of anatomical changes was also closely linked to an increase in FASQoL scores ($p = 0.001$).

4. The primary components of emotional distress reported by patients were self-consciousness (68.0%) and persistent anxiety regarding the irreversible nature of the disfigurement (74.8%).

5. Delayed or omitted dermatological treatment during the acute phase of acne was identified as the main risk factor for the development of the most severe forms of scarring.

The presented empirical evidence unequivocally indicates that the subjective impact of acne scars on quality of life increases with lesion depth, reinforcing the necessity of implementing effective, interdisciplinary interventional procedures (Tan et al., 2021).

Quality of Life Indicators: Methodology for Assessing Patient Well-Being Using the Dermatology Life Quality Index (DLQI)

Contemporary dermatology utilizes various instruments to evaluate the impact of dermatoses on Health-Related Quality of Life (HRQoL). In clinical practice and research settings, the DLQI questionnaire remains the most widely applied tool (Finlay & Khan, 1994). The structure of this instrument relies on 10 standardized items evaluating physical symptom severity, emotional state, impairment of leisure activities, and the impact of the condition on education, interpersonal relationships, sleep quality, and the treatment process (Finlay & Khan, 1994; Eyuboglu et al., 2018). The total score ranges from 0 to 30 points. The minimum score of 0 reflects no negative impact of the condition on daily functioning, whereas the maximum score of 30 signifies extreme disruption of quality of life (Eyuboglu et al., 2018).

The structure of the questionnaire enables problem analysis across six main domains (Syed et al., 2025; Eyuboglu et al., 2018):

1. Symptoms and feelings (items 1 and 2)
2. Daily activities (items 3 and 4)
3. Leisure (items 5 and 6)
4. Work and school (items 7.1 and 7.2)
5. Personal relationships (items 8 and 9)
6. Treatment (item 10)

An increasing cumulative score on the DLQI scale directly reflects a worsening degree of psychosocial and functional impairment in the patient (Eyuboglu et al., 2018).

2. Methodology

To systematize current knowledge, a narrative literature review was conducted regarding the clinical efficacy of autologous platelet concentrates (PRP/PRF) in atrophic acne scar reduction and their role in improving patients' psychosocial quality of life. The objective of this analysis was to provide a synthetic overview of the contemporary state of research, evaluate biological mechanisms and procedural synergies, and highlight existing research gaps.

A comprehensive literature search was performed across electronic medical databases, including PubMed, Scopus, Google Scholar, and Web of Science. A total of 78 scientific publications were selected and analyzed. The selection prioritized recent peer-reviewed literature published between 2018 and 2026, while including selected foundational and methodological studies (e.g., scoring systems and quality of life validation instruments) to maintain historical accuracy and clinical relevance.

The search strategy utilized combinations of Boolean operators (AND, OR) with the following key terms: *acne scars*, *atrophic scarring*, *platelet-rich plasma*, *PRP*, *platelet-rich fibrin*, *PRF*, *i-PRF*, *microneedling*, *subcision*, *fractional CO_2 laser*, *quality of life*, *DLQI*, *psychosocial burden*, and *body dysmorphic disorder*.

3. Technological Innovations in Autologous Biomaterial Harvesting

3.1. Technological Evolution of Cell Separation Systems: Transition from Classical Platelet-Rich Plasma (1st Generation PRP) to Advanced Platelet-Rich Fibrin Technology (2nd Generation PRF)

Autologous platelet concentrates (APCs) represent a dynamically developing class of biomaterials widely utilized in regenerative medicine due to their ability to secrete supraphysiological concentrations of endogenous growth factors (Farshidfar, Amiri, et al., 2025). Among these, transforming growth factor-β (TGF-β), vascular endothelial growth factor (VEGF), and platelet-derived growth factor (PDGF) play a pivotal role as key mediators of tissue repair (Barootchi et al., 2024; Davies & Miron, 2024; Moraschini et al., 2023).

The clinical implementation of autologous platelet-rich plasma (PRP) and liquid/fluid platelet-rich fibrin (f-PRF/i-PRF) has established these matrices as versatile therapeutic modalities across numerous medical disciplines. Current clinical reports particularly confirm their high efficacy in dermatological protocols, with a specific focus on acne scar reduction (Ahramiyanpour et al., 2025; Gaumond et al., 2024)

A fundamental advantage of APCs lies in their entirely autologous origin: the material is isolated directly from the patient's whole blood immediately prior to the procedure. This therapeutic model completely eliminates the risk of immunization, allergic reactions, cross-infections, or transmission of blood-borne pathogens (Marques et al., 2014).

The genesis of cell separation system development dates back to the late 1990s, when the first generation of platelet concentrates was developed in the form of PRP (Farshidfar, Amiri, et al., 2025). This biomaterial represents a complex molecular matrix consisting of growth factors, cytokines, and cellular fractions. These elements act synergistically in orchestrating key phases of the repair cascade, stimulating neovascularization, modulating the inflammatory profile, and inducing extracellular matrix (ECM) remodeling (Rath et al., 2025). Despite its broad spectrum of dermatological applications (Diab et al., 2022), classical PRP exhibits significant kinetic limitations. Elution profile analyses demonstrate that PRP is characterized by a rapid, burst-like release of growth factors immediately post-activation, followed by a swift decline in their concentration over time (Farshidfar, Amiri, et al., 2025; Kobayashi et al., 2016). This kinetics of biologically active molecule release proves suboptimal for long-term bioregeneration and tissue histogenesis (Farshidfar, Amiri, et al., 2025).

In response to these technological constraints, second-generation concentrates – platelet-rich fibrin (PRF) – were developed (Davies & Miron, 2024; Kobayashi et al., 2016). The core rationale behind this new methodology was the complete elimination of synthetic anticoagulants from the procedural protocol (Davies & Miron, 2024; Marx, 2001). The absence of chemical coagulation inhibitors allows for the initiation of a slow, physiological, and spontaneous coagulation cascade during centrifugation. Consequently, a structured three-dimensional fibrin meshwork is formed, which naturally traps activated platelets and leukocytes (Soares et al., 2025). This structural configuration enables a slow, sustained, and prolonged elution of growth factors, significantly surpassing the release kinetics observed during standard wound healing or following PRP application (Amiri et al., 2023; Kobayashi et al., 2016)

The capacity of PRF to generate higher cumulative concentrations of chemical mediators with a controlled release profile establishes this biomaterial as an optimal matrix for long-term stimulation of cellular proliferation and migration (Diab et al., 2022). The superiority of this technology is substantiated by both in vitro and in vivo investigations. Wang et al. confirmed that liquid PRF fractions exert a significantly higher stimulatory effect on the proliferation and metabolic activity of human dermal fibroblasts compared to classical

PRP (Wang et al., 2019). Furthermore, Shashank et al. reported promising clinical outcomes using liquid PRF in the management of androgenetic alopecia, facial skin fold volumization, and comprehensive facial tissue regeneration and rejuvenation. Collectively, these data strongly indicate that advanced PRF modalities serve as a highly efficient and safe alternative to conventional platelet-rich plasma procedures (Shashank & Bhushan, 2020).

3.2. Process Engineering – Centrifugation Physics: The Role of Relative Centrifugal Force (RCF), Time, and Rotor Geometry in Preserving Leukocyte and Stem Cell Viability

Despite the widespread clinical use of platelet-rich plasma (PRP) over many years, a unified standard for its preparation remains lacking, as does a consensus on the minimum platelet concentration required to ensure therapeutic success (Pavlovic et al., 2016). The procedure is based on blood collection, centrifugal separation, and harvest of the concentrate. Commercially available systems differ in relative centrifugal force (g-force), centrifugation time, and number of spin cycles, factors that directly determine the cellular composition as well as the concentration of leukocytes and platelets (Assinger et al., 2026; Ghanem et al., 2025).

The biological efficacy of platelet-rich fibrin (PRF) is likewise dependent on centrifugation parameters (Miron et al., 2023; Quirynen et al., 2024). Key variables, including relative centrifugal force (RCF), time, and rotor tilt angle, shape the architecture of the fibrin network, the elution profile of growth factors, and cellular distribution while protecting cells from mechanical stress (Fujioka-Kobayashi et al., 2020; Miron et al., 2020). A systematic review of thirteen studies revealed that in 84.6% of evaluated cases, horizontal swing-out centrifugation proved superior to fixed-angle systems by achieving better cellular separation, with the remaining studies demonstrating no significant differences between the methods (Farshidfar, Alccayhuaman, et al., 2025).

Quantitative analyses by Miron et al. (2019) confirmed that classical L-PRF protocols (2700 rpm for 12 min) accumulate the majority of cells within a narrow buffy coat layer. Conversely, reducing centrifugal parameters in the A-PRF protocol (1300 rpm for 8 min) yields a more even distribution of platelets throughout the matrix, albeit with a lower leukocyte yield. The implementation of a horizontal rotor enabled up to a fourfold increase in platelet and leukocyte concentrations compared to fixed-angle centrifuges (Miron et al., 2019). This relationship was corroborated by Ferreira Sávio et al., who observed a twofold increase in leukocyte count alongside homogeneous cellular distribution using horizontal centrifugation (H-PRF: 700 g, 8 min) (De Souza Ferreira Sávio et al., 2023), as well as by Feng et al., who obtained a leukocyte-richer H-PRF matrix than that produced via fixed-angle L-PRF (Feng et al., 2020).

Centrifugation physics also alters protein architecture and release kinetics (Miron et al., 2023). Centrifugal forces around 700 g push cells to the bottom of the tube, yielding an inhomogeneous product. In contrast, lower relative forces (~200 g) foster the formation of a uniform fibrin meshwork with a homogeneous distribution of cellular elements, which enhances growth factor retention and promotes tissue regeneration (Miron et al., 2023; Soares et al., 2025).

In PRP research, two-step centrifugation protocols have predominated (most commonly 900 g for 5 min, followed by 2000 g for 15 min), utilizing sodium citrate or EDTA along with calcium chloride as an activator [30]. Protocols for injectable PRF (i-PRF) were more standardized (typically 700 rpm / 60 g for 3 min) without the addition of anticoagulants (Farshidfar, Amiri, et al., 2025). In in vitro investigations, PRP exhibited an initial, rapid burst-like release of growth factors (demonstrating higher concentrations of TGF-β1 and VEGF after 10 days), whereas i-PRF demonstrated a sustained, long-term release (up to 10–14 days) of PDGF-AA, PDGF-AB, EGF, and IGF-1 (Fernández-Medina et al., 2019; Miron et al., 2017).

In the context of acne scar treatment combined with microneedling, clinical trials have evaluated diverse PRP protocols (e.g., 1500/3700 rpm or 1419/2522 g with citrate) alongside i-PRF modalities (700 rpm, 60 g) (Davies & Miron, 2024). Diab et al. (2022), in a randomized controlled trial (RCT) involving 30 patients, demonstrated that intradermal injections and microneedling with both PRP and PRF significantly reduced scarring (yielding a 3-fold and 5-fold improvement, respectively). However, PRF-based therapy was found to be significantly more effective than PRP, offering a safe, simple alternative with superior clinical potential, particularly when combined with microneedling (Diab et al., 2022).

3.3. Elimination of Chemical Additives: Technological Distinction of Omitting Anticoagulants in PRF Technology in Favor of a Natural, Three-Dimensional Fibrin Matrix

Classical platelet-rich plasma (PRP) is characterized by rapid, initial growth factor release kinetics immediately post-application, followed by a swift decline in concentration over time (Kobayashi et al., 2016). To overcome this limitation, platelet-rich fibrin (PRF) technology was introduced. The PRF formulation is prepared without exogenous anticoagulants, allowing for the slow and sustained secretion of cellular mediators released by platelets and leukocytes embedded within the structural fibrin network (Dashore et al., 2021; Kobayashi et al., 2016).

The mandatory use of anticoagulants, such as sodium citrate (SC) or citrate-dextrose-A (ACD), in conventional PRP preparations introduces significant challenges in clinical practice (Assinger et al., 2026). These chemical compounds negatively impact the regenerative and pro-angiogenic potential of the autologous material. The underlying mechanism involves the chelation of calcium ions (Ca2+) by SC and the alteration of platelet activation dynamics and endothelial response caused by the presence of dextrose in ACD, directly impairing tissue repair processes (Aizawa et al., 2020; Ulasli et al., 2021). Furthermore, the application of anticoagulant-containing formulations correlates with localized adverse events, including allergic reactions (Latalski et al., 2019), delayed healing, and the development of post-injection dermal inflammatory papules (Assinger et al., 2026; Oneto et al., 2020).

Fibrin concentrates serve as an effective alternative that eliminates exposure to citrate (Assinger et al., 2026). In point-of-care (POC) systems, a single, low-g-force soft-spin centrifugation procedure is employed to separate whole blood, yielding liquid platelet-rich fibrin (f-PRF) suitable for injection within 30 minutes (Ratajczak et al., 2018). Rich in cellular microaggregates, injected f-PRF naturally forms a three-dimensional fibrin gel meshwork upon administration (Alsabri et al., 2024; Rattanawonsakul et al., 2025). This architecture effectively sequesters growth factors, guaranteeing their sustained secretion for up to 10 days and providing an extended therapeutic window compared to PRP (Rattanawonsakul et al., 2025).

As a second-generation platelet concentrate, PRF eliminates the risk of chemically induced hypersensitivity while optimizing the release kinetics of regulatory proteins (Ehrenfest et al., 2009). The key to separating blood fractions prior to the onset of the coagulation cascade lies in a rapid, brief centrifugation protocol. Within the platelet-rich phase, spontaneous autopolymerization of the fibrin matrix occurs, physically trapping platelets and leukocytes to mediate a slow and prolonged release of growth factors compared to classical PRP (Ehrenfest et al., 2009). The spatial architecture present in liquid PRF modalities thus functions as an advanced, autologous system for controlled growth factor delivery (Diab et al., 2022).

4. Biomechanism of Tissue Regeneration and Remodeling

4.1. Release Kinetic Physics of Growth Factors: Rapid Alpha-Granule Burst in PRP versus Sustained, Controlled Cytokine Release (PDGF, TGF-β, VEGF) from the PRF Fibrin Network (Sustained Release Effect)

Key biological mediators present in platelet-rich plasma (PRP) include platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), insulin-like growth factor (IGF), and fibroblast growth factor (FGF) (Borrione et al., 2010; Yu et al., 2011).

The divergent release kinetics of these biomolecules represent the fundamental distinction between the evaluated concentrates. In activated PRP, growth factors circulate freely in solution, generating an immediate burst-like release. Conversely, in PRF-based biomaterials, these proteins undergo physical sequestration (entrapment) within a dense, three-dimensional fibrin matrix (Assinger et al., 2026). This structural phenomenon underlies the delayed and prolonged cytokine elution profile.

In a study by Zwittnig et al. (2022), the secretion profiles of growth factors in liquid and solid PRF matrices were evaluated, revealing no overall statistically significant differences between the two forms ($p > 0.05$). Across both structural variants, the mean release of VEGF, TGF-β-1, PDGF-BB, and matrix metalloproteinase-9 (MMP-9) reached a maximum at day seven of observation (the fifth measurement timepoint). However, distinct variations were noted in the absolute concentrations of individual proteins: liquid PRF matrices eluted lower absolute amounts of VEGF compared to solid matrices while maintaining higher secretion levels of PDGF-BB and MMP-9 across all analyzed timepoints.

4.2. Biological Macrophage Stimulator: The Role of PRF-Derived Leukocytes in Attenuating Chronic Micro-inflammation and Directing Fibroblasts for Proper Extracellular Matrix Reconstruction

The impact of leukocytes on the tissue microenvironment depends heavily on the specific type of concentrate utilized. Scientific reports indicate that leukocytes can stimulate damaged tissue healing and exert direct antimicrobial effects (Alsousou et al., 2009; Cieslik-Bielecka et al., 2009). Conversely, other analyses demonstrate a directly proportional relationship between the total leukocyte pool in classical PRP and elevated synthesis of pro-inflammatory cytokines, which may subsequently inhibit tissue repair processes (McCarrel et al., 2012; Pavlovic et al., 2016).

Preparations of liquid platelet-rich fibrin (f-PRF) exhibit entirely different cellular dynamics. Fibroblast migration has been shown to occur significantly more intensely under the influence of f-PRF compared to conventional PRP. The application of liquid PRF induces stronger cellular proliferation and generates a marked increase in mRNA expression for key structural components: fibronectin, type I collagen, and TGF-β. These molecular changes directly translate into stronger and more effective stimulation of in situ collagen biosynthesis (Varela et al., 2018).

5. Review of Clinical Efficacy and Combination Procedures

5.1. Monotherapy vs. Innovative Combination Protocols: Limitations of PRP/PRF Alone and the Superiority of Hybrid Procedures

Autologous platelet concentrates (APCs) represent a valuable adjunctive therapy in the management of atrophic acne scars. They demonstrate maximum clinical efficacy when combined with primary remodeling procedures, such as microneedling, fractional CO_2 laser resurfacing, or subcision (Novintan et al., 2026).

The biological rationale for utilizing platelet-rich plasma (PRP) relies on its function as an autologous reservoir of key tissue repair mediators. Upon activation, blood platelets release growth factors from their alpha-granules – including PDGF, TGF-β1/2, EGF, and VEGF – which stimulate chemotaxis, cell proliferation, differentiation, and angiogenesis (Goodman, 2011; Lubkowska et al., 2012). Concurrently, dense granules release vasoactive molecules that transiently increase vascular permeability and modulate the localized immune response (Marx, 2004). Paracrine signaling induced by PRP recruits stem cells, drives their proliferation and targeted differentiation, and attenuates inflammation, thereby significantly accelerating proper re-epithelialization (Foster et al., 2009; Miron et al., 2019).

In a clinical setting, however, monotherapy with platelet concentrates alone rarely achieves complete structural defect remodeling in deep atrophic scars. Consequently, optimal therapeutic outcomes are obtained through hybrid protocols, wherein mechanical or laser-induced tissue disruption creates microchannels and initiates the healing cascade, while co-administered APCs provide the requisite biochemical support for regeneration (Miron et al., 2019).

5.2. Application Techniques of Autologous Platelet Concentrates (APCs)

Transdermal Application: Utilizing Microneedling-Induced Microchannels for Facilitated Growth Factor Delivery

Microneedling also known as percutaneous collagen induction (PCI) represents a minimally invasive, non-surgical, and non-ablative method for skin resurfacing and acne scar management (Davies & Miron, 2024). This procedure involves the controlled disruption of cutaneous integrity using automated devices equipped with a pulsating cartridge (most commonly featuring a 12-microneedle array) operating at frequencies between 3,000 and 5,000 cycles per minute. This enables precise tissue penetration to depths ranging from 0.25 to 2.5 mm (Davies & Miron, 2024; Fernandes, 2005).

The primary biological mechanism of microneedling relies on inducing micro-traumas that stimulate localized neovascularization alongside a cascade of neocollagenesis and structural remodeling. Histological evaluations confirm that mechanical micro-injuries resulting from PCI alone lead to dermal thickening and enhanced cutaneous hydration levels (Aust et al., 2010).

An additional technological advantage of microneedling is the formation of a dense network of microchannels, which serve as pathways for facilitated transdermal delivery of autologous platelet concentrates (APCs) applied topically to the treatment area (Davies & Miron, 2024). Combining both modalities yields a synergistic effect:

1. Local growth factors released in response to mechanical trauma interact with autologous mediators supplied by PRP/PRF, significantly accelerating collagen remodeling and tissue regeneration (Diab et al., 2022; Davies & Miron, 2024; Gentile, 2019).

2. However, the release kinetics of PRP indicate an almost total cytokine burst within the first 15 minutes post-application, which, when used as monotherapy, necessitates repeating sessions at short time intervals (Asif et al., 2016; Dashore et al., 2021; Litchman et al., 2022).

Key clinical advantages of combining microneedling with APCs include a high safety profile, excellent patient tolerance, and a brief recovery period (typically 24 to 48 hours) compared to more invasive interventional procedures (Davies & Miron, 2024; Litchman et al., 2022).

Evaluation of clinical outcomes unequivocally indicates that combining microneedling with APC therapy yields superior efficacy compared to microneedling alone or microneedling combined with topical adjuncts (e.g., vitamin C). This synergy translates into statistically higher improvement rates on objective clinical grading systems (such as the Goodman and Baron Quantitative Acne Scarring Grading System) and significantly elevated patient satisfaction levels (Davies & Miron, 2024).

Intradermal (Deposit) Injections: Precise Delivery into the Dermis (Deep Planes vs. Superficial Deposits/Papules)

As an alternative or complement to microneedling, precise intradermal injections enable the direct delivery of high concentrations of autologous platelet concentrates (APCs) directly into the target area. This technique features an exceptionally high safety profile and minimal invasiveness. The procedure involves depositing small volumes of the product into the intradermal layer or just beneath the dermis using fine needles (recommended size 30G, 4 mm length), allowing for strict depth control and the formation of transient deposits (papules) (Davies & Miron, 2024).

The primary advantage of deposit-based administration lies in the ability to deliver highly targeted therapy to specific, problematic anatomical zones. Compared to transdermal delivery, intradermal injections ensure a locally higher concentration of growth factors and biological mediators directly within the target tissue, serving as an effective and safe biostimulation method (Davies & Miron, 2024).

5.3. Subcision Technology Supported by Liquid Fibrin Matrix (i-PRF)

Subcision represents a crucial dermatological surgery procedure aimed at severing fibrous tethers pulling the scar base deep into the dermis. However, a significant limitation of subcision alone is the high risk of fibrous tissue re-attachment (re-anchoring) and defect recurrence. Applying injectable platelet-rich fibrin (i-PRF) during subcision enables the formation of a biological, three-dimensional bio-scaffold that acts as a physical separation barrier and a reservoir for continuously released growth factors (Diab et al., 2022).

5.4. Comparative Analysis of PRF vs. PRP in Combination Procedures

The application of PRF is characterized by higher clinical efficacy compared to classical PRP, as confirmed by direct comparative studies. In an analysis conducted by Diab et al. (2022), therapeutic response to PRP and PRF applications was evaluated – both as monotherapy and in combination with mechanical fractional resurfacing. Regardless of the chosen application technique, the PRF-treated group achieved a significantly greater reduction in scar severity according to the Goodman and Baron Quantitative Global Acne Scarring Grading System (GSGS) (Diab et al., 2022; Davies & Miron, 2024).

It is worth emphasizing the pronounced superiority of platelet-rich fibrin (PRF) over platelet-rich plasma (PRP) in classical intradermal injections, where the percentage of patients achieving tissue renewal rated as "excellent" was five times higher in the PRF deposit group (33.3%) compared to the PRP injection group (6.7%). Introducing an additional mechanical stimulus via fractional mechanical resurfacing (microneedling) induced a clear biological synergy and elevated optimal outcome rates across both therapeutic variants yielding a threefold increase in patients with an "excellent" effect in the PRP group (from 6.7% to 20%) and nearly a twofold increase in the PRF group, ultimately reaching 53.2% (Diab et al., 2022).

Aggregated clinical data indicate that microneedling techniques combined with autologous concentrates achieve superior outcomes compared to intradermal injections alone. Across all procedural variants, platelet-rich fibrin (PRF) demonstrates higher biological activity and therapeutic superiority over platelet-rich plasma (PRP) (Diab et al., 2022).

Table 1. Comparative Clinical Efficacy of PRP vs. PRF in Monotherapy and Combination Protocols for Atrophic Acne Scar Treatment (Diab et al., 2022; Davies & Miron, 2024)

Treatment Modality	Platelet-Rich Plasma (PRP)	Platelet-Rich Fibrin (PRF)	Relative Advantage / Biological Synergy
Intradermal Injections (Monotherapy)	6.7% "Excellent" outcome	33.3% "Excellent" outcome	5-fold higher rate of "excellent" tissue renewal for PRF ($p < 0.05$)
Microneedling Combination (Hybrid Protocol)	20.0% "Excellent" outcome (3-fold increase vs. PRP injection)	53.2% "Excellent" outcome (1.6-fold increase vs. PRF injection)	2.66-fold higher rate for PRF + Microneedling vs. PRP + Microneedling
Overall GSGS Reduction (Scar Severity Score)	Moderate reduction	Significantly greater reduction	Superior reduction in scar severity across all procedural variants

5.5. Synergy with Physical Technologies (Fractional CO_2 Laser Therapy): Mechanisms and Clinical Profile of Combined AFCL-PRP Therapy

Ablative fractional carbon dioxide laser (AFCL) plays a fundamental role in the combined treatment of persistent structural defects and acne scars (Novintan et al., 2026). The mechanism of action of this technology is based on fractional photothermolysis: the laser microbeam creates controlled microthermal zones (MTZs) within the tissue, inducing focal evaporation (ablation) of the epidermis while sparing surrounding tissue islands, thereby facilitating rapid re-epithelialization (Helbig et al., 2009; Novintan et al., 2026). The delivered thermal energy stimulates the dermis, activating fibroblasts for intense neocollagenesis, synthesis of new extracellular matrix, and reorganization of elastic fibers, ultimately leading to smooth scar contours (Helbig et al., 2009).

Integrating platelet-rich plasma as an adjunctive therapy into the ablative laser procedure (AFCL) generates a pronounced biochemical-physical synergy. Combining controlled thermal injury with a dose of autologous cytokines significantly enhances and prolongs tissue remodeling, resulting in more distinct structural improvement compared to laser monotherapy alone (Guo et al., 2023; Novintan et al., 2026; Sharma & Garg, 2025). Simultaneously, the addition of PRP plays a crucial role in mitigating post-procedure side effects, reducing the severity of post-procedural edema, erythema, and pain (Priya & Patil, 2023). Accelerated re-epithelialization – promoted by the presence of autologous growth factors – not only drastically shortens downtime but also minimizes the risk of post-inflammatory hyperpigmentation (PIH). The efficacy of this hybrid approach is substantiated by clinical trial reviews and split-face comparative analyses, which demonstrate the superiority of combination therapy via both intradermal injection and topical application onto the laser-ablated epidermis manifested by objective reductions in scar depth, evened pigmentation, and higher patient satisfaction rates (Novintan et al., 2026).

The primary barrier to widespread clinical implementation of combined AFCL–PRP protocols remains the lack of unified national guidelines and standardized procedural parameters (regarding both apheresis dosing and laser energy density settings) (Novintan et al., 2026).

6. Discussion: Limitations and Future Perspectives

The application of autologous platelet concentrates (APCs) as an adjunctive therapy in the treatment of atrophic acne scars is strongly supported by clinical studies. The integration of APCs into microneedling or laser therapy procedures achieves superior regenerative efficacy compared to monotherapy while maintaining a high safety profile (Davies & Miron, 2024). Furthermore, a growing body of evidence confirms that stimulation using platelet-rich plasma (PRP) or liquid platelet-rich fibrin (f-PRF/i-PRF) significantly accelerates extracellular matrix repair (Assinger et al., 2026). Despite these promising outcomes, this evaluation requires pointing out substantial methodological limitations, such as the high heterogeneity of commercial APC harvesting systems (which vary in centrifugal force, cellular composition, and growth factor release kinetics) as well as the variability of treatment parameters (Novintan et al., 2026). Additional major

obstacles include inter-individual patient variability (age, lifestyle, cytokine profile) and the lack of standardized, objective metrics for evaluating therapeutic outcomes, which precludes the standardization of meta-analyses (Novintan et al., 2026). In clinical practice, a series of 3 sessions spaced 4 weeks apart is generally recommended, combined with maintenance treatments, proper home skincare, and photoprotection (Davies & Miron, 2024). Future randomized controlled clinical trials (RCTs) should precisely elucidate the advantages of PRF over PRP and evaluate the efficacy of combination protocols in distinct patient cohorts, explicitly differentiating acne scars from burn scars due to their divergent healing pathomechanisms (Diab et al., 2022; Novintan et al., 2026).

7. Summary and Conclusions

Innovative autologous platelet concentrates, encompassing platelet-rich plasma and platelet-rich fibrin, represent a foundational pillar of modern regenerative medicine and interventional dermatology. A review of current scientific evidence unequivocally indicates that monotherapy relying on a single modality is being superseded by advanced combination procedures. Physical and mechanical therapies, such as microneedling, CO_2 laser treatment, or subcision, create an ideal environment for autologous cytokines. Together, they significantly boost neocollagenesis and extracellular matrix remodeling. Liquid platelet-rich fibrin plays a particularly vital role in this process; by forming a three-dimensional biological scaffold with an extended growth factor release profile, it demonstrates therapeutic superiority over classical plasma and effectively prevents the recurrence of fibrous adhesions beneath the scar base. A crucial aspect of combined platelet concentrate administration is the significant improvement in the safety profile of the procedures themselves: the presence of biomediators mitigates post-procedural edema, erythema, and pain, accelerates re-epithelialization, shortens recovery time, and minimizes the risk of post-inflammatory hyperpigmentation. However, the continued dynamic evolution of this field necessitates the establishment of a cohesive international consensus regarding the standardization of apheresis and dosing protocols. Crucially, the ultimate clinical success of modern biostimulators is not measured solely by the degree of anatomical tissue repair, but primarily by breaking down psychological barriers, facilitating effective social reintegration, and achieving lasting improvements in the quality of life for patients affected by persistent structural defects.

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