



---

## **A Review on Advancements in Periodontal Diagnosis and Imaging Techniques**

*<sup>1</sup>Shyaame M, <sup>2</sup>Vasanthi B, <sup>3</sup>Dr. Uma Sudhakar, MDS, Ph. D*

<sup>1,2</sup> Junior Resident, <sup>3</sup> Professor and Head of the Department, Department of Periodontics

<sup>1,2,3</sup> Thai Moogambigai Dental College and Hospital

---

### **ABSTRACT**

Periodontal conditions remain a notable global health issue, impacting a substantial global population. Timely and precise diagnosis holds paramount importance in facilitating effective interventions and mitigating disease advancement. Recent years have witnessed remarkable strides in the realm of periodontal diagnostic methods and imaging technologies, fundamentally transforming the landscape of periodontal disease detection and treatment. This comprehensive review offers an in-depth exploration of the most recent progressions in periodontal diagnostic instruments and imaging modalities, underscoring their clinical relevance, merits, and prospective avenues.

Keywords: Periodontal diseases, diagnosis, imaging techniques, advancements, clinical significance, future directions.

---

### **INTRODUCTION**

Periodontal diseases, comprising a spectrum of inflammatory conditions impacting the supporting structures of teeth, are a formidable global public health challenge. Millions of individuals worldwide grapple with the ramifications of these conditions, which can lead to tooth loss and are increasingly recognized for their systemic implications, including links to cardiovascular disease and diabetes. In light of these multifaceted concerns, the early and precise diagnosis of periodontal diseases emerges as an imperative facet of effective treatment and the deterrence of disease progression. Recent years have witnessed a remarkable upswing in the sphere of periodontal diagnostics and imaging methodologies.<sup>1,2</sup> This surge in innovation has initiated a transformative era in the realm of periodontal care, promising to augment our capacity to detect and manage these intricate conditions. The objective of this comprehensive review article is to offer an extensive exploration of the latest strides in periodontal diagnostic instruments and imaging modalities. This exploration will underscore their clinical relevance, elucidate their inherent advantages, and chart the possible trajectories for future advancements.

---

### **BIOMARKERS IN SALIVA AND GINGIVAL CREVICULAR FLUID**

Periodontal diseases are characterized by inflammatory processes that affect the tissues surrounding and supporting teeth. Traditional methods of diagnosing these conditions often rely on clinical examination and radiographic imaging.<sup>3,4</sup> However, in recent years, there has been a growing recognition of the potential for salivary and gingival crevicular fluid (GCF) biomarkers to play a pivotal role in periodontal disease diagnosis.<sup>5</sup> Saliva contains a variety of inflammatory markers, such as interleukins (IL-1 $\beta$ , IL-6, IL-8), tumor necrosis factor-alpha (TNF- $\alpha$ ), and C-reactive protein (CRP). Elevated levels of these biomarkers have been associated with periodontal inflammation. Salivary IL-1 $\beta$ , in particular, has shown promise as a diagnostic marker for periodontal disease severity. Matrix Metalloproteinases (MMPs) are enzymes involved in tissue remodeling and degradation.<sup>6</sup> Elevated salivary MMP-8 levels have been linked to periodontal tissue destruction. Monitoring MMP-8 in saliva can aid in assessing disease progression. Periodontal pathogens, such as *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans*, can be detected in saliva. Polymerase chain reaction (PCR) and DNA probe techniques allow for the identification and quantification of these pathogens, aiding in early diagnosis and risk assessment. GCF contains various proinflammatory cytokines, including IL-1 $\beta$ , IL-6, and TNF- $\alpha$ .<sup>7</sup> Elevated levels of these cytokines in GCF correlate with periodontal disease severity. Enzymes responsible for collagen degradation, such as matrix metalloproteinases (MMPs), are found in GCF. High levels of MMPs in GCF are indicative of tissue destruction and can serve as a diagnostic marker. GCF can reflect the host's immune response to periodontal pathogens. Markers like leukotriene B4 (LTB4) and prostaglandin E2 (PGE2) can provide insights into the local immune reaction and disease activity.<sup>8</sup> Biomarkers enable the identification of periodontal disease at its earliest stages, facilitating timely intervention and prevention of disease progression. Biomarkers provide objective measures of disease activity, reducing the subjectivity associated with clinical examination alone. Periodic monitoring of biomarkers allows for tracking disease progression and the effectiveness of treatment interventions. Biomarker analysis can aid in tailoring treatment plans to individual patients' needs, improving the precision of therapy.<sup>9</sup>

---

## MICROBIOLOGICAL TESTS

Historically, culture techniques played a pivotal role in periodontal research, aiming to understand the composition of the subgingival microflora. Despite the introduction of various preventive measures, effectively managing periodontal diseases remains challenging, often initiated after lesions are clinically detectable and have caused irreversible damage.<sup>10</sup> Microbiological diagnostic tests have emerged as valuable tools for early detection, allowing for non-invasive treatment before irreversible damage occurs. Several diagnostic methods have been employed, including culture methods, biochemical tests, molecular biology techniques, and genetic tests. Culture methods, although considered the gold standard, have limitations such as the inability to detect non-viable bacteria and the need for specialized equipment and expertise.<sup>11</sup> Chairside tests offer a practical and rapid approach to periodontal diagnosis. They can detect specific periodontal pathogens and inflammation markers, providing real-time results during routine dental check-ups. These tests include methods like BANA analysis, Perioscan, and the Chair-Side Test (CST). Biochemical tests, such as the Toxicity Prescreening Assay (TOPAS) and Evalusite, assess bacterial toxins and inflammatory proteins in gingival crevicular fluid (GCF). These tests aid in differentiating active and inactive periodontal destruction. Molecular biology techniques like Polymerase Chain Reactions (PCR) and DNA probes allow for the identification of specific periodontal pathogens at the genetic level. Fluorescent In-Situ Hybridisation (FISH) and Terminal Restriction Fragment Length Polymorphism (T-RFLP) are also used for microbial analysis.<sup>12</sup> Genetic tests, including the Periodontal Susceptibility Test (PST), assess an individual's genetic predisposition to periodontal diseases. These microbiological diagnostic aids offer a range of benefits, including early detection, personalized treatment planning, and monitoring disease progression. However, their applications in periodontal diagnosis may have limitations, and further research is needed to address these concerns.<sup>13</sup>

---

## BIOCHEMICAL TESTS

Biochemical tests have played a crucial role in periodontal diagnosis, providing valuable insights into various biomarkers and enzymes present in oral fluids. Oral Fluid Nanosensor Test (OFNASET) is an automated point-of-care device that measures various components in saliva, including DNA gene transcripts, electrolytes, proteins, and enzymes like Horse Radish Peroxide (HRP).<sup>14</sup> It detects specific salivary biomarkers such as Thioredoxin, Interleukin (IL)-8, IL-1 $\beta$ , and SAT, offering potential applications in periodontal diagnostics. ElectroTaxis-On-A-Chip (ETC) is a microfluidic lab-on-chip system that facilitates the detection of clinical biomarkers in physiological settings using minimal sample sizes.<sup>15</sup> It can assess periodontal biomarkers like IL-1, MMP-8, and CRP, as well as biomarkers for cancer from whole saliva. Oraquick is an FDA-approved test for the qualitative detection of HIV-1/2 antibodies. While primarily used for HIV detection, it has some limitations, including a higher sensitivity during the acute phase of HIV infection and the need for confirmation via a second ELISA or western blot. Integrated Microfluidic Platform for Oral Diagnostics (IMPOD) is a clinical point-of-care diagnostic test designed to identify oral disease biomarkers in human saliva. It utilizes sample pre-treatment and electrophoretic immunoassays to measure biomarkers like MMP-8, IL-6, and TNF- $\alpha$ . Periogard Periodontal Tissue Monitor measures Aspartate Aminotransferase (AST) levels in gingival crevicular fluid (GCF).<sup>16</sup> It can indicate attachment loss or alveolar bone loss over time, but it has limitations in identifying all degrading sites. PocketWatch measures AST levels in periodontally diseased and healthy sites. It can provide information about cell death and tissue failure, but its evaluation is subjective and technique-dependent. Periocheck detects GCF-derived enzyme behavior, specifically matrix metalloproteinases and neutral protease enzymes. It is a rapid chairside test with high sensitivity and specificity, but it may be affected by saliva contamination.<sup>17</sup> Prognos-Stik detects serine proteinase and elastase in GCF samples. Elevated elastase levels may indicate active disease states. This method has been used to validate clinical outcomes in chronic periodontitis patients preoperatively. Biolise is a test for detecting elastase activity in GCF. It involves a series of reactions and calculations to determine elastase activity, providing insights into periodontal health. MMP-8 Dipstick Test utilizes immunochromatography to detect specific isoforms of MMP-8. It can assist in identifying pathogens like *C.rectus*, *P.gingivalis*, and *F.nucleatum*. However, dipsticks may have limitations in terms of sensitivity and sample volume.<sup>18</sup>

---

## MOLECULAR BIOLOGY TECHNIQUES

Polymerase Chain Reaction (PCR) is a widely used technique in periodontology that allows for the amplification and examination of genes and their RNA transcripts from various sources, including gingival crevicular fluid, blood, skin, hair, and semen. Different PCR variants such as RT-PCR, Q-PCR, Multiplex-PCR, Nested-PCR, Real-time PCR, and Allele-specific PCR have been developed and have played important roles in periodontal research. Modern DNA technology enables the detection of complex nucleic acid sequences, helping to classify bacterial organisms. This technique involves the digestion of DNA with enzymes to generate specific fragments, which are radiolabeled to create a "DNA library" for experiments.<sup>19</sup> DNA probes are highly sensitive and can detect numerous species simultaneously. They have been used to monitor subgingival infections, assess the impact of therapies, and analyze microbial profiles. Checkerboard DNA-DNA Hybridisation, introduced by Socransky et al., facilitates the rapid processing of plaque samples to study the oral microbial community. It does not require bacterial viability and is valuable for epidemiological studies. Checkerboard hybridisations are gradually replacing culture-based methods in periodontal research. Fluorescence In-Situ Hybridisation (FISH) is a technique that uses fluorescently labeled probes to detect and identify specific bacterial species in periodontal diseases.<sup>20</sup> It offers high sensitivity and can detect a single bacterial cell, making it useful for studying the abundance and distribution of various periodontal pathogens. Terminal Restriction Fragment Length Polymorphism (T-RFLP) is a molecular biology technique used to profile microbial populations by analyzing the location of a restriction site in amplified genes. It allows for the rapid diagnosis of periodontal diseases and offers detailed information on bacterial communities' structure and diversity. Next-generation sequencing techniques like 454 pyrosequencing have revolutionized the study of bacterial diversity in oral microbiota.<sup>21</sup> It involves fragmenting DNA, PCR amplification, and sequencing, providing valuable insights into the composition of oral microbiota in different oral health conditions. Supported

Oligonucleotide Ligation and Detection (SOLiD) instrumentation is used for various applications, including whole genome resequencing, transcriptome research, and epigenome analysis. While it offers many advantages, such as comprehensive sequencing capabilities, it has limitations like biased sequence coverage in certain regions.<sup>22</sup>

---

## ADVANCED 2D IMAGING TECHNIQUES

Microradiography is primarily used for quantitatively assessing structural features in mineralized tissues. It can produce a true radiographic image throughout the specimen's total thickness. Two types of microradiography exist: Conventional contact microradiography and parallel beam microradiography, which are employed to analyze the degree of mineralization in dental tissues such as dentinal tubules.<sup>23</sup> However, its use is hindered by limitations like long exposure times and the need for high-intensity X-ray sources. Xeroradiography Introduced by Carbon in 1938 and first used in dentistry by Stronezak in 1963. It enhances edge definition, making it particularly useful for visualizing small structures and areas with minimal density differences. Valuable for evaluating initial osseous changes, assessing osseous repair following periodontal therapy, and clearly visualizing crestal heights.<sup>24</sup> Scanography (Soredex Scanora), A commercially available X-ray unit capable of both rotational and linear scanography. It can perform posteroanterior and lateral linear scans of the maxillofacial complex. It is effective in assessing periodontal disease and detecting periapical lesions.<sup>25</sup> Absorptiometry is most sensitive technique for analyzing periodontal bone changes and can serve as a standard for comparing the sensitivity of other methods. Variants include single photon absorptiometry (measuring the total thickness of the alveolar ridge) and dual photon absorptiometry (determining bone mass). Planar nuclear imaging efficiently images large anatomical areas from a wide variety of directions. It is used to view areas of the alveolar process in the laboratory and clinical studies of periodontitis.<sup>26</sup>

---

## CONE-BEAM COMPUTED TOMOGRAPHY (CBCT)

Cone-beam computed tomography (CBCT) represents a significant shift from 2D to 3D imaging in dentistry. CBCT employs a rotating gantry with an X-ray source and detector to capture images. A cone-shaped beam of radiation passes through the area of interest, striking an X-ray detector on the opposite side. Multiple sequential planar images of the field of view (FoV) are obtained during this rotation, requiring just one gantry rotation for image reconstruction. This cone-beam geometry allows for reduced radiation dosage, making CBCT more accessible and cost-effective for dental imaging. One drawback of CBCT is its susceptibility to scatter radiation, which can reduce contrast and hinder soft tissue imaging. Consequently, CBCT is primarily used for visualizing hard tissues. In recent years, dental CBCT has been introduced in periodontology, proving its diagnostic accuracy in detecting and quantifying periodontal defects in laboratory settings. It has shown promise in assessing intrabony defects, dehiscence and fenestration defects, periodontal cysts, and diagnosing furcation involvement in molars. Studies suggest that CBCT has the potential to replace intraoral imaging for evaluating periodontal architecture and monitoring changes in periodontal bone over time.<sup>27</sup>

---

## ULTRASONOGRAPHIC PROBE

The ultrasonographic probe employs ultrasound waves to detect, image, and map the upper boundary of the periodontal ligament, allowing for earlier detection of periodontal disease activity and non-invasive diagnosis. It was created at the NASA Langley Research Center and features a removable tip housing a small ultrasound transducer. This transducer emits high-frequency ultrasound pulses into the gingival sulcus or periodontal pocket, where they interact with periodontal tissue and return as echoes. By measuring the time it takes for the signals to return, the probe can determine the depth of the pocket. This technology offers several advantages, including the ability to examine areas between teeth where periodontal disease often occurs. It is non-invasive, painless, less prone to examiner variability, potentially more sensitive, and can provide additional histologic information about tissue thickness and inflammation.<sup>28</sup>

---

## SPECTROSCOPY

Optical coherence tomography (OCT) is a non-invasive imaging technique that can provide valuable insights into the microstructure of dental tissues, including periodontal tissue health. It creates high-resolution, three-dimensional cross-sectional images by scanning near-infrared light across the tissue's surface. OCT uses low-coherent light sources that can penetrate tissue deeply without causing harm. This technology can reveal crucial details about periodontal tissue, such as contour, sulcular depth, and connective tissue attachment. By detecting microstructural changes, OCT has the potential to identify active periodontal disease at an earlier stage than conventional methods, before significant bone loss occurs. OCT offers advantages like reproducibility and reliability in measuring attachment levels, as it can directly measure tissue dimensions without compressing soft tissue. This non-contact or short-focus probe can be placed on the tissue surface or within the pocket space. Additionally, infrared (IR) spectroscopy is gaining popularity in biomedical applications, particularly for analyzing gingival crevicular fluid (GCF). IR spectroscopy can differentiate between healthy and diseased tissues by examining molecular vibrations in chemical bonds. The IR spectrum of GCF provides valuable information about oral health, and spectral differences can be used for diagnostic purposes. Near-infrared (NIR) spectroscopy is another optical modality under investigation for periodontal disease diagnosis. It can monitor markers related to tissue hydration, oxygenation, and perfusion, offering insights into inflammation at specific periodontal sites. NIR spectroscopy has shown that tissue oxygenation is significantly reduced in periodontitis compared to gingivitis and healthy tissues. Both IR and NIR spectroscopy provide non-invasive, cost-effective, and reliable methods for assessing periodontal health and inflammation. They have the potential to complement traditional diagnostic approaches and aid in the early detection and monitoring of periodontal disease.<sup>29</sup>

---

## ARTIFICIAL INTELLIGENCE (AI) AND MACHINE LEARNING

Companion introduced an ultrasonographic periodontal probe in 1998 to reduce the pain and inaccuracies associated with manual probing.<sup>30</sup> This probe uses a hollow conical tip filled with water to couple ultrasound into periodontal tissues. Advanced techniques like 3D parallel acoustic finite integration are employed to simulate ultrasound propagation, aiding in the assessment of periodontal pocket depths. Traditional methods for assessing halitosis, such as measuring Volatile Sulfur Compounds (VSCs), have limitations. Artificial olfaction offers a non-invasive approach using nanomaterial-based sensors to analyze the full spectrum of exhaled volatile compounds.<sup>31</sup> AI algorithms and pattern recognition are used to detect oral or extra-oral halitosis and even associate it with systemic diseases. Researchers utilized a linear Support Vector Machine (SVM) and 40 bacterial species to differentiate between Generalized Aggressive Periodontitis (AgP) and Generalized Chronic Periodontitis (ChP).<sup>32,33</sup> Machine learning classifiers are employed to distinguish between healthy and inflamed gums using fluorescence imaging. The classifier uses specific wavelengths of light and biomarker fluorescence to segment regions with gingivitis accurately. Automated Process Using Machine Learning Segmentation and Correlation combines intra-oral fluorescent biomarker imaging, clinical examinations, and machine learning to correlate systemic and periodontal health. Co-occurrence rates between Modified Gingival Index (MGI) and various health factors are analyzed. A computer-aided recognition system was developed to diagnose and predict periodontally compromised teeth (PCT) based on periapical radiographs. The system demonstrated diagnostic and predictive accuracy comparable to that of a board-certified periodontist. Deep learning techniques are used to detect periodontal bone loss on panoramic dental radiographs, showing promising results. Integration of additional imaging data and clinical records can further enhance accuracy.<sup>34</sup>

---

## MOBILE APPLICATIONS FOR DIAGNOSIS IN PERIODONTICS

Mobile applications for diagnosis in periodontics are emerging as valuable tools to bridge the gap between dental professionals and patients, particularly in the context of improving periodontal health and gingivitis monitoring. Two innovative mobile health (mHealth) apps, iGAM and PerioSmart, have shown promise in enhancing periodontal care and facilitating communication between dentists and patients. iGAM is an mHealth app designed to address the common issue of gingivitis, characterized by red, swollen, and bleeding gums. Gingivitis often goes unnoticed until it progresses to a painful stage, making early detection crucial. iGAM offers an innovative solution by enabling users to monitor their gum health remotely. Users can take weekly photos of their gums using the app, allowing them to visually track changes in gum health over time. iGAM facilitates communication between patients and dentists, providing a platform for sharing photographic updates and receiving guidance from dental professionals.<sup>35</sup> PerioSmart is another pioneering mobile app designed to assist dental professionals, including dental students, postgraduate students of periodontology, and professors, in making accurate periodontal diagnoses. It leverages an integral algorithm based on the 2018 classification of periodontal diseases to enhance diagnostic precision and efficiency. PerioSmart enhances the efficiency of periodontal diagnosis by applying the latest classification standards and algorithms. Compared to traditional knowledge-based diagnosis, PerioSmart has shown a better concordance rate in determining diagnosis type and the stage/grade of periodontitis. PerioSmart serves as an educational tool, assisting dental professionals in their clinical decision-making and deepening their understanding of periodontal conditions.<sup>36</sup>

---

## DISCUSSION

Our article provides a thorough overview of the various diagnostic techniques and technologies used in the field of periodontology. It underscores the significance of early detection and continuous monitoring of periodontal diseases to enhance their treatment effectiveness. The utilization of biomarkers such as interleukins, TNF- $\alpha$ , and MMPs in saliva and GCF holds great promise as a means of diagnosing periodontal diseases. These biomarkers offer objective measures and can be instrumental in tailoring treatment plans to individual patients. Microbiological diagnostic tests encompassing culture methods, molecular biology techniques, and genetic tests are valuable for early detection and personalized treatment options. Nevertheless, some limitations in these methods necessitate further research. Biochemical tests like OFNASET and ETC have the capacity to identify specific salivary biomarkers and provide insights into periodontal diagnosis, all while offering non-invasive diagnostic avenues. PCR variants, DNA probes, FISH, and T-RFLP represent potent tools for investigating periodontal pathogens and microbial profiles. Next-generation sequencing techniques furnish detailed insights into the composition of the oral microbiota. Techniques such as microradiography, Xeroradiography, and scanography play a pivotal role in evaluating changes in periodontal tissue and bone. They offer invaluable insights into structural characteristics. Cone-Beam Computed Tomography (CBCT) marks a significant advancement in 3D dental imaging and holds promise for visualizing hard tissues as well as assessing periodontal defects. The ultrasonographic probe is a non-invasive tool utilizing ultrasound waves to detect changes in periodontal tissue. Its advantages include painlessness and high sensitivity. Optical coherence tomography (OCT), IR spectroscopy, and NIR spectroscopy are non-invasive methods for assessing periodontal health and inflammation, providing valuable insights into microstructural details. Artificial Intelligence (AI) and machine learning techniques are being applied to periodontal diagnosis, including ultrasonographic probing, halitosis detection, and the classification of periodontal conditions. These technologies have the potential to enhance diagnostic accuracy and efficiency. Mobile applications like iGAM and PerioSmart are emerging as tools to facilitate communication between patients and dental professionals. They offer innovative solutions for monitoring gingivitis and diagnosing periodontal conditions. In summary, these diagnostic methods and technologies contribute significantly to the enhancement of periodontal care by enabling early detection, personalized treatment planning, and more precise diagnosis. Ongoing research and development efforts in this field are likely to lead to further advancements in periodontal diagnostics and treatment.

---

## CONCLUSION

In conclusion, advancements in periodontal diagnosis and imaging techniques have significantly transformed the landscape of periodontal care and dentistry as a whole. These innovations have provided both dental professionals and patients with enhanced tools for early detection, accurate diagnosis, and improved treatment planning.

## REFERENCES

---

1. Dorairaj, Jayachandran. (2016). Imaging Techniques in Periodontics: A Review Article. 7. 739-747.
2. Chakrapani S, Sirisha K, Srilalitha A, Srinivas M. Choice of diagnostic and therapeutic imaging in periodontics and implantology. *J Indian Soc Periodontol.* 2013 Nov;17(6):711-8. doi: 10.4103/0972-124X.124474. PMID: 24554878; PMCID: PMC3917198.
3. Papagerakis P, Zheng L, Kim D, Said R, Ehlert AA, Chung KKM, Papagerakis S. Saliva and Gingival Crevicular Fluid (GCF) Collection for Biomarker Screening. *Methods Mol Biol.* 2019;1922:549-562. doi: 10.1007/978-1-4939-9012-2\_41. PMID: 30838599.
4. Noha Ayman Ghallab, Diagnostic potential and future directions of biomarkers in gingival crevicular fluid and saliva of periodontal diseases: Review of the current evidence, *Archives of Oral Biology*, Volume 87, 2018, Pages 115-124
5. Grant MM, Taylor JJ, Jaedicke K, Creese A, Gowland C, Burke B, Doudin K, Patel U, Weston P, Milward M, Bissett SM, Cooper HJ, Kooijman G, Rmaile A, de Jager M, Preshaw PM, Chapple ILC. Discovery, validation, and diagnostic ability of multiple protein-based biomarkers in saliva and gingival crevicular fluid to distinguish between health and periodontal diseases. *J Clin Periodontol.* 2022 Jul;49(7):622-632. doi: 10.1111/jcpe.13630. Epub 2022 Apr 29. PMID: 35451104; PMCID: PMC9324935.
6. atsiki, P, Nazmi, K, Loos, BG, et al. Comparing periodontitis biomarkers in saliva, oral rinse and gingival crevicular fluid: A pilot study. *J Clin Periodontol.* 2021; 48: 1250–1259.
7. He W., You M., Wan W., Xu F., Li F., Li A. Point-of-Care Periodontitis Testing: Biomarkers, Current Technologies, and Perspectives. *Trends Biotechnol.* 2018;36:1127–1144. doi: 10.1016/j.tibtech.2018.05.013.
8. Ko TJ, Byrd KM, Kim SA. The Chairside Periodontal Diagnostic Toolkit: Past, Present, and Future. *Diagnostics (Basel).* 2021 May 22;11(6):932. doi: 10.3390/diagnostics11060932. PMID: 34067332; PMCID: PMC8224643.
9. Arweiler, NB, Marx, VK, Laugisch, O, Sculean, A, Ausschil, TM. Clinical evaluation of a newly developed chairside test to determine periodontal pathogens. *J Periodontol.* 2020; 91: 387–395.
10. Meghana Sri Sai Ivatur, Advanced Chairside Diagnostic Aids for Periodontal Diagnosis- A Review, *Journal of Clinical and Diagnostic Research.* 2021 Sep, Vol-15(9): ZE17-ZE22
11. Priyanka N, Kalra N, Shanbhag N, Kumar K, Seema Brijet B, Avani PR. Recent approaches in saliva as a credible periodontal diagnostic and prognostic marker. *AOSR.* 2012;2(1):40-46
12. Herr AE, Hatch AV, Giannobile WV, Throckmorton DJ, Tran HM, Brennan JS, et al. Integrated microfluidic platform for oral diagnostics. *Ann N Y Acad Sci.* 2007;1098:362-74.
13. Herr AE, Hatch AV, Throckmorton DJ, Tran HM, Brennan JS, Giannobile WV, et al. Microfluidic immunoassays as rapid saliva-based clinical diagnostics. *Proc Natl Acad Sci U S A.* 2007;104(13):5268-
14. Park OJ, Yi H, Jeon JH, Kang SS, Koo KT, Kum KY, et al. Pyrosequencing analysis of subgingival microbiota in distinct periodontal conditions. *J Dent Res.* 2015;94(7):921-27.
15. Persson GR, Alves ME, Chambers DA, Clark WB, Cohen R, Crawford JM, et al. A multicenter clinical trial of PerioGard in distinguishing between diseased and healthy periodontal sites. (I). Study design, methodology and therapeutic outcome. *J Clin Periodontol.* 1995;22(10):794-803.
16. Shimada K, Mizuno T, Ohshio K, Kamaga M, Murai S, Ito K. Analysis of aspartate aminotransferase in gingival crevicular fluid assessed by using PocketWatch: A longitudinal study with initial therapy. *J Clin Periodontol.* 2000;27(11):819-23.
17. Hemmings KW, Griffiths GS, Bulman JS. Detection of neutral protease (Periocheck) and BANA hydrolase (Perioscan) compared with traditional clinical methods of diagnosis and monitoring of chronic inflammatory periodontal disease. *J Clin Periodontol.* 1997;24(2):110-14.
18. Herrmann JM, Gonzáles JR, Boedeker RH, Vonholdt J, Meyle J. Microassay for the detection of elastase activity in the gingival crevice. *J Clin Periodontol.* 2001;28(1):31-37.
19. Öztürk VÖ, Emingil G, Umeizudike K, Tervahartiala T, Gieselmann DR, Maier K, et al. Evaluation of active matrix metalloproteinase-8 (aMMP-8) chair-side test as a diagnostic biomarker in the staging of periodontal diseases. *Arch Oral Biol.* 2021;124:104955.

20. Sorsa T, Tervahartiala T, Leppilähti J, Hernandez M, Gamonal J, Tuomainen AM, et al. Collagenase-2 (MMP-8) as a point-of-care biomarker in periodontitis and cardiovascular diseases. Therapeutic response to non-antimicrobial properties of tetracyclines. *Pharmacol Res.* 2011;63(2):108-13
21. Naqvi AZ, Mu L, Hasturk H, Van Dyke TE, Mukamal KJ, Goodson JM. Impact of Docosahexaenoic acid therapy on subgingival plaque microbiota. *J Periodontol.* 2017;88(9):887-95.
22. Voelkerding KV, Dames SA, Durtschi JD. Next-generation sequencing: From basic research to diagnostics. *Clin Chem.* 2009;55(4):641-58.
23. Takagi S, Chow LC, Brown WE, Dobbyn RC, Kuriyama M. Application of an x-ray image magnifier to the microradiography of dental specimens. *J Dent Res.* 1985;64:866-9.
24. Lopez J., Jr Xeroradiography in dentistry. *J Am Dent Assoc.* 1976;92:106-10.
25. White SC, Pharaoh MJ. 5th ed. St. Louis, Missouri: Mosby Publication; 2004. *Oral Radiology Principles and Interpretation*; pp. 248-50.
26. Hausmann E, Ortman LF, McHenry K, Fallon J. Relationship between alveolar bone measured by 125I absorptiometry with analysis of standardized radiographs: 1. Magiscan. *J Periodontol.* 1982;53:307-10.
27. Mol AI imaging methods in periodontology, *Periodontol* 2000, 34 (2004), pp. 34-48
28. Misch KA, Yi ES, Sarment DP Accuracy of cone beam computed tomography for periodontal defect measurements, *J Periodontol*, 77 (2006), pp. 1261-1266
29. Tyndall DA, Rathore S, Cone-beam CT diagnostic applications: caries, periodontal bone assessment, and endodontic applications, *Dent Clin North Am*, 52 (2008), pp. 825-841
30. Sachdeva, Shivani & Mani, Amit & Vora, Hiral & Saluja, Harish & Mani, Shubhangi & Manka, Nishant. (2021). Artificial intelligence in periodontics – A dip in the future. *Journal of Cellular Biotechnology*. 7. 1-6. 10.3233/JCB-210041.
31. Rudd K, Bertocchini C, Hinders M. Simulations of Ultrasonographic Periodontal Probe Using the Finite Integration Technique. *Open Acoust J.* 2009;2:1-9.
32. Nakhleh MK, Quatreteniers M, Haick H. Detection of Halitosis in Breath: Between the Past, Present and Future. *Oral Dis.* 2017;24(5):1- 11. doi:10.1111/odi.12699
33. Yauney G, Rana A, Wong LC, Javia P, Muftu A, Shah P, et al. Automated Process Incorporating Machine Learning Segmentation and Correlation of Oral Diseases with Systemic Health. *Annu Int Conf IEEE Eng Med Biol Soc.* 2019;p. 3387-93. doi:10.1109/EMBC.2019.8857965.
34. Krois J, Ekert T, Meinhold L, Golla T, Kharbot B, Wittemeier A, et al. Deep learning for the radiographic detection of periodontal bone loss. *Scientific Rep.* 2019;9:849
35. Ramani et al. / IP International Journal of Periodontology and Implantology 2023;8(2):71-74 Tobias G, Spanier A Developing a Mobile App (iGAM) to Promote Gingival Health by Professional Monitoring of Dental Selfies: User-Centered Design Approach *JMIR Mhealth Uhealth* 2020;8(8):e19433
36. Sánchez-Otálvaro LM, Jiménez-Rivero Y, Velasquez RA, Botero JE. Development and testing of a mobile application for periodontal diagnosis. *J Clin Exp Dent.* 2022 Mar 1;14(3):e269-e273. doi: 10.4317/jced.59338. PMID: 35317291; PMCID: PMC8916594.