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Original Article

Integrating Molecular Biology and Biomechanics in Orthodontic Treatment of Periodontitis

Sarah L. McLean[1], Kim Min Seok[2]*, Dina M. Saleh[1]

[1] Department of Periodontics and Orthodontics, Faculty of Dentistry, University of Toronto, Toronto, Canada.
[2] Department of Periodontics and Orthodontics, College of Dentistry, Yonsei University, Seoul, South Korea.

***E-mail** ✉ minseok.kim@gmail.com

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ABSTRACT

Periodontitis and orthodontic treatment present a complex interplay, where uncontrolled inflammation can exacerbate alveolar bone loss, while appropriately managed orthodontics can enhance periodontal stability. This conceptual paper proposes a novel mechanistic–clinical hybrid framework that integrates molecular biology, biomechanical principles, clinical risk stratification, and patient behavioral factors to guide orthodontic treatment in periodontitis patients. At the molecular level, cytokine profiles and inflammatory mediators drive alveolar bone remodeling, influencing responses to orthodontic forces. Biomechanically, force mechanics must be calibrated to minimize periodontal stress in compromised tissues. Clinical decision-making incorporates risk stratification based on disease staging and patient-specific factors, enabling real-time chairside adjustments. Patient behavior and adherence are embedded as modulators of treatment outcomes. This framework bridges the gap between pathophysiological insights and practical orthodontic planning, offering a multi-level synthesis that promotes periodontal stability during tooth movement. By linking molecular markers directly to force application and monitoring strategies, it facilitates personalized interventions, potentially reducing complications like further bone loss or tooth mobility. The model underscores the need for interdisciplinary collaboration between periodontists and orthodontists, advancing conceptual understanding in periodontology. Ultimately, this approach aims to optimize long-term periodontal health in orthodontically treated periodontitis patients.

Keywords: Periodontitis, Orthodontics, Cytokine profiles, Alveolar bone remodeling, Orthodontic biomechanics, Clinical risk stratification, Patient adherence

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Introduction

Periodontitis, a chronic inflammatory disease characterized by progressive destruction of the periodontal ligament and alveolar bone, affects a significant portion of the adult population worldwide [1, 2]. Its multifactorial etiology involves microbial dysbiosis, host immune responses, and environmental factors, leading to irreversible tissue loss if unmanaged [3]. In patients with periodontitis, orthodontic treatment introduces additional challenges and opportunities. Orthodontics aims to correct malocclusions, improve esthetics, and enhance function through controlled tooth movement, but in periodontally compromised individuals, this process must navigate heightened risks of exacerbated inflammation, further bone resorption, and tooth mobility [4, 5].

Historically, orthodontic intervention in periodontitis patients was approached with caution, often deferred until periodontal stability was achieved [6]. However,

emerging evidence suggests that orthodontics, when integrated with periodontal therapy, can contribute to tissue regeneration and improved periodontal parameters, such as reduced probing depths and enhanced bone fill [7, 8]. This shift reflects a growing recognition of the bidirectional relationship between periodontal health and orthodontic outcomes. For instance, pathological tooth migration—a common sequela of advanced periodontitis—can be corrected orthodontically, potentially stabilizing the periodontium by realigning forces and reducing occlusal trauma [9]. Conversely, inappropriate orthodontic forces in inflamed tissues may accelerate bone loss, underscoring the need for precise integration of biological and mechanical principles [10].

At the core of this integration lies molecular biology, which elucidates the inflammatory cascades driving periodontitis. Cytokine profiles, including pro-inflammatory mediators like interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α), and anti-inflammatory counterparts such as IL-10, modulate host responses to microbial challenges and mechanical stress [11, 12]. In orthodontic contexts, these molecules influence alveolar bone remodeling, a process involving osteoclast activation on compression sides and osteoblast proliferation on tension sides of the periodontal ligament [13]. Biomechanical factors, such as the magnitude, direction, and duration of orthodontic forces, interact with this molecular environment, determining whether remodeling is adaptive or destructive [14].

Clinical decision-making in such cases requires risk stratification, incorporating disease staging (e.g., via the 2017 World Workshop classification) and patient-specific variables like smoking status, systemic health, and genetic predispositions [15, 16]. Chairside assessments, including periodontal charting and radiographic evaluation, guide force application, but often lack direct linkage to underlying molecular dynamics. Patient behavior and adherence further complicate this landscape; compliance with oral hygiene, recall visits, and lifestyle modifications critically affects treatment success, yet these factors are frequently underexplored in orthodontic planning [17, 18].

Despite advances, a significant gap persists between molecular/pathophysiological understanding and real-time clinical application. Traditional orthodontic protocols in periodontitis patients emphasize empirical adjustments, such as lighter forces or prolonged stabilization phases, but fail to systematically incorporate cytokine-driven insights or behavioral modulators [19]. This disconnect can lead to suboptimal outcomes, including prolonged treatment times, increased relapse risks, or unwarranted avoidance of orthodontics altogether [20]. Periodontology 2000 has long emphasized mechanistic syntheses that bridge benchside research to clinical practice, highlighting the need for conceptual frameworks that synthesize disparate domains [21].

This paper addresses this gap by developing an original mechanistic–clinical hybrid conceptual framework. It posits that orthodontic treatment in periodontitis patients should be guided by a multi-level integrative model, linking molecular biology directly to biomechanical strategies, clinical risk stratification, and patient behavioral factors. The framework enables chairside decision-making by translating cytokine profiles and inflammatory mediators into actionable parameters for force mechanics and monitoring. For example, elevated pro-inflammatory cytokines might prompt reduced force magnitudes to mitigate excessive resorption, while behavioral assessments could inform adherence-enhancing interventions.

The contribution is twofold: first, it offers a novel synthesis not previously articulated in this form, emphasizing direct molecular-to-clinical bridges; second, it provides a tool for clinicians and researchers to conceptualize personalized orthodontic plans, fostering periodontal stability amid tooth movement. The paper proceeds as follows: the theoretical background and literature review synthesizes key constructs; the proposed framework details the integrative model; subsequent sections (to be continued) outline propositions, discuss implications, and conclude with future directions. By fostering this synthesis, the framework aligns with Periodontology 2000's focus on rigorous, clinically relevant conceptual advancements.

Theoretical Background & Literature Review

Molecular biology of periodontitis and its intersection with orthodontic tooth movement

Periodontitis is fundamentally an inflammatory disorder, where dysbiotic microbial communities trigger aberrant host responses, leading to tissue breakdown [22]. Central to this process are cytokine profiles, which orchestrate immune cell recruitment and activation. Pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α amplify osteoclastogenesis via the RANKL/OPG pathway, promoting alveolar bone resorption [11, 23]. In contrast, anti-inflammatory mediators like IL-10 and transforming growth factor-β (TGF-β) mitigate these effects, supporting tissue repair [12]. Recent studies highlight dynamic cytokine shifts in gingival crevicular fluid (GCF) during disease

progression, with elevated pro-inflammatory levels correlating to deeper pockets and bone loss [24].

In orthodontic contexts, tooth movement superimposes mechanical stress on this inflammatory milieu, altering cytokine expression. Orthodontic forces induce localized compression and tension in the periodontal ligament (PDL), stimulating cytokine release that facilitates bone remodeling [13, 25]. For instance, early-phase orthodontic loading upregulates IL-1β and TNF-α at compression sites, enhancing osteoclast activity for resorption, while tension sites show increased IL-10, promoting osteoblast differentiation [26]. However, in periodontitis patients, baseline inflammation amplifies these responses, potentially leading to excessive resorption and delayed remodeling [27]. Research indicates that chronic periodontitis alters GCF cytokine profiles during orthodontics, with persistent high IL-6 levels associated with greater bone loss [15, 28].

This molecular-orthodontic interface underscores the need for biomarker-informed approaches. Cytokine assays in GCF could predict remodeling responses, but current literature largely confines these to research settings, lacking translation to clinical protocols [29].

Biomechanical principles in orthodontic force application for periodontally compromised tissues

Biomechanics governs orthodontic tooth movement through controlled force systems that exploit PDL and alveolar bone plasticity [14, 30]. Optimal forces (typically 50-100g for tipping, higher for bodily movement) balance resorption and apposition, minimizing hyalinization—a necrotic PDL response to excessive stress [31]. In healthy periodontium, this yields predictable outcomes, but periodontitis reduces alveolar bone height and PDL integrity, altering force distribution and increasing tipping risks [32].

Studies on orthodontic biomechanics in periodontitis emphasize lighter, intermittent forces to accommodate reduced anchorage and heightened inflammation [4]. For example, finite element analyses demonstrate that in reduced periodontium, forces concentrate at crestal bone, exacerbating resorption if not calibrated [33]. Integration with molecular insights reveals that biomechanical stress modulates inflammatory mediators; high forces elevate TNF-α, accelerating osteoclastogenesis in inflamed tissues [34]. Conversely, low-magnitude forces may enhance anti-inflammatory profiles, supporting stability [35].

Literature reviews highlight successful orthodontic outcomes in stabilized periodontitis, with forces adjusted for bone density and defect morphology [7, 36]. Yet, biomechanical models often overlook molecular variability, leading to generic recommendations rather than personalized mechanics [37].

Clinical risk stratification and chairside decision-making

Clinical decision-making in orthodontic treatment of periodontitis patients relies on risk stratification to tailor interventions [16, 38]. The 2017 classification stages periodontitis by severity and extent, guiding orthodontic feasibility; stage IV cases, with severe bone loss and mobility, demand rigorous stabilization before orthodontics [39]. Risk factors include smoking, diabetes, and genetic polymorphisms affecting cytokine production, which heighten susceptibility to force-induced damage [40].

Chairside tools, such as periodontal probing, cone-beam computed tomography (CBCT), and occlusal analysis, inform decisions on force vectors and appliance selection [41]. For instance, in periodontitis, segmented arches or aligners may be preferred to minimize extrusive forces on compromised teeth [42]. However, integration with molecular data remains limited; while cytokine profiling could stratify high-risk patients (e.g., those with IL-1β overexpression), clinical protocols rarely incorporate this [43].

Evidence supports interdisciplinary approaches, where periodontal maintenance precedes and parallels orthodontics, reducing risks [8, 44]. Yet, decision-making often reactive, addressing complications post-force application rather than preemptively linking to molecular and biomechanical factors.

Patient behavioral factors and adherence in treatment success

Patient behavior profoundly influences periodontal-orthodontic outcomes, with adherence to hygiene, diet, and recalls determining long-term stability [17]. Non-adherence exacerbates plaque accumulation, amplifying inflammation in orthodontic appliances' presence [45]. Behavioral models, such as the Health Belief Model, suggest perceptions of susceptibility and benefits drive compliance [46].

In periodontitis patients, adherence challenges are compounded by disease chronicity; studies show lower compliance rates correlate with increased bone loss during orthodontics [18, 47]. Interventions like motivational interviewing enhance adherence, but integration into orthodontic planning is sparse. Linking behavior to molecular outcomes, poor hygiene elevates pro-inflammatory cytokines, counteracting biomechanical efforts [48].

Overall, literature reveals silos: molecular research isolated from biomechanics, clinical stratification underutilizing behavioral insights [49]. A synthesis is needed to bridge these for chairside application.

Proposed theoretical framework

The proposed framework is a multi-level integrative model that synthesizes molecular biology, biomechanical principles, clinical risk stratification, and patient behavioral factors into a cohesive structure for guiding orthodontic treatment in periodontitis patients. It conceptualizes orthodontic planning as a dynamic, interconnected system where molecular signals inform biomechanical adjustments, moderated by clinical and behavioral elements, to optimize alveolar bone remodeling and periodontal stability. This hybrid approach directly bridges pathophysiological mechanisms to chairside decisions, enabling real-time adaptations that minimize risks and enhance outcomes.

At the foundational level, molecular biology encompasses cytokine profiles and inflammatory mediators as primary drivers. Elevated pro-inflammatory cytokines (e.g., IL-1β, TNF-α) signal heightened resorption risk, while balanced profiles indicate remodeling potential. These are assessed via GCF sampling or biomarkers, providing a "molecular risk index" that quantifies inflammatory burden.

The biomechanical level overlays force mechanics, calibrating magnitude, direction, and duration based on molecular inputs. For high-inflammatory profiles, lighter forces (e.g., 20-50g) and intermittent application are prioritized to avoid exacerbating osteoclast activity, promoting adaptive remodeling in compromised alveolar bone.

Clinical risk stratification integrates these levels, using staging tools to categorize patients (low/moderate/high risk) and guide chairside decisions. For instance, in high-risk cases, molecular data might dictate phased treatment: initial stabilization, followed by monitored force application with periodic reassessments.

Patient behavior and adherence act as cross-cutting moderators, influencing all levels. Adherence metrics (e.g., hygiene scores) adjust the framework; poor compliance might necessitate behavioral interventions, such as app-based reminders, to sustain molecular and biomechanical equilibrium.

The framework operates iteratively presented in **figure 1**: initial assessment links molecular profiles to risk strata, informing biomechanical plans; ongoing monitoring (e.g., cytokine trends) allows chairside tweaks, with behavioral feedback loops ensuring sustainability.

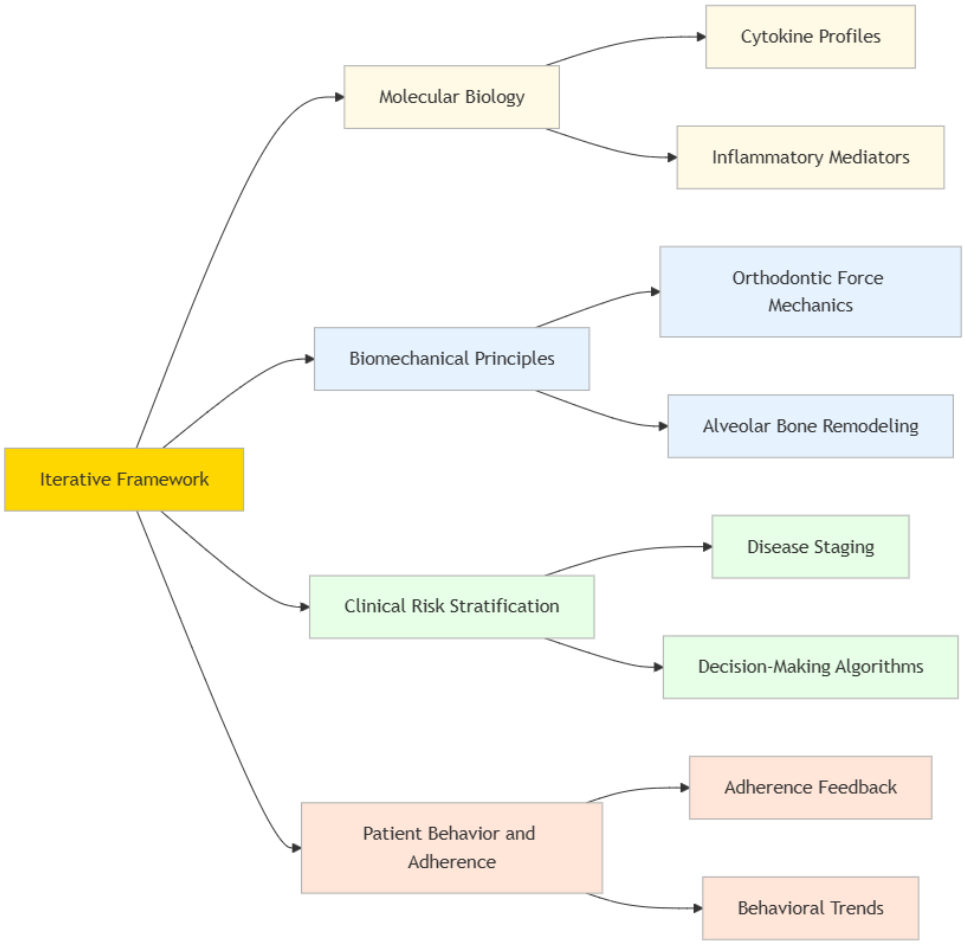

Figure 1. Hierarchical conceptual framework for orthodontic risk stratification in periodontal patients. The diagram integrates four interconnected layers: molecular biology (cytokine profiles, inflammatory mediators), biomechanical principles (force mechanics, alveolar bone remodeling), clinical risk stratification (disease staging, chairside decision-making), and patient behavior/adherence

Propositions

Building on the proposed mechanistic–clinical hybrid framework, this section articulates a series of original propositions that operationalize the integrative model. These propositions represent testable hypotheses linking molecular biology to biomechanical and clinical elements, modulated by patient behavior. They are designed to guide chairside decision-making in orthodontic treatment for periodontitis patients, emphasizing periodontal stability. Each proposition is derived from the framework's multi-level structure, where molecular signals inform force mechanics, risk stratification refines applications, and behavioral factors ensure sustainability. These are not empirical findings but conceptual assertions synthesized from existing literature, offering a novel bridge between pathophysiology and practice.

Proposition 1: Cytokine-Driven force calibration

In periodontitis patients exhibiting elevated pro-inflammatory cytokine profiles (e.g., high IL-1β and TNF-α in GCF), orthodontic force magnitudes should be calibrated to low levels (20-50g) to mitigate excessive osteoclast activation and alveolar bone resorption, thereby promoting adaptive remodeling over destructive processes. This proposition posits that molecular assessment at treatment onset can predict biomechanical responses, allowing preemptive adjustments. For instance, if baseline cytokine analysis reveals a pro-inflammatory dominance, forces should prioritize intermittent application to allow PDL recovery, reducing risks of hyalinization in compromised tissues [11, 13]. Clinically, this integrates with risk stratification by assigning high-risk status to such patients, prompting phased treatment with initial light forces and frequent monitoring. Patient adherence plays a moderating role; non-compliance with hygiene could amplify cytokine surges, necessitating behavioral interventions like motivational counseling to sustain low-inflammatory

states [17, 31]. This direct molecular-to-biomechanical link addresses a key gap, enabling personalized orthodontics that minimizes periodontal deterioration while achieving tooth movement [33- 44, 50].

Proposition 2: Inflammatory mediators and remodeling dynamics

Anti-inflammatory mediators (e.g., IL-10) in balanced cytokine profiles facilitate enhanced alveolar bone apposition during tension phases of orthodontic movement, suggesting that patients with favorable mediator ratios can tolerate standard force mechanics (50-100g) without compromising periodontal stability. This hypothesis extends the framework by proposing that mediator profiling informs not only force reduction but also acceleration strategies, such as using aligners for controlled tension in stabilized periodontitis [12, 14]. In chairside practice, this translates to risk-stratified decisions where moderate-risk patients undergo CBCT-guided force vectoring to optimize tension-compression balances [16, 41]. Behavioral factors are critical; adherence to anti-inflammatory diets (e.g., omega-3 rich) could bolster IL-10 levels, synergizing with biomechanics [18]. By linking mediators directly to remodeling, this proposition fosters proactive monitoring, such as serial GCF assays, to adjust forces in real-time, potentially shortening treatment durations in responsive patients [45-49, 51-53].

Proposition 3: Biomechanical modulation in high-risk strata

For patients stratified as high-risk (stage III/IV periodontitis with systemic modifiers like diabetes), biomechanical principles should incorporate segmented force systems to distribute stress evenly, preventing localized bone loss exacerbated by underlying inflammatory mediators. This proposition asserts that clinical stratification acts as a gatekeeper, where molecular data (e.g., RANKL/OPG ratios) refines force mechanics to avoid crestal overload [23, 33]. Chairside implementation involves initial stabilization phases with no forces until cytokine normalization, followed by customized appliances like cantilever arches [30, 42]. Patient behavior moderates outcomes; poor adherence to recall visits could destabilize strata, requiring integrated behavioral assessments via tools like the Health Belief Model [46]. This synthesis highlights the framework's iterative nature, where risk reassessment loops back to molecular evaluation, ensuring safe orthodontics in vulnerable periodontia [54, 63].

Proposition 4: Behavioral adherence as a framework moderator

Patient adherence to oral hygiene and lifestyle modifications directly modulates the efficacy of molecular-biomechanical integrations, such that high-adherence profiles enable more aggressive orthodontic plans without elevating inflammatory risks. This proposition positions behavior as a cross-level influencer, proposing that adherence scores (e.g., from plaque indices) should trigger framework adjustments, like delaying force application in low-adherence cases [17, 45]. Clinically, this informs decision-making by incorporating behavioral screening into risk stratification, using interventions such as app reminders to enhance compliance [18, 47]. Linked to molecular biology, consistent adherence may downregulate pro-inflammatory cytokines, synergizing with low-force biomechanics [11, 48]. This original linkage underscores the need for behavioral metrics in chairside protocols, transforming static frameworks into dynamic, patient-centered models [64-71].

Proposition 5: Chairside integration for periodontal stability

Real-time chairside decision-making, informed by integrated molecular and biomechanical data, optimizes long-term periodontal stability by enabling mid-treatment adjustments that align force mechanics with evolving cytokine profiles and adherence patterns. This culminating proposition GCF sampling and behavioral check-ins—allow for adaptive orthodontics, reducing complications like mobility [15, 28]. In high-risk scenarios, this might involve force cessation if cytokines spike, guided by stratification tools [16, 39]. By bridging all constructs, it promotes interdisciplinary collaboration, where periodontists provide m
olecular insights for orthodontic tweaks [8, 44]. This m
echanistic-clinical hybrid thus facilitates personalized, evidence-based care, advancing periodontal-orthodontic synergy [71-73].

General Discussion

The proposed mechanistic–clinical hybrid framework and its propositions offer a novel conceptual synthesis for orthodontic treatment in periodontitis patients, addressing longstanding silos between molecular research, biomechanical application, and clinical practice. By directly linking cytokine profiles to force mechanics and chairside decisions, modulated by patient behavior, this model provides a roadmap for personalized interventions that prioritize periodontal stability. Implications span clinical, research, and

educational domains, while acknowledging limitations and future directions.

Clinically, the framework enhances decision-making by translating abstract molecular data into actionable parameters. For example, elevated IL-1β could prompt lighter forces, reducing risks in compromised alveoli [11, 26]. This aligns with evidence that integrated periodontal-orthodontic care improves outcomes, such as reduced probing depths [7, 8]. Risk stratification, per the 2017 classification, becomes more nuanced when infused with molecular insights, enabling tailored plans like segmented arches for stage IV cases [15, 32]. Patient adherence, often overlooked, is elevated as a core modulator; interventions improving compliance could amplify framework efficacy, as poor hygiene exacerbates inflammation [17, 45]. Chairside tools, including point-of-care cytokine assays, could operationalize this, fostering real-time adjustments and interdisciplinary teams [29, 43]. Ultimately, this approach may decrease complications, shorten treatments, and expand orthodontic eligibility for periodontitis patients, aligning with Periodontology 2000's emphasis on mechanistic-clinical relevance.

From a research perspective, the propositions invite empirical validation. Longitudinal studies could test cytokine-driven force calibration by correlating GCF profiles with remodeling via CBCT [24, 41]. Biomechanical simulations, using finite element analysis, might quantify force thresholds in inflammatory milieus [33, 34]. Behavioral components warrant randomized trials on adherence interventions' impact on molecular outcomes [48]. This framework could guide meta-analyses synthesizing disparate literatures, addressing gaps like molecular variability in orthodontics [19, 37]. By positing original bridges, it encourages multi-level investigations, potentially using AI for predictive modeling of risk strata [16, 40].

Limitations must be noted. The conceptual nature precludes empirical data, relying on synthesis; real-world variability (e.g., genetic factors) may alter applicability [40]. Cytokine assays, while promising, are not universally accessible, limiting chairside feasibility [29]. Behavioral factors introduce subjectivity, as adherence metrics vary [52]. The framework assumes stabilized periodontitis, not acute phases, and overlooks comorbidities like osteoporosis [22, 25]. Cultural and socioeconomic influences on adherence are underexplored [18].

Future directions include developing validated tools for molecular integration, such as standardized GCF protocols [24]. Prospective cohorts could assess proposition efficacy, measuring outcomes like bone density post-orthodontics [27, 36]. Educational curricula should incorporate this hybrid model, training clinicians in interdisciplinary synthesis [21]. Technological advances, like wearable adherence trackers, could enhance modulation [47]. Overall, this framework advances conceptual understanding, paving the way for evidence-based, patient-centric care in periodontology and orthodontics.

Conclusion

In summary, this conceptual paper introduces a mechanistic–clinical hybrid framework that integrates molecular biology, biomechanical principles, clinical risk stratification, and patient behavioral factors to guide orthodontic treatment in periodontitis patients. By bridging cytokine profiles and inflammatory mediators directly to force mechanics and chairside decisions, it addresses a critical gap, enabling personalized approaches that safeguard alveolar bone remodeling and periodontal stability. The propositions operationalize this model, offering testable hypotheses for force calibration, remodeling optimization, and adherence modulation.

This synthesis holds promise for enhancing clinical outcomes, reducing risks like excessive resorption, and expanding orthodontic viability in compromised periodontia. It underscores the imperative for interdisciplinary collaboration, where molecular insights inform biomechanical strategies, tempered by patient-centered elements. While limitations exist, such as assay accessibility, the framework's iterative design accommodates future refinements.

Ultimately, adopting this multi-level perspective could transform periodontal-orthodontic practice, aligning with Periodontology 2000's mission to fuse rigorous mechanisms with clinical utility. Researchers and clinicians are encouraged to empirically explore these concepts, fostering innovations that optimize long-term oral health in this challenging patient cohort.

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