

Review a Comprehensive Article on Longitudinal Evaluation of Oral Microbial Changes and Radiation-Induced Dental Caries in Head and Neck Cancer Patients

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Abstract

Radiotherapy is an essential treatment modality for head and neck cancers; however, it is frequently associated with significant oral complications, particularly radiation-induced dental caries. Emerging evidence suggests that radiotherapy not only impairs salivary gland function but also induces substantial alterations in the oral microbiome. Longitudinal studies have demonstrated that oral microbial changes may become evident within 2–3 weeks of treatment initiation, characterized by an increased prevalence of cariogenic microorganisms such as *Streptococcus mutans* and *Lactobacillus* species, along with a reduction in beneficial commensal bacteria including *Neisseria*, *Rothia*, and *Streptococcus sanguinis*. These microbial shifts are often accompanied by decreased microbial diversity, persistent xerostomia, and salivary dysfunction, creating an acidic oral environment that promotes enamel demineralization and accelerates caries progression. In addition, opportunistic fungal organisms, particularly *Candida albicans*, may increase during and after radiotherapy, further contributing to oral dysbiosis and oral complications. This review summarizes the longitudinal microbial changes associated with radiotherapy, examines their role in the pathogenesis of radiation-induced dental caries, and discusses current preventive and therapeutic strategies. Understanding these dynamic microbial alterations may facilitate early intervention, improve oral health outcomes, and support the development of personalized preventive approaches for head and neck cancer patients undergoing radiotherapy.

Keywords: Radiation-induced dental caries, Oral microbiome, Radiotherapy, Head and neck cancer, Xerostomia

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Introduction

Radiotherapy remains one of the primary treatment modalities for head and neck cancers because of its effectiveness in controlling tumor progression and improving survival outcomes [1, 2]. Despite its therapeutic benefits, radiotherapy can produce several adverse effects on the oral cavity, including mucositis, xerostomia, infections, and radiation-induced dental caries [2- 4]. Among these complications, radiation caries is considered particularly severe because of its rapid onset, aggressive progression, and long-term impact on oral health and patient quality of life.

Radiation-induced dental caries is a multifactorial

condition associated with salivary gland dysfunction, alterations in the oral microbiome, and structural damage to dental tissues [5- 7]. Recent studies have demonstrated that radiotherapy not only reduces salivary flow but also causes significant longitudinal shifts in oral microbial composition [8-10]. These changes favor the proliferation of acidogenic and aciduric microorganisms while reducing beneficial commensal species that normally contribute to oral homeostasis.

Although previous studies have separately described xerostomia, microbial dysbiosis, and radiation caries, relatively few review articles have comprehensively

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integrated longitudinal microbial monitoring with caries risk prediction in head and neck cancer patients. Understanding these temporal microbial changes is important for identifying early biomarkers of disease progression and improving preventive oral care strategies during and after radiotherapy.

Therefore, this review focuses on the longitudinal evaluation of oral microbial alterations associated with radiotherapy and their contribution to radiation-induced dental caries. The review also summarizes current preventive and therapeutic approaches while highlighting future directions for personalized oral healthcare in irradiated patients.

Etiology of Radiation-Induced Dental Caries

Radiation-induced dental caries is a multifactorial complication resulting from salivary gland dysfunction, oral microbial dysbiosis, dietary alterations, and direct radiation-induced damage to dental hard tissues [5- 7]. Salivary gland damage leads to xerostomia and reduced buffering capacity, thereby increasing susceptibility to acidogenic microorganisms and dental demineralization [11- 13]. In addition, structural changes in enamel and dentin following radiation exposure further accelerate the caries process [5, 14].

In addition to salivary changes, radiotherapy also affects the balance of microorganisms present in the oral cavity. There is a noticeable shift toward acid-producing and acid-tolerant bacteria such as *Streptococcus mutans* and *Lactobacillus* species [15, 16]. These microorganisms contribute to increased acid production, which accelerates the breakdown of tooth structure.

Another contributing factor is the direct effect of radiation on teeth. Radiation can weaken enamel and dentin by altering their structure, making them more prone to damage. When all these factors act together, they create conditions that promote the rapid development of dental caries.

Oral Microbial Changes during Radiotherapy

Radiotherapy leads to significant changes in the oral microbiome over time. Under normal conditions, the oral cavity contains a balanced mix of microorganisms that help maintain oral health. However, during radiotherapy, this balance is disturbed due to changes in salivary flow, pH levels, and nutrient availability.

As treatment progresses, there is a gradual increase

in cariogenic bacteria, particularly *Streptococcus mutans* and *Lactobacillus* species. These bacteria are well adapted to acidic environments and continue to thrive even when salivary protection is reduced. In addition, fungal organisms such as *Candida albicans* may also increase, further contributing to microbial imbalance.

Recent microbiome-based studies have demonstrated that radiotherapy not only increases cariogenic microorganisms but also significantly reduces beneficial commensal bacteria such as *Neisseria*, *Rothia*, and *Streptococcus sanguinis* [17- 20]. These commensal organisms normally contribute to microbial balance and maintenance of oral pH stability. Their reduction promotes ecological dysbiosis and favors acidogenic microbial colonization.

In addition, longitudinal analyses have reported progressive reductions in microbial alpha diversity along with significant alterations in beta diversity during and after radiotherapy [19, 20]. These findings indicate substantial shifts in microbial composition and reduced microbial stability over time. Studies by Gao et al. and Belström further suggest that antimicrobial therapies such as chlorhexidine may temporarily suppress pathogenic microorganisms; however, prolonged use may also delay the recovery of beneficial oral microbiota and alter microbial recolonization patterns following radiotherapy.

Even after the completion of radiotherapy, these changes often persist for a long time. The continued reduction in salivary flow and altered oral conditions make it difficult for the microbiome to return to its normal state. This long-term imbalance increases the risk of dental caries and other oral complications.

These microbial alterations may persist for several months after radiotherapy, indicating long-term disruption of oral ecological balance and increased risk of radiation-induced dental caries [10, 19, 20]. The longitudinal changes in the oral microbiome observed before, during, and after radiotherapy, together with their dominant microorganisms and clinical implications, are summarized in Table 1.

Pathogenesis of Radiation Caries

The development of radiation-induced dental caries involves a combination of biological and environmental factors. One of the key mechanisms is reduced salivary secretion, which limits the natural protective functions of saliva [11, 13, 21, 22]. Without adequate saliva, the oral cavity becomes more susceptible to bacterial colonization

Table 1. Longitudinal Changes in Oral Microbiome During Radiotherapy.

Phase of Treatment	Microbial Characteristics	Dominant Microorganisms	Clinical Impact
Pre-Radiotherapy	Balanced oral flora with commensal dominance	<i>Streptococcus</i> spp. (non-cariogenic), <i>Actinomyces</i>	Healthy oral environment
During Radiotherapy	Shift toward acidic environment and dysbiosis	<i>Streptococcus mutans</i> , <i>Lactobacillus</i> spp., <i>Candida albicans</i>	Increased caries risk
Post-Radiotherapy	Persistent dysbiosis and reduced diversity	<i>Lactobacillus</i> spp., <i>Candida albicans</i>	Long-term caries susceptibility

Table 2. Etiological Factors and Their Impact on Radiation-Induced Dental Caries.

Factor	Mechanism	Effect on Oral Health
Salivary gland dysfunction	Reduced salivary flow and buffering capacity	Xerostomia and increased caries risk
Microbial dysbiosis	Increase in acidogenic bacteria	Rapid demineralization
Radiation effect on teeth	Structural weakening of enamel and dentin	Increased susceptibility to decay
Dietary changes	Increased intake of soft, carbohydrate-rich food	Promotes cariogenic environment

and acid accumulation.

At the same time, the increased presence of acid-producing bacteria leads to a drop in oral pH and promotes enamel demineralization [15, 16, 23, 24]. This acidic environment promotes the loss of minerals from enamel and dentin, initiating the formation of carious lesions. Radiation also weakens the structural integrity of teeth, making them more vulnerable to chemical and mechanical damage [5, 7, 14]. Collectively, salivary gland dysfunction, microbial dysbiosis, direct radiation-induced damage to dental hard tissues, and dietary alterations contribute to the development and progression of radiation-induced dental caries. The major etiological factors involved in the development of radiation-induced dental caries and their impact on oral health are summarized in Table 2. Furthermore, the overall pathogenesis and interaction of these contributing factors are illustrated in Figure 1

As these processes continue, dental caries progresses rapidly and may affect multiple teeth at once. The pattern of damage is often different from conventional caries, which highlights the unique nature of this condition.

Clinical Features

Radiation-induced dental caries shows distinct clinical features that help differentiate it from typical dental caries. The lesions tend to develop quickly and often involve several teeth simultaneously. Commonly affected areas include the cervical regions, incisal edges, and cusp tips.

Acute manifestations of radiation-induced dental caries may become evident within approximately 3 months after radiotherapy and are commonly associated with rapid enamel demineralization, cervical lesions, and increased tooth sensitivity. Chronic manifestations may develop gradually over 1–2 years and are characterized by progressive structural breakdown, extensive cavitation, crown amputation, and tooth fracture [7, 14, 25].

The affected teeth may show discoloration, ranging from yellowish-brown to dark brown or black. Over time, the enamel may chip off, and the tooth structure becomes weak and brittle. In advanced stages, extensive destruction

can lead to fractures and even tooth loss.

Patients may also experience sensitivity, discomfort, and difficulty in maintaining oral hygiene, which can further worsen the condition.

Complications

Radiation-induced dental caries can lead to several serious complications that significantly affect patient quality of life. The rapid destruction of dental tissues often results in tooth loss, which can impair mastication, speech, and aesthetics. In addition, the altered oral environment increases the risk of bacterial and fungal infections.

Patients may also experience nutritional deficiencies due to difficulty in eating, which can further compromise their overall health. The psychological impact of oral disfigurement and functional impairment should also be considered, as it can affect the patient's emotional well-being.

Diagnosis

The diagnosis of radiation-induced dental caries involves a combination of clinical and laboratory assessments. Clinical examination remains the primary method for detecting carious lesions and assessing the extent of dental damage. Evaluation of salivary flow and symptoms of xerostomia is also essential.

Microbiological analysis can be performed to identify the presence of cariogenic bacteria and fungal organisms. Advanced molecular techniques such as polymerase chain reaction (PCR) provide accurate identification of oral pathogens. Salivary testing, including measurement of flow rate and pH, can further aid in the assessment of caries risk.

Preventive Strategies

Prevention plays a key role in reducing the risk of radiation-induced dental caries, especially in patients undergoing long-term radiotherapy. One of the most commonly recommended approaches is the use of

Table 3. Preventive and Therapeutic Strategies for Radiation-Induced Dental Caries.

Strategy	Approach	Outcome
Fluoride therapy	Topical fluoride, fluoride trays	Enhances remineralization
Saliva substitutes	Artificial saliva, stimulants	Reduces xerostomia
Oral hygiene	Brushing, flossing, mouthwash	Controls microbial load
Antimicrobial therapy	Chlorhexidine, antifungals	Reduces infection risk
Restorative treatment	GIC, composite restorations	Restores tooth structure

Table 4. Longitudinal Microbial Changes Observed During Radiotherapy in Head and Neck Cancer Patients.

Author (Year)	Time of Observation	Microbial Changes Reported	Impact on Oral Health
Almståhl & Finizia (21)	During radiotherapy	↑ <i>S. mutans</i> , ↑ <i>Lactobacillus</i> , ↓ salivary secretion	Increased caries risk
Almståhl & Wikström (8)	Within 2–3 weeks of treatment	Early microbial dysbiosis associated with xerostomia	Predictor of future caries development
Belström (19)	Post-radiotherapy assessment	↓ microbial diversity, ↓ beneficial commensal bacteria	Loss of oral ecological balance
Gao et al. (20)	During and after radiotherapy	↓ <i>Neisseria</i> , ↓ <i>Rothia</i> , ↓ <i>S. sanguinis</i> , altered alpha/beta diversity	Enhanced acidogenic colonization and oral dysbiosis

fluoride, which helps in strengthening tooth enamel and promoting remineralization. Topical fluoride applications, including gels and custom trays, have shown good results in minimizing caries risk.

Management of xerostomia is equally important. The use of saliva substitutes and stimulants can help improve oral lubrication and provide some level of protection against microbial growth. Maintaining proper oral hygiene is essential, and patients should be encouraged to follow regular brushing and flossing practices along with the use of antimicrobial mouth rinses.

Dietary habits also play an important role. Reducing the intake of sugary and sticky foods while maintaining adequate hydration can help in controlling the progression of caries. Overall, a combination of these preventive measures can significantly improve oral health outcomes in patients undergoing radiotherapy. The commonly recommended preventive and therapeutic strategies for radiation-induced dental caries are summarized in Table 3.

Patient compliance represents a major challenge during radiotherapy because painful mucositis, oral ulceration, and trismus frequently impair routine oral hygiene practices. Therefore, adaptive oral care measures such as soft-bristled toothbrushes, sponge brushes, non-alcoholic mouth rinses, and individualized oral hygiene instructions should be recommended to improve compliance and reduce the risk of oral complications [26–30].

Treatment Approaches

The treatment of radiation-induced dental caries requires a comprehensive and patient-specific approach. In the early stages, conservative management techniques such as fluoride therapy and antimicrobial treatments can help control disease progression.

For teeth that have already been damaged, restorative procedures are necessary. Materials such as glass ionomer cement and composite resins are commonly used to restore tooth structure and function. These materials also provide some degree of fluoride release, which can be beneficial in preventing further decay.

In cases where the damage is severe, extraction of the affected teeth may be required. This decision should be made carefully, considering the patient's overall condition and healing capacity. Regular dental follow-up is essential to monitor the condition and ensure timely intervention.

Longitudinal Studies and Findings

Several longitudinal investigations have evaluated oral microbial alterations in head and neck cancer patients undergoing radiotherapy. Almståhl and Finizia [31] reported significant reductions in salivary secretion along with progressive increases in cariogenic microorganisms, particularly *Streptococcus mutans* and *Lactobacillus* species, during the early weeks of radiotherapy. Their findings indicated that microbial imbalance persisted after treatment completion, suggesting long-term ecological disruption.

Almståhl and Wikström [8] further demonstrated that reduced salivary flow was associated with increased counts of acidogenic bacteria and fungal organisms. Oral microbial shifts were observed within 2–3 weeks of treatment initiation and correlated strongly with xerostomia severity.

Belström [19] highlighted the importance of salivary microbiota in maintaining oral ecological balance and reported that reduced microbial diversity contributes to oral dysbiosis and increased susceptibility to dental diseases. Similarly, Gao et al. [20] demonstrated significant alterations in alpha and beta diversity during radiotherapy, characterized by reductions in beneficial commensal bacteria such as *Neisseria*, *Rothia*, and *Streptococcus sanguinis*.

Molecular studies employing PCR and microbiome sequencing techniques confirmed progressive increases in *Streptococcus mutans* and *Candida albicans* populations during and after radiotherapy [20, 31–48]. Furthermore, chlorhexidine-based antimicrobial therapy was shown to temporarily reduce cariogenic bacterial load; however, prolonged use may delay recolonization of beneficial microbiota and interfere with microbiome recovery [19, 20].

Collectively, these studies emphasize the importance of longitudinal microbial monitoring, salivary assessment, and preventive dental interventions for reducing the burden of radiation-induced dental caries. A summary of the major longitudinal studies describing oral microbial changes during radiotherapy and their clinical significance is presented in Table 4.

Recent studies utilizing next-generation sequencing, metagenomic analysis, and salivary microbiome profiling have further confirmed that radiotherapy induces substantial alterations in oral microbial composition and

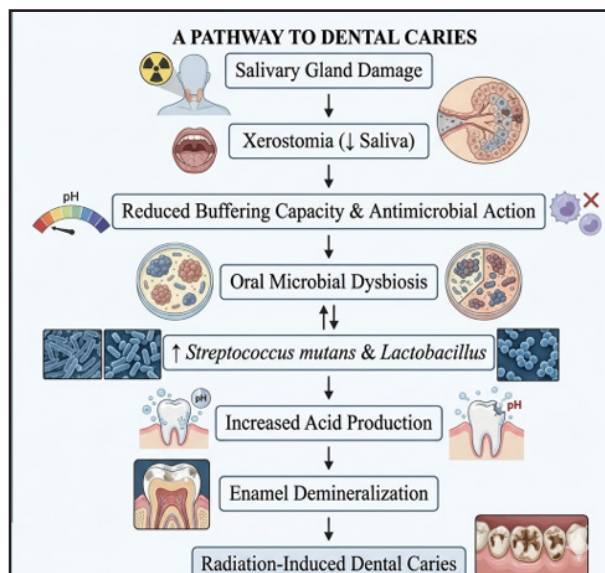


Figure 1. Pathogenesis of Radiation-Induced Dental Caries.

diversity. Longitudinal investigations have demonstrated shifts in microbial community structure during treatment, with persistent dysbiosis observed after radiotherapy completion. These findings support the potential use of microbiome-based biomarkers for early detection of oral complications and individualized preventive strategies in head and neck cancer patients [34- 38].

Future Perspectives

Recent advancements in research have focused on innovative approaches to prevent and manage radiation-induced dental caries. The use of probiotics to restore the balance of the oral microbiome has shown promising results. Additionally, the development of radioprotective agents aims to minimize damage to salivary glands during radiotherapy.

Emerging techniques in regenerative medicine, including salivary gland tissue engineering, offer potential solutions for restoring salivary function. Personalized oral care strategies based on individual microbial profiles are also being explored as a means to improve treatment outcomes. Integration of artificial intelligence and microbiome profiling may further enhance early diagnosis and personalized treatment strategies.

Recent advances in metagenomic sequencing, salivary microbiome profiling, and artificial intelligence-assisted analytical approaches have improved the understanding of microbial dynamics during radiotherapy. These technologies may facilitate the development of predictive biomarkers and personalized preventive strategies for radiation-induced dental caries [34- 38].

Future studies should focus on the identification of microbiome-based biomarkers for the early detection of radiation-induced dysbiosis [39, 40]. Probiotic and microbiome-modulating approaches may help restore oral microbial balance and reduce the burden of radiation-induced dental caries [41, 42]. Artificial

intelligence-assisted risk prediction models may improve individualized patient monitoring and preventive care planning [44, 45]. Furthermore, advances in regenerative medicine and salivary gland tissue engineering may provide innovative strategies for restoring salivary function and improving long-term oral health outcomes in irradiated patients [45- 48].

In conclusion, radiation-induced dental caries remains one of the most challenging complications associated with radiotherapy in head and neck cancer patients. It develops as a result of multiple interacting factors, including reduced salivary function, changes in the oral microbiome, and direct damage to dental tissues.

The findings discussed in this review highlight the importance of early diagnosis and continuous monitoring in managing this condition effectively. Preventive strategies, along with appropriate therapeutic interventions, can help reduce the severity and progression of dental caries.

In addition, a multidisciplinary approach involving oncologists, dentists, microbiologists, and oral medicine specialists is essential for comprehensive patient care. Despite growing evidence regarding oral microbial dysbiosis following radiotherapy, further multi-center longitudinal studies are required to establish standardized predictive biomarkers and targeted preventive strategies for radiation-induced dental caries. Such efforts may significantly improve oral health outcomes and quality of life in head and neck cancer survivors.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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