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INNOVATIVE TECHNOLOGIES FOR EARLY DIAGNOSIS OF PERIODONTAL DISEASES

Yusupjanova Nigora Davronbek qizi
Central Asian Medical University International Medical University Assistant,
Burhoniddin Marg'inoniy Street-64, Phone: +998 95 485 00 70, Email: info@camuf.uz,
Fergana, Uzbekistan
Email: nigorausupzanova79@gmail.com
Orcid: https://orcid.org/0009-0005-7472-7741

Abstract

Early diagnosis of periodontal diseases, such as gingivitis and periodontitis, is crucial for preventing irreversible tissue destruction and tooth loss. Traditional clinical methods—including probing depth measurement and radiographic imaging—often detect the disease only after significant damage has occurred. Recent advances in bioengineering and molecular diagnostics have enabled a paradigm shift toward minimally invasive, real-time, point-of-care detection. Key innovations include salivary biomarkers, lab-on-a-chip biosensors, wearable electrochemical devices, and artificial intelligence–driven analytics. For example, microRNA-based detection platforms such as nanopore sensors can measure periodontitis-associated miRNAs in saliva with high sensitivity. These cutting-edge technologies enable early, non-invasive screening, personalized risk stratification, and better monitoring of therapeutic response in precision periodontology. As these diagnostic tools mature and integrate into clinical workflows, they have the potential to transform periodontal care and improve long-term oral health outcomes.

Keywords

periodontal disease, salivary biomarkers, exosomes, lab-on-a-chip, wearable biosensor, microRNA.

Intradaction: Periodontal diseases represent a significant public health concern worldwide, affecting the supporting structures of the teeth—including gingiva, periodontal ligament, and alveolar bone—and if left untreated, can lead to tooth mobility and loss. Clinically, periodontal disease ranges from reversible gingivitis to more severe, irreversible periodontitis. Traditional diagnostic approaches rely on clinical parameters such as probing pocket depth (PPD),

bleeding on probing (BOP), attachment level, and radiographic imaging to assess bone loss. However, these methods generally detect disease only after tissue destruction has occurred, limiting the efficacy of early intervention. The necessity for earlier, more sensitive diagnostics has led to a growing interest in biomarkers and bioengineering solutions. Biomarkers present in saliva and gingival crevicular fluid (GCF) reflect the biological processes underlying inflammation, tissue breakdown, and host response, offering a non-invasive window into disease activity. Saliva, in particular, is an attractive diagnostic medium because it is easily collected, abundant, and rich in molecules such as cytokines, enzymes, microbial DNA, and microRNAs. These salivary components dynamically change in response to periodontal inflammation and therefore have considerable potential for early disease detection.

Concurrent with biomarker discovery, technological advancements have enabled the development of highly sensitive biosensors and miniaturized diagnostic platforms. Lab-on-a-chip systems integrate microfluidics, molecular recognition elements, and detection modules to perform rapid assays at the point of care. These platforms can simultaneously measure multiple biomarkers, thus enabling a multiplexed approach that enhances diagnostic accuracy.

Wearable biosensors represent another frontier. Devices like mouthguard-based electrochemical sensors can continuously monitor markers of inflammation, such as matrix metalloproteinase-8 (MMP-8), in real time. When combined with advanced data processing—particularly artificial intelligence (AI) and deep learning—such systems can distinguish subtle pathological signals from background noise, stratify risk, and even predict disease progression or response to therapy. Furthermore, molecular techniques such as nanopore sensing allow real-time detection of microRNAs associated with periodontitis (e.g., miR-31) in salivary samples, offering specificity at the molecular level. Exosomal microRNAs, contained in extracellular vesicles from gingival tissues, provide yet another layer of diagnostic information with high discriminatory power.

Together, these innovations move periodontal diagnostics from a reactive, clinic-based model toward a proactive, personalized paradigm. Early detection may enable tailored preventive or therapeutic strategies, reduce the burden of advanced disease, and improve long-term oral health outcomes. This article reviews the most promising emerging technologies for early diagnosis of periodontal diseases, discusses their methodological underpinnings, and considers how they may be integrated into future clinical practice.

Materials and Methods: To investigate the most advanced technologies for early detection of periodontal disease, we conducted a structured literature review

focusing on peer-reviewed research published between 2018 and 2025. We searched PubMed, Scopus, and Google Scholar using combinations of the following search terms: "periodontal disease biomarkers," "salivary microRNA periodontitis," "lab-on-a-chip periodontal diagnostics," "wearable biosensor MMP-8," "electrochemical saliva sensor," and "deep learning periodontal disease."

We included in vitro studies, pilot clinical trials, cohort studies, and proof-of-concept device studies. Exclusion criteria were papers without empirical data (e.g., purely theoretical works), studies not involving human or human-derived saliva/GCF, and older technologies not employing miniaturized or point-of-care systems.

From the identified literature, we extracted key methodological details, including:

1. Type of biomarker assessed — cytokines (e.g., IL-1β, IL-6), enzymes (MMP-8, MMP-9), microRNAs (miR-31, miR-143-3p, miR-155), exosomal miRNAs, and microbial nucleic acids.

2. Detection technology — e.g., nanopore sensors, molecularly imprinted polymer (MIP) electrochemical sensors, lab-on-a-chip microfluidics, magnetic modulation biosensing, AI-enhanced signal processing.

3. Platform design — including microfluidic layout, wearable form factor, electrode composition (e.g., graphene oxide interlayer), sample volume, measurement modality (e.g., impedance, electrical resistance, fluorescence).

4. Analytical performance — sensitivity, specificity, limit of detection, dynamic range, response time, stability, and reproducibility, based on validation in artificial saliva or patient saliva.

5. Clinical validation — when available, details of sample size, study design (cross-sectional, cohort), correlation with clinical periodontal parameters (probing depth, attachment loss), and predictive value (e.g., ROC curves, risk stratification).

We synthesized methodological trends and compared platforms in terms of feasibility, scalability, and readiness for translation to clinical or consumer use. Furthermore, we evaluated challenges and barriers to adoption, such as calibration, biofouling, user acceptability, regulatory hurdles, and cost.

Finally, we organized the findings thematically into three technological categories: (1) salivary molecular biomarkers (miRNAs, exosomes, cytokines), (2) lab-on-a-chip and microfluidic biosensors, and (3) wearable biosensing devices with AI integration. This classification forms the backbone for our results and discussion.

Results: Salivary Molecular Biomarkers A wealth of recent studies has demonstrated that salivary biomarkers reliably reflect periodontal disease activity.

Among these, cytokines such as interleukin-1β (IL-1β), interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and matrix metalloproteinase-8 (MMP-8) are consistently elevated in patients with active periodontitis.

MicroRNAs (miRNAs) in saliva have emerged as powerful diagnostic molecules. A pilot cross-sectional study identified that hsa-miR-381-3p levels in whole saliva significantly correlated with periodontal probing depth and disease severity. A cohort study over two years further revealed that salivary miRNAs (including hsa-miR-5571-5p, hsa-let-7f-5p, miR-99a-5p, miR-28-5p, and miR-320d) predicted progression of periodontitis, suggesting prognostic value.

Moreover, next-generation sequencing combined with qRT-PCR validation identified miR-143-3p as significantly upregulated in chronic periodontitis patients versus healthy controls, indicating its potential as a novel salivary biomarker.

In addition, extracellular vesicle–associated miRNAs (exosomal miRNAs) isolated from saliva have shown even stronger discriminatory power. A pilot study demonstrated that miRNAs such as hsa-miR-140-5p, hsa-miR-146a-5p, and hsa-miR-628-5p in salivary small extracellular vesicles (sEVs) could distinguish periodontitis from healthy controls with high accuracy (AUC = 0.96).

Finally, a more specific miRNA, miR-31, has been detected by nanopore sensing platforms. Using an engineered nanopore, researchers were able to detect miR-31 in human saliva samples in real time, demonstrating high sensitivity and specificity.

In addition to nucleic acids, protein biomarkers remain important. For instance, microRNA-155 (miR-155) was shown in a clinical case-control study to correlate with both periodontal status and coronary heart disease severity, underlining its relevance in systemic inflammation associated with periodontitis.

Lab-on-a-Chip and Microfluidic Biosensors: Advances in microfluidics and lab-on-a-chip (LOC) technologies have enabled miniaturized, rapid, multiplexed assays for periodontal biomarkers. A review study highlighted how LOC devices integrate sample handling, molecular recognition, and detection in a single compact format.

For example, recent work published in Lab on a Chip described a wearable microfluidic patch capable of multimodal sensing. The system integrates biochemical (e.g., cytokine) sensors with microfluidic sample handling and wireless data transmission. Although not yet applied directly to periodontal biomarkers in that study, the design principles can be readily adapted to saliva-based detection of inflammatory proteins or microRNAs.

Another promising approach is magnetic modulation biosensing (MMB), which uses magnetically modulated beads to enhance the sensitivity of biomarker

detection. MMB has been used in other fields to detect proteins and nucleic acids at very low concentrations, with rapid assay times and minimal sample processing. While its direct application to periodontal biomarkers remains in early development, the high sensitivity and low-wash requirement suggest strong potential.

Wearable Biosensors with AI Integration: Perhaps the most exciting technological frontier is the development of wearable, continuously operating biosensors. A landmark study demonstrated an electrochemical sensor built into a mouthguard, using a molecularly imprinted polymer (MIP) matrix targeting MMP-8, a key enzyme associated with periodontal inflammation.

In that device, the MIP sensor includes a graphene oxide interlayer to boost conductivity. The system monitors impedance changes via electrochemical impedance spectroscopy (EIS) in real time as MMP-8 in saliva binds to the sensor. To improve diagnostic accuracy, the raw impedance data are processed with a convolutional neural network (CNN) deep-learning model that filters noise and predicts MMP-8 concentration trends.

Clinical validation with patient saliva showed strong correlation with standard methods, and the wearable platform could alert to early inflammation before clinical symptoms become obvious.

In summary, our review of the literature identifies multiple complementary technological strategies for early periodontal disease diagnosis: molecular biomarkers in saliva (especially miRNAs and exosomal miRNAs), miniaturized lab-on-chip devices for multiplexed assays, and wearable biosensors coupled with AI for continuous monitoring.

Discussion: The early detection of periodontal disease represents a critical unmet need in dentistry. Traditional clinical diagnostics often identify disease only after substantial tissue damage has occurred, limiting the opportunity for meaningful early intervention. The innovative technologies described here offer a compelling solution by enabling non-invasive, sensitive, and real-time detection of molecular changes that precede overt clinical signs.

Significance of Salivary Biomarkers: Salivary biomarkers provide a biological window into early periodontal inflammation. Cytokines such as IL-1β, IL-6, and TNF-α reflect the host immune response, while enzymes like MMP-8 indicate tissue breakdown. Nevertheless, cytokine and enzyme levels can be influenced by multiple factors, including systemic inflammation or oral hygiene, potentially reducing their specificity. The emergence of microRNAs addresses this limitation: miRNAs are more stable than proteins, can be highly specific to pathogenic pathways, and may provide prognostic information.

Among microRNAs, miR-143-3p and miR-31 stand out. miR-143-3p was significantly elevated in chronic periodontitis patients in both NGS-based discovery studies and qRT-PCR validation. miR-31 detection via nanopore sensing demonstrated rapid, label-free, and highly sensitive measurement in saliva. These approaches could eventually allow chairside or even at-home molecular screening.

Exosomal miRNAs further enhance diagnostic accuracy. Since exosomes encapsulate miRNAs released from diseased periodontal tissues, they may enrich for disease-specific signals. The pilot study by Han et al. identified exosomal miRNAs (e.g., miR-146a-5p) that distinguished periodontitis from health with high discriminatory power (AUC = 0.96). Integrating exosomal miRNA profiling into diagnostic workflows may refine risk stratification and disease monitoring.

Furthermore, systemic relevance of some miRNAs has been noted. For instance, miR-155 correlates with both periodontal status and coronary heart disease severity in a clinical study , hinting that periodontal diagnostics might also provide insight into systemic inflammatory burden.

Technological Platforms: Lab-on-a-Chip and Biosensors: Lab-on-a-chip (LOC) devices represent a powerful tool for point-of-care diagnostics. Microfluidic integration allows for minimal sample volume, rapid reaction kinetics, and multiplexed assays. The review of LOC developments shows how these systems can transition biomarker analysis from centralized labs to the dental chair or even remote settings. The wearable microfluidic patch described in Lab on a Chip , although not yet applied to periodontal biomarkers, demonstrates the feasibility of real-time biomarker measurement in a portable format. Magnetic modulation biosensing (MMB) holds additional promise. Because MMB exploits magnetically modulated beads and laser-detected fluorescence, it offers high sensitivity even at very low analyte concentrations without extensive washing steps. While direct applications to periodontitis biomarkers are in early stages, combining MMB with salivary cytokines or nucleic acids could yield rapid, ultrasensitive assays suitable for chairside diagnostics.

Wearable Biosensor Innovations The mouthguard-based biosensor that monitors MMP-8 is particularly transformative. MMP-8 is a well-known biomarker of active tissue destruction in periodontitis, but traditional measurement often requires laboratory assays. The wearable system integrates a molecularly imprinted polymer (MIP) selective for MMP-8, with a conductive graphene oxide layer, enabling continuous, label-free electrochemical detection via impedance measurement. Most importantly, the system uses deep learning (a CNN) to analyze impedance spectra in real time. This AI integration helps distinguish true inflammation signals from biological noise, improving diagnostic accuracy and

potentially predicting flare-ups before they become clinically apparent. The proof-of-concept study showed good correlation with conventional assays and suggests a path toward personalized, continuous periodontal health monitoring.

This approach aligns with the paradigm of "precision periodontology": diagnostics tailored to individual risk, combined with real-time feedback to guide preventive or therapeutic interventions.

Challenges and Limitations

Despite these exciting advances, several challenges remain before these technologies can be widely adopted in clinical practice.

1. Standardization and Calibration. Biosensors must be carefully calibrated for salivary matrices, which are complex and variable. Components such as pH, viscosity, and interfering substances (food, microbes) can affect measurement. Reproducibility across individuals and populations is a major hurdle.

2. Device Stability and Longevity. Wearable devices must maintain stability, sensitivity, and biocompatibility over time. Biofouling (protein or microbial deposition) can degrade sensor performance, especially in the oral environment. Regular calibration or disposable components may be required.

3. Regulatory Approval. New diagnostic devices must undergo rigorous regulatory evaluation for safety, efficacy, and reproducibility. Clinical validation trials in diverse populations are needed before adoption in standard care.

4. User Compliance. For wearable sensors, patient acceptance, comfort, and adherence are critical. A mouthguard sensor, for example, must be ergonomic, safe, and easy to incorporate into daily life.

5. Cost and Accessibility. High-performance devices may be expensive to manufacture, limiting access in low-resource settings. Scaling up production while maintaining quality is essential.

6. Data Management and Privacy. Continuous monitoring generates large volumes of data. Secure transmission, storage, and interpretation (especially using AI) require robust infrastructure and privacy safeguards.

7. Integration into Clinical Workflows. For these technologies to be useful, dentists must incorporate them into their practice. This necessitates training, changes in clinical protocols, and alignment with reimbursement models.

Future Directions

To maximize the potential of these technologies, future research should focus on:

Large-scale clinical studies validating salivary miRNAs and exosomal biomarkers across diverse patient populations and disease stages.

Optimization of lab-on-a-chip devices specifically for periodontal biomarkers, including multiplex panels and microfluidic designs tailored to saliva.

Iterative refinement of wearable biosensors to improve biocompatibility, lifespan, and user comfort.

More sophisticated AI models that not only detect biomarker changes but also predict disease onset, progression, or response to therapy.

Development of integrated tele-dentistry platforms that use these devices to remotely monitor patients and guide preventive or therapeutic interventions.

Economic studies to assess cost-effectiveness and strategies for scaling production.

Conclusion: Innovative diagnostic technologies are rapidly transforming the landscape of periodontal disease detection. Salivary biomarkers—including cytokines, MMPs, microRNAs, and exosomal miRNAs—offer non-invasive insight into inflammatory processes even before overt clinical signs emerge. Lab-on-a-chip platforms bring multiplexed assays to the point of care, while wearable biosensors integrated into mouthguard formats provide continuous monitoring of inflammatory enzymes like MMP-8. Coupled with deep-learning algorithms, these systems can filter noise, stratify risk, and alert to early disease activity. Such advances enable a shift from reactive treatment of established disease to proactive, personalized periodontal care. Patients may soon benefit from early intervention strategies tailored to their molecular profile, reducing the risk of tissue destruction, tooth loss, and systemic complications. However, challenges remain in terms of calibration, regulatory approval, user acceptance, and cost. Continued research, validation, and refinement are essential to bring these promising technologies into routine clinical practice. As they mature, they hold the potential to significantly improve periodontal health outcomes and usher in a new era of precision periodontology.

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