UNIVERSIDADE FEDERAL DE SANTA CATARINA
CENTRO DE CIÊNCIAS DA SAÚDE
PROGRAMA DE PÓS-GRADUAÇÃO EM ODONTOLOGIA

Bruna Venzke Fischer

Reintervenção endodôntica em dentes irradiados: efeito do momento de realização do tratamento endodôntico (pré e pós-irradiação) e da dose de irradiação na quantidade de material obturador remanescente

Florianópolis
2023

Bruna Venzke Fischer

Reintervenção endodôntica em dentes irradiados: efeito do momento de realização do tratamento endodôntico (pré e pós-irradiação) e da dose de irradiação na quantidade de material obturador remanescente

Dissertação submetida ao Programa de Pós-Graduação em Odontologia da Universidade Federal de Santa Catarina (UFSC), como parte dos requisitos para obtenção do título de Mestre em Odontologia, área de concentração em Endodontia.
Orientador: Prof. Dr. Lucas da Fonseca Roberti Garcia
Coorientadora: Profa. Dra. Cleonice da Silveira Teixeira

Florianópolis
2023

Fischer, Bruna Venzke
Reintervenção endodôntica em dentes irradiados : Efeito do momento de realização do tratamento endodôntico (pré e pós-irradiação) e da dose de irradiação na quantidade de material obturador remanescente / Bruna Venzke Fischer ; orientador, Lucas da Fonseca Roberti Garcia, coorientadora, Cleonice da Silveira Teixeira, 2023.
45 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. Endodontia . 3. Radioterapia. 4. Reintervenção endodôntica. 5. Dentina irradiada. 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.

Bruna Venzke Fischer

Reintervenção endodôntica em dentes irradiados: efeito do momento de realização do tratamento endodôntico (pré e pós-irradiação) e da dose de irradiação na quantidade de material obturador remanescente

O presente trabalho em nível de Mestrado foi avaliado e aprovado, em 29 de junho de 2023 pela banca examinadora composta pelos seguintes membros:

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

Prof. Dr. Rogério de Oliveira Gondak
Universidade Federal de Santa Catarina

Profa. Dra. Georgia Ribeiro Martini
Universidade do Oeste Catarinense

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: 13/09/2023 11:29:44-0300
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: 12/09/2023 17:57:34-0300
CPF: ***.929.858-**
Verifique as assinaturas em https://v.ufsc.br

Prof. Dr. Lucas da Fonseca Roberti Garcia
Orientador

Florianópolis, 2023

AGRADECIMENTOS

Agradeço, em primeiro lugar, à minha família. Minha mãe **Ediléia Venzke Fischer**, meu exemplo número 1 de profissional e pessoa a ser seguido, e meu pai **Gilson Fischer** *(in memoriam)* que foi fundamental nos primeiros anos da minha vida e ajudou a formar minha educação e caráter, sinto sua presença eternamente. Obrigada por serem os maiores exemplos da minha vida!

Agradeço também ao meu exemplo profissional, dinda e segunda mãe **Frida Bergmann Venzke**, que foi a inspiração na minha escolha por essa profissão e minha base nos primeiros anos de formada. Obrigada por sempre acreditar em mim!

Agradeço ao meu companheiro e melhor amigo **Alexandre Braga Silveira**, sem ele essa jornada teria se tornando muito mais difícil. Você torna minha caminhada mais leve, obrigada por estar sempre ao meu lado!

Agradeço, especialmente, ao meu orientador **Prof. Dr. Lucas da Fonseca Roberti Garcia**, por todos os conhecimentos compartilhados, por toda dedicação e disponibilidade em ensinar. Obrigada por todo carinho e confiança, o senhor é um exemplo a ser seguido!

Agradeço à minha coorientadora **Profa. Dra. Cleonice da Silveira Teixeira**, uma mulher forte e batalhadora a qual é sempre uma inspiração. Obrigada por ser sempre tão atenciosa e disponível a me ajudar!

Agradeço às demais professoras da Endodontia, **Profa. Dra. Ana Maria Hecke Alves**, **Profa. Dra. Thais Mageste Duque** e **Profa. Dra. Juliana Silva Ribeiro de Andrade**. Todas vocês são exemplos de mulheres na educação e na pesquisa, admiro e tenho um carinho especial por cada uma. Obrigada por tantas conversas, ensinamentos e, principalmente, tornarem nossa rotina mais gostosa. É muito bom a convivência com vocês!

Agradeço aos professores da banca, **Prof. Dr. Rogério de Oliveira Gondak** e **Profa. Dra. Georgia Ribeiro Martini**, por aceitarem o convite e se fazerem presente nesse momento. Tenho certeza que suas colocações serão de extrema importância para a evolução deste trabalho.

Agradeço à minha colega de pós-graduação, **Taynara dos Santos Goulart**, que desde o início foi minha companheira em tantos momentos e compartilhou muito conhecimento. Você me marcou apenas com lembranças positivas e tenho muito orgulho de você!

Agradeço aos meus colegas **Luiz Dias** e **Filipe Vitalli** que compartilharam comigo muitos conhecimentos sobre metodologia, estatística e revisão sistemática, sempre com muita humildade e disposição.

Agradeço aos meus demais colegas de pós-graduação e amigos, **Riéli Elis Schulz**, **Lívia Ribeiro**, **Maria Eduarda Paz Dotto**, **Julia Menezes Savaris**, **Luiz Fernando Czornobay**, **Gabriela Pasqualini Ghidini**, que tornaram minha caminhada na pós-graduação mais leve e divertida. Obrigada por toda troca que tivemos e por serem momentos de paz em meio ao caos.

Impossível deixar de agradecer a minha melhor amiga e companheira dos anos de graduação, **Luiza Freitas Brum Souza**. Você foi fundamental do início ao fim, mesmo de longe foi meu ombro amigo e suporte emocional. Você é muito especial na minha vida!

Por fim, gostaria de agradecer à **Universidade Federal de Santa Catarina (UFSC)**, por me proporcionar um ensino de qualidade e excelência, contribuindo ainda mais para minha vida pessoal e profissional. Orgulho de fazer parte desta Universidade!

RESUMO

A reintervenção endodôntica em dentes irradiados possui poucas evidências científicas e faltam protocolos clínicos para pacientes oncológicos que passaram pela radioterapia de cabeça e pescoço. O objetivo deste estudo *in vitro* foi investigar o efeito da radioterapia na quantidade de material obturador remanescente aderido às paredes do canal radicular após reintervenção endodôntica, em função do momento em que o tratamento endodôntico foi realizado (pré e pós-radiação) e da dosagem de radiação recebida. Sessenta pré-molares inferiores humanos unirradiculares foram distribuídos em 5 grupos (n = 12), de acordo com o tempo e dosagem de radiação (55 Gy ou 70 Gy): NegativoGC (grupo controle negativo) - dentes não irradiados; Endo-pre-RT_{55} - obturação do canal radicular antes da irradiação (55 Gy); Endo-pre-RT_{70} - obturação do canal radicular antes da irradiação (70 Gy); Endo-post-RT_{55} - obturação do canal radicular e reintervenção após irradiação (55 Gy); e Endo-post-RT_{70} - obturação do canal radicular e reintervenção após irradiação (70 Gy). As raízes foram clivadas em hemissecções e analisadas em estereomicroscópio e Microscópio Eletrônico de Varredura (MEV) para quantificar (%) o material obturador remanescente. As comparações intergrupos e intragrupos foram realizadas pelo teste ANOVA de um fator, e teste post hoc de Tukey ($\alpha = 0,05$). Os grupos experimentais apresentaram uma quantidade significativamente maior ($P < 0,05$) de material obturador remanescente nos terços médio e apical do que o grupo controle, com exceção de Endo-pré-RT^{55} no terço médio ($P < 0,0001$). Em todos os grupos, o terço apical apresentou maior quantidade de material obturador remanescente ($P < 0,05$) aderido às paredes do canal radicular. A radioterapia, antes e depois do tratamento endodôntico primário, aumentou a quantidade de material obturador remanescente aderido às paredes do canal radicular após a reintervenção endodôntica, independentemente da dose de radiação aplicada. Sendo assim, pode ocorrer maior dificuldade na remoção de material obturador durante a reintervenção endodôntica em dentes irradiados.

Palavras-chave: Radioterapia; Dentina irradiada; Reintervenção endodôntica; Material obturador.

LISTA DE FIGURAS

Figura 1. Fluxograma do desenho experimental..22

Figura 2. Imagens de um espécime clivado em duas hemissecções capturadas, separadamente, em estereomicroscópio para ser analisada no software Image J...25

Figura 3. Imagens representativas de uma hemissecção radicular analisada no software Image J. **a.** Setas amarelas indicam as delimitações dos terços (cervical, médio e apical). **b.** Contorno externo da área de cada terço do canal radicular. **c.** Seta vermelhas indicam exemplos de remanescente de material obturador presente na hemissecção...26

Figura 4. Box plot mostrando a porcentagem de material obturador remanescente no terço cervical nos grupos controle, Pré 55Gy, Pré 70Gy, Pós 55Gy e Pós 70Gy...29

Figura 5. Box plot mostrando a porcentagem de material obturador remanescente no terço médio nos grupos controle, Pré 55Gy, Pré 70Gy, Pós 55Gy e Pós 70Gy...29

Figura 6. Box plot mostrando a porcentagem de material obturador remanescente no terço apical nos grupos controle, Pré 55Gy, Pré 70Gy, Pós 55Gy e Pós 70Gy...29

Figura 7. Imagens representativas no MEV. A, B e C: Imagens em aumento de 200x do grupo controle negativo dos terços cervical, médio e apical, respectivamente. D: Imagem do terço cervical do grupo controle negativo em aumento de 1000x. Nota-se a formação de tags de cimento obturador no interior dos túbulos dentinários. E, F, G: Imagens em aumento de 200x do grupo G-Endo Pré 70 dos terços cervical, médio e apical, respectivamente. H: Imagem do terço cervical do grupo G-Endo Pré 70 em aumento de 1000x. Nota-se a grande quantidade de material obturador sobre a superfície dentinária. I, J, K: Imagens em aumento de 200x do grupo G-Endo Pós 70 dos terços cervical, médio e apical, respectivamente. L: Imagem do terço cervical do grupo G-Endo Pós 70 em aumento de 1000x. Nota-se obliteração de túbulos dentinários e presença de material obturador sobre eles...30

SUMÁRIO

1. INTRODUÇÃO E CONTEXTUALIZAÇÃO 11
2. OBJETIVOS E HIPÓTESE 14
2.1. Objetivo geral 14
2.2. Objetivos Específicos 14
2.3. Hipóteses 14
3. ARTIGO CIENTÍFICO 15
4. CONCLUSÃO 38
5. REFERÊNCIAS 39
ANEXOS 44
Anexo A - Parecer consubstanciado do Comitê de Ética em Pesquisa com Seres Humanos da UFSC. 44

1. INTRODUÇÃO E CONTEXTUALIZAÇÃO

De acordo com a Organização Mundial da Saúde (OMS), dois terços dos pacientes oncológicos serão submetidos à radioterapia durante seu tratamento (WHO, 2008). A radiação ionizante produzida durante a radioterapia causa quebra do DNA celular, interrompendo sua duplicação (RAY-CHAUDHURI; SHAH; PORTER, 2013). Entretanto, a radiação não atinge apenas os tecidos neoplásicos (RAY-CHAUDHURI; SHAH; PORTER, 2013). Uma grande área adjacente ao tumor também é irradiada, afetando tecidos sadios (RAY-CHAUDHURI; SHAH; PORTER, 2013). Desta forma, a radioterapia em pacientes portadores de câncer de cabeça e pescoço (CCP) compromete a integridade dos tecidos da cavidade oral (MARTA et al., 2014), em especial, mandíbula, maxila e dentes (CAMPI et al., 2019; RODRIGUES et al., 2018; VELO et al., 2018).

Estudos recentes demonstraram que a radioterapia nestes pacientes afeta a adesão de biomateriais ao esmalte e dentina (BODRUMLU et al., 2009; BODRUMLU; BODRUMLU, 2018; MARTINS et al., 2016; PALMIER et al., 2022; RODRIGUES et al., 2018; YAMIN et al., 2018). Devido ao seu alto conteúdo orgânico e solubilidade (HOPPENBROUWERS; DRIESSENS; BORGGREVEN, 1987), a dentina é mais afetada pela radiação ionizante, com grandes alterações em sua matriz colágena (DE BARROS DA CUNHA et al., 2017; GONÇALVES et al., 2014).

Estas alterações em tecidos altamente orgânicos ocorrem principalmente devido a um fenômeno chamado radiólise, que consiste na quebra das moléculas de água pela radiação ionizante, formando radicais livres e peróxido de hidrogênio (COLE; SILVER, 1963). Na dentina radicular e intrarradicular é possível observar intensa desidratação do substrato, colapso da rede de fibrilas colágenas (CAMPI et al., 2019), obliteração dos túbulos dentinários e microfissuras na dentina peri e intertubular (VELO et al., 2018).

Atualmente, os protocolos de radioterapia para o tratamento de CCP se baseiam em doses totais de radiação que podem variar entre 55 Gy e 70 Gy, em frações diárias de aproximadamente 2 Gy, por um período de 5 a 7 semanas, 5 dias por semana (JHAM; FREIRE, 2006). A Terapia de Radioterapia de

Intensidade Modulada (IMRT) é o método mais utilizado, pois permite que o alvo primário receba a quantidade total de radiação necessária ao tratamento, minimizando a concentração de radiação recebida pelos tecidos adjacentes (YU, 1995). Clinicamente, mesmo com o uso do método IMRT para o tratamento de CCP, a exposição dos tecidos dentários localizados próximos à área alvo não pode ser evitada (LIESHOUT; BOTS, 2014; PARAHYBA et al., 2016).

É consenso na literatura que a periodontite apical persistente após tratamento endodôntico primário representa uma situação etiológica e terapêutica mais complexa que a periodontite apical que atinge dentes que não foram submetidos a um tratamento endodôntico anterior (NAIR, 2006). A periodontite apical pós-tratamento endodôntico é geralmente observada quando o tratamento primário não seguiu padrões aceitáveis de prevenção e controle da infecção do sistema de canais radiculares (SIQUEIRA et al., 2005). As modalidades de tratamento nestes casos incluem a reintervenção endodôntica não-cirúrgica, a cirurgia periapical ou a extração dentária (KARAMIFAR; TONDARI; SAGHIRI, 2020).

No entanto, em pacientes portadores de CCP em caso de falha do tratamento endodôntico primário, o procedimento de reintervenção endodôntica não-cirúrgica deve ser a primeira opção de tratamento (RUDDLE, 2004), devendo a cirurgia periapical e a extração dentária serem evitadas ao máximo (RAY-CHAUDHURI; SHAH; PORTER, 2013). Pacientes portadores de CCP que foram submetidos a radioterapia apresentam modificação no seu padrão de vascularização e reparo tecidual, e estão altamente suscetíveis a osteorradionecrose (ORN) (RAY-CHAUDHURI; SHAH; PORTER, 2013). A ORN é uma necrose isquêmica óssea causada pela radiação ionizante (JHAM; FREIRE, 2006). É uma das mais graves consequências da radioterapia, podendo ocorrer espontaneamente ou, mais comumente, após algum trauma, como cirurgias orais e extrações dentárias (JHAM; FREIRE, 2006). Em 95% dos casos, a ORN provoca necrose dos tecidos moles e subsequente exposição óssea, sendo de difícil tratamento e cicatrização (JHAM; FREIRE, 2006).

Assim sendo, o principal objetivo da reintervenção endodôntica não-cirúrgica é promover uma sanificação adequada do sistema de canais radiculares, não atingidas no tratamento primário (CROZETA et al., 2016). A frequente presença de material obturador remanescente (MOR), que pode conter microrganismos e seus subprodutos, impede uma sanificação apropriada do sistema de canais radiculares (SIQUEIRA JUNIOR et al., 2018). Desta forma, o uso de métodos complementares para otimizar a remoção de material obturador é fundamental (MARTINS et al., 2017). Apesar de nenhuma técnica ser capaz de remover completamente o material obturador durante a reintervenção endodôntica, a Irrigação Ultrassônica Passiva (*Passive Ultrasonic Irrigation* - PUI) têm apresentado excelentes resultados (CROZETA et al., 2020; SILVEIRA et al., 2018).

No entanto, estudos que avaliem a reintervenção endodôntica não-cirúrgica em dentes irradiados continuam desconhecidos. Grande parte dos estudos existentes até o momento abordam apenas a interação entre dentina intrarradicular irradiada e sistemas adesivos, cimentos resinosos, pinos de fibra e a capacidade de selamento de cimentos obturadores (BODRUMLU et al., 2009; RODRIGUES et al., 2018; MARTINS et al., 2016; YAMIN et al., 2018; PALMIER et al., 2022). Todos os estudos citados realizaram a radiação dos tecidos dentários previamente ao protocolo de tratamento utilizado.

A escassez de dados que correlacionem os efeitos da radioterapia sobre a interação entre material obturador e dentina intrarradicular de dentes que necessitem reintervenção endodôntica tornam a realização deste tipo de estudo fundamental para o estabelecimento de protocolos clínicos baseados em evidências científicas.

2. OBJETIVOS E HIPÓTESE

2.1. Objetivo geral

Avaliar o efeito da radiação ionizante na quantidade de material obturador remanescente aderido às paredes do canal radicular após reintervenção endodôntica, em função do momento em que o tratamento endodôntico foi realizado (pré e pós-radiação) e da dosagem de radiação recebida.

2.2. Objetivos Específicos

2.2.1. Analisar quantitativamente em estereomicroscópio a quantidade de material obturador remanescente após reintervenção endodôntica em dentes irradiados antes e após o tratamento endodôntico de acordo com a dose total de radiação utilizada (55 ou 70Gy).

2.2.2. Analisar qualitativamente em Microscópio Eletrônico de Varredura o efeito da radiação ionizante sobre o material obturador remanescente e a dentina intrarradicular após reintervenção endodôntica em dentes irradiados antes e após o tratamento endodôntico de acordo com a dose total de radiação utilizada (55 ou 70Gy).

2.3. Hipóteses

2.3.1. Hipótese nula

A irradiação cumulativa, antes ou após o tratamento endodôntico primário, não influenciará na quantidade de material obturador remanescente aderido às paredes do canal radicular após a reintervenção endodôntica.

2.3.2. Hipótese alternativa

A radioterapia afetaria a quantidade de material obturador remanescente aderido às paredes do canal radicular? O momento e a dosagem da radioterapia afetariam a quantidade de material obturador remanescente?

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 Endodontics* (Qualis A1, Fator de Impacto 4.171).

Effect of the timing and dosage of radiation therapy on the filling material removal during endodontic reintervention

Bruna V. Fischer[1], Cleonice da S. Teixeira[1], Lucas da F. R. Garcia[1]

[1]Department of Dentistry - Endodontics Division, Health Sciences Center, Federal University of Santa Catarina, Florianópolis, Santa Catarina, 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) 3721-4853 - E-mail address: drlucas.garcia@gmail.com

Effect of the timing and dosage of radiation therapy on the filling material removal during endodontic reintervention

ABSTRACT

Introduction: Endodontic reintervention in irradiated teeth is a scientific gap to be bridged. This *in vitro* study investigated the effect of the timing and dosage of radiation therapy on the filling material removal during endodontic reintervention.

Method: Sixty single-rooted human mandibular premolars were distributed into 5 groups (n = 12), according to the timing and dosage of radiation (55 Gy or 70 Gy): NegativeCG (negative control group) - non-irradiated teeth; Endo-pre-RT_{55} - root canal obturation before irradiation (55 Gy); Endo-pre-RT_{70} - root canal obturation before irradiation (70 Gy); Endo-post-RT_{55} - root canal obturation and reintervention after irradiation (55 Gy); and Endo-post-RT_{70} - root canal obturation and reintervention after irradiation (70 Gy). The roots were cleaved into hemisections and analyzed under a stereomicroscope and a Scanning Electron Microscope (SEM) to quantify (%) the amount of remaining filling material. Intergroup and intragroup comparisons were performed with the One-way Analysis of Variance (ANOVA) test and post hoc Tukey's test (α = 0.05).

Results: The experimental groups had a significantly greater amount ($P < .05$) of remaining filling material in the middle and apical thirds than the control group, except for Endo-pre-RT_{55} in the middle third ($P < .0001$). In all groups, the apical third had a greater amount of remaining filling material ($P < .05$) attached to the root canal walls.

Conclusion: Radiation therapy, before and after primary endodontic treatment, increased the amount of remaining filling material attached to the root canal walls after endodontic reintervention, regardless of the radiation dose delivered.

KEY WORDS: Radiotherapy; head and neck cancer; dentin; root canal therapy; root canal filling material.

INTRODUCTION

According to the American Society of Oncology (ASCO), adjuvant radiotherapy is widely used to treat head and neck câncer (HNC)[1]. Radiation uses total radiation doses that may range from 55 Gy to 70 Gy[2]. Despite the primary focus of irradiation being concentrated in the tumor area, healthy tissues are also irradiated[3]. Therefore, radiotherapy in HNC patients compromises the integrity of oral tissues[4], especially, the mandible, maxilla, and teeth[5-7].

It is consolidated in the literature that persistent apical periodontitis after primary endodontic treatment represents a complex therapeutic situation[8]. The treatment for these cases includes non-surgical endodontic reintervention, apical surgery, or tooth extraction[9]. However, in HNC patients undergoing radiotherapy, the non-surgical endodontic reintervention procedure should be the first treatment option[3]. Apical surgery and tooth extraction should be avoided due to the high risk of osteoradionecrosis in these patients[3].

Few studies have assessed the sealing capacity and bond strength of endodontic sealers to irradiated dentin, and the results reported so far are controversial[10-14]. Despite being the most recommended treatment for patients undergoing radiation therapy, there are no studies evaluating the possible negative effects of irradiation on the filling material removal during endodontic reintervention.

Therefore, the purpose of this *in vitro* study was to evaluate the amount of filling material attached to the root canal walls, which had been exposed to different dosages of radiation therapy at different time points during the course of endodontic reintervention. The following hypotheses were tested: (I) Would radiation therapy affect the amount of remaining filling material attached to the root canal walls? (II) Would the timing and dosage of radiation therapy affect the amount of remaining filling material?

MATERIALS AND METHODS

Ethical Concerns and Sample Size Calculation

This research consists of a quantitative experimental laboratory study, and it was approved by the Human Research Ethics Committee of the Federal University of Santa Catarina (Protocol No.: 5.915.260 - CAAE: 65558822.0.0000.0121) and performed following the ethical standards laid down in the 2008 Declaration of Helsinki.

The sample size was calculated based on previous studies that used ten specimens per group[15,16]. In the present study, additional specimens were selected by antecipating cases of loss throughout the research. The final sample size was twelve specimens per group.

Specimens Selection

Sixty single-rooted human mandibular premolars, recently extracted for reasons beyond the scope of this research, were selected for this study. The teeth underwent rigorous visual inspection under magnification (×4) and radiographic examination to assess their internal morphology. The inclusion criteria adopted were a straight or slightly curved root (curvature angle between 0° and 5°), a single and completely formed root canal, with no calcifications, no internal or external resorption, and no previous endodontic treatment. Teeth with signs of cracks, fractures, or carious lesions were excluded from the final sampling.

The external surface of the teeth was cleaned with an ultrasonic insert (T1-S; Schuster Equipamentos Odontológicas, Santa Maria, RS, Brazil). Next, the teeth were immersed in a 0.1% thymol solution for disinfection for 48 hours, followed by washing in running water for 24 hours. Then, the teeth was stored in plastic receptacles containing distilled water to avoid dehydration and kept in an oven at 37°C until the beginning of the experiment. All experimental procedures, from the specimen selection to endodontic reintervention, were performed by a single and trained operator, a specialist in endodontics.

Randomization and Specimens Distribution

The teeth were numbered and randomly distributed (www.random.org) into five experimental groups: a negative control group (*n* = 12), and four experimental groups (*n* = 12).

- NegativeCG (negative control group): non-irradiated teeth. The endodontic reintervention was performed 30 days after root canal obturation.
- Endo-pre-RT_{55}: root canals were obturated before irradiation. Then, the teeth were irradiated with a dosage of 55 Gy. After 30 days, endodontic reintervention was performed.

- Endo-pre-RT_{70}: root canals were obturated before irradiation. Then, the teeth were irradiated with a dosage of 70 Gy. After 30 days, endodontic reintervention was performed.
- Endo-post-RT_{55}: the teeth were irradiated with a dosage of 55 Gy and then, endodontically treated. After 30 days, the endodontic reintervention was performed.
- Endo-post-RT_{70}: the teeth were irradiated with a dosage of 70 Gy and then, endodontically treated. After 30 days, the endodontic reintervention was performed.

The study design and experimental group distribution may be seen in Figure 1.

Teeth Irradiation

Teeth irradiation was carried out at the Department of Radiotherapy of the Oncology Research Center (CEPON; Florianópolis, SC, Brazil). The radiation therapy followed the CEPON protocol for the treatment of HNC, with 6MV of energy (photons) and total administration of 55 Gy or 70 Gy, divided into 2 Gy daily, 5 days a week, for 5 or 7 weeks[11]. The irradiation was performed in a linear accelerator (Clinac 2100C; Varian Medical Systems, Inc., Palo Alto, CA, USA) with dynamic collimators (Dynamic Multileaf Collimator - DMLC), by the Intensity Modulated Radiotherapy Technique[17,18]. The teeth were placed inside a plastic receptacle and completely immersed in distilled and deionized water during the whole protocol[19]. The distilled and deionized water was discarded at the end of each irradiation cycle, and replaced by artificial saliva. Then, the teeth were stored in an oven at 37ºC to simulate the oral conditions. The artificial saliva was replaced by distilled and deionized water at each new cycle of radiation therapy.

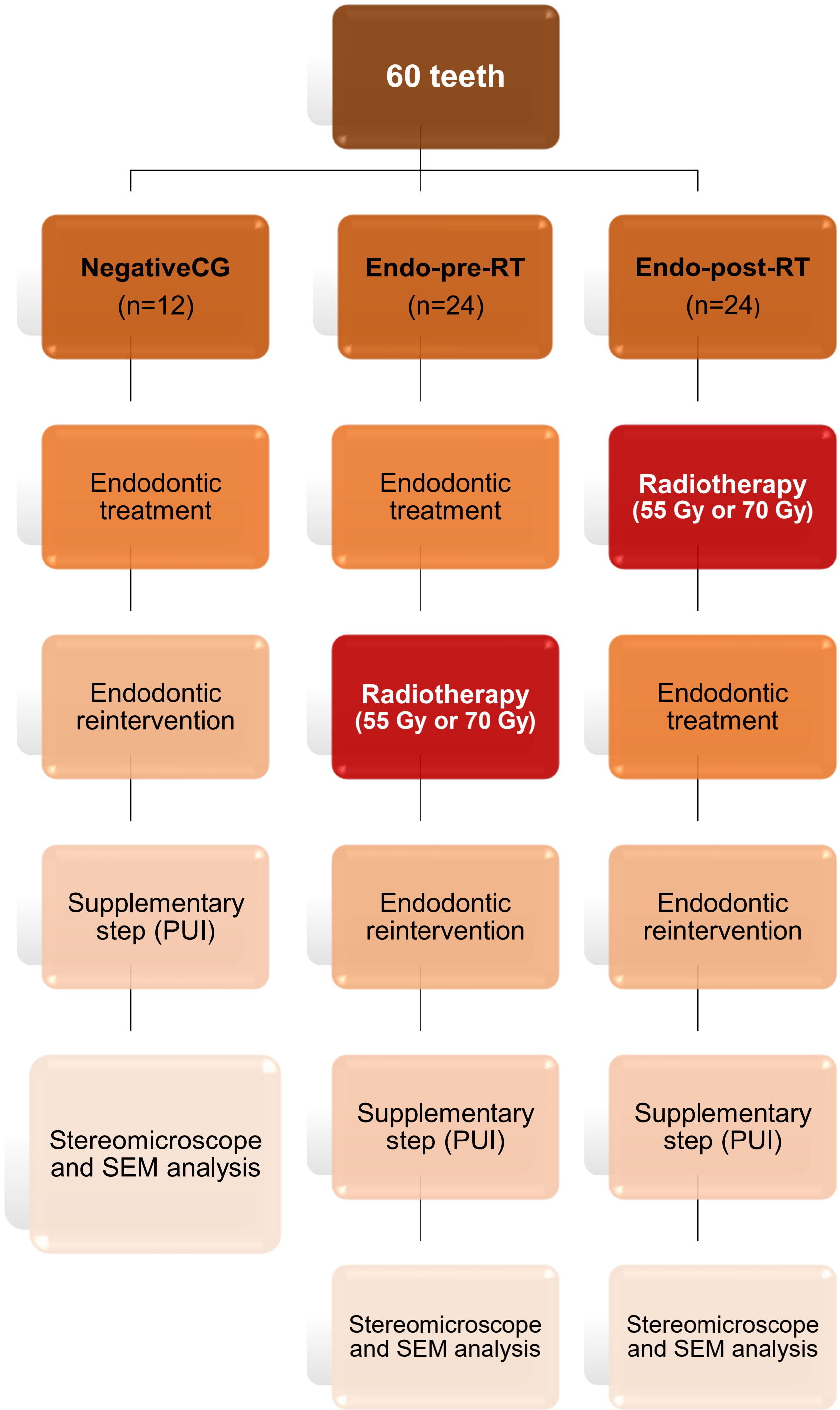

FIGURE 1 - Study design and experimental and control group distribution.

Endodontic Treatment

The teeth were decoronated at the cementoenamel junction with a double-sided diamond disc (No. 7016; American Burs, Palhoça, SC, Brazil) coupled to a straight handpiece, under copious water cooling. The root canals were initially negotiated with a size 10 K-file (Dentsply Maillefer, Ballaigues, Switzerland). The working length (WL) was established 1 mm short of the apical foramen.

Root canal preparation was performed by the crown-down technique with the R40 instrument (40/.06) (Reciproc; VDW GmbH, Munich, Germany) powered by an electric motor (VDW Gold, VDW GmbH), in the “RECIPROC ALL” mode, following the manufacturer's recommendations. At every three pecking movements towards the apical, the instrument was removed and cleaned with gauze soaked in 70% alcohol. The root canal was then irrigated with 2 mL of 2.5% NaOCl solution (Asfer Indústria Química, São Caetano do Sul, SP, Brazil). Irrigation was performed with a 30G needle (NaviTip; Ultradent Products Inc., South Jordan, UT, USA) coupled to a 5-mL plastic syringe (Ultradent Products Inc.), in back-and-forth movements, previously calibrated 2 mm short the WL. The apical patency was maintained by inserting a size 15 K-file (Dentsply Maillefer) through the apical foramen.

These steps were repeated until the instrument reached the WL. On completion of root canal preparation, the canals were irrigated with 3 mL of 17% ethylenediaminetetraacetic acid (EDTA) (Biodinâmica, Ibiporã, PR, Brazil) for 3 minutes, followed by final irrigation with 3 mL of 2.5% NaOCl solution. A final volume of 20 mL of 2.5% NaOCl solution was used per root canal. The root canals were dried with absorbent paper cones (VDW GmbH).

Root Canal Obturation

Root canal obturation was performed using the cold lateral compaction technique. Initially, a size 40 master gutta-percha cone (Reciproc; VDW GmbH) wrapped in endodontic sealer (AH Plus JET; Dentsply DeTrey GmbH, Konstanz, Germany) was inserted into the root canal up to the WL. Then, a size 25 finger spreader (Dentsply Maillefer), calibrated 1 mm short of the WL, was gently inserted into the root canal to laterally compact the master cone and create space for the insertion of size B7 accessory gutta-percha cones (Tanari, São Paulo, SP, Brazil). Before each accessory gutta-percha cone insertion, the use of the finger spreader was necessary, as well as the placement of a thin layer of sealer on the cones’ surface. After maximum placement of accessory gutta-percha cones, they were cut with a pre-heated plugger (Odous de Deus, Belo Horizonte, MG, Brazil) followed by vertical compaction. Digital periapical radiographs were taken in mesiodistal and buccolingual directions to ensure the quality of the root canal obturation. Root canal obturation with gaps and voids was discarded from the final specimen pool, and replaced. The root canal entrance was sealed with composite resin (Opus Bulk Fill; FGM Dental Group, Joinville, SC, Brazil). The specimens were kept in an environment with 100% humidity (gauze soaked in distilled water) and 37°C for 30 days, to achieve a complete setting of the endodontic sealer.

Endodontic Reintervention

Initially, the gutta-percha was perforated with a size 2 Gates-Glidden drill (Dentsply DeTrey GmbH), positioned 5 mm short of the WL. Next, the R40 instrument (Reciproc; VDW GmbH) was used for the filling material removal. The instrument was apically activated, in pecking movements of approximately 3 mm in amplitude. Filling material removal was considered finished when the instrument reached the WL, the filling material was no longer observed in the reflux of the irrigating solution and on the instrument's cutting blades.

The re-instrumentation of the root canals was performed with the R50 instrument (50/.05) (Reciproc; VDW GmbH) until reaching the WL, as described above. The same irrigation protocol used during root canal preparation was performed during endodontic reintervention (filling material removal and re-instrumentation). Apical patency was maintained by inserting a size 15 K-file (Dentsply Maillefer) through the apical foramen.

The root canals were then submitted to a supplementary irrigation protocol (Passive Ultrasonic Irrigation- PUI). The root canals were flooded with 17% EDTA, which was ultrasonically activated with a smooth insert with a diameter of 0.2 mm (E1-Irrisonic; Helse, Santa Rosa do Viterbo, SP, Brazil), positioned 2 mm short of the WL. The insert was activated by a piezoelectric ultrasonic device (JetSonic; Gnatus, Ribeirão Preto, SP, Brazil), at 20% power, with back-and-forth movements in 3 cycles of 20 seconds each. The solution was renewed at each new cycle. Afterward, the final irrigation of the root canals was performed with 3 mL of 2.5% NaOCl solution, following the same protocol used for the 17% EDTA ultrasonic activation.

Stereomicroscope and Scanning Electron Microscope (SEM) Analysis

To quantify the remaining filling material attached to the root canal walls, the specimens were analyzed directly under a stereomicroscope (SteREO Discovery. V12, Carl Zeiss, Jena, Germany)[20-23]. Initially, a gutta-percha cone was inserted into the root canal to prevent the entry of debris. Next, longitudinal grooves were made on each root's buccal and lingual external surfaces with a double-sided diamond disc No. 7016 (American Burrs). Then, the roots were gently cleaved with the aid of a chisel and hammer, obtaining two root hemisections per tooth.

The roots' hemisections were assessed under a stereomicroscope at ×8 magnification (total view of the hemisection area). Each hemisection was individually positioned with its long axis parallel to a calibration ruler. The image acquisition was performed with the AxioVision software (AxioVision LE64 - SteREO Discovery. V12, Carl Zeiss). All images were captured in TIF format and analyzed by a properly calibrated examiner using the Image J 1.53t software (National Institutes of Health, USA - https://imagej.nih.gov/). The percentage of remaining filling material attached to the root canal walls was calculated. The root canal was divided into three thirds (cervical, middle, and apical), according to the WL previously established (mm). Initially, the external contour of the area of each root third was delimited (mm^2). It is important to point out that to delimit the areas of interest more precisely, the images were enlarged. Next, the external contour of the remaining filling material was delimited, and based on a rule of three, the values generated for the areas expressed in mm^2 were transformed into percentages for comparison among control and experimental groups (Figure 2).

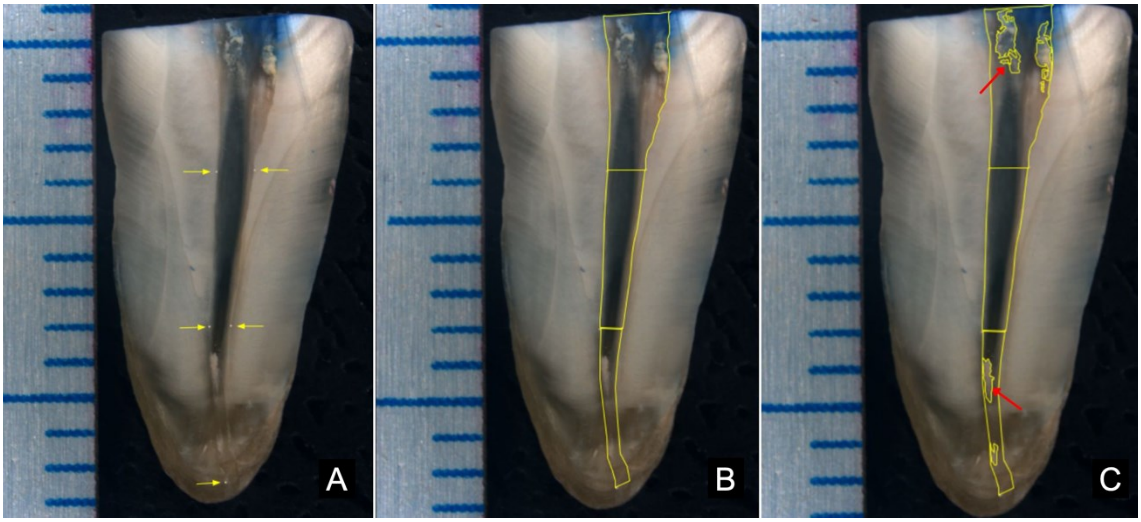

FIGURE 2 - Representative images of the root hemisection in the stereomicroscope analysis (Image J software). (*A*) Yellow arrows indicate the limits of the root thirds (cervical, middle, and apical). (*B*) Delimitation of the external contour of each root third area. (*C*) Delimitation of the external contour of the remaining filling material (red arrows).

After the stereomicroscope analysis, the hemisections were kept in an oven at 37ºC for 48 hours, and then, placed in a vacuum desiccator for the same period to eliminate all traces of moisture. Next, the hemisections were mounted onto metallic stubs, and sputter-coated with a gold/palladium layer (300 Å). Image acquisition of the hemisections was performed under Scanning Electron Microscope (SEM) (Jeol JSM 5410, Sony, Tokyo, Japan), operating at 10 keV, at ×20, ×250, ×1.000 and ×3.000 magnifications.

Statistical Analysis

Statistical analysis was performed using the IBM SPSS Statistics 25.0 software (IBM Corp., Armonk, NY, USA). The normality of data distribution and the homoscedasticity of variances was confirmed using the Shapiro-Wilk and Levene tests, respectively. Intergroup and intragroup comparisons were performed with the One-way Analysis of Variance (ANOVA) test. Post hoc comparisons were conducted using Tukey's test. The significance level was set at 5% (α = 0.05).

RESULTS

Stereomicroscope Analysis

No specimen was lost during the experiment. When the analysis of variance was examined, the different experimental conditions (irradiation timing/dosage) (P < .05) and the root canal third (P < .05) had a significant effect on the amount of remaining filling material. The interaction of these factors was also significant (P < .05).

In the intergroup analysis (Figure 3), Endo-post-RT$_{55}$ had a greater amount of remaining filling material than the NegativeCG, Endo-pre-RT$_{55}$, and Endo-pre-RT$_{70}$ in the cervical third (P = .0025). Endo-post-RT$_{70}$ had no significant difference compared to the other groups (Figure 3). Endo-pre-RT$_{70}$, Endo-post-RT$_{55}$, and Endo-post-RT$_{70}$ showed a greater amount of remaining filling material than NegativeCG and Endo-pre-RT$_{55}$ in the middle third (P < .0001). In the apical third, all experimental groups had a greater amount of remaining filling material than the negative control group (P = .0001).

In the intragroup analysis, the amount of remaining filling material in the apical third was significantly greater than in the cervical and middle thirds for the NegativeCG (P = .038) and Endo-pre-RT$_{55}$ (P = .0037). Endo-pre-RT$_{70}$ (P < .0001), Endo-post-RT$_{55}$ (P = .0079) and Endo-post-RT$_{70}$ (P = .0008) had a greater amount of remaining filling material attached to the root canal walls in the apical and middle thirds than in the cervical third.

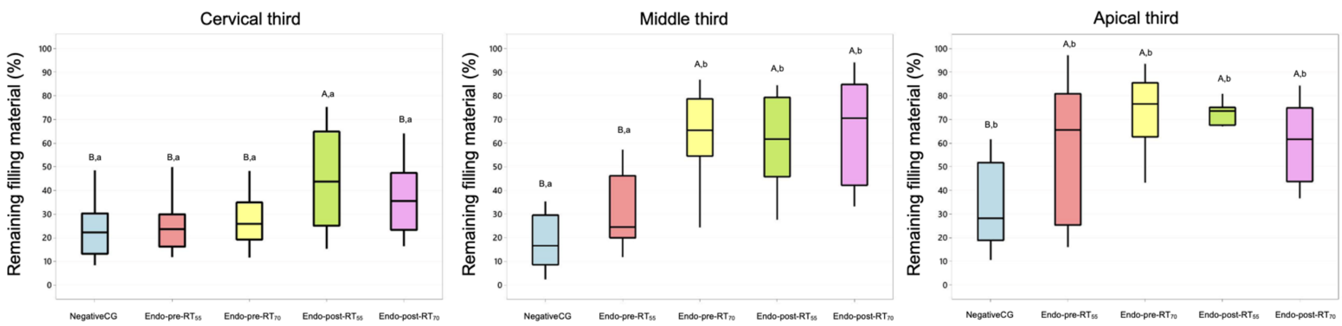

FIGURE 3 - Box plot graphical representation of the amount of remaining filling material attached to the root canal walls (%) at the different root thirds. Different uppercase letters represent a statistically significant difference among groups (intergroup analysis). Different lowercase letters represent a statistically significant difference among root thirds (intragroup analysis). One-way ANOVA test, Tukey posthoc test, P < .05.

SEM Analysis

Representative SEM images may be seen in Figure 4. There were differences between irradiated and non-irradiated specimens in terms of dentin microstructure and morphology; and the amount of remaining filling material attached to the root canal walls. There were distinct differences between the characteristics of the dentin surface before and after radiation therapy.

In the NegativeCG, it was possible to observe more regular dentinal tubules, with no signs of microcracks or radiation induced-dehydration. Most of the dentinal tubules were free of endodontic sealer. However, in some specimens, it was possible to note the presence of sealer tags within the dentinal tubules. A smaller amount of remaining filling material attached to the root canal walls was observed in the specimens of the control group in comparison with the experimental (irradiated) groups (Figure 4*A-D*). In the Endo-pre-RT groups, a greater amount of remaining filling material attached to the root canal walls was evident, regardless of the radiation dosage (55 Gy or 70 Gy) (Figure 4*E-H*). In the Endo-post-RT groups (55 Gy and 70 Gy), in some specimens, it was noted the presence of microcracks along the dentinal surface. Obliteration of the dentinal tubules and a greater amount of filling material covering them was also observed (Figure 4*I-L*).

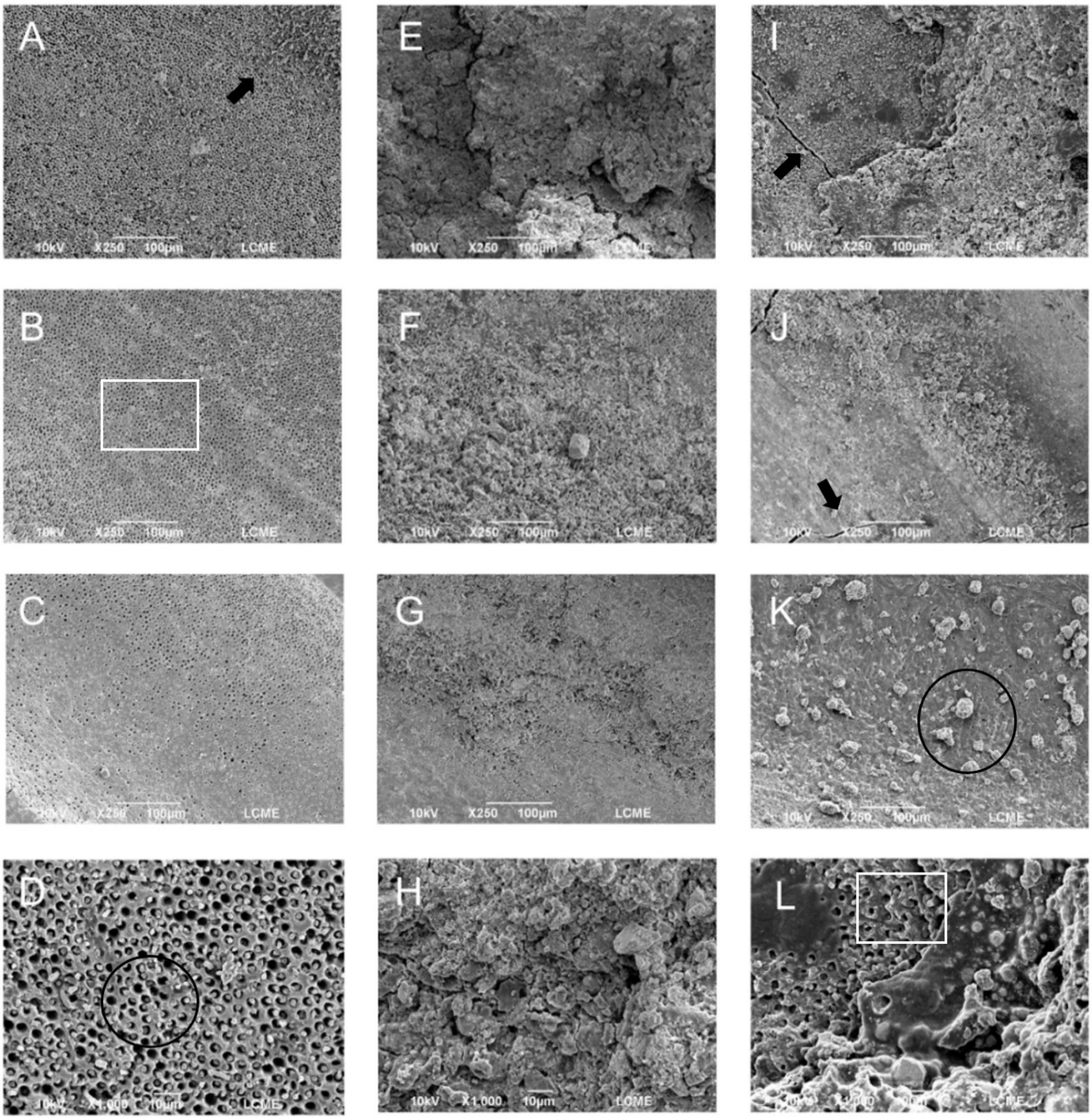

FIGURE 4 - Representative SEM images of specimens from the control and experimental groups. (*A-C*) NegativeCG - cervical, middle, and apical thirds, respectively (×250). Note the regular dentin (box), with no signs of radiation induced-dehydration or micro-cracks, and a few filling material remnants (arrows). (*D*) NegativeCG - cervical third (×1000). Sealer tags within the dentinal tubules (circle). (*E-G*) Endo-pre-RT_{70} - cervical, middle, and apical thirds, respectively (×250). Greater amount of remaining filling material attached to the root canal walls. (*H*) Endo-pre-RT_{70} - cervical third (×1000). Debris produced by the re-instrumentation covering the root canal walls in the cervical third, obliterating the entrance of the dentinal tubules. (*I-K*) Endo-post-RT_{70} - cervical, middle, and apical thirds, respectively (×250). Observe the presence of microcracks along the dentinal surface (arrows), and debris produced by the re-instrumentation covering the root canal walls (circle). (*L*) Endo-post-RT_{70} - cervical third (×1000). Note the signs of radiation induced-dehydration on the dentinal surface (box). Greater amount of filling material.

DISCUSSION

Radiation therapy is defined as the “use of high-energy radiation from X-rays, gamma-rays, neutrons, protons, and other sources to kill cancer cells and shrink tumors”[1]. This *in vitro* study assessed the amount of remaining filling material attached to the root canal walls, which had been exposed to different dosages of radiation therapy at different time points during the course of endodontic reintervention. Based on the results obtained, the first hypothesis tested was confirmed, since irradiated teeth had a greater amount of remaining filling material attached to the root canal walls than non-irradiated teeth, regardless of the timing and dosage of radiation therapy. Therefore, the second hypothesis was rejected.

Parahyba et al.[24] have reported that the irradiation delivered to the teeth of HNC patients depends on several factors, such as the primary tumor location, size, staging, and laterality. According to these authors, the dose received by mandibular premolars, the teeth used in the present study, in a clinical scenario, may range from 38.76 Gy to 64.49 Gy. Therefore, in this research, two radiation therapy dosages (55 Gy and 70 Gy) were tested to verify whether cumulative radiation might lead to harmful effects on endodontic reintervention.

Teeth irradiation was performed by the Intensity Modulated Radiotherapy Technique. This technique consists of a previous elaboration of a dose distribution map by computed tomography[17,18]. Therefore, the intensity of the radiation beam can be controlled from a three-dimensional spatial plane, maximizing disease control and minimizing morbidity and toxicity to healthy tissues adjacent to the targeted tissues (neoplastic cells)[4].

Regardless of the radiation dose received, the amount of remaining filling material attached to the root canal walls in the experimental groups was greater than in the control group, confirming the negative impact of radiotherapy on endodontic reintervention. The experimental groups showed a significantly greater amount of remaining filling material, especially in the middle and apical thirds, in comparison with the control group, except for Endo-pre-RT_{55}, in the cervical and middle thirds.

Bodrumlu et al.[12] reported that teeth irradiation after root canal obturation increased the sealer’s apical flow when compared to non-irradiated teeth. The temperature increase of the irradiated structures is one of the most common phenomena associated with radiotherapy[25]. In the present study, such a phenomenon may have led to thermoplastification of the filling material, especially gutta-percha, in the groups submitted to primary endodontic treatment before irradiation[12], hindering its removal during reintervention[26,27]. Furthermore, to validate the thermoplasticity of the filling material, specimens that had undergone endodontic treatment before radiotherapy displayed an orange hue following irradiation. Additionally, during the removal of the filling material, it became apparent that it exhibited a noticeably softer consistency in comparison with the control group.

On the other hand, the experimental group in which primary endodontic treatment was performed after radiotherapy also showed a greater amount of remaining filling material than the non-irradiated control group. Ionizing radiation causes damage to dentin morphology and microstructure, which hinders its interaction with biomaterials[6,7,10,28], such as endodontic sealers[14]. The most deleterious effects are the collapse of the collagen fibrils network, obliteration of dentinal tubules, and dentin dehydration due to radiolysis[7,28.] Radiolysis is the breakdown of water molecules by ionizing radiation, leading to free radicals and hydrogen peroxide formation[7].

In the present study, an epoxy resin-based endodontic sealer (AH Plus JET) was used for root canal obturation. This type of sealer forms covalent bonds between its epoxy rings and the amine groups of the dentin collagen, increasing its bond strength[29]. Radiotherapy significantly affects the organic portion of dentin[14,30], which highly compromises the adhesion of this endodontic sealer[14]. The collagen fibrils network collapse after irradiation is the most accepted explanation for the lower bond strength of epoxy resin-based endodontic sealer to irradiated intraradicular dentin[14].

Conversely, it is valid to notice that AH Plus JET has a hydrophobic nature[25]. Therefore, it may be suggested that the greater amount of filling material attached to the root canal walls in the groups irradiated before primary endodontic treatment and reintervention is due to a more appropriate interaction between the dehydrated dentin by irradiation and a hydrophobic sealer[29]. Our SEM analysis revealed the presence of microcracks along the dentinal surface and signs of radiation induced-dehydration on the dentinal surface. However, this is an argument that needs further studies to be corroborated. Other studies have shown a significant reduction in the bond strength of this sealer[14] due to changes in the dentin organic matrix after radiotherapy[14,30]. However, it must be emphasized that in the present study, the bond strength of the AH Plus JET was not tested, and it would not be appropriate to associate bond strength values with the amount of remaining filling material after endodontic reintervention.

Despite the different results obtained between experimental (irradiated) and control (non-irradiated) groups, the root canal third seemed to play a key role in these findings. In all groups, the apical third showed a greater amount of remaining filling material. This finding is similar to other studies that demonstrated that filling material removal in the apical third is more challenging[31-33]. The apical third is considered a critical zone because it has great anatomical variation and a high number of lateral, secondary, and accessory canals, and most of them are located in the final 3 mm[34,35].

Therefore, proper sanitization of the apical third is often difficult to achieve[36,37] and the presence of remaining filling material may shelter microorganisms responsible for maintaining periapical diseases[31]. As conventional instrumentation is not enough to completely remove the filling material from the root canal[33], supplementary steps to accomplish the removal, such as sonic and ultrasonic activation of the irrigating solutions, ultrasonic inserts for mechanical filling material removal, and the use of endodontic files that change their shape according to body temperature, have been used and promoted a significant reduction in the amount of remaining filling material attached to the root canal walls[15, 31,32].

In the present study, we opted for ultrasonic activation of the irrigating solution, since previous studies have demonstrated the effectiveness of this protocol as a supplementary step for the remaining filling material removal after initial desobturation with mechanized instruments[38-40]. The acoustic energy produced by the ultrasonic insert provides further mechanical debridement, allowing the irrigating solution to reach hard-to-reach areas not touched by the instruments[38-40]. The constant flow of the irrigating solution against the root canal walls produces an effect named cavitation, which leads to the remaining filling material dislodgement[38-40].

The use of a stereomicroscope to quantify the amount of remaining filling material might be considered a limitation of our study, as it only allows a two-dimensional analysis of the root canal images. On the other hand, micro-CT allows a three-dimensional analysis of the specimens[41,42]. However, it is a high-cost method, which restricts its access to most researchers[41,42]. In addition, it takes a long time to scan each specimen and may generate artifacts due to the presence of radiodense materials (gutta-percha and sealer) within the root canal[41,42]. Despite the limitations of using a stereomicroscope for this type of analysis, it is still widely used[20-23].

The increase in the survival rate of HNC patients reinforces the importance of oral health management[43]. Therefore, the search for clinical protocols based on scientific evidence for dental treatment before, during, and after radiation therapy in HNC patients should be highly encouraged[24]. Despite the advances in cancer treatment, teeth extraction, and oral surgery after head and neck radiation therapy continue to be avoided due to the high risk of osteoradionecrosis[44]. Proper endodontic reintervention will provide a greater chance of treatment success, and avoid periapical surgery or tooth extraction.

It is worth mentioning the clinical relevance of this study, since in the irradiated teeth, regardless of the timing in which the primary endodontic treatment was performed (pre- or post-radiotherapy), there was a greater amount of remaining filling material attached to the root canal walls. This finding proves the effect of radiation on the filling material, and consequently, on the endodontic reintervention. Such a procedure must be carried out with greater acuity than under normal clinical conditions. Furthermore, the use of supplementary steps to accomplish greater filling material removal must be always considered.

CONCLUSION

It is possible to conclude that irradiation of the teeth, before and after primary endodontic treatment, increased the amount of remaining filling material attached to the root canal walls after endodontic reintervention, regardless of the radiation dose delivered.

ACKNOWLEDGMENTS

The authors would like to thank the Department of Radiotherapy of the Oncology Research Center (CEPON - Florianópolis, SC, Brazil) for the teeth irradiation.

REFERENCES

1. American Society of Oncology. Management of the Neck in Squamous

Cell Carcinoma of the Oral Cavity and Oropharynx: ASCO Clinical Practice Guideline. J Clin Oncol. 2019;37:1753-74.

2. Jham BC, Freire ARDS. Oral complications of radiotherapy in the head and neck. Braz J Otorhinolaryngol 2006;72:704–8. https://doi.org/10.1016/S1808-8694(15)31029-6.
3. 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;214:387–93. https://doi.org/10.1038/sj.bdj.2013.380.
4. Marta GN, Silva V, De Andrade Carvalho H, et al. Intensity-modulated radiation therapy for head and neck cancer: Systematic review and meta-analysis. Radiother Oncol 2014;110:9–15. https://doi.org/10.1016/j.radonc.2013.11.010.
5. Campi LB, Lopes FC, Soares LES, et al. Effect of radiotherapy on the chemical composition of root dentin. Head Neck 2019;41:162–9. https://doi.org/10.1002/hed.25493.
6. Rodrigues RB, Soares CJ, Junior PCS, Lara VC, Arana-Chavez VE, Novais VR. Influence of radiotherapy on the dentin properties and bond strength. Clin Oral Investig 2018;22:875–83. https://doi.org/10.1007/s00784-017-2165-4.
7. Velo MM de AC, Farha ALH, da Silva Santos PS, et al. Radiotherapy alters the composition, structural and mechanical properties of root dentin in vitro. Clin Oral Investig 2018;22:2871–8. https://doi.org/10.1007/s00784-018-2373-6.
8. Nair PNR. On the causes of persistent apical periodontitis: A review. Int Endod J 2006;39:249–81. https://doi.org/10.1111/j.1365-2591.2006.01099.x.
9. Karamifar K, Tondari A, Saghiri MA. Endodontic Periapical Lesion: An Overview on the Etiology, Diagnosis and Current Treatment Modalities. Eur Endod J 2020;5:54–67. https://doi.org/10.14744/eej.2020.42714.
10. Palmier NR, Madrid Troconis CC, Normando AGC, et al. Impact of head and neck radiotherapy on the longevity of dental adhesive restorations: A systematic review and meta-analysis. J Prosthet Dent 2022;128:886–96. https://doi.org/10.1016/j.prosdent.2021.02.002.
11. 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;51:1301–12. https://doi.org/10.1111/iej.12945.

12. Bodrumlu E, Avsar A, Meydan AD, Tuloglu M. Can radiotherapy affect the apical sealing ability of resin-based root canal sealers? J Am Dent Assoc 2009;140:326–30. https://doi.org/10.14219/jada.archive.2009.0162.
13. Bodrumlu EH, Bodrumlu E. Effect of radiotherapy on the coronal-sealing ability of two different root canal sealing materials. Niger J Clin Pract 2018;21:1008–11. https://doi.org/10.4103/njcp.njcp_377_17.
14. Martins C V, 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;49:1065–72. https://doi.org/10.1111/iej.12556.
15. Silva EJNL, Belladonna FG, Zuolo AS, et al. Effectiveness of XP-endo Finisher and XP-endo Finisher R in removing root filling remnants: a micro-CT study. Int Endod J 2018;51:86–91. https://doi.org/10.1111/iej.12788.
16. De-Deus G, Belladonna FG, Zuolo AS, et al. XP-endo Finisher R instrument optimizes the removal of root filling remnants in oval-shaped canals. Int Endod J 2019;52:899–907. https://doi.org/10.1111/iej.13077.
17. Cancelier P da A, 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 2022:1–10. https://doi.org/10.1111/aej.12699.
18. 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 2023:1–8. https://doi.org/10.1111/ipd.13073.
19. da Cunha SR de B, Ramos PAMM, Haddad CMK, da Silva JLF, Fregnani ER, Aranha ACC. Effects of Different Radiation Doses on the Bond Strengths of Two Different Adhesive Systems to Enamel and Dentin. J Adhes Dent 2016:151–6. https://doi.org/10.3290/j.jad.a35841
20. da Silveira Bueno CE, de Azevêdo Rios M, Coelho MS, et al. Influence of passive ultrasonic irrigation on the removal of root canal filling material in straight root canals. Eur Endod J 2017;2:1–5. https://doi.org/10.5152/eej.2017.16062.

21. da Silva Machado AP, Câncio Couto de Souza AC, Lima Gonçalves T, Franco Marques AA, da Fonseca Roberti Garcia L, Antunes Bortoluzzi E, Acris de Carvalho FM. Does the ultrasonic activation of sealer hinder the root canal retreatment? Clin Oral Investig 2021;25:4401–4406. https://doi.org/10.1007/s00784-020-03752-0
22. Gomes NN, de Carvalho GM, Sponchiado EC, da Fonseca Roberti Garcia L, Marques AAF, de Carvalho FMA. Filling material removal with reciprocating and rotary systems associated with passive ultrasonic irrigation. Eur Endod J 2017;2:1–7. https://doi.org/10.5152/eej.2017.16037.
23. Purba R, Sonarkar SS, Podar R, Singh S, Babel S, Kulkarni G. Comparative evaluation of retreatment techniques by using different file systems from oval-shaped canals. J Conserv Dent 2020;23:91–6.
24. Parahyba CJ, Moraes FY, Ramos PAM, Haddad CMK, da Silva JLF, Fregnani ER. 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;38:1621–7.
25. Yu CX. Intensity-modulated arc therapy with dynamic multileaf collimation: An alternative to tomotherapy. Phys Med Biol 1995;40:1435–49. https://doi.org/10.1088/0031-9155/40/9/004.
26. Kim H, Kim E, Lee SJ, Shin SJ. Comparisons of the Retreatment Efficacy of Calcium Silicate and Epoxy Resin-based Sealers and Residual Sealer in Dentinal Tubules. J Endod 2015;41:2025–30. https://doi.org/10.1016/j.joen.2015.08.030.
27. Yang R, Tian J, Huang X, et al. A comparative study of dentinal tubule penetration and the retreatability of EndoSequence BC Sealer HiFlow, iRoot SP, and AH Plus with different obturation techniques. Clin Oral Investig 2021;25:4163–73. https://doi.org/10.1007/s00784-020-03747-x.
28. Gonçalves LMN, Palma-Dibb RG, Paula-Silva FWG, et al. Radiation therapy alters microhardness and microstructure of enamel and dentin of permanent human teeth. J Dent 2014;42:986–92. https://doi.org/10.1016/j.jdent.2014.05.011.
29. Marques Ferreira M, Martinho JP, Duarte I, et al. Evaluation of the Sealing

Ability and Bond Strength of Two Endodontic Root Canal Sealers: An In Vitro Study. Dent J 2022;10:1–10. https://doi.org/10.3390/dj10110201.

30. Lopes FC, Roperto R, Akkus A, de Queiroz AM, Francisco de Oliveira H, Sousa-Neto MD. Effect of carbodiimide and chlorhexidine on the bond strength longevity of resin cement to root dentine after radiation therapy. Int Endod J 2020;53:539–52. https://doi.org/10.1111/iej.13252.
31. Crozeta BM, Chaves de Souza L, Correa Silva-Sousa YT, Sousa-Neto MD, Jaramillo DE, Silva RM. Evaluation of Passive Ultrasonic Irrigation and GentleWave System as Adjuvants in Endodontic Retreatment. J Endod 2020;46:1279–85. https://doi.org/10.1016/j.joen.2020.06.001.
32. Martins MP, Duarte MAH, Cavenago BC, Kato AS, da Silveira Bueno CE. Effectiveness of the ProTaper Next and Reciproc Systems in Removing Root Canal Filling Material with Sonic or Ultrasonic Irrigation: A Micro-computed Tomographic Study. J Endod 2017;43:467–71. https://doi.org/10.1016/j.joen.2016.10.040.
33. Silva EJNL, Orlowsky NB, Herrera DR, Machado R, Krebs RL, De Souza Coutinho-Filho T. Effectiveness of rotatory and reciprocating movements in root canal filling material removal. Braz Oral Res 2015;29:1–6. https://doi.org/10.1590/1807-3107BOR-2015.vol29.0008.
34. De Deus QD, Horizonte B. Frequency, location, and direction of the lateral, secondary, and accessory canals. J Endod 1975;1:361–6. https://doi.org/10.1016/S0099-2399(75)80211-1.
35. Simon J. The apex: how critical is it? Gen Dent 1994;42:330–4.
36. Nascimento EHL, Abrahão Elias MR, Vasconcelos VHF, Haiter-Neto F, Mendonça EF, Sousa TO. Ex Vivo Detection of Apical Delta in Premolars: A Comparative Study Using Periapical Radiography, Cone-beam Computed Tomography, and Micro–computed Tomography. J Endod 2019;45:549–53. https://doi.org/10.1016/j.joen.2019.02.022.
37. Ordinola-Zapata R, Martins JNR, Niemczyk S, Bramante CM. Apical root canal anatomy in the mesiobuccal root of maxillary first molars: influence of root apical shape and prevalence of apical foramina – a micro-CT study. Int Endod J 2019;52:1218–27. https://doi.org/10.1111/iej.13109.
38. Bernardes RA, Duarte MAH, Vivan RR, Alcalde MP, Vasconcelos BC, Bramante CM. Comparison of three retreatment techniques with ultrasonic

activation in flattened canals using micro-computed tomography and scanning electron microscopy. Int Endod J 2016;49:890–7. https://doi.org/10.1111/iej.12522.

39. Cavenago BC, Ordinola-Zapata R, Duarte MAH, et al. Efficacy of xylene and passive ultrasonic irrigation on remaining root filling material during retreatment of anatomically complex teeth. Int Endod J 2014;47:1078–83. https://doi.org/10.1111/iej.12253.
40. Silveira SB, Alves FRF, Marceliano-Alves MF, et al. Removal of Root Canal Fillings in Curved Canals Using Either Mani GPR or HyFlex NT Followed by Passive Ultrasonic Irrigation. J Endod 2018;44:299–303. https://doi.org/10.1016/j.joen.2017.09.012.
41. Nair MK, Nair UP. Digital and Advanced Imaging in Endodontics: A Review. J Endod 2007;33:1–6. https://doi.org/10.1016/j.joen.2006.08.013.
42. Baumeier NC, Hungaro Duarte MA, Vivan RR, Lemos AC, Machado R, da Silva Neto UX. Passive ultrasonic irrigation, EndoActivator system and XP-endo Finisher R as additional cleaning techniques to remove residual filling materials from flattened root canals. J Conserv Dent 2022;25:385–91. https://doi.org/10.4103/jcd.jcd_117_22
43. Pulte D, Brenner H. Changes in Survival in Head and Neck Cancers in the Late 20th and Early 21st Century: A Period Analysis. Oncologist 2010;15:994–1001. https://doi.org/10.1634/theoncologist.2009-0289.
44. Moon DH, Moon SH, Wang K, et al. Incidence of, and risk factors for, mandibular osteoradionecrosis in patients with oral cavity and oropharynx cancers. Oral Oncol 2017;72:98–103. https://doi.org/10.1016/j.oraloncology.2017.07.014.

4. CONCLUSÃO

Com base nos resultados obtidos é possível afirmar que a irradiação dos dentes, antes e após o tratamento endodôntico primário, aumentou a quantidade de material obturador remanescente aderido às paredes do canal radicular após a reintervenção endodôntica, independentemente da dose de radiação recebida.

5. REFERÊNCIAS

BAUMEIER, N. C. et al. Passive ultrasonic irrigation, EndoActivator system and XP-endo Finisher R as additional cleaning techniques to remove residual filling materials from flattened root canals. **Journal of Conservative Dentistry**, v. 25, n. 4, p. 385–391, 2022.

BERNARDES, R. A. et al. Comparison of three retreatment techniques with ultrasonic activation in flattened canals using micro-computed tomography and scanning electron microscopy. **International endodontic journal**, v. 49, n. 9, p. 890–897, set. 2016.

BODRUMLU, E. et al. Can radiotherapy affect the apical sealing ability of resin-based root canal sealers? **Journal of the American Dental Association**, v. 140, n. 3, p. 326–330, 2009.

BODRUMLU, E. H.; BODRUMLU, E. Effect of radiotherapy on the coronal-sealing ability of two different root canal sealing materials. **Nigerian journal of clinical practice**, v. 21, n. 8, p. 1008–1011, 2018.

CAMPI, L. B. et al. Effect of radiotherapy on the chemical composition of root dentin. **Head and Neck**, v. 41, n. 1, p. 162–169, 2019.

CANCELIER, P. D. A. et al. Effect of the timing of radiation therapy on the push-out strength of resin cement to root dentine. **Australian Endodontic Journal**, p. 1–10, 2022.

CAVENAGO, B. C. et al. Efficacy of xylene and passive ultrasonic irrigation on remaining root filling material during retreatment of anatomically complex teeth. **International Endodontic Journal**, v. 47, n. 11, p. 1078–1083, 2014.

COELHO, S. M. et al. Effect of radiation therapy on fracture resistance of simulated immature teeth submitted to root reinforcement. **International Journal of Paediatric Dentistry**, p.1–8, 2023.

COLE, T.; SILVER, A. H. Production of hydrogen atoms in teeth by X-irradiation. **Nature**, v. 200, n. 4907, p. 700–701, 1963.

CROZETA, B. M. et al. Micro-Computed Tomography Study of Filling Material Removal from Oval-shaped Canals by Using Rotary, Reciprocating, and Adaptive Motion Systems. **Journal of Endodontics**, v. 42, n. 5, p. 793–797, 2016.

CROZETA, B. M. et al. Evaluation of Passive Ultrasonic Irrigation and GentleWave System as Adjuvants in Endodontic Retreatment. **Journal of Endodontics**, v. 46, n. 9, p. 1279–1285, 2020.

DA SILVA MACHADO, A. P. et al. Does the ultrasonic activation of sealer hinder the root canal retreatment? **Clinical Oral Investigations**, v. 25, n. 7, p. 4401–4406, 2021.

DA SILVEIRA BUENO, C. E. et al. Influence of passive ultrasonic irrigation on the removal of root canal filling material in straight root canals. **European Endodontic Journal**, v. 2, n. 1, 2017.

DE BARROS DA CUNHA, S. R. et al. Effects of different radiation doses on the microhardness, superficial morphology, and mineral components of human enamel. **Archives of Oral Biology**, v. 80, p. 130–135, 2017.

DE-DEUS, G. et al. XP-endo Finisher R instrument optimizes the removal of root filling remnants in oval-shaped canals. International Endodontic Journal, v.52, n.6, p.899–907, 2019.

DE DEUS, Q. D.; HORIZONTE, B. Frequency, location, and direction of the lateral, secondary, and accessory canals. **Journal of Endodontics**, v. 1, n. 11, p. 361–366, 1975.

GOMES, N. N. et al. Filling material removal with reciprocating and rotary systems associated with passive ultrasonic irrigation. **European Endodontic Journal**, v. 2, n. 1, p.1–7, 2017.

GONÇALVES, L. M. N. et al. Radiation therapy alters microhardness and microstructure of enamel and dentin of permanent human teeth. **Journal of Dentistry**, v. 42, n. 8, p. 986–992, 2014.

HOPPENBROUWERS, P. M. M.; DRIESSENS, F. C. M.; BORGGREVEN, J. M. P. M. The mineral solubility of human tooth roots. **Archives of Oral Biology**, v. 32, n. 5, p. 319–322, 1987.

JHAM, B. C.; FREIRE, A. R. D. S. Oral complications of radiotherapy in the head and neck. **Brazilian Journal of Otorhinolaryngology**, v. 72, n. 5, p. 704–708, 2006.

KARAMIFAR, K.; TONDARI, A.; SAGHIRI, M. A. Endodontic Periapical Lesion: An Overview on the Etiology, Diagnosis and Current Treatment Modalities. **European Endodontic Journal**, v. 5, n. 2, p. 54–67, 2020.

KIM, H. et al. Comparisons of the Retreatment Efficacy of Calcium Silicate and Epoxy Resin-based Sealers and Residual Sealer in Dentinal Tubules. **Journal of Endodontics**, v. 41, n. 12, p. 2025–2030, 2015.

LIESHOUT, H. F. J.; BOTS, C. P. The effect of radiotherapy on dental hard tissue- a systematic review. **Clinical Oral Investigations**, v. 18, n. 1, p. 17–24, 2014.

LOPES, F. C. et al. Effect of carbodiimide and chlorhexidine on the bond strength longevity of resin cement to root dentine after radiation therapy. **International Endodontic Journal**, v. 53, n. 4, p. 539–552, 2020.

MARQUES FERREIRA, M. et al. Evaluation of the Sealing Ability and Bond Strength of Two Endodontic Root Canal Sealers: An In Vitro Study. **Dentistry Journal**, v. 10, n. 11, p. 1–10, 2022.

MARTA, G. N. et al. Intensity-modulated radiation therapy for head and neck cancer: Systematic review and meta-analysis. **Radiotherapy and Oncology**, v. 110, n. 1, p. 9–15, 2014.

MARTINS, M. P. et al. Effectiveness of the ProTaper Next and Reciproc Systems in Removing Root Canal Filling Material with Sonic or Ultrasonic Irrigation: A Micro-computed Tomographic Study. **Journal of endodontics**, v. 43, n. 3, p. 467–471, 2017.

MARTINS, C. V. et al. Influence of therapeutic cancer radiation on the bond strength of an epoxy- or an MTA-based sealer to root dentine. **International Endodontic Journal**, v. 49, n. 11, p. 1065–1072, 2016.

MOON, D. H. et al. Incidence of, and risk factors for, mandibular osteoradionecrosis in patients with oral cavity and oropharynx cancers. **Oral Oncology**, v. 72, p. 98–103, 2017.

NAIR, M. K.; NAIR, U. P. Digital and advanced imaging in endodontics: a review. **Journal of Endodontics**, v. 33, n. 1, p. 1–6, 2007.

NAIR, P. N. R. On the causes of persistent apical periodontitis: A review. **International Endodontic Journal**, v. 39, n. 4, p. 249–281, 2006.

NASCIMENTO, E. H. L. et al. Ex Vivo Detection of Apical Delta in Premolars: A Comparative Study Using Periapical Radiography, Cone-beam Computed Tomography, and Micro–computed Tomography. **Journal of Endodontics**, v. 45, n. 5, p. 549–553, 2019.

ORDINOLA-ZAPATA, R. et al. Apical root canal anatomy in the mesiobuccal root of maxillary first molars: influence of root apical shape and prevalence of apical foramina – a micro-CT study. **International Endodontic Journal**, v. 52, n. 8, p. 1218–1227, 2019.

ORGANIZATION., W. H. **Cancer control: knowledge into action: WHO guide for effective programmes: diagnosis and treatment.** Geneva: 2008

PALMIER, N. R. et al. Impact of head and neck radiotherapy on the longevity of dental adhesive restorations: A systematic review and meta-analysis. **Journal of Prosthetic Dentistry**, v. 128, n. 5, p. 886–896, 2022.

PARAHYBA, C. J. 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**, v. 38, n. 11, p. 1621–1627, 2016.

PULTE, D.; BRENNER, H. Changes in Survival in Head and Neck Cancers in the Late 20th and Early 21st Century: A Period Analysis. **The Oncologist**, v. 15, n. 9, p. 994–1001, 2010.

PURBA, R. et al. Comparative evaluation of retreatment techniques by using different file systems from oval-shaped canals. **Journal of Conservative Dentistry**, v. 23, n. 1, p. 91–96, 2020.

RAY-CHAUDHURI, A.; SHAH, K.; PORTER, R. J. The oral management of patients who have received radiotherapy to the head and neck region. **British Dental Journal**, v. 214, n. 8, p. 387–393, 2013.

RODRIGUES, R. B. et al. Influence of radiotherapy on the dentin properties and bond strength. **Clinical Oral Investigations**, v. 22, n. 2, p. 875–883, 2018.

RUDDLE, C. J. Nonsurgical Retreatment. **Journal of Endodontics**, v. 30, n. 12, p. 827–845, 2004.

SILVA, E. J. N. L. et al. Effectiveness of rotatory and reciprocating movements in root canal filling material removal. **Brazilian Oral Research**, v. 29, n. 1, p. 1–6, 2015.

SILVA, E. J. N. L. et al. Effectiveness of XP-endo Finisher and XP-endo Finisher R in removing root filling remnants: a micro-CT study. **International endodontic journal**, v. 51, n. 1, p. 86–91, 2018.

SILVEIRA, S. B. et al. Removal of Root Canal Fillings in Curved Canals Using Either Mani GPR or HyFlex NT Followed by Passive Ultrasonic Irrigation. **Journal of Endodontics**, v. 44, n. 2, p. 299- 303, 2018.

SIMON, J. The apex: how critical is it? **General Dentistry**, v. 42, n. 4, p. 330–334, 1994.

SIQUEIRA, J. F. et al. Periradicular status related to the quality of coronal restorations and root canal fillings in a Brazilian population. **Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology**, v. 100, n. 3, p. 369–374, 2005.

SIQUEIRA JUNIOR, J. F. et al. Unprepared root canal surface areas: Causes, clinical implications, and therapeutic strategies. **Brazilian Oral Research**, v. 32, p. 1–19, 2018.

VELO, M. M. DE A. C. et al. Radiotherapy alters the composition, structural and mechanical properties of root dentin in vitro. **Clinical Oral Investigations**, v. 22, n. 8, p. 2871–2878, 2018.

YAMIN, P. A. et al. Longevity of bond strength of resin cements to root dentine after radiation therapy. **International Endodontic Journal**, v. 51, n. 11, p. 1301–1312, 2018.

YANG, R. et al. A comparative study of dentinal tubule penetration and the retreatability of EndoSequence BC Sealer HiFlow, iRoot SP, and AH Plus with different obturation techniques. **Clinical Oral Investigations**, v. 25, n. 6, p. 4163–4173, 2021.

YU, C. X. Intensity-modulated arc therapy with dynamic multileaf collimation: An alternative to tomotherapy. **Physics in Medicine and Biology**, v. 40, n. 9, p. 1435–1449, 1995.

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: Reintervenção endodôntica em dentes irradiados: efeito do momento de realização do tratamento endodôntico (pré e pós-irradiação) na quantidade de material obturador remanescente

Pesquisador: LUCAS DA FONSECA ROBERTI GARCIA

Área Temática:

Versão: 2

CAAE: 65558822.0.0000.0121

Instituição Proponente: CENTRO DE CIÊNCIAS DA SAÚDE

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 5.915.260

Apresentação do Projeto:

As informações que seguem e as elencadas nos campos "Objetivo da pesquisa" e "Avaliação dos riscos e benefícios" foram retiradas do arquivo PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_2055771.pdf, de 22/12/2022, preenchido pelos pesquisadores.

Segundo os pesquisadores:

RESUMO

"O objetivo do presente estudo será avaliar o efeito da radiação ionizante na quantidade de material obturador remanescente aderido às paredes do canal radicular após reintervenção endodôntica, em função do momento em que o tratamento endodôntico será realizado (pré e pós-radiação). Sessenta pré-molares inferiores humanos unirradiculares serão selecionados e distribuídos em 3 grupos de acordo com o momento da radiação, com 12 amostras no grupo controle e 24 amostras em cada grupo teste: GCN (grupo controle negativo- dentes não irradiados)- será realizado o tratamento endodôntico, após 30 dias, será realizada a reintervenção endodôntica; GEndo-pré (tratamento endodôntico pré-radioterapia) - os dentes serão tratados endodonticamente previamente a irradiação. Após 30 dias, os dentes serão irradiados. Após a

Investigador	Projeto_de_Pesquisa.pdf	22/12/2022 21:46:50	GARCIA	Aceito
Folha de Rosto	folhaDeRosto_assinado.pdf	23/11/2022 19:12:13	LUCAS DA FONSECA ROBERTI GARCIA	Aceito
Declaração de Instituição e Infraestrutura	Declaracao_Infraestrutura_CEPON.pdf	23/11/2022 15:50:54	LUCAS DA FONSECA ROBERTI GARCIA	Aceito
Declaração de Instituição e Infraestrutura	Declaracao_Infraestrutura_UFSC.pdf	23/11/2022 15:50:38	LUCAS DA FONSECA ROBERTI GARCIA	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

FLORIANOPOLIS, 28 de Fevereiro de 2023

Assinado por:
Luciana C Antunes
(Coordenador(a))