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**Efeito da radiação ionizante recebida durante o tratamento simulado de câncer
nasofaríngeo na resistência de união de um cimento obturador à base de resina epóxica à
dentina intrarradicular de pré-molares inferiores**

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Orientador: Prof. Dr. Lucas da Fonseca Roberti Garcia
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O presente trabalho em nível de Doutorado foi avaliado e aprovado, em 17 de novembro de 2025, pela banca examinadora composta pelos seguintes membros:

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Florianópolis, 2026.

*Dedico esta tese aos meus grandes
amores, Carlos Henrique e Miguel - minha
base, meu motivo e minhas maiores alegrias.*

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RESUMO

Este estudo *in vitro* avaliou os efeitos de doses clinicamente realistas de radiação ionizante (30 Gy e 70 Gy) sobre a resistência de união de um cimento endodôntico à base de resina epóxi à dentina radicular, considerando diferentes técnicas de obturação (condensação lateral e técnica híbrida de Tagger). Análises adicionais avaliaram a interface cimento–dentina e a penetração do cimento nos túbulos dentinários. Sessenta pré-molares inferiores unirradiculares foram distribuídos aleatoriamente em três grupos: não irradiados (NoRT), 30 Gy e 70 Gy. A irradiação foi realizada pela técnica de Radioterapia com Intensidade Modulada (IMRT), em frações diárias de 2 Gy, cinco dias por semana. Os canais radiculares foram preparados com o sistema Reciproc R40 e obturados com o cimento AH Plus Jet, utilizando a condensação lateral ou a técnica híbrida de Tagger. A resistência de união foi avaliada por meio do teste push-out, e os modos de falha foram classificados por MEV. A interface cimento–dentina e a penetração dos tags foram analisadas qualitativamente por MEV e MCL. Os dados foram analisados por testes não paramétricos ($\alpha = 0,05$). A exposição à radiação reduziu significativamente a resistência de união do cimento à dentina radicular, mesmo em 30 Gy, independentemente da técnica de obturação ou do terço radicular analisado ($p < 0,05$). Espécimes obturados pela técnica híbrida de Tagger apresentaram maiores valores de resistência de união e melhor adaptação do cimento em comparação à condensação lateral ($p < 0,05$). As análises por MEV e MCL revelaram descontinuidades na interface adesiva, morfologia irregular dos tags e redução da penetração do cimento nos espécimes irradiados, especialmente a 70 Gy. A radiação ionizante em doses clinicamente realistas compromete o desempenho adesivo de cimentos endodônticos à base de resina epóxi, alterando a estrutura da dentina e limitando a penetração do cimento. A técnica de obturação exerce papel fundamental na manutenção da integridade interfacial, destacando a necessidade de estratégias endodônticas individualizadas para pacientes submetidos à radioterapia de cabeça e pescoço.

Palavras-chave: Radioterapia; Resistência de união; Microscopia eletrônica de varredura; Microscopia confocal; Cimento obturador.

ABSTRACT

This *in vitro* study evaluated the effects of clinically realistic doses of ionizing radiation (30 Gy and 70 Gy) on the bond strength of an epoxy resin-based endodontic sealer to root dentin, considering different obturation techniques (lateral condensation and Tagger's hybrid technique). Additional analyses assessed the sealer-dentin interface and sealer penetration into dentinal tubules. Sixty single-rooted mandibular premolars were randomly distributed into three groups: non-irradiated (NoRT), 30 Gy, and 70 Gy. Irradiation was performed using the Intensity-Modulated Radiotherapy (IMRT) technique in daily fractions of 2 Gy, five days per week. Root canals were prepared with the Reciproc R40 system and obturated using AH Plus Jet sealer with either lateral condensation or Tagger's hybrid technique. Push-out bond strength was measured, and failure modes were classified by SEM. The sealer-dentin interface and tag penetration were qualitatively analyzed using SEM and CLSM. Data were analyzed using nonparametric tests ($\alpha = 0.05$). Radiation exposure significantly reduced the bond strength of the sealer to root dentin, even at 30 Gy, irrespective of the obturation technique or root third analyzed ($p < 0.05$). Specimens obturated with Tagger's hybrid technique exhibited higher bond strength values and superior sealer adaptation compared with lateral condensation ($p < 0.05$). SEM and CLSM analyses revealed interfacial gaps, irregular tag morphology, and reduced sealer penetration in irradiated specimens, particularly at 70 Gy. Ionizing radiation at clinically realistic doses compromises the adhesive performance of epoxy resin-based sealers by altering dentin structure and limiting sealer penetration. The obturation technique plays a key role in maintaining interfacial integrity, underscoring the need for tailored endodontic strategies in patients undergoing head and neck radiotherapy.

Keywords: Radiotherapy; Bond strength; Scanning electron microscopy; Confocal laser scanning microscopy; Root canal sealer.

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1 INTRODUÇÃO

Câncer de cabeça e pescoço (CCP) é definido como um grupo de tumores malignos que podem atingir a cavidade oral, a cavidade nasal, os seios paranasais, as glândulas salivares, a faringe e a laringe (MOORE et al., 2020). É caracterizado por alta agressividade, potencial metastático, recorrência e resistência terapêutica (DENG et al., 2025). De acordo com a Agência Internacional para Pesquisa em Câncer (IARC), órgão da Organização Mundial de Saúde (OMS), estima-se que a cada ano cerca de 947.000 novos casos de CCP sejam diagnosticados em todo o mundo. No Brasil, o câncer de cavidade oral é considerado o oitavo grupo de neoplasias mais frequente, acometendo aproximadamente 10.900 homens e 4.200 mulheres, segundo o Instituto Nacional de Câncer (INCA, 2023).

As modalidades de tratamento do CCP são determinadas por diferentes fatores, tais como o tipo de câncer, o estágio de diagnóstico (inicial ou avançado) e a localização do tumor, podendo a intervenção ser a cirurgia, a quimioterapia, a radioterapia, a imunoterapia, ou ainda a associação dessas modalidades, sendo considerada importante a sequência de combinação dessas terapias (CAMPI et al., 2019; ANDRADE, 2020; WORTHINGTON et al., 2023).

A radioterapia (RT) é o tratamento mais comumente utilizado, podendo ser aplicada como tratamento primário, adjuvante a outras terapias, ou também como tratamento paliativo para tumores em estágio avançado (GONÇALVES et al., 2014). O procedimento consiste na utilização de um feixe de radiação ionizante como agente terapêutico, que promove danos ao DNA das células tumorais, levando à sua morte ou perda da capacidade reprodutiva (GONÇALVES et al., 2014; ANDRADE, 2020). O tratamento é realizado de forma fracionada, a fim de diminuir os efeitos adversos causados aos tecidos adjacentes à área do tumor (BHANDARI et al., 2020). Dessa forma, é administrada uma fração de radiação diária de 02 Grays (Gy) durante 05 dias, por um período de 05 a 07 semanas, correspondendo a uma dosagem total entre 50 a 70 Gy ao final do tratamento, variando conforme o tipo de CCP (PELLOSO et al., 2022).

Ao longo dos últimos anos as técnicas radioterápicas evoluíram, passando inicialmente da radioterapia convencional bidimensional (2D) para a radioterapia conformada tridimensional (3D), e logo em seguida para a técnica de radioterapia modulada por intensidade (IMRT), que é a mais utilizada atualmente (CHEN et al., 2019). Essa última tem o objetivo de reduzir os danos causados aos tecidos saudáveis, pois consiste na entrega de doses mais altas de radiação no centro do tumor, minimizando os efeitos colaterais dos tecidos adjacentes à região a ser tratada (BAK et al., 2016; PRARAHYBA et al., 2016).

Pacientes com CCP que serão submetidos à radioterapia devem passar por uma avaliação prévia da saúde bucal, incluindo procedimentos como extração dentária, tratamento endodôntico, restaurador e periodontal (VISSINK et al., 2003). Dessa forma, é essencial um manejo odontológico adequado para promover a saúde bucal a longo prazo e contribuir para o bem-estar geral dos pacientes oncológicos em tratamento radioterápico (PARAHYBA et al., 2016).

Apesar da RT ser um procedimento eficaz e não invasivo, o tratamento provoca diversos efeitos adversos que prejudicam a qualidade de vida dos pacientes (RODRIGUES et al., 2018). O tratamento afeta não somente as células cancerosas, mas também as células saudáveis, causando danos aos ossos, às mucosas, às glândulas salivares e aos dentes localizados na região irradiada, o que resulta em complicações como, mucosite, trismo, hipossalivação, cárie relacionada à radiação e osteorradioneecrose (VELO et al., 2018; ANDRADE, 2020; PELLOSO et al., 2022).

Está consolidado na literatura que a exposição à radiação causa alterações nos tecidos dentários (VELO et al., 2017; RODRIGUES et al., 2018; MOORE et al., 2020). Estudos têm demonstrado que a RT afeta a composição química e as propriedades mecânicas do esmalte e da dentina coronária e radicular, que associadas à xerostomia, à higiene oral deficiente, ao aumento da ingestão de alimentos macios e ricos em carboidratos e às mudanças na microbiota oral, contribuem para o aumento do risco de cárie relacionada à radiação, podendo causar destruição severa da estrutura dentária (BODRUMLU et al., 2015; NOVAIS et al., 2016; RODRIGUES et al., 2018; CAMPI et al., 2019; DE MIRANDA et al., 2019; TURKER et al., 2021). As alterações no tecido dental incluem a perda de estrutura de prismas de esmalte, a degeneração dos processos odontoblásticos, a obliteração dos túbulos dentinários e a formação de *gaps* na junção amelo-dentinária (MOORE et al., 2020).

A dentina é um tecido biológico complexo, altamente solúvel, constituído aproximadamente por 70% de material inorgânico, 20% de material orgânico e 10% de água, sendo a sua porção orgânica formada em 90% por fibrilas colágenas (MARTINS et al., 2015; RODRIGUES et al., 2018; VELO et al., 2018; YAMIN et al., 2018). Em contrapartida, o esmalte contém apenas 4% de matriz orgânica e água combinadas (DE DIOS TERUEL et al., 2015). A presença de uma quantidade considerável de água em sua composição, quando comparada a outros tecidos, torna a dentina extremamente vulnerável aos efeitos da radiação ionizante, resultando em um fenômeno conhecido como radiólise (DE MIRANDA et al., 2019; DOUCHY et al., 2022). A radiação afeta as moléculas de água presentes na dentina, formando radicais livres, como íons de oxigênio (O^{2-}), hidroxila (OH^-) e hidrogênio (H^{+1}) (PELLOSO et

al., 2022). Esses radicais ligam-se a outras moléculas e se reorganizam formando novos compostos, o que causa a desnaturação dos componentes orgânicos, alteração da composição química da dentina, degeneração dos processos odontoblásticos e obliteração dos túbulos dentinários (DE MIRANDA et al., 2019; DOUCHY et al., 2022; PELLOSO et al., 2022). Paralelamente, ocorre a degradação das fibrilas colágenas, o que reduz a resistência de união com materiais resinosos (RODRIGUES et al., 2018; YAMIN et al., 2018; CAMPI et al., 2019).

Além das mudanças na composição química, também são afetadas as propriedades mecânicas da dentina irradiada, como a microdureza e a resistência à tração (RODRIGUES et al., 2018; CAMPI et al., 2019). Como resultado da diminuição da dureza e elasticidade, tem-se uma dentina mais ressecada e friável, aumentando as chances de trincas e fraturas (VELO et al., 2018; TURKER et al., 2021).

A cárie relacionada à radiação é outro efeito adverso da RT, considerada uma das principais complicações bucais que acometem os pacientes com CCP submetidos ao tratamento radioterápico (MARTINS et al., 2015). Ela se caracteriza como uma doença multifatorial, complexa e destrutiva, que difere da cárie convencional por ter uma rápida progressão e por atingir superfícies normalmente livres da doença, como as regiões cervical, incisal e ponta de cúspide, levando à destruição severa dos tecidos mineralizados e, conseqüentemente a alterações pulpares (CAMPI et al., 2019).

No passado, dentes acometidos por cárie severa eram extraídos antes do início do tratamento radioterápico, a fim de evitar o risco de osteorradionecrose (NOVAIS et al., 2016; ANDRADE, 2020; MOORE et al., 2020; GOMES-SILVA et al., 2021). Contudo, o tratamento endodôntico de dentes irradiados tem se mostrado eficaz e deve ser considerado como uma terapia de escolha em relação à extração dentária (NOVAIS et al., 2016; ANDRADE, 2020; MOORE et al., 2020; GOMES-SILVA et al., 2021). Além disso, considerando as alterações na estrutura dentária e a ocorrência de cárie de radiação em pacientes submetidos à RT de cabeça e pescoço, há uma propensão para o desenvolvimento de alterações pulpares, sendo então necessária a realização do tratamento endodôntico (MARTINS et al., 2015).

O objetivo do tratamento endodôntico é a limpeza e desinfecção do sistema de canais radiculares, bem como o selamento de toda a extensão do canal radicular, impedindo assim a sua reinfecção (BODRUMLU et al., 2009). Entretanto, para garantir um selamento eficiente, é necessário que o material obturador tenha adesão às paredes do canal radicular, de modo a impedir e/ou diminuir a infiltração microbiana (TEDESCO et al., 2014).

Martins et al. (2015) avaliaram a resistência de união de diferentes cimentos obturadores à dentina intrarradicular e analisaram a interface cimento/dentina em dentes submetidos à

radiação (60 Gy). Os autores relataram uma diminuição na resistência de união à dentina intrarradicular nos dentes irradiados, quando comparados aos não irradiados, e relacionaram o resultado encontrado a alterações na estrutura da dentina, como desproteção e fragmentação das fibras colágenas; mudanças na dentina inter, peri e intratubular; e obliteração dos túbulos dentinários. Esses resultados foram sustentados por Yamin et al. (2018), que também analisaram a resistência de união e adaptação do cimento à dentina intrarradicular em dentes irradiados com uma dose total de 60 Gy. Foram observadas uma redução na resistência de união e uma menor adaptação na interface cimento/dentina. Resultados semelhantes foram encontrados em um estudo recente de Pelloso et al. (2022), que investigaram as alterações químicas na dentina radicular submetida à radiação ionizante (70 Gy) e como o seu efeito interfere na interação com cimentos resinosos.

Nos diversos estudos laboratoriais publicados até o presente momento foram aplicadas doses de radiação ionizante que variam entre 50 Gy e 70 Gy, dependendo do estágio e da localização do tumor, seguindo o protocolo clínico rotineiramente utilizado para o tratamento de CCP (PELLOSO et al., 2022). Como mencionado, é amplamente relatado em estudos prévios as inúmeras alterações que a radiação provoca na estrutura dental (MARTINS et al., 2015; RODRIGUES et al., 2018; YAMIN et al., 2018; CAMPI et al., 2019; PELLOSO et al., 2022). Walker et al. (2011) constataram que a gravidade de tais alterações está intimamente relacionada com a dose de radiação que o dente recebe. Os autores relataram que ocorre um dano dental mínimo com uma dose abaixo de 30 Gy; que doses entre 30 e 60 Gy aumentam esse risco de 02 a 03 vezes; e que há 10 vezes mais chance de danos à estrutura dental se forem aplicadas doses acima de 60 Gy. Entretanto, os estudos laboratoriais não reproduzem adequadamente os parâmetros dosimétricos e as doses de radiação que realmente atingem a estrutura dental (PARAHYBA et al., 2016; POLCE et al., 2021), podendo levar a resultados inconsistentes. Inúmeros fatores podem influenciar na dose real entregue aos tecidos adjacentes saudáveis, e essa dosagem pode ou não ser tão alta quanto à dose de radiação fornecida ao núcleo do tumor (PARAHYBA et al., 2016).

Nos estudos de Parahyba et al. (2016) e Polce et al. (2021) foram realizados mapas dosimétricos que determinaram as doses média e máxima de radiação administradas a cada dente e aos ossos maxilares e mandibulares em pacientes com diferentes tipos de câncer de cabeça e pescoço. A partir desses estudos foi possível evidenciar que as doses aplicadas em pesquisas anteriores estavam superestimadas, o que pode alterar o impacto do dano causado aos tecidos dentários. Assim sendo, é importante avaliar se doses de radiação inferiores a 70 Gy provocam alterações nas propriedades da dentina e afetam a adesão a esse substrato. Para isso,

tornam-se necessários novos estudos que simulem com maior precisão a quantidade de radiação que de fato incide sobre a estrutura dental.

Complicações dentárias são frequentes em pacientes submetidos à radioterapia para o tratamento de CCP. As alterações orais provocadas pela radiação podem comprometer significativamente a qualidade de vida após o término do tratamento.

Diante do exposto, torna-se essencial aprofundar a compreensão acerca dos efeitos reais da radiação ionizante nos tecidos dentários, uma vez que os danos por ela provocados influenciam diretamente o planejamento de um tratamento adequado antes, durante e após a radioterapia. Assim, é fundamental buscar novos conhecimentos sobre o impacto da radiação nas estruturas dentárias, com o objetivo de preservar, de forma eficaz, a qualidade de vida dos pacientes ao longo de todo o processo terapêutico.

2 OBJETIVOS

2.1 OBJETIVO PRINCIPAL

Avaliar *in vitro* o efeito da dosagem de radiação ionizante entregue no tratamento de câncer nasofaríngeo na resistência de união de um cimento obturador à base de resina epóxica à dentina intrarradicular de pré-molares inferiores.

2.2 OBJETIVOS ESPECÍFICOS

- Avaliar o efeito das dosagens (30 Gy e 70 Gy) de radiação ionizante na resistência de união de um cimento obturador à base de resina epóxica à dentina intrarradicular de pré-molares inferiores, através do teste de união ao cisalhamento por extrusão.
- Avaliar a resistência de união de um cimento obturador à base de resina epóxica à dentina intrarradicular de pré-molares inferiores irradiados (30 Gy e 70 Gy), variando-se as técnicas de obturação do canal radicular (compactação lateral e híbrida de Tagger);
- Avaliar o efeito das dosagens de radiação ionizante (30 Gy e 70 Gy) na interface cimento/dentina de pré-molares inferiores, por meio de análise em Microscopia Eletrônica de Varredura (MEV);
- Avaliar o efeito das dosagens de radiação ionizante (30 Gy e 70 Gy) na capacidade de penetração de um cimento à base de resina epóxica nos túbulos dentinários de pré-molares inferiores, por meio de análise em Microscopia Confocal a Laser (MCL).

2.3 HIPÓTESE NULA

A dosagem de radiação ionizante aplicada não alterará a resistência de união do cimento à base de resina epóxica à dentina intrarradicular, a interface cimento/dentina e a capacidade de penetração do cimento nos túbulos dentinários, independentemente da técnica de obturação realizada.

3 ARTIGO CIENTÍFICO

Impact of clinically realistic radiation doses and obturation techniques on the bond strength, interfacial adaptation, and dentin penetration of an endodontic sealer

Pandolfo, MT; Teixeira, CS; Garcia, LFR

ABSTRACT

Aim: This *in vitro* study evaluated the effects of clinically realistic doses of ionizing radiation (30 Gy and 70 Gy) on the bond strength of an epoxy resin-based endodontic sealer to root dentin, considering different obturation techniques (lateral condensation and Tagger's hybrid technique). Additional analyses assessed the sealer-dentin interface and sealer penetration into dentinal tubules.

Methodology: Sixty single-rooted mandibular premolars were randomly distributed into three groups: non-irradiated (NoRT), 30 Gy, and 70 Gy. Irradiation was performed using the Intensity-Modulated Radiotherapy (IMRT) technique in daily fractions of 2 Gy, five days per week. Root canals were prepared with the Reciproc R40 system and obturated using AH Plus Jet sealer with either lateral condensation or Tagger's hybrid technique. Push-out bond strength was measured, and failure modes were classified by SEM. The sealer-dentin interface and tag penetration were qualitatively analyzed using SEM and CLSM. Data were analyzed using nonparametric tests ($\alpha = 0.05$).

Results: Radiation exposure significantly reduced the bond strength of the sealer to root dentin, even at 30 Gy, irrespective of the obturation technique or root third analyzed ($p < 0.05$). Specimens obturated with Tagger's hybrid technique exhibited higher bond strength values and superior sealer adaptation compared with lateral condensation ($p < 0.05$). SEM and CLSM analyses revealed interfacial gaps, irregular tag morphology, and reduced sealer penetration in irradiated specimens, particularly at 70 Gy.

Conclusions: Ionizing radiation at clinically realistic doses compromises the adhesive performance of epoxy resin-based sealers by altering dentin structure and limiting sealer penetration. The obturation technique plays a key role in maintaining interfacial integrity, underscoring the need for tailored endodontic strategies in patients undergoing head and neck radiotherapy.

Keywords: Radiotherapy; Bond strength; Scanning electron microscopy; Confocal laser scanning microscopy; Root canal sealer

Introduction

Head and neck cancer (HNC) is a prevalent malignancy that affects multiple regions, including the oral cavity, nasal cavity, paranasal sinuses, salivary glands, pharynx, and larynx (Deng et al., 2025). Among the various types of cancer that occur in the head and neck region,

oral cavity cancer is one of the most frequent (Jordani et al., 2024). It may involve structures such as the lips, buccal mucosa, palate, tongue, and floor of the oral cavity (Jordani et al., 2024).

The treatment of HNC is generally performed through surgery, chemotherapy, radiotherapy, immunotherapy, or a combination of these modalities (De Miranda et al., 2019; Worthington et al., 2023). Radiotherapy is a widely employed therapeutic approach in the management of HNC and plays a fundamental role in its treatment (Arid et al., 2020; Bhandari et al., 2020). The ionizing radiation administered during radiotherapy affects not only neoplastic cells but also healthy tissues adjacent to the irradiated area (Parahyba et al., 2016; Pelloso et al., 2022; Jordani et al., 2024). Although radiotherapy achieves high success rates, it can lead to several adverse effects in the oral cavity, including mucositis, trismus, hyposalivation, radiation-related caries, and osteoradionecrosis (Velo et al., 2018; Cunha et al., 2020). Furthermore, structural alterations in enamel and dentin have been observed as a consequence of radiotherapy, becoming more pronounced with increasing radiation doses (Gonçalves et al., 2014; Arid et al., 2020).

Initially, dentition degradation following radiotherapy was considered an indirect effect of the treatment, resulting from radiation-induced alterations in the salivary glands that lead to hyposalivation (Reed et al., 2015). However, it has been demonstrated that the severity of structural changes in dental tissues is also directly correlated with the radiation dose received by each tooth (Gonçalves et al., 2014; Reed et al., 2015; Arid et al., 2020). Radiotherapy exerts direct effects on the chemical composition, structure, and mechanical properties of both coronal and radicular dentin (Turker et al., 2021). The main alterations observed include a reduction in microhardness, attributed to its high water content (approximately 10%); obliteration of dentinal tubules and degeneration of odontoblastic processes due to limited vascularization and metabolic deficits; and degradation of the collagen fibril network caused by free radicals generated through the interaction of radiation with water molecules within the tissue (Martins et al., 2015; Reed et al., 2015; Cunha et al., 2017; Campi et al., 2019).

Polce et al. (2021) demonstrated, using dosimetric maps with individualized estimates for each tooth, that the radiation dose received by teeth can differ substantially from that delivered to the tumor site. For instance, during the treatment of nasopharyngeal cancer, in which radiotherapy protocols range from 50 Gy to 70 Gy, mandibular premolars received doses of approximately 30 Gy. This finding suggests that the radiation doses reported in previous *in vitro* studies (Reed et al., 2015; Qing et al., 2016; Velo et al., 2018; Yamin et al., 2018; Campi et al., 2019; De Miranda et al., 2019; Lopes et al., 2020) may have been overestimated, potentially limiting the interpretation of the actual effects of radiation on dental tissues.

Consequently, it is crucial to investigate whether clinically realistic doses below 70 Gy can alter dentin properties and affect the adhesion of restorative materials and endodontic sealers.

A comprehensive understanding of the effects of radiotherapy on dentin is essential for the planning and implementation of safe and effective dental interventions. Such knowledge provides critical technical and scientific support for clinical decision-making, fostering more precise and evidence-based practices. Therefore, the aim of this *in vitro* study was to evaluate the effects of clinically realistic doses of ionizing radiation (30 Gy and 70 Gy) on the bond strength of an endodontic sealer to root dentin, considering variations in root canal obturation techniques (lateral condensation and Tagger's hybrid technique). Additionally, the effects of these radiation doses on the sealer-dentin interface and on the sealer's penetration into dentinal tubules were assessed.

The null hypotheses tested were that the applied doses of ionizing radiation would not affect (1) the bond strength of the sealer to root dentin, (2) the integrity of the sealer-dentin interface, or (3) the sealer's penetration into dentinal tubules, regardless of the root canal obturation technique employed.

Materials and methods

Ethical approval and sample size calculation

The research project was previously submitted for review by the Human Research Ethics Committee of the Federal University of Santa Catarina (CEPSH-UFSC; approval No. 5.893.644) and by the Department of Radiotherapy of the Oncology Research Center (CEPON, Florianópolis, SC, Brazil; approval No. 6.013.576).

Initially, a sample size calculation was performed using G*Power software (version 3.1.9.7; Universität Düsseldorf, Germany) to determine the minimum number of repetitions required per experimental group to detect a statistically significant difference of 5% among them. Sample size was calculated based on the study by Jordani et al. (2024). The following parameters were considered: α error = 0.05 (significance level = 5%), test power ($1-\beta$) = 0.80, and effect size = 0.5. Wilcoxon signed-rank statistical test (matched pairs) was performed. The type of power analysis was set a priori (compute required sample size - given α , power, and effect size). Based on this calculation, ten specimens per experimental group were required for the bond strength test.

Sample selection and preparation

A total of 60 freshly extracted human teeth were included in the study, specifically mandibular premolars with a single, fully formed canal and no carious lesions, hypoplastic or hypomineralized areas, pulp calcifications, resorptions, or previous endodontic treatment. The teeth were initially examined through rigorous visual inspection under a magnifying lens ($\times 4$) and radiographic analysis using digital periapical radiographs (Digital Sensor Fit; Acteon, Indaiatuba, SP, Brazil) in both mesiodistal and buccolingual directions. Digital radiographic images were also used to measure the root canal dimensions at 2 mm and 5 mm cervical to the apical foramen. Only teeth with a total length of 16 mm and a buccolingual-to-mesiodistal dimension ratio of ≤ 1.5 were selected (Lopes et al., 2020; Jordani et al., 2024). Teeth that did not meet these criteria were excluded from the final sample. Subsequently, the teeth were cleaned using an ultrasonic device (Profi Neo; Dabi Atlante, Ribeirão Preto, SP, Brazil) and immersed in a 0.1% thymol solution for 48 h for disinfection, followed by rinsing under running water for 24 h. After this procedure, to prevent dehydration, the teeth were individually stored in plastic flasks containing distilled water and maintained in an incubator at 37°C until use.

The crowns of the teeth were sectioned transversely 1 mm above the cemento-enamel junction using a double-sided diamond disc (Fava, São Paulo, SP, Brazil) mounted on a low-speed handpiece (Model 605; Kavo, Joinville, SC, Brazil) under copious water cooling. This procedure left a 1 mm coronal remnant and standardized the root length at 16 mm, measured with a digital caliper (Mitutoyo, Kawasaki, Kanagawa, Japan). The teeth were randomly allocated (www.random.org) into three groups ($n = 20$): NoRT - non-irradiated teeth (negative control); 30 Gy - teeth exposed to the total radiation dose delivered to mandibular premolars during radiotherapy for nasopharyngeal cancer (30 Gy) (Polce et al., 2021); and 70 Gy - teeth exposed to the total radiation dose typically delivered to tumor core for nasopharyngeal cancer treatment (70 Gy) (positive control) (Polce et al., 2021). Samples from each group (NoRT, 30 Gy, and 70 Gy) were subsequently subdivided into two subgroups ($n=10$) according to the root canal obturation technique: LC - lateral condensation, and HB - Tagger's hybrid technique (Fig. 1).

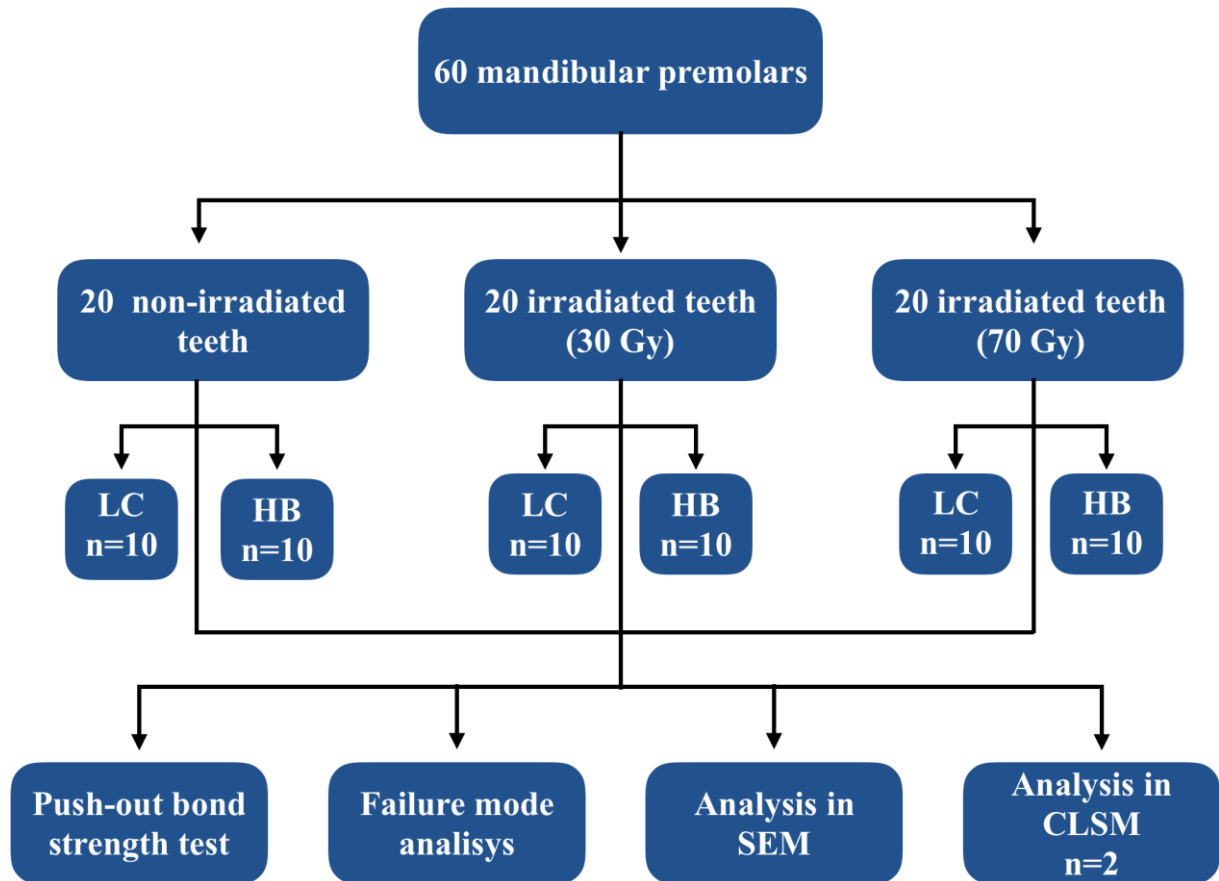


Figure 1. Flowchart of groups distribution

Teeth irradiation

The teeth were irradiated using a linear accelerator (Clinac 2100C; Varian Medical Systems, Inc., Palo Alto, CA, USA) with the Intensity-Modulated Radiation Technique (IMRT) technique and a dynamic multileaf collimator (DMLC) prior to the experimental procedures. For this purpose, the teeth were placed in a plastic holder containing distilled and deionized water, aligned equidistantly from the radiation source to ensure a standardized distribution of the daily radiation dose (400 MU/min) (Cunha et al., 2016). The total radiation doses delivered to the teeth in the 30 Gy (LC and HB) and 70 Gy (LC and HB) groups were fractionated into daily doses of 2 Gy, five days per week, for three or seven weeks, respectively. At the end of each daily irradiation cycle, the distilled and deionized water was replaced with artificial saliva, and the teeth were maintained at 37°C to simulate intraoral conditions. Prior to each new irradiation cycle, the artificial saliva was replaced with distilled and deionized water. The entire radiotherapy procedure was conducted at the Department of Radiotherapy of the Oncology Research Center (CEPON, Florianópolis, SC, Brazil) under the supervision of a

medical physicist and a radiation oncologist. After completing the radiotherapy protocol, the teeth were stored in artificial saliva at 37°C until testing.

Root-canal preparation

Irradiated and non-irradiated root canals were negotiated using a size 10 K-file (Dentsply-Maillefer, Ballaigues, Switzerland), and the working length was established 1.0 mm short of the apical foramen. The canals were shaped with a single-file reciprocating system (40/.06) (Reciproc R40; VDW, Munich, Germany) operated in “RECIPROC ALL” mode using a 6:1 reduction contra-angle handpiece (VDW Silver Reciproc; Dentsply Sirona, Bensheim, Germany). The file was advanced apically with a gentle pecking motion and, after every three strokes, was removed, cleaned with gauze, and reinserted until the working length was reached. Canal patency was maintained throughout the preparation using a size 10 K-file (Dentsply-Maillefer). Irrigation was performed with 2 mL of 2.5% sodium hypochlorite (NaOCl) solution (Biodinâmica, Ibiporã, PR, Brazil) delivered through a disposable syringe and a NaviTip needle (Ultradent Products, South Jordan, UT, USA) positioned 2 mm short of the working length. Simultaneous aspiration was performed using a metallic suction cannula. Final irrigation consisted of 3 mL of 17% EDTA (Biodinâmica, Ibiporã, PR, Brazil) for 3 minutes, followed by 2 mL of 2.5% NaOCl solution. Finally, the canals were dried with R40 paper points (Reciproc R40; VDW).

Root canal obturation

Root canal obturation was performed using an epoxy resin–based sealer (AH Plus Jet; Dentsply DeTrey, Konstanz, Germany), an R40 gutta-percha master cone (Reciproc; VDW, Munich, Germany), and B7 accessory cones (Tanariman; Manaus, AM, Brazil). For Confocal Laser Scanning Microscopy (CLSM) analysis, two samples from each experimental group were obturated with a sealer containing 0.001 g of 0.1% Rhodamine B (Sigma-Aldrich, St. Louis, MO, USA) diluted in 0.05 mL of distilled water and buffered with 0.5% sodium phosphate solution per gram of sealer (Tedesco et al., 2023). The following obturation techniques were performed:

Lateral condensation technique: The master cone was coated with endodontic sealer and inserted into the root canal using circumferential motions until reaching the working length. A 25 mm digital spreader (Dentsply-Maillefer) was then applied laterally to the master cone at the working length, followed by the insertion of accessory cones coated with sealer until the root canal was completely filled. Excess material was removed, and vertical compaction was

performed using a Paiva plugger (Golgran, São Paulo, Brazil) heated to the level of the cemento-enamel junction.

Tagger's hybrid technique: The master cone was coated with sealer and inserted to the working length with gentle circumferential motions. A 25 mm digital spreader (Dentsply-Maillefer) was then placed laterally to the master cone, followed by the insertion of two accessory cones coated with sealer. Subsequently, a size 60 McSpadden compactor (Dentsply-Maillefer), calibrated 3 mm short of the working length and mounted on a low-speed handpiece (Model 605; Kavo), was positioned parallel to the tooth's long axis. A back-and-forth motion was performed until the predetermined working length was reached.

The quality of the obturation was verified using digital periapical radiographs taken in both buccolingual and mesiodistal projections. The access cavities were sealed with the adhesive system Adper Single Bond 2 (3M ESPE, St. Paul, MN, USA) and the composite resin Filtek Z350 XT (3M ESPE, Sumaré, SP, Brazil). The samples were then stored at 37°C and 100% humidity for a period corresponding to three times the sealer's setting time before performing the push-out bond strength test.

Push-out bond-strength test

Each root was transversely sectioned with a double-sided diamond disc (No. 11-4243; Buehler, Lake Bluff, IL, USA) on a metallographic cutting machine (Isomet 1000; Buehler) under a 100 g load at 350 rpm with continuous water cooling. After removal of the coronal portion at the cemento-enamel junction, two dentin slices (1.0 ± 0.1 mm thick) were obtained from each root third for the push-out test, scanning electron microscopy (SEM) analysis, and confocal laser scanning microscopy (CLSM) analysis.

For testing, each dentin slice was positioned with the cervical side facing downward on a stainless-steel jig mounted on a universal testing machine (OM150; Odeme Dental Research, Luzerna, SC, Brazil). Steel plungers with diameters of 0.6, 0.8, 1.0, or 1.2 mm - previously selected to match the root canal diameter in the cervical, middle, or apical third - were used to apply load at a crosshead speed of 0.5 mm/min until the maximum stress required to displace the material was reached. The compressive force was applied in the apical-to-cervical direction of the dentin slices.

The force required for displacement was recorded in Newtons (N) using a 2 N load cell, and subsequently divided by the bonding surface area (mm²). The resulting values were then expressed in megapascals (MPa). The bonding surface area was calculated using the following formula:

$$BS = \pi (R + r) \sqrt{h^2 + (R - r)^2}$$

BS is the bonding surface area, h is the dentin slice thickness (measured with a digital caliper), and R and r are the cervical and apical radii of the canal space, respectively.

Failure mode analysis

After the push-out testing, each dentin slice was inspected under a stereomicroscope (SteREO Discovery V12; Carl Zeiss, Jena, Germany) at 15× and 40× magnifications to determine the failure mode. Representative specimens were then selected and examined under SEM (TESCAN VEGA, Brno, Czech Republic). Specimens were affixed to aluminium stubs with carbon tape, sputter-coated with a 300-500 Å gold-palladium layer (Desk II; Denton Vacuum, Moorestown, NJ, USA) for 120 seconds, and imaged at 500×, 1000×, and 1500× magnifications. Failures were classified as follows: adhesive (root canal walls free of endodontic sealer or disruption of the cementation line), cohesive at the sealer (fracture of the filling material while the dentin remained covered by sealer), cohesive at dentin (fracture of dentin substrate), and mixed (a combination of different failure types occurring within the same specimen) (Jordani et al., 2024).

Adhesive interface analysis (SEM)

Dentin slices that were not subjected to the push-out test were reserved for analysis of the adhesive interface under SEM (JSM-5410; JEOL, Tokyo, Japan). The slices were immersed in a 2.5% glutaraldehyde solution buffered to pH 7.4 with 0.1 M sodium cacodylate (Dermus, Florianópolis, SC, Brazil) for 12 hours at 4 °C. Subsequently, the slices were rinsed with deionized water and dehydrated through ascending concentrations of ethyl alcohol (25% for 20 minutes, 50% for 20 minutes, 75% for 20 minutes, 95% for 30 minutes, and 100% for 1 hour). Each slice was then dried and mounted with double-sided adhesive tape onto Teflon rings (5 mm thickness × 2.0 cm diameter), with the cervical surface facing downward, and embedded in epoxy resin. After resin polymerization, both sides of the samples were polished using a polishing machine (DP-10; Panambra, São Paulo, SP, Brazil) with abrasive papers (Norton, São Paulo, SP, Brazil) applied under light pressure and constant water irrigation in decreasing grit sequence (#400, #600, and #1200), followed by polishing with felt discs and alumina pastes of 0.3 µm and 0.1 µm particle size (Arotec, São Paulo, SP, Brazil). After thorough rinsing with running water, the samples were demineralized with 6 mol/L hydrochloric acid (Dermus) for 30 seconds, followed by deproteinization with 2% sodium hypochlorite solution (Dermus) for

10 minutes (Teixeira et al., 2009). The specimens were then placed in a vacuum chamber and sputter-coated with a 300 Å layer of gold/palladium alloy (80 wt% / 20 wt%) (Bal-Tec SCD 005; Bal-Tec Co., USA). Images of different areas of each dentin slice were obtained at magnifications of 100×, 500×, 1000×, and 2000×.

The following characteristics were evaluated during analysis (Tedesco et al., 2018): the integrity of the adhesive interface between dentin and the endodontic sealer (continuous and homogeneous interface and/or presence of gaps), as well as the density and depth of sealer penetration into the dentinal tubules.

Penetration into dentinal tubules analysis (CLSM)

The analysis of sealer penetration into dentinal tubules was performed using CLSM (Leica SP8; Leica Microsystems, Mannheim, Germany). The second dentin slice from each root third (cervical, middle, and apical) of the two samples in the groups in which 0.1% Rhodamine B was incorporated into the sealer was used. Each slice was polished on both surfaces for one minute using abrasive papers (Norton) in ascending grit sequence (#800, #1200, and #1500) to obtain a smooth and uniform surface. The dentin slices were then placed on glass coverslips (0.17 mm thick).

Using the epifluorescence mode, the excitation and emission wavelengths of the dye applied during the obturation phase were employed: Rhodamine B with a red-light filter (excitation: 552 nm laser; emission: 548/588 nm). The Leica Application Suite-Advanced Fluorescence software (Leica Microsystems) was used to evaluate the extent of endodontic sealer penetration. Samples were analyzed at a depth of 10 µm below the surface under 10× and 20× magnifications.

Statistical analysis

The statistical analysis was performed using SPSS Statistics version 25 software (IBM Corp., Armonk, NY, USA). Due to the non-normal distribution of the data (Shapiro–Wilk test, $p = 0.0019$) and heteroscedasticity (Levene’s test, $p = 0.0192$), the data were analyzed using nonparametric tests. For the bond strength values, the influence of the obturation techniques (LC and HB) was analyzed using the Mann-Whitney test, and the effect of the radiotherapy regimen (NoRT, 30 Gy, and 70 Gy) was assessed using the Kruskal-Wallis test followed by Dunn’s post hoc test. The influence of the root thirds was evaluated using the Friedman test. The distribution of failure modes (adhesive, cohesive, or mixed) in each group was analyzed using Fisher’s exact test. The significance level was set at 5%. The adhesive interface and sealer

penetration into dentinal tubules were qualitatively evaluated by two previously calibrated and blinded examiners. The findings were analyzed using the Kappa test to assess intra- and inter-examiner agreement, with values greater than 0.75 - considered excellent - confirming the validity and reproducibility of the analysis. SEM and CLSM evaluations were performed at different time points, with a 15-day interval between assessments to minimize examiner bias.

Results

Bond strength

No specimens were lost during the push-out bond strength testing. The bond strength of the specimens irradiated with either 30 Gy or 70 Gy were significantly lower than the non-irradiated specimens, in both LC and HB groups, regardless of the root third ($p < 0.05$).

Overall, the HB group showed significantly higher values of bond strength, compared to the LC group, in both non-irradiated specimens, and irradiated with 30 Gy or 70 Gy ($p < 0.05$).

The root thirds did not affect the bond strength values in any of the experimental settings ($p > 0.05$). The complete results of the pairwise comparisons with their respective p-value is demonstrated in Table 1 and Fig. 2.

Table 1. Median and interquartile range values of bond strength of each group, according to the radiotherapy regimen, obturation technique, and root thirds.

Root Thirds	Group	Radiotherapy			p-value
		NoRT	30 Gy	70 Gy	
Cervical	LC	2.93 (1.43) ^{A,a}	1.52 (1.19) ^{B,a}	1.67 (0.95) ^{B,a}	0.002
	HB	4.10 (0.99) ^{A,a}	2.54 (0.48) ^{B,b}	2.21 (0.58) ^{B,a}	<0.001
	p-value	0.82	0.002	0.199	
Middle	LC	3.12 (0.71) ^{A,a}	1.21 (1.09) ^{B,a}	1.86 (0.62) ^{B,a}	<0.001
	HB	4.01 (1.15) ^{A,b}	2.35 (0.45) ^{B,b}	2.57 (1.21) ^{B,b}	0.004
	p-value	0.016	0.023	0.011	
Apical	LC	3.26 (1.09) ^{A,a}	1.97 (0.51) ^{B,a}	1.56 (0.82) ^{B,a}	0.001
	HB	4.13 (1.41) ^{A,a}	2.54 (0.39) ^{B,b}	2.31(0.51) ^{B,a}	<0.001
	p-value	0.143	0.009	0.075	
Overall	LC	3.12 (1.02) ^{A,a}	1.69 (1.03) ^{B,a}	0.89 (0.31) ^{B,a}	<0.001
	HB	4.10 (1.27) ^{A,b}	2.51 (0.48) ^{B,b}	2.26 (0.63) ^{B,b}	<0.001
	p-value	0.001	<0.001	0.001	

Different uppercase letters in a row indicate statistical differences regarding the radiotherapy regimen (Kruskal-Wallis + Dunn). Different lowercase letters in a column indicate statistical difference between obturation techniques (Mann-Whitney).

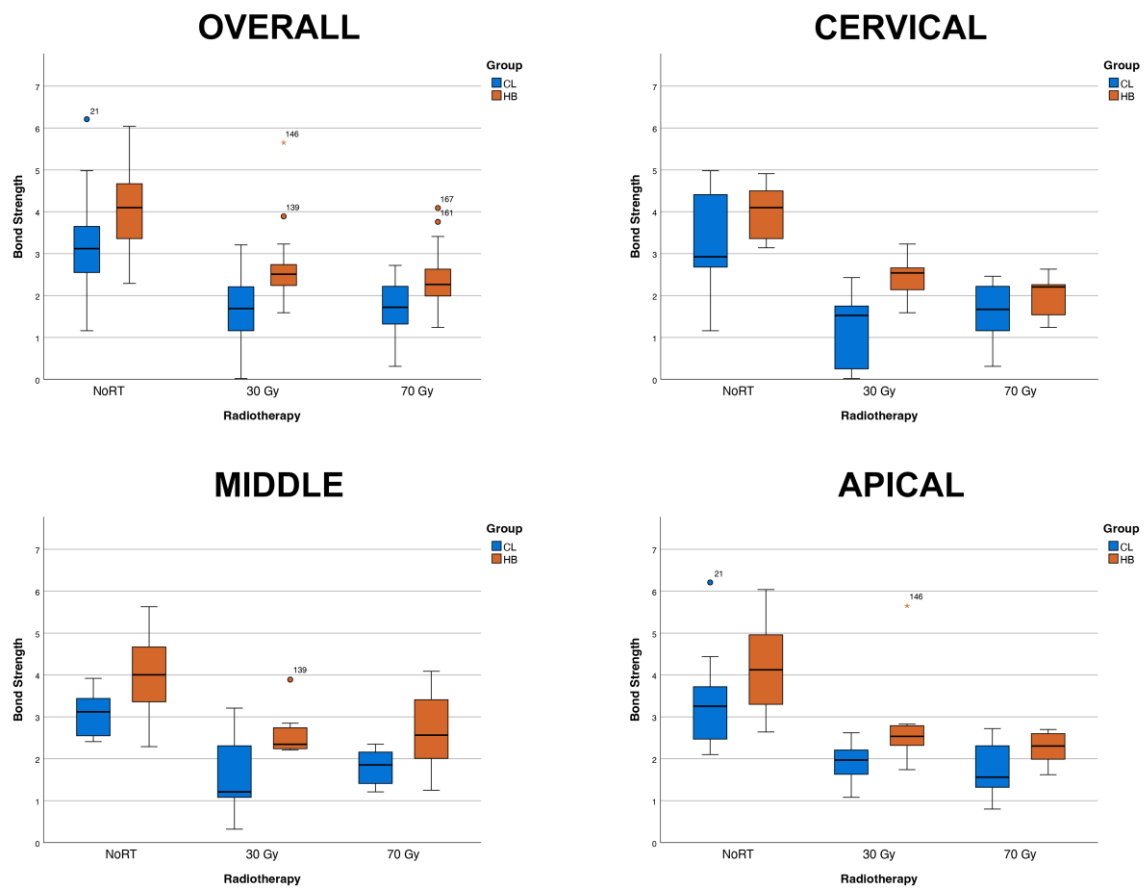


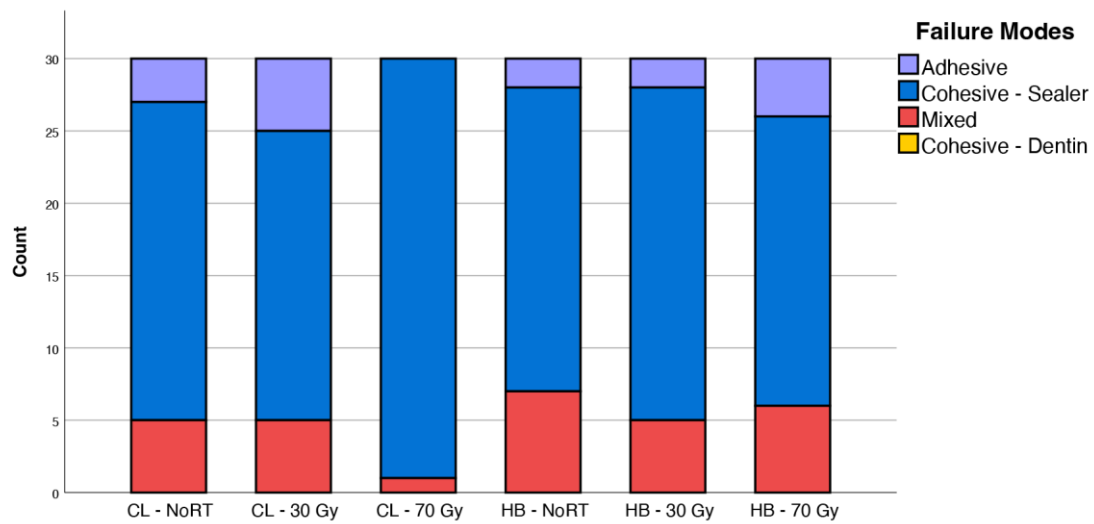
Figure 2. Boxplot of the bond strength values according to the radiotherapy regimen, obturation technique, and root thirds.

Failure mode

Table 2 and Fig. 3 present the distribution and frequency, respectively, of failure modes in each experimental group. Representative SEM images of the failure modes may be seen in Fig. 4. The failure mode analysis revealed that there were no significant differences among the experimental groups ($p > 0.05$). The most common was the cohesive failure at the sealer, followed by mixed failures, and adhesive failures, respectively. None of the specimens presented cohesive failures at dentin.

Table 2. Distribution of failure modes among the experimental groups.

Radiotherapy	Group	Failure mode			
		Adhesive	Cohesive - Sealer	Cohesive - Dentin	Mixed
NoRT	LC	3	22	0	5
	HB	2	21	0	7
30 Gy	LC	5	20	0	5
	HB	2	23	0	5
70 Gy	LC	0	29	0	1
	HB	4	20	0	6

**Figure 3.** Bar chart of the failure modes frequency, according to the obturation technique and radiotherapy regimen.

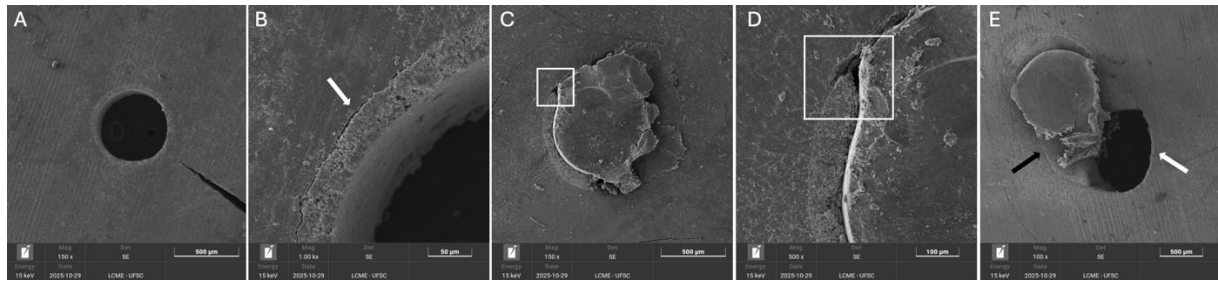


Figure 4. Representative SEM images of the failure modes after the bond strength test. (A) Adhesive failure ($\times 150$). (B) Higher magnification showing disruption of the cementation line (arrow) ($\times 1000$). (C) Cohesive failure within the sealer (box) ($\times 150$). (D) Higher magnification showing fracture of the filling material (box) ($\times 500$). (E) Mixed failure, showing a combination of adhesive (white arrow) and cohesive failure at the sealer (black arrow) within the same specimen ($\times 150$). Images acquired at 15 kV; scale bar = 50, 100 and 500 μm .

Adhesive interface analysis

Representative SEM images of the adhesive interface may be seen in Fig. 5. SEM analysis revealed distinct morphological patterns at the adhesive interface among the experimental groups. In the NoRT-LC specimens, a continuous and compact cementation line was observed, without voids or interfacial gaps, and characterized by the presence of long, well-defined sealer tags. Similarly, the NoRT-HB group showed dense and elongated tags, although occasional discontinuities were evident along the cementation line. In the 30 Gy-LC group, the interface appeared generally uniform; however, small interfacial gaps and partial disruption of some sealer tags were visible. The 30 Gy-HB group presented a denser arrangement of sealer tags compared with the LC subgroup, indicating enhanced adaptation of the sealer to the dentinal surface. In contrast, specimens from the 70 Gy groups demonstrated pronounced interfacial degradation. The 70 Gy-LC samples exhibited evident gaps and severe disruption of the sealer tags, while the 70 Gy-HB samples showed long but irregular tag morphology and discontinuous interfaces. These findings suggest that higher radiation doses adversely affect the integrity of the sealer-dentin interface, compromising both tag formation and interfacial continuity.

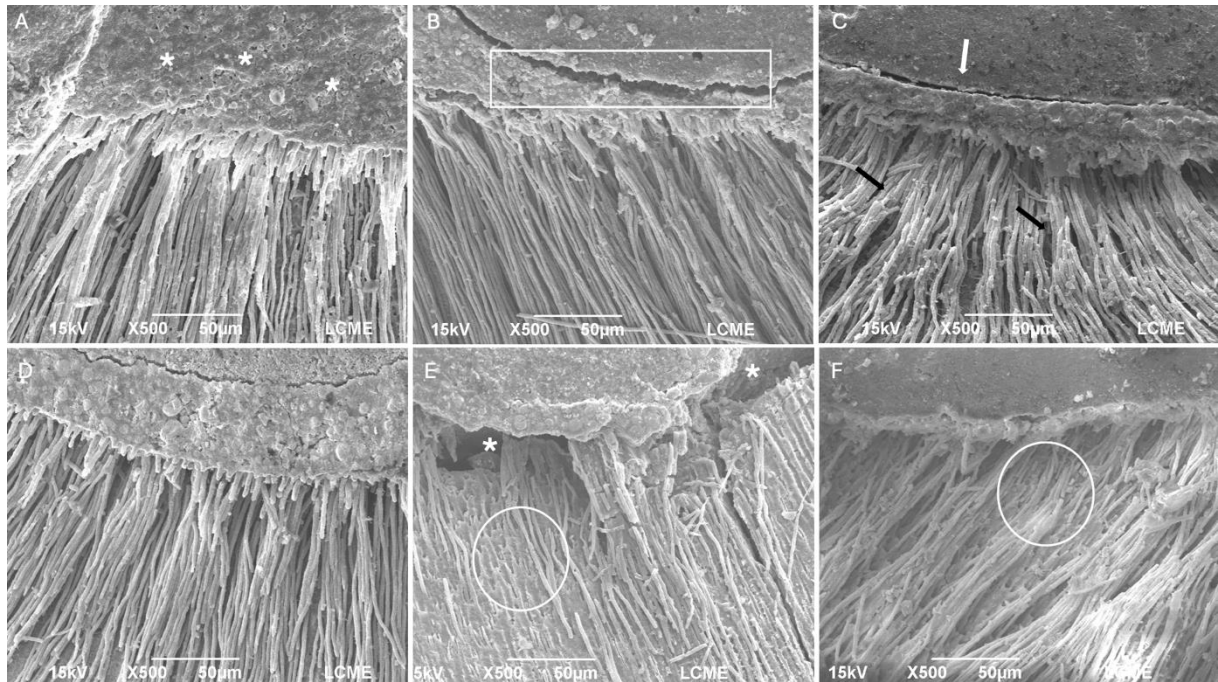


Figure 5. Representative SEM images of the adhesive interface. (A) NoRT-LC: Continuous and compact cementation line (*), without voids or gaps; most sealer tags are long ($\times 500$). (B) NoRT-HB: Discontinuous cementation line (box); however, sealer tags are denser and longer ($\times 500$). (C) 30 Gy-LC: Uniform interface; although white arrow indicates interfacial microgap and disruption of some sealer tags (black arrows) ($\times 500$). (D) 30 Gy-HB: Sealer tags are denser and longer than 30 Gy-LC ($\times 500$). (E) 70 Gy-LC: Interfacial gaps (*) and evident disruption of sealer tags (circle) ($\times 500$). (F) 70 Gy-HB: Interfacial gaps and long but irregular sealer tags are visible (circle) ($\times 500$). Both groups irradiated with 70 Gy exhibited a reduced number of sealer tags compared with the 30 Gy and NoRT groups. Images acquired at 15 kV; scale bar = 50 μm .

Penetration into dentinal tubules analysis

Representative CLSM images for each group, corresponding to the different root thirds (cervical, middle, and apical), are shown in Figure 6. CLSM analysis revealed distinct patterns of sealer penetration into dentinal tubules among the experimental groups. Overall, the 30 Gy and 70 Gy groups exhibited a less pronounced pattern of sealer penetration compared with the NoRT group, regardless of the obturation technique employed (LC or HB). In the NoRT-LC specimens, the sealer showed deep and continuous penetration, with long and uniformly distributed fluorescent tags extending along the entire circumference of the root canal. The NoRT-HB group demonstrated a similar pattern, with even greater tag density, indicating effective sealer adaptation and homogeneous penetration along the dentinal walls. In the 30 Gy-

LC specimens, sealer penetration was still evident but appeared slightly reduced in both depth and density, with areas of partial discontinuity in tag distribution. The 30 Gy-HB specimens exhibited moderately intense fluorescence, with long sealer tags extending along the tubule paths, although small regions of irregular distribution were observed. In contrast, the 70 Gy-LC group displayed a markedly reduced fluorescence signal, suggesting limited sealer penetration and disruption of tag continuity, while the 70 Gy-HB group exhibited sparse and irregular fluorescent tags concentrated mainly near the cementation line.

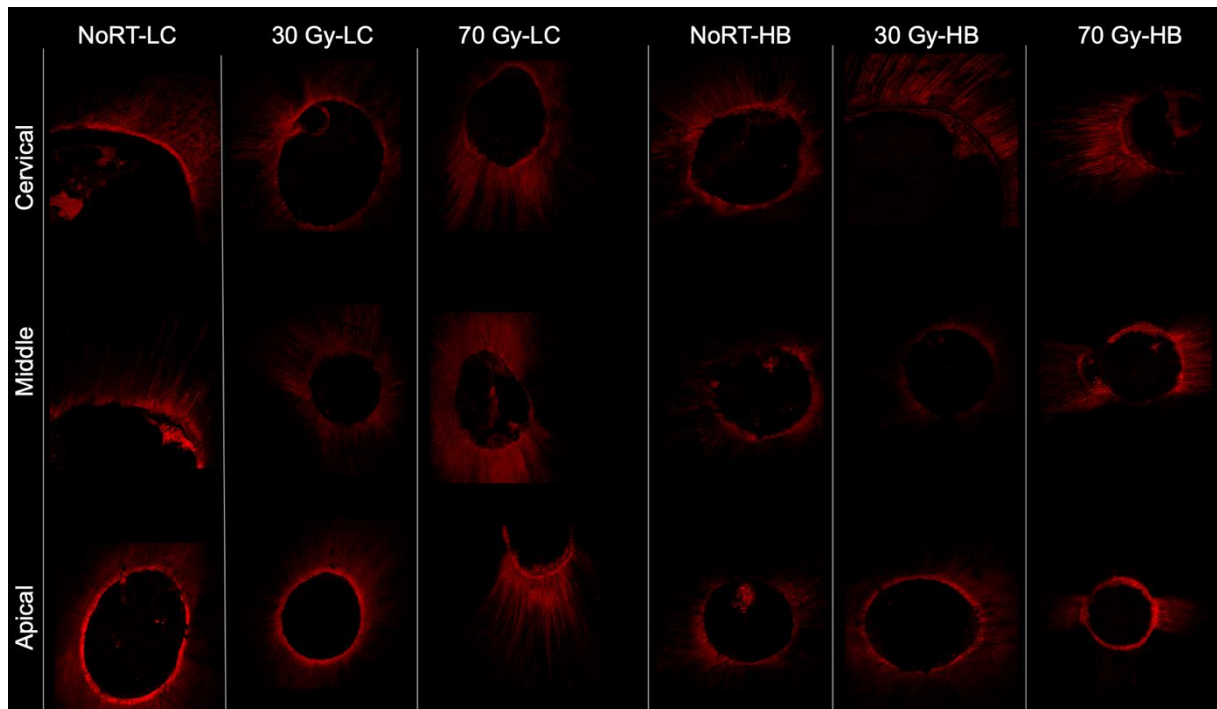


Figure 6. Representative CLSM images of the experimental groups according to root level (cervical, middle, and apical thirds). NoRT-LC and NoRT-HB specimens show deep and continuous sealer penetration with long, uniformly distributed fluorescent tags along the dentinal walls. The 30 Gy-LC and 30 Gy-HB groups display reduced penetration depth and tag density, with areas of partial discontinuity. In contrast, the 70 Gy-LC and 70 Gy-HB specimens exhibit markedly decreased fluorescence intensity, with sparse and irregular sealer tags concentrated mainly near the cementation line.

Discussion

It is well established in the literature that radiotherapy induces multiple alterations in dental structures (Rodrigues et al., 2018; Velo et al., 2018). Ionizing radiation interacts with water molecules, leading to the formation of highly unstable and reactive free radicals through a process known as radiolysis (Rodrigues et al., 2018; Goulart et al., 2024). Consequently, tissues with a higher water content, such as dentin, are especially susceptible to the effects of radiation, exhibiting significant structural damage (Goulart et al., 2024).

This *in vitro* study aimed to evaluate the effects of two clinically realistic doses of ionizing radiation used in the treatment of nasopharyngeal cancer, on the bond strength of an epoxy resin-based endodontic sealer to root dentin of mandibular premolars, considering variations in root canal obturation techniques. The study also evaluated the effects of radiation on the sealer-dentin interface and on the sealer's penetration into dentinal tubules. Based on the results obtained, the null hypotheses were rejected, as both radiation doses affected the bond strength of the sealer, the integrity of the sealer-dentin interface, and the sealer's penetration capacity. Additionally, a significant difference in bond strength was observed between the obturation techniques evaluated, regardless of the radiotherapy regimen.

Studies employing dosimetric maps have demonstrated that radiotherapy administered for different types of HNC results in an uneven distribution of radiation across dental structures (Polce et al., 2021; Garcia & Ribeiro, 2024). As a result, the dose actually absorbed by the teeth often differs from the dose originally prescribed for the tumor (Polce et al., 2021; Garcia & Ribeiro, 2024). Consequently, experimental studies using radiation doses between 60 Gy (Campi et al., 2019; Lopes et al., 2020) and 70 Gy (Reed et al., 2015; Pelloso et al., 2022) may overestimate the true extent of radiation-induced damage to dental tissues (Polce et al., 2021; Garcia & Ribeiro, 2024).

In clinical practice, radiotherapy for HNC typically involves total doses ranging from 50 Gy to 70 Gy (Pelloso et al., 2022). However, tumor extent and location are clinical variables that directly influence the amount of radiation received by the teeth (Polce et al., 2021). Dosimetric map analyses have shown that radiation levels differ between the maxilla and mandible, as well as among various dental groups, during radiotherapy for different HNC types (Polce et al., 2021). For example, in nasopharyngeal cancer cases treated with 60 Gy, only approximately 30 Gy reaches the lower premolar region (Polce et al., 2021), whereas more extensive oropharyngeal lesions can result in doses of up to 63 Gy in the same area (Polce et al., 2021). Clinically, the radiation absorbed by teeth does not always correspond to the prescribed dose for the neoplastic target, particularly in experimental models (Goulart et al., 2024; Garcia & Ribeiro, 2024). Therefore, the present study employed two radiation doses: 30 Gy, representing the amount typically absorbed by mandibular premolars during nasopharyngeal cancer radiotherapy (Polce et al., 2021), and 70 Gy, corresponding to the dose delivered to tumor core for nasopharyngeal cancer treatment, and commonly used in laboratory investigations (Reed et al., 2015; Velo et al., 2018; Pelloso et al., 2022). Specimens were irradiated once daily in 2 Gy fractions, five days per week, following the standard clinical protocol used in HNC treatment (Jham & Freire, 2006).

An additional factor considered to simulate clinical conditions was the storage of teeth in artificial saliva between radiation cycles. Although artificial saliva does not fully reproduce the physicochemical complexity of natural saliva - whose flow, secretion, and composition undergo significant changes in patients undergoing radiotherapy - it remains the most appropriate medium for mimicking clinical conditions (Martins et al., 2015). During radiation exposure, the teeth were immersed in distilled water, following the protocol adopted in previous studies (Martins et al., 2015; Jordani et al., 2024; Goulart et al., 2024), since the viscosity and high ionic concentration of artificial saliva may interfere with the uniform distribution of the radiation dose (Martins et al., 2015).

Root canal obturation was performed using two techniques: lateral condensation, considered the reference method for comparison with other obturation approaches (Araújo et al., 2016), and Tagger's hybrid technique, which provides superior adaptation of the sealer to the complex internal anatomy of the root canal system (Fracassi et al., 2013). Although widely used, the lateral condensation technique may promote the formation of voids and gaps within the filling material, excessive sealer accumulation in specific canal regions, and reduced apical density (Rossetto et al., 2014). These limitations may help explain the findings of the present study, as the group obturated with Tagger's hybrid technique (HB) exhibited significantly higher bond strength values than the group treated with lateral condensation (LC). It is also worth noting that, from a methodological standpoint, this laboratory study sought to ensure specimen standardization by selecting only root canals with comparable buccolingual and mesiodistal dimensions (ratio ≤ 1.5) (Jordani et al., 2024). Consequently, specimens with similar cementation line characteristics were subjected to the push-out bond strength test, thereby minimizing potential sources of bias in the results.

In the present study, the bond strength of the endodontic sealer to root dentin was lower in teeth exposed to radiation compared with non-irradiated teeth, regardless of the radiation dose (30 Gy or 70 Gy), obturation technique, or root third analyzed. This finding confirms that even low radiation doses - similar to those absorbed by certain dental groups during radiotherapy for HNC - are capable of inducing significant deleterious effects on dentin (Gonçalves et al., 2014; Martins et al., 2015; Rodrigues et al., 2018; Yamin et al., 2018; Campi et al., 2019). However, root canals obturated using Tagger's hybrid technique exhibited higher bond strength values, regardless of the experimental condition (irradiated or non-irradiated). This result reinforces that, in addition to the effects of radiotherapy, the obturation technique plays a crucial role in the bond strength of endodontic sealers, particularly in oncologic patients.

The reduction in bond strength observed in irradiated specimens is consistent with the morphological alterations revealed by SEM and CLSM analyses. Under SEM, the 30 Gy and 70 Gy groups exhibited evident interfacial discontinuities, with gaps and partial detachment of the sealer from the dentin surface. The degradation of collagen fibrils and obliteration of dentinal tubules, commonly induced by ionizing radiation, likely compromised the mechanical interlocking between the sealer and the dentin substrate (Gonçalves et al., 2014; Martins et al., 2015; Rodrigues et al., 2018; Yamin et al., 2018; Campi et al., 2019). CLSM findings further supported this interpretation, showing reduced sealer penetration depth and irregular fluorescent tag distribution in irradiated groups, particularly at 70 Gy. This decrease in interaction is likely due to radiation-induced alterations in the mineral components of dentin, which are critical for effective sealer adhesion (Peloso et al., 2022). Together, these structural changes explain the weaker adhesive performance of the sealer when dentin is exposed to radiation.

Conversely, specimens obturated using Tagger's hybrid technique exhibited superior adaptation of the sealer to the dentinal walls and higher bond strength values compared with those obturated by lateral condensation. SEM images of the HB groups revealed a more continuous cementation line and denser sealer tags, while CLSM analysis confirmed deeper and more homogeneous penetration of the fluorescent dye within the dentinal tubules. These morphological patterns suggest that the thermoplasticized gutta-percha used in the hybrid technique enhances sealer flow and penetration (Álvarez-Vásquez et al., 2024), compensating partially for the radiation-induced alterations in dentin (Jordani et al., 2024). Thus, both microscopic and mechanical findings reinforce the strong interdependence between dentin structural integrity and the obturation technique employed.

It is important to note that a 0.1% Rhodamine B fluorescent dye was employed in this study due to its stable fluorescence properties (Tedesco et al., 2023). Additionally, the small particle size of Rhodamine B facilitates its incorporation into the endodontic sealer without compromising its adhesion (Tedesco et al., 2023). Prior to use, the dye was diluted in distilled water and buffered with a 0.5% sodium phosphate solution to prevent any interference with the sealer's bond strength (Tedesco et al., 2023).

Regarding the failure mode analysis, structural alterations in root dentin induced by radiotherapy, combined with the mechanical stress generated during root canal preparation, increase the tooth's susceptibility to fractures and microfractures (Yamin et al., 2018). This condition may explain the predominance of cohesive failures observed in most specimens, regardless of the experimental condition (radiotherapy regimen or obturation technique).

The findings of this study indicate that gradual exposure to radiation at doses of up to 70 Gy has a direct impact on the observed outcomes. Although no statistically significant differences were detected among the administered doses, exposure to as little as 30 Gy was sufficient to compromise the bond strength of the sealer to root dentin. These results suggest that the deleterious effects of radiotherapy may be irreversible, potentially jeopardizing the long-term success of endodontic treatment in patients undergoing head and neck radiotherapy.

Conclusions

Within the limitations of this *in vitro* study, it can be concluded that exposure of root dentin to ionizing radiation, even at clinically realistic doses, negatively affects the adhesion of epoxy resin-based sealers to dentin. Both 30 Gy and 70 Gy radiation regimens reduced the bond strength of the endodontic sealer to root dentin and impaired the integrity of the sealer-dentin interface. However, Tagger's hybrid obturation technique provided superior sealer adaptation and higher bond strength values compared with the lateral condensation technique, regardless of radiation exposure. The morphological findings observed through SEM and CLSM corroborate the mechanical results, demonstrating that radiotherapy alters dentin structure and compromises the adaptation and penetration of the endodontic sealer. These results highlight the importance of considering the effects of radiotherapy during endodontic treatment planning for oncology patients and emphasize the need for further *in vitro* and *in vivo* investigations to establish evidence-based clinical guidelines for this population.

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4 CONSIDERAÇÕES FINAIS

A continuidade das pesquisas *in vitro* deve apoiar-se em dados dosimétricos obtidos em condições clínicas reais. Isso se justifica porque a dose prescrita para o tratamento de CCP representa apenas uma estimativa parcial da radiação efetivamente absorvida pela dentina radicular, influenciada pelo estágio e pela localização do tumor. Dessa forma, cada mapa dosimétrico precisa ser interpretado à luz dessas especificidades, evitando projeções indevidas para outras regiões. Nas condições laboratoriais do presente estudo, observou-se redução significativa da resistência de união das amostras irradiadas com 30 Gy e 70 Gy, em concordância com as alterações morfológicas identificadas nas análises de MEV e de MCL. Ademais, a dose de 30 Gy já se mostrou suficiente para provocar danos estruturais à dentina radicular, comprometendo a adesão dos cimentos obturadores a esse substrato.

Sendo assim, as dificuldades inerentes à adesão de cimentos obturadores às estruturas dentárias em pacientes portadores de CCP submetidos à radioterapia poderão ser minimizadas por meio da implementação de protocolos clínicos fundamentados em evidências científicas robustas, contribuindo para a tomada de decisão e para o aprimoramento dos resultados dos tratamentos odontológicos.

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