UNIVERSIDADE FEDERAL DE SANTA CATARINA

CENTRO DE CIÊNCIAS DA SAÚDE

PROGRAMA DE PÓS-GRADUAÇÃO EM ODONTOLOGIA

Gabriel Hernandez Machado de Souza

Efeito de doses cumulativas de radioterapia na resistência de união de um cimento resinoso universal à dentina intrarradicular

Florianópolis
2023

Gabriel Hernandez Machado de Souza

Efeito de doses cumulativas de radioterapia na resistência de união de um cimento resinoso universal à dentina intrarradicular

Dissertação submetida ao Programa de Pós-Graduação em Odontologia, do Centro de Ciências da Saúde da Universidade Federal de Santa Catarina, como requisito para obtenção do título de Mestre. Área de concentração: Endodontia.
Orientador: Prof. Dr. Lucas da Fonseca Roberti Garcia
Coorientadora: Profa. Dra. Cleonice da Silveira Teixeira

Florianópolis

2023

Souza, Gabriel Hernandez Machado de
Efeito de doses cumulativas de radioterapia na resistência de união de um cimento resinoso universal à dentina intraradicular / Gabriel Hernandez Machado de Souza ; orientador, Lucas da Fonseca Roberti Garcia, coorientadora, Cleonice da Silveira Teixeira, 2023.
39 p.

Dissertação (mestrado) - Universidade Federal de Santa Catarina, Centro de Ciências da Saúde, Programa de Pós-Graduação em Odontologia, Florianópolis, 2023.

Inclui referências.

1. Odontologia. 2. Radioterapia. 3. Cimento resinoso. 4. Resistência de união. I. Garcia, Lucas da Fonseca Roberti. II. Teixeira, Cleonice da Silveira. III. Universidade Federal de Santa Catarina. Programa de Pós-Graduação em Odontologia. IV. Título.

Gabriel Hernandez Machado de Souza

Efeito de doses cumulativas de radioterapia na resistência de união de um cimento resinoso universal à dentina intrarradicular

O presente trabalho em nível de Mestrado foi avaliado e aprovado, em 16 de junho de 2023, pela banca examinadora composta pelos seguintes membros:

Prof. Dr. Lucas da Fonseca Roberti Garcia
Universidade Federal de Santa Catarina

Profa. Dra. Renata Gondo Machado
Universidade Federal de Santa Catarina

Profa. Dra. Índia Olinta de Azevedo Queiroz
Universidade Federal de Santa Catarina

Certificamos que esta é a versão original e final do trabalho de conclusão que foi julgado adequado para obtenção do título de Mestre em Endodontia.

ICP-Edu
Documento assinado digitalmente
Mariane Cardoso Carvalho
Data: 15/09/2023 16:33:14-0300
CPF: ***.647.159-**
Verifique as assinaturas em https://v.ufsc.br

____

Coordenação do Programa de Pós-Graduação

ICP-Edu
Documento assinado digitalmente
Lucas da Fonseca Roberti Garcia
Data: 15/09/2023 12:25:33-0300
CPF: ***.929.858-**
Verifique as assinaturas em https://v.ufsc.br

____

Prof. Dr. Lucas da Fonseca Roberti Garcia
Orientador

Florianópolis, 2023

AGRADECIMENTOS

À minha Mãe, já que tudo que eu tenho e conquistei eu devo a ela, pois se não foi ela quem me deu condições de conquistar, foi ela quem me inspirou a conquistar. Minha mãe é meu porto seguro, uma mulher forte, que me criou sozinha, enfrentou todas as dificuldades que apareceram em seu caminho sem se deixar abater. Me educou com muito amor e dedicação, e esta criação me fez ser quem eu sou hoje. Não foi uma pessoa estudada, porém para lidar com outras pessoas não é necessário estudo, então ela me ensinou a sempre ser respeitoso, buscar fazer o certo, ajudar quem necessita, se dedicar a família e aos amigos e a enfrentar de cabeça erguida as dificuldades da vida. Obrigado Mãe, você é a minha maior inspiração, meu exemplo de como cuidar e educar os filhos, sempre que eu busco me tornar uma pessoa melhor, é para orgulhar você, Mãe.

Ao Meu Orientador, Lucas da Fonseca Roberti Garcia, agradeço por sua compreensão, auxilio e orientação durante a execução deste trabalho. Temos uma relação desde a minha graduação, onde você me orientou na iniciação científica e no meu TCC, se tornando um exemplo para mim. Você guia seus orientados para o caminho certo, sempre com muita humildade e motivação. Obrigado por tudo.

A Professora Renata Gondo Machado, não sei se sou capaz de descrever o carinho que sinto por você. Quando nos conhecemos na graduação, você foi a primeira professora que por meio das palavras e atitudes me fez realmente acreditar que eu poderia me tornar um ótimo profissional, você confiou em mim, me ensinou, e quando foi necessário me apoiou. Estas atitudes fizeram toda a diferença na minha vida. Muito obrigado por todo o carinho!

A professora Cleonice da Silveira Teixeira, muito obrigado por todo o conhecimento compartilhado, por toda disposição e dedicação em ensinar, sempre buscando ajudar.

A Professora India Olinta de Azevedo Queiroz, agradeço por aceitar fazer parte da banca examinadora, dispondo de seu tempo e atenção para tornar este trabalho melhor.

RESUMO

O objetivo deste estudo *in vitro* foi investigar o efeito de doses cumulativas de radiação na resistência de união *push-out* de um cimento resinoso universal utilizados nos modos autocondicionante (AC) e autoadesivo (AA) à dentina intrarradicular. Quarenta e oito dentes humanos unirradiculares foram distribuídos em 3 grupos (n = 16), de acordo com a dose de radioterapia (RT): NoRT (sem radioterapia); 70RT (70 Gy); e 70+70RT (70 Gy+70 Gy). Após o tratamento endodôntico, os dentes foram redistribuídos em dois subgrupos (n = 8), de acordo com a abordagem adesiva para a cimentação de pinos de fibra de vidro: AC (NoRT-AC; 70RT-AC; e 70+70RT-AC) e AA (NoRT- AA; 70RT-AA; e 70+70RT-AA). As raízes foram seccionadas transversalmente em discos de dentina, que foram submetidos ao teste de resistência de união *push-out* em máquina universal de ensaios. Os padrão de falha foi avaliado em estereomicroscópio e microscópio eletrônico de varredura (MEV). Os dados foram comparados estatisticamente (*push-out* - ANOVA e teste post hoc de Tukey; padrão de falha - teste exato de Fisher - $\alpha = 0,05$). No modo AC, a resistência de união foi significativamente maior nos dentes não irradiados em comparação com os grupos 70RT e 70+70RT ($p < 0,0001$). Não houve diferenças significativas entre os modos AC e AA em dentes não irradiados ($p = 0,14$). No grupo 70RT, o modo AC aumentou a resistência de união em relação ao modo AA ($p < 0,0001$). A maioria dos espécimes apresentou falhas adesivas no modo AA. No modo AC, observou-se maior incidência de falhas mistas. O cimento resinoso universal no modo AC apresentou maior resistência de união à dentina intrarradicular irradiada. Quando os dentes foram re-irradiados, o cimento resinoso universal teve desempenho semelhante em termos de resistência de união push-out, independentemente da abordagem adesiva.

Palavras-chave: radioterapia, tratamento endodôntico, câncer de cabeça e pescoço, cimento resinoso, resistência de união.

LISTA DE FIGURAS

LISTA DE TABELAS

SUMÁRIO

1 INTRODUÇÃO

Os cânceres que atingem a região de cabeça e o pescoço (CCP) estão hoje entre os de segunda maior incidência em homens brasileiros acima dos 40 anos segundo o Instituto Nacional do Câncer “José Alencar Gomes da Silva” (INCA, 2022). Somente no ano de 2019, foram registradas 20.722 mortes por CCP (INCA, 2022). O carcinoma de células escamosas é o tipo histológico predominante, e aproximadamente 40% dos pacientes terão a doença diagnosticada em estágio avançado (III e/ou IV) quando avaliados pela primeira vez (INCA, 2022)

O consumo de álcool e tabaco está diretamente relacionado ao desenvolvimento de CCP (MYERS et al., 2003). A interação entre esses dois fatores etiológicos possui efeito multiplicativo, elevando consideravelmente as chances de surgimento destes tipos de cânceres, principalmente os da cavidade oral e faringe (HASHIBE et al., 2009). Segundo o INCA (2022), o álcool e o tabaco são responsáveis por 70% dos casos de CCP. Além desses principais fatores, a exposição à radiação ultravioleta tem papel fundamental no desenvolvimento de câncer de pele na região da face e lábios (KERAWALA et al., 2016). Ainda, o Papiloma vírus, principalmente o tipo 16, tem se mostrado como um fator etiológico importante no desenvolvimento do câncer de orofaringe em pessoas mais jovens (KERAWALA et al., 2016).

Quando diagnosticado em seu estágio inicial, o CCP pode ser tratado apenas com cirurgia e/ou quimioterapia (BRAAKHUIS et al., 2012). Nestes casos, tais modalidades de tratamento podem aumentar as chances de sobrevida dos pacientes entre 70% e 90% (MOORE et al., 2012; CHOW, 2020). Por outro lado, quando diagnosticado em estágio avançado, o CCP apresenta alto risco de recorrência local, variando entre 15% a 40%, e metástase à distância, com prognóstico desfavorável (BRAAKHUIS et al., 2012)

Para estes casos mais avançados, as opções de tratamento tradicionalmente incluem cirurgia seguida de radioterapia adjuvante (utilizada para controlar a doença após ressecção cirúrgica, com a intenção de eliminar tumor residual) ou quimiorradioterapia adjuvante (BRANA et al., 2012). A quimiorradioterapia é preconizada principalmente em casos em que está contraindicada a intervenção cirúrgica e onde não há a possibilidade de cura, atuando como tratamento paliativo para controlar o crescimento do tumor e reduzir os efeitos colaterais da doença (CHOW, 2020).

A radiação ionizante liberada durante o tratamento radioterápico age principalmente em estruturas críticas das células, causando a quebra da molécula de DNA, resultando na morte celular (LOPES et al., 2013). As células que apresentam alta atividade mitótica, como as células tumorais, tendem a ser mais afetadas pela radiação, devido à constante replicação de seu conteúdo genético (LOPES et al., 2013). Apesar de ser altamente eficaz no tratamento do CCP, a radiação ionizante não atinge apenas a massa tumoral, se estendendo também para os tecidos adjacentes (LOPES et al., 2013), promovendo reações adversas (RAY-CHAUDHURI et al., 2013).

Desta forma, um planejamento minucioso da dose de radiação entregue aos tecidos alvo e adjacentes deve ser realizado, levando em consideração a localização e o tamanho da massa tumoral (PARAHYBA et al., 2016). Para o tratamento de CCP, a dose padrão varia entre 55 e 70 Gy, sendo fracionada em doses de 1,5 a 2 Gy diários, por 5 dias consecutivos, até atingir a dose total preconizada (ZACKRISSON et al., 2003; REED et al., 2015). A aplicação desse protocolo de doses visa permitir que as células saudáveis se recuperem, além de permitir que a radiação atinja as células tumorais em diferentes estágios de divisão celular (JHAM & DA SILVA FREIRE, 2006). O prognóstico do tratamento com radioterapia depende de algumas variáveis, incluindo a radiossensibilidade da massa tumoral alvo e a radiossensibilidade dos tecidos normais circundantes (JHAM & DA SILVA FREIRE, 2006).

Apesar do relativo sucesso obtido no tratamento de pacientes portadores de CCP, a recidiva locorregional é comum em casos mais avançados, e menos da metade dos pacientes, neste caso, podem ser submetidos a nova cirurgia (YAMAZAKI et al., 2017; BAHL et al., 2018). A Radioterapia de Intensidade Modulada (IMRT) e seus refinamentos adicionais, como a radioterapia guiada por imagem (IGRT), permitem a re-irradiação destes pacientes, uma vez que é possível direcionar a radiação ionizante para a área tumoral, limitando seus efeitos colaterais nos tecidos adjacentes (YAMAZAKI et al., 2017; BAHL et al., 2018). Ainda assim, efeitos colaterais como a mucosite, hiposalivação, xerostomia e osteorradionecrose são comuns (RAY-CHAUDHURI et al., 2013). Diversas evidências científicas também indicam alterações significativas nas estruturas dentárias (JERVOE 1970; SOARES et al., 2010; DE MELLARA et al., 2014).

A quebra das moléculas de água promovida pela radiação ionizante leva à formação de radicais livres reativos, que, ao interagir com biomoléculas, resultam em danos estruturais (COLE & SILVER, 1963), principalmente na dentina, que possui estrutura altamente orgânica (NAVES et al., 2012). Estes radicais livres promovem a desnaturação dos componentes orgânicos, como o colágeno do tipo I, e a sua proteólise tem impacto direto na integridade estrutural deste tecido (PIOCH et al.,1992).

Os danos causados à matriz orgânica da dentina têm interferência direta nos procedimentos adesivos, levando a falhas na formação de uma camada hibrida adequada e sua longevidade (YADAV & YADAV, 2013). As fibrilas de colágeno presentes na dentina de dentes irradiados apresentaram alto grau de desorganização e fragmentação, dificultando a penetração de agentes adesivos e a formação da camada hibrida. (GONÇALVES et al., 2014). Nesses casos, ainda é possível observar fissuras e obliteração dos túbulos dentinários (GONÇALVES et al., 2014).

Em pacientes submetidos à radioterapia, a extração de dentes com grande perda coronária deve ser evitada, devido à elevada probabilidade de osteorradionecrose (BUGLIONE et al., 2016). Desta forma, a reabilitação destes dentes com pinos de fibra fixados adesivamente é altamente recomendada (FARIA E SILVA et al., 2007).

Durante o processo de adesão dos pinos à dentina intrarradicular, a retenção micromecânica promovida por cimentos resinosos é considerada um dos fatores mais importantes (PERDIGÃO et al., 2013). A retenção ocorre quando os monômeros hidrófilos que compõem os adesivos dentinários interpenetram a rede de fibrilas colágenas expostas, formando uma estrutura mista com fibrilas envolvidas por componentes resinosos e cristais de hidroxiapatita (PERDIGÃO et al., 2013). Quando a rede de fibrilas colágenas está colapsada pela radioterapia há uma deficiência na formação da camada hibrida (RODRIGUES et al., 2017).

Cimentos resinosos universais estão entre as mais recentes evoluções nos tratamentos adesivos (JOSIC et al., 2022; CARDENARO et al., 2023; MARAVIC et al., 2023). Podem ser utilizados em combinação com seu sistema adesivo próprio, ou no modo autoadesivo, dependendo da conduta clínica adotada (JOSIC et al., 2022; CARDENARO et al., 2023; MARAVIC et al., 2023). Breschi et al. (2023) reportaram em um estudo laboratorial resultados promissores quanto ao uso de cimentos resinosos universais, principalmente quando combinado ao seu sistema adesivo específico. Entretanto, não descartaram seu uso no modo autoadesivo, especialmente em casos em que a sensibilidade de uma técnica de múltiplos passos pode comprometer o resultado clínico final.

Alterações nas propriedades da dentina irradiada são comprovadas por diversos estudos (DE MELLARA et al., 2014; REED et al., 2015). Entretanto, não existem achados científicos que correlacionam o efeito de doses cumulativas de radioterapia, como nos casos de pacientes com recidiva locorregional, sobre a resistência de união do cimento resinoso à dentina intrarradicular (NOVAIS et al., 2016). Ainda, avanços recentes nas estratégias adesivas, como o uso de cimentos resinosos universais, podem melhorar significativamente a qualidade de vida de pacientes oncológicos submetidos a radioterapia que necessitem de reabilitação com pinos de fibra de vidro.

2 OBJETIVOS

2.1 OBJETIVO GERAL

- Avaliar o efeito de doses cumulativas de radioterapia na resistência de união de um cimento resinoso universal à dentina intrarradicular.

2.2 OBJETIVO ESPECÍFICO

- Avaliar a resistência de união de um cimento resinoso universal nos modos autocondicionante e autoadesivo à dentina intrarradicular irradiada e re-irradiada.

2.3 HIPÓTESES NULAS

- As doses cumulativas de radioterapia não afetarão a resistência de união do cimento resinoso universal à dentina intrarradicular.

- Os diferentes modos de cimentação (autocondicionante e autoadesivo) não apresentarão diferença na resistência de união do cimento resinoso à dentina intrarradicular irradiada.

3 ARTIGO CIENTÍFICO

Este estudo foi preparado e escrito na forma de artigo científico de acordo com as normas para submissão no periódico Journal of Esthetic and Restorative Dentistry (Qualis A3, Fator de Impacto 3.040).

Effect of cumulative doses of radiation therapy on the push-out bond strength of universal resin cement to intraradicular dentin

Gabriel Hernandez Machado de Souza[1] | Cleonice da Silveira Teixeira[1] | Lucas da Fonseca Roberti Garcia[1]

[1]Department of Dentistry - Endodontics Division, Health Sciences Centre, Federal University of Santa Catarina, Florianópolis, SC, Brazil.

Correspondence

Prof. Lucas F. R. Garcia - Department of Dentistry - Endodontics Division, Health Sciences Centre, Federal University of Santa Catarina, Campus Reitor João David Ferreira Lima, CEP: 88040-900, Florianópolis, Santa Catarina, Brazil. Telephone: +55 (48) 3721-4853E-mail address: drlucas.garcia@gmail.com

ABSTRACT

Objectives: To investigate the effect of cumulative doses of radiation on the push-out bond strength of a universal resin cement used in the self-etch (SE) and self-adhesive (SA) modes to the intraradicular dentin.

Materials and methods: Forty-eight single-rooted human teeth were distributed into 3 groups (n = 16) according to the radiation therapy dose (RT): NoRT (no-radiotherapy); 70RT (70 Gy); and 70+70RT (70 Gy+70 Gy). After endodontic treatment, the teeth were further redistributed into two subgroups (n = 8), according to the adhesive approach for fiberglass posts luting: SE (NoRT-SE; 70RT-SE; and 70+70RT-SE) and SA (NoRT-SA; 70RT-SA; and 70+70RT-SA). The roots were sectioned and submitted to the push-out bond strength test. Failure modes were classified under a stereomicroscope and a Scanning Electron Microscope (SEM). Data were statistically compared (push-out - ANOVA and Tukey's post hoc test; failure mode - Fisher's exact test - $\alpha = 0.05$).

Results: In the SA mode, bond strength was significantly higher in the non-irradiated teeth compared to 70RT and 70+70RT groups ($p < 0.0001$). There were no significant differences between the SE and SA modes in non-irradiated teeth ($p = 0.14$). In the 70RT group, the SE mode increased the bond strength compared to the SA mode ($p < 0.0001$). Most specimens had adhesive failures in the SA mode. In the SE mode, a higher incidence of mixed failures was observed.

Conclusions: The universal resin cement in the SE mode had greater bond strength to the irradiated intraradicular dentin. When teeth were re-irradiated, the universal resin cement had similar performance in terms of push-out bond strength, regardless of the adhesive approach.

Clinical significance: No studies so far have correlated the effect of cumulative doses of radiotherapy and the use of a universal resin cement used in both, self-etch and self-adhesive modes, on the bond strength to intraradicular dentin.

KEYWORDS

radiotherapy, universal resin cement, bond strength, adhesive approaches.

1 I INTRODUCTION

When diagnosed at an early stage, the different types of head and neck cancer (HNC) may be treated only with surgery and/or chemotherapy.[1] In these cases, such treatment protocols may increase the chances of patient survival between 70% and 90%.[2,3] Conversely, when diagnosed at an advanced stage, HNC has a high risk of local recurrence, ranging from 15% to 40%, and metastasis, with an unfavorable prognosis.[1]

In advanced cases, the treatment options for HNC traditionally include surgery followed by adjuvant radiotherapy (used to control the disease after surgical resection, to eliminate residual tumor) or adjuvant chemoradiotherapy.[4] Chemoradiotherapy is especially recommended when surgery is contraindicated, and there is no possibility of cure.[3] It is a palliative treatment to control tumor growth and reduce the side effects of the disease.[3]

The ionizing radiation released during radiotherapy acts on critical cell structures, leading to DNA breakage, and resulting in cell death.[3] Despite being highly effective in the HNC treatment, ionizing radiation does not only reach the tumor area but also extends to adjacent tissues,[3] promoting adverse reactions.[5]

For the HNC treatment, the standard dose of ionizing radiation ranges from 55 to 70 Gy, divided into doses of 1.5 to 2 Gy daily, for 5 consecutive days, until reaching the recommended total dose.[6,7] Despite the relative success obtained in the HNC treatment, locoregional recurrence is common in more advanced cases, and less than half of the patients, in this case, may be submitted to a new surgery.[8,9] The Intensity Modulated Radiotherapy Technique (IMRT) and its additional refinements, such as Image-Guided Radiotherapy (IGRT), allow the re-irradiation of these patients, as it is possible to direct the ionizing radiation to the tumor area, limiting the side effects in the adjacent tissues.[8,9] Even so, side effects such as mucositis, hyposalivation, xerostomia, and osteoradionecrosis are common.[5] Scientific evidence also indicate significant changes in the dental structures.[10-12]

The breakdown of water molecules by ionizing radiation leads to reactive free radicals formation.[13] The free radicals, when interacting with biomolecules, promote structural damage to dentin,[13] which has a high organic content.[14] The denaturation of the organic content, such as type I collagen, and its proteolysis has a direct impact on the structural integrity of dentin.[15]

The damage caused to the organic matrix of dentin directly interferes with the adhesive procedures, leading to failures in the hybrid layer and its longevity.[16] The collagen fibrils of irradiated teeth showed higher levels of disorganization and fragmentation, hindering the adhesive agent's infiltration and the formation of a proper hybrid layer.[17] In these cases, it is still possible to observe fissures and obliteration of the dentinal tubules.[17]

In patients undergoing radiotherapy, teeth extraction should be avoided due to the high risk of osteoradionecrosis.[18] Therefore, rehabilitation of teeth with great coronal destruction using luted fiber posts is highly recommended.[19]

During fiberglass posts luting, the micromechanical retention promoted by resin cement to the intraradicular dentin is considered one of the most important factors.[20] Posts' retention occurs when the hydrophilic monomers from adhesive agents infiltrate the exposed collagen fibrils network, forming a structure containing fibrils surrounded by resinous components and hydroxyapatite crystals.[20] When the collagen fibrils network is collapsed by radiotherapy, the hybrid layer formation is compromised.[21]

The use of universal resin cement is the most recent evolution in adhesive strategies.[22-24] They can be used in combination with their specific adhesive system (etch-and-rinse or self-etch), or in the self-adhesive mode, depending on the clinical approach adopted.[22-24] Breschi et al.[25] have reported in a laboratory study promising results regarding the use of universal resin cements, especially when combined with their specific adhesive system. However, the authors did not discard their use in the self-adhesive mode, especially in cases where the sensitivity of a multi-step technique could compromise the final clinical result.[25]

Changes in the properties of irradiated dentin are highly documented by several studies.[6,7,11,12,14] However, there is no scientific evidence correlating the effect of cumulative doses of radiotherapy (locoregional recurrence)[8] on the bond strength of resin cement to intraradicular dentin.[26] Also, recent advances in adhesive strategies, such as the use of universal resin cements, may improve the life quality of oncological patients undergoing radiotherapy who need rehabilitation with fiberglass posts.

Therefore, this *in vitro* study investigated the effect of cumulative doses of radiation therapy on the push-out bond strength of a universal resin cement used in the self-etch and self-adhesive modes to the intraradicular dentin. The following null hypotheses were tested: I) the cumulative doses of radiotherapy would not affect the bond strength of the universal resin cement to intraradicular dentin; II) the different adhesive approaches (self-etch and self-adhesive) would not affect the bond strength of the resin cement to the irradiated intraradicular dentin.

2 I MATERIALS AND METHODS

2.1 I SAMPLE SELECTION

The present study was previously approved by the Research Ethics Committee (CAAE: 26203019.9.1001.0121) and conducted under the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Based on the study by de Souza et al.,[27] the sample size was calculated with the G*Power software (version 3.1.9.6) (http://www.psycho.uni-duesseldorf.de/abteilungen/aap/gpower3/). The calculation was performed according to the following parameters: $\alpha = 0.05$, Power (1-ß err prob) = 0.95, and effect size f = 0.80. The type of power analysis was set *a priori* (compute required sample size - given α, power, and effect size), and then, the ANOVA (fixed effects, special, main effects, and interactions) statistical test was performed. The calculation allocated a minimum of eight specimens to each control or experimental group.

After rigorous visual inspection under magnifying lens (×4) and radiographic examination, 48 freshly extracted single-rooted mandibular premolars, with a single and straight canal, and closed apex, were selected for this study. The radiographic images were also used to calculate the dimensions of the root canal at the 2- and 5-mm cervical to the apical foramen.[28] Only teeth with a total length of 15 mm and a ratio of the buccolingual and mesiodistal dimension ≤1.5 were selected.[29] Teeth with caries, fractures, cracks, or signs of calcification or internal resorption were discarded from the final sample and replaced.

The teeth were stored in 0.5% chloramine T solution for one month for disinfection and then placed in plastic flasks containing distilled water. The flasks were stored in an oven at 37°C to avoid dehydration until the experiment was carried out. The teeth were decoronated 1 mm above the cementoenamel junction with a double-sided diamond disk (152.4 mm x 0.5 mm x 12.7 mm) (Buehler, Lake Forest, IL, EUA) mounted on a high-precision metallographic cutter (Isomet 1000; Buehler), under abundant water cooling.

2.2 I RADIOTHERAPY PROTOCOL

The roots were randomly distributed (www.random.org) into 3 groups (n = 16), according to the radiotherapy dosage delivered (Figure 1). NoRT was not submitted to radiotherapy, being considered the control group. 70RT was submitted to a total radiation dose of 70 Gy; and 70+70RT to cumulative doses of 70 Gy + 70 Gy.

The irradiation of the specimens was performed at the Department of Radiotherapy of the Oncology Research Center (CEPON - Florianópolis, SC, Brazil) under the supervision of a physicist and a radio-oncologist. The radiotherapy equipment used was a linear accelerator (Clinac 2100C; Varian Medical Systems, Inc., Palo Alto, CA, USA) using the Intensity Modulated Radiotherapy Technique (IMRT) with dynamic collimators (Dynamic Multileaf Collimator - DMLC).

The specimens were immersed in distilled and deionized water inside a plastic support aligned to be equidistant from the center of the beam to allow a proper radiation dose rate distribution (400 UM/min).[30,31] Radiation therapy was fractionated into daily doses of 2 Gy, 5 days a week, for 7 weeks (70RT group), or 14 weeks (70+70RT group) with 6MV of energy (photons).[7,30-32]

The distilled and deionized water was discarded at the end of each irradiation cycle. The specimens were kept in artificial saliva at 37ºC overnight to simulate the oral conditions, and to perform a new cycle, the artificial saliva was replaced with new distilled and deionized water.[30,31] At the end of the radiotherapy protocol (7 or 14 weeks), the specimens were stored in artificial saliva at 37ºC until the experiment.

2.3 I ENDODONTIC PROCEDURES

On completion of the radiotherapy protocol, the specimens from the experimental and control groups were submitted to endodontic treatment. Root canals were negotiated with a size 10 K-file (Dentsply-Maillefer, Ballaigues, Switzerland). The working length (WL) was established at 1.0 mm short of the apical foramen. The chemomechanical preparation was performed with the R40 (40/.06) instrument (Reciproc; VDW GmbH, Munich, Germany) driven by an electric motor (VDW Silver Reciproc; Sirona Dental Systems GmbH, Bensheim, Germany), in the “RECIPROC ALL” mode, according to the manufacturer's instructions. Preparation was performed by root thirds (cervical, middle, and apical). The instrument was gradually inserted in a slow in-and-out pecking motion, for three pecking movements. At the end of each root third preparation, the instrument was removed from the root canal and cleaned with sterile gauze soaked in 70% alcohol. At this moment, the root canal was irrigated with 2 mL of 2.5% sodium hypochlorite solution (Fórmula e Ação, São Paulo, SP, Brazil), using a 30-gauge needle (Ultradent Products Inc., South Jordan, UT, USA) coupled to a 5-mL plastic syringe (Ultradent Products Inc.) 2 mm shorter the WL. Apical patency was performed by inserting a size 15 K-file through the apical foramen. Each reciprocating instrument was used to prepare only one root canal.

On completion of root canal preparation, each root canal was irrigated with 3 mL of 17% ethylenediamine tetra-acetic acid (EDTA) (Biodinâmica, Ibiporã, PR, Brazil) for 3 minutes, followed by irrigation with 2 mL of 2.5% sodium hypochlorite solution (Fórmula e Ação) for another 3 minutes for the smear layer removal. Next, the root canals were dried by aspiration with the aid of a Capillary Tip cannula (Ultradent Products Inc.) and R40 absorbent paper cones (Reciproc; VDW GmbH). Root canal obturation was performed using the lateral compaction technique, with an epoxy resin-based cement (AH Plus Jet; Dentsply, Petrópolis, RJ, Brazil) and gutta-percha cones (VDW GmbH).

2.4 I FIBERGLASS POSTS LUTING

The materials used in the adhesive procedures are described in Table 1. The specimens were redistributed into 6 subgroups (n = 08) according to the adhesive mode of the universal resin cement used for fiberglass posts luting: self-etch (SE) and self-adhesive (SA). Then, the following experimental groups were formed: NoRT-SE, 70RT-SE, and 70+70RT-SE; and NoRT-SA, 70RT-SA, and 70+70RT-SA (Figure 1).

Initially, the roots were inserted into silicone molds (Express XT; 3M, Sumaré, SP, Brazil) to simulate the alveolar bone and prevent the passage of light during light-curing.[27] After a new radiographic examination, 2/3 of the filling material was removed with the aid of Gates-Glidden burs (Dentsply-Malleifer). The endodontic space was prepared with the specific drills of the fiberglass post system (Power Post Nº 2; BM4, Maringá, PR, Brazil). The root canals were rinsed with distilled water and aspirated. The fiberglass posts were tested inside the root canal to ensure proper adaptation and confirm their length. Next, each post was sectioned 4 mm above the cervical limit of the root canal with a diamond bur, under abundant water cooling. The fiberglass posts were cleaned with 70% alcohol for 30 seconds, jet air-dried for 5 seconds, and then, coated with a layer of silane bonding agent (Prosil; FGM, Joinville, SC, Brazil). The silane was applied and rubbed on the post surface for 60 seconds, and jet air-dried for 5 seconds.

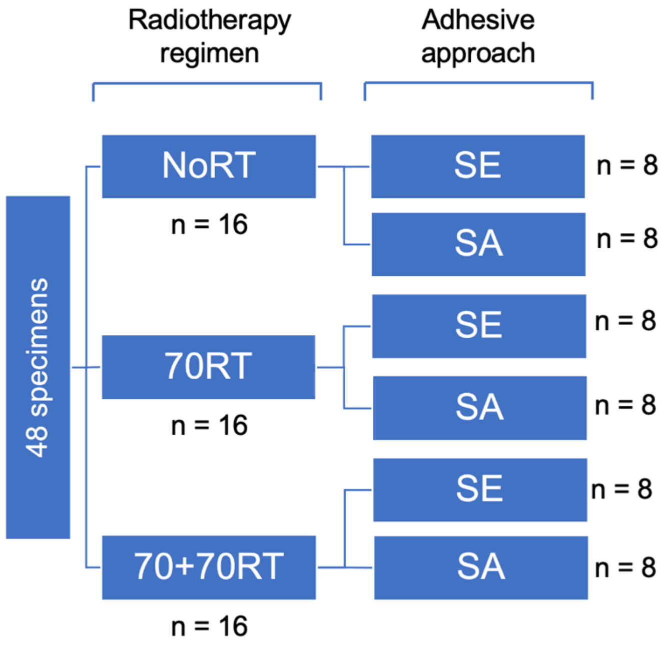

FIGURE 1 Experimental group distribution.

TABLE 1 Materials used for the adhesive procedures.

Material	Composition*	Manufacturer
Scotch Bond Universal Plus (adhesive system)	Brominated dimethacrylate, HEMA, 10-MDP, 2-Propenoic acid, 2-methyl-, 3-(triethoxysilyl) propyl ester, reaction products with silica and 3-(triethoxysilyl)-1-propanamine, ethanol, water, Synthetic amorphous silica, fumed, crystalline-free, γMPTES, Camphorquinone, Copolymer of acrylic and itaconic acid, N,ndimethylbenzocaine, APTES, DEGDMA, Acetic acid, copper(2+) salt, monohydrate.	3M ESPE, Sumaré, SP, Brazil
RelyX Universal (resin cement)	Base paste: γMPTES, reaction products with vitreous silica, DUDMA, TEGDMA, Mixture of GPDMA, bis-GPDMA, and tris-GPDMA, Silane treated silica, t-Amyl Hydroperoxide, 2,6-Di-tert-butyl-pcresol, HEMA, Methyl Methacrylate, Acetic acid, copper(2+) salt, monohydrate. Catalyst paste: Ytterbium (III) fluoride, Silane-treated glass powder, TEGDMA, L-Ascorbic acid, 6-hexadecanoate, hydrate (1:2) Silane treated silica, HEMA, Titanium Dioxide, Triphenyl Phosphite.	

*Composition of the materials according to the manufacturers' websites and documents. Abbreviations: 10-MDP, 10-Methacryloyloxydecyl dihydrogen phosphate; APTES, (3-aminopropyl)triethoxysilane; bis-GPDMA, bis(gliceryldimethacrylate) phosphate; DEGDMA, Diethylene glycol dimethacrylate; DUDMA, diurethane dimethacrylate; HEMA, 2-Hydroxymethacrylate; TEGDMA, Triethyleneglycol dimethacrylate; tris-GPDMA, tris(glyceryldimethacrylate) phosphate; γMPTES, 2-Propenoic acid, 2-methyl-, 3-(trimethoxysilyl)propyl ester.

In the groups where the universal resin cement was used in the SE mode, a thin layer of adhesive (Scotch Bond Universal Plus; 3M ESPE) was applied and rubbed on the silanized post surface for 20 seconds, and jet air-dried for 5 seconds. The posts were reserved until use. The root canal was rinsed with distilled water, and the excess moisture was removed with absorbent paper points. A layer of adhesive was applied and rubbed for 20 seconds on the root canal walls. The excess adhesive was gently removed with an air jet for 5 seconds. Light-curing of the adhesive was performed for 40 seconds (Bluephase N, Ivoclar Vivadent, Schaan, Austria, intensity ≥1200 mW/cm^2, wavelength 460-480 nm). In the groups where the universal resin cement was used in the SA mode, the root canals were also previously rinsed with distilled water, followed by the removal of moisture excess with absorbent paper points. However, no adhesive was applied to the root canal walls.

In all groups (control and experimental), the universal resin cement (RelyX Universal; 3M ESPE) was placed inside the root canal with a self-mixing tip. Next, a thin layer of cement was applied on the fiberglass post, which was apically inserted into the root canal in a rotating motion. After the resin cement excess removal, light-curing was performed for 60 seconds (Bluephase N; Ivoclar Vivadent).

After the fiberglass posts' luting, the coronal portion was protected with composite resin to prevent microleakage. Pre-etching of the dentin surface was performed with 37% phosphoric acid (Fusion-Duralink; Angelus, Londrina, PR, Brazil) for 15 seconds, followed by copious washing with distilled water for 30 seconds, and drying with absorbent paper. Two layers of adhesive (Single Bond; 3M ESPE) were applied on the dentin surface for 20 seconds each, and jet air-dried for 5 seconds. The adhesive was light-cured for 20 seconds. A 2.0-mm thick increment of composite resin (Z100, 3M, Sumaré, SP, Brazil) was placed and light-cured for 40 seconds.

2.5 I PUSH-OUT BOND STRENGTH

On completion of fiberglass posts' luting, the roots were removed from their silicone molds and embedded in colorless self-curing acrylic resin (JET, Clássico, São Paulo, SP, Brazil) to form resin blocks (25.0 mm x 10.0 mm). The resin blocks were coupled to a metallographic cutter (SYJ - 150 Digital Diamond Low-Speed Saw 4, MTI Crystal, Richmond, CA, USA), and transversely sectioned in relation to their longitudinal axis with a double-sided diamond disk Nº 11-4243 (Buehler, Lake Bluff, IL, USA), under abundant water cooling. Two dentin slices 1.0-mm thick (+ 0.1 mm) were obtained per root third (cervical, middle, and apical). The thickness of the dentin slices was checked with a digital caliper (Starret 727; Starret, Itu, SP, Brazil).

Each dentin slice was carefully positioned on a stainless-steel metallic base containing a 2.5 mm diameter hole in its central portion. The base was coupled to the lower portion of the universal testing machine (Model 4444; Instron, Canton, MA, USA). Metallic cylindrical plungers with a diameter similar to the root canal/fiberglass post (0.47 mm to 1.3 mm) in each dentin slice (cervical, middle, and apical third) were fixed in the upper portion of the machine. The metallic plunger diameter was selected according to the proportion of 0.7/1.0.[33] Then, a compressive force was apically applied (crosshead speed of 0.5 mm/min) until dislodgement of the post/resin cement set.[27] The compressive force was applied from the apical to the cervical direction of the dentin slices. The force for the material dislodgement was measured in kiloNewtons (kN), transformed into Newtons (N), and divided by the bonding surface area (mm^2). Then, the values were converted into MPa (MegaPascal). The bonding surface area was obtained with the formula:

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

where, R = root canal radius in its cervical portion; r = root canal radius in its apical portion; and h = height/thickness of the dentin slice.[27]

2.6 I FAILURE MODE ANALYSIS

After the push-out bond strength test, the fractured specimens were analyzed under a stereomicroscope (SteREO Discovery V12; Carl Zeiss, Jena, Germany) at ×40 magnification, for the failure mode classification: a) adhesive - dentin surface free of resin cement; b) cohesive of the cement - fracture of the bonding area, with part of the intraradicular dentin covered by cement; c) cohesive of the fiberglass post - post fracture; and d) mixed - two, or more, different types of failure in the same specimen. The failure mode was expressed as a percentage. The analysis was performed by a single examiner, blinded, and previously calibrated.

Representative samples of the different failure modes were taken to Scanning Electron Microscope (SEM) (Jeol JSM 5410, Sony, Tokyo, Japan) for new image acquisition. The samples were attached with double-sided carbon tape onto metallic stubs and sputter-coated with a gold-palladium alloy layer (300Å to 500Å) under a high vacuum (Denton Vacuum, Desk II, Moorestown, NJ, USA) for 120 seconds. SEM was operated at 15 kV. Samples were examined at ×500, ×1000, and ×1500 magnifications.

2.7 I STATISTICAL ANALYSIS

The statistical analysis was performed using the IBM SPSS Statistics software (IBM Corp., Armonk, NY, USA). The normality of the data distribution, and the equality of variances, were confirmed by the Shapiro-Wilk and Levene tests, respectively ($p > 0.05$). Parametric tests were applied. The effect of radiotherapy, the adhesive approaches, and their interaction, were initially analyzed by the ANOVA test, and complemented by Tukey's post hoc test ($p < 0.05$). The influence of the root thirds was analyzed by the ANOVA test for repeated data, and complemented by Tukey's post hoc test ($p < 0.05$). The failure mode distribution within the experimental and control groups was analyzed by Fisher's exact test ($p < 0.05$). The significance level was set at 5% ($\alpha = 0$ .05).

3 I RESULTS

3.1 I RADIATION THERAPY

Radiotherapy significantly affected the bond strength values ($p < 0.0001$). In the SA mode, the universal resin cement showed greater bond strength in non-irradiated specimens compared to specimens irradiated with 70 Gy and 70+70 Gy ($p < 0.0001$). These differences occurred in the cervical ($p = 0.0003$) and middle thirds ($p = 0.0012$). There were no significant differences in bond strength values between groups irradiated with 70 Gy and 70+70 Gy ($p = 0.375$).

In the SE mode, the universal resin cement also showed greater bond strength in non-irradiated specimens compared to specimens irradiated with 70 Gy and 70+70 Gy ($p < 0.0001$). However, the bond strength in the cervical third in the specimens irradiated with 70 Gy was significantly higher than in specimens irradiated with 70+70 Gy ($p < 0.0001$). In the middle third, non-irradiated specimens and specimens irradiated with 70 Gy showed greater bond strength than specimens irradiated with 70+70 Gy ($p = 0.0005$). In the apical third, the universal resin cement showed greater bond strength in non-irradiated specimens when compared to specimens irradiated with 70+70 Gy ($p = 0.0047$) (Table 2).

3.2 I ADHESIVE APPROACHES

In the non-irradiated specimens, both adhesive approaches (SE and SA) and canal location (root thirds) had no significant effect on the push-out strength of the universal resin cement ($p = 0.121$). On the other hand, in the specimens irradiated with 70 Gy, the universal resin cement in the SE mode showed greater bond strength than in the SA mode ($p < 0.0001$), in all root thirds. In the specimens irradiated with 70+70 Gy, the adhesive approaches had no significant effect on the push-out strength of the universal resin cement ($p = 0.273$) (Table 2).

TABLE 2 Mean values and standard deviation of bond strength (MPa) for universal resin cement considering the radiation therapy regimen and the adhesive approaches.

Root thirds	Adhesive approaches	Radiotherapy regimen			
		Non-irradiated	**70 Gy**	**70+70 Gy**	p-value
Cervical	Self-adhesive	$7.94 \pm 1.86^{A,a}$	$4.84 \pm 1.95^{B,a}$	$3.22 \pm 1.72^{B,a}$	0.0003
	Self-etch	$9.15 \pm 0.93^{A,a}$	$7.19 \pm 2.19^{B,b}$	$4.07 \pm 1.24^{C,a}$	< 0.0001
	p-value	0.1210	0.04	0.2739	
Middle	Self-adhesive	$6.93 \pm 1.90^{A,a}$	$4.13 \pm 1.27^{B,a}$	$3.83 \pm 1.36^{B,a}$	0.0012
	Self-etch	$7.33 \pm 0.77^{A,a}$	$6.31 \pm 0.78^{A,b}$	$4.67 \pm 1.50^{B,a}$	0.0005
	p-value	0.5966	0.001	0.258	
Apical	Self-adhesive	$5.97 \pm 1.75^{A,a}$	$4.09 \pm 1.47^{A,a}$	$4.00 \pm 1.99^{A,a}$	0.0598
	Self-etch	$6.53 \pm 0.65^{A,a}$	$5.63 \pm 1.05^{AB,b}$	$4.40 \pm 1.53^{B,a}$	0.0047
	p-value	0.4206	0.0309	0.6625	

Uppercase letters in lines: radiotherapy comparisons (ANOVA and Tukey's post-test).
Lowercase letters in columns: adhesive approaches (ANOVA and Tukey's post-test).

3.3 I ROOT THIRDS

In the SA mode, there was no significant difference in the bond strength values among root thirds in non-irradiated specimens ($p = 0.1241$), as well as specimens irradiated with 70 Gy (p = 0.5795) or 70+70 Gy ($p = 0.6409$). In the SE mode, significantly greater bond strength values were observed in the cervical third compared to the middle and apical thirds in the non-irradiated specimens. ($p < 0.0001$). When the universal resin cement was used in SE mode, no significant differences were observed among root thirds in the specimens irradiated with 70 Gy ($p = 0.1263$) and 70+70 Gy ($p = 0.7123$) (Table 3).

TABLE 3 Mean values and standard deviation of bond strength (MPa) for universal resin cement considering the different root thirds.

Adhesive approaches	Radiotherapy regimen	Root thirds			
		Cervical	**Middle**	**Apical**	p-value
Self-adhesive	Non-irradiated	7.94 ± 1.86^{A}	6.93 ± 1.90^{A}	5.97 ± 1.75^{A}	0.1241
	70 Gy	4.84 ± 1.95^{A}	4.13 ± 1.27^{A}	4.09 ± 1.47^{A}	0.5795
	70+70 Gy	3.22 ± 1.72^{A}	3.83 ± 1.36^{A}	4.00 ± 1.99^{A}	0.6409
Self-etch	Non-irradiated	9.15 ± 0.93^{A}	7.33 ± 0.77^{B}	6.53 ± 0.65^{B}	< 0.0001
	70 Gy	7.19 ± 2.19^{A}	6.31 ± 0.78^{A}	5.63 ± 1.05^{A}	0.1263
	70+70 Gy	4.07 ± 1.24^{A}	4.67 ± 1.50^{A}	4.40 ± 1.53^{A}	0.7123

Uppercase letters in lines: root thirds comparisons (ANOVA for repeated data and Tukey's post-test)

3.4 I FAILURE MODE ANALYSIS

Figure 2 presents the frequency of failure modes in each experimental and control group. Representative SEM images of the failure modes may be seen in Figure 3. Radiotherapy did not affect the frequency of failure modes in any of the root thirds. Therefore, no significant differences were observed between irradiated and non-irradiated specimens, regardless of the adhesive approach ($p > 0.05$). When the universal resin cement was used in the SA mode, there was a predominance of adhesive-type failures ($p > 0.05$), while in the SE mode, there was a higher incidence of mixed failures, both in non-irradiated ($p = 0.007$) and irradiated with 70 Gy ($p = 0.05$). In the specimens irradiated with 70+70 Gy, there was no difference among the failure modes, regardless of the adhesive approach ($p = 0.385$).

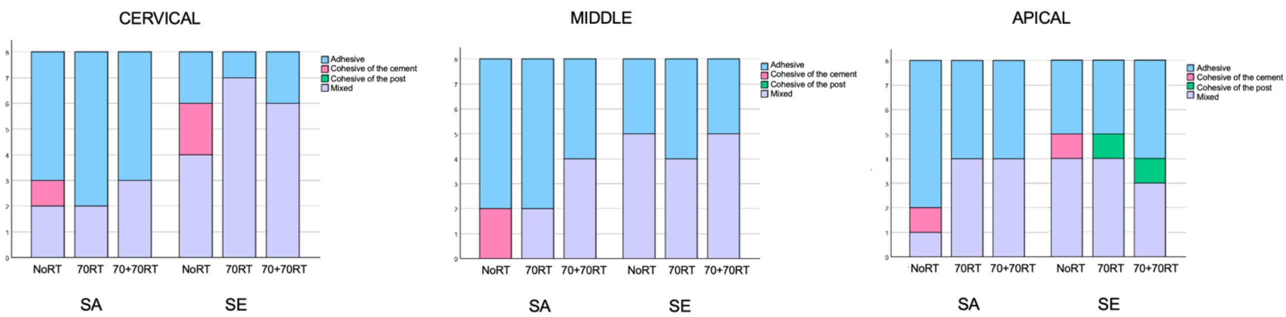

FIGURE 2 Graphical representation of the failure mode (%) at the different root thirds.

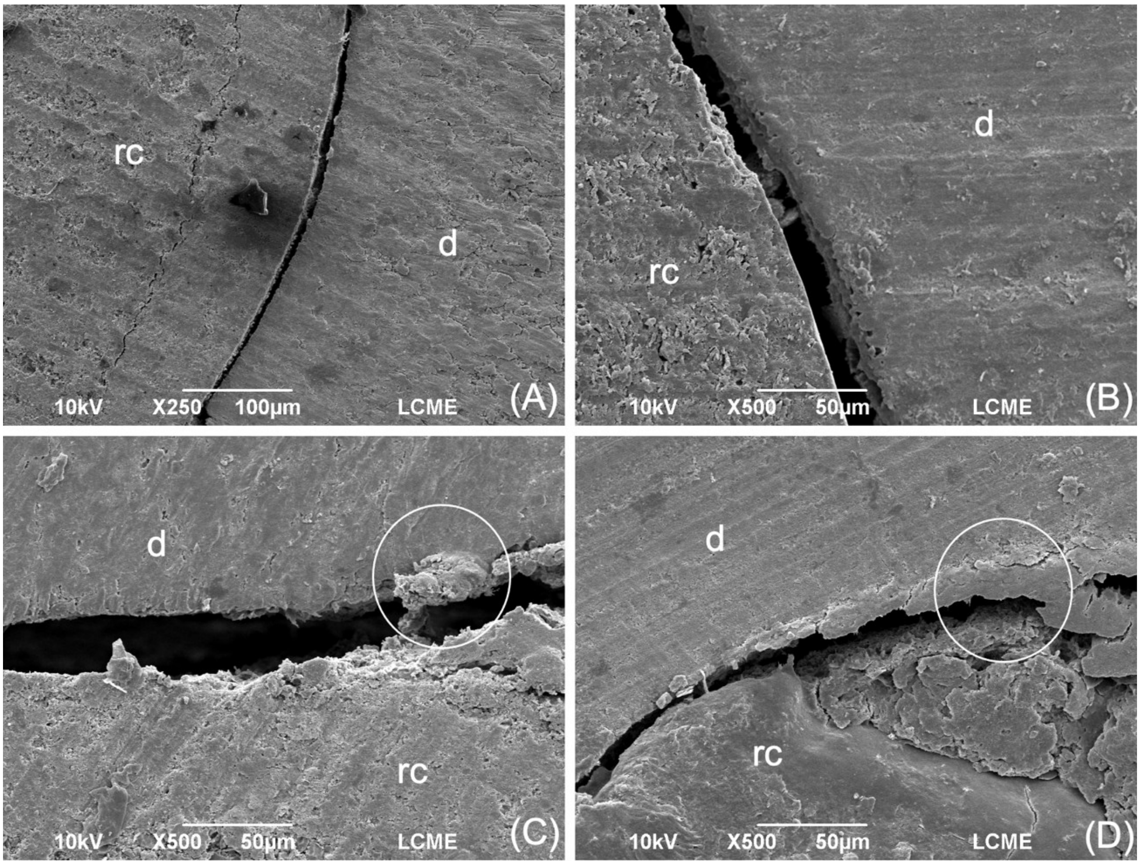

FIGURE 3 Representative SEM images of the failure mode after the push-out bond strength test. (A) Adhesive failure (SA mode/non-irradiated); dentin (d), resin cement (rc). (B) Adhesive failure (SA/70 Gy); dentin (d), resin cement (rc). (C) Mixed failure (SE/70 Gy). Areas corresponding to adhesive and cohesive failures of the resin cement (circle). dentin (d), resin cement (rc). (D) Cohesive failure of the resin cement (SE/non-irradiated). Note the fracture of the bonding area, with part of the intraradicular dentin covered by the adhesive/resin cement (circle). dentin (d), resin cement (rc).

4 I DISCUSSION

The present study assessed the effect of different radiotherapy regimens (70 Gy and 70+70 Gy) on the push-out bond strength of a universal resin cement used in the SE and SA modes to the intraradicular dentin. According to our results, both null hypotheses tested were partially accepted. The different radiotherapy regimens affected the bond strength of the universal resin cement only when it was used in the SE mode. The universal resin cement in the SE mode had greater bond strength than in the SA mode for specimens irradiated with 70 Gy. However, for specimens irradiated with cumulative doses, there were no differences between both adhesive approaches.

Regarding the methodological aspects of this laboratory study, for an appropriate standardization of specimens, only root canals with buccolingual and mesiodistal ratios ≤1.5 were selected.[29] For the push-out test, metallic cylindrical plungers similar in diameter to the root canal/fiberglass post area in the different root thirds were used to properly measure the adhesiveness of the universal resin cement to the intraradicular dentin in the different portions of the root canal.[34]

During radiotherapy, the specimens were completely immersed in distilled and deionized water, as recommended by other similar studies.[30,31] The distilled and deionized water was discarded at the end of each irradiation cycle, and the specimens were kept in artificial saliva overnight to simulate the oral conditions.[30,31] Artificial saliva is mainly composed of water, carboxymethyl cellulose, glycerin, and flavoring agents.[35] The viscosity and ion concentration of artificial saliva might affect the delivery of ionizing radiation to the specimens.[35] Therefore, to avoid dehydration and to allow a uniform distribution of the radiation doses to each one of the specimens, in the present study, they were stored in distilled water during irradiation.[30,31]

Most HNC are treated with radiation doses up to 70 Gy, distributed into 2 Gy fractioned daily doses.[36] However, re-irradiation of patients with locoregional recurrence is a common clinical approach in more advanced cases of HNC.[8,9] Bearing this in mind, in this study, different radiation therapy regimens were tested, simulating clinical protocols in which HNC patients needed to be subjected to new radiotherapy treatment. The IMRT with dynamic collimators was used for specimen irradiation. This technique is widely adopted during the oncological clinical routine, as it allows the delivery of high doses of irradiation to the tumor mass, minimizing exposure of healthy tissues to irradiation.[37,38]

Despite these technical advances, radiation therapy may lead to severe destruction of the adjacent structures to the tumor area, especially the hard and soft tissues of the oral cavity.[17,30,39] The radiation collapses the structure of the dentin collagen matrix, and promotes morphological and chemical changes in the intertubular and peritubular dentin, hindering the adhesion of restorative materials.[17,30,39] Therefore, it is valid to infer that in re-irradiated patients, adhesion protocols are a more challenging procedure.

According to the manufacturer's recommendations, the universal resin cement used in this study (RelyX Universal; 3M ESPE) may be used in the etch-and-rinse, self-etch, and self-adhesive modes. Universal resin cements represent a novelty in dental adhesive strategies, and for this reason, there are few studies assessing this type of resin cement,[23,25] especially, involving irradiated dentin. Therefore, the bond strength of universal resin cements on teeth undergoing radiotherapy is a gap in the scientific literature to be bridged.

In the present study, the universal resin cement was tested only in the SE and SA modes. The difficulty in applying the resin cement inside the root canal, the incomplete evaporation of the adhesive agent solvent, especially in the apical third, and the poor moisture control, are among the greatest difficulties in using multi-step adhesive systems, such as the etch-and-rinse ones.[40] Therefore, SE and SA resin cements are increasingly used to overcome the limitations of posts luting in the deepest portions of the endodontic space.[40] In addition, it is important to note that, pre-etching of the dentin substrate with phosphoric acid might result in greater damage to a tissue largely compromised by the irradiation doses delivered to it.[32]

The results from our laboratory study revealed that radiotherapy negatively affected the bond strength of the universal resin cement to dentin, regardless of the adhesive approach. It is a consensus that bonding on irradiated teeth is highly compromised.[41] However, in the specimens irradiated with 70 Gy, the universal resin cement in the SE mode had greater bond strength than in the SA mode in all root thirds. Breschi et al.[25] have reported that the bonding performance of universal resin cement to dentin is improved when using their specific adhesive systems.

Functional acidic monomers are incorporated into universal resin cements, and/or their respective adhesive systems, to etch, and simultaneously, infiltrate the dentin, forming chemical bonds with the ions calcium from hydroxyapatite and the methacrylate monomers.[23,42-44] Several functional acidic monomers may be used in resinous materials formulation.[23,42-44] However, the gold standard functional acidic monomer currently is the 10-MDP (10-methacryloyloxydecyl dihydrogen thiophosphate).[23,42-44] This phosphoric acid/methacrylate group molecule can create highly stable chemical bonds with the hydroxyapatite, forming 10-MDP-Ca salts, hydrogen bonds with the collagen network, and bond with the carbon chain of the resin monomers.[23,42-44]

Furthermore, 10-MDP-Ca salts can inhibit dentinal matrix-metalloproteinases (MMPs) activity.[23,42-44] Queiroz et al.[45] have reported that radiotherapy increases the MMPs activity. When activated, MMPs are related to several complex phenomena, such as hybrid layer degradation.[20,45] The universal resin cement used in this study contains the functional acidic monomer 10-MDP in its adhesive system.[23,42-44] This fact may explain the better performance of the cement in the self-etch mode on the dentin substrate irradiated with 70 Gy.[23,42-44] Further studies correlating universal resin cements containing 10-MDP to MMPs activity/inhibition on irradiated dentin should be performed.

One of the most important characteristics of universal resin cements is the possibility of associating these two adhesive approaches to benefit from both strategies, depending on the clinical scenario.[25] Conversely, in the re-irradiated specimens, there were no differences between the adhesive approaches. It may be hypothesized that, in this case, the radiotherapy regimen was a key point for determining the bond strength values. Radiotherapy has harmful effects on the organic portion of dentin[17,30,39], and re-irradiation seems to be more relevant in this scenario than the bonding strategy.

Regarding the failure mode, no significant differences were observed between irradiated and non-irradiated specimens, regardless of the adhesive approach. When the universal resin cement was used in the SA mode, there was a predominance of adhesive-type failures, while in the SE mode, a higher incidence of mixed failures, both in non-irradiated and irradiated specimens (70 Gy and 70+70 Gy), was noted. These findings are in line with the push-out bond strength results, as the universal resin cement in the SE mode had a better performance than in the SA mode.

The different forms of HNC are among the most common cancer worldwide.[46] The understanding of the effects of radiation therapy on teeth to properly restore their function and esthetics is essential. Thus, the development of clinical protocols based on scientific evidence must be a basic premise for these oncological patients.

5 I CONCLUSION

This is the first investigation assessing the effect of cumulative doses of radiation therapy on the push-out bond strength of a universal resin cement used in the self-etch and self-adhesive modes to the intraradicular dentin. Within its limitations, the current laboratory data concerning the use of universal resin cement in both adhesive approaches are promising. Radiotherapy negatively affected the bond strength of the universal resin cement to intraradicular dentin, regardless of the adhesive approach. However, in the irradiated specimens, the universal resin cement in the self-etch mode showed greater bond strength than in the re-irradiated specimens. In the self-adhesive mode, the radiotherapy regimen was determinant for decreasing the bond strength of the universal resin cement.

DISCLOSURE

The authors declare that they do not have any financial interest in the companies whose materials are included in this article.

ACKNOWLEDGMENTS

The authors would like to thank the Department of Radiotherapy of the Center for Oncological Research (CEPON - Florianópolis, SC, Brazil) for irradiating the specimens, and the company BM4 – Brasil materials e instrumentalais LTDA (Maringá - PR) for donating the dental fiber post.

DATA AVAILABILITY STATEMENT

Data sharing does not apply to this article as no datasets were generated or analyzed during the current study.

REFERENCES

1. Braakhuis BJ, Brakenhoff RH, Leemans CR. Treatment choice for locally advanced head and neck cancers on the basis of risk factors: biological risk factors. Ann Oncol. 2012;23(Suppl 10):x173-x177.
2. Moore EJ, Janus J, Kasperbauer J. Transoral robotic surgery of the oropharynx: Clinical and anatomic considerations. Clin Anat. 2012;25(1):135-141.
3. Chow LQM. Head and neck cancer. N Engl J Med. 2020;382(1):60-72.
4. Brana I, Siu LL. Locally advanced head and neck squamous cell cancer: treatment choice based on risk factors and optimizing drug prescription. Ann Oncol. 2012;23(Suppl 10):x178-x185.
5. Ray-Chaudhuri A, Shah K, Porter RJ. The oral management of patients who have received radiotherapy to the head and neck region. Br Dent J. 2013;214(8):387-393.
6. Zackrisson B, Mercke C, Strander H, et al. A systematic overview of radiation therapy effects in head and neck cancer. A systematic overview of radiation therapy effects in head and neck cancer. Acta Oncol. 2003;42(5-6):443-461.
7. Reed R, Xu C, Liu Y, et al. Radiotherapy effect on nano-mechanical properties and chemical composition of enamel and dentine. Arch Oral Biol. 2015;60(5):690-697.
8. Yamazaki H, Demizu Y, Okimoto T, et al. Reirradiation for recurrent head and neck cancers using charged particle or photon radiotherapy. Strahlenther Onkol. 2017;193(7):525-533.
9. Bahl A, Oinam AS, Elangovan A, et al. Evaluation of reirradiation in locally advanced head and neck cancers: toxicity and early clinical outcomes. J Oncol. 2018;2018:8183694.
10. Jervoe P. X-ray diffraction investigation on the effect of experimental and in situ radiation on mature human teeth. A preliminary report. Acta Odontol Scand. 1970;28(5):623-631.

11. Soares CJ, Castro CG, Neiva NA, et al. Effect of gamma irradiation on ultimate tensile strength of enamel and dentin. J Dent Res. 2010;89(2):159-164.
12. de Siqueira Mellara T, Palma-Dibb RG, de Oliveira HF, et al. The effect of radiation therapy on the mechanical and morphological properties of the enamel and dentin of deciduous teeth--an in vitro study. Radiat Oncol. 2014;9:30.
13. Cole T, Silver AH. Production of hydrogen atoms in teeth by x-irradiation. Nature. 1963;200:700-701.
14. Naves LZ, Novais VR, Armstrong SR, et al. Effect of gamma radiation on bonding to human enamel and dentin. Support Care Cancer. 2012;20(11):2873-2878.
15. Pioch T, Golfels D, Staehle HJ. An experimental study of the stability of irradiated teeth in the region of the dentinoenamel junction. Endod Dent Traumatol. 1992;8(6):241-244.
16. Yadav S, Yadav H. Ionizing irradiation affects the microtensile resin dentin bond strength under simulated clinical conditions. J Conserv Dent. 2013;16(2):148-151.
17. Gonçalves LM, Palma-Dibb RG, Paula-Silva FW, et al. Radiation therapy alters microhardness and microstructure of enamel and dentin of permanent human teeth. J Dent. 2014;42(8):986-992.
18. Buglione M, Cavagnini R, Di Rosario F, et al. Oral toxicity management in head and neck cancer patients treated with chemotherapy and radiation: Dental pathologies and osteoradionecrosis (Part 1) literature review and consensus statement. Crit Rev Oncol Hematol. 2016;97:131-142.
19. Faria e Silva AL, Casselli DS, Ambrosano GM, et al. Effect of the adhesive application mode and fiber post translucency on the push-out bond strength to dentin. J Endod. 2007;33(9):1078-1081.
20. Perdigão J, Reis A, Loguercio AD. Dentin adhesion and MMPs: a comprehensive review. J Esthet Restor Dent. 2013;25(4):219-241.
21. Rodrigues RB, Soares CJ, Junior PCS, et al. Influence of radiotherapy on the dentin properties and bond strength. Clin Oral Investig. 2018;22(2):875-883.
22. Josic U, Mazzitelli C, Maravic T, et al. Evaluation of fiber post adhesion to root dentin achieved with different composite cements: 1-year in vitro results. J Adhes Dent. 2022;24(1):95-104.
23. Maravić T, Mazzitelli C, Mancuso E, et al. Resin composite cements: Current status and a novel classification proposal. J Esthet Restor Dent. 2023;doi: 10.1111/jerd.13036.
24. Cadenaro M, Josic U, Maravić T, et al. Progress in dental adhesive materials. J Dent Res. 2023;102(3):254-262.

25. Breschi L, Josic U, Maravic T, et al. Selective adhesive luting: A novel technique for improving adhesion achieved by universal resin cements. J Esthet Restor Dent. 2023; doi: 10.1111/jerd.13037.
26. Novais VR, Rodrigues RB, Simamoto Júnior PC, et al. Correlation between the mechanical properties and structural characteristics of different fiber posts systems. Braz Dent J. 2016;27(1):46-51.
27. de Souza GHM, Pandolfo MT, Bortoluzzi EA, et al. Effect of root perforation repair with mineral aggregate-based cements on the retention of customized fiberglass posts. Odontology. 2022;110(3):535-544.
28. Lopes FC, Roperto R, Akkus A, et al. Effect of carbodiimide and chlorhexidine on the bond strength longevity of resin cement to root dentine after radiation therapy. Int Endod J. 2020;53(4):539-552.
29. Pereira RD, Valdívia AD, Bicalho AA, et al. Effect of photoactivation timing on the mechanical properties of resin cements and bond strength of fiberglass post to root dentin. Oper Dent. 2015;40(5):E206-E221.
30. Cancelier PDA, Machado RG, Savaris JM, et al. Effect of the timing of radiation therapy on the push-out strength of resin cement to root dentine. Aust Endod J. 2023; doi: 10.1111/aej.12699.
31. Coelho SM, Pandolfo MT, Bortoluzzi EA, et al. Effect of radiation therapy on fracture resistance of simulated immature teeth submitted to root reinforcement. Int J Paediatr Dent. 2023; doi: 10.1111/ipd.13073.
32. Yamin PA, Pereira RD, Lopes FC, et al. Longevity of bond strength of resin cements to root dentine after radiation therapy. Int Endod J. 2018;51(11):1301-1312.
33. Pane ES, Palamara JE, Messer HH. Critical evaluation of the push-out test for root canal filling materials. J Endod. 2013;39(5):669-673.
34. Martins CV, Leoni GB, Oliveira HF, et al. Influence of therapeutic cancer radiation on the bond strength of an epoxy- or an MTA-based sealer to root dentine. Int Endod J. 2016;49(11):1065-1072.
35. J Pytko-Polonczyk J, Jakubik A, Przeklasa-Bierowiec A, et al. Artificial saliva and its use in biological experiments. J Physiol Pharmacol. 2017;68(6):807-813.
36. Jham BC, da Silva Freire AR. Oral complications of radiotherapy in the head and neck. Braz J Otorhinolaryngol. 2006;72(5):704-708.

37. Verdonck HW, de Jong JM, Granzier ME, et al. Intensity-modulated radiation therapy for oropharyngeal cancer: radiation dosage constraint at the anterior mandible. Oral Oncol. 2009;45(6):511-514.

38. Parahyba CJ, Ynoe Moraes F, Ramos PA, et al. Radiation dose distribution in the teeth, maxilla, and mandible of patients with oropharyngeal and nasopharyngeal tumors who were treated with intensity-modulated radiotherapy. Head Neck. 2016;38(11):1621-1627.

39. de Barros da Cunha SR, Ramos PA, Nesrallah AC, et al. The effects of ionizing radiation on the oral cavity. J Contemp Dent Pract. 2015;16(8):679-687.

40. Ubaldini ALM, Benetti AR, Sato F, et al. Challenges in luting fibre posts: Adhesion to the post and to the dentine. Dent Mater. 2018;34(7):1054-1062.

41. Paiola FG, Lopes FC, Mazzi-Chaves JF, et al. How to improve root canal filling in teeth subjected to radiation therapy for cancer. Braz Oral Res. 2018;32:e121.

42. Yoshihara K, Hayakawa S, Nagaoka N, et al. Etching efficacy of self-etching functional monomers. J Dent Res. 2018;97(9):1010-1016.

43. Breschi L, Maravic T, Cunha SR, et al. Dentin bonding systems: From dentin collagen structure to bond preservation and clinical applications. Dent Mater. 2018;34(1):78-96.

44. Han F, Jin X, Yuan X, et al. Interactions of two phosphate ester monomers with hydroxyapatite and collagen fibers and their contributions to dentine bond performance. J Dent. 2022;122:104159.

45. Queiroz AM, Bonilla CMC, Palma-Dibb RG, et al. Radiotherapy activates and protease inhibitors inactivate matrix metalloproteinases in the dentinoenamel junction of permanent teeth. Caries Res. 2019;53(3):253-259.

46. Globocan - International Agency for Cancer Research, 2018. Available at: http://globocan.iarc.fr/Default.aspx (Accessed on June 27th, 2022).

4 CONCLUSÕES

Considerando-se as limitações de um estudo laboratorial, pode-se concluir que:

1. A radioterapia afetou a resistência de união do cimento resinoso universal a dentina intrarradicular, independentemente da abordagem adesiva.
2. No entanto, nos espécimes irradiados, o cimento resinoso universal no modo autocondicionante apresentou maior resistência de união que nos espécimes re-irradiados.
3. No modo autoadesivo, o regime de radioterapia foi determinante para diminuir a resistência de união do cimento resinoso universal.

ANEXOS

Anexo A - Parecer consubstanciado do Comitê de Ética em Pesquisa com Seres Humanos da UFSC.

UNIVERSIDADE FEDERAL DE SANTA CATARINA - UFSC

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: EFEITO DE DOSES CUMULATIVAS DE RADIAÇÃO IONIZANTE NA RESISTÊNCIA DE UNIÃO DO CIMENTO OBTURADOR A DENTINA RADICULAR

Pesquisador: LUCAS DA FONSECA ROBERTI GARCIA

Área Temática:

Versão: 1

CAAE: 26203019.9.1001.0121

Instituição Proponente: CENTRO DE CIÊNCIAS DA SAÚDE

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 3.761.367

Apresentação do Projeto:

Trata-se o presente parecer da apreciação ética do projeto de conclusão de curso de graduação em Odontologia da Universidade Federal de Santa Catarina de Giovana Aparecida Wosniak orientada pelo prof. Dr. Lucas da Fonseca Roberti Garcia. O estudo pretende avaliar o efeito de doses cumulativas de radiação ionizante na resistência de união do cimento obturador a dentina radicular de dente extraídos por motivos alheios a pesquisa com uma amostra d 60 dentes doados.

Objetivo da Pesquisa:

Objetivo Primário:

Avaliar a resistência de união de cimentos endodônticos à dentina radicular submetida a doses cumulativas de radiação ionizante.

Objetivo Secundário:

Avaliar o efeito de doses cumulativas de radiação ionizante (70 Gy e 70 Gy + 70 Gy) na resistência de união de um cimento endodôntico à base de resina epóxica (AH Plus, Dentsply) e um biocerâmico (BioRoot, Septodont).

Avaliação dos Riscos e Benefícios:

Riscos:

Poderá haver desconforto e sensibilidade no local devido à cirurgia que é uma consequência

Endereço: Universidade Federal de Santa Catarina, Prédio Reitoria II, R: Desembargador Vitor Lima, nº 222, sala 401
Bairro: Trindade **CEP:** 88.040-400
UF: SC **Município:** FLORIANOPOLIS
Telefone: (48)3721-6094 **E-mail:** cep.propesq@contato.ufsc.br

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

FLORIANOPOLIS, 11 de Dezembro de 2019

Assinado por:
Maria Luiza Bazzo
(Coordenador(a))