UNIVERSIDADE FEDERAL DE JUIZ DE FORA
CAMPUS GOVERNADOR VALADARES
PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS APLICADAS À SAÚDE

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Desempenho da ferramenta de redução de artefato metálico em diferentes campos de visão da TCFC para detecção de istmo radicular em molares inferiores com pinos intrarradiculares

Governador Valadares
2021

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Dissertação apresentada ao Programa de Pós-Graduação em Ciências Aplicadas à Saúde, da Universidade Federal de Juiz de Fora, Campus Governador Valadares, como requisito parcial à obtenção do título de Mestra em Ciências Aplicadas à Saúde.

Orientadora: Profa. Dra. Francielle Silvestre Verner

Coorientador: Prof. Dr. Rafael Binato Junqueira

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2021

Ficha catalográfica elaborada através do programa de geração
automática da Biblioteca Universitária da UFJF,
com os dados fornecidos pelo(a) autor(a)

Oliveira, Manuela Lima Barros de .
Desempenho da ferramenta de redução de artefato metálico em diferentes campos de visão da TCFC para detecção de istmo radicular em molares inferiores com pinos intrarradiculares / Manuela Lima Barros de Oliveira. -- 2021.
59 f. : il.

Orientadora: Francielle Silvestre Verner
Coorientador: Rafael Binato Junqueira
Dissertação (mestrado acadêmico) - Universidade Federal de Juiz de Fora, Campus Avançado de Governador Valadares, Instituto de Ciências da Vida - ICV. Programa de Pós-Graduação em Ciências Aplicadas à Saúde, 2021.

1. Artefatos. 2. Tomografia Computadorizada de Feixe Cônico. 3. Diagnóstico. 4. Micro Tomografia Computadorizada. 5. Retentores intrarradiculares. I. Verner, Francielle Silvestre, orient. II. Junqueira, Rafael Binato, coorient. III. Título.

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Aprovada em 23 de março de 2021

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DEDICATÓRIA

À Deus por ser meu capacitador e guia permanente, aquele que me revestiu de perseverança, paciência, fé e sabedoria.

Há dois anos comecei subir esse degrau em minha vida e este, assim como todos os outros, eu também dedico a mulher mais guerreira e correta que conheço, minha fonte de inspiração e dedicação, minha mãe. À você, agradeço pela vida, pelo exemplo que sempre foi e por mais essa conquista que, seu esforço e luta por nós duas, me ajudou a alcançar.

Aos meus professores, orientadores e amigos Francielle e Rafael, por todos esses anos (desde a graduação) de orientação científica e de vida. Vocês enxergaram em mim uma Mestre e me ajudaram ver uma porta aberta, a qual eu insistia em negar e aqui estou. Vocês foram pais, que me mostraram a direção e seguraram minha mão desde que comecei engatinhar. Obrigada carrega pouco significado diante da admiração e gratidão que sempre terei por vocês.

AGRADECIMENTOS

À Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) pela bolsa de pós-graduação concedida, a qual permitiu que eu me dedicasse com mais intensidade e disponibilidade à pesquisa, atingindo uma formação de qualidade.

Na pessoa do Magnífico Reitor, Professor Marcus Vinicius David, e do Diretor, Professor Peterson Marco de Oliveira Andrade, agradeço à Universidade Federal de Juiz de Fora – Campus Governador Valadares, instituição onde me graduei e agora finalizo o mestrado, por todo apoio e incentivo.

Na pessoa do coordenador, Professor Rafael Binato Junqueira, agradeço ao Programa de Pós-Graduação Ciências Aplicadas à Saúde, do qual faço parte, bem como a todos os professores que compõem o mesmo, e se doam sem medir esforços para o nosso crescimento. Me orgulho por ser discente da primeira turma deste programa e fazer parte dessa história.

Aos meus professores orientadores Francielle Silvestre Verner e Rafael Binato Junqueira, pelo exemplo de profissionais e incentivadores que sempre foram, certamente nas curvas dessa história eu não estaria aqui sem vocês.

À Faculdade de Odontologia, da Universidade de Ankara, Turquia, na pessoa do Professor Kivanç Kamburoglu, por ter aberto as portas para a parceria conosco, e ter possibilitado a execução das imagens desta pesquisa.

Às colegas Nejlam Eratam, Esra Ece Cakmak e Gul Sonmez, pelo auxílio durante os procedimentos de aquisição das imagens.

Aos professores da banca, os quais tanto admiro, agradeço por terem aceitado fazer parte desse trabalho contribuindo para lapidarmos esse estudo.

Por fim e não menos importante, a Deus que é o principal provedor de tudo em minha vida e me capacitou diariamente.

No nome da minha super mãe Luci Lima Barros, agradeço à toda minha família, a qual tanto amo, me orgulho e dedico tudo que faço.

Ao meu namorado Luan, pela companhia ao longo das páginas desse trabalho, pelo incentivo e paciência, convivendo com meus estresses, ausências e sonhos.

Aos meus amigos, que mesmo com meu distanciamento físico e (muitas vezes) virtual, sempre são abrigo e compreensão.

À todos, minha eterna gratidão, ao longo desse percurso vivido e evoluído.

"A verdadeira viagem de descobrimento não consiste em procurar novas paisagens, mas em ter novos olhos".

Marcel Prou

RESUMO

O objetivo no presente estudo foi avaliar o desempenho da ferramenta redução de artefato metálico (RAM) em diferentes campos de visão (FOV) de Tomografia Computadorizada de Feixe Cônico (TCFC) para detecção de istmo radicular em molares inferiores restaurados com retentores intrarradiculares. Estudo experimental ex vivo onde vinte e oito molares humanos inferiores foram submetidos ao exame de micro-tomografia computadorizada (micro-TC) e avaliados em conjunto por especialistas para detecção dos istmos e estabelecimento do padrão de referência. Os dentes foram submetidos ao tratamento endodôntico e posteriormente, divididos em três grupos: Grupo Guta-percha: dentes tratados endodonticamente, sem retentor intrarradicular (n=10); Grupo pino metálico: dentes tratados endodonticamente e com pino metálico pré-fabricado (n=9); Grupo pino de fibra de vidro: dentes tratados endodonticamente e com pino de fibra de vidro (n=9). A aquisição das imagens de TCFC foi realizada variando-se o tamanho do FOV (10 x 5,5 e 5 x 5,5 cm) e a utilização da ferramenta RAM ("desabilitada", "baixa", "normal" e "alta"). Os exames de TCFC foram avaliados por três especialistas em Radiologia Odontológica, que identificaram a presença ou ausência dos istmos radiculares nos terços radiculares cervical, médio e apical da raiz mesial dos molares inferiores, de acordo com uma escala de 5 pontos. Quando considerados presentes, os istmos eram classificados em completo ou incompleto. Para verificar a concordância intra e inter-examinador foi utilizado o teste Kappa ponderado. Para verificar a associação entre o terço radicular e o tipo de istmo utilizou-se o teste qui-quadrado. Para comparação dos diferentes protocolos de aquisição com o padrão de referência utilizou-se o teste de McNemar. Foram construídas curvas ROC para obtenção dos valores de acurácia, sensibilidade e especificidade. A comparação desses valores entre os protocolos aplicados e entre os grupos com e sem retentores foi realizada por meio de ANOVA dois fatores, com teste pós hoc de Tukey ($p<0,05$). A concordância intra e interexaminadores variou de moderada a substancial. O teste qui-quadrado demonstrou associação entre o terço radicular e o tipo de istmo ($p < 0,05$). A frequência de diagnóstico correto para avaliação do istmo radicular em comparação ao padrão-ouro variou significativamente em todos os grupos, independentemente do protocolo de aquisição de imagem selecionado ($P <0,05$). No grupo guta-percha, não houve diferença nos valores de acurácia, sensibilidade e especificidade entre os protocolos testados. Nos grupos de pinos de metal e fibra de vidro, os valores de acurácia foram maiores com os modos "desativado" e "baixo" da ferramenta RAM, independentemente do tamanho do FOV selecionado. Isso também foi observado para os valores de sensibilidade no grupo de pino de metal ($P < 0,05$). Concluiu-se que o tamanho do FOV não afetou o desempenho da ferramenta RAM e todos os protocolos testados apresentaram diferenças significativas em comparação ao padrão de referência. No entanto, o uso da ferramenta RAM nos modos "normal" e "alto" produziu resultados piores e, portanto, deve ser contraindicado para condições semelhantes às do presente estudo.

Palavras-chave: Artefatos. Tomografia Computadorizada de Feixe Cônico. Diagnóstico. Micro Tomografia Computadorizada. Retentores intrarradiculares.

ABSTRACT

The objective of the present study was to evaluate the performance of the metal artifact reduction (MAR) algorithms tool in different fields of view (FOV) of Cone Beam Computed Tomography (CBCT) for the detection of root isthmus in mandibular molars with intraradicular posts. This was an ex vivo experimental study. Twenty-eight mandibular human molars were submitted to micro-computed tomography (micro-CT) exam and the data set for isthmus detection and establishment of the reference standard. The teeth were prepared for endodontic treatment and later divided into three groups: Gutta-percha Group: teeth treated endodontically, without intraradicular post (n = 10); Metal pin group: teeth treated endodontically and with prefabricated metal post (n = 9); Fiberglass post group: teeth treated endodontically and with fiberglass post (n = 9). The acquisition of CBCT images was performed by varying the size of the FOV (10 x 5.5 and 5 x 5.5 cm) and the use of the MAR tool (disabled, low, normal and high). The CBCT exams were evaluated by three specialists in Dental Radiology, who identified the presence or absence of the root isthmus in the cervical, middle and apical root thirds of the mesial root of the mandibular molars, according to a 5-point scale. When considered to be present, the isthmus was classified as complete or incomplete. To check the intra- and inter- examiner agreement, the weighted Kappa test was used. To check the association between the root third and the type of isthmus, the chi-square test was used. To compare the different acquisition protocols with the reference standard it was used the McNemar test. ROC curves were constructed to obtain the values of accuracy, sensitivity and specificity. The comparison of values between the tested protocols in groups with and without post was performed using two-way ANOVA, with Tukey's post hoc test ($P < 0.05$). The intra- and inter-examiner agreement varied from moderate to substantial. The chi-square test showed an association between the root third and the type of isthmus ($p < 0.05$). The frequency of correct diagnosis for assessing the root isthmus compared to the reference standard varied complementarily in all groups, regardless of the selected image acquisition protocol ($P < 0.05$). In the gutta-percha group, there was no difference in the values of accuracy, sensitivity and specificity between the protocols tested. In the groups of metal and fiberglass posts, the accuracy values were higher with the “disabled” and “low” modes of the MAR tool, regardless of the size of the selected FOV. This was also observed for the sensitivity values in the metal post group ($P < 0.05$). It was concluded that the size of the FOV did not affect the performance of the MAR tool and all protocols differed to the reference standard. However, the use of the MAR tool in normal and high modes produced worse results and, therefore, should be contraindicated for conditions similar to the present study.

Keywords: Artefacts. Cone Beam Computed Tomography. Diagnosis. Micro CT. Root retainer.

SUMÁRIO

1 INTRODUÇÃO

A realização de tratamento endodôntico em molares inferiores representa um desafio, em virtude da variabilidade da anatomia do sistema de canais radiculares, com destaque para a presença dos istmos radiculares (SERT et al., 2004; FAN et al., 2010; PABLO et al., 2010; VILLAS-BÔAS et al., 2011; VERSIANI et al., 2016; TAHMASBI et al., 2017). O istmo constitui uma comunicação estreita, em forma de fita, entre dois canais radiculares, que contêm tecido pulpar, também conhecido como corredor ou anastomose transversa (KIM et al., 2016).

Estudos têm mostrado que a presença de canais acessórios ou de um istmo radicular são fatores limitantes durante o tratamento endodôntico cirúrgico ou não-cirúrgico, sendo uma das principais razões para o insucesso (MANNOCCI et al., 2005; PABLO et al., 2010; VILLAS-BÔAS et al., 2011; PABLO et al., 2012; DUQUE et al., 2017; TAHMASBI et al., 2017; KELEŞ; KESKIN, 2018). Tal situação relaciona-se com o fato de instrumentos de limpeza mecânica, bem como de soluções irrigantes apresentarem pouca eficiência nessas regiões (ENDAL et al., 2011; KELEŞ et al., 2016; DUQUE et al., 2017; KELEŞ et al., 2018; KIM et al., 2018). Consequentemente acontece a persistência de micro-organismos, mesmo quando o tratamento foi realizado com padrões aceitáveis e por um clínico experiente (ENDAL et al., 2011; PÉCORA et al., 2013; VON ARX 2016; SILVA et al., 2019; SIQUEIRA-JUNIOR et al., 2018).

De acordo com Von Arx (2016) a elevada prevalência de istmo nos primeiros molares superiores e inferiores relatada *in vitro* por alguns estudos, foi confirmada em seu trabalho *in vivo* através da inspeção durante cirurgia endoscópica perirradicular. O istmo se mostrou presente em 76% das raízes mesiovestibulares dos primeiros molares superiores, em 83% de raízes mesiais de primeiros molares inferiores, e em 36% de raízes distais dos primeiros molares inferiores. Tal peculiaridade dos primeiros molares inferiores serem os dentes que apresentam maior variabilidade de anatomia radicular, assim como alta incidência de istmo, foi relatada por diversos estudos na literatura (MARKVART et al., 2012; HARRIS et al., 2013; PÉCORA et al., 2013; ESTRELA et al., 2015; WOLF et al., 2016; KELEŞ; KESKIN, 2018, MARCELIANO-ALVES et al., 2018).

Buscando solucionar esses desafios, exames de imagem são muito usados na Endodontia clínica e laboratorial (ESTRELA et al., 2015), com destaque para a radiografia periapical (SOUSA et al., 2017a; KOÇ et al., 2019). Entretanto, conforme relatado por Pécora et al. (2013), para avaliar a microconfiguração do sistema de canais radiculares esta é insatisfatória, por ser um exame bidimensional. Assim, os recursos tecnológicos mais avançados e que tem tido melhores resultados, são exames tridimensionais, como a tomografia computadorizada de feixe cônico (TCFC) na prática clínica (MATHERNE et al., 2008; HASSAN et al., 2012; HELVACIOGLU-YIGIT et al., 2016; NIKBIN et al., 2018; KOÇ et al., 2019), e a microtomografia computadorizada (micro-TC) na investigação laboratorial (ENDAL et al., 2011; ORDINOLA-ZAPATA et al., 2017; KELEŞ; KESKIN, 2018, TOLENTINO et al., 2018).

A acessibilidade, o alto custo e a necessidade de conhecimento técnico elevado são limitações da micro-TC (KELEŞ; KESKIN, 2018). Apesar de não ser possível seu uso clínico, ela fornece informações mais precisas do que a TCFC (HARRIS et al., 2013; ORDINOLA-ZAPATA et al., 2017; TOLENTINO et al., 2018). Isso é um dos fatores que pode explicar resultados de investigações da morfologia tridimensional de canais *in vitro* serem consideradas superiores aos métodos *in vivo* (WOLF et al., 2016).

Ademais, a micro-TC é um método usado para investigar raízes de forma não destrutiva, sendo importante na reconstrução e análise dos sistemas de canais radiculares, permitindo por exemplo, a comparação da morfologia dos canais antes e depois de alguma intervenção, utilizando dentes extraídos (FAN et al., 2010; ORDINOLA-ZAPATA et al., 2017; SIQUEIRA-JUNIOR et al., 2018). Os primeiros relatos de sua aplicação na pesquisa endodôntica estavam vinculados à medição de espessura do esmalte dos dentes e à comparação de técnicas de instrumentação, sendo posteriormente aplicada em pesquisas na detecção de istmos (MANNOCCI et al., 2005). Atualmente, este é o método mais detalhado e preciso na investigação da morfologia interna dos canais radiculares, a partir da reconstrução de imagens em softwares que permitem a avaliação tridimensional, sendo considerado padrão de referência (ORDINOLA-ZAPATA et al., 2017; MARCELIANO-ALVES et al., 2018; SIQUEIRA-JUNIOR et al., 2018).

A utilização da TCFC tem ampliado consideravelmente nos últimos anos, tanto na prática clínica como em pesquisa científica (KIM et al., 2018; TOLENTINO et al., 2018; CAMPELLO et al., 2019; KOÇ et al., 2019; PATEL et al., 2019b). De acordo com as diretrizes da Associação Americana de Endodontia e da Academia Americana de Radiologia Oral e Maxilofacial (2015), a TCFC deve ser usada apenas quando a história do paciente e um exame clínico demonstram que os benefícios para o paciente superam os riscos potenciais da exposição à radiação X, bem como quando as informações necessárias não puderem ser alcançadas por radiografia bidimensional de dose mais baixa (PATEL et al., 2019a; PATEL et al., 2019b). Dessa forma, em casos de tratamento endodôntico de dentes com morfologia complexa, a TCFC com campo de visão (*field of view* – FOV) limitado deve ser considerada uma modalidade de imagem de escolha, desde que os critérios citados anteriormente sejam respeitados. Destaca-se que a TCFC não deve ser usada como exame de rotina na Endodontia, sendo individualmente indicada (AAE, 2015; PATEL et al., 2019a).

Segundo a literatura, a obtenção de uma imagem com boa qualidade para adequada visualização de estruturas anatômicas na TCFC, é diretamente influenciada pelo protocolo de aquisição de imagens selecionado (HASSAN et al., 2012; NEVES et al., 2014; CODARI et al., 2017). Esses protocolos vem sendo cada vez mais pesquisados, visto a relevância de uma correta indicação de acordo com as informações clínicas de cada caso (SOUSA et al., 2017a; MARCELIANO-ALVES et al., 2018). O projeto SEDENTEXCT e a Sociedade Europeia de Endodontia (SEDENTEXCT, 2009; PATEL et al., 2019a), também destacaram importantes diretrizes baseadas em evidências sobre o uso da TCFC aplicada à Endodontia, como a importância no ajuste desses protocolos para a radioproteção, destacando que a dose de radiação depende do tipo de equipamento e dos parâmetros de exposição, especialmente o FOV selecionado.

O FOV dos exames de TCFC é um fator importante para a visualização dos canais, uma vez que quanto menor o FOV utilizado, maior a resolução espacial da imagem (TOLENTINO et al., 2018). Dessa forma, exames que utilizam FOV maior apresentam pior qualidade da imagem, consequentemente, dificultando o diagnóstico (HASSAN et al., 2012; HELVACIOGLU-YIGIT et al., 2016; QUEIROZ et al., 2017b; SOUSA et al., 2017a; TOLENTINO et al., 2018; KOÇ et al., 2019).

A inter-relação do efeito de volume parcial com a qualidade da imagem, existe pelo fato deste efeito limitar o diagnóstico de estruturas pequenas e complexas, influenciando nos resultados de sensibilidade (TOLENTINO et al., 2018). Isso ocorre quando a resolução do voxel da varredura é maior do que a resolução espacial do objeto analisado (TOLENTINO et al., 2018; TOLENTINO et al., 2020).

O voxel por sua vez, é definido como o menor elemento de imagem, sendo determinado por sua altura, largura e espessura (OZER, 2011). O tamanho do voxel está diretamente ligado à resolução espacial, sendo que quanto menor o tamanho do voxel melhor a resolução da imagem. O alto contraste e resolução espacial é um fator essencial, devido à necessidade da riqueza de detalhes para examinar pequenas estruturas como istmos radiculares (TOLENTINO et al., 2018).

Outro fator limitante em exames de TCFC é a formação de artefatos em casos onde existem materiais de alta densidade presentes, tais como guta percha, pinos metálicos ou implantes (NEVES et al., 2014; BEZERRA et al., 2015; HELVACIOGLU-YIGIT et al., 2016; KAMBUROĞLU et al., 2016; RABELO et al., 2017; FREITAS et al., 2018; NIKBIN et al., 2018). Estes podem ser gerados e influenciados por diversos fatores, como efeito de volume parcial (TOLENTINO et al., 2018), radiação secundária dispersa (RABELO et al., 2017; VASCONCELOS et al., 2019), protocolos de aquisição de imagens (BEZERRA et al., 2015; HELVACIOGLU-YIGIT et al., 2016; FREITAS et al., 2018) e, principalmente, em função das diferenças na atenuação e absorção dos raios X por materiais de alta densidade, levando ao aumento da energia média do feixe de radiação, fenômeno conhecido como endurecimento do feixe (KAMBUROĞLU et al., 2016; KAJAN et al., 2018). A imagem resultante então apresentará estrias hipodensas (faixas escuras), estrias hiperdensas (faixas brancas) e distorção de objetos metálicos, que podem interferir na interpretação do exame, acarretando erros de diagnóstico (BEZERRA et al., 2015; QUEIROZ et al., 2017a).

Neste contexto, diversos métodos e algoritmos têm sido propostos para reduzir os artefatos em TCFC. Um deles é a ferramenta de redução de artefato metálico (RAM), que é um conjunto de algoritmos que atuam na homogeneização das variações dos valores de cinza e aumentam a relação de contraste-ruído (QUEIROZ et al., 2017a; KOÇ et al., 2019). Seu uso tem sido testado em diversos estudos que buscam ferramentas para aprimorar o diagnóstico de condições como fraturas radiculares, instrumentos fraturados, perfurações de furca, doenças periodontais e periimplantites em regiões que apresentem materiais de alta densidade e/ou elevado número atômico (BEZERRA et al., 2015; KAMBUROĞLU et al., 2016; QUEIROZ et al., 2017b; FREITAS et al., 2018; NIKBIN et al., 2018; CANDEMIL et al., 2019; KOÇ et al., 2019; VASCONCELOS et al., 2019; COSTA et al., 2020).

Apesar dos recentes avanços, o diagnóstico por imagem dos istmos radiculares ainda permanece um desafio na prática clínica. Tolentino et al. (2018) relataram em que mesmo utilizando parâmetros de aquisição que contribuam para uma maior resolução espacial na TCFC, os resultados não permitiram uma detecção confiável de presença de istmo em comparação com o grupo controle, analisado com micro-TC.

Helvacioglu-Yigit et al. (2016) realizaram avaliação do efeito de diferentes protocolos de aquisição de TCFC, em relação a redução de artefatos metálicos produzidos, em dentes obturados com quatro materiais obturadores distintos. Os autores destacaram que determinadas variáveis como o dente escolhido, o tipo de material obturador, kVp, *voxel* e a configuração da ferramenta RAM, resultaram em diferenças significantes quanto a quantificação dos artefatos gerados. Ainda conforme relatado por Vasconcelos et al. (2019), a ferramenta de RAM apresenta comportamentos distintos em diferentes FOV e na presença de artefatos gerados por materiais de diferentes números atômicos, indicando que ainda são necessários estudos sobre a aplicação e indicação desses algoritmos de reconstrução em diversas situações.

Diante de tais relatos na literatura científica, pode-se destacar que a qualidade da imagem e os protocolos de aquisição estão inter-relacionados, ressaltando-se a importância da escolha adequada das configurações de exposição,a fim de otimizar a qualidade da imagem, considerando também a redução das doses de radiação segundo o princípio *As Low As Diagnostically Accpetable* (ALADA) (NEVES et al., 2014; HELVACIOGLU-YIGIT et al., 2016; QUEIROZ et al., 2017b; RABELO et al., 2017; NIKBIN et al., 2018; KOÇ et al., 2019).

O uso de micro-TC e TCFC na pesquisa é cada dia mais comum (PÉCORA et al., 2013; HELVACIOGLU-YIGIT et al., 2016; KELEŞ et al., 2018). Ambos são úteis em estudos sobre a complexidade anatômica do sistema de canais radiculares, incluindo o diagnóstico dos istmos, principalmente em situações desafiadoras, como a presença de retentores intrarradiculares.

Com base no exposto, a hipótese nula testada foi a de que a ferramenta RAM não influencia o diagnóstico de istmo radicular em molares inferiores com retentores intrarradiculares em imagens de TCFC obtidas com diferentes FOV. Este estudo teve como objetivo avaliar o desempenho da ferramenta RAM em diferentes FOV de TCFC para detecção de istmo radicular em molares inferiores com retentores intrarradiculares.

2 ARTIGO CIENTÍFICO

Artigo científico enviado para publicação no periódico *International Endodontic Journal*, qualis CAPES Interdisciplinar A1. A estruturação do artigo baseou-se nas instruções aos autores preconizadas pelo periódico (ANEXO B).

Title Page

Assessment of the metal artifact reduction tool in CBCT scans with different fields of view for the detection of root isthmus in mandibular molars with intraradicular posts

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Running Title: Assessment of the MAR tool in CBCT

Keywords: Artefacts; Cone Beam Computed Tomography; Diagnosis; Micro CT; Tooth Root; Root Canal Filling Materials.

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Abstract

Aim: To evaluate the performance of metal artefact reduction (MAR) tool in cone-beam computed tomography (CBCT) scans by using different fields of views (FOVs) in the detection of root isthmus in mandibular molars with intraradicular posts.

Methodology: This was an experimental ex vivo study. Twenty-eight human mandibular molars were scanned by using micro-computed tomography in order to serve as reference standard images. Thereafter, specimens were treated endodontically and allocated into different groups according to the presence and/or material of the intraradicular post: Gutta-percha group (teeth with no posts) (n = 10); Prefabricated metal post group (n = 9); Fiberglass post group (n = 9). CBCT scans were taken by using CBCT ProMax 3D Max device. Eight different image acquisition protocols, with variations in the size of the FOV (10 cm x 5.5 cm and 5 cm x 5.5 cm) and MAR tool (disabled, low, normal, and high mode) were utilized. The presence of root isthmus was determined in the cervical, middle, and apical thirds of the mesial root considering a 5-point scale. If present, root isthmuses were classified as either complete or incomplete. Data were analysed by using weighted Kappa, Chi-square, Mc Nemar tests, ROC curves (accuracy, sensitivity, and specificity), and two-way ANOVA with Tukey's post hoc test (α = 5%).

Results: Intra- and inter-examiner agreement varied from moderate to substantial. Chi-square test demonstrated an association between the root third and the type of isthmus (P <0.05). The frequency of correct diagnosis for root isthmus assessment in comparison to reference standard varied significantly in all groups, regardless of the image acquisition protocol selected (P <0.05). In the gutta-percha group, there was no difference in accuracy, sensitivity, and specificity values between the tested protocols. In the metal and fiberglass post groups, accuracy values were higher with the “disabled” and “low” modes of the MAR tool, regardless of the FOV size selected. This was also observed for sensitivity values in the metal post group (P <0.05).

Conclusion: The MAR tool was not effective in reducing metallic artifacts, during the diagnosis of root isthmus, regardless of the FOV used, in molars with intraradicular posts.

Introduction

The variability in the anatomy of root canal system poses a challenge for the endodontic treatment of mandibular molars, specifically in the presence of root isthmus (Sert *et al.* 2004, Fan *et al.* 2010, Pablo *et al.* 2010, Villas-Bôas *et al.* 2011, Versiani *et al.* 2016, Tahmasbi *et al.* 2017). Previous studies showed that accessory canals or root isthmuses could limit and negatively affect surgical or non-surgical endodontic treatment leading to treatment failure (Mannocci *et al.* 2005, Pablo *et al.* 2010, Villas-Bôas *et al.* 2011, Pablo *et al.* 2012, Duque *et al.* 2017, Tahmasbi *et al.* 2017, Keleş & Keskin 2018). Hitherto, in order to assess three-dimensional microconfiguration of the root canal system micro-computed tomography (micro CT) and cone-beam computed tomography (CBCT) were successfully utilized, for *in vitro* research (Endal *et al.* 2011, Ordinola-Zapata *et al.* 2017, Keleş & Keskin 2018, Tolentino *et al.* 2018) and clinical practice (Matherne *et al.* 2008, Hassan *et al.* 2012, Helvacioglu-Yigit *et al.* 2016, Nikbin *et al.* 2018, Koç *et al.* 2019), respectively. Micro CT provides more accurate information than CBCT, however its clinical use is not allowed mainly due to high doses of radiation emitted to the patient, in addition to difficult accessibility, high cost and the need for high technical knowledge (KELEŞ; KESKIN, 2018).

Usage of CBCT showed a significant jump over the last years both in terms of clinical practice and scientific research, once the three-dimensional images provide great details, that even with limitations, allows changes in acquisition parameters in order to improve quality of image (Kim *et al.* 2018, Tolentino *et al.* 2018, Campello *et al.* 2019, Koç *et al.* 2019, Patel *et al.* 2019b). According to the guidelines of the American Association of Endodontics and the American Academy of Oral and Maxillofacial Radiology (2015), CBCT should only be used when the patient's history and clinical examination indicate that the benefits of the tomographic scanning outweigh the risks of radiation exposure, or when two-dimensional radiography is insufficient to provide the required diagnostic information (Patel *et al.* 2019a, Patel *et al.* 2019b). Therefore, considering radioprotection factors, CBCT with a limited field of view (FOV) should be the imaging modality of choice for the endodontic treatment or retreatment of teeth with complex morphology, as is the case of those with root isthmus (AAE 2015, Patel *et al.* 2019a).

Artefact formation due to the presence of high-density restorative materials, such as; amalgams, crowns, implants, gutta-percha and metal posts, may drastically reduce the diagnostic accuracy of CBCT scans (Neves *et al.* 2014, Bezerra *et al.* 2015, Helvacioglu-Yigit *et al.* 2016, Kamburoğlu *et al.* 2016, Rabelo *et al.* 2017, Freitas *et al.* 2018, Nikbin *et al*. 2018). High-density materials may produce variations in the attenuation and absorption of X-rays, leading to an increase in the average energy of the radiation beam, a phenomenon known as beam hardening (Kamburoğlu *et al.* 2016, Kajan *et al.* 2018). The resulting image presents hypodense or hyperdense bands, and distortion of metallic objects, which can interfere with the interpretation of the image and result in misdiagnosis (Bezerra *et al.* 2015, Queiroz *et al.* 2017a). In addition, factors, such as; the partial volume effect (Tolentino *et al.* 2018), scattered secondary radiation (Rabelo *et al.* 2017, Vasconcelos *et al.* 2019), and different image acquisition protocols (Bezerra *et al.* 2015, Helvacioglu-Yigit *et al.* 2016, Freitas *et al.* 2018) may all affect the formation of metallic artefacts.

Several methods and algorithms were proposed in order to reduce the extent of artefact formation in reconstructed CBCT images. One of them is the metal artefact reduction (MAR) tool, which is a set of algorithms that homogenize variations in grayscale values and increase the contrast-to-noise ratio (Queiroz *et al.* 2017a, Koç *et al.* 2019). This tool was tested in several studies in order to improve the diagnosis of root fractures, fractured instruments, furcation perforations, periodontal diseases, and peri-implantitis, in areas with high-density and/or high atomic number materials (Bechara *et al.* 2013, Kamburoğlu *et al.* 2013, Bezerra *et al.* 2015, Kamburoğlu *et al.* 2016, Queiroz *et al.* 2017b, Freitas *et al.* 2018, Nikbin *et al.* 2018, Candemil *et al.* 2019, Koç *et al.* 2019, Vasconcelos *et al.* 2019, Costa *et al.* 2020).

Helvacioglu-Yigit et al. (2016) assessed the effectiveness of different CBCT acquisition protocols in reducing metallic artefact formation. The authors concluded that the configurations of the MAR tool significantly affected the average number of artefacts. The MAR tool presented different characteristics depending on the FOV and the presence of artefacts generated by materials with different atomic numbers (Vasconcelos *et al.* 2019). Hence, further studies indicating the application of these reconstruction algorithms in diverse situations should be encouraged.

Despite the most recent advances, diagnostic imaging of root isthmuses still remains as a challenge for the clinician. Even when acquisition parameters with higher spatial resolution are used in CBCT scanning, the detection of isthmus may be less accurate in comparison to micro CT (Tolentino *et al.* 2018). Previous literature suggest that the image quality and acquisition protocols are interrelated, emphasizing the importance of correctly choosing exposure settings to optimize the image quality while reducing radiation doses, according to the As Low As Diagnostically Acceptable (ALADA) principle (Neves *et al.* 2014, Helvacioglu-Yigit *et al.* 2016, Queiroz *et al.* 2017b, Rabelo *et al.* 2017, Nikbin *et al.* 2018, Koç *et al.* 2019).

The anatomical complexity of the root canal system should be thoroughly examined for endodontic success, especially in challenging situations due to artefact formation and due to the influence of different acquisition protocols on the image quality. To the best of our knowledge, the present study is the first to address such parameters in teeth with a high prevalence of root isthmuses and in need of endodontic retreatment. Therefore, the null hypothesis tested was that the MAR tool did not influence the diagnosis of root isthmus in mandibular molars with intraradicular posts when CBCT images obtained by using different FOVs were assessed. This study aimed to evaluate the performance of the MAR tool in CBCT scans taken with different FOVs in the detection of root isthmus in mandibular molars with intraradicular posts.

Materials and Methods

This study was previously approved by the Human Research Ethics Committee at the Federal University of Juiz de Fora, under Protocol No: 3.675.856/2019, and was structured according to the Standards for the Reporting of Diagnostic Accuracy Studies (STARD) for of diagnostic accuracy studies (Bossuyt *et al.* 2015, Cohen *et al.* 2015).

Sample Selection

Forty-five first and second human mandibular molars recently extracted for different purposes were obtained from a biorepository and used in this experimental *ex vivo* study. Teeth were clinically and radiographically inspected for eligibility and mandibular molars only with sound roots were included. Teeth with lacerated and/or fused roots, endodontic treatment, intraradicular posts, fractured file in the canals, internal or external root resorption, obliterated canals, pulp calcifications, and roots with incomplete rhizogenesis, were excluded from the study. Teeth with cracks and root fractures were also excluded according to diagnosis through transillumination technique by using a high-power LED 1200 mW/cm^2 (Radii Cal, SDI, Victoria, Australia). Finally, 13 teeth were excluded resulting in an *n* of 32. Thereafter, scaling and root planning were performed on teeth, followed by bathing in an ultrasonic bath for 30 minutes (Cristófoli, Londrina, Paraná, Brazil), in order to remove possible calculus or remaining cementum and bone tissue. All crowns were then sectioned at the level of the cementoenamel junction by using ISOMET 1000 Precision Saw metallographic cutter (Buehler, Lake Bluff, IL, USA) in order to avoid identification of the teeth by the examiners.

Micro CT acquisition and evaluation (Reference Standard)

After sample preparation, all teeth were subjected to micro CT scanning (Super-argus PET/CT, Sedecal USA Inc., Madrid, Spain), which served as reference standard (Tayman et al. 2018). The images were obtained at 40 kVp, 140 mA and a voxel size of 0.03 mm. Micro CT images were evaluated by consensus of an Endodontist and a Dentomaxillofacial Radiology specialist to establish the reference standard - presence/absence of isthmus in the cervical, middle, and apical root thirds, as well as the type of isthmus (complete or incomplete) **(Figure 1)**. The analysis of micro CT scans was performed under the same observation conditions by using AMIDE software (Amide's, a Medical Imaging Data Examiner, available at amide.sf.net, public domain) on a 24" LCD screen (LG Electronics, Seoul, South Korea) with a screen resolution of 1920 x 1200 pixels and 16-bit color depth in a room with dimmed lighting.

Endodontic treatment

Once micro CT scans were obtained, endodontic treatment was performed on the specimens by a single specialist, with 8 years of experience, in a standardized manner. The length of the root canal was established when the tip of a file #10 (LK-flexofile, Dentsply, Petrópolis, RJ, Brazil) reached the apex of the root patency. The file length was measured, and the working length was set 1 mm below the actual length. The teeth were then instrumented by using rotary files (ProTaper Universal, Dentsply / Maillefer, Petrópolis, RJ, Brazil). During instrumentation, four teeth suffered instrument fracture inside the root canal, resulting in a final sample of 28 teeth. Statistical power of the sample was calculated and indicated that the minimum sample size was reached. All teeth were irrigated with 2.5% sodium hypochlorite, cleaned with 17% EDTA, and dried with absorbent paper tips (Dentsply / Maillefer, Petrópolis, RJ, Brazil). The filling was performed with gutta-percha cones and zinc oxide and eugenol cement (Endofill, Dentsply/Maillefer, Petrópolis, RJ, Brazil) through lateral condensation technique.

Following endodontic treatment, specimens were randomly divided into three groups based on the presence and/or material of the intraradicular posts (cemented after clearance of 2/3 of the root length), as follows: GPG – gutta-percha group, teeth with no posts (*n* = 10); PMG - teeth with a prefabricated metal post (*n* = 9); FGG - teeth with a fiberglass post (*n* = 9).

CBCT acquisition and evaluation

For CBCT imaging, each tooth was placed in the appropriately prepared mandibular molar sockets of a dry skull along with its mandible. The dry skull along with its mandible was covered with 2 cm. red wax as a soft tissue equivalent material. ProMax 3D Max CT scanner (Planmeca, Helsinki, Finland) was set to the following fixed parameters: 96 kVp, 7.1 mA, 15 s, 0.15 mm voxel size, varying FOVs (10 x 5.5 cm - DAP 1153 mGy*cm^2; 5 x 5.5 cm - DAP 657 mGy*cm^2) **(Table 1)**. The MAR tool was tested in disabled, low, normal, and high modes **(Table 1 and Figure 2)**. The artefact removal tool in Romexis software (Planmeca Oy) works as follows: the software algorithm recognizes metal areas in the basic frames and corrects them by interpolation, after which a three-dimensional volume is calculated from the corrected basic frames and artefacts are reduced. The low–medium–high selection is the threshold value to recognize the metal areas and the user can set the threshold value for recognition. The threshold values are fixed and determined in the scanner: 8000 for low, 4000 for medium and 3500 for high MAR. The scale is 0–8191 (13 bit). CBCT scans were evaluated by L.A.S., L.M.F. e I.S.Q.B, three previously instructed and trained specialists in CBCT image reading. During training sessions, images of eight teeth which were not included in the present study were analyzed under the same conditions of the full-length study. The examiners classified the presence or absence of root isthmus in the cervical, middle, and apical root thirds of the mesial root, according to a 5-point scale (Bezerra *et al.* 2015, Kamburoğlu *et al.* 2016, Koç *et al.* 2019, Rosado *et al.* 2020), as follows: 1 - definitely absent; 2 - probably absent; 3 - unclear; 4 - probably present; 5 - definitely present. The cases that scored 4 or 5 were further classified according to the type of isthmus either as complete or incomplete.

Reconstructed CBCT images were analyzed under the same observation conditions by using Romexis Viewer Software (Planmeca, Helsinki, Finland) on a 24″ LCD screen (LG Electronics, Seoul, South Korea) with a screen resolution of 1920 x 1200 pixels and 16-bit color depth in a room with dimmed lighting. Tools for image enhancement, zoom, brightness, and contrast were also used, if needed. 3 weeks after the initial evaluations, 20% of the sample was reevaluated (Bezerra *et al.* 2015), as previously described, in order to calculate intra-examiner agreement.

Data analysis

Kappa test was used to assess intra- and inter-examiner agreement. The statistics were interpreted based on the following criteria: < 0.00 = poor agreement; 0.00 - 0.20 = slight agreement; 0.21 - 0.40 = fair agreement; 0.41 - 0.60 = moderate agreement; 0.61 - 0.80 = substantial agreement; 0.81 - 1.00 = almost perfect agreement (Landis & Koch 1977). The association between the type of isthmus and the root third was determined by using the Chi-square test. The responses of the examiners for different acquisition protocols in comparison to the reference standard were analyzed by Mc Nemar test. Receiver Operating Characteristic (ROC) curves were constructed to obtain accuracy, sensitivity, and specificity values for each imaging protocol. In order to compare these values in relation to FOV and MAR tool, two-way ANOVA with Tukey's post hoc test, was used. Data were analyzed in the MedCalc version 11.2.1.0 (MedCalc Software, Oostende, Belgium) and Jamovi version 1.2 (Jamovi Software, Sydney, Australia), considering a 5% significance level.

Results

The Chi-square test showed an association between the root third and the type of isthmus ($P < 0.05$). A high prevalence of isthmus was observed in the cervical third (85.70%, of which 60.70% were complete and 25% were incomplete) and apical third (85.70%, of which 78.60% were complete 7.10% were incomplete). While the middle root third had a lower overall prevalence of isthmus, it showed the highest prevalence of the incomplete type (60.70%, of which 32.10% were complete and 28.60% were incomplete).

Weighted Kappa statistics indicated moderate to substantial intra- and inter-examiner agreement, as described in **Table 2**.

The frequency of correct diagnosis of root isthmus in comparison to reference standard (micro CT) varied significantly for all groups, regardless of the image acquisition protocol (FOV and MAR) ($P < 0.05$) **(Table 3)**. Nevertheless, the use of MAR in “disabled” and “low” modes was significantly related to a higher frequency of correct diagnosis **(Table 3)**.

Accuracy, sensitivity, and specificity values for the gutta-percha, prefabricated metal post, and fiberglass post groups are shown in **Tables 4, 5, and 6**, respectively. The gutta-percha group showed accuracy, sensitivity, and specificity values ranging from 0.612 to 0.719, 0.333 to 0.628, and 0.714 to 1.0, respectively. However, there was no significant difference related to the FOV and the MAR tool.

In the prefabricated metal post group, accuracy values ranged between 0.565 to 0.854; sensitivity values ranged between 0.133 to 0.866, and specificity values ranged between 0.666 to 1.0. Greater accuracy and sensitivity were observed in the "disabled" and "low" modes of the MAR tool ($P < 0.05$), regardless of the FOV.

In the fiberglass post group, the values of accuracy, sensitivity, and specificity ranged from 0.506 to 0.788, 0.111 to 0.777, and 0.388 to 0.944, respectively. Higher accuracy values were observed in the "disabled" and "low" modes of the MAR tool, regardless of the FOV ($P < 0.05$). There was no significant difference in terms of sensitivity and specificity related to the FOV and MAR tool.

Discussion

Knowledge regarding the complexity of the root canal anatomy and its variations is critical for the success of endodontic therapy (Marceliano-Alves *et al.* 2019, Tolentino *et al.* 2020). The first and second molars are considered as teeth which mostly present variations in the root canal morphology (Harris *et al.* 2013, Pécora *et al.* 2013, Estrela *et al.* 2015, Wolf *et al.* 2016, Keleş & Keskin 2018, Marceliano-Alves *et al.* 2018, Tolentino *et al.* 2020). An example of the complexity of canal anatomy is the presence of root isthmus, which is one of the leading causes of endodontic treatment failure (Mannocci *et al.* 2005). Therefore, in the present study, we simulated the real clinical conditions present in endodontically-treated teeth with intraradicular posts, treatment failure, recurrence of symptoms, and the need for endodontic retreatment.

Despite all advances in imaging technologies, metallic artefacts continue to be a limitation for CBCT scanning of the root canal anatomy, commonly resulting in misdiagnosis and overlooking the need for endodontic retreatment, as broadly discussed elsewhere (Bechara *et al.* 2013, Kamburoğlu *et al.* 2013, Bezerra *et al.* 2015, Kamburoğlu *et al.* 2016, Queiroz *et al.* 2017b, Freitas *et al.* 2018, Nikbin *et al.* 2018, Candemil *et al.* 2019, Koç *et al.* 2019, Vasconcelos *et al.* 2019, Costa *et al.* 2020). There is mounting evidence in the literature on image acquisition protocols, artefact behaviour, and how to minimize them, in clinical conditions, such as; root fractures, peri-implantitis, periodontal defects, root perforations, as well as under- and over-instrumentation (Bechara *et al.* 2013, Kamburoğlu *et al.* 2013, Bezerra *et al.* 2015, Koç *et al.* 2019). Nevertheless, to the best of our knowledge, the present study is the first to address such parameters in teeth with a high prevalence of root isthmuses and in need of endodontic retreatment.

The apical third is the most critical area of the root due to the predominance of isthmus and frequently incomplete cleaning by mechanical instruments and irrigation solutions (Mannocci *et al.* 2005, Harris *et* al. 2013, Siqueira-Junior *et al.* 2018). The findings of our study are in line with the existing literature, suggesting that there was an association between the root third and the type of isthmus (Mannocci *et al.* 2005, Harris *et al.* 2013, Pécora *et al.* 2013). We found a predominance for specific classifications according to the root third. For example, complete isthmus was more prevalent in the apical (78.6%) and cervical (60.7%) thirds, respectively, while the middle third had a higher percentage for the absence of isthmus (39.3%).

Despite the continuous and cutting-edge progress in endodontic research, cleaning and disinfecting root canal isthmuses remain as a clinical challenge since it is considered the main reason for symptoms and bacterial persistence (Siqueira-Junior *et al.* 2018, Tolentino *et al.* 2020). Therefore, imaging exams may provide accurate diagnostic information in order to support treatment planning. Micro CT was used in this study as the reference standard modality images since it is the most detailed and accurate non-destructive approach to examine the internal morphology of root canals, generating high-quality images (Ordinola-zapata *et al.* 2017, Marceliano-Alves *et al.* 2018, Siqueira-Junior *et al.* 2018). Since use of micro CT in clinical practice is not feasible due to ultra-high radiation doses, CBCT serves as the preferred imaging method for the analysis of complex root anatomy in the clinical scenario (Sedentexct 2009, AAE 2015, Patel *et al.* 2019a). In addition, CBCT is also a non-destructive, accurate technique that allows for a three-dimensional analysis of anatomical structures and their variations (Baratto-Filho *et al.* 2020), although artefact formation in the presence of high-density materials is a major limitation of CBCT (Patel *et al.* 2019b, Vasconcelos *et al.* 2019).

In our study, the null hypothesis tested was that the MAR tool does not influence the diagnosis of root isthmus in mandibular molars with intraradicular pins in CBCT images obtained with different FOVs, which was accepted. Our findings indicated that the CBCT images differed from those of the reference standard, regardless of the image acquisition protocol used ($P < 0.05$). This finding highlights how challenging it may be to diagnose root isthmuses in the presence of metallic artefacts. Despite this, in the group with prefabricated metallic posts, there was a higher percentage of correct diagnosis when using the protocol with reduced FOV (5 x 5.5 cm) associated with the use of MAR tool in “low” mode. This can be explained by the fact that small FOVs provide higher spatial resolutions (Tolentino *et al.* 2020) and that the effectiveness of the MAR tool in homogenizing of grayscale values and increasing the contrast-to-noise ratio is directly related to the intensity of the artifacts, where the most pronounced ones (usually caused by materials with a high atomic number, such as prefabricated metal poles) make the MAR tool more effective (Queiroz *et al.* 2017a, Freitas *et al.* 2018, Koç *et al.* 2019, Fontenele *et al.* 2020, Gaêta-Araujo *et al.* 2020).

The second-highest percentage of correct diagnosis of root isthmus was also observed in the group of specimens with prefabricated metal posts, despite the use of larger FOV (10 x 5.5 cm) and “disabled” MAR tool. This result suggests that MAR was unnecessary for an extended FOV in the presence of more pronounced metallic artefacts.

While it has been established that the size of the FOV is related to the quality of the image because of the effect of scattered radiation and increased spatial resolution (Brüllmann & Schulze 2015, Kamburoğlu *et al.* 2016), little is known about the performance of MAR algorithms in different sizes of the FOV (Vasconcelos *et al.* 2019). We found that there was no difference between the size of the FOV and MAR tool settings. However, it is important to note that in both groups with posts (whether metallic or fiberglass), the highest percentage of success was found with the smallest 5 x 5.5 cm FOV. These results should be interpreted with caution since the factor “intracanal material” is a variable that can also be directly involved in the outcome (Helvacioglu-Yigit, *et al.* 2016, Codari *et al.* 2017). Furthermore, one must consider the direct relationship between the FOV and the radiation dose emitted to the patient. Of note, the dose area product (DAP) is almost doubled when large FOVs are used, which goes against the recommendations of the American Association of Endodontics (AAE 2015). Taken altogether, our findings indicate that the use of a smaller FOV is preferred to optimize the radiation dose administered and to avoid misdiagnosis during the analysis of tomographic images.

The fiberglass post group showed the lowest percentage of correct diagnosis of root isthmus in comparison to reference standard when a larger FOV (10 x 5.5 cm) and the MAR tool in "normal" mode were applied. This is consistent with the findings mentioned earlier, which suggested that a larger FOV reduced the quality of spatial resolution and that the use of MAR tool was not effective in the presence of a fiberglass post. This can be explained by the low atomic number of the fiberglass and, consequently, its discreet artefact formation characteristics (Helvacioglu-Yigit, *et al.* 2016, Patel *et al.* 2019b, Vasconcelos *et al.* 2019, Gaêta-Araujo *et al.* 2020).

Fontenele *et al.* (2020) showed that the MAR algorithm was effective in reducing artefact formation, especially when artefacts were more noticeable. Thus, it can be said that the effectiveness of the MAR tool is causally associated with the intensity of artefact formation in the presence of high-density materials, which explains why fiberglass posts tend to form less pronounced artefacts (Queiroz *et al.* 2017, Patel *et al.* 2019b, Vasconcelos *et al.* 2019). These findings are in line with those published elsewhere suggesting that there was no significant difference between fiberglass posts and the control group in terms of hypodense halo artefact formation ($P > 0.05$) (Rabelo *et al.* 2017).

In the gutta-percha group, FOV and MAR settings did not significantly change accuracy, sensitivity, and specificity values. These results disagree with those reported by Kajan *et al.* (2018), who analysed the complexity of the root canal anatomy and reported an increase in the number of correct diagnoses in all groups when using the MAR tool in CBCT images, including specimens filled with gutta-percha. However, mentioned authors suggested that the percentage of correct diagnoses was not related to the use of MAR tool (Kajan *et al.* 2018). Likewise, Queiroz *et al.* (2017) evaluated the effectiveness of the MAR tool in different materials and found that its application was unnecessary in the presence of gutta-percha, since the artefacts formed by this material were insufficient to meet the requirements for the optimal performance of the MAR tool.

In prefabricated metal posts, greater accuracy and sensitivity were obtained with the MAR tool “disabled” or set to “low” mode ($P < 0.05$), regardless of selected FOV. Koç *et al.* (2019) evaluated the diagnosis of endodontic conditions, such as instrument fracture, strip perforation, canal underfilling and canal overfilling, by using the MAR tool in different modes and were unable to find any significant difference related to the use of the MAR tool. As the prefabricated metal post has a high atomic number, possibly it generates major artefacts and thereby meets the requirements of the MAR tool, although better outcomes were observed with the MAR tool disabled and/or in “low” mode.

Collectively, our results suggest that "medium" and "high" mode MAR tends to generate grayscale homogenization and alter the noise-to-contrast ratio. Although it reduces metallic artefacts, as reported by Bezerra *et al.* (2015), when dealing with the diagnosis of complex structures, such changes make it difficult to distinguish root canal features (*e.g.*, root isthmuses) from artefacts as well as from the surrounding dentin. Therefore, we do not recommend using the MAR tool in normal and high modes to detect root isthmuses in endodontically-treated teeth with intraradicular posts.

Using the same device, we used in the present study (ProMax 3D), Vasconcelos *et al.* (2019) demonstrated that the MAR tool performed better if it was associated with the largest FOV tested by them (10 x 5 cm). However, although these results indicated a good performance for the MAR tool in the ProMax 3D device operating with a large FOV (10 x 5 cm), our study simulated *ex vivo* conditions that mimicked almost the same real clinical environment.

As previously reported, the performance of the MAR tool may be satisfactory in reducing artifacts, but not necessarily when it comes to improving the diagnosis of conditions and variations of the root anatomy, in the case of detecting the second mesiobuccal canal in first molars (Rosado *et al.* 2020), root fractures (Bechara *et al.* 2013, Bezerra *et al.* 2015, Koç *et al.* 2019), peri-implantitis and periodontal defects (Kamburoğlu *et al.* 2013), root perforations (Koç *et al.* 2019), under- and over-instrumentation (Koç *et al.* 2019) and root isthmus.

Although we used a dry skull with the mandible coated with 2 cm-thick wax to position the teeth and simulate soft tissues, the patient's positioning and movement variables were not evaluated in this study ex vivo, which can directly influence the quality and resolution of the image obtained, it is important to consider that due to these factors, clinically different results can be obtained. Despite their limitations, *ex vivo* CBCT studies are the only methodological approach through which it is possible to obtain repeated images in order to compare different protocols, which is not allowed in patients due to radioprotection concerns (AAE 2015). Moreover, micro CT is a laboratory examination method that cannot be used in routine clinical practice (Harris *et al.* 2013, Ordinola-Zapata *et al.* 2017, Tolentino *et al.* 2018).

Further research is needed to clarify current conflicting evidence and to evaluate other image acquisition protocols associated with the MAR tool for the diagnosis of root isthmus and other conditions of the root canal system. The diagnosis of root isthmus continues to be a challenge and this fact was also confirmed by poor accuracy and sensitivity and high specificity values associated with significant variations of all protocols in comparison to the reference standard.

Conclusion

Within the limitations of the present research, the MAR tool was not effective in reducing metallic artifacts, during the diagnosis of root isthmus, regardless of the FOV used. All tested protocols showed significant differences in comparison to the reference standard. However, the use of the MAR tool in normal and high modes yielded poorer outcomes and therefore should be contraindicated for conditions similar to those of the present study.

Conflict of interest

The authors deny any conflict of interest.

Acknowledgment

The main author is grateful to CAPES Foundation, Brazil.

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Figures

Figure 1: Axial micro-CT sections showing representative cases of missing isthmus (a), incomplete isthmus (b) and complete isthmus (c).

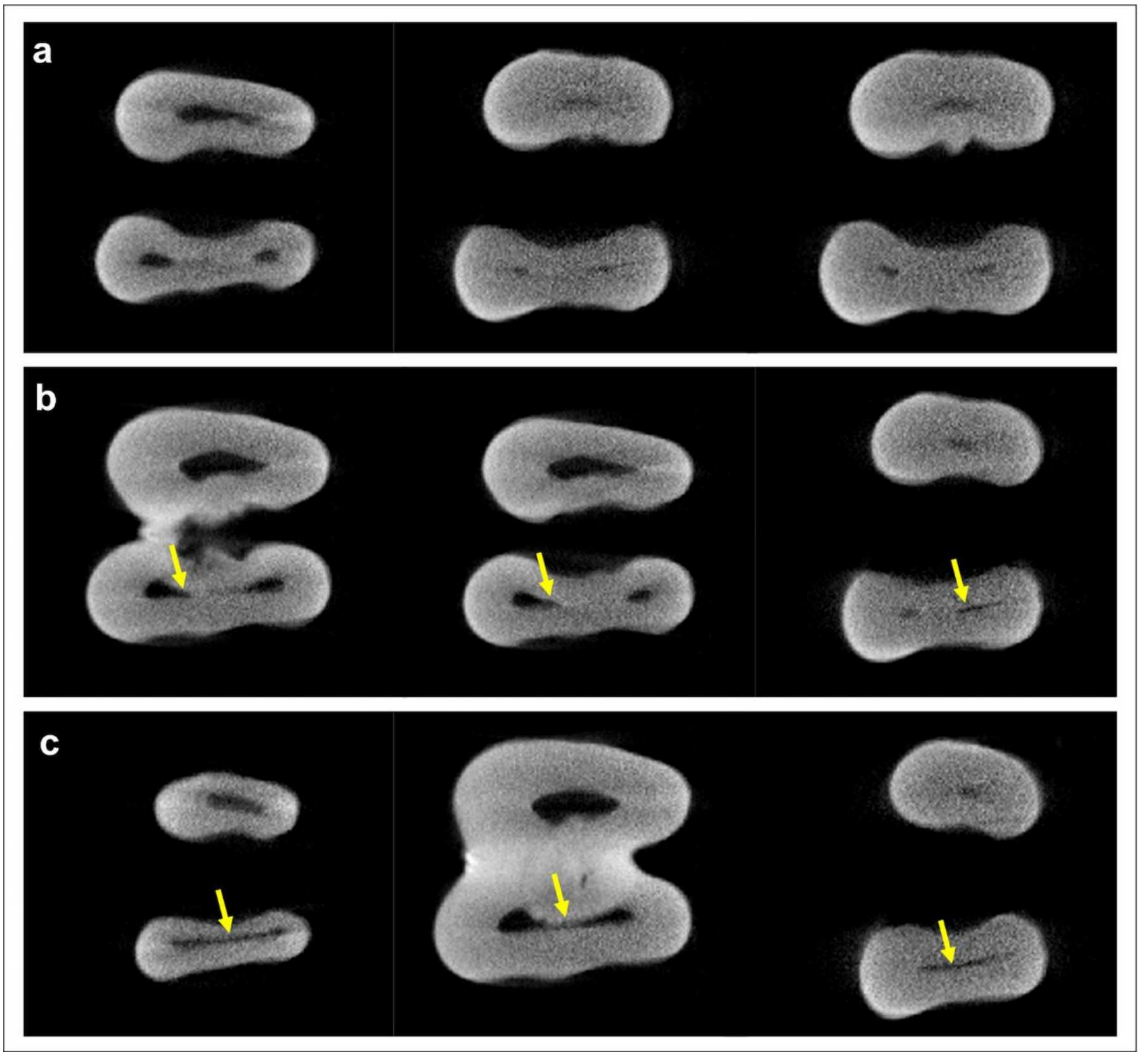
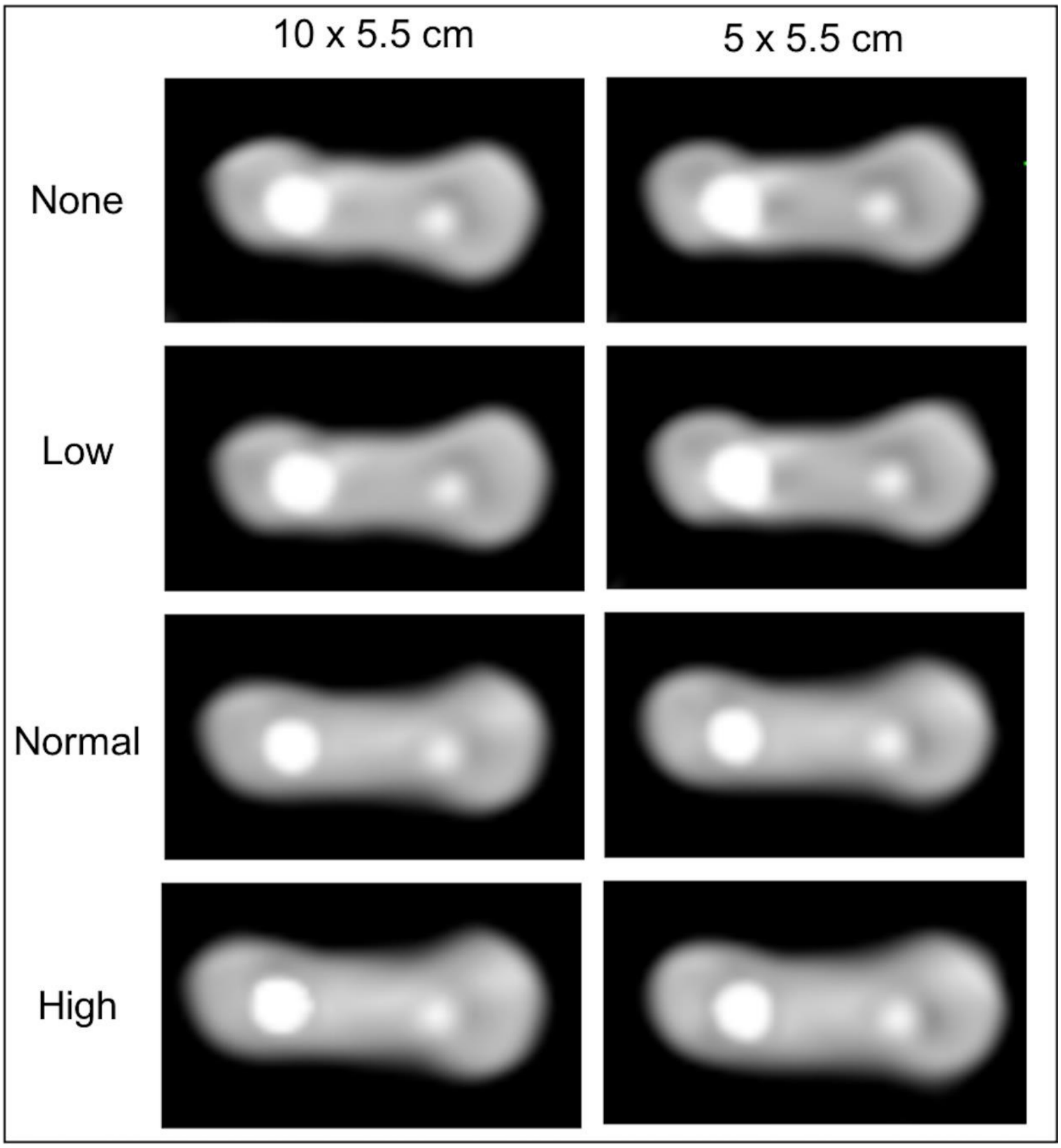


Figure 2: ProMax® 3D Max axial slices of a teeth with prefabricated metal post, with the tested protocols.



Tables

Table 1: ProMax 3D Max protocols tested.

Protocol	KV	mA	t (s)	DAP (mGy*cm^2)	FOV (cm)	VOXEL (cm)	MAR
1	96	7.1	15	1153	10 X 5.5	0.015	disabled
2	96	7.1	15	657	5 x 5.5	0.015	disabled
3	96	7.1	15	1153	10 X 5.5	0.015	low
4	96	7.1	15	657	5 x 5.5	0.015	low
5	96	7.1	15	1153	10 X 5.5	0.015	normal
6	96	7.1	15	657	5 x 5.5	0.015	normal
7	96	7.1	15	1153	10 X 5.5	0.015	high
8	96	7.1	15	657	5 x 5.5	0.015	high

Table 2: Weighted Kappa values for intra and inter-examiner agreement.

	Evaluator 1	Evaluator 2	Evaluator 3
Evaluator 1	0.795	0.489	0.598
Evaluator 2	-	0.732	0.521
Evaluator 3	-	-	0.706

Table 3: Frequency of correct diagnosis of the root isthmus according to the CBCT protocols, for each group, in relation to the reference standard (microTC).

MAR	Gutta-percha				Prefabricated metal post				Fiberglass post			
	FOV (cm)				FOV (cm)				FOV (cm)			
	10 x 5.5		5 x 5.5		10 x 5.5		5 x 5.5		10 x 5.5		5 x 5.5	
	%	P VALUE*	%	P VALUE*	%	P VALUE*	%	P VALUE*	%	P VALUE*	%	P VALUE*
Disabled	42.06	P < 0.0001	44.44	P < 0.0001	71.42	P = 0.0001	69.84	P = 0.0192	57.14	P < 0.0001	63.49	P < 0.0001
Low	50.79	P < 0.0001	44.44	P < 0.0001	69.84	P = 0.0007	73.01	P = 0.0127	57.14	P < 0.0001	57.14	P < 0.0001
Normal	39.68	P < 0.0001	39.68	P < 0.0001	38.09	P < 0.0001	44.44	P < 0.0001	31.74	P < 0.0001	34.92	P < 0.0001
High	39.68	P < 0.0001	38.88	P < 0.0001	42.85	P < 0.0001	34.92	P < 0.0001	34.92	P < 0.0001	33.33	P < 0.0001

* P Value: McNemar Test

Table 4: Values of accuracy, sensitivity and specificity, according to the CBCT protocols, for the gutta-percha group.

MAR	Accuracy FOV (cm)		Sensitivity FOV (cm)		Specificity FOV (cm)	
	10 x 5.5	**5 x 5.5**	**10 x 5.5**	**10 x 5.5**	**5 x 5.5**	**10 x 5.5**
Disabled	0.654 Aa	0.717 Aa	0.485 Aa	0.628 Aa	0.809 Aa	0.714 Aa
Low	0.719 Aa	0.633 Aa	0.590 Aa	0.457 Aa	0.809 Aa	0.809 Aa
Normal	0.656 Aa	0.617 Aa	0.333 Aa	0.333 Aa	0.952 Aa	0.904 Aa
High	0.670 Aa	0.612 Aa	0.333 Aa	0.361 Aa	1.000 Aa	0.904 Aa

Different capital letters indicate a significant difference between the different FOV in the same line ($P < 0.05$, ANOVA two factors, Tukey post hoc test).
Different lowercase letters indicate a significant difference between the MAR tool in the same column ($P < 0.05$, ANOVA two factors, Tukey post hoc test).

Table 5 Values of accuracy, sensitivity and specificity, according to the CBCT protocols, for the prefabricated metal post group.

MAR	Accuracy		Sensitivity		Specificity	
	FOV (cm)		FOV (cm)		FOV (cm)	
	10 x 5.5	5 x 5.5	10 x 5.5	5 x 5.5	10 x 5.5	5 x 5.5
Disabled	0.854 Aa	0.782 Aa	0.777 Aa	0.866 Aa	0.888 Aa	0.666 Aa
Low	0.828 Aa	0.797 Aa	0.755 Aa	0.800 Aa	0.888 Aa	0.777 Aa
Normal	0.565 Ab	0.605 Ab	0.133 Ab	0.222 Ab	1.000 Aa	1.000 Aa
High	0.598 Ab	0.620 Ab	0.200 Ab	0.400 Ab	1.000 Aa	0.833 Aa

Different capital letters indicate a significant difference between the different FOV in the same line ($P < 0.05$, ANOVA two factors, Tukey post hoc test).
Different lowercase letters indicate a significant difference between the MAR tool in the same column ($P < 0.05$, ANOVA two factors, Tukey post hoc test).

Table 6: Values of accuracy, sensitivity and specificity, according to the CBCT protocols, for the fiberglass post group.

	Accuracy		**Sensitivity**		**Specificity**	
MAR	**FOV (cm)**		**FOV (cm)**		**FOV (cm)**	
	10 x 5.5	**5 x 5.5**	**10 x 5.5**	**5 x 5.5**	**10 x 5.5**	**5 x 5.5**
Disabled	0.719 Aa	0.788 Aa	0.533 Aa	0.622 Aa	0.833 Aa	0.888 Aa
Low	0.738 Aa	0.741 Aa	0.422 Aa	0.711 Aa	0.944 Aa	0.722 Aa
Normal	0.524 Ab	0.506 Ab	0.355 Aa	0.133 Aa	0.722 Aa	0.944 Aa
High	0.527 Ab	0.570 Ab	0.111 Aa	0.777 Aa	0.944 Aa	0.388 Aa

Different capital letters indicate a significant difference between the different FOV in the same line ($P < 0.05$, ANOVA two factors, Tukey post hoc test).
Different lowercase letters indicate a significant difference between the MAR tool in the same column ($P < 0.05$, ANOVA two factors, Tukey post hoc test).

3 CONCLUSÃO

A ferramenta RAM não se mostrou eficaz na redução de artefatos metálicos, durante o diagnóstico de istmos radiculares, independentemente do FOV utilizado. No entanto, o uso da ferramenta RAM nos modos “normal” e “alto” apresentou desempenho pior e, portanto, devem ser contraindicados para em situações semelhantes às do presente estudo.

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ANEXOS

ANEXO A – Aprovação do Comitê de Ética em Pesquisa com Seres Humanos

UFJF - UNIVERSIDADE FEDERAL DE JUIZ DE FORA - MG

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Avaliação do istmo radicular em molares inferiores por tomografia computadorizada de feixe cônico

Pesquisador: FRANCIELLE SILVESTRE VERNER

Área Temática:

Versão: 2

CAAE: 18990319.7.0000.5147

Instituição Proponente: UNIVERSIDADE FEDERAL DE JUIZ DE FORA UFJF

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 3.675.856

Apresentação do Projeto:

Apresentação do projeto esta clara, detalhada de forma objetiva, descreve as bases científicas que justificam o estudo, de acordo com as atribuições definidas na Resolução CNS 466/12 de 2012.

Objetivo da Pesquisa:

Objetivo da pesquisa é comparar a influência de diferentes protocolos de aquisição das imagens de TCFC na detecção de istmos radiculares em molares inferiores. Está bem delineado, apresenta clareza e compatibilidade com a proposta, tendo adequação da metodologia aos objetivos pretendido, de acordo com as atribuições definidas na Norma Operacional CNS 001 de 2013, item 3.4.1 - 4.

Avaliação dos Riscos e Benefícios:

Os riscos que o projeto apresenta estão caracterizados e adequadamente descritos, considerando que os indivíduos não sofrerão qualquer dano ou prejuízo pela participação ou pela negação de participação na pesquisa e benefícios esperados. Estão caracterizados como riscos mínimos, e as formas de mitigação também foram apresentadas:" Os riscos envolvidos na pesquisa consistem em risco mínimo, tanto para os voluntários doadores de dentes (que não serão afetados por nenhum procedimento da metodologia desta pesquisa, nem serão identificados a partir dos dentes), quanto para os pesquisadores que executarão as etapas metodológicas. Estes manipularão os

Endereço: JOSE LOURENCO KELMER S/N
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dentes utilizando equipamentos de proteção individual, minimizando os riscos de contaminação"

Comentários e Considerações sobre a Pesquisa:

O projeto está bem estruturado, delineado e fundamentado, sustenta os objetivos do estudo em sua metodologia de forma clara e objetiva, e se apresenta em consonância com os princípios éticos norteadores da ética na pesquisa científica envolvendo seres humanos elencados na resolução 466/12 do CNS e com a Norma Operacional Nº 001/2013 CNS.

Considerações sobre os Termos de apresentação obrigatória:

Foram adequadamente apresentados FOLHA DE ROSTO devidamente preenchida, TERMO DE CONSENTIMENTO LIVRE ESCLARECIDO e DECLARAÇÃO de infraestrutura e de concordância com a realização da pesquisa de acordo com as atribuições definidas na Norma Operacional CNS 001 de 2013 item 3.3 letra h.

Conclusões ou Pendências e Lista de Inadequações:

Diante do exposto, o projeto está aprovado, pois está de acordo com os princípios éticos norteadores da ética em pesquisa estabelecido na Res. 466/12 CNS e com a Norma Operacional Nº 001/2013 CNS. Data prevista para o término da pesquisa:dezembro de 2021.

Considerações Finais a critério do CEP:

Diante do exposto, o Comitê de Ética em Pesquisa CEP/UFJF, de acordo com as atribuições definidas na Res. CNS 466/12 e com a Norma Operacional Nº001/2013 CNS, manifesta-se pela APROVAÇÃO do protocolo de pesquisa proposto. Vale lembrar ao pesquisador responsável pelo projeto, o compromisso de envio ao CEP de relatórios parciais e/ou total de sua pesquisa informando o andamento da mesma, comunicando também eventos adversos e eventuais modificações no protocolo.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1408767.pdf	09/10/2019 13:57:22		Aceito
Projeto Detalhado / Brochura Investigador	projetodetalhadoalt.pdf	09/10/2019 13:57:06	FRANCIELLE SILVESTRE VERNER	Aceito
Folha de Rosto	_folha_de_rosto_.pdf	09/08/2019 12:27:18	FRANCIELLE SILVESTRE	Aceito

TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE_Biorrepositorio.pdf	05/08/2019 16:44:40	FRANCIELLE SILVESTRE VERNER	Aceito
Declaração de Manuseio Material Biológico / Biorepositório / Biobanco	declaracao_biorrepositorio.pdf	05/08/2019 16:43:40	FRANCIELLE SILVESTRE VERNER	Aceito
Declaração de Instituição e Infraestrutura	declaracao_infraestrutura.pdf	05/08/2019 16:43:16	FRANCIELLE SILVESTRE VERNER	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

JUIZ DE FORA, 01 de Novembro de 2019

Assinado por:
Jubel Barreto
(Coordenador(a))

ANEXO B – Instruções aos autores preconizadas pelo periódico *International Endodontic Journal*

INTERNATIONAL ENDODONTIC JOURNAL
The official journal of the British Endodontic Society and the European Society of Endodontology

Author Guidelines

Content of Author Guidelines:

Useful Websites: Submission Site, Articles published in *International Endodontic Journal*, Author Services, Wiley's Ethical Guidelines, Guidelines for Figures

The journal to which you are submitting your manuscript employs a plagiarism detection system. By submitting your manuscript to this journal you accept that your manuscript may be screened for plagiarism against previously published works.

1. GENERAL

International Endodontic Journal publishes original scientific articles, reviews, clinical articles and case reports in the field of Endodontology; the branch of dental sciences dealing with health, injuries to and diseases of the pulp and periradicular region, and their relationship with systemic well-being and health. Original scientific articles are published in the areas of biomedical science, applied materials science, bioengineering, epidemiology and social science relevant to endodontic disease and its management, and to the restoration of root-treated teeth. In addition, review articles, reports of clinical cases, book reviews, summaries and abstracts of scientific meetings and news items are accepted.

Preprints and Data Sharing

International Endodontic Journal will consider for review articles previously available as preprints. Authors may also post the submitted version of a manuscript to a preprint server at any time. Authors are requested to update any pre-publication versions with a link to the final published article.

International Endodontic Journal encourages authors to share the data and other artefacts supporting the results in the paper by archiving it in an appropriate public repository. Authors should include a data accessibility statement, including a link to the repository they have used, in order that this statement can be published alongside their paper. All accepted manuscripts may elect to publish a data availability statement to confirm the presence or absence of shared data. If you have shared data, this statement will describe how the data can be accessed, and include a persistent identifier (e.g., a DOI for the data, or an accession number) from the repository where you shared the data. Sample statements are available here. If published, statements will be placed in the heading of your manuscript.

Please read the instructions below carefully for details on the submission of manuscripts, the journal's requirements and standards as well as information concerning the procedure after a manuscript has been accepted for publication in *International Endodontic Journal*. Authors are encouraged to visit Wiley Author Services for further information on the preparation and submission of articles and figures.

2. ETHICAL GUIDELINES

International Endodontic Journal adheres to the below ethical guidelines for publication and research.

2.1 Authorship and Acknowledgements

The policy of the journal is that only ONE corresponding author is accepted.

Authors submitting a paper do so on the understanding that the manuscript has been read and approved by all authors and that all authors agree to the submission of the manuscript to the Journal.

International Endodontic Journal adheres to the definition of authorship set up by The International Committee of Medical Journal Editors (ICMJE). According to the ICMJE, authorship criteria should be based on 1) substantial contributions to conception and design of, or acquisiation of data or analysis and interpretation of data, 2) drafting the article or revising it critically for important intellectual content and 3) final approval of the version to be published. Authors should meet conditions 1, 2 and 3.

Acknowledgements: Under acknowledgements please specify contributors to the article other than the authors accredited. Please also include specifications of the source of funding for the study and any potential conflict of interests if appropriate. Please find more information on the conflict of interest form in section 2.6.

2.2 Ethical Approvals

Experimentation involving human subjects will only be published if such research has been conducted in full accordance with ethical principles, including the World Medical Association Declaration of Helsinki (version 2008) and the additional requirements, if any, of the country where the research has been carried out. Manuscripts must be accompanied by a statement that the experiments were undertaken with the understanding and written consent of each subject and according to the above mentioned principles. A statement regarding the fact that the study has been independently reviewed and approved by an ethical board should also be included. Editors reserve the right to reject papers if there are doubts as to whether appropriate procedures have been used.

When experimental animals are used the methods section must clearly indicate that adequate measures were taken to minimize pain or discomfort. Experiments should be carried out in accordance with the Guidelines laid down by the National Institute of Health (NIH) in the USA regarding the care and use of animals for experimental procedures or with the European Communities Council Directive of 24 November 1986 (86/609/EEC) and in accordance with local laws and regulations.

All studies using human or animal subjects should include an explicit statement in the Material and Methods section identifying the review and ethics committee approval for each study. The authors MUST upload a copy of the ethical approval letter when submitting their manuscript and a separate English translation. Editors reserve the right to reject papers if there is doubt as to whether appropriate procedures have been used.

2.3 Clinical Trials

The International Endodontic Journal asks that authors submitting manuscripts reporting from a clinical trial to register the trial *a priori* in any of the following public clinical trials registries: www.clinicaltrials.gov, https://www.clinicaltrialsregister.eu/, http://isrctn.org/. Other primary registries if named in the WHO network will also be considered acceptable. The clinical trial registration number and name of the trial register should be included in the Acknowledgements at the submission stage.

2.3.1 Randomised control clinical trials

Randomised clinical trials should be reported using the Preferred Reporting Items for RAndomized Trials in Endodontics (PRIRATE) 2020 guidelines. A PRIRATE checklist and flowchart (as a Figure) should also be completed and included in the submission material. The PRIRATE 2020 checklist and flowchart can be downloaded from: http://pride-endodonticguidelines.org/prirate/

It is recommended that authors consult the following papers, which explains the rationale for the PRIRATE 2020 guidelines and their importance when writing manuscripts:

Nagendrababu V, Duncan HF, Bjørndal L, Kvist T, Priya E, Jayaraman J, Pulikkotil SJ, Pigg M, Rechenberg DK, Vaeth M, Dummer P. PRIRATE 2020 guidelines for reporting randomized trials in Endodontics: a consensus-based development. Int Endod J. 2020 Mar 20. doi: 10.1111/iej.13294. (https://onlinelibrary.wiley.com/doi/abs/10.1111/iej.13294)

Nagendrababu V, Duncan HF, Bjørndal L, Kvist T, Priya E, Jayaraman J, Pulikkotil SJ, Dummer P. PRIRATE 2020 guidelines for reporting randomized trials in Endodontics: Explanation and elaboration. Int Endod J. 2020 April 8. doi: 10.1111/iej.13304 (https://onlinelibrary.wiley.com/doi/abs/10.1111/iej.13304)

2.3.2 Epidemiological observational trials

Submitting authors of epidemiological human observations studies are required to review and submit a 'strengthening the reporting of observational studies in Epidemiology' (STROBE) checklist and statement. Compliance with this should be detailed in the materials and methods section. (www.strobe-statement.org)

2.4 Systematic Reviews

The abstract and main body of the systematic review should be reported using the PRISMA for Abstract and PRISMA guidelines respectively (http://www.prisma-statement.org/). Authors submitting a systematic review should register the protocol in a readily-accessible source at the time of project inception (e.g. PROSPERO database, previously published review protocol in journal). The protocol registration number, name of the database or journal reference should be provided at the submission stage in the "Registration" section in the abstract and 'Methods' section in the main body of the text. A PRISMA checklist and flow diagram (as a Figure) should also be included in the submission material. Source of funding (grant number, if available) should be added in 'Acknowledgements' section.

It is recommended that authors consult the following papers, which help in the production of high quality reviews:

1. Nagendrababu V, Duncan HF, Tsesis I, Sathorn C, Pulikkotil SJ, Dharmarajan L, Dummer PMH. PRISMA for abstracts: best practice for reporting abstracts of systematic reviews in Endodontology. Int Endod J. 2019 Mar 19:1096-07. doi: 10.1111/iej.13118.
2. Nagendrababu V, Dilokthornsakul P, Jinatongthai P, Veettil SK, Pulikkotil SJ, Duncan HF, Dummer PMH. Glossary for systematic reviews and meta-analyses. Int Endod J. 2020 Feb;53(2):232-249. doi: 10.1111/iej.13217. Epub 2019 Nov 25.

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Papers reporting protein or DNA sequences and crystallographic structure determinations will not be accepted without a Genbank or Brookhaven accession number, respectively. Other supporting data sets must be made available on the publication date from the authors directly.

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• You are required to upload your files.

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3.4. Blinded Review

Manuscript that do not conform to the general aims and scope of the journal will be returned immediately without review. All other manuscripts will be reviewed by experts in the field (generally two referees). International Endodontic Journal aims to forward referees' comments and to inform the corresponding author of the result of the review process. Manuscripts will be considered for fast-track publication under special circumstances after consultation with the Editor.
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All documents uploaded under the file designation 'title page' will not be viewable in the html and pdf format you are asked to review in the end of the submission process. The files viewable in the html and pdf format are the files available to the reviewer in the review process.

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You may suspend a submission at any phase before clicking the 'Submit' button and save it to submit later. The manuscript can then be located under 'Unsubmitted Manuscripts' and you can click on 'Continue Submission' to continue your submission when you choose to.

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Review Articles (systematic and narrative): are accepted for their broad general interest; all are refereed by experts in the field who are asked to comment on issues such as timeliness, general interest and balanced treatment of controversies, as well as on scientific accuracy. Reviews should generally include a clearly defined search strategy and take a broad view of the field rather than merely summarizing the literature. Extensive or unbalanced citation of the authors' own publications is discouraged.

Clinical Techniques: are suited to describe significant improvements in clinical practice such as the report of a novel technique, a breakthrough in technology or practical approaches to recognised clinical challenges. They should conform to the highest scientific and clinical practice standards.

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5. MANUSCRIPT FORMAT AND STRUCTURE

5.1. Format

Language: The language of publication is English. It is preferred that manuscript is professionally edited.

Presentation: Authors should pay special attention to the presentation of their research findings or clinical reports so that they may be communicated clearly. Technical jargon should be avoided as much as possible and clearly explained where its use is unavoidable. Abbreviations should also be kept to a minimum, particularly those that are not standard. The background and hypotheses underlying the study, as well as its main conclusions, should be clearly explained. Titles and abstracts especially should be written in language that will be readily intelligible to any scientist.

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Abbreviations: International Endodontic Journal adheres to the conventions outlined in Units, Symbols and Abbreviations: A Guide for Medical and Scientific Editors and Authors. When non-standard terms appearing 3 or more times in the manuscript are to be abbreviated, they should be written out completely in the text when first used with the abbreviation in parenthesis.

5.2. Structure

All manuscripts submitted to *International Endodontic Journal* should include Title Page, Abstract, Main Text, References and Acknowledgements, Tables, Figures and Figure Legends as appropriate

Title Page: The title page should bear: (i) Title, which should be concise as well as descriptive; (ii) Initial(s) and last (family) name of each author; (iii) Name and address of department, hospital or institution to which work should be attributed; (iv) Running title (no more than 30 letters and spaces); (v) No more than six keywords (in alphabetical order); (vi) Name, full postal address, telephone, fax number and e-mail address of author responsible for correspondence.

Abstract for Original Scientific Articles should be no more than 350 words giving details of what was done using the following structure:

• **Aim**: Give a clear statement of the main aim of the study and the main hypothesis tested, if any.
• **Methodology**: Describe the methods adopted including, as appropriate, the design of the study, the setting, entry requirements for subjects, use of materials, outcome measures and statistical tests.
• **Results**: Give the main results of the study, including the outcome of any statistical analysis.
• **Conclusions**: State the primary conclusions of the study and their implications. Suggest areas for further research, if appropriate.

Abstract for Systematic Review Articles should be no more than 350 words using the following structure where applicable:

• **Title**: Identify the report as a systematic review, meta-analysis, or both.
• **Background:** Provide a brief introduction of the subject and why it is important.
• **Objectives:** The research question including components such as participants, interventions, comparators, and outcomes. Use PICO format.
• **Methods:** Briefly describe i) the inclusion criteria, ii) provide databases searched and dates, iii) mention the method used to assess study quality (risk of bias) iv) meta-analysis methodology (if appropriate).
• **Results:** i) Number and type of included studies and participants ii) results for main outcomes (benefits and harms). If a meta-analysis was undertaken, include summary measures and confidence intervals. iii) direction of the effect in terms that are meaningful to clinicians and patients.
• **Discussion:** i) Strengths and ii) limitations of evidence.
• **Conclusions**: General interpretation of the results and important implications.

• **Funding:** Primary source of funding for the review (if no funding: say 'none').
• **Registration**: Registration number and name.

Abstract for Review Articles (narrative)
The Abstract should be unstructured and no more than 350 words.

Abstract for Clinical Techniques and Case Reports should be no more than 350 words using the following structure:

• **Aim**: Give a clear statement of the main aim of the report and the clinical problem which is addressed.
• **Summary**: Describe briefly the clinical technique(s) or the case report(s).
• **Key learning points**: Provide up to 5 short, bullet-pointed statements to highlight the key messages of the report. All points must be fully justified by material presented in the report.

Main Text of Original Scientific Article should include Introduction, Materials and Methods, Results, Discussion and Conclusion:

• **Introduction**: should be focused, outlining the historical or logical origins of the study and gaps in knowledge. Exhaustive literature reviews are not appropriate. It should close with the explicit statement of the specific aims of the investigation, or hypothesis to be tested.
• **Material and Methods**: must contain sufficient detail such that, in combination with the references cited, all clinical trials and experiments reported can be fully reproduced.

(i) Clinical Trials should be reported using the PRIRATE 2020 guidelines. A PRIRATE 2020 checklist must be completed and included along with a flow diagram (as a Figure) in the submission material. These are available at http://pride-endodonticguidelines.org/prirate/.

(ii) Experimental Subjects: experimentation involving human subjects will only be published if such research has been conducted in full accordance with ethical principles, including the World Medical Association Declaration of Helsinki (version 2008) and the additional requirements, if any, of the country where the research has been carried out. Manuscripts must be accompanied by a statement that the experiments were undertaken with the understanding and written consent of each subject and according to the above mentioned principles. A statement regarding the fact that the study has been independently reviewed and approved by an ethical board should also be included. Editors reserve the right to reject papers if there are doubts as to whether appropriate procedures have been used.

When experimental animals are used the methods section must clearly indicate that adequate measures were taken to minimize pain or discomfort. Experiments should be carried out in accordance with the Guidelines laid down by the National Institute of Health (NIH) in the USA regarding the care and use of animals for experimental procedures or with the European Communities Council Directive of 24 November 1986 (86/609/EEC) and in accordance with local laws and regulations.

All studies using human or animal subjects should include an explicit statement in the Material and Methods section identifying the review and ethics committee approval for each study, if applicable. Editors reserve the right to reject papers if there is doubt as to whether appropriate procedures have been used.

(iii) Suppliers: Suppliers of materials should be named and their location (Company, town/city, state, country) included.

• **Results**: should present the observations with minimal reference to earlier literature or to possible interpretations. Data should not be duplicated in Tables and Figures.
• **Discussion**: may usefully start with a brief summary of the major findings, but repetition of parts of the abstract or of the results section should be avoided. The Discussion section should progress with a review of the methodology before discussing the results in light of previous work in the field. The Discussion

should end with a brief conclusion and a comment on the potential clinical relevance of the findings. Statements and interpretation of the data should be appropriately supported by original references.
• **Conclusion**: should contain a summary of the findings.

Main Text of Systematic Review Articles should be divided into Introduction, Methods, Results and Conclusions:

• **Introduction:** Should be focused to place the subject matter in context and to justify the need for the review.
• **Method:** Divide into logical sub-sections in order to improve readability and enhance understanding (e.g. details of protocol registration, literature search process, inclusion/exclusion criteria, data extraction, quality assessment, outcome(s) of interest, data synthesis and statistical analysis, quality of evidence).
• **Results:** Present in structured fashion (e.g. results of the search process, characteristics of the included studies, results of primary meta-analysis, additional analysis, publication bias, quality of evidence).
• **Discussion:** Should summarize the results, highlighting completeness and applicability of evidence, quality of evidence, agreements and disagreements with other studies or reviews, strength and limitations, implications for practice and research.
• **Conclusion(s):** Section should reach clear conclusions and/or recommendations on the basis of the evidence presented.

Main Text of Review Articles should be divided into Introduction, Review and Conclusions. The Introduction section should be focused to place the subject matter in context and to justify the need for the review. The Review section should be divided into logical sub-sections in order to improve readability and enhance understanding. Search strategies must be described and the use of state-of-the-art evidence-based systematic approaches is expected. The use of tabulated and illustrative material is encouraged. The Conclusion section should reach clear conclusions and/or recommendations on the basis of the evidence presented.

Main Text of Clinical Techniques and Case Reports should be divided into Introduction, Report, Discussion and Conclusion,. They should be well illustrated with clinical images, radiographs, diagrams and, where appropriate, supporting tables and graphs. However, all illustrations must be of the highest quality.

Case reports should be written using the Preferred Reporting Items for Case reports in Endodontics (PRICE) 2020 guidelines. A PRICE checklist and flowchart (as a Figure) should also be completed and included in the submission material. The PRICE 2020 checklist and flowchart can be downloaded from: http://pride-endodonticguidelines.org/price/.

It is recommended that authors consult the following papers, which explains the rationale for the PRICE 2020 guidelines and their importance when writing manuscripts:

Nagendrababu V, Chong BS, McCabe P, Shah PK, Priya E, Jayaraman J, Pulikkotil SJ, Setzer FC, Sunde PT, Dummer PMH. PRICE 2020 guidelines for reporting case reports in Endodontics: a consensus-based development. Int Endod J. 2020 Feb 23. doi: 10.1111/iej.13285. (https://www.ncbi.nlm.nih.gov/pubmed/32090342)

Nagendrababu V, Chong BS, McCabe P, Shah PK, Priya E, Jayaraman J, Pulikkotil SJ, Dummer PMH. PRICE 2020 guidelines for reporting case reports in Endodontics: Explanation and elaboration. Int Endod J. (https://onlinelibrary.wiley.com/doi/abs/10.1111/iej.13300)

Acknowledgements: *International Endodontic Journal* requires that all sources of institutional, private and corporate financial support for the work within the manuscript must be fully acknowledged, and any potential conflicts of interest noted. Grant or contribution numbers may be acknowledged, and principal grant holders should be listed. Acknowledgments should be brief and should not include thanks to anonymous referees and editors. See also above under Ethical Guidelines.

5.3. References
It is the policy of the Journal to encourage reference to the original papers rather than to literature reviews. Authors should therefore keep citations of reviews to the absolute minimum.

We recommend the use of a tool such as EndNote or Reference Manager for reference management and formatting. The EndNote reference style can be obtained upon request to the editorial office (iejeditor@cardiff.ac.uk). Reference Manager reference styles can be searched for here: www.refman.com/support/rmstyles.asp

In the text: single or double authors should be acknowledged together with the year of publication, e.g. (Pitt Ford & Roberts 1990). If more than two authors the first author followed by *et al.* is sufficient, e.g. (Tobias *et al.* 1991). If more than 1 paper is cited the references should be in year order and separated by "," e.g. (Pitt Ford & Roberts 1990, Tobias *et al.* 1991).

Reference list: All references should be brought together at the end of the paper in alphabetical order and should be in the following form.

(i) Names and initials of up to six authors. When there are seven or more, list the first three and add *et al.*
(ii)Year of publication in parentheses
(iii) Full title of paper followed by a full stop (.)
(iv) Title of journal in full (in italics)
(v) Volume number (bold) followed by a comma (,)
(vi) First and last pages

Examples of correct forms of reference follow:

Standard journal article
Bergenholtz G, Nagaoka S, Jontell M (1991) Class II antigen-expressing cells in experimentally induced pulpitis. *International Endodontic Journal* **24**, 8-14.

Corporate author
British Endodontic Society (1983) Guidelines for root canal treatment. *International Endodontic Journal* **16**, 192-5.

Journal supplement
Frumin AM, Nussbaum J, Esposito M (1979) Functional asplenia: demonstration of splenic activity by bone marrow scan (Abstract). *Blood* **54** (Suppl. 1), 26a.

Books and other monographs

Personal author(s)
Gutmann J, Harrison JW (1991) *Surgical Endodontics*, 1st edn Boston, MA, USA: Blackwell Scientific Publications.

Chapter in a book
Wesselink P (1990) Conventional root-canal therapy III: root filling. In: Harty FJ, ed. *Endodontics in Clinical Practice*, 3rd edn; pp. 186-223. London, UK: Butterworth.

Published proceedings paper
DuPont B (1974) Bone marrow transplantation in severe combined immunodeficiency with an unrelated MLC compatible donor. In: White HJ, Smith R, eds. Proceedings of the Third Annual Meeting of the International Society for Experimental Rematology; pp. 44-46. Houston, TX, USA: International Society for Experimental Hematology.

Agency publication
Ranofsky AL (1978) Surgical Operations in Short-Stay Hospitals: United States-1975. DHEW publication no. (PHS) 78-1785 (Vital and Health Statistics; Series 13; no. 34.) Hyattsville, MD, USA: National Centre for Health Statistics.8

Dissertation or thesis
Saunders EM (1988) In vitro and in vivo investigations into root-canal obturation using thermally softened

gutta-percha techniques (PhD Thesis). Dundee, UK: University of Dundee.

URLs
Full reference details must be given along with the URL, i.e. authorship, year, title of document/report and URL. If this information is not available, the reference should be removed and only the web address cited in the text.
Smith A (1999) Select committee report into social care in the community [WWW document]. URL http://www.dhss.gov.uk/reports/report015285.html
[accessed on 7 November 2003]

5.4. Tables, Figures and Figure Legends

Tables: Tables should be double-spaced with no vertical rulings, with a single bold ruling beneath the column titles. Units of measurements must be included in the column title.

Figures: All figures should be planned to fit within either 1 column width (8.0 cm), 1.5 column widths (13.0 cm) or 2 column widths (17.0 cm), and must be suitable for photocopy reproduction from the printed version of the manuscript. Lettering on figures should be in a clear, sans serif typeface (e.g. Helvetica); if possible, the same typeface should be used for all figures in a paper. After reduction for publication, upper-case text and numbers should be at least 1.5-2.0 mm high (10 point Helvetica). After reduction, symbols should be at least 2.0-3.0 mm high (10 point). All half-tone photographs should be submitted at final reproduction size. In general, multi-part figures should be arranged as they would appear in the final version. Reduction to the scale that will be used on the page is not necessary, but any special requirements (such as the separation distance of stereo pairs) should be clearly specified.

Unnecessary figures and parts (panels) of figures should be avoided: data presented in small tables or histograms, for instance, can generally be stated briefly in the text instead. Figures should not contain more than one panel unless the parts are logically connected; each panel of a multipart figure should be sized so that the whole figure can be reduced by the same amount and reproduced on the printed page at the smallest size at which essential details are visible.

Figures should be on a white background, and should avoid excessive boxing, unnecessary colour, shading and/or decorative effects (e.g. 3-dimensional skyscraper histograms) and highly pixelated computer drawings. The vertical axis of histograms should not be truncated to exaggerate small differences. The line spacing should be wide enough to remain clear on reduction to the minimum acceptable printed size.

Figures divided into parts should be labelled with a lower-case, boldface, roman letter, a, b, and so on, in the same typesize as used elsewhere in the figure. Lettering in figures should be in lower-case type, with the first letter capitalized. Units should have a single space between the number and the unit, and follow SI nomenclature or the nomenclature common to a particular field. Thousands should be separated by a thin space (1 000). Unusual units or abbreviations should be spelled out in full or defined in the legend. Scale bars should be used rather than magnification factors, with the length of the bar defined in the legend rather than on the bar itself. In general, visual cues (on the figures themselves) are preferred to verbal explanations in the legend (e.g. broken line, open red triangles etc.)

Figure legends: Figure legends should begin with a brief title for the whole figure and continue with a short description of each panel and the symbols used; they should not contain any details of methods.

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Further information can be obtained at Wiley Blackwell's guidelines for figures: http:/authorservices.wiley.com/bauthor/illustration.asp.

Check your electronic artwork before submitting it: http://authorservices.wiley.com/bauthor/eachecklist.asp

5.6. Guidelines for reporting of DNA microarray data
The *International Endodontic Journal* gives authors notice that, with effect from 1st January 2011, submission to the *International Endodontic Journal* requires the reporting of microarray data to conform to the MIAME guidelines. After this date, submissions will be assessed according to MIAME standards. The complete current guidelines are available at http://www.mged.org/Workgroups/MIAME/miame_2.0.html. Also, manuscripts will be published only after the complete data has been submitted into the public repositories, such as GEO (http://www.ncbi.nlm.nih.gov/geo/) or ArrayExpress (http://www.ebi.ac.uk/microarray/submissions_overview.html), in MIAME compliant format, with the data accession number (the identification number of the data set in the database) quoted in the manuscript. Both databases are committed to keeping the data private until the associated manuscript is published, if requested.

Prospective authors are also encouraged to search for previously published microarray data with relevance to their own data, and to report whether such data exists. Furthermore, they are encouraged to use the previously published data for qualitative and/or quantitative comparison with their own data, whenever suitable. To fully acknowledge the original work, an appropriate reference should be given not only to the database in question, but also to the original article in which the data was first published. This open approach will increase the availability and use of these large-scale data sets and improve the reporting and interpretation of the findings, and in increasing the comprehensive understanding of the physiology and pathology of endodontically related tissues and diseases, result eventually in better patient care.

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Publication in electronic formats has created opportunities for adding details or whole sections in the electronic version only. Authors need to work closely with the editors in developing or using such new publication formats.

Supporting information, such as data sets or additional figures or tables, that will not be published in the print edition of the journal, but which will be viewable via the online edition, can be submitted. It should be clearly stated at the time of submission that the supporting information is intended to be made available through the online edition. If the size or format of the supporting information is such that it cannot be accommodated on the journal's website, the author agrees to make the supporting information available free of charge on a permanent Web site, to which links will be set up from the journal's website. The author must advise Wiley Blackwell if the URL of the website where the supporting information is located changes. The content of the supporting information must not be altered after the paper has been accepted for publication.

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6. GRAPHICAL ABSTRACT

Authors are invited to submit a graphical abstract along with their manuscript to be published in the International Endodontic Journal's:

- Online table of contents.
- Content alert emails.
- Within the article.

The graphical abstract should visually convey the key findings of the report and present a clear message to the reader. It should be used as a means of attracting the readers' attention and promoting further engagement with the article.

To create an effective graphical abstract, authors should focus on presenting to the reader what they can learn from the report, communicating only the key message.

Guidelines for designing a Graphical Abstract:

1. Creating a graphical abstract does ***not*** mean just copying and pasting a figure from the manuscript.
2. Use text sparingly, so the graphical abstract does not become cluttered, but ensure that you have clearly stated the purpose of the report, research design, clinical case and the outcome of the study or case. Use language consistent with terms and definitions in the article that are free of editorialization (personal opinion) or bias.
3. Use only images that you have a legal right to use. Authors are responsible for obtaining permission to use any images that they include from outside sources, including articles, web pages, stock photo sites or Google image searches. Any needed permissions must be submitted along with your graphical abstract or identified in the Acknowledgements section of your manuscript.
4. Exclude imagery that can be viewed as advertisement, such as trade names, logos, or images of trademarked items.
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6. Required file properties:
    - Resolution: 700 pixels (width) x 600 pixels (height).

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Please contact the editorial office at IEJeditor@cardiff.ac.uk if you have any questions.

7. AFTER ACCEPTANCE

Upon acceptance of a paper for publication, the manuscript will be forwarded to the Production Editor who is responsible for the production of the journal.

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Hard copies of all figures and tables are required when the manuscript is ready for publication. These will be requested by the Editor when required. Each Figure copy should be marked on the reverse with the figure number and the corresponding author's name.

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