

A Review of the Biological and Clinical Aspects of Radiation Caries

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Abstract

Aim: The aim of this article is to review the clinical and biological features underlying the development and progression of radiation caries.

Background: Although radiotherapy (RT) plays an important role in the management of patients with head and neck cancer (HNC), it is also associated with several undesired side effects such as radiation caries which is a common, yet serious, complication. To review the condition, the Pubmed database was searched using the keywords “radiotherapy,” “radiation,” “caries,” “hyposalivation,” “prevention” and “management”. Only studies published in the English language were selected. Cross-referencing identified additionally relevant studies.

Review Results: RT leads to alterations in the dentition, saliva, oral microflora, and diet of patients. Consequently, irradiated patients are at increased risk for the development of a rapid, rampant carious process known as radiation caries. Motivation of patients, adequate plaque control, stimulation of salivary flow, fluoride use, and nutritional orientation are essential to reduce the incidence of radiation caries and ultimately improve the quality of life for HNC patients.

Conclusion: Radiation caries is an aggressive side effect of RT. Dentists play an important role in the prevention of the condition via comprehensive oral healthcare before, during, and after the active cancer therapy.

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Clinical Significance: Dentists should understand the clinical and biological aspects underlying radiation caries to prevent the development of lesions and provide optimal treatment when needed.

Keywords: Radiotherapy, RT, caries, head and neck cancer, HNC, xerostomia, literature review

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Introduction

Although radiotherapy (RT) plays an important role in the management of patients with head and neck cancer (HNC), it is also associated with several undesired reactions. The RT field of exposure frequently includes the salivary glands, oral mucosa, and jaws, thus, leading to various side effects including hyposalivation, xerostomia, mucositis, and taste loss.¹⁻³

Irradiated patients are also at increased risk for the development of a rapid, rampant carious process known as radiation caries. Lesions tend to develop four weeks after completion of RT and affect atypical areas of teeth, such as the lingual surface, incisal edges, and cusp tips. Clinically, three different patterns have been identified. The most common pattern (Type 1) affects the cervical aspect of the teeth and extends along the cementoenamel junction. A circumferential injury develops and crown amputation often occurs (Figure 1A).

The second pattern (Type 2) presents with areas of demineralization on all dental surfaces. Generalized erosions and worn occlusal and incisal surfaces are not uncommon (Figure 1B). The third and least common pattern (Type 3) presents as color changes in the dentin. The crown becomes dark brown/black and occlusal and incisal wear may be seen (Figure 1C). The same individual can present with more than one pattern. Importantly, even teeth located outside the RT field are at risk.¹⁻⁴

The aim of this article is to review the clinical and biological features that underlie the development and progression of radiation caries. Radiation-induced alterations in the dentition, saliva, microflora, and diet involved in the pathogenesis of radiation caries are discussed. In addition, special emphasis is given to management of the lesions.



Figure 1. Different types of radiation caries. **A.** Type 1 are lesions affecting the cervical aspect of the teeth and extending along the cementoenamel junction. **B.** Type 2 presents with demineralized and worn occlusal surfaces. **C.** Type 3 lesions present as color changes in the dentin. The crown is dark brown/black, along with occlusal wear.

Changes Following Radiotherapy (RT)

The Dentition

Conflicting studies have been published regarding the effect of radiation on teeth and the exact nature of direct radiation damage is yet to be

elucidated.⁵ Some state demineralization in irradiated teeth is histologically characterized by total loss of the prismatic structure. Enamel would then be less resistant to acid attack after irradiation. In contrast, others claim there are no differences in structure or composition between irradiated and non-irradiated enamel.³ Fränzel et al.⁶ found irradiation dramatically decreased the mechanical parameters of enamel. In non-irradiated teeth demineralization had nearly the same effects of irradiation on the mechanical properties. In irradiated teeth the effects of demineralization were negligible in comparison to non-irradiated teeth.⁶ Similarly, one study showed irradiation does not influence *in vitro* demineralization or *in situ* remineralization of human teeth.⁷

Similarly to enamel caries, dentin radiation caries usually begin with apatite dissolution. Changes in the organic components of dentin promote instability at the dentinoenamel junction (DEJ), causing the dentin to lose its capacity to support enamel. Tooth deterioration secondary to masticatory forces can lead to gap formation at the DEJ, favoring increased bacterial colonization.⁸ Following bacterial acid attack upon mineral tissues, enzymatic degradation of dentin organic components occurs. In addition, hydrogen free radicals and hydrogen peroxide present within the dentin denature its organic components and alter dentin micro-hardness.⁹ Activation of salivary matrix metalloproteinases may also play a role in the pathogenesis of dentin radiation caries.⁸

Al-Nawas et al.¹⁰ employed ultrasound transmission velocity to evaluate the effects of radiation on dentin. These investigators verified irradiation had only a minor effect on the mechanical properties of dentin under RT conditions. The mechanical properties were affected only after high experimental dosages, suggesting direct radiogenic damage without further cofactors does not significantly affect mineralized dental hard tissue. Nevertheless, damage of the organic components of the dentin, collagen matrix, and odontoblastic processes must also be taken into consideration. In addition, the irradiated dentin may acquire a rubbery texture, due to damage to collagen peptide chains. In any case, the literature strongly

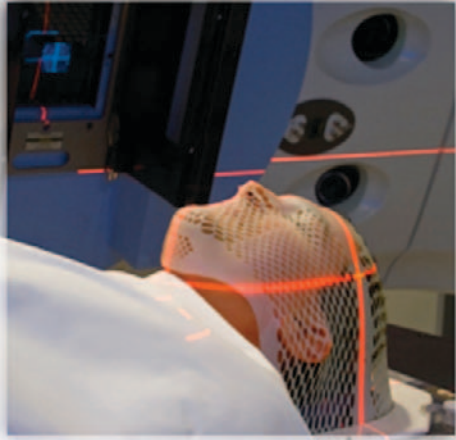
indicates RT-induced dentin changes are less important than enamel modifications in the pathogenesis of radiation caries.

When vital teeth are located within the field of radiation, hypovascularity leads to a decrease in circulation to pulp tissue. In addition, dental pulp alterations, including fibrosis, hyalinization, and calcifications, may be seen. Springer et al.⁵ found significant differences in the pulp collagen of irradiated teeth, indicating increased amounts of collagen fragments by direct radiogenic destruction.⁵ In contrast, cobalt-60 radiation in a dose range up to 70 Gy had no demonstrable adverse effect on the dental pulps of mature permanent teeth of monkeys.¹¹

The Saliva

Radiation has a rapid effect on the salivary glands. The saliva becomes thicker, leading to difficulties in chewing and speaking, taste loss, and increased caries risk. In the absence of saliva demineralization is more likely to occur and it is also more difficult to stop or revert.^{1,12} In the first two weeks, with a cumulative RT dose of 20 Gy, around 80% of salivary function is lost.¹³ Immediately following completion of RT, a reduction of 95% of salivary flow may be present.¹⁴ Indeed, Someya et al.¹⁵ evaluated the relationship between salivary flow and radiation dose. The authors found above 58 Gy there was a complete loss of salivary gland function, even following stimulation. These findings have been corroborated in other studies.^{14,16}

In addition to quantitative alterations, the saliva also develops qualitative changes during RT. In irradiated patients alterations in salivary composition include changes in its antibacterial properties and ionic concentration, with consequent reductions of buffering capacity and the pH.^{3,17,18} The average post-irradiation pH falls from about 7.0 to 5.0, which is definitively cariogenic.³ The buffer capacity of saliva is responsible for increasing pH and switching the demineralization/remineralization equilibrium towards remineralization. A reduced buffering capacity of saliva is a consequence of RT.¹⁹ Because of the lowered pH and buffering capacity, the minerals of enamel and dentin can easily dissolve following RT. Transient high concentrations of salivary total proteins, IgA,



albumin, lactoferrin, lysozyme, hexosamines, salivary peroxidase, and myeloperoxidase have been identified during RT.^{20,21} In addition, reduction of low molecular weight salivary proteins (including acidic and basic proline-rich proteins, cystatins, histatins, and statherin) is seen in irradiated patients.²² Also, increased levels of sodium, calcium, potassium, and phosphate are seen during RT.¹⁹

The Oral Microflora

RT of the head and neck induces physiological changes in the oral cavity in relation to the radiation dose given. Thus, low doses of 10–30 Gy are usually tolerated while higher doses rapidly increase oral problems.²³ In addition, the reduced salivary flow results in significant changes of the oral flora in patients treated with RT. These changes occur from the onset of RT up to three months after completion and remain more or less constant thereafter.³ An increase in acidogenic and cariogenic micro-organisms (*Streptococcus mutans*, *Lactobacillus*, and *Candida* species), along with a reduction in non-cariogenic microorganisms such as *Streptococcus sanguis*, *Neisseria*, and fusobacterium, is seen.^{17,24-26} Interestingly, one study showed some genotypes of *S. mutans* might not adapt to the alterations of the oral environment seen during and after RT.²⁷ Despite intensive oral hygiene, no reduction of cariogenic pathogens is seen in HNC patients undergoing RT, leading to high caries risk even 12 months following RT.¹⁰

A number of different therapeutic and prophylactic modalities targeting the reduction of the microbial

burden on the mucosal membranes have been studied. Oral rinses with antiseptic solution, systemic administration of immunoglobulin, and local administration of G-CSF have all been tried.²³ The effect of fluorides upon the oral microflora has also been assessed. The use of topically applied fluoride during RT does not seem to quantitatively affect the oral microflora.^{18,24,28} The only evident fluoride effect is a temporal delay in the microbiological population shift. Nonetheless, the slower rates of increased acidogenic microflora seen in fluoride gel users could lead to inhibition of bacterial growth.²⁴

In addition to salivary flow, other side effects of RT may have an indirect effect on oral microorganisms. Mucositis, trismus, and teeth hypersensitivity can negatively affect oral hygiene and plaque control and, consequently, increase caries risk.^{1,3}

The Diet

Maintenance of adequate nutritional status is a major concern regarding cancer patients. Significant weight loss and deterioration of nutritional status is further aggravated by pain during mastication and swallowing, loss of appetite, nausea, and physical discomfort. Aiming to maintain a good nutritional status without the need for enteral nutrition, physicians, and nutritionists commonly recommend diet changes that include sticky, soft, non-detergent, carbohydrate-rich foods. However, these, along with a higher frequency of intake, will contribute to the onset of caries.^{1,3,24} In addition, acute RT side effects, such as mucositis, also contribute to changes in the composition and frequency of food intake.¹⁻³

Alteration in taste is an early response to radiation. Loss of taste is not only due to the effect of irradiation on the taste buds but is also related to hyposalivation. Taste sensation decreases exponentially with a cumulative dose of about 30 Gy.^{29,30} This change in taste also greatly affects susceptibility to caries, since intake of carbohydrates will be increased in many cases.³

Prevention and Management of Radiation Caries

Although radiation caries is a multifactorial condition, its main risk factor in HNC patients is RT-induced reduction of salivary flow. Thus, the

ideal approach to prevent radiation caries would be to avoid radiation-induced hyposalivation caused by damage to the salivary glands. This could be achieved with exclusion of the major and minor salivary glands from the irradiation field.^{1,23} In this context the integration of intensity-modulated radiotherapy (IMRT) techniques into broad routine will be of great benefit to patients.³¹

If protection of glands is not possible and radiation-induced hyposalivation occurs, current treatment options are restricted to the stimulation of the residual salivary flow (gustatory, mechanical, or pharmaceutical) or to the use of saliva substitutes.³²⁻³⁴ It has been shown sugar-free gums may stimulate salivary flow, buffering, and sugar clearance. Further, adding xylitol to chewing gum could enhance its caries-preventing effects.³² Unfortunately, mechanical stimulation of residual secretion is often insufficient to relieve patients' complaints.¹ In addition, acidic substances have been shown to increase saliva secretion. However, such a procedure is not recommended, since acidity contributes to dental demineralization.³⁵ Overall, the literature seems to indicate mechanical stimulation of saliva to prevent radiation caries is not convenient and frequently leads to low patient compliance.

There are also artificial salivas (saliva substitutes) capable of increasing tissue lubrication, hydration, salivary clearance, and pH neutralization.³⁶ Saliva substitutes contain substances capable of inhibiting bacterial growth and enzymes that stabilize the oral environment.³⁷ Artificial salivas apparently have a remineralization potential which cannot be ignored. Olsson and Axell³⁸ compared artificial saliva with water for the treatment of xerostomia. With artificial saliva, the mean duration of improvement was approximately two times greater than water. Epstein et al.³⁹ evaluated salivary flow, xerostomia, and cariogenic microorganisms in patients using artificial saliva. Patients reported improvement of oral lubrication, although without statistical significance. However, there were no effects on the colonization by cariogenic microorganisms. According to Turssi et al.⁴⁰ saliva substitutes may provide partial remineralization to preformed caries-like lesions. Further, the addition of inorganic substances to the composition of artificial salivas, such as calcium, phosphates, and fluoride ions, can stabilize caries

by reducing the solubility of apatite.⁴¹ Based on the findings of this literature review, the use of artificial saliva represents a good option against RT-induced xerostomia even though the efficacy of preventing radiation caries remains arguable. It is a safe method that may be attempted by dentists due to little risk of side effects. The major drawback is short duration, which requires patients to frequently employ the product.

Systemic sialogogues are a third option to stimulate salivary flow and, consequently, reduce the risk of radiation caries. Among sialogogues, pilocarpine is the most widely used and is considered an effective therapeutic option for the treatment of radiation-induced hyposalivation.^{32,39,42} Johnson et al.⁴³ evaluated 5 mg pilocarpine used three times a day, during 12 weeks in previously irradiated patients. There was significant reduction of xerostomia, reported by 54% of the patients. Similarly, Rieke et al.⁴⁴ verified pilocarpine led to an increase in salivary flow, in addition to reduction of xerostomia. Disadvantages of systemic medications include potential adverse reactions and loss of effect once the drug is withdrawn. Nonetheless, dentists should consider implementing this therapy, especially when dealing with patients with high caries risk and severe hyposalivation.

In addition to targeting quantitative saliva reduction it is also important to approach factors related to salivary qualitative alterations. In this context topically applied fluorides have been successfully used to inhibit the formation of dental caries.⁴⁵ Importantly, neutral fluoride solutions are generally



preferable, since acidic solutions can cause damage to the oral mucosa already sensitized by radiation.^{2,25,46,47} In addition, the chemical preparations of NaF are preferred due to fewer side effects and with this higher compliance. Still, stannous fluoride has been recommended without experiencing problems.⁴⁸

Based on their ten year experience with 935 patients, Horiot et al.⁴⁹ claimed a five minute daily application of fluoride gel is the most reliable method for the prevention of post-irradiation dental caries. The classic study by Dreizen et al.⁵⁰ showed an application of a 1% neutral sodium fluoride gel applied daily in custom trays could significantly reduce caries in irradiated patients. Similarly, Meyerowitz et al.⁵¹ showed rinsing daily with a 0.05% NaF mouthrinse prevented demineralization and increased enamel remineralization in irradiated patients. Spak et al.¹² compared the application of NaF gel 0.42% and 1.23% in individual trays and found the use of the former is sufficient to inhibit caries formation. Similarly, Bonan et al.⁵² suggested NaF 1.23% daily gel application using a tooth brushing technique. However, because an intensive daily self-application of fluoride is required compliance is an issue. To address this matter, Chambers et al.⁴⁵ recently conducted a pilot study testing an intraoral fluoride-releasing system. The system provided similar rates of control for caries formation to a fluoride-gel-containing tray. Together, these studies demonstrate the use of fluoride to prevent radiation caries enjoys a consensus in the literature and should always be employed by dentists when treating patients submitted to head and neck radiation.

Besides fluorides, other alternatives have been studied. A clinical trial⁵³ compared the caries preventive efficacy of a mouthrinse solution containing casein derivatives coupled with calcium phosphate (CD-CP) with a 0.05% sodium fluoride mouthrinse. It was found CD-CP preparations hold promise as caries preventive agents for individuals with dry mouth. Similarly, the efficacy of remineralizing toothpastes (which also deliver soluble calcium and phosphate ions) was recently investigated with the results indicating this toothpaste may prevent root caries in irradiated patients.⁵⁴ However, these remineralizing compounds need to be further studied before

they can be routinely recommended. Furthermore, chemotherapeutic prevention with topically applied bactericidal or bacteriostatic drugs has also been recommended to prevent radiation caries. Chlorhexidine has beneficial effects on plaque control in irradiated patients.³ In addition, a combination of fluoride and chlorhexidine used daily has been shown to offer better results for patients with a high risk of developing radiation caries. Joyston-Bechal et al.²⁵ verified the periodic use of 1% chlorhexidine gel, combined with the daily fluoride rinse, was sufficient to prevent caries. When using chlorhexidine, it is very important to avoid using an alcoholic formulation in order to prevent further dehydration of the already dry irradiated oral mucosa.

Unfortunately, it is not always possible to prevent the development of radiation caries. The restoration of radiation caries can be extremely challenging for a number of reasons. Difficult access to cervical lesions can lead to incomplete excavation of caries. Further, the cavity preparation can be difficult to define and might provide little mechanical retention.⁵⁵ In addition to technical issues, selection of the most appropriate restorative material is difficult due to the challenging oral environment found in irradiated patients. Ideally, the chosen material should demonstrate appropriate adhesion, prevent secondary caries, and resist dehydration and acid erosion.

Some believe amalgam or polymeric materials capable of delivering fluoride should be employed. Indeed, McComb et al.⁵⁶ confirmed the effectiveness of fluoride-releasing materials in the prevention of recurrent caries in irradiated patients. Composite resins have been proven to prevent *in vitro* recurrent decay, and retention of these materials has been demonstrated even for long periods.⁵⁷ However, when time is limited, glass ionomer cements seem to be effective temporary treatments.^{55,56} Indeed, Hu et al.⁵⁵ showed glass ionomers can prevent secondary caries development, even when restorations were lost. Moreover, glass ionomers appear to offer satisfactory handling, adhesion, and physical properties. However, lack of salivary buffering in xerostomic patients may lead to a reduction of normal plaque pH and in turn lead to the formation of hydrofluoric acid and erosion of the glass ionomer.⁵⁶ However, it should be noted most

evidence in the literature regarding the optimal restoration method for irradiated patients is based only on empirical studies. Therefore, it is difficult to determine the ideal restorative material for irradiated patients. Importantly, it is imperative the patient is kept under close supervision regardless of which material is chosen. Also, adequate oral hygiene and plaque control are crucial for clinical success.

Conclusion

RT leads to alterations in the dentition, saliva, oral microflora, and nutrition of HNC patients. Despite a multifactorial etiology, radiation caries is primarily a consequence of hyposalivation. Therefore, radiation caries would ideally be

prevented by sparing salivary glands from radiation. In cases where this is not possible, prevention is achieved with comprehensive dental care before, during, and after RT. In this context, motivation of patients, adequate plaque control, stimulation of salivary flow, fluoride use, and nutritional orientation are essential to reduce the incidence of radiation caries and ultimately improve the quality of life of HNC patients.

Clinical Significance

Since radiation caries is a common yet serious complication of RT, dentists should understand the clinical and biological aspects underlying the disease to prevent development of lesions and provide optimal treatment when needed.

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