**UNIVERSIDADE FEDERAL DO CEARÁ**
**FACULDADE DE FARMÁCIA, ODONTOLOGIA E ENFERMAGEM**
**PROGRAMA DE PÓS-GRADUAÇÃO EM ODONTOLOGIA**

**DIEGO SANTIAGO DE MENDONÇA**

# ACURÁCIA DE MEDIDAS LINEARES DOS SEIOS MAXILAR E FRONTAL NA ESTIMATIVA DO SEXO DE INDIVÍDUOS DO NORDESTE BRASILEIRO: UM ESTUDO COM TOMOGRAFIAS COMPUTADORIZADAS *MULTISLICE*

**FORTALEZA**
**2020**

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Dissertação apresentada ao Programa de Pós-Graduação em Odontologia da Faculdade de Farmácia, Odontologia e Enfermagem da Universidade Federal do Ceará, como um dos requisitos para a obtenção do título de Mestre em Odontologia.

Área de Concentração: Clínica Odontológica

Orientador: Prof. Dr. Fábio Wildson Gurgel Costa.
Coorientadora: Profa. Dra. Andréa Silvia Walter de Aguiar

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Aprovada em: ___/___/_____.

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Ao meu pai, José Audísio de Mendonça Lima
*(in memoriam).*

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Salmo 23:4

## RESUMO

O processo de identificação humana representa um dos aspectos mais relevantes no campo das ciências forenses. Poucos estudos relacionados ao dimorfismo sexual avaliaram a acurácia de medidas lineares dos seios frontal e maxilares em tomografias computadorizadas *multislice* (TCM). A presente investigação teve como objetivos: (1) avaliar parâmetros de acurácia na estimativa do sexo através dos seios maxilar e frontal em TCM de indivíduos adultos brasileiros; (2) desenvolver e validar uma nova fórmula matemática para diferenciar homens e mulheres. Uma pesquisa transversal em duas fases foi conduzida com uma amostra estatisticamente estimada de 140 TCM: fase 1) desenvolvimento de uma fórmula baseada em ambos os seios (50 homens e 50 mulheres); fase 2) estudo de validação (20 homens e 20 mulheres). As medidas lineares dos seios frontal e maxilares (altura, largura e diâmetro) foram avaliadas usando o *software* RadiAnt DICOM. Com base em uma abordagem estatística multivariada, uma nova fórmula combinando os seios paranasais foi desenvolvida e validada. Foram criadas curvas *receiver operating characteristic* (ROC) e obtidos valores de sensibilidade, especificidade, valores preditivos positivos e negativos, acurácia e razão de verossimilhança. Além disso, a influência da idade foi avaliada por meio de análise estatística de subgrupo. Os homens apresentaram maiores valores médios de largura, altura e diâmetro dos seios paranasais estudados ($p < 0,05$). Os seios maxilares foram melhores preditores para estimar o sexo do que os seios frontais (acurácia entre 61-74% e 58-69%, respectivamente). A maior precisão foi encontrada com a distância entre os seios maxilares direito e esquerdo (74%). A fórmula para estimativa do sexo mostrou sensibilidade de 80%, especificidade de 95,5% e uma acurácia de 87,5%. Em indivíduos com idade superior a 30 anos houve uma redução de 63,1% no número de valores preditivos para estimativa do sexo. As medidas dos seios frontal e maxilar foram preditores adequados de dimorfismo sexual em uma amostra brasileira. Ambos os seios paranasais apresentaram melhor estimativa do sexo masculino e a acurácia mais significativa ocorreu nos seios maxilares. Foi encontrada alta precisão com a distância entre os seios maxilares direito e esquerdo. A fórmula baseada em abordagem estatística multivariada forneceu uma melhor precisão na discriminação de homens e mulheres.



**Palavras-chave:** seios paranasais, dimorfismo sexual, seio maxilar, seio frontal, tomografia computadorizada.

## ABSTRACT

The human identification process represents one of the most relevant aspects of the forensic sciences field. Few studies related to sex dimorphism have evaluated the accuracy of linear measurements of frontal and maxillary sinuses on *multislice* computed tomographies (MCT). This investigation aimed to: (1) evaluate parameters of accuracy in sex estimation of maxillary and frontal sinuses on MCT of Brazilian adult individuals; (2) develop and cross-validate a new formula for discriminating males and females. Two-phase cross-sectional research was conducted with a statistically estimated sample of 140 MCTs: phase 1) development of a formula based on both sinuses (50 males and 50 females); phase 2) validation study (20 males and 20 females). Frontal and maxillary sinuses linear measurements (height, width, and diameter) were assessed using the RadiAnt DICOM software. Based on a multivariate statistical approach, a new formula combining both paranasal sinuses was developed and further validated. Receiver operating characteristic (ROC) curves, the area under the curve (AUC), sensitivity, specificity, positive and negative predictive values, accuracy, and likelihood ratio were obtained. Also, the influence of age was evaluated by subgroup statistical analysis. Men showed higher mean values of width, height, and diameter of the studied paranasal sinuses ($p<0.05$). The maxillary sinuses were a better predictor of sex estimation than frontal sinus (accuracy between 61-74% and 58-69%, respectively). The highest accuracy was found with the distance between the right and left maxillary sinuses (74%).The formula for sex estimation showed a sensitivity of 80%, specificity of 95.5%, and an accuracy of 87.5%. In individuals aged > 30 years, there was a 63.1% reduction in predictive values for sex estimation. Frontal and maxillary sinuses measurements were adequate predictors for sexual dimorphism in a Brazilian sample. Both paranasal sinuses showed a better estimation of males, and the most significant accuracy occurred with maxillary sinuses. High precision was found with the distance between the right and left maxillary sinuses. The multivariate statistics-based formula provided a better precision in discriminating males and females.



**Keywords:** paranasal sinuses, sexual dimorphism, maxillary sinus, frontal sinus, computed tomography.

## LISTA DE ABREVIATURAS E SIGLAS

| | |
|---|---|
| DS | Dimorfismo sexual |
| SF | Seio frontal |
| SM | Seio maxilar |
| SP | Seios paranasais |
| TC | Tomografia computadorizada |
| TCFC | Tomografia computadorizada de feixe cônico |
| TCM | Tomografia computadorizada *multislice* |

**SUMÁRIO**

## 1 INTRODUÇÃO GERAL

Os conceitos anatômicos dos seios paranasais (SP) tornaram-se amplamente estudados desde o final do século XIX e início do século XX (VIVEK; KHANDELWAL, 2010), o que torna a função dos SP ainda um tema de debate. O desenvolvimento e persistência dos seios em humanos tem estimulado a discussão sobre a vantagem evolutiva de manter um sistema tão complexo (ARSLAN; AYDINLIOĞLU; BOZKURT; EGELI, 1999).

Nesse contexto, as fossas nasais e os SP são áreas de significativa variabilidade e complexidade estruturais, em que a tomografia computadorizada (TC) constitui-se em um exame de eleição na avaliação pré-operatória e no estudo de doenças inflamatórias nasossinusais. Este exame, particularmente com o sistema de reconstrução tridimiensional, tem sido crescentemente utilizado nas últimas décadas visando à definição de parâmetros de imagem nasossinusais. Além disso, tal modalidade de exame tem mostrando concordância com os resultados de estudos de dissecção anatômica (ARSLAN; AYDINLIOĞLU; BOZKURT; EGELI, 1999).

A integração tridimensional na avaliação imaginológica corresponde a uma ferramenta de suporte para um bom planejamento cirúrgico. Contudo, a aquisição de imagem e os relatórios imaginológicos são frequentemente incompletos no que diz respeito a variações anatômicas, cuja importância é reconhecida na cirurgia endoscópica e em cirurgias relacionadas, principalmente pelo seu possível envolvimento patogênico e pelos riscos operatórios associados (MARQUES *et al.*, 2011).

Dessa maneira, os SP assumiram uma significância maior nos últimos tempos devido a avanços tanto no campo de procedimentos cirúrgicos como no uso de tecnologias de imagem. Entretanto, é mister reportar que, além dessas aplicabilidades anteriormente citadas, tais estruturas anatômicas passaram a ter o seu devido reconhecimento no âmbito das ciências forenses, especialmente no que diz respeito ao processo de identificação humana. Este, por sua vez, é definido como um processo pelo qual se determina a identificação de uma pessoa ou de uma coisa (DELWING, 2013).

De fato, a identificação de restos humanos é um dos aspectos de grande relevância no contexto da antropologia forense. A determinação do sexo de indivíduos desconhecidos tem sido considerada de grande importância no processo de investigação para se obter a correta identificação *post-mortem* (HAMED; EL-BADRAWY; ABDEL FATTAH, 2014; VIDYA; *et al.*, 2013). Esse processo ganha maior destaque em circunstâncias de desastres em massa

naturais ou provocados pelo homem e nos casos em que o corpo é decomposto ou desmembrado, como nas tentativas de ocultar deliberadamente a identidade do indivíduo (MATHUR; *et al.*, 2013).

A estimativa do sexo é considerada um passo importante na reconstrução do perfil biológico de um indivíduo desconhecido no âmbito forense. Pesquisas com esse propósito têm utilizado, por exemplo, os dentes como ferramenta adicional para a distinção entre indivíduos do sexo masculino e feminino devido a sua capacidade de resistir à destruição no período pós-morte. Entretanto, vale destacar que o dimorfismo sexual (DS) pode ser realizado utilizando-se outras estruturas do corpo humano e as variações esqueléticas mais proeminentes entre os sexos são as da pelve óssea e dos ossos adjacentes, especialmente aquelas que contribuem para a formação da articulação do quadril, ou seja, o acetábulo e a cabeça do fêmur (PAPALOUCAS; FISKA; DEMETRIOU, 2008; ZORBA; MORAITIS; MANOLIS, 2011).

Em situações extremas como explosões, guerras e outros desastres em massa, o crânio e outros ossos, com frequência, apresentam-se gravemente desfigurados. Em tais casos, como o de vítimas que são incineradas, tem sido relatada a utilização do seio maxilar (SM) no processo de identificação em virtude de o mesmo permanecer intacto (KAJOAK *et al.*, 2013). Da mesma maneira, o seio frontal (SF) é considerado como sendo uma estrutura anatômica muito resistente a um trauma, sendo provável que esteja preservado em cadáveres desmembrados ou mesmo carbonizados (AKHLAGHI *et al.*, 2016).

Diferentes métodos de aquisição de imagem têm sido empregados para estimativa do sexo em osteologia forense, tais como radiografias digitais, imagens de ressonância nuclear magnética e exames tomográficos (KRISHAN *et al.*, 2016). Um exemplo atual que ilustra a relevância de métodos modernos de imagem consiste no uso da *virtopsy*, que vem ganhando destaque no campo da investigação forense. Esta técnica emprega métodos de imagem tridimensionais (3D) rotineiramente usados na medicina, além de patologia forense, radiologia, computação gráfica, biomecânica e física. Ela consiste em uma varredura de superfície 3D usada para mapear a superfície externa do corpo em que é possível gravar e documentar imagens com riqueza de detalhes (BADAM *et al*, 2017).

Embora pesquisas relacionadas ao estudo do DS venham também sendo realizadas com tomografias computadorizadas de feixe cônico (TCFC) (GAMBA *et al.*, 2017), a tomografia computadorizada *mulitslice* (TCM), ou multidetectores, oferece informação útil previamente à necropsia, auxiliando, por exemplo, no desvendamento de características de corpos severamente desfigurados (NAIKMASUR *et al.*, 2009). Além disso, as medidas lineares

obtidas em imagens de TCM (resolução de 0,6 mm) e TCFC (resolução de 0,25 mm) foram consideradas precisas e exatas (GAIA *et al.,* 2014).

A realização do presente trabalho é justificada pela importância da estimativa do sexo através dos seios paranasais e a escassez de estudos brasileiros de acurácia com TCM cuja avaliação tenha considerado em conjunto medidas lineares dos seios maxilar e frontal.

Na literatura pertinente ao tema, observa-se uma lacuna nas pesquisas empreendidas na área, que tenham desenvolvido e validado uma fórmula matemática que envolva medidas de diferentes seios paranasais para fins de distinção entre homens e mulheres.

# 2 REVISÃO DE LITERATURA

## 2.1 Aspectos gerais do SM e SF

Os SM são cavidades preenchidas por ar, localizados no osso maxilar, que podem exibir variados tamanhos e formas. Suas paredes são delgadas, revestidas internamente por uma membrana, e seu ápice pode se estender ao processo zigomático e ocupar o osso zigomático (UTHMAN *et al.*, 2010). Além disso, na região de assoalho constituído pelo processo alveolar, as raízes dos primeiros, segundos e terceiros molares, bem como as raízes dos caninos podem elevar tais SP ou, em algumas situações, ocasionar a perfuração do assoalho sinusal (KAJOAK *et al.*, 2013).

Geralmente, os SM, não são vistos no exame de imagem ao nascer. Nessa fase do desenvolvimento humano apresentam-se como um saco arredondado e raso. Logo entre o primeiro e o quarto ano de vida o processo de pneumatização ocorre de forma rápida. Por volta dos 7 anos de idade, o assoalho do SM atinge o nível do meato inferior. Entre os 12 e 14 anos, o indivíduo exibe o assoalho do SM ao nível do assoalho da cavidade nasal. Após isso, um processo lento de pneumatização continua até os 20 anos de idade.

Além das diversas variações anatômicas, como hipoplasia, pneumatização, presença de septos antrais ou exostose óssea, alterações patológicas também são bastante comuns; as quais incluem espessamento da mucosa, sinusite, cisto de retenção de muco, descontinuidade do assoalho do seio, lesões polipóides, descontinuidade da parede lateral do seio ou presença de corpos estranhos.

Dentre as estruturas anatômicas mais estudadas e com repercussão clínica cita-se o septo maxilar, cuja anatomia pode ser fator de complicação durante osteotomia para fins de confecção e posterior remoção de janela óssea de acesso durante o procedimento cirúrgico de elevação do assoalho do SM (BETTS; MILORO, 1994). Como resultado, essa variação anatômica está frequentemente associada à perfuração da membrana sinusal (ARDEKIAN2006; HERNÁNDEZ-ALFARO; TORRADEFLOT; MARTI, 2008). Dessa maneira, o conhecimento da localização e morfologia dos septos do seio é essencial na fase de planejamento quanto à melhor abordagem cirúrgica (LOZANO-CARRASCAL *et al.*, 2017; WEN; CHAN; WANG, 2013).

Os SF, por sua vez, desenvolvem-se como extensão das células aéreas etmoidais anteriores. Na população em geral, estão ausentes em 5% e hipoplásicos em 4% dos indivíduos. Os SF bem pneumatizados apresentam margens típicas recortadas com septos internos intactos. Deiscências focais dentro da parede posterior dos seios frontais podem ser identificadas no plano sagital. Seu desenvolvimento embriológico é formado pela continuação do recesso frontal

(STAMMBERGER; KENNEDY, 1995). A pneumatização do SF é altamente variável, alernando de aplasia a hiperplasia, mesmo entre gêmeos monozigóticos e dentro do mesmo indivíduo (KJÆR; PALLISGAARD; BROCK-JACOBSEN, 2012).

Encontram-se comumente em número de dois, no espaço da díploe, entre as paredes externa e interna do osso frontal, geralmente de tamanho e extensão diferentes e separados por um septo ósseo na linha média. Ocasionalmente, um dos SF apresenta tamanho reduzido ou mesmo pode encontrar-se ausente. A drenagem do seio é realizada através do recesso frontal, uma estrutura em formato de ampulheta, que geralmente drena para o meato médio em 62% dos pacientes e para o infundíbulo etmoidal em 38% dos casos (LANDSBERG; FRIEDMAN, 2001). É considerado o seio mais desafiador frente a abordagens cirúrgicas devido a sua anatomia complexa e proximidade com a órbita e a lamela lateral da placa cribiforme (NAIDOO *et al.*, 2012; WORMALD, 2005).

**2.2 Estimativa do sexo por meio do SM e SF**

A avaliação do DS é uma alternativa que vem sendo utilizado há muitos anos dentro das ciências forenses com fins de identificação humana. Esta avaliação mostra-se mais acurada em indivíduos adultos, uma vez que sofrem menos influências morfológicas do que as estruturas ósseas de indivíduos mais jovens na fase de puberdade, como por hormônios que controlam o crescimento e desenvolvimento dos ossos (ANUTHAMA *et al.*, 2011; FRANKLIN *et al.*, 2012).

Na população contemporânea existe uma relativa escassez de padrões morfométricos específicos para a estimativa do sexo em achados ósseos de pessoas desconhecidas. Esta é basicamente uma comprovação histórica da falta ou da má documentação do aproveitamento de esqueletos humanos disponíveis para o estudo (KHANPETCH *et al.*, 2012; NAIKMASUR; SHRIVASTAVA; MUTALIK, 2010; REJTAROVA *et al.*, 2009).

A TC tem a capacidade de facilitar o trabalho de antropólogos e patologistas forenses, proporcionando aos mesmos uma identificação mais rápida e precisa (KHANPETCH *et al.*, 2012). Estudos anteriores indicaram que a análise morfométrica do seio maxilar TC é um método bem-sucedido. Além disso, foi apresentado como um método rápido e eficaz de identificação (AMIN; HASSAN, 2012; TEKE *et al.*, 2007; UTHMAN *et al.*, 2011).

Embora tenham sido reportados estudos sobre a anatomia dos seios paranasais, considera-se que ainda existam dimensões do SM e de estruturas circundantes que precisam ser melhor investigadas (SAHLSTRAND-JOHNSON *et al.*, 2011). Diferentes estudos que utilizaram os SM como fatores para determinação do sexo mostraram que o tamanho e outras

medições tomográficas podem ser úteis no contexto da medicina forense. (AKHLAGHI *et al.*, 2017; AKHLAGHI *et al.*, 2016; AMIN; HASSAN, 2012; JEHAN; BHADKARIA *et al.*, 2014; KANTHEM *et al.*, 2015; SAHLSTRAND-JOHNSON *et al.*, 2011; TAMBAWALA *et al.*, 2016; TEKE *et al.*, 2007).

# 3 OBJETIVOS

## 3.1 Objetivo Geral

Estimar o sexo por meio de parâmetros morfométricos dos seios frontal e maxilar em TCM de indivíduos adultos do nordeste brasileiro.

## 3.2 Objetivos Específicos

- Avaliar especificidade, sensibilidade e acurácia de medidas lineares relativas ao SF, na estimativa do sexo, em TCM de indivíduos brasileiros;
- Avaliar especificidade, sensibilidade e acurácia de medidas lineares relativas aos SM, na estimativa do sexo, TCM de indivíduos brasileiros;
- Desenvolver e validar uma fórmula matemática (equação da reta) de estimativa do sexo a partir da combinação de parâmetros quantitativos dos SF e SM em TCM de indivíduos brasileiros.

## 4 PROPOSIÇÃO

A presente dissertação será apresentada por meio do seguinte capítulo: *Forensic assessment of maxillary and frontal sinuses measurements in sex estimation based on multislice computed tomography among Brazilian adults: a STROBE-compliant study*.

## 5 CAPÍTULO

A presente dissertação será baseada no Artigo 46 do Regimento Interno do Programa de Pós-Graduação em Odontologia da Universidade Federal do Ceará que regulamenta o formato alternativo para dissertações de Mestrado e teses de Doutorado e permite a inserção de artigos científicos de autoria ou coautoria do candidato. Por se tratar, em parte, de pesquisa envolvendo seres humanos, o projeto de pesquisa referente ao trabalho desenvolvido foi submetido à apreciação prévia pelo Comitê de Ética em Pesquisa Envolvendo Seres Humanos do Instituto Dr. José Frota, em conformidade com a Resolução nº 466, de 12 de dezembro de 2012, do Conselho Nacional de Saúde, sob número de parecer de aprovação 2.253.923 (CAAE 67591217.2.0000.5047) (Anexo A).

Desta forma, a dissertação é composta pelo capítulo único descrito: *Forensic assessment of combined maxillary and frontal sinuses measurements in sex estimation based on multislice computed tomography among Brazilian adults: a STROBE-compliant study*. O presente artigo será submetido à publicação na revista "Forensic Science International" (On-line version ISSN 0379-0738; Fator de impacto: 1.990; Qualis CAPES vigente: A2) (Anexo B).

## 5.1 CAPÍTULO ÚNICO

**TITLE:**

**Forensic assessment of maxillary and frontal sinuses measurements in sex estimation based on *multislice* computed tomography among Brazilian adults: a STROBE-compliant study**

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**Highlights:**

- Frontal and maxillary sinuses measurements were adequate predictors for sexual dimorphism in a Brazilian sample.
- A new formula for sex estimating was developed and validated, considering linear measurements of two paranasal sinuses.
- Men showed higher mean values of width, height, and diameter of the studied paranasal sinuses.
- The highest accuracy value was found with the distance between the right and left maxillary sinuses.

**ABSTRACT**

The human identification process represents one of the most relevant aspects of the forensic sciences field. Few studies related to sex dimorphism have evaluated the accuracy of linear measurements of frontal and maxillary sinuses on multislice computed tomographies (MCT). This investigation aimed to: (1) evaluate parameters of accuracy in sex estimation of maxillary and frontal sinuses on MCT of Brazilian adult individuals; (2) develop and cross-validate a new formula for discriminating males and females. Two-phase cross-sectional research was conducted with a statistically estimated sample of 140 MCTs: phase 1) development of a formula based on both sinuses (50 males and 50 females); phase 2) validation study (20 males and 20 females). Frontal and maxillary sinuses linear measurements (height, width, and diameter) were assessed using the RadiAnt DICOM software. Based on a multivariate statistical approach, a new formula combining both paranasal sinuses was developed and further validated. Receiver operating characteristic (ROC) curves, the area under the curve (AUC), sensitivity, specificity, positive and negative predictive values, accuracy, and likelihood ratio were obtained. Also, the influence of age was evaluated by subgroup statistical analysis. Men showed higher mean values of width, height, and diameter of the studied paranasal sinuses ($p<0.05$). The maxillary sinuses were a better predictor of sex estimation than frontal sinus (accuracy between 61-74% and 58-69%, respectively). The highest accuracy was found with the distance between the right and left maxillary sinuses (74%).The formula for sex estimation showed a sensitivity of 80%, specificity of 95.5%, and an accuracy of 87.5%. In individuals aged > 30 years, there was a 63.1% reduction in predictive values for sex estimation. Frontal and maxillary sinuses measurements were adequate predictors for sexual dimorphism in a Brazilian sample. Both paranasal sinuses showed a better estimation of males, and the most significant accuracy occurred with

maxillary sinuses. High precision was found with the distance between the right and left maxillary sinuses. The multivariate statistics-based formula provided a better precision in discriminating males and females.

**Keywords:** paranasal sinuses, sexual dimorphism, maxillary sinus, frontal sinus, computed tomography.

## Introduction

The process for human remains identification is one of the most relevant aspects of forensic sciences. This process has received considerable attention in circumstances of individuals involved in natural calamities or mass disasters where the deceased person is decomposed, dismembered, skeletonized, or burnt, as well as in criminal situations related to attempts of hiding individual's identity [1, 2].

It is noteworthy that sexual determination tools are useful in biological profile reconstruction, especially in unknown individuals. In forensic odontology, human teeth have been commonly used for the distinction between males and females since dental units can resist postmortem period deterioration. Sexual dimorphism is a well-recognized prominent area in forensic and anthropological fields that can assess several body-related structures, including the skull, pelvis, long bones, foramen magnum, and paranasal sinuses [3, 4]. Among human bones, after pelvis, skull components have been considered the second part of the skeleton estimation of sex [5].

Osteometry has been a preferable approach to discriminate males and females since high accuracy values, such as 77-92% [6] and 72-95.5 [7], are described in the literature. In extreme situations such as explosions, wars, and different types of mass disasters, the skull and other bones may be severely disfigured. However, in cases of incinerated victims, it has been reported that the maxillary sinus (MS) remains intact and, thus, this anatomic structure can be used for identification purposes [8]. Similarly, the frontal sinus (FS) has been preserved in dismembered or carbonized corpses mainly because of its high resistance to traumatic injuries, as previously reported [9].

Skull-related morphological aspects have been reported as a potential method for sexual dimorphism; however, there is no specific feature [5]. Thus, the estimation of sex based on the craniofacial structures, such as paranasal sinuses, should be considered a

topic of interest in forensic research because it may address population-specific parameters to the current literature. Considering that the paranasal sinuses show a significant inter-individual variation [10], imaging studies may provide substantial scientific evidence about paranasal sinus-based sex estimation.

Nowadays, computed tomography is a usual imaging technique among forensic institutes worldwide, and its application on skeletal bones has received continuous attention in attempts of sex estimation [11]. Additional aspects that favor the use of this x-ray exam in *postmortem* investigations are its common clinical application in the preoperative assessment of paranasal sinus and adjacent structures, as well as its high accuracy of details even in severely disfigured corpses [12]. Also, computed tomography assessment has been validated by different forensic science groups [13-15].

Few *in vivo* studies related to sex dimorphism have evaluated accuracy parameters of linear measurements of frontal [9, 16] or maxillary [17-21] sinuses on *multislice* computed tomography (MCT). Thus, the study's primary goal was to evaluate the specificity, sensitivity, and accuracy in sex estimation of maxillary and frontal sinuses linear measurements based on MCT of Brazilian adult individuals. Furthermore, this research aimed to develop and cross-validate a new formula for discriminating males and females.

## Material and Methods

### *Study design and ethics statement*

This cross-sectional investigation was performed after approval by the Ethics and Research Committee (number 2.253.923) of Dr. José Frota Hospital (Ceará, Brazil) and followed the Declaration of Helsinki principles. It was conducted according to the

*Strengthening the Reporting of Observational studies in Epidemiology* (STROBE) Statement [22].

*Sample*

It was evaluated MCT data from individuals who were referred to Dr. José Frota Hospital imaging between May and June 2017. Two investigators initially analyzed the image hospital database until obtaining the necessary sample since it included all MCT scans required for different clinical purposes (e.g., cranial trauma and maxillofacial injuries assessment).

One hundred and forty MCT volumes were used in a two-phase study: (1) development of a formula based on maxillary and frontal sinuses measurements (n=100 images from 50 males and 50 females); (2) validation of the new formula through a random Brazilian sample of MCTs that was not used in phase 1 (n=40 images from 20 males and 20 females). All MCT scans were evaluated according to the eligibility criteria by two investigators (DSM and ASWA). The inclusion criteria were imaging exams from individuals aged 18 to 40 years, clearly showing at least the frontal and maxillary sinuses, and the presence of posterior maxillary teeth (at least first premolar to the second upper molar). Data from duplicated exams, images that revealed pathology or fractures signs, signs suggesting facial growth disorders or craniofacial syndromes, any metallic (maxillary dental implants and osteosynthesis materials) or motion artifacts, and low-quality diagnostic images impairing the sinus-related structure's assessment were excluded.

The Student's t-test estimated 50 MCT per group to obtain a representative sample (90% of power and assuming a 95% confidence interval). About the sample size estimation, it was considered the study of Sherif et al., [23] that found a statistically

significant difference between males and females regarding an FS anteroposterior measurement (6.90±2.30 vs. 8.76±3.25 mm, respectively).

*Variables*

The dichotomic variable analyzed in the present study included sex. Quantitative data were linear measurements.

*Image acquisition process*

MCT data were obtained using a single scanner (Somatom Emotion 6, Siemens, Forchheim, Medical Solutions, Germany) under the following acquisition protocol: 1mm of table increment, 130 kVp, milliamperage ranging from 80 to 120 mA, cross-section image thickness up to 2.0 mm, 180 mm FOV, and 0.6 seconds of rotation time. The same computer (Dell Inc., model G3 3590, Intel® Core ™ processor i5-9300H CPU @ 2.40GHz, 2400 Mhz, 4 colors, 8 logic processors - LED HD backlight screen) was used to perform all analyses, and the *Digital Imaging and Communications in Medicine* (DICOM) files were imported to the free software RadiAnt (Medixant, Poznan- Poland), version 4.6.9.18463 (64 bit).

A trained observer (DSM) performed all evaluations in a dedicated room with dimmed light. The evaluator was free to modify the brightness of the screen during the analysis, and up two exams were evaluated per study shift aiming to prevent visual fatigue since an approximate total of 45 minutes per scan was necessary to perform all measurements. Initially, head orientation and tomographic alignment were performed to ensure that all measurements were perpendicular to the horizontal plane. Then, axial, sagittal, and coronal sections were obtained to guide the observer. During this process, an axial view-related parallel plane to the hard palate, in the coincident sagittal section with anterior nasal spine and posterior nasal spine, was used as a reference landmark in this study (Figure 1).

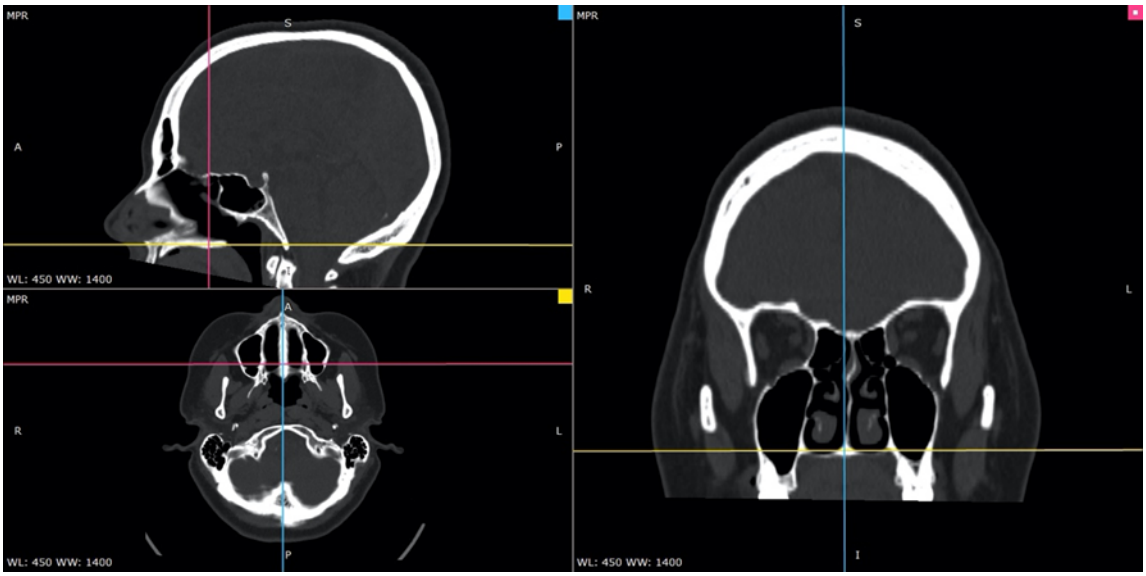


Figure 1 - Definition of positioning parameters to measure frontal and maxillary sinuses in the sagittal, axial, and coronal planes.

Through axial and coronal images, the highest linear measurements were estimated (Table 1 and Figure 2). Also, to improve the accuracy of the measurements, after determining the section with the largest measurement (main image), all linear assessments were repeated in two slices above and two sections below the main segment. Then, for each evaluated variable in this study, the mean of these five values was adopted (Figures 1 and 2).

Table 1 - Definition of the adopted morphometric parameters.

| | **Spatial view** | **Parameter** | **Paranasal sinus** |
|---|---|---|---|
| **Maximum distance between upper and lower sinus borders** | Coronal | Height | Frontal and maxillary |
| **Maximum distance between anterior and posterior sinus walls** | Axial | Diameter | Frontal and maxillary |
| **Maximum distance between medial and lateral sinus walls** | Axial | Individual width | Maxillary |

| | | | |
|---|---|---|---|
| **Maximum distance between external limits of the sinus walls** | Axial | Maximum width | Frontal and maxillary |

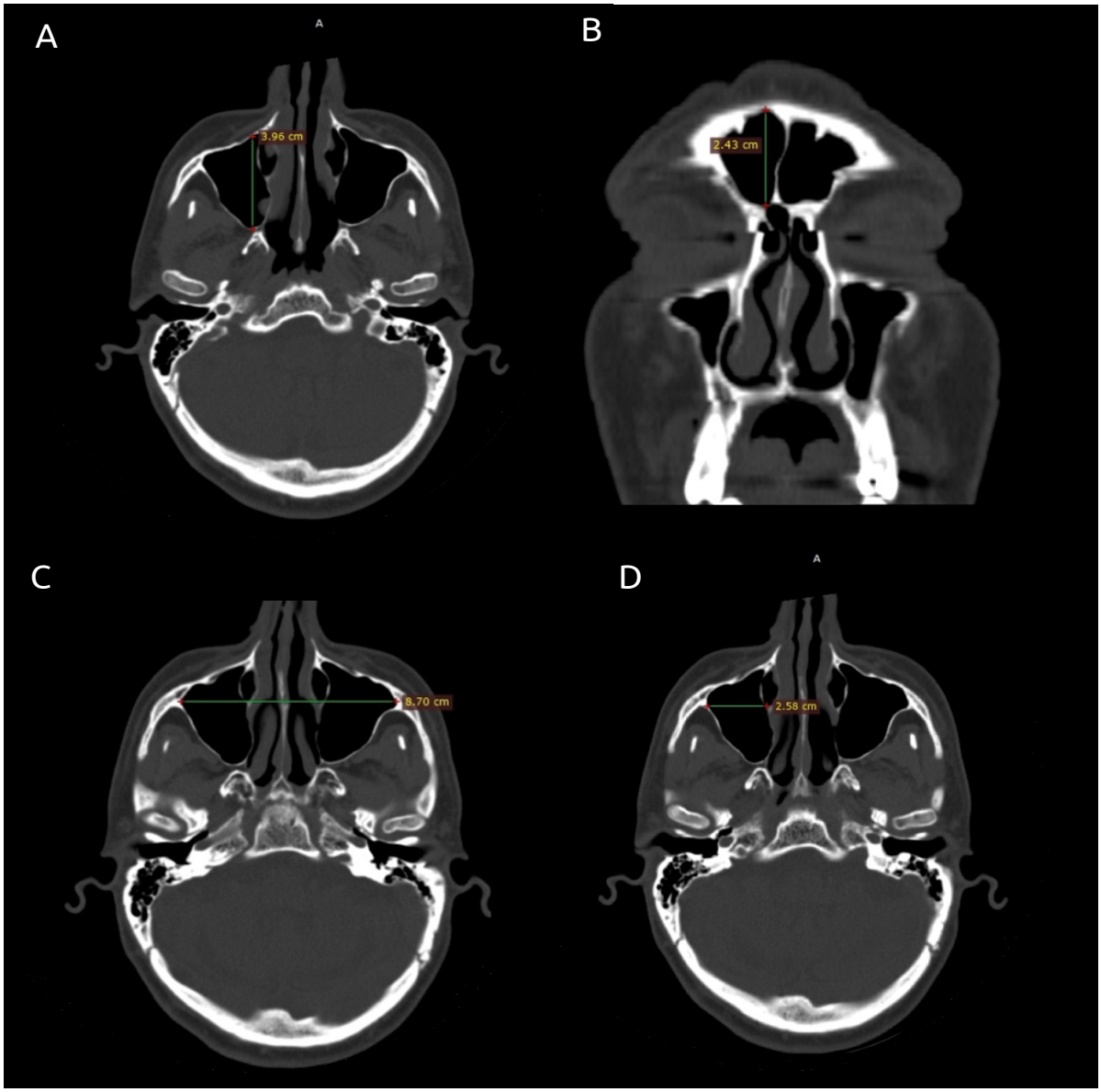


Figure 2 - A) Maximum distance between anterior and posterior sinus walls (diameter); B) maximum distance between upper and lower sinus borders (height); C) maximum distance between the external limits of the MS (maximum width); D) Maximum distance between medial and lateral sinus walls of the MS (individual width).

*Measurement training and study error*

To minimize the occurrence of measurement bias, the observer (DSM) that performed the analysis in this study was previously trained by senior investigators (FWGC and LMK) with experience in oral and maxillofacial radiology. Firstly, an image dataset of randomly selected MCT scans was evaluated in a blind process. After a 15-day interval, the same procedure was repeated to obtain the intrarater agreement. Data were assessed using SPSS version 20.0 (IBM Corporation, Sommers, NY, USA) for Windows (Microsoft Corporation, Redmond, WA, USA), and their analysis was based on a paired t-test, Pearson's correlation, and intraclass correlation coefficient (ICC) to assess systematic errors. A random bidirectional effect model with a 95% confidence interval and $p < 0.05$ were used to estimate the ICC. The intraclass correlation coefficient (ICC) assessed intraobserver reproducibility according to the Koo and Li [25] reliability criteria: poor (< 0.5), moderate (0.5-0.74), good (0.75-0.9), and excellent (> 0.9).

*Development and validation of a sex estimation-related formula*

A linear regression model was estimated for each measurement to predict female and male sex correctly. Correlation coefficients were used to create a mathematical formula using the frontal and maxillary sinuses (isolated or combined). To validate the formula, a random sample of MCT scans from Brazilian individuals (20 males and 20 females) was assessed. The validation method followed the recommendations of Farias-Gomes et al., [26], which were the selection of tomographic images in a broader age range and inclusion of individuals regardless of the presence or absence of posterior maxillary teeth.

*Bias*

Some aspects were considered to minimize the occurrence of bias [20]: (1) selection bias - planning was carried out regarding the sample size calculation to estimate

adequate and equally divided samples between males and females; (2) sample selection - the dental status was standardized, and potential confounding factors (i.e., suggestive signs of pathological changes or bone fractures) were avoided; (3) measurement errors - image examinations were conducted by a trained observer, who was blind to the gender of each image, and it was performed the reliability of the measurements.

*Statistical methods*

All analyses were performed by an investigator (PGBS) using SPSS version 20.0 (IBM Corporation, Armonk, NY, USA), with a 95% confidence level. Regarding the validation of the five measurements per MTC volume, the Cronbach's alpha was used as a measure of internal consistency, the ICC was obtained to evaluate systematic error, and the Hotelling's T-Squared statistic (multivariate counterpart of the t-test) was performed to calculate the random error.

The Kolmogorov-Smirnov test was used to test the normality of the data. The linear measurements are expressed as mean and standard deviation (SD), and categorical data are expressed in absolute and relative frequencies. Bivariate analysis was performed using the Student t-test (linear measurements between males and females). The coefficient of variation was also calculated, and the variance regarding sex was compared using the Levene test. The measurements of the MS on the right and left sides were compared using the paired t-test.

Receiver operating characteristic (ROC) curves were developed to identify cutoff points related to sexual dimorphism and obtain the area under the curve (AUC), sensitivity, specificity, positive and negative predictive values, accuracy, and likelihood ratio. In an age-related subgroup analysis, sensitivity, specificity, positive and negative predictive values, accuracy, and likelihood ratio for individuals up to 30 years of age and those older than 30 years were calculated.

## Results

*Reliability*

The confidence of the method was significant for linear sinus measurements, varying from satisfactory (r = 0.822) to highly satisfactory (r = 0.997). The paired t-test did not reveal a statistically significant difference between the first and second measurements. The ICC showed satisfactory values, ranging from 0.896 to 0.998.

*Reproducibility analysis*

The validation analysis (Table 2) of the FS measurements showed excellent Cronbach's alpha (> 0.800) and ICC (> 0.800) values, as well as significant Hotelling's T-Squared correlation (p <0.001). The measurements of the MS, on both sides, showed excellent values for maximum height and maximum width regarding the Cronbach's alpha (> 0.800), ICC (> 0.800), and Hotelling's T-Squared correlation (p <0.001).

*Men showed higher mean values of paranasal sinuses measurements.*

The mean maximum height (p = 0.018) and width (p = 0.201), as well as the diameter (p <0.001) of the FS (both sides), were significantly higher in men (Table 3). Also, males showed increased values of the following MS measurements in comparison with females: maximum height (right side, p <0.001; left side, p = 0.001), maximum width (right side, p =0.011; left side, p = 0.001), diameters (right side, p=0.011; left side, p=0.004).

Regarding data variance, this measure of statistical dispersion was significantly higher for maximum height (p = 0.035) and diameter (p = 0.001) of the FS. In the MS, the diameter was significantly higher in men than in women when evaluated the right (p = 0.015) and left (p = 0.048) sides (Table 2).

Table 2: Sample characterization and reproducibility analysis of the MS to discriminate males and females.

| | **Validation coefficients** | | | **Mean±SD (cm)** | | | | **Variation coefficient** | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Cronbach´s alpha** | **Hotelling's T-Squared** | **ICC** | **Total** | **Females** | **Males** | **p-value[a]** | **Females** | **Males** | **p-value[b]** |
| FS height | 0.999 | <0.001 | 0.997 | 2.92±1.13 | 2.65±0.93 | 3.19±1.26 | 0.018 | 35.1% | 39.5% | 0.035 |
| FS width | 0,993 | <0.001 | 0.967 | 5.21±1.73 | 4.99±1.59 | 5.43±1.85 | 0.201 | 31.9% | 34.1% | 0.406 |
| FS diameter | 0.993 | <0.001 | 0.967 | 1.12±0.39 | 0.96±0.26 | 1.28±0.43 | <0.001 | 27.1% | 33.6% | 0.001 |
| RMS height | 0.999 | <0.001 | 0.994 | 3.65±0.49 | 3.48±0.45 | 3.82±0.47 | <0.001 | 12.9% | 12.3% | 0.699 |
| RMS width | 0.999 | <0.001 | 0.994 | 2.83±0.51 | 2.70±0.42 | 2.95±0.56 | 0.011 | 15.6% | 19.0% | 0.337 |
| RMS diameter | 0.998 | 0.074 | 0.998 | 3.92±0.38 | 3.83±0.25 | 4.02±0.46 | 0.011 | 6.5% | 11.4% | 0.015 |
| LMS height | 0.999 | <0.001 | 0.999 | 3.67±0.50 | 3.51±0.45 | 3.84±0.49 | 0.001 | 12.8% | 12.8% | 0.966 |
| LMS width | 0.999 | <0.001 | 0.994 | 2.82±0.49 | 2.66±0.41 | 2.98±0.51 | 0.001 | 15.4% | 17.1% | 0.287 |
| LMS diameter | 0.947 | 0.351 | 0.781 | 3.92±0.36 | 3.82±0.27 | 4.02±0.41 | 0.004 | 7.1% | 10.2% | 0.048 |
| $MS_{(x--[R;L])}$ | 1.000 | 0.028 | 0.998 | 8.59±0.94 | 8.21±0.97 | 8.96±0.74 | <0.001 | 11.8% | 8.3% | 0.467 |

SD, standard deviation; FS, frontal sinus; MS, maxillary sinus; R, right; L, left; ($\bar{x}$[R;L]), arithmetic mean between R and L measurements; [a]Student t-test; [b]Levene's test; ICC = intraclass correlation coeficient.

*MS were significant predictors of sexual dimorphism*

The ROC curves-based (Figure 3) cutoff points for estimating sexual dimorphism are shown in Table 4. Most AUCs were significantly higher than the null axis of the ROC curve (> 0.500). The higher AUC value was observed in the maximum width of the MS (0.756±0.049).

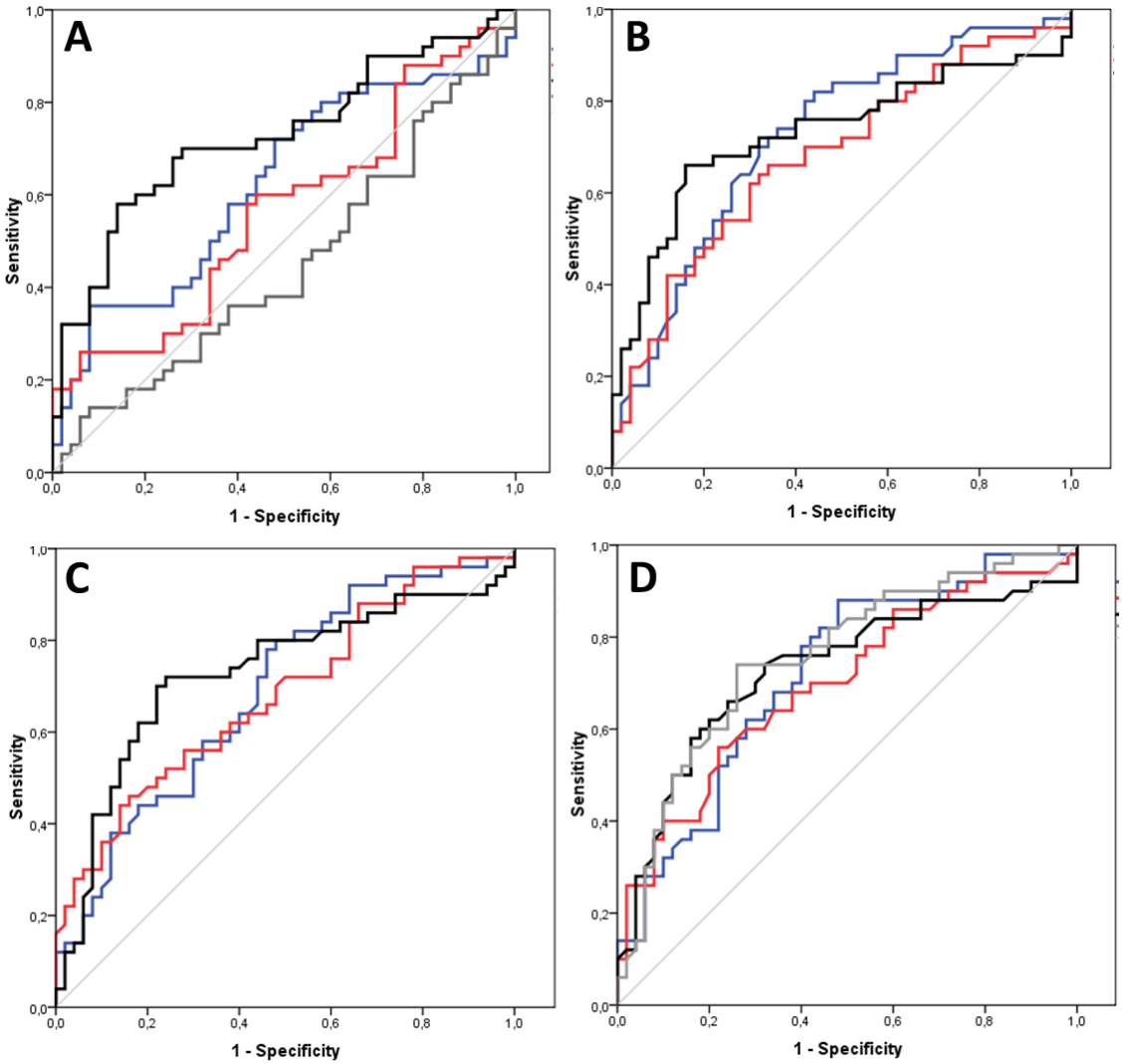


Figure 3 - ROC curves demonstrating cutoff values, sensitivities, and specificities of the FS (A), right MS (B) and left MS (C), and both MS (D). Blue line = maximum height; red line = RS maximum width or MS individual width; black line = diameter; grey line = MS maximum width.

According to Table 3, the best sensitivity in estimating male sex was observed in the maximum MS width (74.0%). Among females, the MS diameters on the left (82.0%) and right (78.0%) sides, and the mean diameters of both sides (80.0%) showed the most significant values of specificity. The highest accuracy was observed in the mean maximum width (74.0%) with the highest likelihood ratio (8.10; 95% CI = 3.31-19.80).

*Age-related subgroup analysis*

Age-frequency distribution based on gender is shown in Table 4. Patients aged up to 30 years showed a reduction in the number of predictive values for sex estimation (35.4%). In the 30 years old age subgroup, this reduction was 63.1 %.

In the 30 years old age subgroup, the highest sensitivity in identifying the male sex was observed in the width between both MS (76.9%), and the highest specificities in identifying the female sex were found in the left MS diameter (83.9%). The highest accuracy was observed in the width between both MS (78.6%). In CT scans of patients over 30 years of age, the highest sensitivity in identifying the male gender was observed in the FS height (90.9%), the highest specificity in identifying the female gender was found in the FS diameter (84.2%). The highest accuracy was observed in the FS diameter measure (80.0%).

Table 3: Summary of sensitivity, specificity, positive/negative predictive values, accuracy, and likelihood ratio for the study variables (cm) to estimate sex.

| | **Estimated sex** | | **Sens.** | **Spec.** | **PPV** | **PNV** | **Accuracy** | **LR** |
|---|---|---|---|---|---|---|---|---|
| | **F** | **M** | **(M)** | **(F)** | **(M)** | **(F)** | | **(95% CI)** |
| | **(n=50)** | **(n=50)** | | | | | | |
| FS height | 26 | 35 | 70.0% | 52.0% | 59.3% | 63.4% | 61.0% | 2.53 (1.11-5.74) |
| FS width | 29 | 29 | 58.0% | 58.0% | 58.0% | 58.0% | 58.0% | 1.91 (0.86-4.22) |
| FS diameter | 34 | 35 | 70.0% | 68.0% | 68.6% | 69.4% | 69.0% | 4.96 (2.12-11.58) |
| RMS height | 34 | 34 | 68.0% | 68.0% | 68.0% | 68.0% | 68.0% | 4.52 (1.95-10.46) |
| RMS width | 34 | 32 | 64.0% | 68.0% | 66.7% | 65.4% | 66.0% | 3.78 (1.65-8.65) |
| RMS diameter | 39 | 33 | 66.0% | 78.0% | 75.0% | 69.6% | 72.0% | 6.88 (2.83-16.74) |
| LMS height | 32 | 29 | 58.0% | 64.0% | 61.7% | 60.4% | 61.0% | 2.46 (1.10-5.49) |
| LMS width | 37 | 26 | 52.0% | 74.0% | 66.7% | 60.7% | 63.0% | 3,08 (1.33-7.15) |
| LMS diameter | 41 | 30 | 60.0% | 82.0% | 76.9% | 67.2% | 71.0% | 6.83 (2.73-17.09) |
| MS height$_{(x\text{--}[R;L])}$ | 34 | 31 | 62.0% | 68.0% | 66.0% | 64.2% | 65.0% | 3.47 (1.52-7.90) |
| MS width$_{(x\text{--}[R;L])}$ | 35 | 30 | 60.0% | 70.0% | 66.7% | 63.6% | 65.0% | 3.50 (1.53-8.01) |
| MS diameter$_{(x\text{--}[R;L])}$ | 40 | 30 | 60.0% | 80.0% | 75.0% | 66.7% | 70.0% | 6.00 (2.45-14.68) |
| Width between both MS | 37 | 37 | 74.0% | 74.0% | 74.0% | 74.0% | 74.0% | 8.10 (3.31-19.80) |

M, male; F, female; FS, frontal sinus; MS, maxillary sinus; R, right; L, left; ($x^{--}$[R;L]), arithmetic mean between R and L measurements; Sens., sensibility; spec., specificity; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood; CI, confidence interval.

Table 4: Variation of predictive values of sex estimation according to age groups.

| | Up to 30 years | | | | | > 30 years | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Sens. (M) | Spec. (F) | PPV (M) | PNV (F) | Accuracy | Sens. (M) | Spec. (F) | PPV (M) | PNV (F) | Accuracy |
| Frontal sinus height | **-5.9%** | **-0.4%** | 3.2% | **10.1%** | **-2.4%** | 20.9% | 0.6% | **-6.7%** | 27.5% | 5.7% |
| Frontal sinus width | 3.5% | **-9.6%** | 2.0% | **-8.0%** | **-2.3%** | **-12.5%** | 15.7% | **-8.0%** | 12.0% | 5.3% |
| Frontal sinus diameter | **-0.8%** | **-9.9%** | **-1.1%** | **-9.4%** | **-4.7%** | 2.7% | 16.2% | 4.1% | 14.8% | 11.0% |
| R maxillary sinus height | 1.2% | 3.0% | 7.0% | **-3.3%** | 2.0% | **-4.4%** | **-4.8%** | **-18.0%** | 7.0% | **-4.7%** |
| R maxillary sinus width | 2.7% | 6.2% | 9.8% | **-1.5%** | 4.0% | **-9.5%** | **-10.1%** | **-23.8%** | 3.4% | **-9.3%** |
| R maxillary sinus diameter | 0.7% | **-0.6%** | 3.8% | **-4.7%** | **-0.6%** | **-2.4%** | 0.9% | **-11.4%** | 9.3% | 1.3% |
| L maxillary sinus height | 3.5% | 3.7% | 8.9% | **-2.1%** | 3.3% | **-12.5%** | **-6.1%** | **-23.2%** | 4.3% | **-7.7%** |
| L maxillary sinus width | 4.4% | 3.4% | 9.2% | **-2.2%** | 2.7% | **-15.6%** | **-5.6%** | **-26.7%** | 4.3% | **-6.3%** |
| L maxillary sinus diameter | 4.1% | 1.9% | 6.4% | **-2.2%** | 1.9% | **-14.5%** | **-3.1%** | **-21.3%** | 4.2% | **-4.3%** |
| Maxillary sinus height ($x^{--}$[R;L]) | 2.1% | 6.2% | 9.8% | **-2.0%** | 3.6% | **-7.5%** | **-10.1%** | **-23.1%** | 4.6% | **-8.3%** |
| Maxillary sinus width ($x^{--}$[R;L]) | 4.1% | 10.6% | 13.9% | 0.5% | 6.4% | **-14.5%** | **-17.4%** | **-31.0%** | **-1.1%** | **-15.0%** |
| Maxillary sinus diameter ($x^{--}$[R;L]) | 1.5% | 0.6% | 5.0% | **-4.2%** | 0.0% | **-5.5%** | **-1.1%** | **-15.0%** | 8.3% | 0.0% |
| Width between both maxillary sinuses | 2.9% | 6.6% | 9.3% | **-0.5%** | 4.6% | **-10.4%** | **-10.8%** | **-24.0%** | 1.0% | **-10.7%** |

M, male; F, female; FS, frontal sinus; MS, maxillary sinus; R, right; L, left; ($x^{--}$[R;L]), arithmetic mean between R and L measurements; Sens., sensibility; spec., specificity; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood; CI, confidence interval; $x^{--}$ = arithmetic mean between left and right measurements. Bold numbers represent reduced values of accuracy measures.

*Formula for sex estimation and external validation*

A multiple linear regression model was designed to obtain adjusted beta values, which were inserted in a linear formula to estimate sex [26]. Based on coefficients of collinearity with sex, the following formula was constructed to discriminate females (value < 0) and males (value > 0):

| | |
|---|---|
| Sex = | 0.196*(A) - 0.406*(B) + 0.446*(C) + 0.318*(D) + 0.176*(E) – 0.168*(F) + 0.060*(G) |

Where: A, FS height; B, FS width; C, FS diameter; D, MS width; E, arithmetic mean between right and left MS height; F, arithmetic mean between right and left MS width; G, arithmetic mean between right and left MS diameter.

Then, a ROC curve with a statistically significant AUC (0.757±0.002; [CI 95% = 0.619 - 0.894]; p = 0.002) was plotted, and it was estimated an optimal cutoff point value of 2.23 (Figure 4). Additionally, we performed a sample size calculation to estimate the number of cases to external validation. Based on the best measurement of this study (frontal sinus diameter: females = 0.96±0.26, males = 1.28±0.43), 20 patients per group were necessary to perform the validation of the formula according to a statistical approach (power 80% and confidence 95%; t-test).

In an independent sample consisting of 20 CT scans of females and 20 CT scans of males that were not part of the original studied sample, this cutoff point showed a sensitivity of 80.0% (males), a specificity of 95.5% (females), the positive predictive value of 94.1% (males), the negative predictive value of 82.6% (females), and likelihood ratio of 76.00 (CI05% = 7.70 – 750.49) as shown in Table 5.

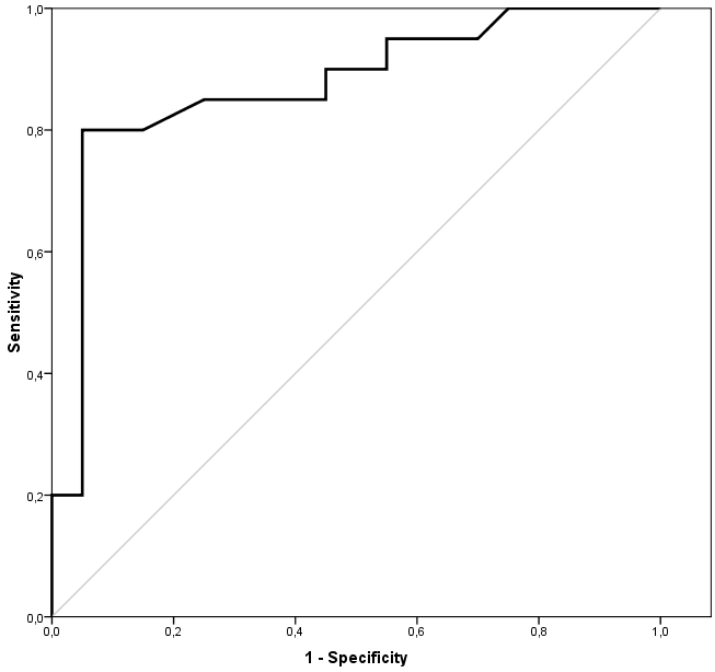


Figure 4 - ROC to establish an optimal cutoff point value for estimating sex.

Table 5 - Summary of sensitivity, specificity, positive/negative predictive values, accuracy, and likelihood ratio for the external validation of the formula created to estimate sex.

| **Estimated sex** | | **Sens.** | **Spec.** | **PPV** | **PNV** | **Accuracy** | **LR** |
|---|---|---|---|---|---|---|---|
| **F** | **M** | **(M)** | **(F)** | **(M)** | **(F)** | | **(95% CI)** |
| **(n=20)** | **(n=20)** | | | | | | |
| 19 | 16 | 80.0% | 95.5% | 94.1% | 82.6% | 87.5% | 76.00 (7.70-750.49) |

Sens., sensibility; spec., specificity; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood; CI, confidence interval; M, male; F, female.

**Discussion**

The present research evaluated MTC images for maxillary and frontal sinuses sexual dimorphism purposes. Previous studies have used conventional radiographs of the craniofacial complex [5, 27, 28], cone beam computed tomography (CBCT) [12], and magnetic resonance imaging to estimate sex. There are scarce studies on MTC that developed and validated formula for estimating sex combining frontal and maxillary sinuses morphometric (linear distances) measurements [23]. To the best of our knowledge, there are no published Brazilian studies with similar methodological aspects to date.

Besides applications of MTC in surgical procedures, the usefulness of this method in estimating sex has been limited explored through the years for both frontal and maxillary sinuses; in fact, a few numbers of diagnostic accuracy studies evaluating both paranasal sinuses on MTC has been published to date (Table 9). Since this imaging method requires standardized measurement methods to obtain reliable results, the present investigation used validated coefficients (Cronbach´s alpha, Hotelling's T-Squared, and ICC) to assess the intraobserver agreement. We found an almost perfect agreement, which was similar to Sahlstrand-Johnson et al [10]. Also, it should be highlighted that a mean value was obtained considering five consecutive MTC slices, which guaranteed higher fidelity in the measures.

This crossectional investigation adopted a convenience sample of MCT scans to compare males and females based on maxillary and frontal sinuses tridimensional measurements. It was used a dataset of MCT with large FOV since imaging exams following this parameter were necessary and justified regarding clinical and surgical planning purposes. Although MCT is an x-ray exam that emits a higher dose of radiation than CBCT [29], most patients with cranial trauma and maxillofacial injuries have been referred to hospital radiology departments to perform craniofacial MCT. A previous study

showed similar precision and accuracy of linear measurements obtained from MCT (0.6 mm resolution) and CBCT (0.25 mm resolution). Another advantage of MCT in comparison to CBCT is the high accuracy in measuring soft tissues, which plays substantial importance during orthognathic surgery preoperative planning [30].

In the context of forensic sciences, the paranasal sinuses are highly individual, comparable to fingerprints. This finding supports the use of the FS contours in situations that require quantitative reasoning for forensic identification [16]. Regarding the MS, although there are published studies focused on their anatomical aspects, Sahlstrand-Johnson et al., [10] mentioned that there are still dimensions related to these structures that need to be investigated. Thus, both paranasal sinuses assessed in this study are currently recommended in the literature on sex dimorphism. Also, the development of a formula combining measurements from two paranasal sinuses has not been reported to date, which reinforces the relevance of this research. Further studies in other population-based samples may be conducted with a similar study design to evaluate the accuracy of frontal and maxillary sinuses in discriminating males and females.

Both paranasal sinuses showed significantly higher measurement values among males than in females, which are in agreement with FS-related data of studies from Brazil [31] and Iraq [32], and MS findings among individuals from Iraq [17, 21] and Turkey [33]. Also, the present results were obtained from a miscegenated population, since its ancestry has shown the mixture to be predominantly European and Amerindian populations (refer), which partially explains different values compared with other studies. Farias-Gomes et al., [26] highlighted some factors that can influence these differences: sample size, age, type of imaging exam, measurement methods, and statistical protocol.

The right MS height showed a sensitivity of 68% in identifying the male gender, which was higher than in female individuals. Previous studies from non-Brazilian

populations [9, 10, 17, 18, 33-36] also showed the height as a useful variable in sex estimation due to their ability to provide a faster identification and facilitate the work of anthropologists [37]. Other sinus linear measurements performed in this study (width and diameter) have been considered significant for gender differentiation among computed tomograph-designed studies [38, 39].

The FS was assessed for sexual dimorphism in 2014 by Belaldavar et al., [40], who evaluated width, height, and sinus area on posteroanterior plain radiographs from an Indian sample. These authors found a sex estimation index of 64.6%, a value found within the present study range (61% to 69% for linear measurements). Regarding FS measurements, Luo et al., [24] considered medium significance for sex estimation when they used the area and an index calculated between the height and width. The accuracy of the FS height and width in our study was 61 to 58%, respectively, confirming its significance when used as parameter for discriminating males and females.

The most significant accuracy values for the estimation of sex regarding the type of paranasal sinus were 74% (MS) and 69% (FS) in this research. In a Turkish population study [33], the MS accuracy rate was 69.3%. Ekizoglu et al., [20], with a similar population and methods, found an accuracy of 77.1%. Uthman et al., [21] measured the MS, also employing CT evaluation, in an Iraqi population, and the authors found an overall accuracy of 73.9% for sex estimation. Akhlaghi and collaborators concluded two distinct investigations with Iraqis individuals. Their first study [9] did not recommend FS parameters to estimate sex among Persian adults. The study performed in 2017 [17] showed that in young Iranian adults, the MS width had a considerable accuracy (65.6%) in identifying the correct sex.

The mean width between the right and left MS showed an accuracy of 74% and a likelihood ratio of 8.10 for correctly identifying men, emphasizing the role of this

measurement on MCT scans in the field of sex dimorphism investigation. This finding was similarly found in the Iranian population-based studies [9, 17, 21] that also observed a high sensitivity in identifying the male gender using the MS.

Our study obtained accuracy values for the diameter of the right and left MS of 72% and 71%, respectively; right and left MS width were 66% and 63%, respectively; the height of the right MS showed a 68% rate. Regarding males, Ekizoglu et al., [20] obtained the highest precision rates when assessed the diameter of the right MS (75.7%) and the mean height between both MS (71.4%). Uthman et al., [21] found a 60.5% accuracy rate for the right MS width and 72.1% for the opposite side.

High precision for sex estimation was observed with the maximum distance between both MS (74%) and the FS diameter (69%), while the low accuracy rate was related to the left MS width and FS width. In a study evaluating the MS, the best variables were the height and the anteroposterior diameter of the left MS [21]. Teke et al., [33] reported low accuracy (67.7%) for linear measurements in the left MS and the distance between both MS, which contrast with the present results. Concerning the FS, Akhlaghi et al, [17] reported precision of 61.3% for the left side height and a low rate (51.3%) for the width of the right side.

We also developed and validated a mathematical equation to estimate sex in a sample of adult individuals from Northeast Brazil. There is a limited comparison with Brazilian published data due to differences in methodological approaches. Farias-Gomes et al., [26] reached an accuracy of 84% with a formula based on the three-dimensional volume of MS in CBCT images from a south-west Brazilian sample; however, that study used a single paranasal sinus, while our formula used a multivariate statistical approach based on frontal and MS linear measurements. Wanzeler et al, [41] reported that the chances of correctly estimating sex through CBCT-based volumetric analyzes were

96.2% and 92.7% for men and women from North Brazil, respectively. Nevertheless, these authors included the sphenoidal sinus in their formula, which was not performed in the present study.

Regarding the validation study, the formula reliability was tested in another sample of Brazilians without restriction for age or the presence of posterior teeth as recommended in a previous investigation of sex dimorphism [26]. The cross-validated formula showed moderate accuracy (74%) and lower error. Although the present formula used simple and relatively easy-to-apply anthropometric measures of selected paranasal sinuses, it should be previously validated if applied to other ethnic groups in further investigations.

In the current investigation, with advancing age, the accuracy measures related to the MS were significantly reduced, which may be explained by bone resorption and age-related degenerative changes. Akhlaghi et al., [17] found an age influence on the reduction of predictive MS anthropometric indices for sex estimation. Regarding individuals aged over 30 years, the FS provided better measures of accuracy to estimate sex, which was also reported in the literature [17].

This investigation presents some limitations. Due to rigorous eligibility criteria, a sample of one hundred MCT scans was included. Although a non-larger population was included in this study, which was similar to Sherif et al., [23] that evaluates MCT of 100 adult Egyptians, we adopted a sample size calculation to minimize selection bias. There was a relatively subjective selection of the slice with the highest measure; however, it was found substantial intrarater observer agreement, and a mean for five consecutive measurements (thickness of 0.6-2.0 mm) was adopted in the present methodology. The developed formula was based on a linear relationship between specific measurements and a category (0 = female; 1 = male), which does not always exist in gender estimation;

therefore, intersection ranges between variables can influence the final sex estimation. However, we must highlight that the adopted multivariate model was able to determine different weights for each measurement in an inter-associated approach. After this adjustment, it was possible to develop a formula with a sensitivity of 80% and specificity of 95.5%, which are substantial values for forensic studies purposes.

We believe that a multivariate statistics-based formula may provide a better precision in discriminating males and females. We suggested this approach in future investigations using other imaging exam modalities or evaluating other bones for sex dimorphism purposes.

## Conclusion

In this investigation, higher mean values of the studied paranasal sinuses were mainly found in men. The most significant accuracy values for sex estimation were observed with MS, followed by FS. High precision was observed with the distance between the right and left MS. Also, the developed and validated formula showed high precision for sex estimation. In the field of forensic sciences, the present data highlight the importance of MCT-based morphometric assessment of FS and MS as a complementary tool for sex estimation.

## Conflict of interest

The authors declare that they have no conflict of interest.

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None declared.

## Credit Author Statement

**Diego Santiago de Mendonça:** Methodology, Investigation, Writing- Original draft preparation

**Francisco Samuel Rodrigues Carvalho:** Software, Validation, Visualization

**Paulo Goberlânio de Barros Silva:** Data curation, Formal analysis

**Lúcio Mitsuo Kurita:** Data curation, Review and Editing

**Andréa Silvia Walter de Aguiar:** Writing- Review and Editing

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Table 6 – Characterization of accuracy studies in sexual dimorphism using MCT to evaluate linear measurements in frontal and maxillary sinuses.

| Authors | Continent | Country | Sample (F/M) | MCT unit | Paranasal sinus | Linear measurements | Best linear measurement | AUC | Cutoff point (mm) | Sens. (%) | Spec. (%) | PPV (%) | NPV (%) | Accuracy (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Akhlaghi et al.[9] | Asia | Iran | 100/100 | Siemens 64 Slice | Frontal | Maximum AP dimension, width, and height | Left max. height | NI | 21 | 61 | 59 | 60 | 40 | 61.3 |
| Uthman et al., [16] | Asia | Iraq | 45/45 | Siemens Somatom Plus 4 | Frontal | Width, height, AP length, distance between the highest points of the two sinuses, distance between the highest points of each sinus to its max. lateral limit | Left height | NI | NI | NI | NI | NI | NI | 76.95 |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Akhlaghi et al.[17] | Asia | Iran | 144/144 | NI | Maxillary | Max. AP dimension, width, height, and distance between the sinuses | Max. distance between the sinuses | 0.656 | 83.5 | 56.3 | 75 | 69.2 | 63.2 | 65.6 |
| Uthman et al.[21] | Asia | Iraq | 45/43 | Siemens Somatom Emotion | Maxillary | Max. width, length, height, and total distance across both sinuses | Left height | NI | 42 | 76.7 | 68.9 | 71.2 | NI | 72.7 |
| Amin and Hassan[18] | Africa | Egypt | 48/48 | GE Medical Systems | Maxillary | AP, transverse and cephalocaudal diameters, and size | Left cephalocaudal diameter and size | NI | NI | NI | NI | NI | NI | 70.8 |
| Ekizoglu et al.[20] | Europe | Turkey | 70/70 | Siemens Medical Solutions | Maxillary | AP, transverse, and cephalocaudal diameters | Right AP diameter | NI | 35.7 | 74.3 | 80.7 | 78.8 | NI | NI |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Attia et al., [19] | Africa | Egypt | 34/39 | NI | Maxillary | Max. width, length, height, and total distance across both sinuses | Right height | 0.706 | NI | 74 | 38 | 66 | 70 | 68 |
| Dangore-Kashbage & Bhowate [42] | Asia | India | 100/100 | Siemens Healthnineers | Maxillary | Mediolateral, superoinferior and anteroposterior | Left superoinferior | NI | NI | NI | NI | NI | NI | 71.5 |

F, Female; M, male; Max., maximum; AP, anteroposterior; AUC, area under the curve; Sens., sensitivity; Spec., specificity; PPV, positive predictive value; NPV, negative predictive value; NI, not informed.

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# 6 CONCLUSÃO

Considerando-se os resultados obtidos e as limitações inerentes ao presente estudo, as conclusões podem ser sumarizadas da seguinte forma:

1. A análise do seio frontal mostrou que a maior sensibilidade em identificar o sexo masculino foi observada através da altura máxima e diâmetro, bem como as maiores especificidades em identificar o sexo feminino foram observadas com base no diâmetro. A maior acurácia foi observada por meio da média da largura máxima e a maior razão de verossimilhança foi encontrada por meio do diâmetro.

2. A análise dos seios maxilares mostrou que a maior sensibilidade em identificar o sexo masculino foi relativa à largura máxima e a maior especificidade em identificar o sexo feminino foi observada com o diâmetro do lado esquerdo. A maior acurácia foi obtida por meio da média da largura máxima, a qual apresentou a maior razão de verossimilhança.

3. Baseado nos coeficientes de colinearidade com o sexo, obtidos das medidas lineares do seio frontal e da média dos seios maxilares, foi possível elaborar e validar uma equação, que demonstrou adequadas medidas de acurácia para fins de dimorfismo sexual (sensibilidade de 80,0% para o sexo masculino e especificidade de 95,5% para o sexo feminino).

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# ANEXO A - PARECER DO COMITÊ DE ÉTICA EM PESQUISA

INSTITUTO DR. JOSÉ FROTA - IJF/ PREFEITURA DE FORTALEZA

## PARECER CONSUBSTANCIADO DO CEP

**DADOS DA EMENDA**

**Título da Pesquisa:** Tomografia computadorizada em feixe em leque em traumatologia bucomaxilo facial.

**Pesquisador:** Andréa Silvia Walter de Aguiar
**Área Temática:**
**Versão:** 2
**CAAE:** 67591217.2.0000.5047
**Instituição Proponente:** Instituto Dr. José Frota - IJF/ Prefeitura de Fortaleza
**Patrocinador Principal:** Financiamento Próprio

**DADOS DO PARECER**

**Número do Parecer:** 2.253.923

**Apresentação do Projeto:**
O trauma é causa mais comum de morbidade e mortalidade, em especial em jovens e adultos-jovens. As fraturas faciais, por sua vez, configuram-se em 18% de todos os traumatismos do corpo humano. As fraturas faciais apresentam critérios peculiares no diagnóstico e planejamento cirúrgico, visto que são frequentemente múltiplas, complexas e assimétricas. Para uma melhor compreensão, análises a tomografia computadorizada (TC)
tornou-se uma ferramenta imprescindível principalmente na interpretação de fraturas
complexas, assim como na possibilidade de classificação de severidade das fraturas.A
sobreposição de imagens e de fragmentos ósseos faz com que a TC se torne método
radiográfico de primeira escolha para esta finalidade, definindo os traços de fratura, localização, extensão e deslocamentos. Inúmeros trabalhos vêm demonstrando a real viabilidade de se obter a reconstrução em 3D, aprimorando a qualidade da imagem e sua aplicabilidade na área da traumatologia. A TC com reconstrução multiplanar (RMP) produz uma interpretação mais correta que as radiografias convencionais para muitas fraturas.
O diagnóstico precoce das fraturas faciais é fundamental para o seu tratamento adequado e para o estabelecimento de um prognóstico favorável. Será realizado primário, observacional, longitudinal, prospectivo e individualizado em exames tomográficos

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de face, de um grande hospital de referência em Fortaleza. Trata-se de um estudo quantitativo, observacional, individuado, descritivo, transversal baseado em investigações que observaram causa e efeito, simultaneamente.

**Objetivo da Pesquisa:**

Geral: Estudar a severidade dos traumatismos faciais a partir de exames tomográficos, em pacientes atendidos em um hospital de emergência de uma cidade do Nordeste brasileiro.

Objetivos Específicos:

1.Traçar perfil epidemiológico das fraturas faciais no período de um ano;

2. Realizar avaliação objetiva das fraturas faciais a partir de exame tomográfico;

3. Classificar a severidade do traumatismo facial a partir da classificação da AO para fraturas do esqueleto craniomaxilo facial;

4. Elaborar um algoritmo de severidade de traumatismo facial de interesse ao exame tomográfico.

**Avaliação dos Riscos e Benefícios:**

Para realização da pesquisa serão obedecidos e respeitados todos os aspectos éticos expressos na Resolução nº 466 de 2012, do Conselho Nacional de Saúde/ Ministério da Saúde, que traz as Diretrizes e Normas Regulamentadoras de pesquisas com seres humanos e em conformidade com a norma do CONEP (Comissão Nacional de Ética em Pesquisa) (BRASIL, 2012). Em virtude de implicações legais, e a fim de manter os princípios éticos, as identidades dos sujeitos se configuram como sigilosos.

Como benefícios vão ser estudados os graus de severidade de traumatismos. Haverá a possibilidade de institucionalização de protocolos imaginológico de severidade do trauma na assistência às vítimas acidentes e violência. O benefício para sociedade é traduzido na detecção precoce de graus de fraturas faciais, e no conhecimento procedente da pesquisa que contribuirá para desenvolvimento de métodos efetivos de diagnóstico imaginológico de pacientes internados vítimas de acidentes ou violência física interpessoal.

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**Comentários e Considerações sobre a Pesquisa:**

Pesquisa de grande relevância à cirurgia bucomaxilo facial para o estudo da severidade de fraturas faciais e desenvolvimento de métodos efetivos de diagnóstico imaginológico de pacientes internados vítimas de acidentes ou violência física interpessoal. A pesquisadora solicitou uma emenda ao projeto, já aprovado anteriormente pelo CEP/IJF, solicitado a inclusão deuma pesquisadora para colaborar na coleta de dados do estudo.

**Considerações sobre os Termos de apresentação obrigatória:**

Apresentados corretamente: Folha de rosto, Carta de Anuência (Chefe da Odontologia e Chefe do Serviço de Imagem), TCLE.

**Recomendações:**

Sem recomendações.

**Conclusões ou Pendências e Lista de Inadequações:**

Aprovado

**Considerações Finais a critério do CEP:**

Solicita-se ao pesquisador que após o término da pesquisa que seja enviado para o CEP/IJF os resultados, discussão e conclusão, via Plataforma Brasil, como notificação.

**Este parecer foi elaborado baseado nos documentos abaixo relacionados:**

| Tipo Documento | Arquivo | Postagem | Autor | Situação |
|---|---|---|---|---|
| Informações Básicas do Projeto | PB_INFORMAÇÕES_BÁSICAS_982107_E1.pdf | 19/08/2017 14:01:58 | | Aceito |
| Outros | Solicitacao_Coletador.jpeg | 19/08/2017 13:58:14 | Andréa Silvia Walter de Aguiar | Aceito |
| Outros | Curriculo_Juliana.pdf | 25/04/2017 10:19:54 | Andréa Silvia Walter de Aguiar | Aceito |
| Projeto Detalhado / Brochura Investigador | IJF_TC_Severidade_BMF_ProjetoFinal.pdf | 25/04/2017 10:18:26 | Andréa Silvia Walter de Aguiar | Aceito |
| Outros | IJF_TC_Severidade_BMF_Instrumento.pdf | 25/04/2017 10:11:45 | Andréa Silvia Walter de Aguiar | Aceito |
| Outros | CARTA_DE_ANUENCIA_TAMIA_VARELA.pdf | 25/04/2017 10:11:13 | Andréa Silvia Walter de Aguiar | Aceito |
| Outros | CARTA_DE_ANUENCIA_MANOEL_MELLO.pdf | 25/04/2017 10:10:45 | Andréa Silvia Walter de Aguiar | Aceito |
| Outros | IJF_Tomografia_Severidade_Cartaencaminhamento.pdf | 25/04/2017 10:09:13 | Andréa Silvia Walter de Aguiar | Aceito |

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| TCLE / Termos de Assentimento / Justificativa de Ausência | TERMO_FIEL_DEPOSITARIO_VICENTE.pdf | 25/04/2017 10:08:33 | Andréa Silvia Walter de Aguiar | Aceito |
| Folha de Rosto | IJF_TC_Folhaderosto.pdf | 25/04/2017 10:06:06 | Andréa Silvia Walter de Aguiar | Aceito |

**Situação do Parecer:**
Aprovado

**Necessita Apreciação da CONEP:**
Não

FORTALEZA, 01 de Setembro de 2017

**Assinado por:**
**Márcia Maria Pinheiro Dantas**
**(Coordenador)**

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# ANEXO B – NORMAS DE SUBMISSÃO DO PERIÓDICO *FORENSIC SCIENCE INTERNATIONAL*

**FORENSIC SCIENCE INTERNATIONAL**
An international journal dedicated to the applications of medicine and science in the administration of justice.

**AUTHOR INFORMATION PACK**

## TABLE OF CONTENTS



**ISSN:** 0379-0738

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### INTRODUCTION

*Forensic Science International* is a peer-reviewed, international journal for the publication of original contributions in the many different scientific disciplines comprising the forensic sciences. These fields include, but are not limited to, forensic pathology and histochemistry, toxicology (including drugs, alcohol, etc.), serology, chemistry, biochemistry, biology (including the identification of hairs and fibres), odontology, psychiatry, anthropology, the physical sciences, firearms, and document examination, as well as the many other disciplines where science and medicine interact with the law.

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2. Review Articles
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7. Preliminary Communications
8.Letters to the Editor
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**Announcement of Population Data**: these types of articles will be published in Forensic Science International: Genetics, only. Please submit these articles via https://www.evise.com/profile/api/navigate/FSIGEN.

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**Forensic Anthropology Population Data:** Although the main focus of the anthropology section of the journal remains on the publication of original research, authors are invited to submit their forensic anthropology population data articles by selecting the "Forensic Anthropology Population Data" article type on the online submission system. When submitting a Forensic Anthropology Population data article, please assure that "Forensic Anthropology Population Data" is included as one of the keywords. These forensic anthropology population data articles involve the application of already published and standardised methods of aging, sexing, determination of ancestry and stature and other well known diagnoses on different populations. This is at the heart of applied forensic anthropology. For example, in order to correctly assess age, stature or even sex of individuals of different ancestry or from different populations, it is fundamental that the method be tested on the specific population one is working on. In building the biological profile of a skeleton in order to aid identification, one needs to calibrate such techniques on the population of interest before applying them. The same may be true in a completely different scenario of anthropology, for example identifying criminals taped on video surveillance systems and aging victims of juvenile pornography. This section is dedicated to forensic anthropological population data and other types of updates (state of the art of particular issues, etc.), particularly concerning the following:

- Sexing
- Aging sub adult skeletal remains
- Aging adult skeletal remains
- Aging living sub adults and adults
- Determining ancestry
- Stature estimation
- Facial reconstruction
- Non metric trait distribution, pathology and trauma
- Positive identification of human skeletal remains
- Positive identification of the living

Forensic Anthropology Population Data articles will be published in abridged form in print (a clear, descriptive summary taken from the abstract), and the full length article will be published online only. Full citation details and a reference to the online article, including e-page numbers, will be published in the relevant print issue of the journal. All submitted manuscripts will be evaluated by a strict peer review process.

**Case Reports** will be accepted only if they contain some important new information for the readers.

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**Technical Notes** report new developments, significant advances and novel aspects of experimental and theoretical methods and techniques which are relevant for scientific investigations within the journal scope. Manuscripts of this type should be short (a few pages only). Highly detailed and specific technical information such as computer programme code or user manuals can be included as electronic supplements. The manuscript title must start with "Technical Note:".

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