UNIVERSIDADE FEDERAL DO RIO DE JANEIRO
Centro de Ciências da Saúde
Faculdade de Odontologia

DIAGNÓSTICO E DECISÕES DE TRATAMENTO PARA CÁRIE INDUZIDO POR LUZ: APLICAÇÃO DE UMA CÂMERA INTRAORAL COM FLUORESCÊNCIA

Luciana Pereira da Silva

Rio de Janeiro
2022

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Tese de doutorado submetida ao Programa de Pós-graduação em Odontologia (Área de Concentração: Odontopediatria) da Faculdade de Odontologia da Universidade Federal do Rio de Janeiro como parte dos requisitos para obtenção do título de Doutor em Odontologia (Área de Concentração: Odontopediatria).

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Tese de Doutorado submetida ao Programa de Pós-Graduação em Odontologia, Faculdade de Odontologia, Universidade Federal do Rio de Janeiro-UFRJ, como parte dos requisitos necessários à obtenção do título de Doutor em Odontologia (Odontopediatria).

Rio de Janeiro, 08 de novembro de 2022.

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DEDICATÓRIA

Aos meus pais, **João Carlos Lima da Silva** e **Marilza Pereira da Silva**, por tudo que eu sou. Vocês me presentearam com a câmera intraoral utilizada nesta tese. Me fizeram crer que este sonho era possível. Ao longo desses cinco anos, tivemos momentos difíceis, mas em todos eles, me ensinaram a ter fé.

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RESUMO

DA SILVA, Luciana Pereira. Diagnóstico e decisões de tratamento para cárie induzido por luz: aplicação de uma câmera intraoral com fluorescência. Rio de Janeiro, 2022. Tese (Doutorado em Odontologia – Área de Concentração: Odontopediatria) – Faculdade de Odontologia, Universidade Federal do Rio de Janeiro, Rio de Janeiro, 2022.

Objetivou-se verificar se 1) o diagnóstico por fluorescência (DF) e o exame visual (EV), são igualmente eficazes em detectar lesões de mancha branca (MB); 2) verificar se imagens obtidas por uma câmera intraoral, no modo luz branca (LB) ou fluorescente (LF) são comparáveis à radiografia digital (RD) no diagnóstico e no auxílio às decisões de tratamento para cárie oclusal e 3) verificar se a câmera intraoral, no modo LF, comporta-se com precisão, ao definir se a remoção químico-mecânica (RQM) de dentina cariada com gel de papaína estabelece um adequado limite para o preparo. Neste contexto, três estudos foram propostos. O primeiro estudo contou com uma revisão sistemática da literatura, a fim de verificar se o DF e o EV, são comparáveis em detectar lesões de MB relacionada a ortodontia fixa. Cinco estudos foram incluídos nesta revisão. O diagnóstico de MB relacionada a ortodontia fixa, realizado por fluorescência, foi satisfatório em relação ao EV, porém com baixa qualidade das evidências. O segundo estudo contou com uma pesquisa *ex vivo*, com 10 molares permanentes e 26 dentistas avaliadores, e propôs verificar se imagens obtidas pela câmera intraoral SoproLife®, no modo LB e LF, e as RD, são comparáveis no diagnóstico e decisões de tratamento de cárie oclusal, comparado a um padrão-ouro em microtomografia computadorizada (micro-CT). Para o diagnóstico de cárie, não foi encontrada diferença entre os três métodos ($p=0,415$), com uma concordância geral baixa (média de 15,3%), enquanto para as decisões de tratamento, o percentual de acertos entre os três métodos foi maior para a LB (48,1%) e LF (51,2%) em relação a RD (30,4%) ($p<0,001$). O terceiro estudo foi realizado *ex vivo*, a fim de verificar se a câmera intraoral SoproLife®, no modo LF, comporta-se com precisão, ao definir se a RQM de dentina cariada pelo gel é suficiente comparado a um padrão-ouro em micro-CT. A efetividade de dois géis de papaína na remoção de cárie em dentina também foi estudada. Após o escaneamento inicial, 20 molares permanentes foram pareados e divididos em grupos, (G1) Papacárie Duo® e (G2) Brix3000®. O limiar para a detecção de tecido cariado de <1,11 g/cm^3, foi utilizado. A eficácia da RQM foi menor para o Papacárie Duo® comparado ao Brix3000® ($p<0,05$). Ambos os grupos apresentaram falsos positivos quando a câmera intraoral SoproLife® considerou tecido cariado presente. Deste modo, conclui-se que: 1) O diagnóstico de MB relacionada a ortodontia fixa por DF, mostrou-se satisfatório em relação ao EV; 2) Imagens em LB, LF e RD, foram eficazes nas decisões de tratamento de cárie oclusal; 3) a câmera intraoral SoproLife® não definiu apropriadamente se a RQM pelo gel foi suficiente; 4) a utilização dos géis de papaína resultou em remoção de tecido cariado conservativa, preservando tecido dental sadio.

Palavras-chave: Cárie Dentária, Fluorescência Quantitativa Induzida por Luz, Microtomografia por Raio-X.

ABSTRACT

DA SILVA, Luciana Pereira. Diagnóstico e decisões de tratamento para cárie induzido por luz: aplicação de uma câmera intraoral com fluorescência. Rio de Janeiro, 2022. Tese (Doutorado em Odontologia – Área de Concentração: Odontopediatria) – Faculdade de Odontologia, Universidade Federal do Rio de Janeiro, Rio de Janeiro, 2022.

The aim was to verify if 1) fluorescence diagnosis (FD) and visual examination (VE) are equally effective in detecting white spot (WS) lesions; 2) to verify whether images transmitted by an intraoral camera in white light (WL) mode or fluorescent (FL) are comparable to digital radiography (DR) in diagnosing and aiding treatment decisions for occlusal caries and 3) verify whether the intraoral camera, in FL mode, behaves accurately, when defining whether chemical-mechanical removal (CMR) of carious dentin with papain gel results in appropriate threshold for cavity preparation. In this context, three studies were proposed. The first study was a systematic review of the literature, in order to verify if FD and VE are comparable in detecting WS lesions related to fixed orthodontics. Five studies were included in this review. The diagnosis of WS, performed by fluorescence, was satisfactory in relation to VE, but with very low quality of evidence. The second study included an *ex vivo* survey, with 10 permanent molars and 26 examiners, and verified whether images obtained by the SoproLife® intraoral camera, in WL and FL mode, and the DR, are comparable in the diagnosis and treatment decisions of occlusal caries compared to a gold standard in micro-computed tomography (micro-CT). For caries diagnosis, no difference was found between the three methods ($p=0.415$), with a low overall agreement (mean of 15.3%), while for treatment decisions, the percentage of correct answers between the three methods was higher for WL (48.1%) and FL (51.2%) compared to DR (30.4%) ($p<0.001$). The third study was performed *ex vivo*, in order to verify whether SoproLife® intraoral camera, in FL mode, behaves accurately, when defining whether the CMR of carious dentin is sufficient compared to a gold standard in micro-CT. The effectiveness of two papain gels in removing caries in dentin was also studied. After the initial scan, 20 permanent molars were paired and divided into groups, (G1) Papacárie Duo® and (G2) Brix3000®. A threshold for carious tissue (<1.11 g/cm3) was used. The effectiveness of CMR was lower for Papacárie Duo® compared to Brix3000® ($p<0.05$). Both groups showed false positives when SoproLife® intraoral camera evaluated carious tissue present. Thus, it is concluded that: 1) The diagnosis of WS related to fixed orthodontics due to FD, was satisfactory in relation to VE; 2) WL, FL and DR images were effective in defining occlusal caries treatment decisions and 3) SoproLife® intraoral camera did not properly define whether CMR sufficient and 4) the use of papain gels resulted in conservative removal of carious tissue, preserving sound dental tissue.

Keywords: Dental Caries, Quantitative Light-Induced Fluorescence, X-Ray Microtomography.

RESUMEN

DA SILVA, Luciana Pereira. Diagnóstico e decisões de tratamento para cárie induzido por luz: aplicação de uma câmera intraoral com fluorescência. Rio de Janeiro, 2022. Tese (Doutorado em Odontologia – Área de Concentração: Odontopediatria) – Faculdade de Odontologia, Universidade Federal do Rio de Janeiro, Rio de Janeiro, 2022.

El objetivo fue verificar si 1) el diagnóstico de fluorescencia (DF) y el examen visual (VE) son igualmente efectivos para detectar lesiones de mancha blanca (MB); 2) verificar si las imágenes obtenidas por una cámara intraoral, en modo de luz blanca (LB) o fluorescente (LF), son comparables a la radiografía digital (RD) en el diagnóstico y para ayudar a las decisiones de tratamiento de la carie oclusal y 3) verificar si la cámara intraoral, en modo LF, se comporta con precisión a la hora de definir si la eliminación químico-mecánica (EQM) de dentina cariada con gel de la papaína establece un umbral adecuado para la preparación. Em este contexto, se propusieron tres estudios. El primer estudio incluyó una revisión sistemática de la literatura para verificar si el DF y el VE son comparables en la detección de lesiones de MB relacionadas con la ortodoncia fija. En esta revisión se incluyeron cinco estudios. El diagnóstico de MB relacionado con ortodoncia fija, realizado por fluorescencia, fue satisfactorio en relación a la VE, pero con baja calidad de la evidencia. El segundo estudio fue hecho con una encuesta *ex vivo*, con 10 molares permanentes y 26 odontólogos evaluadores, y propuso verificar si las imágenes obtenidas por la cámara intraoral SoproLife®, en modo LB y LF, y RD, son comparables en las decisiones de diagnóstico y tratamiento de carie oclusal, en comparación con um estándar de oro en microtomografia computadorizada (micro-CT). Para el diagnóstico de caries, no se encontró diferencia entre los tres métodos ($p=0,415$), con un acuerdo general bajo (promedio de 15,3%), mientras que para las decisiones de tratamiento, el porcentaje de respuestas correctas entre los tres métodos fue mayor para LB (48,1%) y LF (51,2%) em relación a RD (30,4%) ($p<0,001$). El tercer estudio se realizó *ex vivo*, con el fin de verificar si la cámara intraoral SoproLife®, en modo LF, se comporta con precisión, al momento de definir si el EQM de la dentina cariada por el gel es suficiente en comparación con un padrón oro en micro-CT. También se estudió la eficacia de dos geles de papaína para eliminar la caries dentinaria. Después del escaneo inicial, 20 molares permanentes fueron emparejados y divididos en grupos, (G1) Paracárie Duo® y (G2) Brix3000®. Se utilizó el umbral para la detección de tejido cariado de <1,11 g/cm^3. La eficacia de EQM fue menor para Paracárie Duo® en comparación con Brix3000® ($p<0,05$). Ambos grupos tuvieron falsos positivos cuando la cámara intraoral SoproLife® considero presencia de tejido descompuesto. Así, se concluye que: 1) El diagnóstico de MB relacionado con ortodoncia fija por DF resultó ser satisfactorio en relación a VE; 2) las imágenes LB, LF y RD fueron efectivas em las decisiones de tratamiento de caries oclusales; 3) la cámara intraoral SoproLife® no ha definido correctamente si el gel EQM fue suficiente; 4) el uso de geles de Paracárie Duo® como resultado la eliminación conservadora del tejido cariado, preservando el tejido dental sano.

Palavras clave: Caries Dental, Fluorescencia Cuantitativa Inducida por la Luz, Microtomografía por Rayos X.

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LISTA DE SIGLAS

BBO	Bibliografia Brasileira de Odontologia
CAAE	Certificado de Apresentação de Apreciação Ética
CEP	Código de Endereçamento Postal
COPPE	Instituto Alberto Luiz Coimbra de Pós-Graduação e Pesquisa de Engenharia, Universidade Federal do Rio de Janeiro
DF	Diagnóstico Fluorescente; por Fluorescência
DFM	Digital Fluorescent Method
DR	Digital Radiography
DV	Desvio Padrão
ECV	Exame Clínico Visual
Email	Correio Eletrônico; Eletronic Mail
EUA	Estados Unidos da América United States of America
USA	United States of America
FACE	Fluorescence-aided Caries Excavation
FL	Fluorescent Light
FO	Faculdade de Odontologia
GEE	Generalized Estimating Equations
GRADE	Grading Recommendations, Assessments, Development, and Evaluations
HGeRJ	Hospital Militar do Estado do Rio de Janeiro
HMI	Hipomineralização de Molares e Incisivos
HUCFF	Hospital Universitário Clementino Fraga Filho
IC	Initial caries
ICDAS	Sistema Internacional de Detecção e Avaliação de Cárie, International Caries Detection and Assessment System
LB	Luz Branca
LED	Light Emitting Diode
LF	Luz Fluorescente
LIFE-D.T.	Light-induced Fluorescence Evaluator for Diagnosis and Treatment

LILACS	Literatura Latino-Americana e do Caribe em Ciências da Saúde
LIN	Laboratório de Instrumentação Nuclear
MB	Mancha Branca
MeSH	Medical Subject Headings
PBOCI	Pesquisa Brasileira em Odontopediatria e Clínica Integrada
PICO	Population, Intervention, Comparison e Outcome
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols
PROSPERO	International Prospective Register of Systematic Reviews
QLF	Quantitative Light-induced Fluorescence
QUADAS	Avaliação de Qualidade de Estudos de Acurácia Diagnóstica, Quality Assessment of Diagnostic Accuracy
RC	Residual Caries
RD	Radiografia Digital; Exame Radiográfico Digital
RDV	Removed Dentine Volume
RJ	Rio de Janeiro
RQM	Remoção Químico-mecânico
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
STARD	Standard for Reporting of Dianostic Accuracy
TCLE	Termo de Consentimento Livre e Esclarecido
UFRJ	Universidade Federal do Rio de Janeiro
VCE	Visual Clinical Examination
VI	Volume Inicial
VTDR	Volume Total de Dentina Removida
WL	White Light
WSL	White Spot Lesion

LISTA DE ABREVIATURAS

3D	Tridimensional
cm	Centímetro
phD	do Latim Philosophiae Doctor, Doctor Philosophiae
et al.	E outros; do latim et alia
H_2HPO_4	Fosfato de Potássio Dibásico
g/cm^3	Grama por Centímetro Cúbico
h	Hora; Hour
IC	Intervalo de Confiança; Confidence Interval
Pixel	Menor Unidade de uma Imagem Digital
μA	Microampère; Microampere
μμ	Micrômetros; Micrometers
Micro-CT	Microtomografia Computadorizada; Micro-computed
mm^3	Milímetro Cúbico
mm	Milímetros; Millimeters
nm	Nanômetro
n	Número Absoluto
pH	Potencial Hidrogeniônico
Prof	Professor(a)
kV	Quilovolts; Kilovolts
s	Segundo; Second
TIFF	Tag Image File Format
p	Valor-p; P-value
v	Versão; Version

LISTA DE SÍMBOLOS

α	Alfa
€	Euros
°	Grau Celsius, Degree Celsius
=	Igual
>	Maior que
±	Mais ou Menos
®	Marca Registrada
≤	Menor ou igual
<	Menor que
%	Porcentagem
R$	Real
TM	Trademark Symbol

SUMÁRIO

1. INTRODUÇÃO

A cárie dentária é resultado de um processo dinâmico que ocorre na superfície dos dentes em resultado da atividade metabólica no biofilme dental (Kidd *et al.*, 2004), impulsionada pela ingestão frequente de carboidratos fermentáveis. Uma mudança na população de microrganismos de baixa cariogenicidade para outra de alta cariogenicidade (mais acidúrica e acidogênica), leva a um aumento na produção de ácidos orgânicos, que promovem a perda mineral de tecido duro dental e resulta no aparecimento de uma lesão de cárie (Fejerskov *et al.*, 2015). De acordo com o "*The Global Burden of Disease Study*", cerca de 2,3 bilhões de pessoas sofrem com a doença e dessas, 530 milhões são crianças. Embora sejam dados estimativos, eles devem ser olhados com atenção (Bernabe *et al.*, 2020).

Os episódios de desmineralização dentária podem ser compensados pelo ganho mineral promovido pela saliva e potencializados pelo fluoreto no meio bucal (Machiulskiene e Carvalho, 2018). A cárie dentária manifesta-se clinicamente em diferentes estágios de desenvolvimento e progressão. Ao reconhecê-la como um processo, que varia de sinais subclínicos até cavidades evidentes, entende-se que estimar a sua magnitude é essencial para estabelecer o limiar para detecção clínica de seus sinais e sintomas (Machiulskiene e Carvalho, 2018).

Na prática clínica, o exame visual (EV), por si só, é o método de inspeção mais adequado e o mais específico para a detecção de lesões de cárie, comparado ao exame radiográfico (RD) e ao método de diagnóstico por fluorescência (DF), induzido por luz (Gimenez *et al.*, 2021). Entretanto, há uma dificuldade visual e táctil em se reconhecer o limite exato entre o tecido cariado infectado e aquele mais profundo, onde a fonte de contaminação ainda não penetrou (Neves *et al.*, 2011), o que faz com que essa etapa do tratamento ainda não seja objetiva (Ricketts *et al.*, 2018; Zhang *et al.*, 2013).

Na inspeção de lesões iniciais (mais conhecidas da terminologia ortodôntica como manchas brancas) (MBs), o DF apresentou boa acurácia na distinção da presença ou ausência de lesões (Sardana *et al.*, 2022). Na inspeção de lesões avançadas em dentes permanentes, o DF comportou-se ligeiramente melhor, comparado ao EV, tanto no ambiente laboratorial quanto clínico (Gimenez *et al.*, 2021). Embora seja considerado que o DF sirva pouco para identificar lesões em estágios avançados, fáceis de distinguir visualmente, alguns autores a sugerem como método auxiliar no processo de tomada de decisão clínica, nomeando-a como "Avaliação de Fluorescência induzida Por Luz para Diagnóstico e Tratamento", sigla em inglês (LIFE-DT) (Salama *et al.*, 2022; Terrer *et al.*, 2009; Terrer *et al.*, 2010).

A câmera intraoral SoproLife® (Sopro-Acteon group, La Ciotat, França) combina a magnificação da imagem digital (modo luz branca) com a tecnologia da fluorescência (modo luz violeta) induzida por um diodo emissor de luz (LED) com comprimento de onda de 450 nanômetros (nm), para analisar as diferenças de densidade, estrutura e/ou composição química do tecido biológico dental (Terrer *et al.*, 2009; Terrer *et al.*, 2010). Segundo o fabricante, a câmera detecta a presença ou ausência de lesão de cárie, de acordo com a cor emitida pelo tecido dental (verde/azul, indicando ausência, enquanto vermelho/marrom, presença), e a atividade das lesões de acordo a intensidade da fluorescência (brilhante, indicando ativo, enquanto escuro, inativo) (Alkahtani *et al.*, 2021).

O ônus atribuído a câmera intraoral SoproLife® refere-se ao custo, cerca de € 3500 a € 4000, que no Brasil correspondem cerca de R$ 20.000,00 (Alkahtani *et al.*, 2021). Ainda para Alkahtani *et al*. (2021), este é um fator que merece ser ponderado, relacionando o benefício pretendido com a câmera na prática clínica. Ressalta-se que há uma escassez de estudos que validam a câmera para a função de auxiliar nas decisões de tratamento, ao avaliar atividade das lesões e qualidade da dentina cariada.

Os métodos convencionais de remoção de cárie e preparo cavitário usam instrumentos mecânicos (Neves *et al.*, 2011), em especial os rotatórios (Barros *et al.*, 2020), frequentemente associados a dor e ao medo, especialmente em crianças (Dorri *et al.*, 2017). Além disso, podem representar um risco potencial para a remoção de tecido saudável do dente e causar danos irreversíveis da polpa (Bussadori *et al.*, 2005). Embora sejam amplamente aceitos e rápidos, há uma forte tendência de substituí-los por abordagens terapêuticas mais modernas, como o método de remoção químico-mecânico (RQM) de cárie (Alkhouli *et al.*, 2020; Neves *et al.*, 2015; Neves *et al.*, 2011; Zambrano-Achig *et al.*, 2022).

O princípio de ação da RQM é amolecer a dentina infectada e facilitar a sua remoção, através da aplicação de um agente (gel) bactericida, bacteriostático e anti-inflamatório, composto basicamente por papaína, cloramina, azul de toluidina, sais e veículo espessante (Bussadori *et al.*, 2005). A papaína é uma enzima proteolítica, extraída do látex das folhas e frutos do mamão verde. Após a aplicação do gel na cavidade, surgem bolhas pela liberação de oxigênio e a partir daí, o processo de remoção de dentina cariada pode ser iniciado, por meio do lado oposto de uma colher de dentina, com movimentos pendulares e sem corte (Bussadori *et al.*, 2005). Dentre as vantagens do gel base-enzimático para a RQM, estão: uma menor dor induzida (Cardoso *et al.*, 2020) e custo relativamente baixo (Bottega *et al.*, 2018; Bussadori *et al.*, 2005), e as marcas atualmente presentes no mercado brasileiro, são: Papacárie Duo® (Fórmula & Ação, São Paulo, Brasil) (Bussadori *et al.*, 2005) e Brix 3000® (Brix SRL, Cacarañá, Argentina) (Alkhouli *et al.*, 2020).

A dentina residual após a RQM com gel base-enzimático de papaína, apresenta características microbiológicas semelhantes às da dentina residual, quando removida por método tradicional (Motta *et al.*, 2014). Este recurso pode ser atribuído ao fato de que o gel não afeta as fibras colágenas de dentina hígida, degrada apenas as células mortas (Bussadori *et al.*, 2005).

Perante o exposto, verifica-se a importância de realizar pesquisas sobre classificações diagnósticas e decisões de tratamento para cárie, por meio de fluorescência induzida por luz, além de avaliar, também por fluorescência, se a dentina cariada escavada, pela RQM com gel enzimático, foi suficiente e a partir daí, estabelecer um marcador biológico entre tecido infectado e o um mais profundo.

2. PROPOSIÇÃO

2.1 Objetivo geral

Verificar a acurácia das decisões de tratamento para cárie, auxiliadas por luz branca ou fluorescente, a partir de imagens digitais obtidas através de uma câmera intraoral.

2.2 Objetivos específicos

- Verificar, por meio de uma revisão sistemática da literatura, se existem evidências que o diagnóstico por fluorescência e o exame clínico visual, são igualmente eficazes na detecção de lesões de mancha branca relacionadas a ortodontia fixa.
- Verificar, por meio de um estudo *ex vivo*, se há concordância entre imagens obtidas por uma câmera intraoral, em modo luz branca ou fluorescente, e a radiografia digital, no diagnóstico e decisões de tratamento para cárie oclusal, comparado à um padrão-ouro em microtomografia computadorizada (micro-CT).
- Verificar, por meio de um estudo *ex vivo*, se uma câmera intraoral, no modo luz fluorescente, é eficaz na definição de um limite para remoção químico mecânica de dentina cariada comparado a um padrão-ouro em micro-CT; além de comparar a eficácia de diferentes géis de papaína na escavação.

3. DELINEAMENTO DA PESQUISA

3.1 Tipo de estudo

Com o propósito de responder a cada objetivo específico, a presente tese é composta por três estudos: 1) Uma revisão sistemática da literatura; 2) Um estudo laboratorial *ex vivo*, observacional comparativo, com diferentes testes diagnósticos e 3) um estudo laboratorial *ex vivo*, observacional comparativo, com diferentes técnicas para remoção de cárie.

3.2 Locais de execução do estudo

O projeto de pesquisa foi submetido e aprovado pelo Comitê de Ética em Pesquisa do Hospital Universitário Clementino Fraga Filho (HUCFF–UFRJ, Rio de Janeiro, Brasil), sob o número 3.442.162, CAAE: 02161018.3.0000.5257 (ANEXO A).

Os estudos de 1 a 3, foram realizados no Departamento de Odontopediatria e Ortodontia da Faculdade de Odontologia da Universidade Federal do Rio de Janeiro (FO/UFRJ, Rio de Janeiro, Brasil).

As coletas das amostras dos estudos 2 e 3, foram realizadas no Hospital Militar Geral do Estado do Rio de Janeiro (HGeRJ), e suas análises, no Departamento de Patologia e Diagnóstico Oral, área de Radiologia, da Faculdade de Odontologia da Universidade Federal do Rio de Janeiro (FO/UFRJ, Rio de Janeiro, Brasil). Já as aquisições das imagens em micro-CT ocorreram no Laboratório de Instrumentação Nuclear (LIN) afiliado ao Instituto Alberto Luiz Coimbra de Pós-Graduação e Pesquisa de Engenharia (COPPE/UFRJ, Rio de Janeiro, Brasil).

3.3 Primeiro estudo

Avaliou, através de uma revisão sistemática da literatura, se o diagnóstico por fluorescência (DF) e o exame clínico visual (ECV), são igualmente eficazes na detecção de lesões de mancha branca relacionadas à ortodontia fixa.

O protocolo do estudo foi registrado em um banco de registros internacional de revisões sistemáticas, o PROSPERO (International Prospective Register of

Systematic Reviews), sob o número CRD42018109453. Além disso, a revisão foi relatada seguindo um conjunto de itens com base em evidências para relatar revisões sistemáticas e meta-análises, o PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols).

As chaves de busca foram elaboradas com base na estratégia PIRO (P = pacientes tratados com ortodontia fixa, I = diagnóstico por fluorescência, R = exame clínico visual, O = lesões de cárie ao redor de aparatos ortodônticos) e incluíram termos MeSH (Medical Subject Headings) e seus sinônimos, além de palavras-chave, sendo desenvolvidas de forma distinta para cada base de dados, sob a orientação de uma bibliotecária com experiência em revisões sistemáticas (DMF).

A busca sistemática da literatura foi realizada nas seguintes bases de dados: PubMed, Scopus, Web of Science, The Cochrane Library, Biblioteca Virtual em Saúde (LILACS e BBO) e literatura cinzenta (Google Scholar e Trip database) até outubro de 2022. Após a seleção dos artigos, uma busca manual nas listas de referências de cada artigo incluído, foi efetuada. Não houve restrições de idioma ou data de publicação.

Ainda seguindo os critérios da estratégia PIRO, foram incluídos na revisão estudos clínicos com pacientes tratados com ortodontia fixa, nos quais a avaliação diagnóstica de lesões de mancha branca por DF foi comparada ao ECV, para detectar, precocemente, lesões de cárie relacionadas a aparatos ortodônticos fixos. Foram excluídos relatos de caso, revisões da literatura, editoriais, cartas aos editores e ensaios laboratoriais. Além disso, estudos que apresentassem amostras sobrepostas e aqueles em que, outras patologias, que não lesões de cárie, como fluorose dental ou hipomineralização de molares e incisivos (HMI) e manchas de outra origem (uma vez que dispositivos fluorescentes são sensíveis a qualquer mancha, por exemplo, aquelas causadas por consumo de determinados alimentos), foram excluídos.

A busca e a seleção dos estudos, bem como a extração de dados de interesse, foram realizadas de forma independente por dois dos autores (LPS e FMFS). Em caso de divergência entre os autores, reuniões de consenso foram realizadas com um especialista em revisões sistemáticas (LCM). Os dados extraídos foram: autor; ano de publicação; país; pacientes (n); idade (anos); dentes (n); tempo de tratamento (meses); aparatos ortodônticos fixos (banda e/ou bráquete); metodologia diagnóstica; repetição das mensurações; método fluorescente; método clínico visual e desfechos. Os autor(es) do estudo foram contactados na ausência de dados.

Os avaliadores examinaram, independentemente, a qualidade metodológica e risco de viés(es) de cada artigo, de acordo com os critérios da ferramenta de Avaliação da Qualidade de Estudos de Acurácia Diagnóstica-2 (QUADAS-2). Esta é uma ferramenta baseada em 4 domínios: seleção de pacientes; teste índice; padrão de referência; fluxo e tempo. Para a revisão, a aplicabilidade do domínio 1, buscou saber se pacientes incluídos no estudo e suas configurações, correspondiam a questão da revisão; domínio 2, se o DF, ‘teste índice’, foi realizado de acordo com as recomendações do fabricante, se o avaliador era experiente e/ou calibrado e se foi realizada uma limpeza prévia da superfície do dente a ser examinado; domínio 3, se o ECV, ‘padrão de referência’, definia uma condição alvo diferente daquela descrita na questão da revisão. Foi considerado para este domínio os ECV validados para a avaliação de lesões de cárie; e, por último, domínio 4, se houve intervalo adequado entre as avaliações ‘teste índice’ e ‘padrão de referência’, se todos os pacientes receberam o mesmo ‘padrão de referência’ e se a análise do estudo abrangeu todos os pacientes recrutados.

Os riscos de vieses e preocupações com a aplicabilidade, foram classificados como ‘baixo’, ‘alto’ ou ‘não claro’ da seguinte forma: se todas as perguntas de um domínio foram respondidas com ‘sim’, o estudo foi classificado como ‘baixo risco’ de viés, com pelo menos uma resposta ‘não’, classificou-o como ‘alto risco’ de viés, e com ‘não claro’, quando algum dado apresentado foi considerado insuficiente. Autor(es) do estudo foram contactados na ausência de dados.

O julgamento geral do risco de viés(es) e a aplicabilidade foi definido usando os critérios: ‘baixo’ em todos os domínios, o estudo foi julgado como ‘baixo risco de viés’ ou ‘baixa preocupação quanto a sua aplicabilidade’; ‘alto’ ou ‘pouco claro’ em pelo menos um domínio, o estudo foi julgado como ‘com risco de viés’ ou ‘preocupação quanto a sua aplicabilidade’. Similar a etapa de seleção dos estudos, um autor experiente (ACRC) foi consultado em caso de divergência entre avaliadores.

A qualidade das evidências foi avaliada através da aplicação das recomendações GRADE (Grading Recommendations Assessments, Development, anda Evaluations) utilizando programa GRADEpro GDT (https://gradepro.org/; McMaster University, Hamilton, On, Canada and Evidence Prime, Inc., Hamilton, On, Canada). Sendo categorizada como ‘alta’, ‘moderada’, ‘baixa’ ou ‘muito baixa’, por dois avaliadores experientes (MBM e LPS) de forma independente.

3.4 Segundo estudo

Este estudo foi categorizado como um estudo *ex vivo*, observacional comparativo, que objetivou verificar a concordância entre imagens obtidas por uma câmera intraoral, em modo luz branca (LB) ou fluorescente (LF), e a radiografia digital (RD), no diagnóstico e decisões de tratamento para cárie oclusal, comparado à um padrão-ouro em microtomografia computadorizada (micro-CT).

O projeto de pesquisa foi submetido e aprovado pelo Comitê de Ética em Pesquisa do Hospital Universitário Clementino Fraga Filho (HUCFF–UFRJ, Rio de Janeiro, Brasil), sob o número 3.442.162, CAAE: 02161018.3.0000.5257 (ANEXO A). Os indivíduos que cederam seus dentes foram informados sobre os objetivos deste estudo, bem como seus benefícios e potenciais riscos, e em seguida, declararam a sua anuência em participar através da assinatura de um termo de consentimento livre e esclarecido (APÊNDICE 1).

Seleção da amostra e critérios de elegibilidade

Foram elegíveis para a pesquisa molares permanentes apresentando lesão de cárie oclusal em esmalte e/ou dentina. Os dentes cedidos foram extraídos, com finalidade ortodôntica, no serviço de Cirurgia Buco Maxilo Facial do Hospital Militar Geral do Estado do Rio de Janeiro (HGeRJ).

Dentes hígidos, restaurados ou com alterações não relacionadas a lesão de cárie (hipomineralização e hipoplasia), foram inelegíveis. Imediatamente após a exodontia, os dentes selecionados (10) foram armazenados em soro fisiológico, até três meses do início deste estudo.

Exame visual baseado em imagem

Os dentes foram limpos e incorporados pelas raízes em uma base de cera. Cada dente foi colocado em contato proximal com dois outros molares permanentes hígidos, um de cada lado, com intuito de simular a posição de um segundo molar permanente, na cavidade oral (Figura 1).

Figura 1: Exemplo de uma amostra montada para exame fotográfico e radiográfico, simulando posições na cavidade oral.

As imagens da superfície oclusal foram obtidas pela câmera intraoral SoproLife®, no modo LB e LF, com os espécimes no interior de uma caixa escura, enquanto as RD, na incidência interproximal, foram tomadas por um aparelho de raios-X intraoral Focus® (Instrumentarium Imaging, Tuusula, Finlândia) e um sistema digital semidireto Kavo Express® (DK Equipamentos, São Paulo, Brasil). Após, foram organizadas em 03 blocos de apresentação, na sequência: RD (10), LB (10) e LF (10).

Para cada bloco de apresentação, as imagens foram apresentadas da primeira a décima e dentro de cada bloco de apresentação as imagens foram misturadas, a fim de evitar viés de sequência pelos avaliadores.

Uma escala, adaptada do estudo de Ekstrand (Ekstrand *et al*., 1995) foi utilizada para a pontuação da presença de cárie oclusal em todas as imagens: (0) superfície oclusal hígida, (1) desmineralização limitada ao esmalte sem cavitação, (2) desmineralização limitada ao esmalte com cavitação, (3) desmineralização em dentina sem cavitação ou (4) desmineralização em dentina com cavitação. Outra escala foi utilizada para pontuação de decisões de tratamento: (0) nenhum tratamento específico, (1) tratamento preventivo (educação em saúde e instruções de higiene oral), (2) tratamento não-cirúrgico (uso de verniz fluoretado e/ ou selante) ou (3) tratamento cirúrgico (remoção da lesão e restauração).

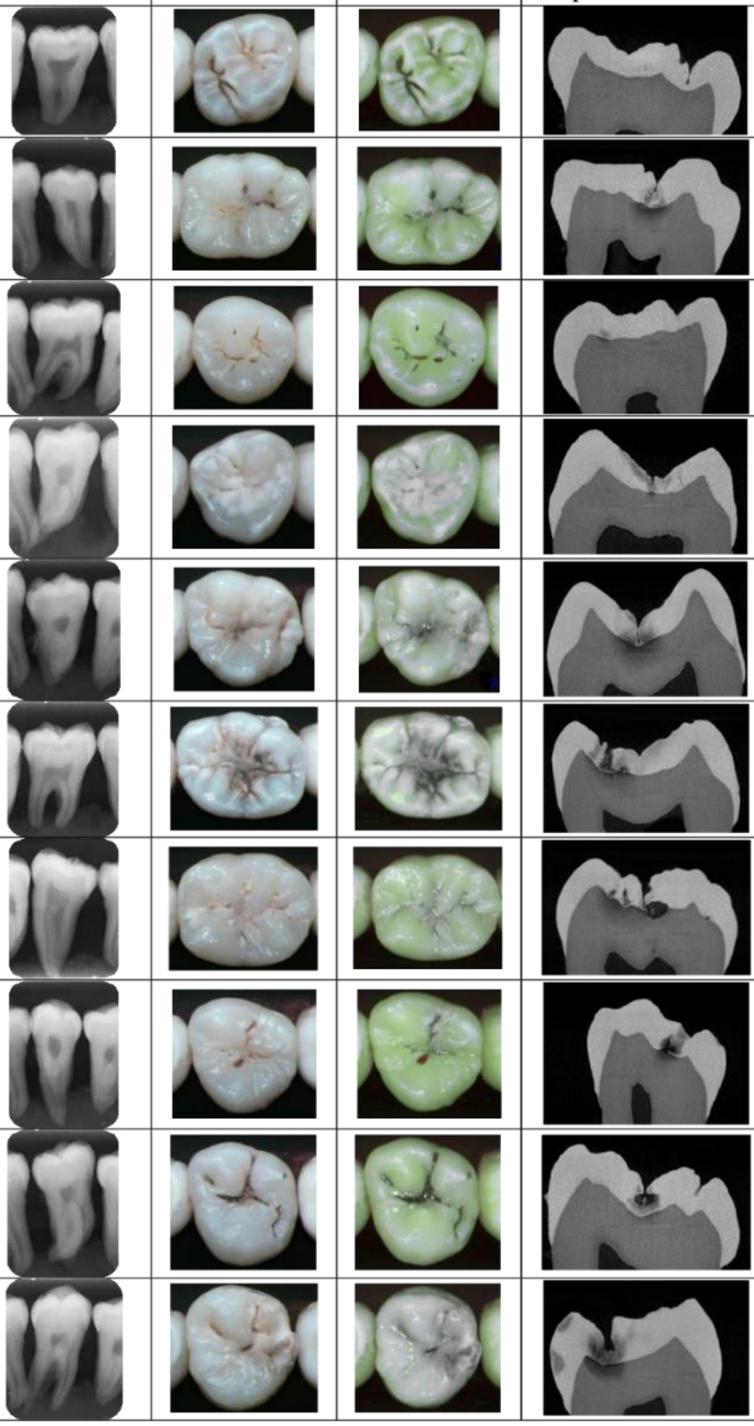
Seleção de Examinadores

Cirurgiões-dentistas (n=26), atuantes na atenção básica em um Hospital Militar Geral do Estado do Rio de Janeiro (HGeRJ), com experiência rotineira no diagnóstico de lesões de cárie, porém, sem formação específica na área de Cariologia, foram abordados por conveniência e convidados a participarem da avaliação. Foram coletados dados sociodemográficos, como: sexo, escolaridade (especialização, mestrado e doutorado), idade e tempo de formação.

Os avaliadores receberam, individualmente, uma explicação sobre a interpretação das cores fluorescentes, visualizadas nas imagens produzidas pela câmera intra-oral, assim como na pontuação dos escores para diagnóstico e decisões de tratamento.

Padrão-ouro (micro-CT) para cárie oclusal e opções de tratamento

Cada espécime foi escaneado utilizando-se um microtomógrafo de alta energia (Skyscan 1173, Bruker, Kontich, Bélgica) com os seguintes parâmetros de aquisição: 100kV, 80μA, tamanho de pixel 6,47μm, exposição 1s, passo de rotação de 0,5° a 360° e movimentos aleatórios de 20 linhas, usando um filtro de alumínio de 1 mm de espessura. As imagens obtidas foram reconstruídas em um programa específico (NRecon v.1.7.0.4, Bruker) utilizando os seguintes parâmetros: correção de artefatos em anel (10), correção de endurecimento do feixe (52%) e limites de contraste padronizados entre 0 e 0,05, fornecendo um conjunto de imagens transversais das amostras com características semelhantes. Após, os dentes foram alinhados pelo programa (Data Viewer, Bruker) e foi selecionado o corte da parte mais profunda da lesão, que foi utilizada para a definição do padrão-ouro para o diagnóstico e as decisões de tratamento para cárie oclusal (Figura 2). Os escores padrão-ouro para o diagnóstico e decisões de tratamento foram atribuídos após consenso entre os pesquisadores.



	Digital images			Gold standard		
Tooth	**DR**	**WL**	**FL**	**Micro-CT representative slice**	**Dental caries score**	**Treatment decision scores**
1					1	1, 2
2					3	1, 2
3					3	1, 2
4					3	1, 2
5					3	1, 2
6					4	3
7					4	3
8					4	3
9					3	1, 2
10					3	1, 2

Figura 2: Imagens provenientes de RD, LB e LF dos dentes selecionados, seus respectivos cortes representativos em micro-CT, a classificação padrão-ouro das lesões de cárie e de seus respectivos tratamentos.

Análise estatística

Os dados coletados foram analisados no software SPSS, versão 25.0 (IBM Corporations, Armonk, NY, EUA). Dados demográficos foram representados por frequências absolutas e relativas. O modelo Generalized Estimation Equations (GEE Model) foi utilizado para comparar proporções de acertos entre os três métodos RD, LB e LF e quando significativos, o teste post-hoc de Bonferroni identificou as diferenças. A significância foi estabelecida em 5% ($p \leq 0,05$).

3.5 Terceiro estudo

Trata-se de um estudo laboratorial *ex vivo*, observacional comparativo, que objetivou verificar se uma câmera intraoral, no modo luz fluorescente, é eficaz na definição de um limite de escavação para a remoção químico mecânica de dentina cariada comparado a um padrão-ouro em micro-CT; além de comparar a eficácia de dois géis de papaína na escavação.

O projeto de pesquisa foi submetido e aprovado pelo Comitê de Ética em Pesquisa do Hospital Universitário Clementino Fraga Filho (HUCFF–UFRJ, Rio de Janeiro, Brasil), sob o número 3.442.162, CAAE: 02161018.3.0000.5257 (ANEXO A). Os indivíduos que cederam seus dentes foram informados sobre os objetivos deste estudo, bem como seus benefícios e potenciais riscos, e em seguida, declararam a sua anuência em participar através da assinatura de um termo de consentimento livre e esclarecido (APÊNDICE 1).

Seleção da amostra e critérios de elegibilidade

Foram elegíveis para a pesquisa molares permanentes com lesão de cárie em dentina. Os dentes cedidos foram extraídos com finalidade ortodôntica, no serviço de Cirurgia Buco Maxilo Facial do Hospital Militar Geral do Estado do Rio de Janeiro (HGeRJ).

Dentes hígidos, restaurados, com alterações não relacionadas a lesões profundas de cárie (hipomineralização e hipoplasia) ou com lesão de cárie em dentina (<2 mm de distância da câmara pulpar) foram inelegíveis. Imediatamente após a exodontia, os dentes selecionados (20) foram armazenados em soro fisiológico, por até três meses do início deste estudo. Após a microtomografia inicial de cada espécime, o volume inicial de dentina cariada foi quantificado (mm^3). A partir deste resultado, os dentes foram pareados em dois grupos de remoção químico-mecânica com géis de papaína: (G1) Papacárie Duo® (Fórmula & Ação Laboratório Farmacêutico, São Paulo, Brasil) e (G2) Brix3000® (Brix Medical Science, Carcañá, Argentina) (Tabela 1). A identificação dos grupos manteve-se em sigilo, durante todo o estudo, para o avaliador (AAN) que realizou a análises.

Tabela 1. Pareamento entre os espécimes dos dois grupos para a remoção de dentina cariada.

Papacárie Duo®		**Brix3000®**	
Dente	Volume inicial (mm^3)	Dente	Volume inicial (mm^3)
7	0,44	15	1,24
16	5,95	10	6,02
4	12,61	1	11,82
2	7,41	8	7,48
18	20,92	6	24,23
17	25,43	14	30,80
19	38,17	13	37,01
5	0,32	12	1,94
20	4,35	9	4,87
3	38,65	11	41,60
Média (± DP)	15,42 ± 13,87	Média (± DP)	16,70 ± 14,52

DP: Desvio padrão.

<u>Exame visual baseado em imagem</u>

As imagens da superfície oclusal de cada espécime obtidas pela câmera intraoral SoproLife®, no modo LF, após a remoção da dentina cariada, com os espécimes no interior de uma caixa escura.

<u>Remoção químico-mecânica de dentina cariada</u>

A dentina cariada foi removida escavada usando dois géis de papaína: Papacárie Duo® e Brix3000®. O gel foi inserido na cavidade, com uma seringa própria, e deixado para agir durante 1 min. Para a remoção de dentina cariada, foi usado o lado oposto de uma colher de dentina, com movimentos pendulares e sem corte; e foi tida como suficiente, após o gel não exibir mais alteração de cor e a cavidade assumir um aspecto vítreo.

Procedimentos de digitalização e reconstrução por micro-CT

Cada espécime foi escaneado utilizando-se um microtomógrafo de alta energia (Skyscan 1173, Bruker, Kontich, Bélgica) com os seguintes parâmetros de aquisição: 100kV, 80μA, tamanho de pixel 6,47μm, exposição 1s, passo de rotação de 0,5° a 360° e movimentos aleatórios de 20 linhas, usando um filtro de alumínio de 1 mm de espessura. As imagens obtidas foram reconstruídas em um programa específico (NRecon v.1.7.0.4, Bruker) utilizando os seguintes parâmetros: correção de artefatos em anel (10), correção de endurecimento do feixe (52%) e limites de contraste padronizados entre 0 e 0,05, o que forneceu um conjunto de imagens transversais das amostras com características semelhantes. Foram realizados dois escaneamentos, antes e após remoção de dentina cariada, utilizando as mesmas configurações.

Calibração da densidade mineral

Os valores de tons de cinza em micro-CT foram calibrados em valores de densidade mineral dentinária, usando um conjunto de padrões aquosos de fosfato de potássio dibásico (K_2HPO_4) nas seguintes concentrações: 0,3; 0,6; 0,8; 1,2; 1,5 e 1,8 g/mm^3. O conjunto de padrões foi escaneado e reconstruído utilizando os mesmos parâmetros das amostras de dentes, e os valores de densidade mineral foram então obtidos em g/cm^3.

Análise das imagens digitais

Cada conjunto de imagens, antes e após a remoção de dentina cariada foi registrado entre si, utilizando um algoritmo de registro geral pelo programa aberto 3D Slicer. Foi implementada a segmentação do tecido, pelo programa FIJI, usando um limite pré-estabelecido na literatura de 1,11 g/cm^3 (Neves *et al.*, 2010). Valores de volume abaixo deste limite, foram considerados como tecido cariado.

Avaliação da eficácia da remoção químico mecânica da cárie

A eficácia da remoção de cárie foi avaliada, após a escavação da dentina cariada, a partir dos seguintes parâmetros: 1) volume relativo médio de cárie residual e 2) densidade mineral média no fundo da cavidade, de acordo com literatura anterior (Neves *et al.*, 2010). Quanto menor foi o valor da diferença entre os parâmetros, mais eficaz foi a técnica de remoção de dentina cariada. A densidade mineral no fundo da cavidade foi calculada após examinar cortes transversais da superfície oclusal e identificar aquele com uma dentina escavada mais profunda. Nesse corte, uma região de interesse circular com raio de 1 cm era delimitada e a densidade mineral foi então calculada (Figura 3).

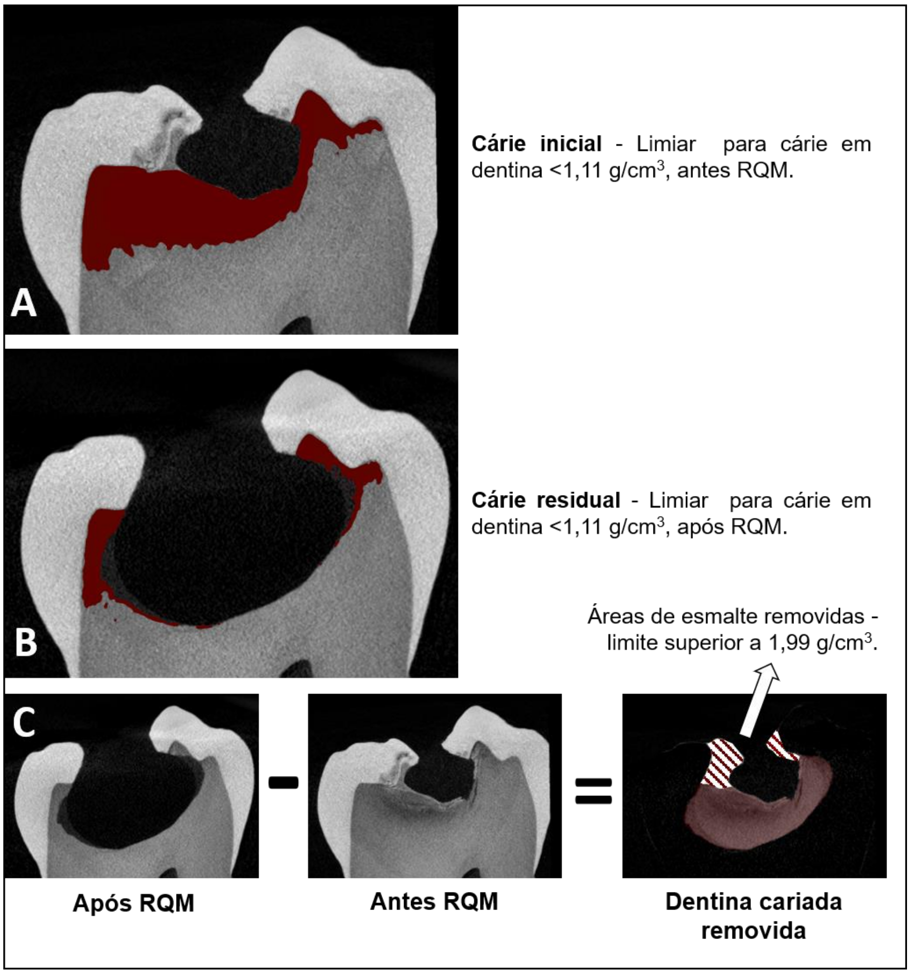


Figura 3: Avaliação da eficácia da RQM de dentina cariada.*RQM – Remoção químico-mecânica; g/cm^3 – grama por centímetro cúbico.

<u>Avaliação do potencial invasivo do gel de papaína</u>

O potencial de invasividade dos dois géis de papaína foi mensurado a partir do “tamanho relativo da cavidade”. Para cada dente, a partir de um conjunto de imagens, o volume de dentina cariada após a utilização dos géis foi subtraído do volume inicial (VI) da lesão, afim de obter o volume total de dentina removida (VTDR). O VTDR foi divido pelo VI, e assim o gel com o menor potencial invasivo, seria aquele com valor mais próximo de 1, a partir desta divisão (Neves *et al.*, 2015).

Análise estatística

Para testar a normalidade dos dados, foi utilizado teste de Shapiro-Wilk, enquanto para comparar variáveis de resultados entre remoção de cárie e géis, o teste Combinado-t. O nível de significância estabelecido foi de 5% ($p \leq 0,05$).

4. DESENVOLVIMENTO DA PESQUISA

Artigo 1: Comparison between detection of orthodontic-related carious lesions with fluorescence or visual method: A systematic review.
Artigo a ser enviado para publicação no periódico científico.

Artigo 2: Comparison between radiographs, white and fluorescent images in the diagnosis and treatment decisions for occlusal caries in permanent molars: An *ex vivo* study.
Artigo aceito no periódico científico “Pesquisa Brasileira em Odontopediatria e Clínica Integrada – PBOCI”.

Artigo 3: Could fluorescence images help in setting a cut-off point for dentin caries removal?
Artigo a ser enviado para publicação em periódico científico.

4.1 Artigo 1: Comparison between detection of orthodontic-related carious lesions with fluorescence or visual method: A systematic review.

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ABSTRACT

Clinical studies in patients treated with fixed orthodontics (P), in which a diagnostic method with a fluorescent method (I) was compared to the visual clinical examination (R), in order to detect carious lesions involving orthodontic appliances (O), were considered eligible. Five databases and grey literature were searched until October 2022. Clinical studies, comparing at least one digital fluorescent method (DFM) with visual clinical examination (VCE), in patients who completed treatment with fixed orthodontic appliances, were eligible. After extracting the data, the risk of bias and the certainty of the evidence were evaluated through the QUADAS-2 and the GRADE approaches, respectively. A total of 40 studies were read in full and five were included in the final synthesis, all with cross-sectional designs. The quantitative light-induced fluorescence (QLF™) method presented a higher correlation with VCE when diagnosing demineralized surfaces. An average loss of fluorescence of 12.5% and greater than 15%, were detected by QLF™ and VCE, respectively to result in clinically detectable lesions. The included studies were judged at risk of bias with very low certainty of evidence on the comparison between DFMs and VCE. The diagnosis of non-cavitated carious lesions related to fixed orthodontic appliances by DFMs was satisfactory relative to VCE.

Keywords: quantitative light-induced fluorescence; orthodontics; dental white spot; photographs; Diagnosis; fluorescence.

INTRODUCTION

Orthodontic fixed appliances constitute a mechanical obstacle for biofilm removal, favoring thus, enamel demineralization and further caries development.[1,2] Indeed, there is already evidence to show that the presence of orthodontic appliances directly influences the quantity and quality of the oral microbiota.[3,4] The incidence of white spot lesions (WSL), in patients undergoing orthodontic treatment is around 38-40% in the first six-months of treatment,[5] increasing to 43-46% in a 12-month period, supporting the idea that fixed appliances potentially become a risk factor for carious lesions.[6,7] Studies have shown that approximately one third of patients undergoing orthodontic treatments with fixed appliances developed at least one WS lesions.[8,9,10] In such cases, early detection may be a challenge due to the presence of the bonded accessories.[11]

Caries diagnosis is a clinical judgement, integrating detection and assessment of signs, such as the presence of lesions, to determine presence of the disease and define the course of treatment.[12] In the clinical routine, it can be performed through visual clinical examination (VCE), at various thresholds and stages of detection. Nowadays, a widespread index used is the International Caries Detection and Assessment System (ICDAS-II),[13] aided by complementary exams such as radiographs, optical and electrical methods.[14]

The use of digital fluorescent methods (DFMs) has been increasing,[15] in order to assist early enamel caries diagnosis. In the clinical practice, instruments such as QLF™,[16,17] DIAGNOdent Pen™,[10,11,18] and Vista Proof™,[10] are frequently used for detection of early caries. The carious lesion can be detected by light-induced fluorescence, when its value decreases at the lesion site.[19] Although intraoral cameras still have a significant cost,[10] its advantages include no emission of ionizing radiation, the possibility of storing standardized images throughout the consultations to provide an independent review of the images at different times, and the possibility of classifying the presence or absence of the lesion according to the intensity of the fluorescence.[10]

Considering all these methods and their possible applicability in clinical practice, the present systematic review intended to answer the following focused question: Are DFM and visual clinical examination comparable in detecting early carious lesions related to fixed orthodontic appliances?

MATERIAL AND METHODS

Protocol registration

Registered in PROSPERO under the number CRD42018109453. The authors also followed the recommendations of the PRISMA statement.[20]

Search strategy

Searches were performed in the following electronic bibliographic data sources: PubMed, Scopus, Web of Science, The Cochrane Library, Lilacs, BBO, as well as in the grey literature (Google Scholar and Trip Database). Medical Subject Headings

(MeSH) terms and keywords were used to identify published papers. The search strategy was appropriately modified for each database according to their syntaxes rules (Table 1). The search was carried out including studies published until October 2022. Hand search in the references list of the included papers was also performed. No date or language restriction was applied.

Two investigators performed the search independently (LPS and FMFS), under the guidance of a librarian (DM). All titles, abstracts and full-text manuscripts retrieved from database searches were screened, excluding irrelevant records. In the case of any inconsistency, a third author (LCM) was consulted. All references were imported into a reference manager online software (EndNote Web; Thomson Reuters Inc., Philadelphia, PA, USA) and duplicated references were considered only once.

Eligibility criteria based on PIRO strategy and selection criteria

The PIRO strategy consists of an acronym for (P) patient, (I) intervention, (R) standard reference and (O) outcomes. Clinical studies in patients treated with fixed orthodontics (P), in which the evaluation within a fluorescent method (I) was compared to the visual clinical examination (R), in order to detect carious lesions involving orthodontic appliances (O), were considered eligible.

The following exclusion criteria were considered: studies in which pathologies other than carious lesions, such as dental fluorosis or molar incisor hypomineralization (MIH) and stains of other origin (since fluorescent devices are sensitive to any stain, for example, caused by the accumulation of biofilm) were excluded from this systematic review.

Data extraction

A data extraction spreadsheet was developed, and data were collected independently by two researchers (LPS and FMFS). For each selected study, the following information was collected: author/country/publication year, patient age/number of teeth evaluated, treatment time, orthodontic appliances, methodological evaluation, repetition of measurements, fluorescent method, visual clinical method, and outcomes. The authors of the primary studies were contacted in case of lack of relevant data.

Risk of bias analysis and methodological quality of the studies

The evaluation of methodological quality in the included studies was performed according to the quality assessment of diagnostic accuracy studies (QUADAS-2).[21]

In domain 1, the risk of bias regarding 'patient selection' was assessed using questions such as: Did the study involve a consecutive or random sample of patients? Have case-control design and inappropriate exclusions been avoided? The applicability of domain 1 was concerned to whether patients included in the study and settings corresponded to the review question.

In domain 2, the risk of bias regarding the use or interpretation of the 'index test', was assessed through questions referring to DFMs, whether they were interpreted without knowledge of the results of the reference standard (VCE), and whether a threshold was used and / or pre-specified. The interpretation of this domain considered the following aspects: if the index test was performed according to manufacturer's recommendations, if the evaluator was experienced and / or calibrated and if a previous surface cleaning of the examined tooth was performed. The applicability of this domain was concerned to whether the 'index test' methods differed from those defined in the review question.

In domain 3, the risk of bias regarding the use or interpretation of the 'reference standard', was assessed through questions referring to VCEs, whether they were able to correctly classify the target condition and if its results were interpreted without knowledge of the 'test index' (DFMs). The interpretation of this domain considered validated VCE methods as reference standards for carious lesions assessment. The applicability of this domain was concerned to whether the 'reference standard' defined a target condition different from that described in the review question.

The fourth domain, 'flow and time', was concerned to investigate whether the patient flow might have introduced bias, considering if there was an adequate interval between the 'index test' and 'reference standard' assessments; if all patients received the same 'reference standard'; and if the study analysis comprised all the patients recruited.

Risk of bias and concerns regarding applicability were rated as 'low', 'high', or 'unclear', as follows: if all questions for a domain were answered with 'yes', the study was classified at 'low risk' of bias; if any question was answered with 'no', it was classified at 'high risk' of bias; and an 'unclear' status was assigned when insufficient data was provided. Therefore, the 'overall judgment' of the risk of bias and applicability was defining using the following criteria: if the risk of bias and / or applicability was rated as 'low' on all domains, the study was judged as 'low risk of bias' or 'low concern regarding applicability'; and if it was rated as 'high' or unclear' in one or more domains, the study was judged 'at risk of bias' or with 'concerns regarding applicability'.[21]

Certainty of evidence

GRADE (Grading of Recommendations Assessment, Development and Evaluation) was used to analyze the certainty of evidence.[22] When serious or extremely serious issues related to risk of bias, inconsistency, indirect evidence, inaccuracy, and publication bias are observed, the quality or certainty of evidence decreases by one or two points. Conversely, if there is large or very large magnitude of an effect, a dose-response was observed, or if the effect of all plausible confounding factors is minimized or suggest a spurious effect, the quality of evidence tends to increase by two points. In this respect, the certainty of evidence in GRADE may range between very low, low, moderate or high.

For the criterion 'risk of bias', it was considered a 'not serious' problem if all included studies presented low risk of bias and a 'very serious problem' if the included studies presented 'high' risk of bias. For the "inconsistency" criterion, it was considered a very serious problem if the studies included in the systematic review presented a large variation in the effect estimates between studies.

The external validity was assessed when the pooled results partially addressed the issue of interest for revision in the population (bands and brackets), fluorescent method (quantity of fluorescent methods) and visual clinical method (quantity of visual clinical methods used). If there was a limitation in one of these criteria, the problem was judged to be 'serious'; if there was a problem in two or three criteria, the problem was judged to be 'very serious'. In the analysis of 'imprecision', a serious problem was considered if the total number of teeth evaluated was less than 300.

The criterion 'publication bias' was judged to be 'undetected' since the search was done in white and gray databases, with no date or language limitation. The criterion 'dose-response' does not apply to the studies included in this systematic review and was classified in such a way as not to modify the final classification of the evidence. For the 'magnitude effect', it was considered with a very large magnitude effect if all studies included reported strong correlation (>0.7 or <0.7) or high accuracy (>0.9).

RESULTS

Literature search

All of the 591 articles found were exported to EndNote Web software®. All duplicates were removed, and 371 articles remained from which, after reading titles and abstracts, 331 were excluded. Forty full text articles were subsequently assessed for eligibility and 36 were excluded for the following reasons: "*in vitro*" studies (n = 8), did not use a fluorescent method (n = 12), did not use VCE as comparison (n = 10), used orthodontic clear aligners (n = 1), evaluated only photographs (n = 2), review (n = 1), meeting abstracts (n = 1) and overlapped sample (n = 1). The five remaining studies[10,11,16,18,23] were included in the qualitative synthesis (Figure 1).

Study characteristics

All studies (n = 5) [10,11,16,18,23] included in the synthesis were cross-sectional, in Table 2, with similar methodological assessments, carried out in Saudi Arabia,[18,23] the Netherlands,[16] Greece,[10] and Hong Kong.[11] The number of patients included in the studies ranged from 13 to 99, aged between 12 to 28 years, but for one study,[11] this was not reported, even after attempts to contact the authors. The number of evaluated teeth varied from 137 to 1653, but for one study,[16] this was not reported, even after attempts to contact the authors. The time of orthodontic treatment ranged from 18 to 24 months, but this information was also not reported by two studies,[10,11] despite the attempts to contact the authors. Some studies evaluated early carious lesions involving only orthodontic brackets,[10,11,23] and others, bands and brackets.[16,18]

Regarding DFMs, one study used DIAGNOdent™ (KaVo, Biberach, Germany),[18] three used DIAGNOdent Pen™ (KaVo, Biberach, Germany),[10,11,23] of these, one also used Vista Proof™ (Dürr Dental, AG, Munich, Germany),[10] and one used QLF™ (Inspektor Research Systems BV, Amsterdam, The Netherlands).[16] For comparison, a modified Ekstrand criteria,[31] an ICDAS-II modified (original scores transformed into four: 0 - healthy tooth, 1 - enamel caries, 2 - deep enamel caries, 3 - dentin caries),[23] and Gorelick's criteria,[10,11] one used the scores: 1 - early enamel caries, 2 - extended enamel caries and 3 - caries into dentine;[10] and the other,[11] the scores: 0 - no lesion, 1 - slight lesion (linear shape), 2 - severe lesion (band shape) and 3 - cavitation, were used as VCE scores. Boersma et al.,[16] performed a VCE considering as a white spot lesion the enamel surface showing a white, discolored or cavitated region. Measurements with DFMs were performed at the pre-bonding,[11] at the time with the brackets,[10,11], repeated 6, 12 and 18 months later, at the time of debonding,[10,16,18,23] and repeated 7 days later,[18] and 6 weeks later.[16] For indirect VCE, the measurement was performed at the time with the brackets.[10] For VCEs, these measurements were performed at the time of debonding,[10,16,18,23] and repeated 6 weeks thereafter.[16] Almosa et al.[23] and Kavvadia et al.[10] only performed one follow-up measurement after debonding, either with DFM or with the VCE.

Four studies[10,11,16,18] documented the entire tooth surface analysis with a digital photography taken with the digital camera Nikon COOLPIX®, Japan. The digital images were saved, printed and used for location to guide the DFM measurements. Two studies[10,11] also used digital photography to perform an indirect visual examination by two experienced examiners.

The Spearman correlation coefficient between DFMs and VCE scores in the studies ranged from 0.40 to 0.71.[18,23] These findings indicated how well the methods related to each other,[24] but in general, there was a clear trend that, with higher VCE scores, DFM values were also increased.[23]

Almosa et al.,[23] revealed that the DFM scores were well correlated to clinical scores (ICDAS-II modified). This correlation was assessed based on the chances of DFM being in accordance with a modified ICDAS-II in the diagnosis of different carious lesion scores. The opposite thus, the chances of different modified ICDAS-II scores being in accordance with the DFM did not achieve the same correlation. Twelve of the 14 teeth classified by the VCE with the modified ICDAS-II score 3 (dentin caries) had the same score when the DFM was used. On the other hand, of the 159 teeth diagnosed with the ICDAS-II modified score 3 by the DFM, only 12 teeth obtained the same score when using the VCE. The results show that fluorescent methods tend to detect more positive cases, with less specificity, being more accurate when there are clear differences in the diagnosis of completely sound and dentin-affected carious teeth.[23]

In the study by Boersma et al.,[16] almost all participants (97%) had one or more early enamel lesions measured by DFM and VCE. A total of 406 and 427 surfaces with caries were recorded by the QLF™ device, after debonding (T0) and 6 weeks later (T1), respectively, with an average loss of fluorescence for the lesions of 10.7% ± 5.8 (T0) and 10.3% ± 5.8 (T1). As for the surfaces recorded by the VCE, there were 284 (T0) and 285 (T1), with average loss of fluorescence of 12.5% and greater than 15%, when detected by QLF™ and VCE, respectively.[16] This corroborate the outcomes presented by another study.[23]

In another study, both DIAGNOdent Pen™ and Vista Proof™ overestimated the record of early carious lesions, compared to VCE based on Gorelick's criteria (gold standard).[10] A greater diagnostic accuracy was found for direct and indirect VCE ($P > 0.90$), compared to DFM ($P = 0.64$),[10] contrary to the other outcomes.[18,23] Analyzing the outcomes of Gorelick´s scores 1 and 2, the DFM sensitivity for score 1 was low, 0.32 and 0.25, for DIAGNOdent Pen™ and Vista Proof™, respectively, while the specificity and accuracy of both were good. For early carious lesions, the VCE method was superior to the DFM.[10] On the other hand, and corroborating with the results of previous studies,[16,18,23] in scores 2 and 3 of Gorelick's criteria (extended carious lesions and cavitation, respectively), the DFM and VCE methods did not differ among themselves, where sensitivity and precision were higher in score 2 and 3 lesions, compared to score 1 lesions.[10]

In the study by Sardana et al.,[11] the values of sensitivity (78%) and specificity (82%) of DIAGNOdent Pen™ in delineating the presence or absence of WSLs were found to be significant ($p<0.001$), revealing a good instrument accuracy, whereas the values of sensitivity (30%) and specificity (83%) were not significant ($p=0.490$) for distinguishing severity of WSLs, indicating instrument failure.

Risk of bias analysis and methodological quality

In the overall judgment of risk of bias and applicability concerns,[21] all studies[10,11,16,18,23] were considered 'at risk of bias' with 'low concern regarding applicability', respectively (Figure 2). Regarding each domain assessment, three studies[10,11,18] (60%) received 'unclear' scores in 'patient selection'; four studies[10,11,18,23] (80%) were scored as 'high risk' in 'index text'; one study[16] (25%) was scored as 'high risk' in 'reference standard', and all studies[10,11,16,18,23] were considered at 'low risk' regarding study flow and timing (Figure 3).[21]

Certainty of evidence

The certainty of evidence from studies in this review was 'very low' since the included studies were cross-sectional and present serious problems in 'risk of bias' for example, some studies made it unclear patients allocation methods,[10,18] number of teeth[16] and not blinding at least one evaluator (Table 3).

DISCUSSION

Regarding DFM for detecting carious lesions, previous systematic reviews[12,25-30] and meta-analysis[15] were performed, however, none of them referred to the detection of carious lesions related to orthodontic appliances. The results of this review showed how well the methods agreed with each other, in addition to that, in Sardana et al.'s study,[11] it was implied that DIAGNOdent Pen™ can correctly identify about 78% of visual WSLs around the brackets, and delineate 83% correct negative results when patients do not have them. This result can be useful for clinicians in making decisions regarding the management of patients under fixed orthodontic therapy.

As for the sensitivity of the DFM to distinguish the severity of the WSLs,[11] it did not have good visual performance (30%), which is in agreement with the value of sensitivity of 32% in Kavvadia et al.[10] for identifying mild WSLs.

In the overall judgment of the risk of bias for each domain, all studies were classified as 'at risk of bias', due to: 'unclear' risk scores in domain 1,[10,11,18] by not reporting how their patients were selected; 'high risk' scores in domain 2,[10,11,18,23] as the 'index test' was not interpreted without knowledge of the reference standard results; and a 'high risk' score in domain 3,[16] as the 'reference standard' was not a validated VCE method. Even knowing that histopathology is the gold standard for the diagnosis of carious lesions,[31] validated VCE methods were considered the reference standard in this review, due to its clinical applicability. Moreover, demineralization found under histopathology might not be clinically symptomatic and relevant for clinical decision-making.[11]

A significant number of variables can adversely affect the accuracy of DFMs, such as moisture over the dental surface, the presence of biofilm, calculus or stains.[15] In this review, the selected studies were careful to control and minimize these confounding factors,[10,16,18,23] except for one study,[11] patients performed their own brushing. However, as with any method involving technology, performance is also mediated in part by the examiner's experience in using the equipment and the application technique.[18] That subjectively may lead to measurement bias.[17]

Visual inspection alone is adequate for most patients in daily clinical,[12] but it is still a relevant challenge for clinicians, since there is a difficulty in predicting lesion volume through VCE, just by assessing the surface area.[32] Methods that accurately report the depth and volume of the lesion would be ideal for future studies, in order to evaluate the behavior of the carious lesions, including progression or regression. Although fluorescence-based technologies measure bacterial metabolites that penetrate the pores of the surface, they do not directly detect changes in the structure of the enamel and, therefore, are not necessarily a measurement of size and / or depth.[25]

Almosa et al.,[23] agree that the clinical advantages of using the DFM for the diagnosis of carious lesions is that it is objective and images can be displayed to the patient, having thus also an educational value.[9] Despite it is more time consuming and may incur in extra costs to the practice,[18] it's non-invasive characteristics support its use.[33] In the case of VCE, despite being an inexpensive, subjective method, which involves little time in the clinic, it does not estimate intervention invasiveness and patient discomfort.[18,29]

CONCLUSIONS

- The diagnosis of non-cavitated carious lesions related to fixed orthodontic appliances by DFMs was satisfactory relative to VCE.
- Moreover, the quantitative results and imaging possibilities may be useful in making clinical decisions about the management of patients.

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Table 1. Systematic search strategy (PIRO).

Database	Search Estrategy
Pubmed	#1 (Optical Imaging[Mesh] OR Fluorescenc* [tiab] OR Photography[Mesh] OR Photograph*[tiab])) #2 ((Orthodontic*[Tiab] OR Orthodontics[Mesh] OR Orthodontic Brackets[Mesh] OR Bracket*[tiab]))) #3 (((Dental Caries[Mesh] OR Carie*[Tiab] or White Spot Dental[tiab] OR white spot[tiab] OR Demineralization Dental[tiab])))) #1 AND #2 AND #3
Scopus	#1 TITLE-ABS-KEY ("optical imaging" OR "fluorescence imaging" OR fluorescence* OR photograph*) #2 (orthodontic* OR bracket* OR "brace orthodontic") #3 (carie* OR "White spot" OR "demineralization dental") #1 AND #2 AND #3
ISI Web of Science	#1 ("optical imaging" OR "fluorescence imaging" OR fluorescence* OR photograph*) #2 (orthodontic* OR bracket* OR "brace orthodontic") #3 (carie* OR "White spot" OR "demineralization dental") #1 AND #2 AND #3
The Cochrane Library	#1 MeSH descriptor: [Dental Caries] #2 ((Carie* OR "White Spot")):ti,ab,kw #3 MeSH descriptor: [Orthodontic Brackets] #4 ((Brackets Orthodontic* OR Bracket*)):ti,ab,kw #5 MeSH descriptor: [Optical Imaging] #6 (("Fluorescence Imaging" OR "Imaging Autofluorescence" OR Photography)):ti,ab,kw #7 #1 OR #2 #8 #3 OR #4 #9 #5 OR #6 #10 #7 AND #8 AND #9
Lilacs/BBO	((mh:(optical imaging)) OR (mh:(fluorescence)) OR (mh:(photography)) OR (tw:(fluorescence imaging)) OR (tw:(imaging autofluorescence)) OR (tw:(photograph*)) OR (tw:(photography dental)) OR (tw:(photography orthodontic*)) OR (tw:(photographies intraoral))) AND ((mh:(orthodontic*)) OR (tw:(orthodontic treatment)) OR (mh:(orthodontic brackets)) OR (tw:(brackets orthodontic*)) OR (tw:(bracket*)) OR (tw:(brace orthodontic*))) AND ((mh:(dental caries)) OR (tw:(carie*)) OR (tw:(white spot dental)) OR (tw:(white spot)) OR (tw:(demineralization dental))) AND (db:("LILACS" OR "BBO") AND type:("article"))
Open Grey	((Carie*)) AND ((Bracket*)) AND ((Fluorescence*))

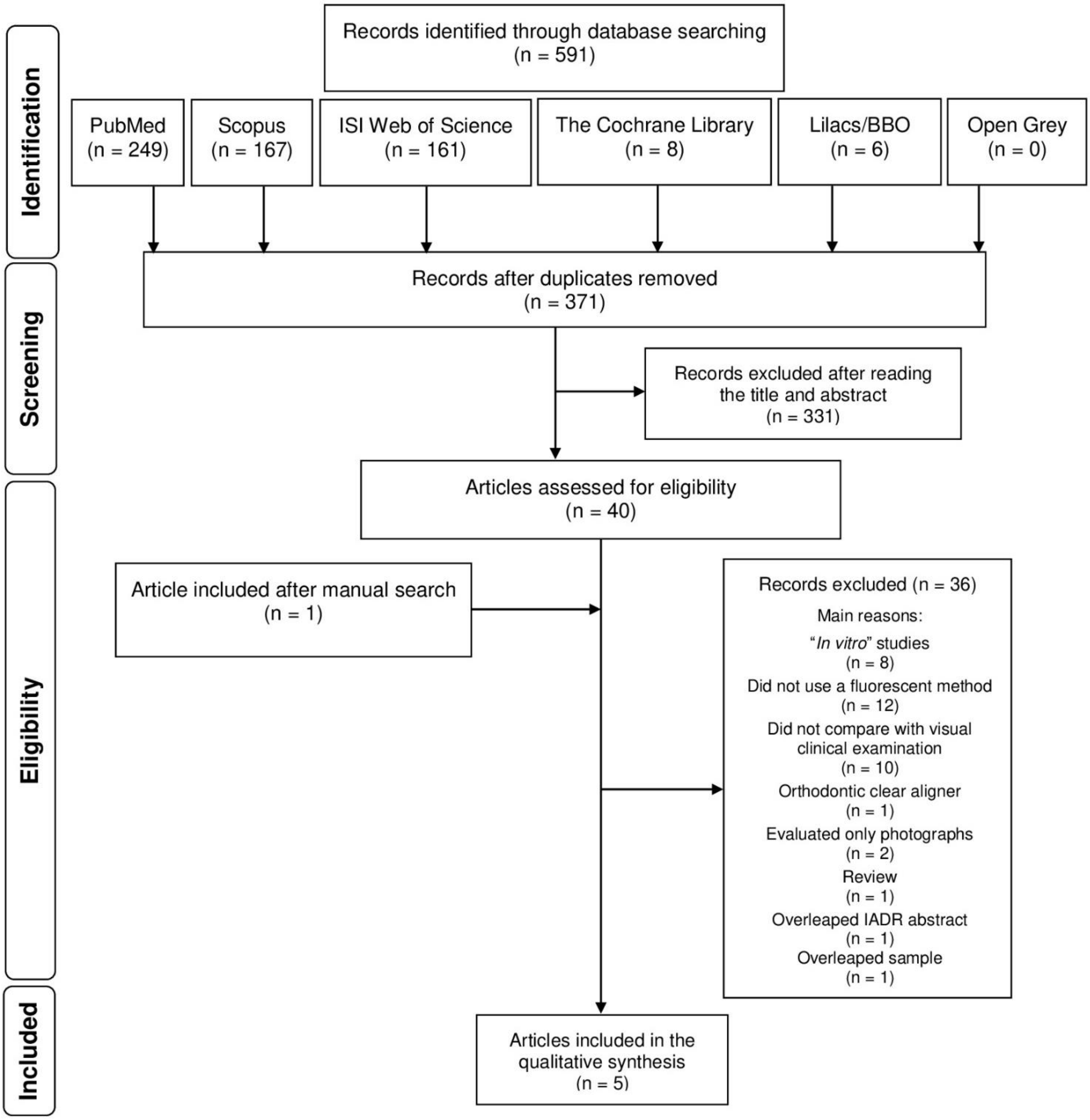

Figure 1. Flow diagram of the screening and selection process.

Table 2. Included studies.

<table>
<tr><th>Author
Year
Country</th><th>Patients (n)
Age (Years)
Tooth (n)</th><th>Treatment time (months)</th><th>Orthodontic appliances</th><th>Caries evaluation</th><th>Repetition of measurements</th><th>Fluorescent method</th><th>Visual clinical method</th><th>Outcomes</th></tr>
<tr><td>Aljehani et al.[18]
(2006)
Saudi Arabia</td><td>13
13-17
137</td><td>24</td><td>Bands and brackets</td><td>Visual examination, DIAGNOdent™ and documented with a digital camera.</td><td>Fluorescent method after debonding and 7 days later.</td><td>DIAGNOdent™</td><td>Modified Ekstrand criterion</td><td>Spearman correlation coefficient between the fluorescent and visual method was 0.40. Readings of both methods were proportional.</td></tr>
<tr><td>Almosa et al.[23]
(2014)
Saudi Arabia</td><td>89
21.2-22.5
1653</td><td>18-24</td><td>Brackets</td><td>Visual examination and DIAGNOdent Pen™.</td><td>NA</td><td>DIAGNOdent Pen™</td><td>ICDAS-II modified</td><td>Spearman correlation coefficient between the fluorescent and visual method was 0.71.
Correlation between methods: In tooth with ICDAS II scores 0 and 3, the reading with DIAGNOdent Pen™ was similar in 97% and 86% of cases.
In those with ICDAS II scores 1 and 2, the reading with DIAGNOdent Pen™ was similar in 14% and 22% of cases.</td></tr>
<tr><td>Boersma et al.[16]
(2005)
Netherlands</td><td>62
12-18
NR</td><td>23.9-25.4</td><td>Bands and brackets</td><td>Visual examination, QLF™ and documented with a digital camera.</td><td>Fluorescent method after debonding and 6 weeks later. Visual method after debonding and 6 weeks later.</td><td>QLF™</td><td>Conventional visual examination</td><td>Sensitivity: Visual method: more than 15%
QLF™: 12.6%
Readings of both methods were proportional.</td></tr>
<tr><td>Kavvadia et al.[10]
(2018)
Greece</td><td>31
13-28
619</td><td>NR</td><td>Brackets</td><td>Direct and indirect (photos) visual examination, DIAGNOdent Pen™ Vista Proof™</td><td>NA</td><td>DIAGNOdent Pen™
Vista Proof™</td><td>Gorelick's criterion</td><td><table><tr><th></th><th>Specificity</th><th>Sensitivity</th><th>Accuracy</th></tr><tr><td>Direct visual method</td><td>97%</td><td>75%</td><td>95%</td></tr><tr><td>Indirect visual method</td><td>96%</td><td>64%</td><td>92%</td></tr><tr><td>DIAGNOdent Pen™</td><td>64%</td><td>69%</td><td>65%</td></tr><tr><td>Vista Proof™</td><td>64%</td><td>71%</td><td>65%</td></tr></table></td></tr>
<tr><td>Sardana et al.[11]
(2022)
Hong Kong</td><td>99
NR
1607</td><td>NR</td><td>Brackets</td><td>Visual examination, DIAGNOdent Pen™ and documented with a digital camera.</td><td>Pre-bonding.
Immediate post-bonding.
At 6, 12 and 18-month later.</td><td>DIAGNOdent Pen™</td><td>Gorelick's criterion</td><td>Correlation between methods: In the tooth with Gorelick´s score 3, the DIAGNOdent Pen™ score had the highest mean: 19.0, compared to 0, 1 and 2: 4.56, 12.9 and 13.8.<table><tr><th></th><th>Specificity</th><th>Sensitivity</th></tr><tr><td>DIAGNOdent Pen™</td><td>83%</td><td>78%</td></tr></table></td></tr>
</table>

*NR: Not reported; NA: Not applied.

Study	RISK OF BIAS					APPLICABILITY CONCERNS			
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	OVERALL JUDGEMENT	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	OVERALL JUDGEMENT
Aljehani et al.[illegible] (2006)	?	☹	☺	☺	At risk of bias	☺	☺	☺	Low concern regarding aplicability
Almosa et al.[20] (2014)	☺	☹	☺	☺	At risk of bias	☺	☺	☺	Low concern regarding aplicability
Boersma et al.[illegible] (2005)	☺	?	☹	☺	At risk of bias	☺	☺	☺	Low concern regarding aplicability
Kavvadia et al.[illegible] (2018)	?	☹	☺	☺	At risk of bias	☺	☺	☺	Low concern regarding aplicability
Sardana et al.[11] (2022)	?	☹	☺	☺	At risk of bias	☺	☺	☺	Low concern regarding aplicability

Figure 2. Assessment of the risk of bias in the included studies.

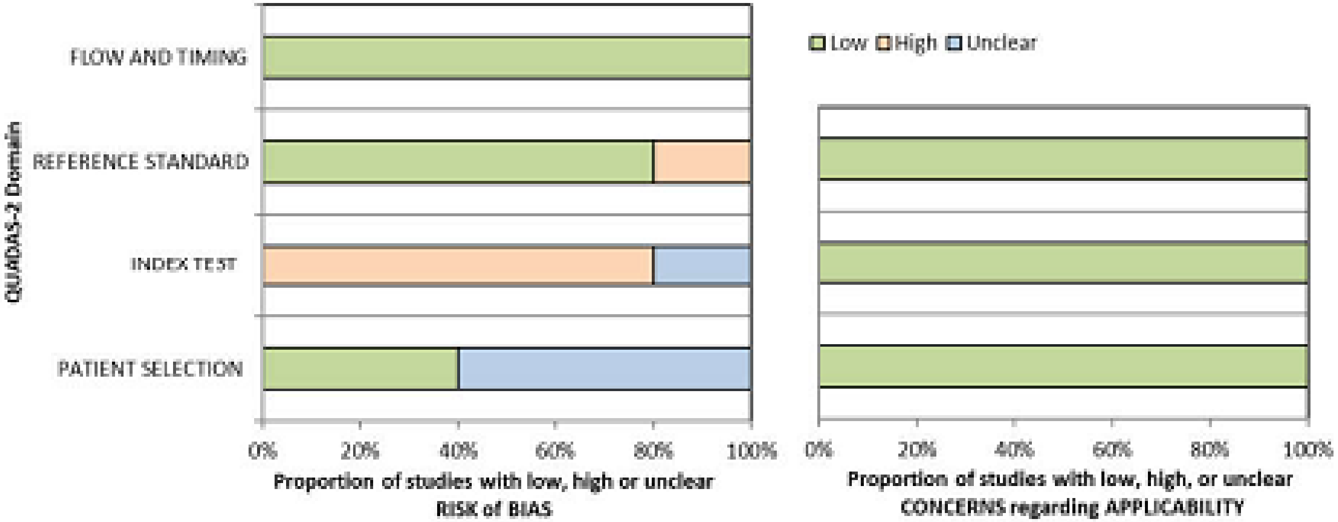

Figure 3. Graphical summary of study quality considering the QUADAS-2 checklist.

Table 3. Certainty of evidence.

Certainty assessment							Summary of findings
Number of tooth (studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Overall certainty of evidence	Effect
Correlation							
1790 (2 cross-sectional)	serious [a]	not serious	not serious	not serious	none	⊕○○○ VERY LOW	Range from 0.4 to 0.71
Sensitivity and specificity							
2226 (2 cross-sectional)	serious [b]	serious	not serious	not serious	none	⊕○○○ VERY LOW	Pooled sensitivity 0,755 [0,695-0.810]* Pooled specificity 0.777 [0.758, 0.795]*

4.2 Artigo 2: Comparison between radiographs, white and fluorescent images in the diagnosis and treatment decisions for occlusal caries in permanent molars: An *ex vivo* study.

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ABSTRACT

The aim of this *ex vivo* study was to compare the agreement of images in white light (WL), fluorescence (FL) and digital radiographs (DR), on the diagnosis and treatment decisions for occlusal caries lesions against a micro-CT gold standard. Ten extracted third molars, with enamel and/or dentin caries (ICDAS 2-4) were included in the study. Occlusal surface images were acquired with an intraoral camera (SoproLife®) in WL and FL mode. DR were obtained using an intraoral X-ray and a semi-direct digital system. A total of 780 images of the same teeth were needed for the present study. The images were organized in a template, so that they could later be examined by twenty-six dentists, invited to compose the study. They were given instructions on how to use the scoring system for occlusal caries lesions, and treatment decisions, using standardized examination conditions. The Generalized Estimation Equations model was used to compare the proportions of the correct answers between the three methods and the gold standard. When significant, Bonferroni post-hoc test was used to identify differences (α=5%). Results: Most of the examiners were specialists (76.9%), with 14.5 years of experience. All diagnostic methods were similar, and showed low agreement (DR 12.7%, WL 16.5%, and FL 16.5%) compared with gold standard caries diagnostic scores. Regarding treatment decisions, mean agreement for all diagnostic methods were higher (43.2%; $p<0.001$), and among all methods, WL (48.1%) and FL (51.2%) modes performed better than DR (30.4%, $p<0.001$). SoproLife® images could help clinicians to propose rational minimally invasive treatments for occlusal caries lesions, considering that the total proportion of correct answers in the treatment decisions prevailed when compared to the diagnosis, for all diagnostic methods.

Keywords: diagnostic imaging; occlusal caries; clinical decision making; caries lesion treatment; X-ray microtomography.

INTRODUCTION

Diagnosing the occlusal surface is still a challenge for clinicians in practice, but the current accuracy of visual examination in detecting the full extent of the lesions can be considered good if a well-established index is used by trained examiners [1]. However, results from other recent systematic review on the subject performed by the same authors pointed out that studies on the accuracy of the visual method for caries detection should consider clinically relevant outcomes [2] since a "correct" diagnosis made by clinicians is not necessarily translated into a direct benefit for patients in terms of more conservative treatment approaches [3]. The gap between an accurate diagnosis and a rational and minimally invasive operative treatment decision should be bridged, if patient-centered outcomes are being put into the spotlight of evidence-based dentistry.

Clinical guidelines still recommend intraoral radiographs as an auxiliary method to the visual clinical examination in detecting caries lesions [4, 5] with the claim that solely; its use may result in failure to detect some lesions. Therefore, the combination of both visual and radiographic methods would provide greater diagnostic sensibility while keeping good sensitivity [6]. Although a digital radiographic examination is easy to perform and provides images in a few seconds, it has strict indications because of health risk hazards associated with ionizing radiation [7]. In this context, it is important to validate and implement diagnostic methods that do not use ionizing radiation sources, to minimize exposure to patients and professionals [8, 9]. Moreover, as mentioned, desirable clinical diagnostic aids should also improve treatment decisions towards more rational and minimally invasive approaches, resulting in a clear benefit for patients [2].

SoproLife® intraoral camera (Sopro-Acteon group, La Ciotat, France) is a light-induced fluorescence caries diagnostic system based on the auto-fluorescence of dental tissues when illuminated by a wavelength of 450 nanometers [10]. It offers two lighting modes: white and fluorescent (blue color). The fluorescent mode is indicated for caries diagnosis, with the colors blue and acid green indicating sound enamel and dentin, while the colors bright red and black green indicate the presence and activity of the lesion, active and inactive, respectively [11]. Caries activity assessments are essential to propose rational treatment plans for occlusal caries lesions because for example, arrested caries generally do not need operative treatment [12].

To measure sensitivity, specificity and accuracy of digital diagnostic alternatives for caries, a micro-CT technique has been proposed as a gold standard to validate caries severity under laboratory conditions [13, 14] especially because histological methods have low accuracy in detecting the real depth of dentin lesions [15]. Thus, the aim of the present *ex vivo* study was to compare the agreement on caries diagnosis and treatment decisions of occlusal surfaces images of permanent carious teeth obtained by SoproLife®, in white light and fluorescence mode, and digital radiographs, against a micro-CT gold standard. The hypothesis tested was that all caries diagnostic methods result in similar agreement when used for detecting/diagnosing lesions or when used to help define treatment decisions.

METHODOLOGY

Ethical aspects and study design

This study was approved by the institution's Research Ethics Committee (#3.442.162). This was an *in vitro* accuracy study with a cross-sectional design, which followed the recommendations of the Standard for Reporting of Diagnostic Accuracy (STARD) steering committee [16].

Sample power

Prior to the beginning of this study, a power calculation was performed using WinPepi v.11.65 [17] to estimate the sample size needed to compare the proportion of correct answers given by examiners using three diagnostic methods. For each individual evaluating 30 images of the same teeth (10 images per diagnostic method group), a total of 690 images of teeth would be needed to disclose significant results and thus, 23 individuals would have to be recruited for this study. This calculation would detect a 15% difference between the proportions of the methodologies as significant, with the estimated hit ratio of the image without fluorescence of 84.9% [18] with a power of 90% and a significance level of 5%. Approximately extra 10% of images were added to this calculation to prevent possible losses, resulting in a total of 780 images of the same teeth and thus, 26 examiners were needed for the present study.

Tooth specimens

Initially, 20 third molars presenting enamel and/or dentin caries lesion on the occlusal surface ranging from ICDAS 2-4 [19], previously detected by an experienced and calibrated examiner (MMA), were selected from a biorepository organized for this specific study. Tooth specimens presenting enamel defects other than carious lesions (hypomineralization, hypoplasia, etc) were excluded from the sample. The selected teeth were kept in saline, to avoid dehydration for a maximum of three months before the start of the study [20]. Sound, restored or teeth presenting changes not related to carious involvement were not considered for the study.

Ten teeth were randomly drawn from this selection (page: https://sorteador.com.br/) and included in the sample (3 teeth with ICDAS 2, two with ICDAS 3 and five with ICDAS 4). After selection, the specimens were cleaned with ultrasonic tips to remove calculus and debris and were subsequently incorporated by the roots using utility wax on a plastic base to facilitate manipulation. Each specimen was placed in approximal contact with two other sound molars, one on each side, in order to simulate the position of a second permanent molar in the oral cavity, as shown in Figure 1. The 10 tooth specimens sets were kept in a closed container under 100% humidity conditions during the course of the study.

Visual and image-based examination

Acquisition of occlusal surface images was performed with the SoproLife® intraoral camera (Sopro-Acteon group, La Ciotat, France) using a dark box, both in white light (WL) and fluorescent light (FL) mode, with the flat surface of the camera slightly touching the occlusal surface of the tooth. Digital radiographic (DR) images were acquired by means of an interproximal incidence, using a Focus® intraoral X-ray device (Instrumentarium Imaging, Tuusula, Finland) and a semi-direct digital system Kavo Express® (DK Equipamentos, São Paulo, Brazil).

The images were acquired by an experienced operator (LPS), exported in "TIFF" format and were later organized into presentation blocks in a PowerPoint® template (Office 365, Microsoft Corporation, United States) in order to be scored by the examiners. All examinations were performed using the same computer (Dell notebook, model Inspiron 5570, Dell, Brazil), in the same location, using identical brightness and contrast settings for all participants. The monitor was placed on a flat surface, which could not be moved and the focal distance between the evaluator and the monitor was 40 centimeters. The images were presented in sequence to one examiner at a time, who should keep them confidential from the others.

The PowerPoint® template presentation was divided into three blocks in the following sequence: (1) 10 digital radiographs; (2) 10 images in WL; (3) 10 images in FL. For each presentation block, the images were presented in turn, from the first to the tenth image, after which a new presentation block was started. Within each presentation block, the images were mixed (page: https://sorteador.com.br/), in order to avoid sequential bias on the part of the examiners.

The examiners were instructed to score the images of the occlusal surface of each selected tooth in each set (middle tooth) acquired with each method (DR, WL and FL) using a modified dental caries scores (Table 1). These scores included just five simple progressive categories, from sound surfaces to dentin cavitation. After that, and for each tooth specimen image, the examiners should also score one best treatment option for each examined tooth (no specific treatment, preventive treatment, non-operative and operative treatment), based on the most recent and comprehensive guidelines [21] (Table 1).

Selection of examiners

From a universe of thirty dentists working in a public clinical setting, twenty-six with routine experience of diagnosing carious lesions, but without specific academic background in the field of Cariology were approached by convenience and were invited to participate in the study. They all provided their written consent before enrolling in the study procedures. Sociodemographic data were collected, such as gender, educational level (specialist, master and PhD), age and time since graduation.

They have been individually provided with a 10-minute explanation on how to score the tooth images using the proposed scores (Table 1) and the interpretation of the fluorescent colors.

Gold standard for dental caries and treatment options

After acquisition of the occlusal surface images and radiographs, the teeth were scanned in a high-energy 1173 micro-CT (Bruker, Kontich, Belgium) using the following acquisition parameters: 100kV, 80µA, 6.47µm pixel size, 1mm thick Al filter, 1s exposure, 0.5° rotation step at 360°, and 20 lines random movements. After this, the acquired projections were reconstructed using the NRecon software version 1.7.0.4, NRecon, Bruker) using standardized parameters: ring artifact correction (10), beam hardening correction (52%), and standardized contrast limits between 0 and 0.05. After reconstruction, the teeth were aligned with the occlusal surface parallel to the ground using a dedicated software (Data Viewer, Bruker) and the slice with the deepest part of the lesion was detected. This slice was classified according to the dental caries scores presented in Table 1, by an experienced operator (LPS), and defined as the gold standard for caries presence in this study (Figure 2).

Possible gold standard for treatment options were defined based on the summary of the best available evidence [21]. Table 2 shows corresponding matched dental caries and treatment option scores.

Statistical analysis

Categorical variables related to demographic data of the examiners were represented by absolute and relative frequencies. The variable "age" and "time since graduation" were represented by mean, standard deviation (SD) and amplitude. The Generalized Estimation Equations model (GEE Model) [22, 23] was used to compare the proportions of the correct answers between the three methods evaluated by the same examiner. This analysis was chosen because it considers related samples. The model was composed by an independent work correlation matrix, and a robust estimator covariance matrix. When significant, the Bonferroni post-hoc test was used to identify the different categories. The level of significance adopted was 5%. All analysis were performed in SPSS software, version 25.0 (IBM Corporations, Armonk, NY, USA).

RESULTS

Most of the examiners were female, (n=21; 80.8%), with an average age of 38.4 years. The most prevalent education level was that of specialist (n=20; 76.9%), with a mean of 14.5 years of experience, as shown in Table 3.

Figure 2 illustrates the teeth included in the study, its respective DR, WL and FL images, and the corresponding micro-CT slice showing the deepest part of the caries lesion. For each tooth, the gold standard dental caries and treatment options scores are also detailed.

Table 4 shows a comparison of the proportions of correct answers (as agreed with the gold standard scores) given by the examiners on the diagnosis of caries at the occlusal surface of the specimens. In general, no difference was found among the three methods ($p=0.415$) with a general low agreement (mean 15.3%) between the assigned caries scores and the gold standard for caries diagnosis. In tooth 6 (ICDAS 4), the evaluators responded better to the images in WL (50% correct answers) compared to DR (15.4%) and FL (19.2%) while in tooth 8 (ICDAS 4), DR underperformed compared to FL, while this was better than WL. As tooth 4 (ICDAS 3) resulted in no correct answers for DR and FL, it was not possible to estimate the p value.

Table 5 shows the comparison of the proportions of correct answers given by the evaluators in relation to treatment decisions proposed for the specimens. The mean percentage of correct answers among the methods was higher for WL (48.1%) and LF (51.2%) compared to DR (30.4%) ($p<0.001$). The total proportion of correct answers were different among the methods also in teeth 4, 6 and 8 ($p<0.05$). For tooth 4 (ICDAS 3), the examiners responded better to the images in WL (88.5%) and FL (80.8%) compared to DR (11.5%). For tooth 6 (ICDAS 4), the evaluators responded better to the images in WL (84.6%) compared to FL (53.8%), but without difference from DR (57.7%). As for tooth 8 (ICDAS 4), the evaluators responded better to the images in FL (88.5%) compared to DR (34.6%) and WL (50%). The remaining teeth did not show a more assertive method.

DISCUSSION

The results of the present study confirms that imaging methods alone underperform in diagnosis of occlusal caries, with a general low mean of correct hits (15.3%) based on the golden standard used. Regarding treatment options, the image obtained by the intraoral camera in WL (48.1%) or FL (51.2%) resulted in statistically significant higher correct hits than DR alone in establishing an acceptable treatment plan. Thus, these imaging methods have aided the examiners in making rational treatment decisions for occlusal caries based on minimally invasive approaches.

Reasons for the low agreement among the diagnostic methods in relation to the diagnosis of caries are probably related to the definition of lesion severity provided by the golden standard used in the present study (microtomography). Although histological processing and analysis is still used as a gold standard for dental caries detection, it is fundamentally a destructive method, because it requires sectioning of the sample for microscopic examination. The micro-CT technique used as golden standard in the present study has been recently proposed and validated to define caries severity under laboratory conditions [13, 14, 24, 25] especially because histological methods have generally low accuracy in detecting the depth of dentin lesions [15].

Evaluation of tooth 4 (ICDAS 3) resulted in no correct answers for caries diagnosis for DR and FL. This could be explained by the fact that a small dentin demineralization area, very near to the threshold between ICDAS 2 and 3 was detected by the micro-CT. This technique has, indeed an improved accuracy in detecting the actual depth of the lesion [24]. However, in line with the general findings of this study, treatment decisions were much better scored using the WL (88.5%) and FL (80.8%) mode, compared to the DR (11.5%) mode, ($p<0.001$).

Tooth 6 (ICDAS 4) resulted in better agreement for caries diagnosis when WL was used and this was probably because the FL pushed the diagnosis towards the activity of the lesion (inactive – color black). Other study has, in fact, not been able to confirm the validity of SoproLife® in determining the actual lesion activity [20]. Caries severity and activity are two different criteria and ideally, treatment options should include both. However, in tooth 6, the enamel cavitation evidenced by WL favored the correct treatment decision – operative treatment focused on the cavitation.

Tooth 8 (ICDAS 4) was favored by the FL mode also due to the lesion activity. In this tooth, the red color of the dentin cavitation area would have called the attention of the examiner towards more correct hits for caries diagnosis and treatment decisions. For the other teeth, no statistically significant differences were detected, but in general, FL and WL resulted in higher correct hits for treatment decisions in the present study.

Fluorescent caries diagnostic devices are considered attractive for their simplicity of use, compact size and absence of exposure to radiation [26]. By combining the advantages of a fluorescent device with an intraoral camera, SoproLife® proves to be a non-destructive and clinically applicable diagnostic method to aid in caries detection. In fact, compared to a gold standard visual examination based on ICDAS, sensitivity values of both SoproLife® imaging modes range from 0.75-0.86 while specificity values are around 0.81-0.89 [27, 28]. Indeed, SoproLife® has an acceptable accuracy to detect the presence (sensitivity) and absence (specificity) of lesions [29] but the gold standard caries detection used are based on clinically scored teeth. In the present study however, no sensitivity/specificity values were calculated. We have rather employed an agreement evaluation using a laboratory and "true" gold standard for caries detection, as mentioned before.

Although the location where the images were presented was the same for all examiners, with the screen calibrated with the same amplitude and brightness, there were still concerns expressed by the examiners regarding the difficulty in detecting occlusal caries through digital images in view of the activity and depth of pigmented grooves. Although most professional evaluators were specialists (n=20; 76%), with experience in the caries diagnosis, they reported a lack of intimacy with the digital fluorescent device and the practice of diagnosing and treatment decision for occlusal caries using digital images. A previous study reported that the ability to evaluate intraoral photographs on a screen at a convenient time and place was considered advantageous by cohort of dentists with experience in epidemiological studies [30] and to facilitate distance diagnosis, such as remote and difficult to access areas [31].

The limitations of this study include the *ex vivo* conditions in which the evaluations were carried out, that may be different from the in vivo dynamic complex of caries initiation and arrestment. Indeed, it is known that caries activity detection can be facilitated in the clinical situation when characteristics such as biofilm accumulation and gingival inflammation can be used as surrogates to whether the lesion is active or inactive [32]. However, it is still possible to detect caries activity by considering some lesion characteristics, such as luster, roughness and staining of the surface [33], and these characteristics were considered in the present study. Moreover, treatment decision gold standards in the present study were broader (more options) due to the nature of the minimally invasive approaches, what could have influenced higher agreement for treatment decisions compared to caries diagnosis. Finally, it is important to mention that the initial implementation costs generally associated with improved imaging detection methods may soon be worth its effectiveness in reducing the cost of care and preventing unnecessary operative treatments for the patient and the healthcare services.

CONCLUSION

The total proportion of correct answers was greater for all diagnostic methods relative to the treatment decisions compared to the current diagnosis of carious lesion in permanent molars. White-light or fluorescent SoproLife® images may help clinicians to propose rational minimally invasive treatments for occlusal caries lesions.

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Figure 1. Example of one sample assembled for photography and radiographic examination, simulating positions in the oral cavity.

Table 1. Scores for dental caries and treatment options used by the examiners to evaluate the sample in this study.

Dental caries scores	Description
0	Sound teeth surface
1	Enamel-limited demineralization without enamel cavitation
2	Enamel-limited demineralization with enamel cavitation
3	Dentin demineralization without dentin cavitation
4	Dentin demineralization with dentin cavitation
Treatment options scores	**Description**
0	No specific treatment
1	Preventive treatment (patient education and oral hygiene instructions)
2	Non-operative treatment (fluoride varnish and/or sealant applications)
3	Operative treatment (caries removal and restoration)

Table 2: Gold standard treatment options related to the dental caries scores.

Dental caries scores	Treatment options scores
0	0, 1
1	1, 2
2	1, 2
3	1, 2
4	2, 3

Table 3. Socio-demographic characterization of the evaluators (n = 26).

Gender	**n (%)**	
Female	21 (80.8)	
Male	5 (19.2)	
Education level	**n (%)**	
PhD	1 (3.8)	
Specialist	20 (76.9)	
Master	5 (19.2)	
	Mean (SD)	**Min-Max**
Age (years)	38.4 (5.6)	31-53
Graduate time (years)	14.5 (5.4)	8-28

SD = standard deviation.

Table 4. Comparison of the proportions of correct answers in the diagnosis of occlusal caries in each teeth and diagnostic method.

Teeth	**All methods**	**Methods**			**p**
		DR (n = 26)	**WL (n = 26)**	**FL (n = 26)**	
	% [IC 95%]	**% [IC 95%]**	**% [IC 95%]**	**% [IC 95%]**	
1	15.4 [8.7; 24.6]	11.5 [3.4; 28.5]	7.7 [1.6; 23.7]	26.9 [12.9; 46.1]	0.163
2	5.1 [1.8; 11.7]	3.8 [0.4; 18.9]	7.7 [1.6; 23.7]	3.8 [0.4; 18.9]	0.789
3	11.5 [5.9; 20]	15.4 [5.4; 33.2]	0 [0; 0]	19.2 [7.7; 37.6]	0.739
4	2.6 [0.5; 8]	0 [0; 0]	7.7 [1.6; 23.7]	0 [0; 0]	-
5	29.5 [20.3; 40.2]	30.8 [15.7; 50.1]	34.6 [18.6; 54]	23.1 [10.2; 41.9]	0.588
6	28.2 [19.1; 38.8]	15.4^{a} [5.4; 33.2]	50^{b} [31.5; 68.5]	19.2^{a} [7.7; 37.6]	**0.003**
7	5.1 [1.8; 11.7]	3.8 [0.4; 18.9]	7.7 [1.6; 23.7]	3.8 [0.4; 18.9]	0.52
8	20.5 [12.7; 30.4]	7.7^{a} [1.6; 23.7]	15.4^{ab} [5,4; 33,2]	38.5^{b} [21,7; 57,8]	**0.005**
9	15.4 [8.7; 24.6]	26.9 [12.9; 46.1]	7.7 [1.6; 23.7]	11.5 [3.4; 28.5]	0.217
10	19.2 [11.7; 29]	11.5 [3.4; 28.5]	26.9 [12.9; 46.1]	19.2 [7.7; 37.6]	0.353
Mean	15.3 [12.9; 17.9]	12.7 [8.8; 17.7]	16.5 [11.7; 22.5]	16.5 [12.4; 21.4]	0.415

DR = Digital radiographic. WL: White light. FL: Fluorescent light. GEE Model: The Generalized Estimation Equations model. TP = Total proportion. Post-hoc comparison using the Bonferroni test. Different letters represent statistically different proportions. IC95% = 95% confidence interval.

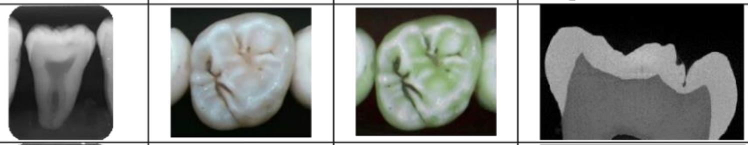
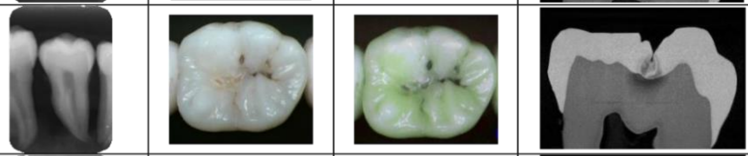
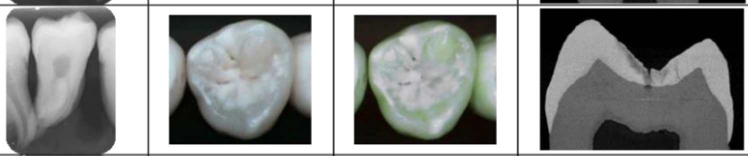
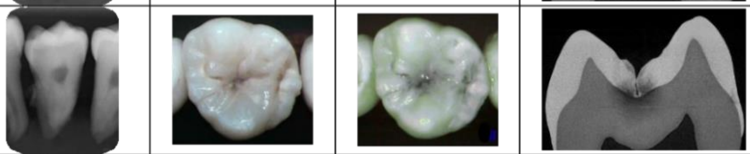
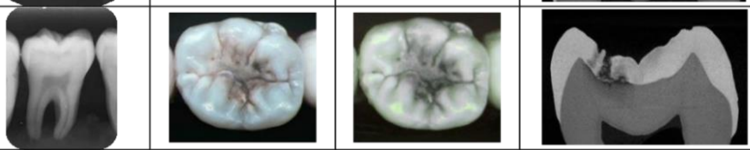
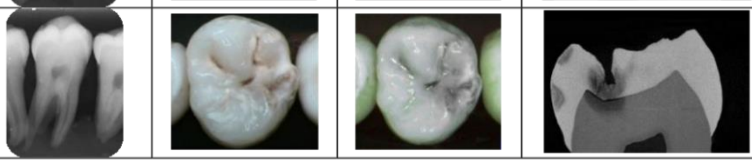
	Digital images			Gold standard		
Tooth	**DR**	**WL**	**FL**	**Micro-CT representative slice**	**Dental caries score**	**Treatment decision scores**
1					1	1, 2
2					3	1, 2
3					3	1, 2
4					3	1, 2
5					3	1, 2
6					4	3
7					4	3
8					4	3
9					3	1, 2
10					3	1, 2

Figure 2. DR, WL and FL images of the selected teeth, their respective representative slices, gold standard classification of caries lesions and respective treatments.

Table 5. Comparison of the proportions of correct answers in the treatment decision.

Teeth	All methods	Methods			p
		DR (n = 26)	WL (n = 26)	FL (n = 26)	
	% [IC 95%]	% [IC 95%]	% [IC 95%]	% [IC 95%]	
1	51.3 [40.3; 62.2]	50 [31.5; 68.5]	50 [31.5; 68.5]	53.8 [35; 71.9]	0.823
2	39.7 [29.4; 50.8]	26.9 [12.9; 46.1]	38.5 [21.7; 57.8]	53.8 [35; 71.9]	0.089
3	33.3 [23.6; 44.3]	23.1 [10.2; 41.9]	42.3 [24.9; 61.4]	34.6 [18.6; 54]	0.281
4	60.3 [49.2; 70.6]	11.5[a] [3.4; 28.5]	88.5[b] [71.5; 96.6]	80.8[b] [62.4; 92.3]	**<0.001**
5	28.2 [19.1; 38.8]	11.5 [3.4; 28.5]	38.5 [21.7; 57.8]	34.6 [18.6; 54]	0.086
6	65.4 [54.4; 75.2]	57.7[ab] [38.6; 75.1]	84.6[a] [66.8; 94.6]	53.8[b] [35; 71.9]	**0.005**
7	17.9 [10.7; 27.5]	11.5 [3.4; 28.5]	23.1 [10.2; 41.9]	19.2 [7.7; 37.6]	0.602
8	57.7 [46.6; 68.2]	34.6[a] [18.6; 54]	50[a] [31.5; 68.5]	88.5[b] [71.5; 96.6]	**<0.001**
9	38.5 [28.2; 49.5]	38.5 [21.7; 57.8]	26.9 [12.9; 46.1]	50 [31.5; 68.5]	0.259
10	39.7 [29.4; 50.8]	38.5 [21.7; 57.8]	38.5 [21.7; 57.8]	42.3 [24.9; 61.4]	0.949
Mean	43.2 [39.8; 46.7]	30.4[a] [24; 37.5]	48.1[b] [42.3; 53.9]	51.2[b] [44.7; 57.6]	**<0.001**

DR = Digital radiographic. WL: White light. FL: Fluorescent light. GEE Model: The Generalized Estimation Equations model. TP = Total proportion. Different letters represent statistically different proportions. IC95% = 95% confidence interval.

4.3 Artigo 3: Could fluorescence images help in setting a cut-off point for dentin caries removal?

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ABSTRACT

Aim: To investigate the accuracy of an intraoral camera, with fluorescent light (FL), in defining a threshold for carious dentin removal, validated a by pre-established computed microtomography (micro-CT) threshold. Moreover, it also investigated the efficacy of different papain gels for selective removal of carious dentin. Materials and Methods: Twenty extracted third molars, with dentin caries were included in the study. After an initial micro-CT, the specimens were matched by the initial volume of carious dentin and divided into two groups of carious dentin removal: Papacárie Duo® and Brix3000®. Images of the occlusal surfaces of each specimen were acquired with SoproLife®, in FL mode. A pre-defined threshold for carious tissue (<1.11 g/cm^3) was used as a standard. The efficacy of carious dentin remove by the different gels was determined by the difference between the mean relative volume of residual caries and the mineral density at the bottom of the cavity. Paired t-tests were used to compare the outcome variables between the two caries removal and the significance level use α was 5%. Results: The effectiveness of carious dentin removal was lower for Papacárie Duo® compared to Brix3000® ($p<0.05$). Mean mineral density at the bottom of the cavity between the groups was not statistically significant different. Excavated cavities from Papacárie Duo® ($n = 4$) and Brix3000® ($n = 7$) showed false positives when the fluorescent camera results were considered as carious tissue (<1.11 g/cm^3). Conclusion: Fluorescent light-induced method behaved imprecisely, when inducing cut-off points for chemical-mechanical caries excavation. Predictably, the gels behaved conservatively, in the biological sense, for carious dentin removal.

Keywords: carious dentin; quantitative light-induced fluorescence; X-ray microtomography.

INTRODUCTION

Mechanically-driven rotary instruments are the most popular technique for carious tissue removal, also proving to be faster when compared to other excavation methods.[1] The use of these instruments however, has drawbacks, such as the potential for thermal damage to dental pulp tissue, the excessive "noise" which can affect patient cooperation in the dental clinic,[2] and its non-selectivity regarding removal of intact dental tissue.[3] In this context, chemo-mechanical removal (CMR) methods have become an alternative to the use of mechanically-driven rotary instruments, leading to a more minimally invasive caries treatment.[4,5]

At present, two chemomechanical caries removing agents are being marketed, both based on the enzyme papain as the main active component. Papacárie Duo® (Fórmula & Ação Laboratório Farmacêutico, São Paulo, Brazil) contains chloramine and toluidine blue,[6] while Brix3000® (Brix Medical Science, Carcañá, Argentina) is a chloramine-free gel with a higher concentration of a bioencapsulated version of papain.[7] Both have similar mechanism of action, degrading altered collagen fibers in the infected dentin, allowing greater selectivity of caries removal, without pain and with preservation of residual tissue that can be repaired.[6] It is known that chemomechanical caries removal results in the closest to the ideal residual dentin cut-off point on the cavity floor, showing thus its suitability and minimal invasive potential.[8,9]

In practice, achieving satisfactory dentin tissue repair and avoiding damage to pulp tissue, requires the dentist to know how to distinguish between: "How much soft dentine need to be removed to avoid failure of restorations, and "What really needs to be removed to result in pulp preservation?".[10] In the literature, the terminology "selective removal" is presented as a synonym for partial and/or incomplete excavation of carious dentin.[9] However, the nomenclature "partial" and "incomplete" are still considered inadequate, as they convey the idea of suboptimal caries treatment, impairing the acceptance of this treatment as a reliable caries excavation method.[11]

Relying on the visual and tactile sense to decide on the ideal cut-off point for residual dentin to be left on the cavity floor [8] can be a risk for the dentist, given the subjectivity of criteria.[11] Fluorescent light-induced diagnostic methods have has been suggested for this purpose, to assist in decision making process.[12] SoproLife® intraoral camera (Sopro, Acteon Group, La Ciotat, France) is an example of this technology that uses the autofluorescence of the carious dental tissue, when illuminated by a wavelength of 450 nanometers.[13] The "brown" color of the caries lesion in daylight is superimposable on the fluorescent and/or dark red, detected by the camera. Sound dentin self-fluoresces green, while enamel does not, despite the "bluish" color is observed from the diffusion of green light emitted by the dentin.[14] This method has demonstrated high repeatability and reliability between evaluators, in distinguishing occlusal caries lesions in permanent teeth.[14,15]

Micro-CT has become popular as a non-destructive technique to investigate mineralized tissues.[16] In the diagnosis[17] and treatment of caries lesions[18] it allows hard tissues to be volumetrically measured and evaluated for their mineral density,[19] in addition to providing complete-detailed quantitative data on carious tissue, before and after its removal.[8]

In this context, it is desirable to find alternative visual markers that could help the practitioner in this decision making process, distinguishing "what to excavate and what to preserve" from carious dentin, and thus helping to standardize an excavation method. So, the aim of this *in vitro* study is to investigate whether an intraoral camera used, in fluorescent light mode, is effective in defining an excavation threshold for the mechanical chemical removal of carious dentin compared to a pre-defined gold standard in micro-CT. Secondarily, the effectiveness of papain gels in caries excavation will also be compared.

MATERIALS AND METHODS

Ethical aspects and study design

This study was approved by the institution's Research Ethics Committee (#3.442.162). This was an *in vitro* laboratory study, of accuracy, for a treatment of dental caries, which followed the recommendations of the Standard for Reporting of Diagnostic Accuracy (STARD) steering committee.[20]

Tooth specimens

From a selection of extracted third molars, those presenting dentin caries lesions ranging from ICDAS 4-6 [21] were selected by an experienced and calibrated examiner (AAN). Tooth specimens presenting restorations or enamel defects other than caries were excluded (hypomineralisation, hypoplasia, and others). After, a digital interproximal radiograph (Focus®, Instrumentarium Imaging, Tuusula, Finland; Kavo Express®, DK Equipamentos, São Paulo, Brazil) was obtained to evaluate the distance between the carious lesion and the pulp. If the lesion was less than 2 millimeters away from the pulp chamber, the specimen would be excluded.

The selected teeth were kept in saline, to avoid dehydration for a maximum of three months before the start of the study.[22]

A first micro-CT scan of the coronal part of tooth specimens was performed by a high-energy 1173 micro-CT (Bruker, Kontich, Belgium), and the baseline (initial caries volume was quantified. After obtaining this parameter, 20 specimens were matched by the initial carious dentin volume and divided in two experimental groups of different caries removal gels, as shown in Table 1. Identification of the groups has remained blind throughout the study.

After selection, the specimens were cleaned with ultrasonic tips to remove calculus and debris and were subsequently incorporated by the roots using utility wax on a plastic base to facilitate manipulation. The 20 tooth specimens sets were kept in a closed container under 100% humidity conditions during the course of the study.

Fluorescence image acquisition

Acquisition of occlusal surface images was performed after caries removal procedures with the SoproLife® intraoral camera (Acteon Group, La Ciotat, France) using the fluorescent light (FL) mode, with the flat surface of the camera slightly touching the occlusal surface of the tooth. The images were acquired by an experienced operator (LPS) and stored in "TIFF" format.

Caries-excavation procedures

Caries removal was performed by an experienced operator (LPS). When necessary, enamel was removed with a spherical diamond bur 1012 (Microdont, Brazil) and a high-speed water-cooled air turbine, in order to expose the underlying dentin lesion. The carious dentin was excavated using papain gels following the manufacturer's recommendations. Papacárie Duo® and Brix3000®. The gel was inserted into the cavity, with a proper syringe, and left for 1 min between sessions. For the removal of carious dentin, the opposite side of a blunt excavator was use, with pendulum movements. Excavation was finished after the gel showed no color change and the cavity assumed a vitreous appearance.

Micro-CT scanning procedures

Micro-CT image acquisition was performed using a high-energy 1173 micro-CT (Bruker, Kontich, Belgium) using the following acquisition parameters: 100kV, 80µA, 6.47µm pixel size, 1mm thick Al filter, 1s exposure, 0.5° rotation step at 360°, and 20 lines random movements. After this, the acquired projections were reconstructed using the NRecon software (version 1.7.0.4, NRecon, Bruker) using standardized parameters: ring artifact correction (10), beam hardening correction (52%), and standardized contrast limits between 0 and 0.05. Two micro-CT scans were performed: the first at baseline and the second after caries excavation, using the same acquisition settings described above.

Mineral density calibration

Micro-CT gray values were calibrated into dentin mineral density values using a set of aqueous K_2HPO_4 phantoms prepared in the following concentrations: 0.3, 0.6, 0.8, 1.2, 1.5 and 1.8 g/cm^3, as described earlier. [23] Phantoms were scanned and reconstructed using similar parameters used for the tooth specimens and a calibration curve was constructed and applied to the micro-CT gray values. Mineral density values in dentin were obtained in g/cm^3.

Digital Image analysis

The baseline and excavated micro-CT stacks were registered using a general registration algorithm within the open-source software platform of 3DSlicer.[24] After this, preprocessing with a 5 voxel kernel 3D median filter was performed to remove background noise. Segmentation of carious tissue was implemented within the FIJI software platform using a pre-selected threshold of 1.1g/cm^3, meaning that any voxel detected below this threshold would be considered as carious tissue.[19] Enamel was segmented from dentin by applying a fixed threshold of 1.99 g/cm^3 [25] and by manually removing residual remaining enamel areas in some stacks.

Evaluation of caries removal effectiveness

The effectiveness of caries removal was evaluated by means of two parameters measured after caries excavation: (1) the (mean) relative volume of residual caries and (2) the mean mineral density (MD) at the bottom of the cavity, as described previously.[8] The mean relative residual caries volume (RC/IC) was obtained as the ratio of the residual carious volume (RC) by the initial caries (IC) volume (to correct for the different volumes of baseline carious tissue). Consequently, the lower this parameter was, the better the technique would be in removing all carious tissue. The mineral density at the bottom of the cavities was calculated after examining the cross-sectional slices of the occlusal surface and identifying the one with the deepest dentin. A 1-mm circular region of interest was drawn on the middle part of the residual dentin and mean mineral density values were obtained by means of a histogram.

Evaluation of minimal invasive potential

The minimal invasive potential of the two chemo-mechanical gels was evaluated by means of the "Relative Cavity Size".[8] From each specimen, the excavated caries' stack was subtracted from the baseline volume, by which the total volume of removed dentin (RDV) was obtained. The RDV was divided by IC to provide the "Relative Cavity Size". The closest this parameter was to 1, the more accurate the minimal invasive potential of the technique would be, as the volume of the removed tissue (RDV) would correspond to the volume of the initial carious lesion (IC volume) (Figure 1).

Statistical analysis

The Shapiro-Wilk test was used to test the normality of the data. All variables tested (initial caries, residual caries, removed dentin and mineral density at the bottom of the cavity) were found to follow the normal distribution and therefore, parametric tests were used throughout the analysis. Paired t-tests were used to compare the outcome variables between the caries removal materials groups. Significance level was set to 5% throughout the analysis.

RESULTS

Results of specimen pairing is shown in Table 1. No statistically significant differences were seen between the groups (bilateral p=0.08, paired t-Test) and for this reason, comparisons made throughout the study could be considered as valid. The caries removal effectiveness was lower for Papacárie Duo® as represented by the higher relative residual caries volume resulted from excavation in this group compared to Brix3000® (Table 2, $p<0.05$, paired T-test). Regarding the mean mineral density at the bottom of the cavities, table 3 shows no statistically significantly different between Papacárie Duo® and Brix3000®.

Regarding the minimal invasive potential of the gels, the total volume of dentine removed was also similar between the caries removing gel groups (Table 2).

Figure 2 shows the fluorescence image taken with the intra-oral camera after caries removal procedures for both groups, together with mineral density data. False positives for caries presence at the bottom of the cavity is indicated by cases where a red color is detected at the residual level of the cavity, but mineral density values are higher than the carious dentin threshold. In total, 11 of the 20 specimens showed false positives when the results of the fluorescent camera were regarded as carious tissue. For the Brix3000® group, where only one specimen showed residual dentin with a value lower than the threshold, 7 out of 10 specimens were deemed as false-positives when the fluorescent camera was used.

DISCUSSION

In this study, Papacárie Duo® gel was less effective (49%), for CMR, compared to Brix3000® (30%), represented by the higher relative residual caries volume resulted from excavation in this group, On the other hand, the total volume of dentin removed was similar between groups (Papacárie Duo® with 1.03 g/cm^3 and Brix3000® with 1.13 g/cm^3), which corroborates the use of CMR for "Minimally Invasive Dentistry".[3] The CMR can be affected by adverse factors such as operator, excavator and dentin hardness,[3] and in order to avoid these biases, all teeth in this study were excavated by a single experienced operator, with the same type of manual excavator. In a previous study,[8] the demineralized enamel of the samples was mechanically removed before the micro-CT analysis to avoid interference by the similarity in the gray values between enamel caries and sound dentin.[19] However, this may have also resulted in the exclusion of some carious dentin areas, making the assessment inaccurate. In this study, eventual areas of enamel caries were removed before the micro-CT scans to avoid this bias. Moreover, the carious dentin CMR was performed by a single operator, obtaining sample homogeneity, therefore, precision in the evaluations.

Chemomechanical caries remove does not require special instruments or equipment. It is an easy-to-perform technique, with the availability of gel for manipulation, that can be used in conventional or field dental treatments, where there is no professional equipment.[2]

The time required for CMR was not measured in this study, however, the manufacturer's recommendations regarding the action and replacement of the gel were followed. Alkhouli et al. (2020),[3] reported that the mean time for caries removal with Brix3000® was 5 min (±1.60 min), and that the time was shorter compared to the conventional rotary method, regardless of the gel. Moreover, using a visual scale, the pain threshold experienced by patients undergoing caries removal by CMR was also lower.[26]

The threshold for caries removal using the CMR method was delineated by the visual-tactile method (no change in gel color and dentin scratch resistance)[27] and by the SoproLife® intraoral camera (Acteon Group, La Ciotat, France) in FL mode. Of the twenty excavated tooth, eleven showed false positives when the results of the fluorescent camera were considered carious tissue (<1,11g/cm^3) (4 in Papacárie Duo® group and 7 in Brix3000® group).

The quantification of caries by FL mode depends on the amount of bacterial by-products, protoporphyrin and the color of the carious dentin. Thus, the presence of discolored dentin, postoperatively, may be a reason that high FL values were obtained after carious dentin CMR, due to the particularity of the technique to selectively remove only soft infected carious tissue.[27] Terrer et al. (2009),[28] pointed out that unlike the DIAGNOdent™ (Kavo, Biberach, Germany), which provides a point-to-point delineation, the SoproLife® provides a global picture of the clinical situation, with over 50X magnification of images, viewed on a large screen monitor, assisting the clinician in judging and choosing appropriate caries treatment therapies (varnish, sealant and/or risk monitoring).[28]

Ideally, the histology of carious tooth surfaces is used as a standard for comparison and establishing relatively defined boundaries between sound and carious dental tissue.[29] In this study, the micro-CT was chosen as the standard for comparison, pre- and postoperatively, due to its validation in previous studies.[16,19] Its advantages include: its non-destructive nature, allowing comparison between results from the same sample, 3D volumetric evaluation convention of micro-CT into values.[16]

In view of the literature studied,[19,27] this was the first study in which SoproLife® intraoral camera fluorescence diagnostic functionality has been tested as a gold standard, to define a cut-off for presence of carious dentin after CMR.

CONCLUSION

The fluorescent light-induced method behaved imprecisely, when indicating cut-off points for the chemical-mechanical caries excavation. In view of the high amount of false positive results for the samples of both groups, making SoproLife® is unfeasible for this purpose. Regarding the behavior of the gels, the total volume of dentin removed was similar between the groups.

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Table 1. Pairing of specimens according to the initial dentin caries volume between the two experimental groups of chemomechanical caries removal.

Papacárie Duo®		Brix3000®	
Specimen	Initial caries volume (mm³)	Specimen	Initial caries volume (mm³)
7	0.44	15	1.24
16	5.95	10	6.02
4	12.61	1	11.82
2	7.41	8	7.48
18	20.92	6	24.23
17	25.43	14	30.80
19	38.17	13	37.01
5	0.32	12	1.94
20	4.35	9	4.87
3	38.65	11	41.60
Mean (± sd)	15.42 ± 13.87	Mean (± sd)	16.70 ± 14.52

Sd: standard deviation; mm³: cubic millimeter.

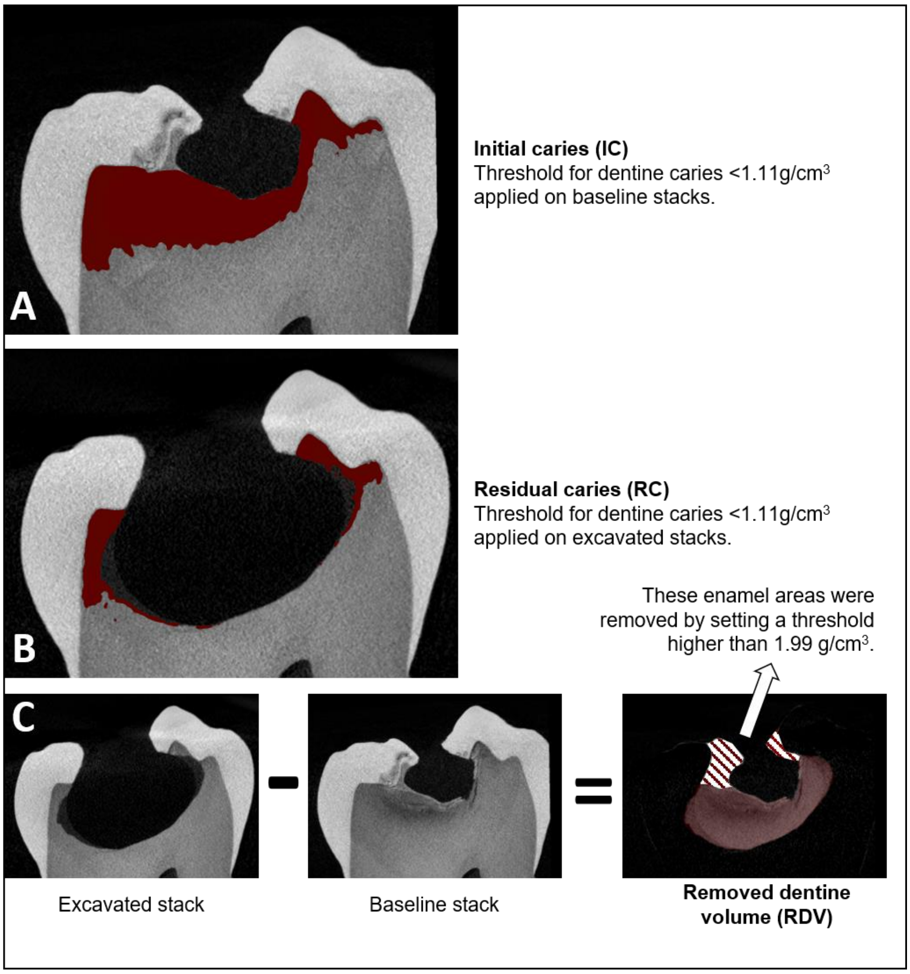


Figure 1: A) Bidimensional representation of segmented initial (baseline) dentine caries (IC). Carious dentine tissue was segmented by applying a connected pixel threshold (<1.11 g/cm^3); B) Bidimensional representation of residual dentine caries left at the bottom of the excavated cavity (RC). Carious tissue was segmented by applying a connected pixel threshold (<1.11 g/cm^3); C) Calculation of total removed dentin volume (RDV). Excavated stack was subtracted from the baseline stack and enamel was removed by applying a threshold (>1.99g/cm^3). *g/cm^3: gram per cubic centimeter

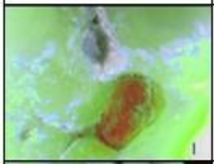
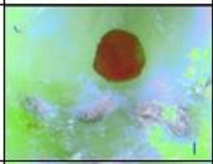
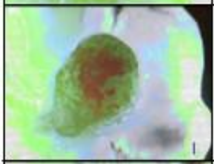
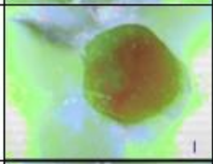
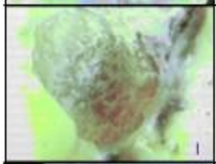
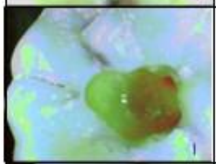
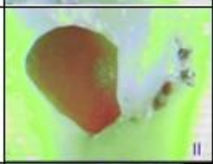
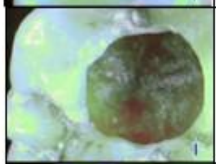
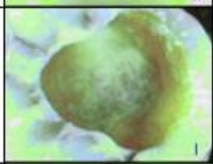
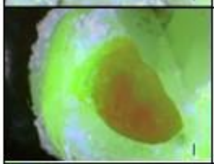
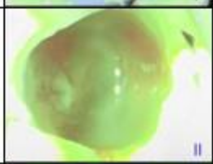
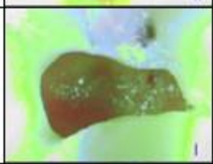
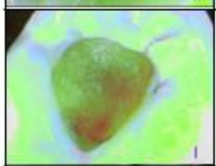
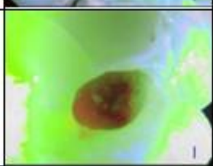
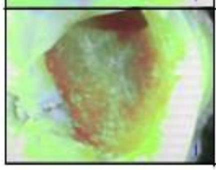
Papacárie Duo®			Brix3000®		
Fluorescent image	Mineral density (g/cm^3)	False-positive	Fluorescent image	Mineral density (g/cm^3)	False-positive
	1.33	yes		1.22	yes
	0.47	no		1.49	yes
	0.59	no		1.37	yes
	1.35	yes		1.48	yes
	1.39	yes		1.34	yes
	1.08	no		0.94	no
	1.18	no		1.21	yes
	0.66	no		1.52	no
	1.01	no		1.24	yes
	1.24	yes		1.15	no

Figure 2: Accuracy of fluorescent signals in indicating presence of residual caries.*g/cm^3: Gram per cubic centimeter.

Table 2: Distribution and mean of residual carious dentin volume and total removed dentin among the caries removing gel groups.

	Papacárie Duo®		Brix3000®	
	Specimen	RC/IC	Specimen	RC/IC
Relative residual carious dentin volume	7	1.00	15	0.58
	16	0.50	10	0.14
	4	0.40	1	0.20
	2	0.32	8	0.15
	18	0.37	6	0.39
	17	0.32	14	0.17
	19	0.47	13	0.41
	5	1.00	12	0.39
	20	0.36	9	0.33
	3	0.22	11	0.26
Mean	-	**0.49 ± 0.28[a]**	-	**0.30 ± 0.14[b]**
	Specimen	RDV/IC	Specimen	RDV/IC
Relative cavity size	7	2.53	15	1.85
	16	0.32	10	1.47
	4	0.67	1	1.01
	2	1.26	8	1.27
	18	1.96	6	0.93
	17	0.62	14	1.05
	19	0.50	13	0.56
	5	1.00	12	0.97
	20	0.71	9	1.46
	3	0.74	11	0.72
Mean	-	**1.03 ± 0.70[a]**	-	**1.13 ± 0.39[a]**

RC: Residual caries; IC: Initial caries; RDV: Removed dentine volume; [a,b]: $p<0.05$, paired T-test).

Table 3: Mineral density at the bottom of the excavated cavities among the caries removing gel groups.

	Papacárie Duo®		Brix3000®	
	Specimen	g/cm³	Specimen	g/cm³
Mineral density at the bottom of the excavated cavity (g/cm³)	7	1.33	15	1.22
	16	0.47*	10	1.49
	4	0.59*	1	1.37
	2	1.35	8	1.48
	18	1.39	6	1.34
	17	1.08*	14	0.94*
	19	1.18	13	1.21
	5	0.66*	12	1.52
	20	1.01*	9	1.24
	3	1.24	11	1.15
Mean	-	**1.03 ± 0.32**	-	**1.30 ± 0.17**

Values marked with (*) are lower than the sound dentin threshold used in the present study (1.11g/cm³); *g/cm³: gram per cubic centimeter.

5. CONSIDERAÇÕES FINAIS

Apesar da limitada certeza da evidência, os estudos mostraram que o DF, quando comparado com o EV, foi capaz de identificar corretamente a presença de lesões de MB relacionadas a ortodontia fixa (Aljehani *et al.*, 2006; Almosa *et al.*, 2014; Boersma *et al.*, 2005; Kavvadia *et al.*, 2018; Sardana *et al.*, 2022). No entanto, quanto a sensibilidade para distinguir a gravidade dessas lesões, em leve e grave, o DF mostrou-se impreciso (Kavvadia *et al.*, 2018; Sardana *et al.*, 2022), podendo ser prejudicado pela presença de biofilme e manchas hipoplásicas nas superfícies dentais (Aljehani *et al.*, 2006) e após ataque ácido e o agente adesivo para a colagem de bráquetes (Sardana *et al.*, 2022).

O sistema que combina câmera e fluorescência, o QLF®, é o sistema considerado padrão-ouro para DF de cárie (Boersma *et al.*, 2005). Um estudo mostrou que a quantidade de lesões de MB encontradas com o QLF® são equivalentes às encontradas pelo EV, e quando uma MB é detectada pelo EV, concomitantemente, pelo QLF®, um perda de fluorescência acontece em várias partes periféricas desta lesão (>15%), favorecendo assim, um possível diagnóstico precoce (Boersma *et al.*, 2005). Tem crescido o uso de fotografias digitais para a detecção de áreas desmineralizadas durante o tratamento ortodôntico fixo, pois é um método confiável, reprodutível e preciso (Sardana *et al.*, 2022). Dentre as suas vantagens clínicas, estão: a objetividade e o valor pedagógico embutido, quando as mensurações são apresentadas ao paciente simultaneamente; e suas desvantagens incluem o maior tempo clínico e dispositivos mais caros (Almosa *et al.*, 2014).

Através de uma análise sistemática da literatura, Gimenez et al. (2021) mostraram que o EV se comportou melhor que a RD, na detecção de cáries oclusais, tanto em dentes permanentes quanto em decíduos, em ambiente clínico e *in vitro*; e quando comparado ao DF, comportou-se com equivalência. Apenas para a detecção de cárie proximal em decíduos, EV e RD foram equivalentes (Gimenez *et al.*, 2021). Apesar do seu caráter subjetivo, o EV é comprovadamente o melhor método diagnóstico para a detecção de cárie, de baixo custo e tempo de trabalho mínimo (Gimenez *et al.*, 2021).

Os dentistas participantes do estudo 2 desta tese, relataram satisfação para o diagnóstico de cárie oclusal por meio de fotografias digitais. Para a maioria, foi o primeiro contato com a câmera intraoral SoproLife®, utilizada nesta tese, e com as imagens fluorescentes obtidas por ela. Eles a elogiaram pela qualidade das imagens, pela magnificação, e pela cor vermelho fluorescente, sugerindo a presença de cárie oclusal, e criticaram a dificuldade em estabelecer a profundidade da lesão, inerente ao método de diagnóstico por imagem.

Nos estudos 2 e 3 desta tese, um padrão-ouro em micro-CT foi associado as análises de imagens digitais, obtidas pela câmera intraoral SoproLife® e as RD, por não ser destrutivo e permitir a comparação dos resultados obtidos da mesma amostra dental, antes e após a remoção de cárie. A natureza tridimensional conferida a micro-CT permite a ela obter resultados de todo o volume da amostra, além de permitir calibrar padrões de hidroxiapatita, em g/cm^3, para obter dados reais de densidade mineral dentinária (Neves *et al.*, 2010).

Para a remoção seletiva de cárie, diferentes critérios para escavação são aplicáveis, mas o “ideal” é que todos confluam para a periferia da cavidade com esmalte “sadio” e uma dentina residual “dura” em direção a parede pulpar, com características visuais e táteis de saúde (Innes *et al.*, 2016). A utilização de métodos químico-mecânicos para a remoção de cárie, Carisolv® e SFC-V® experimental, foram comparados a remoção convencional por broca e a remoção por laser, e apresentaram melhor concordância com os preceitos de seletividade, que implicam em remoção “completa” de cárie e adequado potencial minimamente invasivo (Neves *et al.*, 2011). A eficácia para a remoção de cárie foi menor para o gel Papacárie Duo® (G1), comparado ao gel Brix3000® (G2), em detrimento ao maior volume relativo de cárie residual resultante após escavação; apenas um espécime dental do G2, apresentou no fundo da cavidade, uma densidade mineral compatível com cárie ($<1.11\ g/cm^3$), analisada por micro-CT, após escavação.

A história pregressa de cáries e as avaliações de risco, são os melhores preditores para cáries futuras (Panayotov *et al.*, 2013). Pensar em tecnologias que quantifiquem e detectem lesões de cárie e suas atividades, pode ser uma via para identificar pacientes que requerem intervenções preventivas intensivas (Zero *et al.*, 2001). A SoproLife®, câmera intraoral utilizada neste tese, amplifica seletivamente os sinais de fluorescência, a partir dos componentes orgânicos dos dente, e acentua a especificidade das imagens fluorescentes, para diagnóstico e decisões de tratamento da cárie (Domejean *et al.*, 2016).

Foram sugeridas hipóteses, por Panayotov et al. (2013), para a origem da fluorescência, induzida por luz, dos tecidos dentais, sendo elas: desmineralização, destruição da matriz orgânica de dentina desmineralizada pelas metaloproteinases e produto final da glicação avançada, na matriz orgânica dentinária, pela reação de Maillard (Panayotov *et al.*, 2013), responsável pela coloração da cárie dental, conhecida como glicação ou escurecimento não enzimático (Panayotov *et al.*, 2013). Os produtos finais pela reação de Maillard são altamente fluorescentes, e a fluorescência *in vitro* aumenta em função do tempo de incubação. O aumento da cor da cárie é tempo-dependente e revela uma reação bioquímica que leva ao acúmulo desses produtos altamente fluorescentes (Panayotov *et al.*, 2013). Os espécimes dentais selecionados para esta tese, foram armazenados em soro fisiológico por três meses, fato que pode ser considerado um viés do aumento de fluorescência nas imagens pela câmera intraoral SoproLife®.

A câmera intraoral SoproLife® , no modo LF, apresentou imprecisão ao definir um limite para a escavação, na RQM de dentina cariada pelo gel de papaína, apresentando resultados (n=11) falso-positivos, quando a câmera considera o tecido como cariado. Porém, Panayotov et al. (2013) relataram, que no modelo cárie-*in vitro*, estes resultados devem ser vistos com cautela, pois a dentina anormal no fundo da cavidade, após a escavação, de cor cinza esverdeada ou rosa transparente, à luz do dia, com fluorescência rosa, não é um sinal de falso-positivo, apenas indica que não precisa mais ser removida (Panayotov *et al.*, 2013).

Como em todos os métodos que envolvem tecnologia, o desempenho é determinado, em parte, pela experiência do examinador, no uso do equipamento e na técnica de aplicação (Aljehani *et al.*, 2006). Neste contexto, reforça-se a importância de promover novos estudos para determinar se o DF é aplicável, na prática geral, no diagnóstico da cárie, através de imagens, e nas decisões de tratamento destinadas a interromper ou reverter a progressão das lesões.

6. CONCLUSÕES

Os resultados apresentados nesta tese, fornecem informações importantes sobre a concordância entre exame visual e diagnóstico fluorescente, induzido por luz, para detecção de lesões de mancha branca relacionadas a ortodontia fixa. A câmera intraoral SoproLife® amplificou, seletivamente, os sinais de fluorescência dos tecidos duros dentais, auxiliando no diagnóstico e decisões de tratamento para cárie oclusal. Porém, mostrou-se imprecisa ao definir um limite para a escavação de dentina cariada, por remoção químico-mecânica com gel de papaína.

- Por meio da revisão sistemática da literatura, foi possível mostrar que o diagnóstico fluorescente e o exame visual, concordaram entre si, na detecção de lesões de mancha branca relacionadas a ortodontia fixa, apesar da ‘baixa’ certeza das evidencias, segundo o GRADE. De acordo com QUADAS-2, todos os estudos foram classificados ‘com risco de viés’ e ‘baixa preocupação quanto à aplicabilidade’.
- Na concordância entre imagens obtidas pela câmera intraoral SoproLife®, modo luz branca ou fluorescente, e a radiografia digital, a proporção de acertos foi maior, em todos os métodos, para as decisões de tratamento comparado ao diagnóstico de cárie oclusal. Um padrão-ouro em microtomografia computadorizada (micro-CT), foi criado para este estudo.
- O modo fluorescente, induzido por luz, da câmera intraoral SoproLife®, mostrou-se impreciso, ao induzir um limite para a escavação, pela remoção químico-mecânica com gel de papaína, tendo em vista os resultados falso-positivos para as amostras dentais, em ambos os grupos (G1) Papacárie Duo® e (G2) Brix3000®, revelando a limitação da câmera intraoral para este fim.

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ANEXOS

ANEXO A - Parecer do comitê de ética sobre o segundo e terceiro estudo.

UFRJ - HOSPITAL
UNIVERSITÁRIO CLEMENTINO
FRAGA FILHO DA

PARECER CONSUBSTANCIADO DO CEP

DADOS DA EMENDA

Título da Pesquisa: REMOÇÃO SELETIVA DE DENTINA COM CÁRIE POR MEIO DE LUZ FLUORESCENTE E QUANTIFICAÇÃO DO VOLUME E DA DENSIDADE MINERAL DO TECIDO CARIADO REMOVIDO E RESIDUAL ATRAVÉS DE

Pesquisador: LUCIANA PEREIRA DA SILVA

Área Temática:

Versão: 3

CAAE: 02161018.3.0000.5257

Instituição Proponente: UNIVERSIDADE FEDERAL DO RIO DE JANEIRO

Patrocinador Principal: UNIVERSIDADE FEDERAL DO RIO DE JANEIRO

DADOS DO PARECER

Número do Parecer: 3.442.162

Apresentação do Projeto:

Protocolo 355-18. Emenda E1 recebida em 3.6.2019.

As informações colocadas nos campos denominados "Apresentação do Projeto", "Objetivo da Pesquisa" e "Avaliação dos Riscos e Benefícios" foram retiradas do documento intitulado "PB_INFORMAÇÕES_BÁSICAS_1370928_E1.pdf " (submetido na Plataforma Brasil em 03/06/2019).

INTRODUÇÃO

O Sistema Internacional de Avaliação e Detecção de Cárie (ICDAS II) [1] e o exame radiográfico interproximal são dois critérios clínicos validados comumente usados em estudos de prevalência, incidência ou controle de lesões de cárie [2, 3] porém ambas as técnicas só são otimizadas quando usadas de forma combinada [4]. Paralelo a esses exames, novas tecnologias baseadas em imagens digitais foram desenvolvidas com o mesmo propósito de tornar a detecção de cárie mais objetiva. Alguns autores as chamam de 'terceiros métodos de diagnóstico' [2, 5]. Uma revisão sistemática sobre esse assunto [6], demonstrou que os dispositivos baseados em fluorescência – DIAGNOdent® (Kavo, Biberach, Alemanha), DIAGNOpen® (Kavo, Biberach, Alemanha), QLFTM (Inspektor BV, Amsterdam, Países Baixos) e FC® (Vista Proof, Dürr Dental, Alemanha) – apresentaram baixa qualidade para avaliação e detecção de cárie, de acordo com o sistema

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APÊNDICES

APÊNDICE 1 - Termo de consentimento livre e esclarecido destinado aos participantes do estudo.

UNIVERSIDADE DO BRASIL UFRJ

CENTRO DE CIÊNCIAS DA SAÚDE
FACULDADE DE ODONTOLOGIA
DEP. ODONTOPEDIATRIA E ORTODONTIA

"Remoção seletiva de dentina cariada induzida por luz fluorescente: quantificação do volume e da densidade mineral do tecido cariado removido e residual através do micro-CT"

O Sr (a) está sendo convidado (a) a participar deste projeto de pesquisa na Universidade Federal do Rio de Janeiro, sob-responsabilidade da pesquisadora doutoranda **LUCIANA PEREIRA DA SILVA**, com as seguintes características:
<u>Objetivo do estudo</u>: avaliar, *ex vivo*, (dente depois de ter sido removido da boca) a concordância do método de remoção seletiva (apenas uma parte) de dentina cariada (parte do dente com doença), induzida por luz fluorescente, através da contagem do volume e da densidade mineral do tecido cariado (quantidade de tecido dentário doente), antes e após sua remoção, por meio do micro-CT (exame de imagem).
<u>Riscos</u>: Os riscos que envolvem o desenvolvimento desse estudo são mínimos e relacionam-se ao ato de ceder os dentes e aos próprios dentes que irão compor a amostra. Os riscos para o paciente durante o procedimento de extração dentária são aqueles inerentes ao procedimento cirúrgico, que não possuem nenhuma relação com o estudo. Existe a possibilidade de sangramento excessivo, dor, inchaço e edema. Todos os riscos serão minimizados, pois o procedimento de extração ocorrerá durante a clínica de Cirurgia sob supervisão do professor. Caso haja algum dano, o atendimento será imediato e de responsabilidade da Instituição (FO/UFRJ). O risco de identificação do paciente que irá ceder seu dente será minimizado ao máximo, pois os pesquisadores irão fazer a identificação da amostra por meio de um sistema de etiquetas e códigos. O risco inerente à possibilidade de danos aos dentes cedidos durante o desenvolvimento do estudo será minimizado através do manuseio dos mesmos por equipe devidamente treinada. Os dentes serão armazenados em potes plásticos com tampa, contendo timol a 0,1% (líquido próprio para armazenar dentes) em seu interior. Todos os dentes serão posteriormente microtomografados (serão realizadas imagens dos dentes) e isso não trará nenhum dano. Não haverá a possibilidade de utilizar esses dentes para outro projeto de pesquisa.
<u>Biorrepositório transitório atrelado a um projeto de pesquisa específico (dente que será utilizado apenas para essa pesquisa</u>: Os dentes cedidos serão utilizados para o exame clínico visual (avaliar o dente apenas olhando), exame de imagem através da câmera IntraCam (Activeware®, São Paulo, Brasil) (câmera que faz a imagem do dente), que passará pelo crivo de cirurgiões-dentistas experientes afim de se obter o diagnóstico e decisão de tratamento para cárie por meio de fotografias digitais, remoção seletiva de dentina cariada induzida por luz fluorescente (remoção de parte do tecido dentário doente) e micro-CT (tipo de exame de imagem). Após ceder o dente, você não terá mais nenhum compromisso com a pesquisa. O ato de retirar o dente (devido ao seu tratamento) e cedê-lo à pesquisa terá duração máxima de um dia. Você apenas contribuirá com a pesquisa cedendo o dente, não havendo nenhum outro compromisso. Durante a execução da pesquisa os dentes serão armazenados no laboratório de Odontopediatria da FO/UFRJ, em refrigerador (geladeira) próprio para armazenamento. A identificação do material será realizada por meio de etiquetas e códigos e não será possível identificar os participantes que irão ceder os dentes. Durante toda a pesquisa a equipe se compromete em manter o material armazenado de forma segura. Ao final do estudo o material será destruído sob incineração (os restos do dente serão queimados). Vale ressaltar que esses dentes serão utilizados <u>apenas</u> para esse estudo específico intitulado "Remoção seletiva de dentina cariada induzida por luz fluorescente: quantificação do volume e da densidade mineral do tecido cariado removido e residual através do Micro-CT".

Benefício: Os benefícios desse estudo são indiretos, não serão específicos para você. Os resultados obtidos poderão contribuir para melhorar o diagnóstico de cárie (doença do dente) e consequente o tratamento proposto.
Garantia de acesso: Em qualquer fase do estudo você terá pleno acesso a pesquisadora responsável, doutoranda **LUCIANA PEREIRA DA SILVA**, no Departamento de Odontopediatria e Ortodontia da Faculdade de Odontologia/UFRJ (Av. Prof Paulo Rocco, 325; 2° andar; Cidade Universitária, Rio de Janeiro) de segunda à sexta-feira das 09:00h às 16:00h, ou pelos telefones: (21) 39382043; (21) 39382095 ou [redacted].
Caso surja alguma dúvida quanto à ética do estudo, o (a) Sr. (a) deverá entrar em contato com o Comitê de Ética em Pesquisas envolvendo seres humanos – subordinado ao Conselho Nacional de Ética em Pesquisa, órgão do Ministério da Saúde, através de solicitação ao representante de pesquisa, que estará sob contato permanente, ou contatando o Comitê de Ética em Pesquisa do Hospital Universitário Clementino Fraga Filho/HUCFF/UFRJ – R. Prof. Rodolpho Paulo Rocco, n.º 255 – Cidade Universitária/Ilha do Fundão - 7° andar – ALA E, pelo telefone 3938-2480, de segunda a sexta-feira, das 8 às 16 horas, ou através do e-mail: cep@hucff.ufrj.br. **O Comitê de Ética em Pesquisa é um órgão que controla as questões éticas das pesquisas na instituição e tem como uma das principais funções proteger os participantes da pesquisa de qualquer problema.**
Garantia de liberdade: A participação neste estudo é absolutamente voluntária. Você está livre para, a qualquer momento, negar o consentimento ou desistir de participar e retirar o consentimento, sem que isto traga qualquer tipo de dano ou impedimento. Lembramos, assim, que a recusa não trará nenhum prejuízo à relação com o pesquisador ou com a Instituição e que a participação não é obrigatória. Mediante a aceitação, você cederá o dente que foi extraído por motivo terapêutico (o dente será retirado por causa do seu tratamento) e que não tem nada a ver com esta pesquisa.
Direito de confidencialidade e acessibilidade: os dados colhidos no presente estudo serão utilizados para elaborar a tese de doutorado da pesquisadora responsável. Porém, todas as informações obtidas através dessa pesquisa serão confidenciais e asseguramos o absoluto sigilo dos que aceitarem participar. Os dados não serão divulgados de forma a possibilitar a identificação do participante e ninguém, com exceção dos próprios pesquisadores, poderá ter acesso aos resultados da pesquisa. Cada participante somente poderá ter acesso aos próprios resultados. É assegurado o completo sigilo da identidade do participante quanto à participação neste estudo, incluindo a eventualidade da apresentação dos resultados deste estudo em congressos e periódicos científicos.
Despesas e compensações: o participante não terá, em momento algum, despesas financeiras pessoais. As despesas, assim, se por ventura ocorrerem, serão de responsabilidade dos pesquisadores. Também, não haverá compensação financeira relacionada à participação nesta pesquisa. A participação nesta pesquisa não gera custos e a extração do dente na Instituição, e cedido pelo participante, é gratuita.
Garantia de indenização: Em caso de eventuais danos pessoais, causados por danos comprovadamente ligados a participação neste estudo, o participante terá direito aos tratamentos dentário e médico na Instituição, bem como às indenizações legalmente estabelecidas.
Uma via deste documento será entregue a você, assinada por você e pelo pesquisador. Tanto o pesquisador como o participante deverão rubricar todas as folhas desse TCLE e assinar à última. Em caso de dúvidas ou questionamentos, pode se manifestar agora ou em qualquer momento do estudo para explicações adicionais.

Li e concordo em participar do estudo,

____

Nome do participante de pesquisa

____

Luciana Pereira da Silva

Pesquisadora Responsável

____

Assinatura do participante de pesquisa

Rio de Janeiro, ____/_____/________