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Alessiana Helena Machado

INFLUÊNCIA DA REGIÃO ANATÔMICA NA FORMAÇÃO DE ARTEFATOS METÁLICOS PRODUZIDOS POR IMPLANTES DENTÁRIOS EM IMAGENS DE TOMOGRAFIA COMPUTADORIZADA DE FEIXE CÔNICO

Juiz de Fora
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Exame de Defesa apresentado ao Programa de Pós-Graduação em Clínica Odontológica, da Faculdade de Odontologia da Universidade Federal de Juiz de Fora, como requisito para obtenção do título de Mestre. Área de concentração em Clínica Odontológica.

Orientadora: Profa. Dra. Karina Lopes Devito

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Aprovada em:___/___/___

Banca examinadora

Profa. Dra. Karina Lopes Devito
Universidade Federal de Juiz de Fora

Profa. Dra. Francielle Silvestre Verner
Universidade Federal de Juiz de Fora

Profa. Dra. Andréa de Castro Domingos Vieira
Universidade Federal do Rio de Janeiro

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Eduardo Galeano

MACHADO, A. H. **Influência da região anatômica na formação de artefatos metálicos produzidos por implantes dentários em imagens de tomografia computadorizada de feixe cônico**. Juiz de Fora (MG), 2017. 59 f. Apresentação da Dissertação (Mestrado em Clínica Odontológica) - Faculdade de Odontologia, Universidade Federal de Juiz de Fora (MG).

RESUMO

O objetivo no presente estudo foi comparar, quantitativamente, os artefatos metálicos produzidos em imagens de tomografia computadorizada de feixe cônico (TCFC) por implantes instalados em diferentes regiões maxilomandibulares. Para isso, um total de 200 implantes, selecionados de exames de TCFC, foi dividido em quatro grupos: Grupo 1 (n = 50) - implantes localizados na região anterior da maxila; Grupo 2 (n = 50) - implantes localizados na região posterior da maxila; Grupo 3 (n = 50) - implantes localizados na região anterior da mandíbula e Grupo 4 (n = 50) - implantes localizados na região posterior da mandíbula. Os implantes ainda foram classificados em isolados ou adjacentes a outros implantes. Foram selecionados três cortes axiais de cada implante incluído na amostra (apical, médio e cervical). Nesses cortes foram mensurados os artefatos produzidos pelos implantes. Para comparar as variáveis com dois grupos foi aplicado o teste U de Mann-Whitney. Para a comparação entre os cortes axiais foram aplicados os testes de Kruskal-Wallis e Student-Newman-Keuls. A mandíbula apresentou uma quantidade de artefatos maior que a maxila (corte apical: $p = 0,0024$; corte médio: $p < 0,0001$). A região anterior produziu mais artefatos que a região posterior (corte apical: $p = 0,0105$; corte médio: $p < 0,0316$). Não houve diferença significativa na quantidade de artefatos entre implantes isolados e adjacentes e o corte cervical foi o mais acometido por artefatos. Pode-se concluir que os implantes dentários sempre produzem artefatos metálicos em imagens de TCFC, sendo esses artefatos influenciados pela localização anatômica na arcada dentária.

PALAVRAS-CHAVES: tomografia computadorizada de feixe cônico, implante dentário, artefato metálico.

MACHADO, A. H. ***Effect of anatomical region on the formation of metal artifacts produced by dental implants in cone beam computed tomographic images***. Juiz de Fora (MG), 2017. 59 f. Apresentação da Dissertação (Mestrado em Clínica Odontológica) – Faculdade de Odontologia, Universidade Federal de Juiz de Fora (MG).

ABSTRACT

The objective of the present study was to compare, quantitatively, the metal artifacts produced in cone beam computed tomography (CBCT) images by dental implants installed in different maxillomandibular regions. A total of 200 implants selected from CBCT examinations were divided into four groups: Group 1 (n = 50) - implants located in the anterior maxilla; Group 2 (n = 50) - implants located in the posterior maxilla; Group 3 (n = 50) - implants located in the anterior mandible; and Group 4 (n = 50) - implants located in the posterior mandible. The implants were further classified as isolated or adjacent to other implants. Three axial slices were selected for each sampled implant (apical, middle and cervical). On each slice, the artifacts produced by the implants were counted. The Mann-Whitney U test was used to compare the variables between groups. The Kruskal-Wallis and Student-Newman-Keuls tests were used to compare the axial slices. The mandible showed a greater number of artifacts than the maxilla (apical slice: $p = 0.0024$; middle slice: $p < 0.0001$). The anterior region produced more artifacts than the posterior region (apical slice: $p = 0.0105$; middle slice: $p < 0.0316$). There was no significant difference in the number of artifacts between isolated and adjacent implants, and the cervical slice was most affected by artifacts. It can be concluded that dental implants always produce metal artifacts in CBCT images, and these artifacts are affected by the anatomical location in the dental arch.

KEYWORDS: *cone beam computed tomography, dental implant, metal artifact.*

LISTA DE ABREVIATURAS E SIGLAS

Bit	*Binary digit*
CAPES	Coordenação de Aperfeiçoamento de Pessoal de Nível Superior
CBCT	*Cone beam computed tomography*
CEP	Comitê de Ética em Pesquisa
Cm	Centímetros
DICOM	*Digital imaging and communications in medicine*
DP	Desvio padrão
et al	*Et alii*
EUA	Estados Unidos da América
FO	Faculdade de Odontologia
FOV	*Field of View*
G1	Grupo 1
G2	Grupo 2
G3	Grupo 3
G4	Grupo 4
H	*Height*
kV	Quilovolt
mA	Miliampère
Mm	Milímetro
N	Número da amostra
ROI	*Region of interest*
S	Segundo
SD	*Standard deviation*
SPSS	*Statistical Package for Social Sciences*
TCFC	Tomografia computadorizada de feixe cônico
UFJF	Universidade Federal de Juiz de Fora
USA	*United States of America*
W	*Width*

LISTA DE SÍMBOLOS

-	Menos
%	Por cento
/	Dividido
<	Menor
=	Igual
≤	Menor igual
E	Equação 1, Cochran (1963)
P	Nível de significância
Q	1 – p
R	Coeficiente de Pearson
X	Vezes/ versus
Z	Número atômico
Z^2	Abscissa da curva normal que corta uma área α bicaudal
A	Referência de nível de confiança

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SUMÁRIO

1 INTRODUÇÃO

A utilização do exame de tomografia computadorizada de feixe cônico (TCFC) é cada vez mais frequente na Odontologia, principalmente na Implantodontia, pois é uma ferramenta útil para diagnóstico e planejamento de tratamentos, permitindo a localização de estruturas anatômicas e fornecendo informações precisas sobre morfologia e dimensões ósseas (BECHARA et al., 2013; DRAENERT et al., 2007; ESMAEILI et al., 2012; ESMAEILI et al., 2013; KAMBUROGLU et al., 2013; NAGARAJAPPA et al., 2015, SANCHO-PUCHADES et al., 2015).

Como se trata de um exame tridimensional e sem sobreposições, a TCFC também vem sendo indicada no acompanhamento do tratamento com implantes dentários, como na monitoração da regeneração óssea, detecção de possíveis perdas de osso marginal e sinais de falha na osseointegração (SANCHO-PUCHADES et al., 2015). No entanto, após a instalação dos implantes dentários existe um fator limitador associado às imagens tomográficas: a formação dos artefatos metálicos (NAGARAJAPPA et al., 2015; SANCHO-PUCHADES et al., 2015). Um artefato pode ser definido como qualquer distorção ou erro na imagem, visualizado nos dados reconstruídos e que não está presente no objeto sob investigação (KAMBUROGLU et al., 2013; KUUSISTO et al., 2015; RÓZYTO-KALINOWSKA et al., 2014; SANCHO-PUCHADES et al., 2015).

A formação dos artefatos acontece em consequência das diferenças de atenuação e absorção dos feixes de raios X quando entram em contato com materiais de alta densidade física. Essa interação provoca um efeito chamado de "endurecimento" do feixe (*beam hardening*). A imagem resultante é alterada com a formação de bandas hipodensas (*dark bands*), estrias hiperdensas (*white streaks*) e distorção dos objetos metálicos (*cupping artefacts*) (BECHARA et al., 2013; JAJU et al., 2013). Alguns fatores de exposição, como miliamperagem e quilovoltagem baixas, problemas na regulagem do aparelho, movimentação do paciente durante aquisição da imagem, limitação dos algoritmos utilizados na reconstrução das imagens e uso de materiais odontológicos de alta densidade, como os metais, são citados como prováveis causadores de artefatos (ESMAEILI et al., 2013; JAJU et al., 2013; KUUSISTO et al., 2015; NAGARAJAPPA et al., 2015).

A imagem gerada na TCFC é composta por diferentes tons de cinza, originados dos processos de atenuação do feixe de raios X quando em contato com os tecidos expostos. Os artefatos provenientes de materiais metálicos contribuem para a não homogeneidade dos valores de cinza em TCFC (MOUDI et al., 2015; PAUWELS et al., 2013), pois causam uma atenuação não linear da radiação, o que resulta em uma variação do valor médio de energia do feixe de raios X. Durante o processo de reconstrução das imagens, essa atenuação não linear acarreta em uma redução da qualidade da imagem (KRATZ et al., 2012), que pode prejudicar o diagnóstico, levando a interpretações falso-positivas e/ou falso-negativas (DRAENERT et al., 2007; ESMAEILI et al., 2013; GAMBA et al., 2014; JAJU et al., 2013; PAUWELS et al., 2013; SANCHO-PUCHADES et al., 2015; SCHULZE et al., 2010). Os artefatos causados pelos implantes dentários dificultam a visualização e a avaliação do osso adjacente ao redor desses implantes, sendo praticamente impossível a interpretação de regiões próximas aos implantes na avaliação pós-operatória da osseointegração (PARSA et al., 2014; SANCHO-PUCHADES et al., 2015).

Alguns estudos sugerem que a formação dos artefatos metálicos pode ser influenciada pela região anatômica, pela posição do objeto no interior do FOV (*field of view* - campo de visão) e pelas estruturas anatômicas adjacentes fora do campo de visão (OLIVEIRA et al., 2013; VALIZADEH et al., 2015), porém não existe um consenso em afirmar quais as regiões (maxila ou mandíbula, anterior ou posterior) estão mais relacionadas à formação de artefatos ou quais são os efeitos da localização do objeto no interior do FOV. Sendo assim, o objetivo do presente estudo foi quantificar a formação de artefatos metálicos produzidos por implantes dentários de titânio, instalados em diferentes regiões maxilo-mandibulares.

2 PROPOSIÇÃO

O objetivo no presente estudo foi avaliar, em imagens de TCFC, os artefatos metálicos produzidos por implantes dentários de titânio, comparando:

- a quantidade de artefatos produzida na maxila e mandíbula;
- a quantidade de artefatos produzida nas regiões anterior e posterior;
- a quantidade de artefatos produzida nas proximidades de implantes unitários isolados e adjacentes a outros.

3 MATERIAL E MÉTODOS

3.1 DESENHO DO ESTUDO

Trata-se de um estudo retrospectivo observacional transversal.

3.2 COMITÊ DE ÉTICA

Este estudo foi aprovado pelo Comitê de Ética em Pesquisa da Universidade Federal de Juiz de Fora (CEP/UFJF, Juiz de Fora, Minas Gerais, Brasil), sob o parecer n^{o}. 1.403.545/2016 (ANEXO A)

3.3 DESCRIÇÃO DA AMOSTRA

Foram selecionadas imagens de TCFC com presença de implantes dentários em pacientes de ambos os sexos e de qualquer idade, pertencentes ao arquivo (banco de dados) da clínica de Radiologia Odontológica da Faculdade de Odontologia da Universidade Federal de Juiz de Fora (FO/UFJF) (Minas Gerais, Brasil).

Na amostra da pesquisa, foram incluídos exames apresentando imagem de qualidade, com implantes de titânio, instalados em qualquer região maxila ou mandíbula, com presença da prótese sobre implante, sendo isolados ou adjacentes a outros implantes. Foram excluídos os exames de pacientes que apresentaram implantes nos ossos zigomáticos, restaurações metálicas extensas e/ou pinos metálicos em dentes adjacentes aos implantes, implantes adjacentes a dentes com tratamento endodôntico e implantes sem a presença de prótese.

3.4 GRUPOS DE ESTUDO

Um total de 200 implantes foi dividido em quatro grupos de acordo com sua localização anatômica: Grupo 1 (G1) – implantes localizados na região anterior da maxila; Grupo 2 (G2) – implantes localizados na região posterior da maxila; Grupo 3 (G3) – implantes localizados na região anterior da mandíbula e Grupo 4 (G4) – implantes localizados na região posterior da mandíbula. A seleção da amostra foi definida de maneira aleatória e por conveniência, até que cada grupo tivesse 50 implantes incluídos (uma fórmula foi aplicada para calcular o tamanho da amostra = Z^2 p q/ e^2 (equação 1, Cochran, 1963), onde Z^2 é a abscissa da curva normal que corta uma área α nas caudas (1 - α é igual ao nível de confiança desejado, por exemplo, 95%), sendo o nível de precisão desejado; p é a proporção estimada de um atributo que está presente na população; e q é 1 - p. O valor de Z é encontrado em tabelas estatísticas que contêm a área sob a curva normal. Considerando α = 5%, Z = 1,96, p = 0,80 (sensibilidade) e q = 0,20; o tamanho mínimo da amostra é de 42 implantes.

Os implantes ainda foram classificados em implantes unitários isolados e implantes adjacentes a outros. Foram considerados implantes adjacentes aqueles que possuíam uma distância máxima entre eles de 5 mm.

A distribuição dos grupos de estudo e o respectivo número da amostra encontram-se apresentados na Tabela 1.

Tabela 1. Distribuição dos implantes dentários nos diferentes grupos de estudo

Região	**Implantes Isolados n (%)**	**Implantes Adjacentes n (%)**	**TOTAL n (%)**
Maxila Anterior (G1)	7 (3.5)	43 (21.5)	50 (25.0)
Maxila Posterior (G2)	13 (6.5)	37 (18.5)	50 (25.0)
Mandíbula Anterior (G3)	5 (2.5)	45 (22.5)	50 (25.0)
Mandíbula Posterior (G4)	3 (1.5)	47 (23.5)	50 (25.0)
TOTAL	28 (14.0)	172 (86.0)	200 (100.0)

3.5 SELEÇÃO DOS EXAMES TOMOGRÁFICOS

Todas as imagens, pertencentes ao banco de dados da clínica de Radiologia da FO/UFJF, foram adquiridas pelo mesmo tomógrafo (I-Cat® Next Generation, Imaging Sciences International, Hatfield, Pensilvânia, EUA), com o seguinte protocolo de aquisição: 120 kV, 8 mA, 26,9 s de rotação, voxel de 0,25 mm e FOV (*field of view* - campo de visão) pequeno (variando entre 6 x 13 cm e 8 x 13 cm).

Reconstruções panorâmicas, visualizadas no *software* XoranCat (versão 3.1.62, XoranTechnologies, Ann Arbor, Michigan, EUA), foram utilizadas para seleção de exames de pacientes que se enquadravam nos critérios de inclusão. Para os pacientes com vários implantes incluídos na amostra, os mesmos foram numerados sequencialmente da direita para esquerda, seguindo a sequência dos quadrantes, e diferenciados quanto à localização (maxila e mandíbula) (Figura 1).

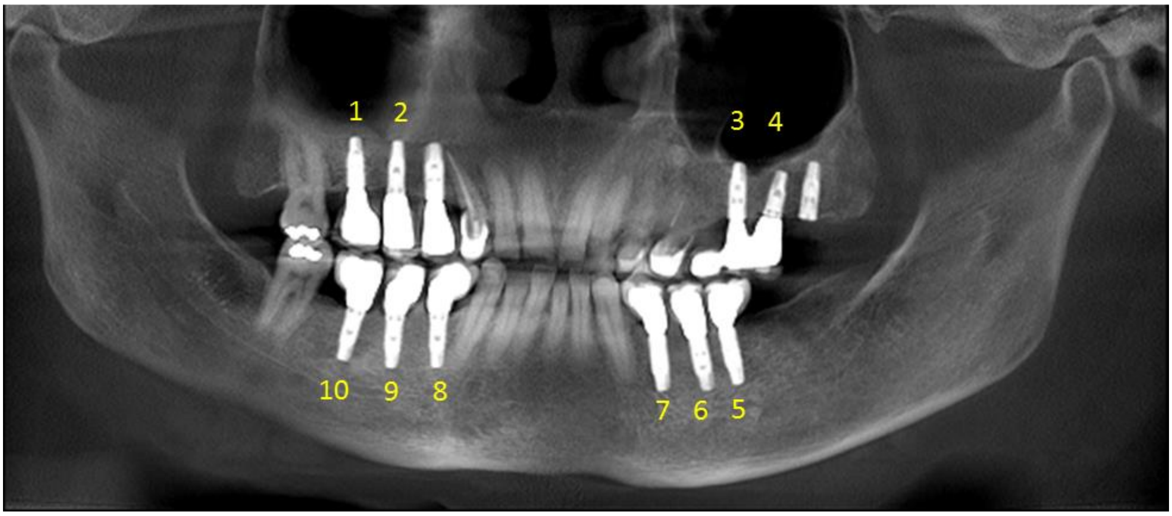

Figura 1. Corte panorâmico de TCFC evidenciando os implantes numerados sequencialmente e identificados quanto à localização.

Fonte: Banco de Dados Radiologia – FO/UFJF

Após a seleção dos exames, as imagens em formato *DICOM* (*Digital Imaging and Communications in Medicine*), descomprimidas, foram submetidas ao *software RadiantDICOM* (Medixant, Poznan, Polônia) para seleção de três cortes axiais de cada implante incluído na amostra, sendo um no terço apical, um no terço médio e um no terço cervical, para posterior quantificação dos artefatos metálicos produzidos por esses implantes. O corte apical foi definido como o corte mais apical do implante que permita a visualização de todo o seu diâmetro. O corte cervical foi definido como o corte mais cervical do implante que permita a visualização de todo o seu diâmetro. O corte médio foi definido como o corte central entre os dois cortes (apical e cervical) previamente selecionados para cada implante individualmente.

Um único examinador radiologista, com experiência em imagens de TCFC, foi o responsável pela seleção das imagens, bem como dos cortes axiais para cada implante selecionado.

3.6 QUANTIFICAÇÃO DOS ARTEFATOS METÁLICOS

Após a seleção dos cortes axiais de cada implante, estes foram avaliados individualmente no *software* ImageJ (U. S. National Institutes of Health, Bethesda, Maryland, EUA), baseando-se na metodologia de Pauwels et al. (2013). Uma ROI (*ROI - region of interest* - região de interesse) circular de dimensões padronizadas (10 x 10 mm) foi construída abrangendo toda a região do implante além do tecido ósseo adjacente. O centro da ROI deveria obrigatoriamente coincidir com o centro do implante (Figura 2).

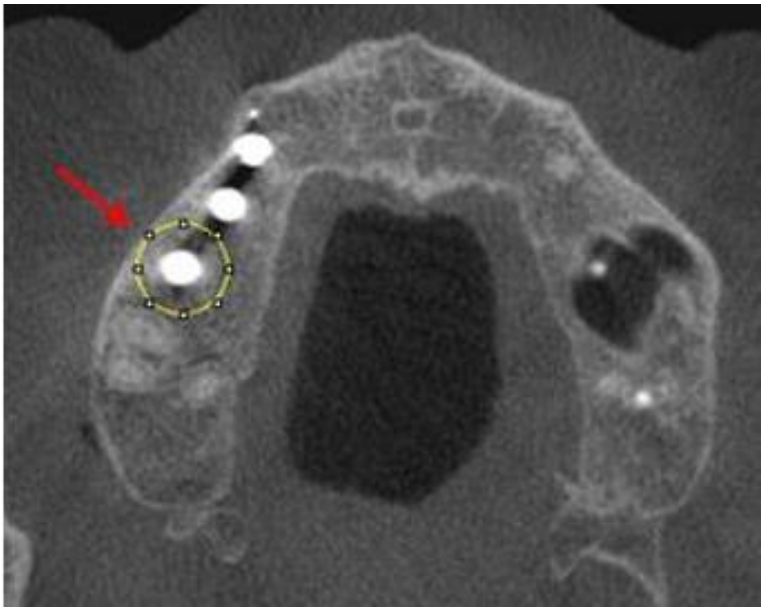

Figura 2. Corte axial apical de um implante com o posicionamento da ROI definida no ImageJ.

Fonte: Banco de Dados Radiologia – FO/UFJF

Para cada ROI selecionada, foram quantificados os artefatos presentes. Ainda no *software* ImageJ, por meio das ferramentas "*Analyze – Histogram*" os valores mínimo e máximo de cinza foram determinados para o cálculo do desvio-padrão (DP) efetivo (Figura 3). O cálculo matemático do DP efetivo foi realizado no programa Excel, versão 2010 (Windows XP, Microsoft, EUA). Utilizando-se uma escala de 16 bits (65.536 valores de cinza), já que as imagens tomográficas geradas a partir do tomógrafo utilizado nesse estudo possuem essa característica, foi determinado o DP teórico máximo, cujo valor é metade dos valores de cinza de uma imagem de 16 bits, ou seja, 32.768. Foi considerado o valor de 32.768 tons de cinza, uma vez que metade dos voxels de uma imagem é preto e metade é branco, assim o DP máximo deveria ser exatamente a metade dos valores de cinza de uma determinada imagem. O cálculo foi realizado da seguinte forma:

(DP efetivo / DP teórico máximo) x 100 = quantificação de artefato

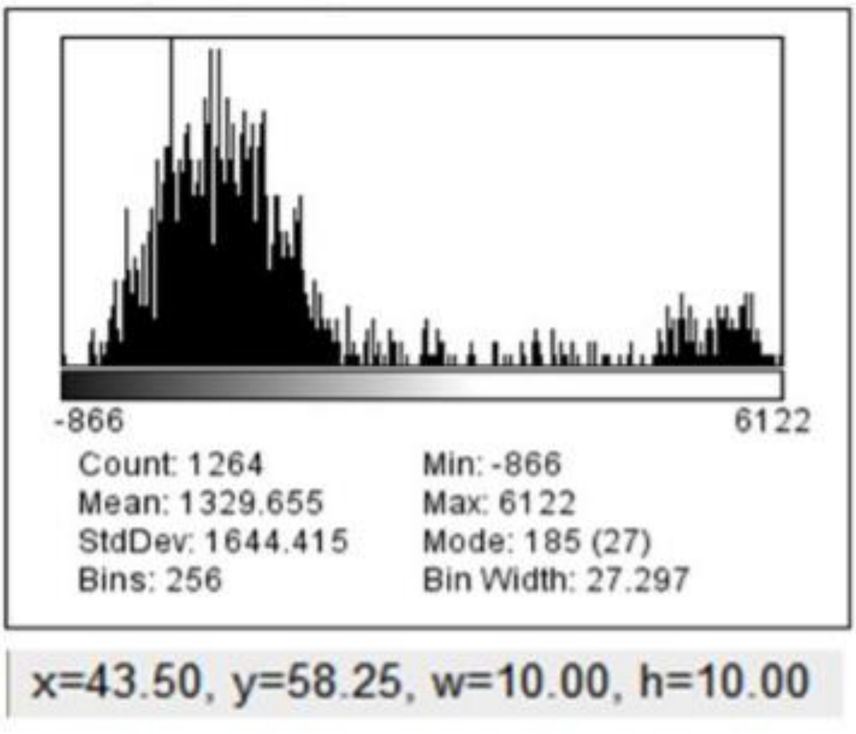

Figura 3. Histograma do *software* ImageJ evidenciando coordenadas da ROI utilizada (x e y), o tamanho da ROI (w e h, respectivamente *width* - largura e *height* - altura) e valores mínimo e máximo de cinza.

Fonte: O Autor

As mensurações foram realizadas pelo mesmo examinador radiologista que realizou a seleção dos cortes tomográficos. Para mensurar a reprodutibilidade do método, 20% dos exames foram avaliados em dois momentos distintos, com intervalo de duas semanas entre eles para o cálculo da concordância intraobservador.

3.7 ANÁLISE ESTATÍSTICA

Os dados obtidos foram tabulados em planilhas do programa Excel (Windows XP, Microsoft, EUA) e analisados estatisticamente no programa *Statistical Package for Social Sciences* (SPSS) (Chicago IL, EUA). O nível de significância adotado foi de 5% ($p \leq 0,05$). Para comparar as variáveis com dois grupos de estudo foi aplicado o teste U de Mann-Whitney. Para a comparação entre os cortes axiais foram aplicados os testes de Kruskal-Wallis e Student-Newman-Keuls.

4 ARTIGO

O artigo a seguir está apresentado nas normas do periódico *Clinical Oral Implants Research*, classificado no Qualis da CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior), na Área de Avaliação de Odontologia, como A1 (ANEXO B). O comprovante de submissão do artigo ao periódico, datado de 14 de junho de 2017, está apresentado no ANEXO C.

EFFECT OF ANATOMICAL REGION ON THE FORMATION OF METAL ARTIFACTS PRODUCED BY DENTAL IMPLANTS IN CONE BEAM COMPUTED TOMOGRAPHIC IMAGES

Authors:

Alessiana Helena Machado*

Karolina Aparecida Castilho Fardim*

Camila Furtado de Souza*

Bruno Salles Sotto-Maior**

Neuza Maria Souza Picorelli Assis***

Karina Lopes Devito***

Authors' affiliations:

* Master's Program in Dental Clinic, School of Dentistry, Federal University of Juiz de Fora, Juiz de Fora, Minas Gerais, Brazil.

** Department of Restorative Dentistry, School of Dentistry, Federal University of Juiz de Fora, Juiz de Fora, Minas Gerais, Brazil.

*** Department of Dental Clinic, School of Dentistry, Federal University of Juiz de Fora, Juiz de Fora, Minas Gerais, Brazil.

Running title:

Metal artifacts produced by dental implants in CBCT

Corresponding author:

Karina Lopes Devito

Department of Dental Clinic, School of Dentistry, Federal University of Juiz de Fora, Campus Universitário, s/n.

CEP: 36036-900 - Juiz de Fora, MG, Brazil

E-mail: karina.devito@ufjf.edu.br

Key Words:

Cone beam computed tomography, dental implant, metal artifact.

EFFECT OF ANATOMICAL REGION ON THE FORMATION OF METAL ARTIFACTS PRODUCED BY DENTAL IMPLANTS IN CONE BEAM COMPUTED TOMOGRAPHIC IMAGES

Abstract

Objective: To quantitatively compare metal artifacts produced by implants in different maxillomandibular regions on cone beam computed tomography (CBCT) images.

Material and Methods: A total of 200 implants selected from CBCT examinations were divided into four groups: Group 1 (n = 50) - implants located in the anterior maxilla; Group 2 (n = 50) - implants located in the posterior maxilla; Group 3 (n = 50) - implants located in the anterior mandible; and Group 4 (n = 50) - implants located in the posterior mandible. The implants were further classified as isolated or adjacent to other implants. Three axial slices were selected for each sampled implant (apical, middle and cervical). On each slice, the artifacts produced by the implants were counted. The Mann-Whitney U test was used to compare the variables between groups. The Kruskal-Wallis and Student-Newman-Keuls tests were used to compare the axial slices.

Results: The mandible showed a greater number of artifacts than the maxilla (apical slice: $p = 0.0024$; middle slice: $p < 0.0001$). The anterior region produced more artifacts than the posterior region (apical slice: $p = 0.0105$; middle slice: $p < 0.0316$). There was no significant difference in the number of artifacts between isolated and adjacent implants, and the cervical slice was most affected by artifacts.

Conclusions: Dental implants always produce metal artifacts in CBCT images, and these artifacts are affected by the anatomical location in the dental arch.

Introduction

Oral rehabilitation with dental implants has become a frequent dental practice due to its high degree of predictability and clinical success (de-Azevedo-Vaz et al. 2016). Radiographic bone tissue examination is an important tool in diagnosis and monitoring in implantology (Benic et al. 2013; Schulze et al. 2010). Periapical radiography, routinely used in dentistry, is used to detect peri-implant bone loss and to evaluate osseointegration (Sancho-Puchades et al. 2015). However, as periapical radiography is a two-dimensional exam, its diagnostic value has limitations due to overlaps and geometric distortions (Benic et al. 2013; Sancho-Puchades et al. 2015).

Cone beam computed tomography (CBCT) has become the most widely used test in implantology, as it minimizes the limitations of two-dimensional images (Cremonini et al. 2011; Pauwels et al. 2013; Sancho-Puchades et al. 2015; Valizadeh et al. 2015). Due to its capacity to provide three-dimensional information, CBCT provides high image quality, diagnostic accuracy and linear measurement precision, thus increasing dental implant installation safety and treatment success rates (Benic et al. 2013; Cremonini et al. 2011; Oliveira et al. 2013; Pauwels et al. 2013; Schulze et al. 2010; Smeets et al. 2017; Valizadeh et al. 2015). However, in the post-surgical follow-up phase, after implant placement, metal artifacts form inside the field of view (FOV), affecting tomographic image quality (Benic et al. 2013; Chindasombatjaroen et al. 2011; Cremonini et al. 2011; de-Azevedo-Vaz et al. 2016; Luckow et al. 2011; Pauwels et al. 2013; Sancho-Puchades et al. 2015; Schulze et al. 2010; Smeets et al. 2017), affecting, for example, the visibility of fenestrations and peri-implant dehiscence (de-Azevedo-Vaz et al. 2016; Vasconcelos et al. 2017).

Metal objects such as titanium implants lead to the formation of artifacts by hardening the X-ray beam (i.e., beam hardening) (de-Azevedo-Vaz et al. 2016; Schulze et al. 2010; Vasconcelos et al. 2017), which is observed in the tomographic image as hyperdense linear streaks irradiating from a high-density object with hypodense areas interspersed between them (de-Azevedo-Vaz et al. 2016; Jaju et al. 2013; Pauwels et al. 2013; Schulze et al. 2010). The artifacts caused by beam hardening occur as a result of differences in the attenuation and absorption of X-ray beams when in contact with high-density material (Bechara et al. 2013; Schulze et al. 2010; Vasconcelos et al. 2017). When crossing the dental implant, the low-energy X-ray photons are absorbed by the metal, and only the high-energy photons are used to form the image, increasing the average energy of the X-ray beam and changing the tomographic reconstruction process (Chindasombatjaroen et al. 2011; Pauwels et al. 2013; Schulze et al. 2010). These artifacts tend to cause excessive variation in gray values near the metal structure (Benic et al. 2013), affecting image quality and making it difficult to evaluate osseointegration and inflammatory processes near the implants (Parsa et al. 2014; Sancho-Puchades et al. 2015; Smeets et al. 2017; Valizadeh et al. 2015).

Some studies suggest that the formation of metal artifacts can be affected by anatomical region, the position of the object within the FOV and the adjacent anatomical structures outside of the FOV (Oliveira et al. 2013; Valizadeh et al. 2015), but there is no consensus regarding which regions (maxilla or mandible, anterior or posterior) are more involved in the formation of artifacts or what the effects of the object's location within the FOV are. Thus, the aim of this study was to use CBCT images to quantify the formation of metal artifacts produced by titanium dental implants installed in different maxillomandibular regions.

Material and methods

This retrospective, cross-sectional, observational study was approved by the Research Ethics Committee of the Federal University of Juiz de Fora (UFJF, Juiz de Fora, Minas Gerais, Brazil), under protocol no. 1,403,545/2016.

CBCT images showing dental implants in the jaw were selected from the archive of the Dental Radiology Clinic at the UFJF Dental School (Minas Gerais, Brazil). All images were acquired in the same scanner (I-Cat ®, Imaging Sciences International, Hatfield, Pennsylvania, USA), with an acquisition protocol of 120 kV, 8 mA, 26.9 s rotation, 0.25 mm voxel and an FOV between 6 x 13 and 8 x 13 cm.

CBCT examinations of patients of either sex and of any age were included that showed isolated titanium dental implants or those with other adjacent implants and that were situated in any region of the maxilla and/or mandible. Implants installed in the zygomatic bone, without the presence of prosthesis and adjacent to teeth with fillings/crowns/metal posts, were excluded.

Study groups

A total of 200 implants were divided into four groups: Group 1 - implants located in the anterior maxilla; Group 2 - implants located in the posterior maxilla; Group 3 - implants located in the anterior mandible; and Group 4 - implants located in the posterior mandible.

The sample selection was defined randomly and by convenience, until each group had 50 implants. The formula applied to calculate the sample size was $n = Z^2 p q / e^2$ (equation 1, by Cochran, 1963), where Z^2 is the abscissa of the normal curve that cuts off an area α at the tails (1 - α equals the desired confidence level, e.g., 95%), e is the desired level of precision, p is the estimated proportion of an attribute that is present in the population, and q is 1 - p. The value for Z is found in statistical tables that contain the area under the normal curve. Considering $\alpha = 5\%$, $Z = 1.96$, $p = 0.80$ (sensitivity), and $q = 0.20$, the minimum sample size was 42 implants.

The implants were further classified as isolated or adjacent to other implants. Adjacent implants were deemed to be those with a maximum distance between them of 5 mm.

Image selection

After exam selection, the images, in uncompressed Digital Imaging and Communications in Medicine (DICOM) format, were imported into RadiantDICOM software (Medixant, Poznan, Poland) for selection of three axial slices for each implant in the sample; one in the apical third, one in the middle third and one in the cervical third. The apical slice was defined as the most apical that allowed the entire diameter to be viewed. The cervical slice was defined as the most cervical that allowed the entire diameter to be viewed before prosthetic connection. The middle slice was that midway between the apical and cervical slices previously selected for each individual implant (Figure 1).

Figure 1

Quantification of metal artifacts

The axial slices selected for each implant were individually evaluated using ImageJ software (US National Institutes of Health, Bethesda, Maryland, USA) to count the artifacts. A circular region of interest (ROI) was selected with standardized dimensions (10 x 10 mm). This ROI covered the entire area of the implant and the adjacent bone tissue. The ROI's center coincided with the implant's center.

The artifacts present in each selected ROI were counted based on the method described by Pauwels et al. (2013). The minimum and maximum gray values were determined using the ImageJ histogram tool to calculate the actual standard deviation (SD). The actual SD calculation was performed in Excel, version 2010 (Windows 10, Microsoft, USA).

According to Pauwels et al. (2013), artifact quantification is defined as follows: actual SD / theoretical maximum SD x 100. A 16-bit scale (65,536 gray values) was used to determine the maximum theoretical SD, as images generated by the CT scanner used have this characteristic. The maximum theoretical SD corresponds to half of the gray values of a 16-bit image (i.e., 32,768 values). This correction is needed to allow comparison of images across different devices and based on different acquisition protocols. Therefore, the actual SD was converted into a percentage of the maximum theoretical SD, where higher percentages indicate more pronounced artifacts.

CT scans, axial slices and ROI definitions were selected by a single examiner who was a radiologist with expertise in interpreting CBCT images. To determine method reproducibility, 20% of the exams were re-evaluated two weeks after the first evaluation, and intra-rater agreement was considered strong (r Pearson: 0.93).

Statistical analysis

The obtained data were statistically analyzed using the Statistical Package for Social Sciences program (SPSS, version 15.0; IBM Corp, Armonk, New York, EUA). The significance level adopted was 5% ($p \leq 0.05$). The Mann-Whitney U test was applied to compare variables between groups (maxilla x mandible; anterior x posterior; isolated x adjacent). The Kruskal-Wallis and Student-Newman-Keuls tests were used to compare the axial, middle and cervical slices.

Results

A total of 200 titanium dental implants were evaluated and divided into groups according to their anatomical location and proximity to other implants (Table 1). The implants had lengths of 4 to 13 mm and diameters of 3.5 to 4 mm.

Table 1

When comparing the number of metal artifacts in the mandible and maxilla, the mandible showed significantly higher numbers of artifacts in the apical and middle slices (Table 2).

Table 2

When comparing the number of artifacts in implants installed in the anterior and posterior regions, the anterior region implants showed significantly higher numbers of artifacts in the apical and middle slices (Table 3).

Table 3

The formation of metal artifacts was also compared according to whether the implants were installed in isolation or adjacent to other implants. There was no significant difference in the number of artifacts between isolated and adjacent implants (Table 4).

Table 4

Comparing the slices (apical, middle and cervical), a significantly higher number of artifacts was always observed in the cervical slices (Table 5).

Table 5

Figure 2 shows various axial slices of the implants and their respective artifacts.

Figure 2

Discussion

CBCT is widely used in the pre-operative stage of dental implant treatment to evaluate bone quantity and quality (de-Azevedo-Vaz et al. 2016; Pauwels et al. 2013). However, it is known that in the post-operative phase, in the presence of previously installed implants, tomographic images show metal artifacts, which reduces the indication for CBCT at this stage.

CBCT image information is composed of voxels. These voxels are each identified by a gray value, reflecting the degree of X-ray attenuation when passing through the object under study. The gray values in CBCT are strongly affected by the object's characteristics, such as density and atomic number (Z) (Oliveira et al. 2013; Schulze et al. 2010). As metals have higher physical densities and atomic numbers than the constituent elements of soft tissue and bone (Cremonini et al. 2011), they promote greater hardening of the X-ray beam. In this interaction, lower energy photons are absorbed by the object in preference to higher energy photons, resulting in increased average power of the beam and the production of artifacts, which appear as hyperdense streaks radiating from a high-density object and interspersed by hypodense areas (de-Azevedo-Vaz et al. 2016; Jaju et al. 2013; Moudi et al. 2015; Pauwels et al. 2013; Schulze et al. 2010).

Titanium (Z = 22), the constituent material of the implants evaluated in this study, is considered a metal and, as expected, produced artifacts in the tomographic images of all of the maxillomandibular anatomical regions. However, a difference in the number of formed artifacts was observed according to implant location. The number of artifacts was higher in the mandible and in anterior regions (incisors and canines), showing that the gray values of a given object differ depending on its location and adjacent anatomical structures. Variations in density and thickness of maxillary and mandibular bone tissue may explain the difference in the number of artifacts, which is consistent with Oliveira et al.'s (2013) findings, who evaluated the effect of anatomical location on the gray values in CBCT images and demonstrated that the same object may have different values depending on anatomical location. Queiroz et al. (2017), evaluating the effect of a metal artifact reduction tool when an artifact generator object was placed in different positions within the FOV, also observed that noise levels were different according to changes in position.

According to Valizadeh et al. (2015), the object's location within the FOV affects the gray values of a tomographic image. In certain positions, X-rays traverse the long axis of the maxilla or mandible, interacting with dental implants, teeth and adjacent bone on a single plane (Luckow et al. 2011), leading to more artifact formation. Another possible explanation for this variation in artifacts relative to anatomical location is the effect of the exomass, i.e., the entire craniofacial area located within and outside the FOV. A significant amount of the patient's tissue attenuates X-rays but is not included in the final image (Benic et al. 2013; Oliveira et al. 2013; Pauwels et al. 2013; Sancho-Puchades et al. 2015). The presence of adjacent anatomical structures, such as the skull and spinal column, affects gray value measurements in the maxilla and mandible (Sancho-Puchades et al. 2015; Smeets et al. 2017).

In the present study, a greater number of artifacts was observed in the dental implants' cervical third, likely due to the presence of the prosthesis over the implant. Titanium, the implant's constituent metal, has a smaller atomic number (Sancho-Puchades et al. 2015; Smeets et al. 2017) than prosthetic crown alloy materials, such as cobalt-chromium (Chindasombatjaroen et al. 2011). As stated previously, the higher the atomic number, the greater the number of artifacts. Therefore, the presence of the prosthesis would have further increased the number of artifacts in the implant's cervical region.

As metals attenuate X-ray beams more than soft tissue and bone (Cremonini et al. 2011), a larger gray value range, i.e., more artifact formation, was expected between adjacent implants. However, when comparing the number of artifacts around isolated implants with those around implants adjacent to others, no significant difference was observed. This result may be explained by the small ROI defined for measuring the artifacts, which was standardized at 10 x 10 mm and therefore suffered little or no effect from neighboring implants.

In the present study, it was possible to quantify the effect of artifacts on the tomographic images' gray values, providing an estimate of the extent of these unwanted images caused by dental implants. However, it is important to note that other factors may also affect artifact formation, such as voxel size, slice thickness and FOV size (Valizadeh et al. 2015). Therefore, it is important to develop future *in vitro* studies that take these variables into account when counting the artifacts generated by implants. Moreover, it is essential to develop research that associates the number of artifacts with diagnostic accuracy to ascertain the real level of interference of these unwanted images on clinical dental practice.

Considering the above results, it can be concluded that metal artifacts are always present in CBCT images and that the anatomical region in which the implant is installed affects the number of metal artifacts produced, with more artifacts in the mandible and in anterior regions (incisors and canines).

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Figure Legends

Fig. 1. (a) CBCT panoramic slices showing the apical (b), middle (c) and cervical (d) slices of an implant installed in the mandible.

Fig. 2. Examples of metal artifacts in CBCT images of dental implants in axial slices.

Table 1. Distribution of dental implants in different study groups

Region	Isolated Implants n (%)	Adjacent Implants n (%)	TOTAL n (%)
Anterior Maxilla (G1)	7 (3.5)	43 (21.5)	50 (25.0)
Posterior Maxilla (G2)	13 (6.5)	37 (18.5)	50 (25.0)
Anterior Mandible (G3)	5 (2.5)	45 (22.5)	50 (25.0)
Posterior Mandible (G4)	3 (1.5)	47 (23.5)	50 (25.0)
TOTAL	28 (14.0)	172 (86.0)	200 (100.0)

Table 2. Comparison of the number of metal artifacts produced by implants installed in the maxilla and mandible

Axial Slice	Region	Median	P value
Apical	Maxilla	16.74	0.0024*
	Mandible	17.69	
Middle	Maxilla	16.98	<0.0001*
	Mandible	18.48	
Cervical	Maxilla	19.75	0.9601
	Mandible	19.54	

* Statistically significant differences according to the U de Mann-Whitney.

Table 3. Comparison of the number of metal artifacts produced by implants installed in the anterior and posterior regions

Axial Slice	Region	Median	P value
Apical	Anterior	17.48	0.0105*
	Posterior	16.93	
Middle	Anterior	17.93	0.0316*
	Posterior	17.24	
Cervical	Anterior	19.57	0.6285
	Posterior	19.53	

* Statistically significant differences according to the U de Mann-Whitney.

Table 4. Comparison of the number of metal artifacts produced by isolated and adjacent implants

Axial Slice	Implant	Median	P value
Apical	Isolated	17.19	0.8880
	Adjacent	17.22	
Middle	Isolated	16.75	0.3981
	Adjacent	17.50	
Cervical	Isolated	20.69	0.7553
	Adjacent	19.52	

Table 5. Comparison of the number of metal artifacts produced between the apical, middle and cervical slices of dental implants

Comparison	Region	Difference between posts	P value
Apical x Middle	Maxilla	1.80	0.8800
	Mandible	11.55	0.3465
	Anterior	6.64	0.5881
	Posterior	6.16	0.6156
	Isolated	1.46	0.8223
	Adjacent	15.75	0.3273
Apical x Cervical	Maxilla	57.72	<0.0001*
	Mandible	66.15	<0.0001*
	Anterior	62.17	<0.0001*
	Posterior	69.36	<0.0001*
	Isolated	15.07	0.0208*
	Adjacent	117.70	<0.0001*
Middle x Cervical	Maxilla	59.53	<0.0001*
	Mandible	54.60	<0.0001*
	Anterior	55.53	<0.0001*
	Posterior	63.20	<0.0001*
	Isolated	16.53	0.0112
	Adjacent	101.95	<0.0001*

* Statistically significant differences according to the Kruskal-Wallis and Student- Newman-Keuls

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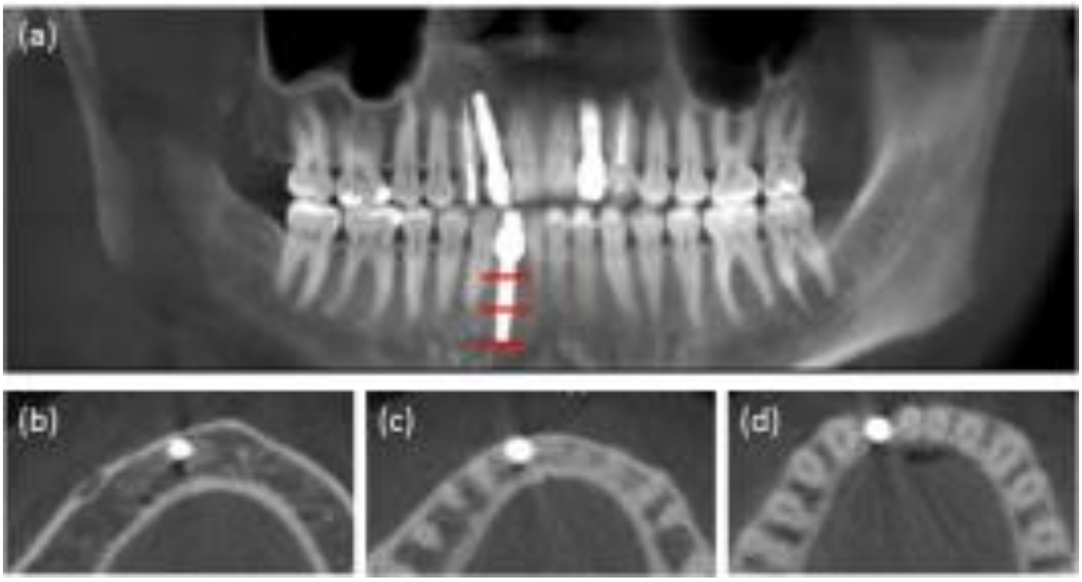

Fig. 2. (a) CBCT panoramic slices showing the apical (b), middle (c) and cervical (d) slices of an implant installed in the mandible.

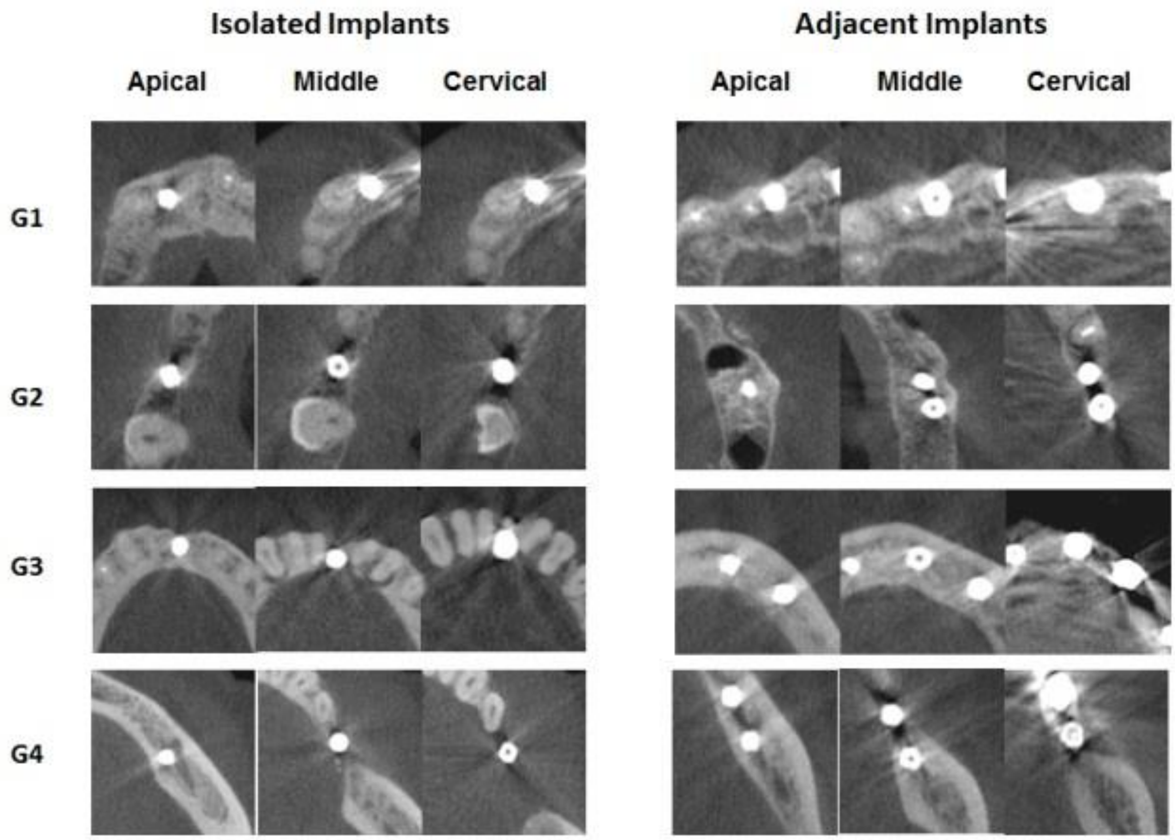

Fig. 2. Examples of metal artifacts in CBCT images of dental implants in axial slices.

5 CONSIDERAÇÕES FINAIS

Sabendo do prejuízo da presença de artefatos metálicos nas imagens de TCFC e da necessidade de conhecer os efeitos da localização dos implantes dentários na produção desses artefatos, esse estudo, que quantificou os artefatos metálicos produzidos por implantes dentários de titânio, indicou que a quantidade de artefatos está relacionada com a localização dos implantes, sendo que a mandíbula foi a arcada mais acometida e a região anterior (incisivos e caninos) foi a área mais afetada pelos artefatos.

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ANEXO A – Parecer do Comitê de Ética

UNIVERSIDADE FEDERAL DE JUIZ DE FORA/MG

Plataforma Brasil

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Influência de um algoritmo de redução de artefato metálico na avaliação de implantes dentários em imagens de tomografia computadorizada de feixe cônico

Pesquisador: Karina Lopes Devito
Área Temática:
Versão: 1
CAAE: 52595216.4.0000.5147
Instituição Proponente: FACULDADE DE ODONTOLOGIA
Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 1.403.545

Apresentação do Projeto:
Apresentação do projeto esta clara e detalhada de forma objetiva. Descreve as bases científicas que justificam o estudo.

Objetivo da Pesquisa:
Apresenta clareza e compatibilidade com a proposta de estudo.

Avaliação dos Riscos e Benefícios:
O risco que o projeto apresenta é caracterizado como risco mínimo, considerando que os indivíduos não sofrerão qualquer dano ou sofrerão prejuízo pela participação ou pela negação de participação na pesquisa e benefícios esperados, estão adequadamente descritos.

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:
O projeto está em configuração adequada e há apresentação de declaração de infraestrutura e de

Endereço: JOSE LOURENCO KELMER S/N
Bairro: SAO PEDRO **CEP:** 36.036-900
UF: MG **Município:** JUIZ DE FORA
Telefone: (32)2102-3788 **Fax:** (32)1102-3788 **E-mail:** cep.propesq@ufjf.edu.br

concordância com a realização da pesquisa, assinada pelo responsável da instituição onde será realizada a pesquisa. O Pesquisador apresenta titulação e experiência compatível com o projeto de pesquisa.

Recomendações:

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: Setembro de 2016.

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_644853.pdf	19/01/2016 19:42:48		Aceito
Outros	DispensaTCLE.pdf	19/01/2016 19:41:38	Karina Lopes Devito	Aceito
Outros	Karina.pdf	11/01/2016 16:03:51	Karina Lopes Devito	Aceito
Outros	Alessiana.pdf	11/01/2016 16:03:29	Karina Lopes Devito	Aceito
Outros	AcessoArquivo.pdf	11/01/2016 16:01:53	Karina Lopes Devito	Aceito
Declaração de Instituição e Infraestrutura	Infraestrutura.pdf	11/01/2016 16:00:10	Karina Lopes Devito	Aceito
Projeto Detalhado / Brochura Investigador	ProjetoCEP.pdf	20/12/2015 23:33:03	Karina Lopes Devito	Aceito
Folha de Rosto	folhaDeRosto.pdf	20/12/2015 23:22:32	Karina Lopes Devito	Aceito

UNIVERSIDADE FEDERAL DE
JUIZ DE FORA/MG

Continuação do Parecer: 1.403.545

Situação do Parecer:
Aprovado
Necessita Apreciação da CONEP:
Não

JUIZ DE FORA, 04 de Fevereiro de 2016

Assinado por:
Francis Ricardo dos Reis Justi
(Coordenador)

Endereço: JOSE LOURENCO KELMER S/N
Bairro: SAO PEDRO **CEP:** 36.036-900
UF: MG **Município:** JUIZ DE FORA
Telefone: (32)2102-3788 **Fax:** (32)1102-3788 **E-mail:** cep.propesq@ufjf.edu.br

ANEXO B – Normas para publicação

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Clinical Oral Implants Research

Edited By: Lisa J. A. Heitz-Mayfield

Impact Factor: 3.464

ISI Journal Citation Reports © Ranking: 2015: 7/91 (Dentistry Oral Surgery & Medicine); 11/76 (Engineering Biomedical)

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Author Guidelines

Author Guidelines

Content of Author Guidelines: 1. General, 2. Ethical Guidelines, 3. Submission of Manuscripts, 4. Manuscript Types Accepted, 5. Manuscript Format and Structure, 6. After Acceptance.

Useful Websites: Submission Site, Articles published in *Clinical Oral Implants Research*, 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

Clinical Oral Implants Research conveys scientific progress in the field of implant dentistry and its related areas to clinicians, teachers and researchers concerned with the application of this information for the benefit of patients in need of oral implants. The journal addresses itself to clinicians, general practitioners, periodontists, oral and maxillofacial surgeons and prosthodontists, as well as to teachers, academicians and scholars involved in the education of professionals and in the scientific promotion of the field of implant dentistry.

Clinical Oral Implants Research publishes:

Original research articles of high scientific merit in the field of material sciences, physiology of wound healing, biology of tissue integration of implants, diagnosis and treatment planning, prevention of pathologic processes jeopardizing the longevity of implants, clinical trials on implant systems, stoma-tognathic physiology related to oral implants, new developments in therapeutic concepts and prosthetic rehabilitation.

Review articles by experts on new developments in basic sciences related to implant dentistry and clinically applied concepts.

Case reports and case series only if they provide or document new fundamental knowledge.

Novel developments if they provide a technical novelty for any implant system.

Short communications of important research findings in a concise format and for rapid publication.

Treatment rational by experts with evidence-based treatment approach.

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 *Clinical Oral Implants Research*. Authors are encouraged to visit Wiley-Blackwell Author Services for further information on the preparation and submission of articles and figures.

2. ETHICAL GUIDELINES
Clinical Oral Implants Research adheres to the below ethical guidelines for publication and research.

2.1. Authorship and Acknowledgements
Authors submitting a paper do so on the understanding that the manuscript have been read and approved by all authors and that all authors agree to the submission of the manuscript to the Journal. ALL named authors must have made an active contribution to the conception and design and/or analysis and interpretation of the data and/or the drafting of the paper and ALL must have critically reviewed its content and have approved the final version submitted for publication. Participation solely in the acquisition of funding or the collection of data does not justify authorship.

Clinical Oral Implants Research 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 acquisition 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.

Up to 6 authors are accepted without need for justification. In the case of a specific and detailed justification of the role of every author, up to 8 authors may be mentioned. It is a requirement that all authors have been accredited as appropriate upon submission of the manuscript. Contributors who do not qualify as authors should be mentioned under Acknowledgements.

Acknowledgements: Under acknowledgements please specify contributors to the article other than the authors accredited. Acknowledge only persons who have made substantive contributions to the study. Authors are responsible for obtaining written permission from everyone acknowledged by name because readers may infer their endorsement of the data and conclusions.

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, 2013) 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. Editor 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.

Clinical Oral Implants Research requires authors of pre-clinical animal studies submit with their manuscript the Animal Research: Reporting In Vivo Experiments (ARRIVE) guidelines checklist.

Clinical Oral Implants Research requires authors of human observations studies in epidemiology to review and submit a STROBE statement. Authors who have completed the ARRIVE guidelines or STROBE checklist should include as the last sentence in the Methods section a sentence stating compliance with the appropriate guidelines/checklist. Checklists should be included in the submission material under "Supplementary Files for Review". Please indicate on the STROBE checklist the page number where the corresponding item can be located within the manuscript e.g Page 4.

3. SUBMISSION OF MANUSCRIPTS

Manuscripts should be submitted electronically via the online submission site http://mc.manuscriptcentral.com/coir. The use of an online submission and peer review site enables immediate distribution of manuscripts and consequentially speeds up the review process. It also allows authors to track the status of their own manuscripts. Complete instructions for submitting a paper is available online and below. Further assistance can be obtained from the Editorial Office at CLRoffice@wiley.com.

3.1. Getting Started
Launch your web browser and go to the journal's online Submission Site:
http://mc.manuscriptcentral.com/coir

• Log-in or click the 'Create Account' option if you are a first-time user.
• If you are creating a new account.
- After clicking on 'Create Account', enter your name and e-mail information and click 'Next'. Your e-mail information is very important.
- Enter your institution and address information as appropriate, and then click 'Next.'
- Enter a user ID and password of your choice (we recommend using your e-mail address as your user ID), and then select your area of expertise. Click 'Finish'.
• If you have an account, but have forgotten your log in details, go to Password Help on the journals online submission system http://mc.manuscriptcentral.com/coir and enter your e-mail address. The system will send you an automatic user ID and a new temporary password.
• Log-in and select Corresponding Author Center.

3.2. Submitting Your Manuscript
• After you have logged in, click the 'Submit a Manuscript' link in the menu bar.
• Enter data and answer questions as appropriate. You may copy and paste directly from your manuscript and you may upload your pre-prepared covering letter.
• Click the 'Next' button on each screen to save your work and advance to the next screen.
• You are required to upload your files.
- Click on the 'Browse' button and locate the file on your computer.
- Select the designation of each file in the drop-down menu next to the Browse button.
- When you have selected all files you wish to upload, click the 'Upload Files' button.
• Review your submission (in HTML and PDF format) before sending to the Journal. Click the 'Submit' button when you are finished reviewing.

3.3. Manuscript Files Accepted
Manuscripts should be uploaded as Word (.doc) or Rich Text Format (.rft) files (not write-protected) plus separate figure files. GIF, JPEG, PICT or Bitmap files are acceptable for submission, but only high-resolution TIF or EPS files are suitable for printing. The files will be automatically converted to HTML and PDF on upload and will be used for the review process. The text file must contain the entire manuscript including title page, abstract, text, references, tables, and figure legends, but no embedded figures. In the text, please reference figures as for instance 'Figure 1', 'Figure 2' etc to match the tag name you choose for the individual figure files uploaded. Manuscripts should be formatted as described in the Author Guidelines below.

3.4. Single Blind Review
All manuscripts submitted to *Clinical Oral Implants Research* will be reviewed by two experts in the field. *Clinical Oral Implants Research* uses single blinded review. The names of the reviewers will thus not be disclosed to the author submitting a paper.

3.5. Suggest a Reviewer
Clinical Oral Implants Research attempts to keep the review process as short as possible to enable rapid publication of new scientific data. In order to facilitate this process, please suggest the names and current email addresses of one potential international reviewer whom you consider capable of reviewing your manuscript. In addition to your choice the journal editor will choose one or two reviewers as well.

3.6. Suspension of Submission Mid-way in the Submission Process
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.

3.7. E-mail Confirmation of Submission
After submission you will receive an e-mail to confirm receipt of your manuscript. If you do not receive the confirmation email after 24 hours, please check your e-mail address carefully in the system. If the e-mail address is correct please contact your IT department. The error may be caused by some sort of spam filtering on your e-mail server. Also, the e-mails should be received if the IT department adds our email server (uranus.scholarone.com) to their whitelist.

3.8. Manuscript Status
You can access ScholarOne Manuscripts (formerly known as Manuscript Central) any time to check your 'Author Centre' for the status of your manuscript. The Journal will inform you by e-mail once a decision has been made.

3.9. Submission of Revised Manuscripts
To submit your revised manuscript, locate your manuscript under 'Manuscripts with Decisions' and click on 'Submit a Revision' . Please remember to delete any old files uploaded when you upload your revised manuscript.

4. MANUSCRIPT TYPES ACCEPTED
Original research articles of high scientific merit in the field of material sciences, physiology of wound healing, biology of tissue integration of implants, diagnosis and treatment planning, prevention of pathologic processes jeopardizing the longevity of implants, clinical trials on implant systems, stomatognathic physiology related to oral implants, new developments in therapeutic concepts and prosthetic rehabilitation.

Review articles by experts on new developments in basic sciences related to implant dentistry and clinically applied concepts. Reviews are generally by invitation only and have to be approved by the Editor-in-Chief before submission.

Case reports and case series, but only if they provide or document new fundamental knowledge and if they use language understandable to the clinician.

Novel developments if they provide a technical novelty for any implant system.

Short communications of important research findings in a concise format and for rapid publication.

Treatment rational by experts with evidence-based treatment approach.

Proceedings of international meetings may also be considered for publication at the discretion of the Editor.

5. MANUSCRIPT FORMAT AND STRUCTURE

5.1. Page Charge
Articles exceeding 10 published pages are subject to a charge of USD 160 per additional page. One published page amounts approximately to 5,500 characters (excluding figures and tables).

5.2. Format

Language: The language of publication is English. Authors for whom English is a second language might choose to have their manuscript professionally edited by an English speaking person before submission to make sure the English is of high quality. A list of independent suppliers of editing services can be found at http://authorservices.wiley.com/bauthor/english_language.asp. All services are paid for and arranged by the author, and use of one of these services does not guarantee acceptance or preference for publication

Abbreviations, Symbols and Nomenclature: The symbol % is to be used for percent, h for hour, min for minute, and s for second. In vitro, in vivo, in situ and other Latin expressions are to be italicised. Use only standard abbreviations. All units will be metric. Use no roman numerals in the text. In decimals, a decimal point and not a comma will be used. Avoid abbreviations in the title. The full term for which an abbreviation stands should precede its first use in the text unless it is a standard unit of measurement. In cases of doubt, the spelling orthodoxy of Webster's third new international dictionary will be adhered to.

Scientific Names: Proper names of bacteria should be binomial and should be singly underlined on the typescript. The full proper name (e.g., Streptococcus sanguis) must be given upon first mention. The generic name may be abbreviated thereafter with the first letter of the genus (e.g., S. sanguis). If abbreviation of the generic name could cause confusion, the full name should be used. If the vernacular form of a genus name (e.g., streptococci) is used, the first letter of the vernacular name is not capitalised and the name is not underlined. Use of two letters of the genus (e.g., Ps. for Peptostreptococcus) is incorrect, even though it might avoid ambiguity. With regard to drugs, generic names should be used instead of proprietary names. If a proprietary name is used, it must be attached when the term is first used.

5.2. Structure
All manuscripts submitted to *Clinical Oral Implants Research* should include Title Page, Abstract, Main Text and Acknowledgements, Tables, Figures and Figure Legends as appropriate.

Title Page: should contain the title of the article, full name(s) of the authors (no more than 6) and institutional affiliation(s), a running title not exceeding 60 letters and spaces, and the name, telephone and fax numbers, email and complete mailing address of the author responsible for correspondence. The author must list appropriate key words for indexing purposes.

Abstract: should not to exceed 250 words. This should be structured into: objectives, material and methods, results, conclusions, and no other information.

Main Text of Original Research Article should include Introduction, Material and Methods, Results and Discussion.

Introduction: Summarise the rationale and purpose of the study, giving only strictly pertinent references. Do not review existing literature extensively. State clearly the working hypothesis.

Material and Methods: Material and methods should be presented in sufficient detail to allow confirmation of the observations. Published methods should be referenced and discussed only briefly, unless modifications have been made. Indicate the statistical methods used, if applicable.

Clinical trial registration number and name of the trial register should be included in the Materials and Methods at the submission stage.

Authors who have completed the ARRIVE guidelines or STROBE checklist should include as the last sentence in the Methods section a sentence stating compliance with the appropriate guidelines/checklist.

Results: Present your results in a logical sequence in the text, tables, and illustrations. Do not repeat in the text all data in the tables and illustrations. The important observations should be emphasised.

Discussion: Summarise the findings without repeating in detail the data given in the Results section. Relate your observations to other relevant studies and point out the implications of the findings and their limitations. Cite other relevant studies.

Acknowledgements: Acknowledge only persons who have made substantive contributions to the study. Authors are responsible for obtaining written permission from everyone acknowledged by name because readers may infer their endorsement of the data and conclusions. Sources of financial support should be acknowledged.

5.3. References
References should quote the last name(s) of the author(s) and the year of publication (Black & Miller 1988). Three or more authors should always be referred to as, for example, (Fox et al. 1977).
A list of references should be given at the end of the paper and should follow the recommendations in Units, symbols and abbreviations: a guide for biological and medical editors and authors (1988), p. 52, London: The Royal Society of Medicine.

a) The arrangement of the references should be alphabetical by author's surname.

b) The order of the items in each reference should be:
(i) for journal references:
name(s) of author(s), year, title of paper, title of journal, volume number, first and last page numbers.
(ii) for book references:
name(s) of author(s), year, title of book, edition, volume, chapter and/ or page number, town of publication, publisher.

c) Author's names should be arranged thus: Daniels, J.A., Kelly, R.A. & Til, T.C.
Note the use of the ampersand and omission of comma before it. Author's names when repeated in the next reference are always spelled out in full.

d) The year of publication should be surrounded by parentheses: (1966).

c) The title of the paper should be included, without quotation marks.

f) The journal title should be written in full, italicised, and followed by volume number in bold type, and page numbers.
Examples:
Tonetti, M. S., Schmid, J., Hämmerle,C. H. & Lang, N. P. (1993) Intraepithelial antigen-presenting cells in the keratinized mucosa around teeth and osseointegrated implants. *Clinical Oral Implants Research* **4**: 177-186.
Poole, B., Ohkuma, S. & Warburton, M. (1978) Some aspects of the intracellular breakdown of erogenous and endogenous proteins. In: Segal, H.S. & Doyle, D.J., eds. Protein turnover and lysosome function, 1st edition, p. 43. New York: Academic Press.

We recommend the use of a tool such as Reference Manager for reference management and formatting. Reference Manager reference styles can be searched for here: www.refman.com/support/rmstyles.asp

5.4. Tables, Figures and Figure Legends

Tables: Tables should be numbered consecutively with Arabic numerals. Type each table on a separate sheet, with titles making them self-explanatory. Due regard should be given to the proportions of the printed page.

Figures: All figures should clarify the text and their number should be kept to a minimum. Details must be large enough to retain their clarity after reduction in size. Illustrations should preferably fill a single-column width (81 mm) after reduction, although in exceptional cases 120mm (double-column) and 168 mm (full page) widths will be accepted. Micrographs should be designed to be reproduced without reduction, and they should be dressed directly on the micrograph with a linear size scale, arrows, and other designators as needed. Each figure should have a legend

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