Universidade de Brasília – UnB

Faculdade de Ciências da Saúde – FS

Programa de Pós-Graduação em Odontologia - PPGODT

Tese de Doutorado.

IMPACTO DA RADIAÇÃO IONIZANTE NA COMPOSIÇÃO QUÍMICA DA DENTINA RADICULAR SADIA E CARIADA E NA RESISTÊNCIA DE UNIÃO DE SISTEMAS ADESIVOS E CIMENTOS IONÔMERO DE VIDRO

Brenda Lisseth Pineda Mancia

Brasília, 02 de fevereiro de 2024.

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Tese apresentada ao Programa de Pós-Graduação em Odontologia da Faculdade de Ciências da Saúde da Universidade de Brasília como requisito parcial à obtenção do título de Doutor em Odontologia.

Orientadora: Profa. Dra. Ana Paula Dias Ribeiro

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Tese aprovada, como requisito parcial para obtenção do grau de Doutor em Odontologia, Programa de Pós-Graduação em Odontologia da Faculdade de Ciências da Saúde da Universidade de Brasília.

Data da defesa: 02/02/2024

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Profa. Dr. Rodrigo Antonio de Medeiros (Suplente)

Dedico este trabalho à minha família, que sempre me apoiou, me incentivou e acreditou em min.

AGRADECIMENTOS

Agradeço a minha orientadora Ana Paula Dias Ribeiro pela orientação durante todo o doutorado. Obrigada por contribuir no meu crescimento profissional, pelos ensinamentos, por sempre me corrigir com cuidado e carinho e pelo apoio emocional. Agradeço a Deus por ter a senhora como orientadora; minha gratidão e admiração.

Agradeço a meu co-orientador Lucas Fernando Tabata Obrigada pelas orientações e partilha de conhecimentos, por me orientar no processo laboratorial mesmo durante a pandemia, pelas inumeras horas de dedicaçao no meu trabalho. Sua experiência como professor é um presente inestimável; obrigada por tudo.

Profa. Soraya Leal, foi uma honra ter a senhora como professora, agradeço todas as orientações mesmo desde antes de começar a doutorado; saiba que sua orientação foi essencial para conseguir cumprir todos os requisitos. Obrigada por me fazer sentir acolhida no programa de pós graduação.

Prof. Leandro Hilgert, quando soube que o senhor seria meu professor me senti muito privilegiada e ainda mais quando o senhor se disponibilizou para me acompanhar em diferentes etapas do doutorado. Sentir que o senhor acredita em mim me faz ser melhor profissional. Obrigada pelos ensinamentos e por sempre estar disponível para me ajudar. Seu compromisso com o aprendizado é imensurável; minha gratidão e admiração.

Profa. Fernanda e Profa. Liliana, obrigada pelos ensinamentos, pelo apoio e disponibilidade.

A minha amiga e colega de pós-graduação Patrícia Ferronato, obrigada pela parceria, por me acompanhar principalmente durante a época da pandemia e por sempre me incentivar cada vez que quis desistir, minha eterna gratidão.

Ao Departamento de Oncologia do Hospital de Brasília (HUB), ao Instituto de Química da Universidade de Brasília, a GC Company e ao Laboratório de dentística e materiais dentários da Universidade de Brasília.

A Organização dos Estados Americanos (OEA), e a Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), pela concessão da bolsa de estudos.

Ao Programa de Pós-graduação em Odontologia da Universidade de Brasília, pela oportunidade de cursar uma pós-graduação stricto sensu de excelente qualidade.

Aos professores da banca, muito obrigada pelas considerações e contribuições que fizeram para o meu trabalho.

“Não fui eu que ordenei a você? Seja forte e corajoso!

Não se apavore nem desanime, pois o Senhor,

o seu Deus, estará com você por onde você andar"

Josué 1:9

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1 CAPÍTULO 1: INTRODUÇÃO, REVISÃO DA LITERATURA E OBJETIVOS

1.1 INTRODUÇÃO E REVISÃO DA LITERATURA

De acordo com o Instituto Nacional do Câncer, neoplasias malignas é um termo dado a um conjunto de mais de cem doenças que têm em comum o crescimento desordenado de células, que invadem tecidos e órgãos, com possibilidade de ocasionar metástase para outras regiões do corpo (Instituto Nacional do Câncer José Alencar Gomes da Silva - INCA) e são popularmente conhecidas como câncer. O câncer é um problema de saúde pública no mundo, figurando como uma das principais causas de morte e, como consequência, uma das principais barreiras para o aumento da expectativa de vida em todo o mundo. Na maioria dos países, corresponde à primeira ou à segunda causa de morte prematura, antes dos 70 anos. (Instituto Nacional do Câncer José Alencar Gomes da Silva - INCA). O Instituto Nacional do Câncer (INCA) publica uma estimativa para o acometimento de câncer na população brasileira. Na publicação mais recente, estima-se 704 mil para novos casos de câncer, esse total é para cada ano do triênio 2023 – 2025, o que significa que serão 2,1 milhões em três anos. Especificamente para a região de cabeça e pescoço em três anos surgirão 118.650, já que a previsão do Inca é de que 39.550 novos casos aparecerão a cada ano do triênio 2023-2025 (2023 - INCA). Esses valores correspondem a um risco alto, sendo o cancer de boca o quarto tumor mais frequente apresentado mais comunmente no sexo masculino, acima de 40 anos. A maioria dos casos é diagnosticada em estágios avançados. (INCA 2023).

Radiação ionizante e seus efeitos

Os cânceres de cabeça e pescoço são frequentemente tratados com radioterapia, uma técnica que utiliza radiação ionizante e danifica de forma semi-seletiva material genético de células malignas vulneráveis, ou através da produção de radicais livres, levando à morte celular (de Felice et al., 2018). A radioterapia pode ser utilizada de forma exclusiva ou associada à cirurgia e à quimioterapia (Kielbassa et al., 2006; Lazarus et al., 2007; de Felice et al., 2018).

A unidade empregada para medir a quantidade de radiação é o Gray (Gy), que informa a dose de radiação absorvida por qualquer material ou tecido humano (INCA 2023). No geral, a dose total de radiação para tratamento de câncer de cabeça e pescoço varia de 30 a 72 Gy, sendo muito comum o esquema de fracionamento, com aplicação de 2 Gy diários, 5 dias por semanas até atingir a totalidade de Gy planejados (Jham & Freire, 2006; Epstein et al., 2012). Apesar de um planejamento cuidadoso, é inevitável que ela cause algum dano aos tecidos saudáveis localizados no campo da radiação (Ping Qing et al.,2015).

Efeitos locais da radiação ionizante

A radioterapia está tipicamente associada a toxicidades agudas e tardias aos tecidos saudáveis localizados no campo da radiação. Os efeitos mais comuns da toxicidade aguda na cavidade oral incluem mucosite, disfagia, hipossalivação, tecidos moles sensíveis ou dolorosos e infecções por fungos (Vissink et al., 2003; Jham & Freire, 2006). Outras consequências têm um caráter mais tardio como o trismo, a hipossalivação, a osteorradionecrose da mandíbula, as alterações nas estruturas dentárias e a cárie relacionada à radiação (Jham & Freire, 2006; Kielbassa et al., 2006; Tolentino et al., 2011; Jawad et al., 2015; Hong et al., 2017). Pacientes que receberam radioterapia de cabeça e pescoço apresentam risco aumentado de cárie dentária.

Efeitos da radiação ionizante nos tecidos dentários

Existem trabalhos na literatura que comprovem os efeitos da radioterapia na estrutura dental no que diz respeito às alterações em suas propriedades mecânicas e químicas, na microestrutura/morfologia, na estrutura cristalina, na solubilidade do esmalte e da dentina (Vissink et al., 2003; Soares et al., 2010; Gonçalves et al., 2014; Lieshout & Bots 2014; Qing et al., 2015; Reed et al., 2015; Liang et al., 2016; Qing et al., 2016; Campi et al. 2018; de Miranda et al., 2018; Lopes et al., 2018; Rodrigues et al., 2018; Velo et al., 2018). A gravidade e a extensão dos efeitos da radiação dependem do conteúdo mineral e orgânico das estruturas do dente, sendo que a dentina pode ser mais vulnerável aos efeitos da radiação (Gonçalves et al., 2014).

Os primeiros sinais de deterioração do tecido duro dos dentes podem ser vistos dentro de três meses após a finalização da radioterapia (Vissink et al., 2003). Esses sinais são áreas de porosidade do esmalte, formação de cavitações com a exposição do esmalte subsuperficial, ou até mesmo da dentina subjacente. À esta deterioração dá se o nome de cárie relacionada à radiação (Vissink et al., 2003; Kielbassa et al., 2006).

Carie relacionada a radiação

A cárie relacionada à radiação se diferencia da cárie convencional, pois se desenvolve rapidamente, é altamente destrutiva e na maior parte manifesta-se sem dor (Jansma et al., 1993; Walker et al., 2011; Kielbassa et al., 2006, Abdalla et al., 2018). Afeta aproximadamente 37% dos pacientes que receberam radioterapia aparecendo entre 3 a 12 meses após a conclusão do tratamento (Moore et al 2020). Possui como etiologia a combinação de efeitos indiretos da radioterapia somados aos efeitos diretos na estrutura dentária (Moore et al 2020, Kielbassa et al., 2006), como alterações na microdureza, composição química e micromorfologia do esmalte e dentina (Lishout & Bots, 2014; Deng et al., 2015; Qing et al., 2016), predispondo a dentição a uma maior ocorrência deste tipo de lesão.

Cárie radicular

As lesões de cárie radicular ativa nas áreas cervicais tem sido descrita como um processo bastante rápido, deixando o esmalte sem suporte coronalmente ao redor da junção cimento-esmalte (Meyer-Luecke et al.; 2019).

As superfícies radiculares diferem das superfícies do esmalte pelo menor conteúdo mineral e maior quantidade de matéria orgânica. Devido ao tamanho menor dos cristais de apatita, as superfícies radiculares são altamente receptivas à absorção mineral no ambiente oral. As lesões de cárie radicular apresentam um tipo de perda mineral subsuperficial, semelhante às lesões de cárie em esmalte e podem ocorrer em todas as superfícies radiculares expostas, mas são encontradas principalmente em locais de retenção de biofilme, como ao longo da junção amelo-cementária (Heasman et al.; 2017).

A lesão de cárie relacionada à radiação tende a ocorrer na região cervical, próximo à junção entre a coroa e a raiz (Jawad et al., 2015). que incluem a lesão da raiz como uma complicação clínica notável (Velo et al 2018). A dentina humana é um tecido complexo (Mjör et al 1972) e altamente solúvel, possivelmente devido ao seu menor conteúdo mineral quando comparado ao esmalte e maiores teores de carbonato e magnésio (Hoppenbrouwers et al 1987). É muito comum observar uma área de desmineralização circunferencial na cervical do dente, afetando superfícies lisas do esmalte que normalmente são resistentes à cárie dentária, bem como superfícies expostas de cemento (Abdalla et al., 2017). Portanto, a cárie radicular da dentina progride, podendo até mesmo levar a fratura da coroa nesta região, e como consequencia exodondia, afetando severamente a mastigação e a estética desses pacientes e também aumenta o risco de desenvolver osteorradionecrose após a exodontia, impactando negativamente a qualidade de vida do paciente (Andrews et al., 2001; Franzel et al., 2006, Lieshout et al 2014).Ela também se difere em relação à sua aparência. Na maioria das vezes, essas lesões apresentam-se com uma coloração marrom e com alteração da translucidez da estrutura dentária.

Efeitos da radiação ionizante nos tratamentos restauradores

A restauração de lesões de cárie relacionada à radiação pode ser extremamente desgastante para pacientes e dentistas (Vissink et al., 2003; Velo et al., 2018). A restauração fica comprometida pelo efeito prejudicial da radiação ionizante na resistência de união ao esmalte e à dentina (Naves et al., 2012; Rodrigues et al., 2018). Diferentes estudos avaliam o impacto da radioterapia na estrutura dos materiais dentários restauradores (Hu et al., 2002, Troconis et al., 2017, Brandeburski et al., 2017) apresentando resultados controversos.

Estudos clínicos demostram que os materiais restauradores mais usados nestes pacientes são: Resinas Compostas, Cimentos de ionômero de vidro convencionais e cimentos de ionômero de vidro modificados por resina, (Palmier et al 2020, Hu et al., 2002, McComb et al., 2002, De Moor et al., 2011)os quais apresentam resultados controversos. Entretanto, a literatura ainda não tem definido o material de escolha para restaurações de dentes acometidos por lesões de cárie relacionadas à radiação.

1.2 OBJETIVOS

1.2.1 OBJETIVO GERAL

Avaliar o impacto da radiação ionizante na composição química da dentina radicular sadia e cariada e na resistência de união ao microcisalhamento de diferentes cimentos de ionômero de vidro e diferentes sistemas adesivos. A realização deste estudo vai permitiu determinar o material com menos falhas adesivas para restaurar lesões de cárie relacionada à radiação em dentina radicular, melhorando assim a qualidade de vida e a função mastigatória e estética de pacientes de câncer de cabeça e pescoço que receberam radioterapia.

1.2.2 OBJETIVOS ESPECÍFICOS

1. Realizar uma revisão de literatura e analisar a literatura sobre o tratamento de lesões de cárie relacionada à radiação, materiais usados, falhas no tratamento e manejo com melhores resultados.
2. Avaliar o impacto da radiação ionizante de cabeça e pescoço na composição química da dentina radicular sadia e cariada.
3. Avaliar o impacto da radiação ionizante de cabeça e pescoço na resistência de união ao microcisalhamento de cimentos ionômero de vidro à dentina radicular sadia e cariada.
4. Avaliar o impacto da radiação ionizante de cabeça e pescoço na resistência de união ao microcisalhamento de sistemas adesivos à dentina radicular sadia e cariada.

1.3 HIPÓTESE NULA

A hipótese nula deste trabalho é de que a radiação ionizante não tem impacto na resistência de união de diferentes sistemas adesivos e cimentos de ionômeros de vidro, tanto em dentina radicular sadia como cariada e na composiçao química destes tecidos.

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2 CAPITULO 2: RADIATION-RELATED CARIES TREATMENT: A LITERATURE REVIEW

ANEXO I

(ARTIGO PUBLICADO NA ODONTOESTOMATOLOGIA)

http://www.scielo.edu.uy/scielo.php?script=sci_arttext&pid=S1688-93392022000101310

3 CAPITULO 3: EFFECT OF IONIZING RADIATION ON THE CHEMICAL STRUCTURE OF SOUND AND CARIES-AFFECTED ROOT DENTINE AND ON THE BOND STRENGTH TO GLASS IONOMER CEMENTS AND ADHESIVES SYSTEMS

ANEXO II

(ARTIGO SUBMETIDO NA OPERATIVE DENTISTRY)

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4 CAPÍTULO 4: DISCUSSÃO GERAL E CONCLUSÕES DA TESE

4.1 DISCUSSÃO GERAL

Neste estudo inicialmete foi realizada uma revisão de literatura com a finalidade de analisar literatura sobre o tratamento de cárie relacionada à radiação, materiais usados, falhas no tratamento e manejo com melhores resultados, no qual a literatura mostrou que a cárie relacionada à radiação é comumente restaurada com cimento de ionômero de vidro convencional, cimento de ionômero de vidro modificado por resina e resina composta com aplicações de flúor e concluimos que mais estudos são necessários para determinar o melhor tratamento, incluindo técnica de preparo cavitário e material restaurador com melhores resultados. Sugerimos a realização de estudos comparando vários sistemas adesivos, concentrações de flúor e restaurações de dentina radicular.

Diante disso, foi realizado um estudo laboratorial avaliando o impacto da radiação ionizante na resistência de união ao microcisalhamento de cimentos de ionômero de vidro e sistemas adesivos à dentina radicular sadia e afetada por cárie, bem como seu impacto na composição química da dentina radicular.

Nesse estudo, as hipóteses nulas foram rejeitadas, uma vez que a resistência de união e a composição química da dentina radicular hígida e afetada por cárie foram alteradas pela radiação ionizante. Nossos resultados demonstraram que os valores de resistência de união da dentina radicular irradiada diferiram daqueles da dentina radicular não irradiada para cimentos ionômero de vidro e sistemas adesivos.

A cárie relacionada à radiação afeta aproximadamente 37% dos pacientes que receberam radioterapia para tratamento de câncer de cabeça e pescoço, aparecendo entre 3 e 12 meses após o término do tratamento (Lieshout et al., 2014). Há um número crescente de pacientes com câncer de cabeça e pescoço que foram submetidos à radiação ionizante que apresentam efeitos colaterais como redução do fluxo salivar (Wijers., et al 2002) adicionando os efeitos diretos da radiação ionizante na estrutura dentária, incluindo alterações na composição química, aumentam o risco de cárie dentária nestes pacientes (Kielbassa et al., 2006; Lieshout et al., 2014; Moore et al 2020). Neste estudo foram observadas alterações no conteúdo mineral principalmente nos grupos de dentina radicular afetada por cárie associada à radiação ionizante.

Considerando que os materiais restauradores mais usados para restaurar cárie relacionada a radiação são resinas compostas, cimentos de ionômero de vidro convencionais e cimentos de ionômeros de vidro modificados por resina, (Palmier et al 2020, Hu et al., 2002, McComb et al., 2002, De Moor et al., 2011), este estudo avaliou diferentes cimentos de ionômero de vidro e diferentes sistemas adesivos. Os achados deste trabalho contribuem para a tomada de decisão sobre materiais restauradores em casos clínicos de cárie radicular após protocolos de radiação ionizante.

Foi observado que após o tratamento de radiação ionizante foi alterada a composição química e alteração na adesão de diferentes materiais restauradores recomenda-se estratégias de prevenção. A literatura mostra que os cuidados bucais, como instruções de higiene com acompanhamento odontológico regular e flúor diário, parecem ser estratégias promissoras para prevenir a cárie relaionada a radiação e o monitoramento periódico desses pacientes é uma das estratégias mais importantes (de Carvalho et al.; 2023).

4.2 CONCLUSÕES

Com base nas limitações do presente estudo, pode-se concluir que a radiação ionizante e a cárie afeta a composição química da dentina radicular e reduz os valores de resistência de união para todos os materiais restauradores avaliados.

Mais estudos clínicos são necessários para abordar as limitações e complementar os resultados deste estudo in vitro.

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5 CAPITULO 5: PRESS RELEASE

A odontologia tem como um dos principais desafios o tratamento da doença cárie. Existe um tipo de lesão de cárie de avanço rápido em pacientes que receberam tratamento de radioterapia para cáncer de cabeça e pescoço e precisa ser tratada. Existem alguns materiais restauradores que podem ser usados para restaurar este tipo de lesão de carie; neste estudo foram avaliados diferentes materiais por meio de estudos laboratorias que precisam ser testados em estudos clinicos para assim definir o material para usar nestes pacientes.

6 ANEXO

ANEXO I

Radiation-related caries treatment: a literature review

Tratamiento de caries relacionada a radiación: una revisión de literatura

Tratamento de cárie relacionada à radiação: uma revisão de literatura

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Abstract

Radiation-related caries are a frequent late complication caused by the direct and indirect effects of head and neck cancer radiotherapy. This study aimed to review and analyze the literature on managing radiation-related caries, restorative materials, treatment failures, and treatment protocols. A search was conducted in Pubmed, Lilacs, and Web of Science by three independent reviewers, and inclusion and exclusion criteria were used for paper selection. According to clinical studies and literature reviews, the most used materials are conventional glass-ionomer cement, resin-modified glass-ionomer cement, and composite resin with fluoride applications. More studies are needed to determine the best treatment, including cavity preparation technique and restorative material with better results. We suggest conducting studies comparing various adhesive systems, fluoride concentrations, and root dentin restorations.

Keywords: radiotherapy, dental caries, head and neck cancer.

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Received on: 25/08/2021 - Accepted on: 30/11/2021

Resumen

Caries relacionada a radiación es una complicación tardía frecuente de la radioterapia de cáncer de cabeza y cuello, ocasionada por efectos directos e indirectos de la radioterapia. El objetivo del presente trabajo es realizar una revisión y analizar literatura sobre el manejo de caries relacionada a radiación, materiales usados, fallas en el tratamiento y protocolo con mejores resultados; tres revisores independientes realizaron una búsqueda en diferentes bases de datos: PubMed, Lilacs y Web of Science, determinando criterios de inclusión y exclusión para la selección. Estudios clínicos y revisiones indicaron que los materiales más usados son cemento ionómero de vidrio convencional, cemento ionómero de vidrio modificado con resina y resina compuesta con aplicaciones de flúor. Son necesarios más estudios para definir el mejor tratamiento que incluya técnica de preparación de la cavidad y material restaurador con mejores resultados. Se recomienda realizar estudios comparando diferentes sistemas adhesivos, concentraciones de flúor y restauraciones en dentina radicular.

Palabras clave: Radioterapia, Caries dental, Cáncer de cabeza y cuello

Resumo

Cárie relacionada à radiação é uma complicação tardia frequente da radioterapia de câncer de cabeça e pescoço, ocasionada por efeitos diretos e indiretos da radioterapia. O objetivo do presente trabalho é realizar uma revisão e analisar literatura sobre o tratamento de cárie relacionada à radiação, materiais usados, falhas no tratamento e manejo com melhores resultados; foi realizada uma bus- ca em diferentes bases de dados: PubMed, Lilacs e Web Of Science, por três revisores independentes, usando critérios de inclusão e exclusão. Estudos clínicos e revisões de literatura indicam que os materiais mais usados são cimento de ionômero de vidro convencional, cimento de ionômero de vidro modificado com resina e resina composta com aplicações de flúor. Mais estudos são necessários para definir o melhor tratamento que inclua a técnica de preparo cavitário e material restaurador com melhores resultados. Recomenda-se a realização de estudos comparando diferentes sistemas adesivos, concentrações de flúor e restaurações em dentina radicular.

Palavras-chave: Radioterapia, Cárie dental, Câncer de cabeça e pescoço.

Introduction

Radiotherapy for head and neck cancer is commonly associated with acute and late complications in healthy tissues located in the irradiated area. Common acute oral complications include mucositis, dysphagia, xerostomia, tender or painful soft tissues, and fungal infections.(1,2) Other late complications include trismus, hyposalivation, osteoradionecrosis, changes in dental structures, and radiation-related caries.(2-4) Radiation-related caries affect approximate- ly 37% of irradiated head and neck cancer patients: it appears between 3 and 12 months after treatment is complete and is considered a late complication.(5)

Radiation-related caries is caused by a combination of the indirect effects of radiotherapy, such as damage to the salivary glands that modify the oral flora and reduce remineralization, damage to the temporomandibular joint and masticatory muscles causing trismus, and damage to the mucous membranes, which causes mucositis and limits adequate oral hygiene. There are also direct consequences on tooth structure,(3,5) such as changes in microhardness, chemical composition, and micromorphology of enamel and dentin,(6,7) predisposing patients to an increased risk of caries. It differs from conventional caries because it develops rapidly, is highly destructi- ve, and is mostly painless.(3,8-10) It mainly affects the root area near the cementoenamel junction(4) and includes root-dentin caries.(11)

Restorative treatments for this type of caries are compromised by the harmful effect of radiotherapy on the bonding strength of the materials to enamel and dentin.(12,13) This entails ineffective adhesion between the restoration and the dental substrate, mainly after high doses of radiotherapy.

This study aimed to review and analyze the literature on managing radiation-related caries, restorative materials, treatment failures, and treatment protocols with the best clinical outcomes.

Methods

An advanced search was conducted in PubMed, LILACS, and Web of Science databases using the following keywords in English, Spanish, and Portuguese: "radiation-related caries," "radiotherapy," "ionizing radiation," "permanent dental restoration," "composite resins," "glass-ionomer cements," "modified glass-ionomer cement," "conventional glass-ionomer cement," and "direct restoration." The literature search was conducted from april to june 2021. The studies included fulfilled the following inclusion criteria: patients with head cancer treated with radiotherapy and treated for caries lesions, patients with any direct restoration with or without fluoride, clinical studies, randomized clinical trials, case-control, cohort, reviews without follow-up period restrictions. Exclusion criteria: reviews, letters, opinions, editorials, books, book chapters, in vitro or in situ studies, and other design studies different from those described in the inclusion criteria, and studies written in non-Latin script.

Development

We found the following studies on managing radiation-related caries: seven clinical studies, one case report, two systematic reviews, and one narrative review. One case report was excluded because it referred to indirect restorations, and one clinical study was excluded because it was written in non-Latin script. The studies inclu- ded were in English, all available in full text and mainly in PubMed (Table 1)

Table 1: Main methodological data obtained from the studies on treating radiation-related caries.

Author	Country	Year	Type of study	Materials analyzed	Was fluoride used?	Period
Wood et al.[14]	Canada	1993	NRS	GIC and AG	Yes	2
McCombe et al.[15]	Canada	2002	NRS	GIC, RMGIC, and CR	Yes	2
Hu et al.[16]	China	2002	NRS	GIC	No	2
Haveman et al.[17]	USA	2003	NRS	RMGIC, and AG	Yes	2
Hu et al.[18]	China	2005	NRS	GIC	No	2
De Moor et al.[19]	Belgium	2011	NRS	GIC, RMGIC, CR	Yes	2
Gupta et al.[20]	India	2015	SR			2
Palmier et al.[21]	Brazil	2020	NR			
Palmier et al.[22]	Brazil	2021	SR			

NRS: non-randomized study; SR: systematic review; NR: narrative review; GIC: glass-ionomer cement; AG: amalgam; RMGIC: resin-modified glass-ionomer cement, ART: atraumatic restorative treatment.

The oldest study was conducted in 1993 by Wood et al.[14] They clinically compared VIC and AG restorations in the treatment of Class V caries in xerostomic patients with head and neck can- cer. They divided the patients into fluoride users and non-fluoride users. They found that GIC fai- led, and AG restorations did not in patients using a slightly acidic sodium fluoride gel (pH 5.8) dai- ly. In patients who stopped using topical fluoride as indicated, GIC restorations did not fail, but AG restorations did. The mean time to loss of resto- ration for both materials was 8.5 months.

In a 2002 study, Mc Comb et al.[15] clinically com- pared GIC, RMGIC, and CR + conventional two- step adhesive system restorations to treat root caries in patients treated with radiotherapy for head and neck cancer. Each patient underwent a restoration with each of these materials. In addition, the daily use of a pH-neutral sodium fluoride gel in customized trays was indicated. Follow-up appointments were made after 6, 12, 18, and 24 months, and the restorations were examined for loss of material, marginal integrity, and recurrent caries at the restoration margin. No statistical differences were found between GIC and RMGIC, but statistical differences were found between these materials and CR in each recovery period. Reductions in recurrent caries in GIC and RMGIC restorations compared to CR were greater than 80% in patients using topical fluoride supplementation. The authors conclu- ded that this clinical comparison provided evi- dence of the therapeutic efficacy of fluoride ma- terials in reducing recurrent caries regardless of the material. They also concluded that fluo- ride-releasing restorative materials may offer a different clinical approach to the overall disease management of high-caries-risk patients.

In 2002, Hu et al. conducted a clinical study on 15 adult patients with radiation-related caries. They used two high-viscosity GICs in each patient to restore 146 caries lesions in exposed dentin and 93 in cementum areas. The restorations were monitored directly for two years to detect reten- tion, secondary caries, anatomical shape, margi- nal integrity, marginal discoloration, and surface texture, and all patients received oral hygiene education. The authors found that placing highly viscous GIC in highcariesrisk patients seemed to prevent secondary caries, even when the resto- rations were subsequently lost.[16]

In 2003, Haveman et al. conducted a clinical study comparing RMGIC and AG restorations. They showed that fluoride-releasing materials could reduce caries around restorations in pa- tients who do not use topical fluoride regularly. [17]

In 2005, Hu et al. conducted a clinical study resto- ring radiation-related caries at the root surface: GIC was placed in 72 conventional and 74 atrau- matic restorative treatment (ART) preparations. Two professionals evaluated the restorations af- ter 6, 12, and 24 months for retention, marginal defects and surface wear, and recurrent caries. They concluded that using hand instruments and the ART method was an equally effective alterna- tive to conventional rotary instrumentation for cavity preparation. More extensive restorations had greater failure rates, usually due to loose- ning.[18]

In 2011, De Moor et al. evaluated the clinical performance of adhesive materials in Class V ca- vities in patients with head and neck cancer in terms of marginal adaptation, anatomical shape, and recurrent caries. Thirty-five adult patients with radiation-related caries with three or more root caries lesions in the same arch were selec- ted. Each patient was treated with a restoration with GIC, RMGIC, CR + conventional 3-step ad- hesive system. Patients were instructed to use 1% neutral sodium fluoride gel in custom trays daily. After 6, 12, 18, and 24 months, the resto- rations were examined for loss of material, mar- ginal integrity, and recurrent caries. The authors concluded that GIC is an optimal option to treat radiation-related root caries since its use is asso- ciated with protection against secondary caries (even after the loss of filling material). However, adaptation and disintegration are more marked in glass-ionomer cements than in composite resins. If glass ionomer cements fail, the defecti- ve restorative materials can be replaced, prefera- bly preserving the remains of the glass-ionomer filling and restoring the tooth with a sandwich technique (with a composite covering the remains of the glass-ionomer cement).[19]

In 2015, a systematic review was published by Gupta et al. on the treatment and prevention of radiation-related caries. They state that, although this type of caries occurs for several reasons, hyposalivation remains the primary cause. Therefore, radiation-related caries can be prevented by preserving the salivary glands, or through prevention, by providing comprehensive dental care before, during, and after radiotherapy.[20]

In 2020, Palmier et al. wrote a narrative review on current diagnostic, prognostic, and management paradigms with clinical relevance. They found that several factors, such as xerostomia and dietary changes, may influence the development of radiation-related caries. CR with fluoride application appears to be the ideal option to manage radiation-related caries.[21]The most recent study found in the literature is a systematic review and meta-analysis conducted by Palmier et al. in 2021 on the impact of head and neck radiotherapy on the longevity of adhesive restorations, which includes the studies above. [14-16,19] They concluded that head and neck radiotherapy affects the longevity of dental adhesive, and better survival rates were observed for CR restorations compared to GIC and RMGIC restorations. They also found that fluoride application showed a positive result in CR restorations and that CR restorations associated with fluoride gel applications appear to be the best method to restore Class V lesions in patients treated with head and neck radiotherapy.[22]

Discussion

Studies show that the direct materials used to restore radiation-related caries are AG, CR, GIC, and RMGIC.[14-16, 19, 21,22] GIC has the lowest success rate. Regarding the cavity restoration technique, only one study compared the conventional technique and ART and found no differences.[18] Radiotherapy may induce a reduction in enamel crystallinity and enlarged crystals, contributing to reduced enamel wear resistance.[7] Chemical alterations in dentin can occur during radiotherapy since its chemical components reorganize, thus altering the structures. This leads to a change in the structural organization of collagen.

[13] This causes the decarboxylation of the carboxylate side bonds in collagen, and this bond is responsible for the interaction of the mineral matrix and hydroxyapatite crystals.[23] Morphologically, a disorganized dentin structure can be observed after radiotherapy using a scanning electron microscope. This can be associated with the reorganization of the collagen structure and compromises the dentin's mechanical and adhesive properties.[13] Performing direct restorations on patients undergoing radiotherapy is important since the literature shows that restorations can be compromised by the harmful effect of ionizing radiation on the bond strength to enamel and dentin, affecting the formation of the hybrid layer.[12,13]

CR restorations with fluoride gel applications seem to be a suitable alternative to restore Class V lesions in patients who have undergone radiotherapy.[22] As irradiated patients present a high risk of caries, fluoride is recommended as it can reduce recurrent caries[16,17] at defined specific concentrations and use instructions. The num- ber of clinical studies is too small to determine the best management and protocol to follow to obtain better long-term results. Studies inclu- ding CR as a restorative material did not analyze several adhesive systems.

The most analyzed failures in the studies were loss of material, marginal integrity, and recu- rrent caries at the restoration margin. Patient motivation, adequate plaque control, stimulation of salivary flow, and fluoride are essential to re- duce the incidence of radiation-related caries.[20] The follow-up period of the studies was two years, so long-term clinical studies are needed. These lesions most typically appear on roots. As the lesion progresses rapidly and salivary fluid decreases, the condition can advance and affect the root.[11] In 2018, Velo et al. demonstrated that irradiated root dentin was less mineralized in vitro study. This could have decreased the subs- trate's permeability and solubility[11] and conse- quently affected the adhesion of restorative ma- terials.

Conclusions

Based on the literature, it is concluded that radiation-related caries is commonly restored with conventional glass-ionomer cement, resin-modified glass-ionomer cement, and composite resin with fluoride applications. More studies are needed to determine the best treatment, including cavity preparation technique and restorative material with better results. We suggest conducting studies comparing various adhesive systems, fluoride concentrations, and root dentin restorations.

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Conflict of interest declaration:

The authors have no conflict of interest regarding the publication of this paper.

Authorship contribution

1. Conception and design of study
2. Acquisition of data
3. Data analysis
4. Discussion of results
5. Drafting of the manuscript
6. Approval of the final version of the manuscript

BLPM has contributed in: 1, 2, 3, 4, 5, 6.
LVMLR has contributed in: 1, 2, 3, 4, 5, 6.
LFT has contributed in: 1, 4, 5, 6.
FCPG has contributed in: 1, 4, 5, 6.
APDR has contributed in: 1, 3, 4, 5, 6.

ANEXO II

Effect of ionizing radiation on the chemical structure of sound and caries-affected root dentine and on the bond strength to glass ionomer cements and adhesives systems

Running title: Root Dentin chemical and mechanical changes after ionizing radiation exposure

Clinical relevance

Ionizing radiation of head and neck cancer and dental caries interferes with the bond strength of glass ionomer cements and adhesive systems to the root dentine and also affects the chemical composition of this substrate increasing the challenge for restorative treatments.

SUMMARY

Objective: To evaluate the impact of ionizing radiation on the microshear bond strength of glass ionomer cements and adhesive systems to sound and caries-affected root dentine as well as its impact on the chemical composition of root dentin.

Methods and Materials: Sound human third molars were divided in 16 groups according to exposure to radiation (irradiated and non-irradiated) and artificial caries challenge (sound and caries-affected dentin). Subsequently, the root dentin specimens were restored with: conventional glass ionomer cement (GIC), resin-modified glass ionomer cement (RMGIC); two-step self-etch adhesive (Clearfil SE) or three-step etch-and-rinse adhesive (Optibond FL). The bond strength of glass ionomer cements and adhesive system to sound and caries-affected dentin was assessed by microshear bond testing, and the failure modes were evaluated using scanning electron microscopy (SEM). Elemental analysis of root dentin was performed using an EDS. Statistical analysis was performed using non-parametric statistical tests (Kruskal-Wallis and Mann-Whitney).

Results: For GICs, all groups submitted to IR presented significantly lower bond strength values when compared to non-irradiated groups in the presence or not of the cariogenic

challenge. For the adhesive systems, the association of IR and artificial caries significantly reduced the bond strength when compared to the other groups. Ionizing radiation and the artificial carious process affected the chemical composition of root dentin, leading to a significant reduction in carbon, oxygen, phosphate, and calcium contents.

Conclusions: Ionizing radiation affects the chemical composition of root dentin and subsequently influencing the bond strength of adhesive systems and glass ionomer cements to root dentin.

INTRODUCTION

The incidence of radiation-related caries (RRC) in patients who received head and neck ionizing radiation (HNIR) is approximately 29%, as reported in previous studies.[1] Its etiology involves a combination of indirect factors, including a decrease in salivary flow, trismus, mucositis, poor plaque control, and taste loss,[1-4] added to the direct effects on the tooth structure. These direct effects include changes in the chemical, structural, and mechanical properties of enamel and dentin[1,3-16], thereby increasing the risk of dental caries in head and neck ionizing radiation (HNIR) patients. [1-3,9-11,17]

In terms of location, RRC tend to occur in the cervical region, close to the enamel-dentine junction.[17-19] Dentinal root caries is a notable and highly prevalent clinical complication.[10,20-22] The severity and extent of the effects of IR depend on the mineral and organic composition of tooth structures, with dentin being identified as a more vulnerable substrate.[23] Clinically, radiation-related caries (RRC) may appear on unconventional surfaces, complicating diagnosis, staging of cavitation, and treatment planning.[24]

Restorative treatment of RRC is compromised by the detrimental effect of IR on the bond strength to enamel and dentin. [12,25-28] Clinical studies have shown that the most used restorative materials in these patients are composite resin (CR), conventional glass ionomer cement (CGIC), and resin-modified glass ionomer cement (RM-GIC).[29-33]

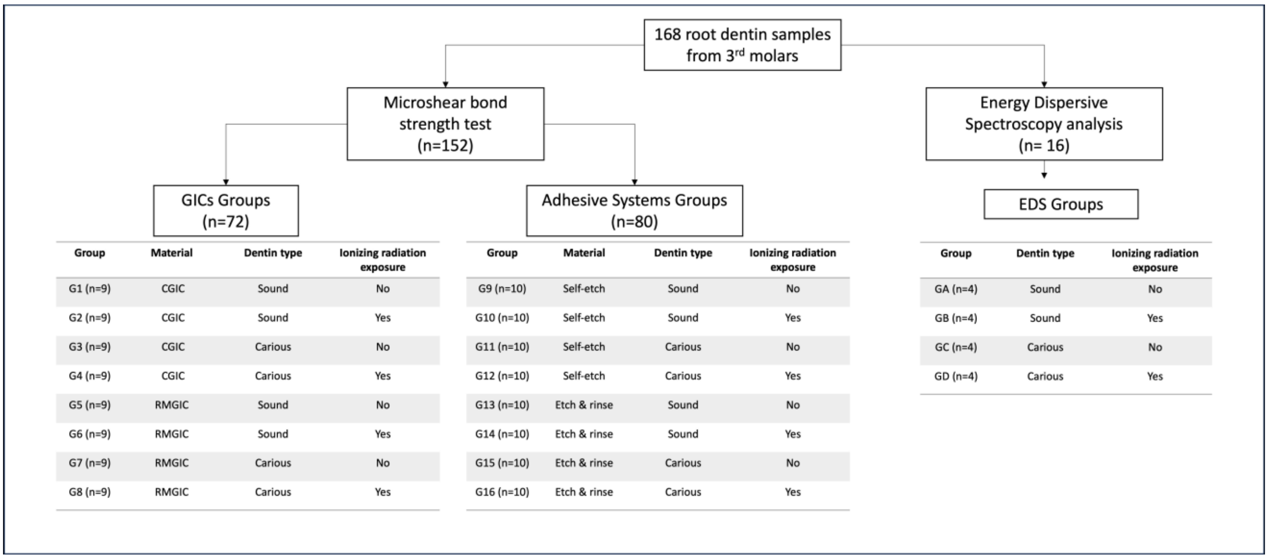
However, the scientific literature has not yet defined the material of choice for restoration of teeth affected by RRC. Glass ionomer cements (GICs) have often been the material of choice for cervical lesions with a longevity similar to that of resin-based composites. [34-38] However, restorative treatments using adhesive procedures are also suggested as a treatment option for related-radiation caries[33]. Thus, the aim of the present study is to investigate the effect of ionizing radiation on the microshear bond strength of two GICs and two different adhesives systems to sound and caries-affected root dentin and its possible effect on the chemical composition of sound and caries-affected root dentin. The hypotheses tested were the following: 1) HNIR has no effect on the bond strength of different GICs and adhesive systems to both sound and caries-affected root dentin. 2) HNIR has no effect on the chemical composition of sound and caries-affected root dentin.

METHODS AND MATERIALS

Specimen Preparation

Tooth selection and groups distribution

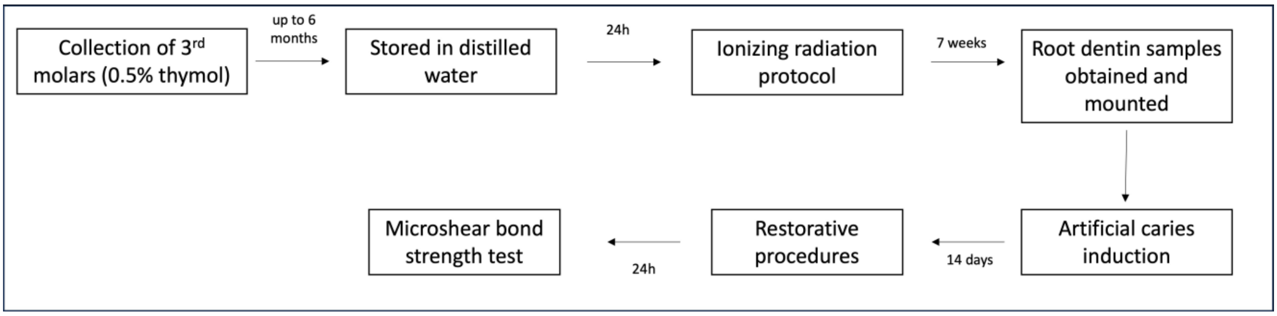
Ethical approval for this study involving human teeth was granted by the local ethics committee (no. 28896620.9.0000.0030). A hundred sixty-eight sound caries-free human third molars, from individuals 18 to 30 years old, were collected with informed donor consent. The teeth were stored for less than six months in a solution of 0.5% thymol after extraction. After cleaning off debris, they were stored in distilled water for 24 h before the beginning of the experiment. The teeth were randomly assigned to sixteen groups for the bond strength test: 8 groups for the GICs (n=9) and 8 groups for the adhesive systems (n=10). The remaining teeth were randomly assigned to four groups for the Energy Dispersive Spectroscopy analysis (n=4). The experimental groups are presented in Figure 1 and the study design flow is presented in Figure 2.



Group	Material	Dentin type	Ionizing radiation exposure
G1 (n=9)	CGIC	Sound	No
G2 (n=9)	CGIC	Sound	Yes
G3 (n=9)	CGIC	Carious	No
G4 (n=9)	CGIC	Carious	Yes
G5 (n=9)	RMGIC	Sound	No
G6 (n=9)	RMGIC	Sound	Yes
G7 (n=9)	RMGIC	Carious	No
G8 (n=9)	RMGIC	Carious	Yes

Group	Material	Dentin type	Ionizing radiation exposure
G9 (n=10)	Self-etch	Sound	No
G10 (n=10)	Self-etch	Sound	Yes
G11 (n=10)	Self-etch	Carious	No
G12 (n=10)	Self-etch	Carious	Yes
G13 (n=10)	Etch & rinse	Sound	No
G14 (n=10)	Etch & rinse	Sound	Yes
G15 (n=10)	Etch & rinse	Carious	No
G16 (n=10)	Etch & rinse	Carious	Yes

Group	Dentin type	Ionizing radiation exposure
GA (n=4)	Sound	No
GB (n=4)	Sound	Yes
GC (n=4)	Carious	No
GD (n=4)	Carious	Yes



Ionizing radiation exposure

The samples from groups that required ionizing radiation exposure (G2, G4, G6, G8, G10, G12, G14, G16 GB, GD) were submitted to the following protocol: fractionated IRconsisted of 2 Gy daily, applied 5 days per week for 7 weeks (total of 70 Gy) using X-rays a linear accelerator (Siemens, Primus, 6MV, LA, USA).[2,39] (The IR used in this study was based on intensity-modulated radiotherapy). During IR exposure, the specimens were mounted on stubs and completely submerged in 5 mL of distilled water per specimen, with the water changed weekly. Control specimens (non-irradiated) were also stored in this manner but did not receive radiation (G1, G3, G5, G7, G9, G11, G13, G15, GA and GB).

Root dentin samples preparation

Following the irradiation protocol, each tooth was sectioned 1 mm coronal to the cervical line, using a diamond disc on a semi-precision cutter (Isomet 1000, Buehler ltd. Lake Buff, Illinois, USA). Flat buccal root dentin surfaces were obtained after removal of the cementum root using 600-grit silicon carbide abrasive paper for 60 s under water cooling. After, the root dentin was polished with 1200-grit silicon carbide abrasive paper for 20 s using a polisher machine (Teclago, São Paulo, Brazil). The buccal root dentin samples were individually included in a 25x20 mm PVC short-reduction bushings filled with transparent self-curing acrylic resin (VIPI Flash, São Paulo, Brazil).

Artificial caries induction

The specimens from the artificial caries groups (G3, G4, G7, G8, G11, G12, G15, G16, GC, GD) were individually immersed for 14 days in demineralizing solution (2.2 mM

CaCl2, 2.2 mM NaH2PO4, 0.05 M acetic acid, pH = 4.5) for 8 h and remineralizing solution (1.5 mM CaCl2, 0.9 mM NaH2PO4, 0.15 mM KCL, pH = 7.0) for 16 h at room temperature without agitation.[40-42] After each 24-hour period, the specimens were washed and dried, and a new solution was used. The solutions were checked periodically using a pH meter.[40-43] After 14 days, a caries detector (Caries Detector, Kuraray, Japan) was used for 25 s to detect dentinal demineralization and to visualize the affected dentin. Control specimens (sound dentin) were stored in distilled water, which was changed every week.

Restorative procedures

The restorative protocols were performed by a single trained operator and followed the manufacturer's instructions according to the type of material used (Table 1). The materials evaluated in this study were: Conventional glass ionomer cement- CGIC (GC Gold Label 9 R-GC, Alsip, Illinois, USA); Resin-modified glass ionomer cement- RM-GIC (GC Gold Label 2 LC R–GC, Alsip, Illinois, USA); Two-step self-etching- SE adhesive system (Clearfil SE Bond – CSE; Kuraray, Chiyoda-ku Tokyo, Japan); Three-step etch-and rinse- E&R adhesive system (Optibond fl; Kerr, Joinville, Santa Catarina, Brazil).

Table 1: Restorative materials and application protocol

Material	Classification	Protocol
GC Fuji IX	Conventional glass-ionomer cement	Polyacrylic acid applied for 10s. Powder agitated for 5s. One powder scoop for two liquid droplets. Half of powder mixed with liquid for 10s on a glass plate; other half mixed thoroughly for 12–20s. Cement inserted to the silicone matrix with the use of a centrix syringe (needle tip).
GC Fuji II LC	Resin-modified glass-ionomer cement	Polyacrylic acid applied for 10s. One powder scoop for two liquid droplets. Half of powder mixed with liquid for 15s on a glass plate; other half mixed thoroughly until obtaining a glossy consistency. Cement inserted to the silicone matrix with

		the use of a centrix syringe (needle tip). Polymerization for 20s.
Clearfil SE Bond	Self-etch adhesive system	Primer applied actively for 20 seconds. Air for 5 seconds. Adhesive applied actively for 10 seconds. Polymerization for 20s. Tetric N-Flow (Flowable resin composite) inserted to the silicone matrix and polymerized for 20s.
Optibond Fl	Etch-and-rinse adhesive system	Phosphoric acid applied for 15s on dentin. Primer applied actively for 15s. Air spray for 5 seconds. Adhesive applied actively for 15s. Air spray for 3s. Polymerization for 20s. Tetric N-Flow (Flowable resin composite) inserted to the silicone matrix and polymerized for 20s.

A silicone matrix with a perforation of 1 mm in diameter and 0.95 mm in height was used to produce the cement and resin rods (restorations). For the GICs groups, prior to cement placement, 20% polyacrylic acid solution (cavity conditioner GC, Alsip, Illinois, USA) was applied to the root dentin surface for 10 s using with a cotton-tip applicator, rinsed with water and dried without desiccation. The CGIC and RMGIC were hand-mixed and placed into the silicone matrix using a centrix-type pistol with a fine tip (Precision applicator, Maquira, Londrina, PR, Brasil). For the RMGIC, the light curing step was completed using a LED light-curing unit (Bluephase G2, Ivoclar Vivadent, Barueri, SP, Brasil) with power intensity of 1,000 mW/cm^2.

For the adhesive groups, after conditioning the root dentin specimens according to the protocol described in Table 1, both adhesive systems were actively applied and the polymerization was carried out using a LED light-curing unit (Bluephase G2, Ivoclar

Vivadent, Barueri, SP, Brasil) with power intensity of 1,000 mW/cm^2. The silicone matrix perforation was filled with a flowable resin composite (Tetric N-Flow) and polymerized for 20 seconds (Bluephase G2, Ivoclar Vivadent, Barueri, SP, Brasil) with power intensity of 1,000 mW/cm^2. The root dentin specimens allowed for 2 restorations in specimen.

Microshear bond strength testing

The specimens were stored in distilled water at 37°C for 24 h to prepare for microshear bond strength testing. The specimen was placed in a universal machine Shimadzu (Shimadzu Corp, Kyoto, Japan) for microshear testing at a speed of 0.55 mm/min. The bond strength, initially recorded in Newtons (N), was subsequently converted to megapascals (MPa).

Failure mode analysis

The fractured specimens were analyzed using a stereoscopic magnifying glass (40X) to determine the mode of failure. The failures were classified as follows: 1) adhesive failure, when the failure occurred in the hybrid layer; 2) cohesive failure, when the failure was entirely in the dentin or ionomer; and 3) mixed failure, when the failure involved part of the adhesive layer and the dentin or ionomer.[41,44] Representative samples of the fractured specimens were evaluated by scanning electron microscopy (SEM) to obtain more detailed images.

X-ray Energy-Dispersive Spectroscopy (EDS) Analysis

Sixteen third molars were used for the EDS analysis and randomly assigned to four groups as indicated in Figure 1 (n=4). Elemental analysis of root dentin was performed using an EDS (X-act, Oxford Instruments. Abingdon, UK) spectrometer equipped with a rhodium X-ray tube and a liquid nitrogen (N2) cooled semiconductor detector, operating at 15 kV. Chemical characterization (wt%) was performed and the concentrations of the following elements were evaluated: Carbon (C), Oxygen (O), Magnesium (Mg), Phosphate (Ph), Calcium (Ca).

Statistical analysis

A pilot study was conducted to determine means and standard deviations for control and experimental groups, providing essential parameters for sample size calculation. The sample size was determined as n=9 for the GIC groups and n=10 for the adhesive system groups based on the results of the pilot study, with an alpha value of 0.05 and statistical power set to 80%. The bond strength values obtained in the microshear test were evaluated for normal distribution using the Shapiro–Wilk test and histogram. Data were analyzed using Kruskal–Wallis and Mann–Whitney nonparametric tests (α=.05) with a statistical software program (Stata/SE 15.1; Stata Corp LLC, Texas, USA). The chemical composition values obtained in the EDS were evaluated for normal distribution using the Shapiro–Wilk test and data were analyzed using Kruskal–Wallis and Mann–Whitney nonparametric tests (α=.05).

Results

Microshear bond strength for GICs (CGIC X RMGIC)

Table 2 presents the mean and standard deviation values as well as the median and interquartile range for the GIC cements. The data rejected the null hypothesis demonstrating a statistically significant difference between the groups (Kruskal-Wallis, p=0.0001). RMGIC presented statistically higher bond strength values than the conventional GIC, except for G1. When considering only the CGIC groups, the control group (G1) had higher bond strength values, which were significantly different from those of the other groups (Mann-Whitney, $p<0.05$). The groups of caries-affected dentin (G3 and G4), whether irradiated or not, did not present significant differences between them (p=0.44). The group with sound and irradiated dentin had the lowest bond strength values, which was statistically different from all the other groups ($p< 0.0001$). When comparing only the RMGIC groups, the control and caries-affected dentin groups had the highest bond strength values and were not significantly different from each other (p= 0.86). The irradiated groups, caries-affected or not, did not present significant differences among them (p=0.44), but they presented values significantly lower than those of the control and caries-affected groups ($p< 0.0001$). Overall, the groups subjected to ionizing radiation exhibited the lowest values of bond strength for both GICs.

Table 2: Mean and standard deviation of the CGICs and RMGIC bond strength values obtained by the microshear test.

Groups	Mean (SD)	Median (IQR)
G1- CGIC (Sound and no radiation)	23.4 (6.1) [a]	22.5 (18.6–25.5)
G2- CGIC (Sound and irradiated)	9.1 (3.3) [b]	7.8 (6.3–12.4)
G3- CGIC (Carious and no radiation)	17.7 (5.6) [c]	16.6 (12.6–21.9)
G4- CGIC (Carious and irradiated)	15.8 (6.7) [c]	16.1 (9.2–22.4)
G5- RM-GIC (Sound and no radiation)	30.5 (5.1) [d]	29.9 (28.1–34.2)
G6- RM-GIC (Sound and irradiated)	24.9 (6.7) [a]	27.1 (18.6–29.7)
G7- RM-GIC (Carious and no radiation)	34.1 (11.6) [d]	29.9 (24.4–44.6)
G8- RM-GIC (Carious and irradiated)	23.4 (7.9) [a]	23.8 (14.6–30.0)

Different letters identify significant difference among the groups ($p<0.05$, Mann–Whitney)

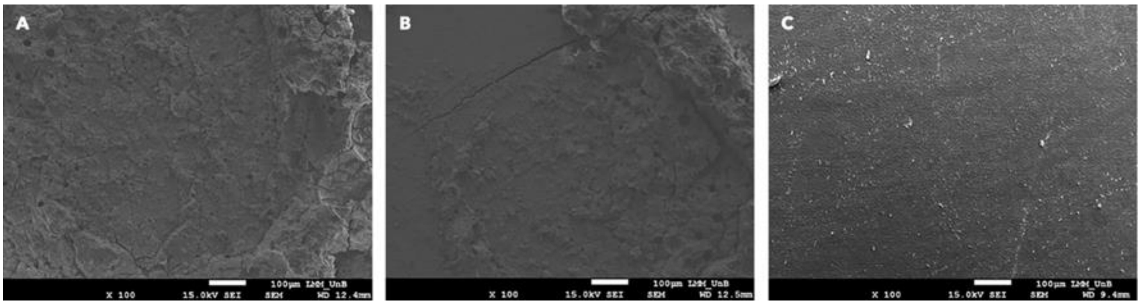
Figure 3 presents the types of failure distribution for both GICs. For both GICs, the controls (G1 and G5) presented with approximately 78% of cohesive failures, whereas the other groups presented a variation between mixed, cohesive, and adhesive failures.

Table 3: Mean and standard deviation of the self-etch and ethc & rinse adhesive systems bond strength values obtained by the microshear test.

Groups	Mean (SD)	Median (IQR)
G9- SE (Sound and no radiation)	45.77 (8.6)[a]	42.3 (38.5-53.8)
G10- SE (Sound and irradiated)	40.5 (9.5)[a,b]	40.0 (32.9-48.3)
G11- SE (Carious and no radiation)	29.9 (6.6) [c]	30.7 (23.7-33.1)
G12- SE (Carious and irradiated)	22.0 (5.4) [d]	20.6 (17.3-25.5)
G13- E&R (Sound and no radiation)	35.1 (4.6) [b,e]	35.4 (31.1-37.1)
G14- E&R (Sound and irradiated)	31.3 (5.3)[e,c]	31.1 (27.4-34.2)
G15- E&R (Carious and no radiation)	23.5 (4.8) [d]	23.7 (19.9-26.5)
G16- E&R (Carious and irradiated)	21.8 (5.4) [d]	22.7 (16.9-27.5)

Different letters identify significant difference among the groups ($p<0.05$, Mann–Whitney)

Figure 4 presents representative samples of cohesive, mixed and adhesive failures for GIC groups.



Microshear bond strength for Adhesive systems (Self-etch X etch and rinse)

Table 3 presents the mean and standard deviation values, as well as the median and interquartile distance for the adhesive systems. The data obtained rejected the null hypothesis and indicate that there is a statistically significant difference between the groups (Kruskal-Wallis, p=0.0001). The self-etch adhesive system presented statistically higher bond strength values for its control (G9) than the etch & rinse system (G13). When considering only the self-etch adhesive system groups, G9 had higher bond strength values and was significantly different from the others ($p < 0.05$), except for G10 (p=0.074). The same was observed for the etch & rinse system: no difference among the control (G13) and the irradiated group (G14) (p= 0.107). For both adhesives, the caries-affected dentin groups (G11 and G15) and its association with the ionizing radiation (G12 and G16) significantly reduced the bond strength ($p < 0.05$).

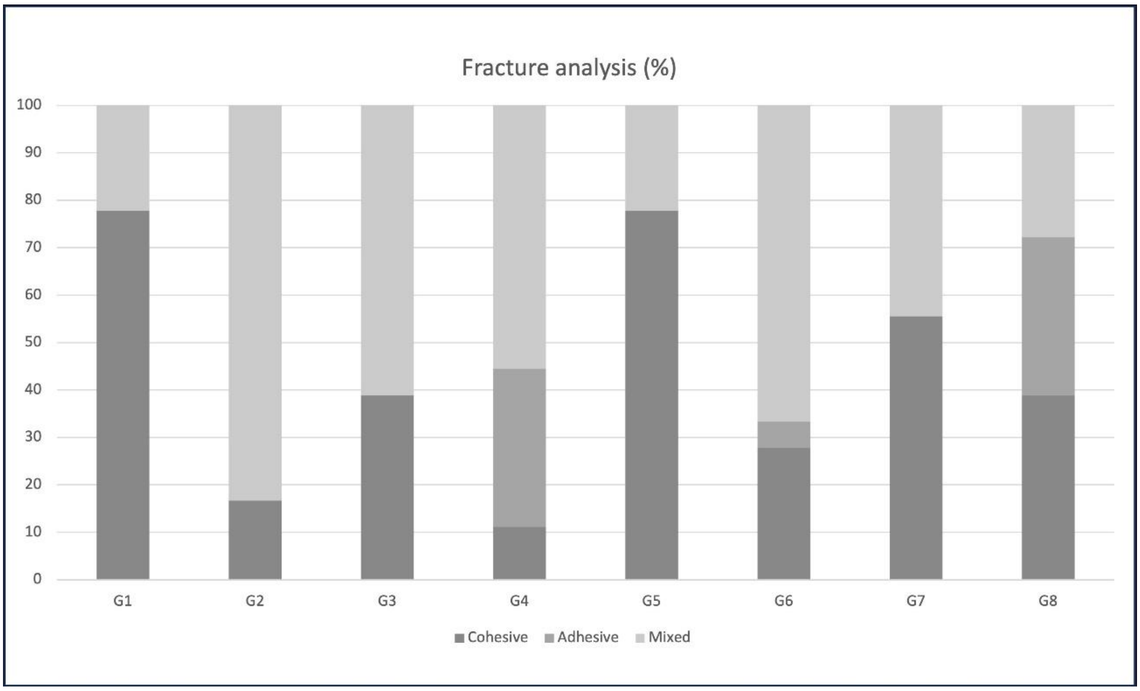
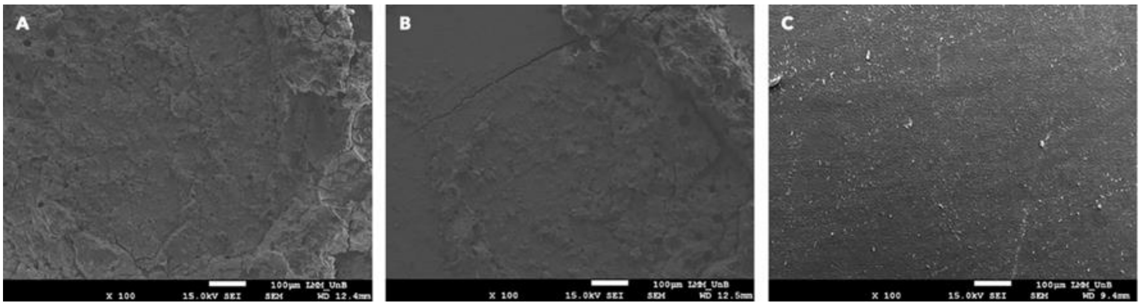
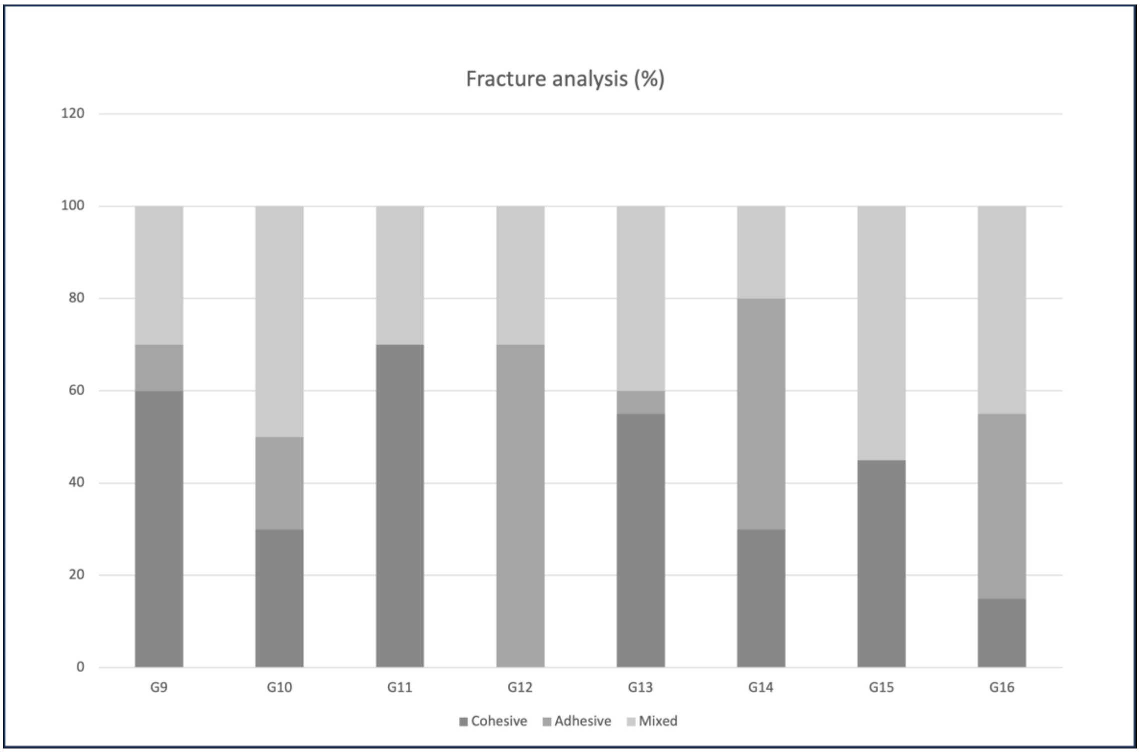
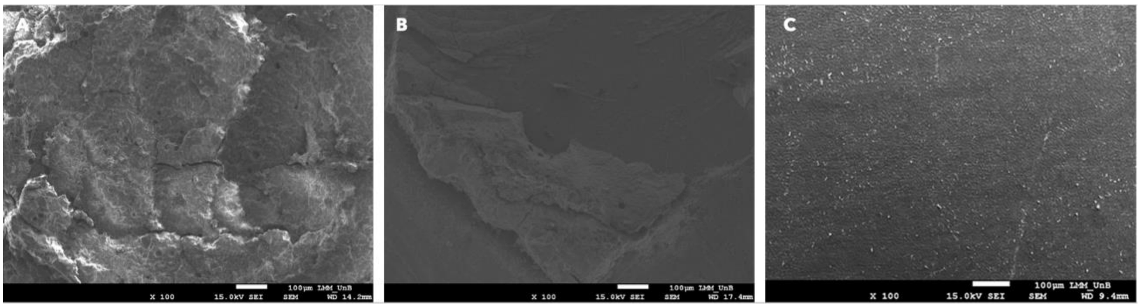


Figure 5 presents the types of failure distribution for both adhesive systems. For the self-etch adhesive, it was observed that in the G9 (control) and G11 (caries-affected dentin) groups there were approximately 60% and 70% of cohesive fractures, respectively. For G10 (irradiated), the mixed-type fracture was predominant (50%), while for G12 (caries-affected and irradiated), the predominant fracture was adhesive (70%). For the etch & rinse system, G13 had approximately 55% of cohesive fractures and G14 (irradiated) had a predominance of adhesive fractures (50%). For G15 (caries-affected dentin) and G16 (caries-affected and irradiated), most fractures were mixed (55%) and 45%, respectively.





Representative samples of the failed specimens were evaluated by scanning electron microscopy (SEM) to obtain more detailed images (Figure 6A, 6B, 6C).



EDS analysis

There was a significant difference between the groups on the amount (%) of carbon, oxygen, phosphate, and calcium (Mann-Whitney, $p<0.05$), while no difference was observed for the component magnesium ($p=0.553$). The groups submitted to the artificial caries process showed significantly reduced amount of carbon, oxygen, phosphate, and calcium ($p<0.05$) when compared to the control (GA) and irradiated (GB) groups. When both challenges were present (GD- caries-affected dentin and ionizing radiation), the phosphate and calcium content were significantly reduced even when compared to the caries-affected group (GC) ($p<0.05$).

Discussion

In the present study, both null hypotheses were rejected as the bond strength and chemical composition of sound and caries-affected root dentin was altered by the ionizing radiation. Our results demonstrated that the bond strength values of irradiated root dentin differed from those of non-irradiated root dentin for GICs and adhesive systems.

As life expectancy increases, root caries is becoming one of the most prevalent and severe diseases in the aging population.[20-22] Additionally, there is a growing number of head and neck cancer patients who have undergone ionizing radiation, surviving the treatment but presenting side effects such as reduced salivary flow.[4] Direct effects of ionizing radiation on the tooth structure, including changes in chemical composition, increase the risk of dental caries in head and neck radiation patients [1,2,3]. In this study, mineral content alterations were observed in the groups of caries-affect root dentin and caries-affected associated to ionizing radiation. The latter (GD- caries-affected associated to radiation) showed significantly lower values of calcium and phosphate when compared to all the other experimental and control groups. For this analysis, EDS spectroscopy was used, a specific method to determine the concentration of chemical elements in the teeth[47]. A recent systematic review confirmed that both organic and inorganic matrixes are altered after ionizing radiation. [48] Consequently, these alterations including reduced calcium and phosphate could negatively interfere with the adhesion of both evaluated restorative dental materials (GICs and adhesive systems)[10].

The radiotherapy protocol used in this study was fractionated, totaling 70 Gy and consisting of 2 Gy daily applied 5 days per week for 7 weeks.[2,39] This amount of radiation is currently used for the treatment of patients with head and neck cancer treated in the radiotherapy sector of our institution and was selected in our study aiming to simulate a clinical situation. Human teeth were used in accordance with ISO/DTS 11405 and ISO/TC 106 D standards,34 Dentistry — Test of adhesion to tooth structure that indicated preference for the use of permanent third molars and post-extraction time less than 6 months.[44]

The cervical area was chosen because studies have shown that radiation-related caries (RRC) develops mainly in the cervical areas of the anterior and posterior teeth with diffuse and advanced dental destruction. [2,18,19] Moreover, the root dentin substrate has shown to be more susceptible to a rapid caries development, especially in the elderly population associated with other comorbidities. [20-22] Radiation also affects the structural, chemical, and mechanical properties of the root dentin. [5,10, 48] These alterations, combined with a decrease in salivary flow due to radiotherapy and poor plaque control, might particularly predispose cervical dentin to develop root caries.[10]

Both independent variables (ionizing irradiation and artificial caries) influenced the bond strength values for the GICs and adhesives. The irradiation factor had a greater effect, significantly reducing bond strength for both cements and adhesives, independent of its combination with or without artificial demineralization. The groups subjected to the radiation protocol presented the lowest bond strength values and more adhesive failures when compared with all the other groups for the different restorative materials. For the conventional GIC, there was a reduction of approximately 61% in the bond strength compared with the control group (G1). For the RMGIC, this reduction was around 23%. For both GICs, the irradiate group and caries-affected + radiation presented significant lowers bond strength when compared to the controls and the highest number of adhesive failures. CGICs are derived from organic acids and glass components and are referred to as acid-base reaction cements.[37] These acid-base reactions that occur in the CGICs result in ionic bonding between the glass ionomer and the calcium within the tooth structure; specifically, an ionic bond occurs between the carboxylate functional groups on the polyalkenoic acid molecules (COO–) in the cement and the calcium (Ca++) ions in the hydroxyapatite surface.[37] In this study, RM-GIC presented overall better bond strength results, including the irradiated ones, when compared with conventional cement. The RMGICs act through an acid-base reaction characteristic of GICs, in addition to the polymerization of the resinous monomer, which starts with activation by photopolymerization, forming a polymeric matrix.[38] There is still controversy on the inclusion of a “hybrid layer” for the RMGIC and the higher bond strength is probably associated to the enhanced micromechanical interlocking of the treated substrate. Therefore, both GICs’ bond strengths values were impacted by the reduction of Calcium as observed in the EDS assay. The chemical reaction between these cements and the dentin requires the chelation of the carboxyl groups with the calcium in the apatite and reduced availability of the Ca+ results in lower values of bond strength.

Regarding the adhesive systems, the groups associating caries-affect dentin plus the ionizing radiation (G12 and G16) presented the lowest bond strength values for the self-etch and etch & rinse bonding agents. Moreover, these groups presented with the highest number of adhesive failures when compared to the others (approximately 70% for Self-etch and 50% for etch & rinse). The self-etching adhesive system contains acidic resin monomers that simultaneously condition and prepare the dental substrate and contain solvents to dissolve the monomers expanding the collagen network and allowing the monomers to fill the spaces in and around the collagen fibrils. Then comes the polymerization activated by the polymerization light, thus forming a thin hybrid layer[49]. It also contains the functional monomer (10-MDP) that allows a chemical interaction between the adhesive and the hydroxyapatite creating MDP-Ca salts with low solubility[50]. The important role of Ca is reduced in the carious and irradiated groups, as demonstrated in the spectroscopy analysis. The reduction of Ca on the surface was approximately in 50% and the bond strength for the irradiated and carious groups was also reduced in approximately 52%. For the etch & rinse system, the substrate is initially pretreated with phosphoric acid, which dissolves the minerals in depth and makes the dentin collagen highly porous[49]. Afterward, the adhesive system is applied to fill the porous dentin and create a thicker hybrid layer, when compared to the self-etch approach. The stronger acidic action of the phosphoric acid in a less mineralized substrate such as the root dentin already chemically altered by the ionizing radiation possibly resulted in reduced microshear bond strength when compared to the self-etch technique.

As reported in the literature, ionizing radiation can affect the teeth through radiative destruction.[13] The interaction of apatite crystals with the organic matrix proceeds from the electrostatic binding of mineral phosphate groups and collagen side chains carboxylate.[13] Ionizing radiation causes decarboxylation and a loss of acidic phosphate groups, causing the formation of new calcium-ion-bridged phosphate groups. The mineral-organic ratio also is reduced, and the development of carbon dioxide may induce microcracks in the hydroxyapatite.[13] Progressive micromorphological alterations, such as dentinal tubule obliteration and fragmentation of collagen fibers, have been observed in dentin.[23] Therefore, as these restorative materials depends on the calcium and dentin structure, these changes caused by radiation justify the lower bond strength values observed for these groups.

As it is difficult to extract teeth affected by RRC in patients with head and neck cancer, a cyclic pH model was chosen to simulate the caries process artificially, because it provides superficial, morphologically demineralized caries-affected dentin.[20,43] For the CGICs, a reduction of 25% to 33% was observed in the bond strength, and most of the failures were adhesive-type failures. Fracture types for self-etching adhesive system, the irradiated + carious dentin group (G12), the predominant fracture was adhesive (70%) and irradiated group (G10), the mixed-type fracture was predominant (50%). For etch and rinse adhesive system, in caries-affected dentin (G15) and irradiated + caries-affected dentin (G16) groups, most of the failures were mixed (55%) and 45%, respectively. For the irradiation-only group (G14), most fractures were of the adhesive type (50%). These results demonstrate that adhesive and mixed failures were observed mainly in the irradiated and carious groups or combined groups. In caries-affected dentin, there is a lower calcium and phosphate content caused by caries[22] and the dentinal tubule morphology of artificial caries-affected dentin is also different due to the lack of mineral casts.[45] Both factors, added to the chemical changes in the structure of collagen and in the mineral: matrix ratio after radiotherapy, can directly interfere with the bond strength of the adhesive materials, thereby interfering with the prognosis and longevity of the restorative treatment.[5,15-16,23]

Our study had some limitations, including the use of an artificial caries process, the use of distilled water instead of human saliva for immersion, and the use of only third molars. However, the present findings contribute to decision-making for restorative materials in clinical cases of root caries after radiation protocols. More clinical studies are needed to address these limitations and complement the findings of this in vitro study.

CONCLUSIONS

Based on the limitations of the present study, the following conclusions can be made:

IR affects the chemical composition of root dentin

IR affects the root dentin substrate and reduces the bond strength values for all the evaluated restorative materials.

The groups that the ionizing irradiation and caries-affected were present, an increase in adhesive and mixed-type failures was observed.

Conflict of Interest

The authors certify that they have no proprietary, financial, or other personal interests of any nature or kind in any product, service, and/or company presented in this article.

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Anexo III

UNB - FACULDADE DE CIÊNCIAS DA SAÚDE DA UNIVERSIDADE DE BRASÍLIA

Plataforma Brasil

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Impacto da radioterapia de cabeça e pescoço na resistência de união de sistemas adesivos e cimentos ionômero de vidro à dentina radicular sadia e cariada

Pesquisador: Brenda Lisseth Pineda Mancia
Área Temática:
Versão: 3
CAAE: 28896620.9.0000.0030
Instituição Proponente: FACULDADE DE SAÚDE - FS
Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 4.093.373

Anexo IV

Universidade de Brasília – UnB

Faculdade de Ciências da Saúde – FS

Programa de Pós-Graduação em Odontologia - PPGODT

Termo de Consentimento Livre e Esclarecido - TCLE

Convidamos o(a) Senhor(a) a participar voluntariamente do projeto de pesquisa “Impacto da radioterapia de cabeça e pescoço na resistência de união a microtração de sistemas adesivos e cimentos ionômero de vidro à dentina radicular sadia e cariada”, sob a responsabilidade da pesquisadora Brenda Lisseth Pineda Mancia. O projeto é referente ao doutorado da aluna juntamente à UnB.

O objetivo desta pesquisa é avaliar o impacto da radioterapia de cabeça e pescoço na resistência de união a microtração de sistemas adesivos e cimentos ionômero de vidro à dentina radicular sadia e cariada visando à contribuição clínica dessa análise em benefício da atividade clínica odontológica.

O (a) senhor (a) receberá todos os esclarecimentos necessários antes e no decorrer da pesquisa e lhe asseguramos que seu nome não aparecerá sendo mantido o mais rigoroso sigilo pela omissão total de quaisquer informações que permitam identificá-lo (a).

Este trabalho não apresenta nenhuma possibilidade de danos à dimensão física, psíquica, moral, intelectual, social, cultural do ser humano, em qualquer etapa da pesquisa e dela decorrente. A sua participação se dará por meio da concessão voluntária de seus terceiros molares hígidos extraídos (dentes do siso), que seriam descartados após o procedimento cirúrgico, realizado sob-responsabilidade do cirurgião-dentista de sua escolha. A indicação de extração do dente não tem qualquer relação com a pesquisa. Os riscos e possíveis danos da cirurgia serão descritos pelo seu dentista de forma a esclarecer a complexidade do procedimento. Os dentes concedidos serão limpos com instrumental especifico e armazenados em Timol 0,5% e submetidos a teste no Laboratório de Pesquisa em Dentística e Materiais Dentários - Faculdade de Ciências da Saúde - Universidade de Brasília (UnB). A concessão se dará no dia escolhido pelo(a) senhor(a) para a realização de sua cirurgia eletiva junto ao profissional responsável, de sua escolha, junto ao local de trabalho do mesmo. A duração do procedimento será avaliada pelo profissional responsável para sua realização e a guarda e utilização do material biológico pode ser retirado a qualquer momento pela pesquisadora responsável.

Quanto à concessão de seu dente ao projeto de pesquisa, se tratando de um dente que seria descartado, não haverá riscos de saúde e/ou de sua imagem, pois todos os dados serão preservados e mantidos de forma confidencial. Além disso, pode retirar seu dente concedido a qualquer momento desistindo de participar da pesquisa. Se o (a) senhor (a) aceitar participar, estará contribuindo para o benefício da atividade clínica odontológica visando o aprimoramento de técnicas que possam melhorar a qualidade e longevidade das restaurações dentárias.

O (a) Senhor (a) pode se recusar a responder (ou participar de qualquer procedimento) qualquer questão que lhe traga constrangimento, podendo desistir de participar da pesquisa em qualquer momento sem nenhum prejuízo para o (a) senhor (a). Sua participação é voluntária, isto é, não há pagamento por sua colaboração e embora esta pesquisa não tem previstos gastos para o (a) senhor (a), tem garantia de ressarcimento de despesas decorrentes da participação na pesquisa.

Despesas que o (a) senhor (a) tiver relacionadas diretamente ao procedimento de extração dos terceiros molares (tais como passagem para o local da cirurgia, alimentação no local ou exames) serão de sua responsabilidade, visto que o procedimento clínico cirúrgico será realizado mediante indicação e motivação própria, não sendo o foco da pesquisa atual que busca apenas solicitação de concessão voluntária do dente extraído.

Caso haja algum dano direto ou indireto decorrente de sua participação na pesquisa (após a concessão do dente), o (a) senhor (a) deverá buscar ser indenizado, obedecendo-se as disposições legais vigentes no Brasil.

Os resultados da pesquisa serão divulgados na Universidade de Brasília podendo ser publicados posteriormente. Os dados e materiais serão utilizados somente para esta pesquisa e ficarão sob a guarda do pesquisador por um período de cinco anos, após isso serão destruídos. Se houver a intenção de utilização futura do material biológico, existe a possibilidade de uso e o reconsentimento do(a) senhor(a) de pesquisa por meio de um TCLE específico referente ao novo projeto de pesquisa, que deverá ser aprovado pelo Comitê de Ética em Pesquisa (CEP).

Se o(a) Senhor(a) tiver qualquer dúvida em relação à pesquisa, por favor telefone para: Brenda Lisseth Pineda Mancia, na Universidade de Brasília no telefone (34) 99265-8684, disponível inclusive para ligação a cobrar ou através do e-maildrapinedamancia@gmail.com. .

Este projeto foi aprovado pelo Comitê de Ética em Pesquisa da Faculdade de Ciências da Saúde (CEP/FS) da Universidade de Brasília. O CEP é composto por profissionais de diferentes áreas cuja função é defender os interesses dos participantes da pesquisa em sua integridade e dignidade e contribuir no desenvolvimento da pesquisa dentro de padrões éticos. As dúvidas com relação à assinatura do TCLE ou os direitos do participante da pesquisa podem ser esclarecidos pelo telefone (61) 3107-1947 ou do e-mail cepfs@unb.br ou cepfsunb@gmail.com, horário de atendimento de 10h00minhs às 12h00minhs e de 13:30hs às 15:30hs, de segunda a sexta-feira. O CEP/FS se localiza na Faculdade de Ciências da Saúde, Campus Universitário Darcy Ribeiro, Universidade de Brasília, Asa Norte.

Caso concorde em participar, pedimos que assine este documento que foi elaborado em duas vias, uma ficará com o pesquisador responsável e a outra com o (a) Senhor (a).

____

Nome e assinatura do Participante de Pesquisa

____

Nome e assinatura do Pesquisador Responsável

Brasília, ___ de __________de _________.