

Challenges in cephalometric landmark identification in syndromic craniosynostoses: the role of 3D multislice computed tomography

Desafios na identificação de pontos cefalométricos nas craniossinostoses síndrômicas: o papel da tomografia computadorizada multislice 3D

Desafíos en la identificación de puntos cefalométricos en las craniosinostosis síndrómicas: el papel de la tomografía computarizada multislice 3D

DOI: 10.46919/archv7n2-002

Originals received: 4/6/2026

Acceptance for publication: 4/27/2026

Michelle Protzenko

PhD student in Health Sciences

Institution: Instituto Fernandes Figueira (FIOCRUZ)

Address: Av. Rui Barbosa, 716, Flamengo, Rio de Janeiro - RJ, CEP: 22250-020

E-mail: michelle.protzenko@gmail.com

Cesar Augusto Vianna de Araújo

PhD student in Health Sciences

Institution: Universidade Federal do Rio de Janeiro (UFRJ)

Address: R. Antônio Barros de Castro, 119, Cidade Universitária, Rio de Janeiro - RJ, CEP: 21941-853

E-mail: cesaraugusto06@gmail.com

Fernanda Rolemberg Riba

PhD in Biological Sciences – Biophysics

Institution: Instituto Fernandes Figueira (FIOCRUZ)

Address: Av. Rui Barbosa, 716, Flamengo, Rio de Janeiro - RJ, CEP: 22250-020

E-mail: fernanda.riba@fiocruz.br

Sayonara Maria de Carvalho Gonzalez

PhD in Biological Sciences – Biophysics

Institution: Universidade Federal do Rio de Janeiro (UFRJ)

Address: R. Antônio Barros de Castro, 119, Cidade Universitária, Rio de Janeiro - RJ, CEP: 21941-853

E-mail: sayonara.gonzalez@fiocruz.br

Juan Clinton Llerena Junior

PhD in Biological Sciences – Biophysics

Institution: Universidade Federal do Rio de Janeiro (UFRJ)

Address: R. Antônio Barros de Castro, 119, Cidade Universitária, Rio de Janeiro - RJ, CEP: 21941-853

E-mail: juan.llerena@fiocruz.br

ABSTRACT

Syndromic craniosynostoses are genetic disorders characterized by the premature fusion of cranial sutures, frequently associated with intracranial hypertension, remodeling of the inner cranial table, and midfacial hypoplasia. The "copper beaten" skull sign, resulting from the continuous action of cerebral pulsations on immature bone, produces digitiform impressions and a lace-like appearance of the calvaria, reflecting

structural alterations that compromise the definition of anatomical boundaries. Additionally, compression of anatomical structures in the hypoplastic midface contributes to difficulties in identifying cephalometric landmarks, particularly in two-dimensional imaging methods. This study aimed to evaluate the impact of these alterations on cephalometric landmark identification and to compare the accuracy of conventional radiography with three-dimensional multislice computed tomography. Patients with clinically and molecularly confirmed syndromic craniosynostoses were analyzed using radiographic and tomographic examinations, with cephalometric assessment performed in a three-dimensional multiplanar environment. A high prevalence of the copper beaten skull sign (85.7%) was observed, predominantly in Crouzon, Apert, and Pfeiffer syndromes, and was associated with greater difficulty in identifying cephalometric landmarks, particularly at the cranial base and midface. Multislice computed tomography demonstrated significant superiority over conventional radiography, providing improved anatomical definition, tissue differentiation based on Hounsfield units, and greater measurement reproducibility. It can be concluded that three-dimensional multislice computed tomography represents the method of choice for cephalometric evaluation in patients with syndromic craniosynostoses, contributing to improved diagnostic accuracy and more precise therapeutic planning.

Keywords: craniosynostosis, cephalometry, computed tomography, cranial base, craniofacial phenotype.

RESUMO

As craniossinostoses sindrômicas são distúrbios genéticos caracterizados pela fusão prematura de suturas cranianas, frequentemente associadas à hipertensão intracraniana, remodelação da tábua interna do crânio e hipoplasia de terço médio facial. O sinal do crânio "em cunha de cobre" (copper beaten skull), resultante da ação contínua das pulsações cerebrais sobre o osso imaturo, produz impressões digitiformes e aspecto rendilhado da calvária, refletindo alterações estruturais que comprometem a definição dos limites anatômicos. Além disso, a compressão das estruturas anatômicas na face média hipoplásica contribui para dificuldades na identificação de pontos cefalométricos, especialmente nos métodos de imagem bidimensionais. Este estudo objetivou avaliar o impacto dessas alterações na identificação de pontos cefalométricos e comparar a acurácia da radiografia convencional com a tomografia computadorizada multislice tridimensional. Pacientes com craniossinostoses sindrômicas confirmadas clínica e molecularmente foram analisados por meio de exames radiográficos e tomográficos, com avaliação cefalométrica realizada em ambiente multiplanar tridimensional. Observou-se alta prevalência do sinal do crânio em cunha de cobre (85,7%), predominantemente nas síndromes de Crouzon, Apert e Pfeiffer, associada à maior dificuldade na identificação dos pontos cefalométricos, especialmente na base do crânio e no terço médio facial. A tomografia computadorizada multislice demonstrou superioridade significativa em relação à radiografia convencional, proporcionando melhor definição anatômica, diferenciação tecidual baseada em unidades Hounsfield e maior reprodutibilidade das medidas. Conclui-se que a tomografia computadorizada multislice tridimensional representa o método de escolha para avaliação cefalométrica em pacientes com craniossinostoses sindrômicas, contribuindo para maior acurácia diagnóstica e planejamento terapêutico mais preciso.

Palavras-chave: craniossinostose, cefalometria, tomografia computadorizada, base do crânio, fenótipo craniofacial.

RESUMEN

Las craniosinostosis sindrômicas son trastornos genéticos caracterizados por la fusión prematura de suturas craneales, frecuentemente asociados con hipertensión intracranial, remodelación de la tabla interna del cráneo e hipoplasia del tercio medio facial. El signo del cráneo "batido en cobre" (copper beaten skull), resultante de la acción continua de las pulsaciones cerebrales sobre el hueso inmaduro, produce impresiones digitiformes y un aspecto encajado de la calvaria, reflejando alteraciones estructurales que comprometen la definición de los límites anatómicos. Además, la compresión de las estructuras anatómicas en el tercio

medio hipoplásico contribuye a las dificultades en la identificación de los puntos cefalométricos, especialmente en los métodos de imagen bidimensionales. Este estudio tuvo como objetivo evaluar el impacto de estas alteraciones en la identificación de puntos cefalométricos y comparar la precisión de la radiografía convencional con la tomografía computarizada multislice tridimensional. Se analizaron pacientes con craniosinostosis sindrómicas confirmadas clínica y molecularmente mediante exámenes radiográficos y tomográficos, con evaluación cefalométrica realizada en un entorno multiplanar tridimensional. Se observó una alta prevalencia del signo del cráneo batido en cobre (85,7%), predominantemente en los síndromes de Crouzon, Apert y Pfeiffer, asociada a una mayor dificultad en la identificación de los puntos cefalométricos, especialmente en la base del cráneo y el tercio medio facial. La tomografía computarizada multislice demostró una superioridad significativa sobre la radiografía convencional, proporcionando mejor definición anatómica, diferenciación tisular basada en unidades Hounsfield y mayor reproducibilidad de las medidas. Se concluye que la tomografía computarizada multislice tridimensional representa el método de elección para la evaluación cefalométrica en pacientes con craniosinostosis sindrómicas, contribuyendo a una mayor precisión diagnóstica y a una planificación terapéutica más precisa.

Palabras clave: craniosinostosis, cefalometría, tomografía computarizada, base del cráneo, fenotipo craneofacial.

1 INTRODUCTION

Syndromic craniosynostoses comprise a heterogeneous group of genetic disorders characterized by the premature fusion of one or more cranial sutures, most commonly associated with pathogenic variants in the *FGFR1*, *FGFR2*, *FGFR3*, and *TWIST1* genes, which play a critical role in osteoblastic differentiation, cellular proliferation, and craniofacial development (Blaser et al., 2015; Carinci et al., 2005). Premature suture fusion disrupts normal cranial growth by preventing expansion perpendicular to the affected sutures, leading to compensatory growth patterns, complex craniofacial deformities, shortening of the cranial base, and midfacial hypoplasia (Alonso; Carpes; Hallinan, 2009; Renier et al., 2000)

The cranial base plays a pivotal role in craniofacial growth, with the spheno-occipital synchondrosis representing a major center of anteroposterior development. Alterations in this region directly affect maxillomandibular relationships, contributing to skeletal discrepancies, facial asymmetries, and profile disharmony. In particular, midface hypoplasia—frequently observed in syndromes associated with *FGFR2* mutations—results in maxillary retrusion, reduction of anatomical spaces, and compression of midfacial structures, leading to reduced separation between adjacent osseous landmarks and impaired anatomical delineation (Goodrich, 2005).

From a pathophysiological perspective, the restriction of cranial growth in the presence of ongoing brain expansion leads to increased intracranial pressure. This imbalance promotes continuous remodeling of the inner cranial table, driven by the combined effects of cerebral pulsations and bone resorption. As a result, digitiform impressions corresponding to the cerebral gyri develop on the inner surface of the calvaria,

producing the characteristic “copper beaten” skull appearance (Taylor et al., 2001). Beyond serving as an indirect marker of chronic intracranial hypertension, this radiologic feature reflects significant alterations in bone microarchitecture, with direct implications for image interpretation (Kim et al., 2019; Protzenko et al., 2026)

These morphological changes pose substantial challenges for cephalometric analysis. The combination of midfacial hypoplasia, anatomical compression, and irregularities of the inner cranial table compromises the definition of structural boundaries and hinders the identification of key cephalometric landmarks, including Nasion, Orbitale, Porion, Point A, and Posterior Nasal Spine. In conventional two-dimensional imaging, these limitations are exacerbated by structural superimposition and lack of depth, resulting in reduced measurement accuracy and reproducibility (ACCORSI, 2007; Tng et al., 1993).

In this context, multislice computed tomography (MSCT) has emerged as the imaging modality of choice for craniofacial assessment in syndromic craniosynostosis. MSCT enables high-resolution 3D reconstructions combined with integrated multiplanar analysis, effectively eliminating superimposition and improving spatial localization of anatomical landmarks (Branson; Shroff, 2011). Furthermore, the use of Hounsfield units allows for quantitative tissue characterization, enhancing the differentiation between osseous and cartilaginous structures, particularly in transitional anatomical regions (Greenway; Campos; Knipe, 2023; Pauwels et al., 2013).

Therefore, an integrated understanding of the genetic background, cranial base involvement, intracranial hypertension, and their effects on craniofacial morphology is essential for accurate cephalometric landmark identification. Overcoming the limitations imposed by structural alterations in syndromic craniosynostoses relies on advanced 3D imaging techniques, with MSCT playing a crucial role in improving diagnostic accuracy, measurement reproducibility, and therapeutic planning.

2 THEORETICAL FRAMEWORKS

2.1 SYNDROMIC CRANIOSYNOSTOSES: GENETIC AND PATHOPHYSIOLOGICAL BASES

Syndromic craniosynostoses result from pathogenic variants in genes regulating fibroblast growth factor signaling, particularly *FGFR1*, *FGFR2*, and *FGFR3*, as well as the *TWIST1* gene, all of which play a critical role in osteoblastic differentiation, cellular proliferation, and craniofacial development (Blaser et al., 2015; Carinci et al., 2005). Crouzon and Apert syndromes are classically associated with mutations in *FGFR2*, while Muenke syndrome is related to a specific and recurrent mutation in *FGFR3*, and Saethre-Chotzen syndrome results from *TWIST1* alterations (Cohen, 2000).

Premature fusion of cranial sutures disrupts normal neurocranial and skull base growth, generating complex compensatory deformities. The restriction imposed by the fused suture results in excessive growth in perpendicular directions, producing the characteristic alterations of each syndrome (Renier et al., 2000). The skull base, particularly through the spheno-occipital synchondrosis, represents a fundamental center of anteroposterior development, and its involvement is a major determinant of the skeletal discrepancies and facial asymmetries observed in these patients (Goodrich, 2005).

From a pathophysiological standpoint, increased intracranial pressure is one of the main complications of syndromic craniosynostoses. Chronic intracranial hypertension promotes continuous interaction between cerebral pulsations and the still-developing inner cranial table, resulting in progressive bone resorption and formation of digitiform impressions on the calvaria (Taylor et al., 2001; Delashaw et al., 1989).

2.2 THE COPPER BEATEN SKULL SIGN

The copper beaten skull sign consists of digitiform impressions on the inner surface of the calvaria, corresponding to cerebral gyri, produced by the pressure exerted by the expanding brain on immature bone. It represents an indirect radiological marker of chronic intracranial hypertension with direct implications for image interpretation in patients with syndromic craniosynostoses (Badve et al., 2013).

In syndromic craniosynostoses, particularly those associated with *FGFR2* mutations, its prevalence is high and its presence reflects significant alterations in bone microarchitecture. Although classically associated with intracranial hypertension, the sign may also be observed as a normal variant in children under six years of age (Desai; Priyadarshinni; Sharma, 2014). Historical reports of skulls exhibiting this morphological pattern further reinforce its relevance as a long-standing diagnostic finding (Rühli; Nicklisch; Alt, 2007).

Beyond its value as an indirect marker of intracranial hypertension, the sign compromises the definition of osseous contours on imaging, hindering the identification of cephalometric landmarks, particularly at the cranial base. Three-dimensional computed tomography reconstructions allow assessment of this pattern with greater spatial and densitometric detail, enabling a more comprehensive understanding of its structural impact (KIM et al., 2019; BRANSON; SHROFF, 2011).

2.3 MIDFACIAL HYPOPLASIA AND CEPHALOMETRIC IMPLICATIONS

Midfacial hypoplasia is one of the most prominent phenotypic features of syndromic craniosynostoses associated with *FGFR2* mutations. Maxillary retrusion resulting from premature fusion

of skull base sutures leads to reduction of anatomical spaces, compression of midfacial structures, and approximation of adjacent cephalometric landmarks, compromising their individual delineation on imaging (Katzen; Mccarthy, 2000; Cohen, 2000).

Recent studies have demonstrated that anatomical morphometric analysis can be used to predict craniofacial growth in patients with syndromic midfacial hypoplasia, underscoring the importance of accurate imaging methodologies for surgical and orthodontic planning (Hariri et al., 2024). This quantitative approach reinforces the need for methods capable of overcoming the limitations of two-dimensional analysis.

In conventional two-dimensional cephalometry, structural superimposition resulting from facial hypoplasia hinders the identification of landmarks such as Point A, Anterior Nasal Spine (ANS), and Posterior Nasal Spine (PNS). Three-dimensional computed tomography analysis allows these limitations to be overcome through integrated multiplanar evaluation with validation in each orthogonal plane (Zamora et al., 2012).

2.4 THREE-DIMENSIONAL CEPHALOMETRY AND MULTISLICE COMPUTED TOMOGRAPHY

Three-dimensional cephalometry represents a significant advance over conventional cephalometry, particularly in cases of complex craniofacial anatomy. Analysis across three orthogonal planes — axial, sagittal, and coronal — allows spatial validation of cephalometric landmarks, reducing observer variability and improving measurement reproducibility (Accorsi, 2007; Cattaneo et al., 2008).

Multislice computed tomography (MSCT) offers additional advantages over cone-beam computed tomography (CBCT) in the context of syndromic craniosynostoses. MSCT provides standardized tissue density values in Hounsfield units, enabling quantitative differentiation between osseous, cartilaginous, and soft tissues — a capacity particularly relevant for identifying cephalometric landmarks at osteocartilaginous interfaces, such as the Posterior Nasal Spine (Branson; Shroff, 2011; Pauwels Et Al., 2013). CBCT, in turn, presents limitations regarding the standardization of gray-scale values, compromising densitometric analysis in complex anatomical regions (Katsumata et al., 2007).

Accuracy studies have demonstrated that linear measurements obtained from three-dimensional spiral computed tomography images are comparable or superior to those obtained by conventional digital cephalometry, reinforcing the role of MSCT in high-complexity craniofacial assessment (Varghese et al., 2014). Recent systematic reviews indicate that multimodal imaging analysis should be considered the gold standard for the evaluation of craniosynostoses, particularly in syndromic forms (Micovic et al., 2025).

3 METHODOLOGY

This was a descriptive observational study approved by the Research Ethics Committee of the Instituto Nacional de Saúde da Mulher, da Criança e do Adolescente Fernandes Figueira – Fiocruz, Rio de Janeiro, Brazil (CAAE 13127519.5.000.5269; approval no. 3,381,275). Written informed consent was obtained from all legal guardians.

The sample consisted of patients with clinically and molecularly confirmed syndromic craniosynostoses, followed at the Medical Genetics and Neurosurgery outpatient clinics of the institution. Molecular analysis was performed at the Laboratory of Molecular Biology/Molecular Genomic Medicine (IFF/Fiocruz) using the Oswaldo Cruz Foundation Sequencing Platform, with an ABI PRISM™ 3100 Capillary DNA Sequencer (Applied Biosystems), according to the Sanger sequencing method (Crossley et al., 2020)

Patients with a history of prior craniofacial surgery or orthopedic facial treatment were excluded to avoid interference with craniofacial morphology and cephalometric measurements.

Imaging examinations included conventional radiographs and multislice computed tomography (MSCT) scans of the skull and face, performed using a GE BrightSpeed 16-slice scanner (GE Healthcare).

Cephalometric analyses were conducted on an ADW 4.6 workstation (AW VolumeShare 5 software – GE Healthcare), using axial, sagittal, and coronal images combined with multiplanar reformations and 3D reconstructions employing volume rendering and transparent bone techniques.

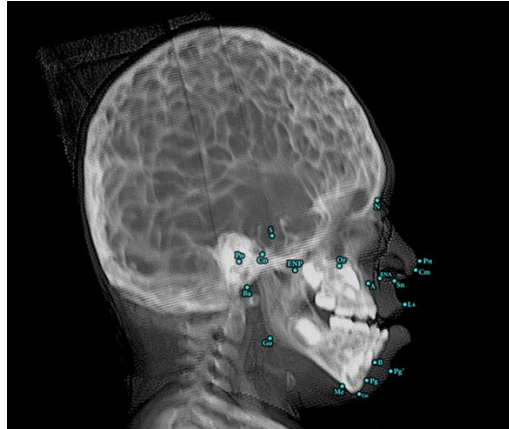
Prior to measurements, all images were standardized with the Frankfurt and bi-orbital planes oriented parallel to the horizontal plane. Cephalometric landmark identification was performed through integrated analysis of the three orthogonal planes, allowing 3D validation of anatomical reference points.

The cephalometric landmarks analyzed included: S (Sella), Ba (Basion), N (Nasion), Po (Porion), Or (Orbitale), Pt (Pterygomaxillary fissure), A (Point A), ANS (Anterior Nasal Spine), PNS (Posterior Nasal Spine), B (Point B), Pg (Pogonion), Gn (Gnathion), Me (Menton), and Go (Gonion).

This 3D approach was particularly relevant for identifying landmarks in complex anatomical regions, such as the cranial base and pterygoid process, as well as in osteocartilaginous interfaces, such as the posterior nasal spine, where tissue differentiation and multiplanar analysis are essential for improved accuracy.

All measurements were performed by a single trained observer to reduce intraobserver variability and enhance measurement reproducibility.

Figure 1. Lateral reconstruction of a cranial computed tomography scan from a patient with syndromic craniosynostosis, showing the main cephalometric landmarks (S, N, Ba, Po, Or, Pt, A, ANS, PNS, B, Pg, Gn, Me, Go). Difficulty in defining the cranial base can be observed.



Source: Authors' own archive (2026)

4 RESULTS AND DISCUSSION

The analysis of the sample revealed a high prevalence of the “copper beaten” skull sign, observed in 85.7% of cases, with predominant occurrence in Crouzon, Apert, and Pfeiffer syndromes. In contrast, this finding was absent in patients with Muenke and Saethre-Chotzen syndromes.

The presence of the copper beaten skull sign was directly associated with increased difficulty in identifying cephalometric landmarks, particularly at the cranial base. The most affected anatomical points were Sella (S), Basion (Ba), and the pterygoid region (Pt), which exhibited greater variability in localization, reflecting structural alterations resulting from remodeling of the inner cranial table.

In two-dimensional imaging, landmark identification was limited by structural superimposition and lack of depth, compromising measurement accuracy. In contrast, multislice computed tomography provided improved anatomical definition, allowing greater precision and reproducibility in the identification of cephalometric landmarks.

Notably, the posterior nasal spine was more clearly delineated in tomographic images, highlighting the importance of 3D analysis combined with tissue differentiation based on Hounsfield units, particularly in osteocartilaginous interface regions.

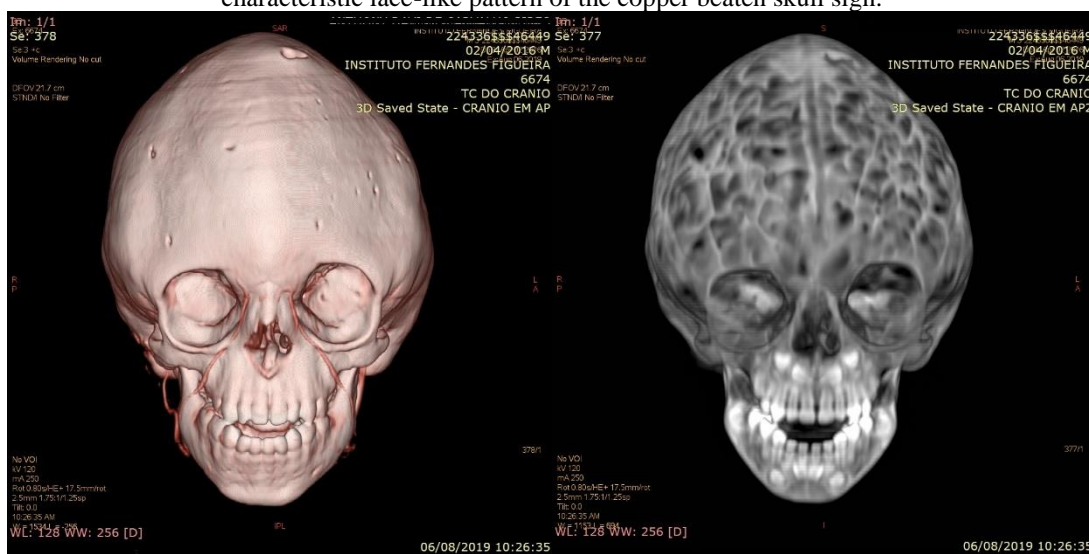
The distribution of syndromes and the presence of the copper beaten skull sign, along with their respective 95% confidence intervals, are presented in Table 1.

Table 1 – Distribution of syndromic craniosynostoses and presence of the copper beaten skull sign with 95% confidence intervals (95% CI).

Syndrome	n (patients)	% sample	(%) copper beaten skull	IC95% copper beaten skull
Crouzon	11	33,3%	100%	74,1 – 100%
Apert	11	33,3%	100%	74,1 – 100%
Pfeiffer	3	9,1%	100%	43,8 – 100%
Muenke	3	9,1%	0%	0 – 56,2%
Saethre-Chotzen	1	3,0%	0%	0 – 79,3%
Total	29	100%	86,2%	—

Legend: Distribution of craniosynostotic syndromes in the sample, including the frequency of the copper beaten (CB) skull sign and corresponding 95% confidence intervals (95% CI), calculated using the Wilson method. Source: prepared by the Source: Authors (2026)

Figure 2. Computed tomography with 3D reconstruction (A) and transparent bone rendering (B) demonstrating the characteristic lace-like pattern of the copper beaten skull sign.



Source: Authors' own archive (2026)

The findings of the present study demonstrate that the identification of cephalometric landmarks in patients with syndromic craniosynostoses is significantly influenced by complex structural factors, including intracranial hypertension, bone remodeling, and midfacial hypoplasia. The high prevalence of the “copper beaten” skull sign observed in the sample reinforces its role as an indirect marker of these alterations, reflecting a dynamic and pathologically remodeled cranial environment (Badve et al., 2013; Desai; Priyadarshinni; Sharma, 2014; Rühli; Nicklisch; Alt, 2007).

From a pathophysiological standpoint, persistent intracranial hypertension in a developing skull promotes continuous interaction between cerebral pulsations and immature bone, resulting in remodeling of the inner cranial table through combined mechanisms of mechanical compression and bone resorption. This process gives rise to digitiform impressions corresponding to the cerebral gyri, producing the characteristic copper beaten appearance. Beyond indicating chronic intracranial hypertension, this pattern reflects significant alterations in bone microarchitecture and compromises the definition of anatomical boundaries on imaging (Badve et al., 2013; Delashaw et al., 1989)

These structural changes have a direct impact on cephalometric analysis, particularly at the cranial base, where accurate identification of landmarks such as Sella (S) and Basion (Ba) depends on well-defined osseous contours. The present results corroborate previous findings by demonstrating increased variability in the localization of these points, as well as in the pterygoid region (Pt), highlighting the sensitivity of these structures to morphological alterations (Katsumata et al., 2007; Zamora et al., 2012)

In addition, midfacial hypoplasia plays a critical role in impairing cephalometric landmark identification. Reduced maxillary growth leads to decreased anatomical spaces and compression of facial structures, promoting structural superimposition and loss of anatomical definition, particularly in 2D imaging. In this context, landmarks such as Point A, Anterior Nasal Spine (ANS), and Posterior Nasal Spine (PNS) become especially difficult to delineate due to structural proximity and morphological variability (Cohen, 2000; Hariri et al., 2024; Katzen; McCarthy, 2000; Zamora et al., 2012).

The limitations of conventional radiography become particularly evident under these conditions. The inherently 2D nature of this modality results in structural superimposition, lack of depth, and dependence on geometric projection, all of which significantly reduce measurement accuracy and reproducibility, especially in anatomically altered skulls.

In contrast, multislice computed tomography (MSCT) provides substantial advantages that support its superiority in cephalometric analysis of syndromic craniosynostoses. Integrated multiplanar analysis—encompassing axial, sagittal, and coronal views—enables progressive and confirmatory localization of cephalometric landmarks, allowing true 3D validation and reducing observer-dependent subjectivity. Each imaging plane contributes uniquely: axial sections are essential for evaluating the cranial base and deep structures; sagittal sections facilitate analysis of midline structures and anteroposterior relationships; and coronal sections allow improved assessment of craniofacial symmetry and lateral anatomical structures (ACCORSI, 2007; Cattaneo et al., 2008; Varghese et al., 2014)..

Another key advantage of MSCT is its ability to provide quantitative tissue density information through Hounsfield units. This feature allows more precise differentiation between osseous, cartilaginous, and soft tissues, which is particularly relevant for identifying cephalometric landmarks located at osteocartilaginous interfaces. The posterior nasal spine represents a paradigmatic example, as its accurate delineation depends on the ability to distinguish between tissues of different densities (Branson; Shroff, 2011; Pauwels et al., 2013).

In contrast, cone-beam computed tomography (CBCT), although widely used in dental practice, presents important limitations in this context. The lack of standardized gray values, which do not directly correspond to Hounsfield units, compromises densitometric analysis and reduces reliability in tissue differentiation, particularly in complex anatomical regions (Branson; Shroff, 2011; Katsumata et al., 2007; Pauwels et al., 2013).

Furthermore, 3D analysis provided by MSCT allows more accurate identification of craniofacial asymmetries, revealing true spatial displacement of cephalometric landmarks. In patients with craniosynostoses, such asymmetries are common and reflect altered and compensatory growth patterns. Therefore, cephalometric analysis must be individualized, taking into account patient-specific anatomy rather than assuming idealized symmetry.

From a genotype–phenotype perspective, syndromes associated with *FGFR2* mutations, such as Crouzon and Apert syndromes, tend to present more severe phenotypic manifestations, including greater cranial base involvement and higher prevalence of the copper beaten skull sign. In contrast, Muenke syndrome, associated with *FGFR3*, typically exhibits a milder phenotype with less structural impact and lower frequency of this radiological finding (Cohen, 2000)

In this context, recent studies have demonstrated that 3D analysis significantly improves cephalometric accuracy and should be considered the gold standard in complex conditions such as syndromic craniosynostoses (Micovic et al., 2025)

From a clinical standpoint, accurate identification of cephalometric landmarks is essential for treatment planning in orthodontics, dentofacial orthopedics, and craniofacial surgery. Even minor variations in landmark localization may result in significant differences in skeletal interpretation, directly impacting clinical decision-making.

Finally, the present findings emphasize that reliance on two-dimensional imaging alone in patients with syndromic craniosynostoses—particularly in the presence of the copper beaten skull sign—may lead to inaccurate interpretations. Multislice computed tomography with 3D reconstruction should be considered the method of choice in these cases, as it integrates spatial and densitometric information, providing greater diagnostic accuracy, measurement reproducibility, and reliability for therapeutic planning.

5 CONCLUSION

The findings of this study demonstrate that the identification of cephalometric landmarks in patients with syndromic craniosynostoses is significantly compromised by structural alterations associated with intracranial hypertension, remodeling of the inner cranial table, and midfacial hypoplasia. The “copper beaten” skull sign represents an important marker of these changes and is directly related to difficulties in defining anatomical boundaries, particularly at the cranial base and in regions of greater morphological complexity.

Additionally, midfacial hypoplasia contributes to compression of anatomical structures and reduction of spatial dimensions, promoting structural superimposition and further hindering accurate landmark identification, especially in two-dimensional imaging modalities.

In this context, multislice computed tomography with 3D reconstruction demonstrated clear superiority by enabling integrated multiplanar analysis and tissue differentiation based on Hounsfield units, resulting in greater accuracy, reproducibility, and reliability in cephalometric landmark localization, including those located at osteocartilaginous interfaces.

Therefore, 3D multislice computed tomography should be considered the method of choice for cephalometric evaluation in patients with syndromic craniosynostoses, contributing to improved diagnostic accuracy and more precise therapeutic planning.

REFERENCES

- ACCORSI, M. A. O. **Comparação de grandezas cefalométricas obtidas por meio de telerradiografias e tomografias computadorizadas multislice em crânios secos humanos.** São Paulo: USP, 2007.
- ALONSO, Nivaldo; CARPES, Arturo; HALLINAN, Márcia. Achados polissonográficos em pacientes com síndromes de Apert e Crouzon. **Polissonographic findings in patients with Apert and Crouzon syndromes.** *Rev Bras Cir Craniomaxilofac*, v. 12, n. 3, p. 98–104, 2009.
- BADVE, Chaitra A. *et al.* Craniosynostosis: imaging review and primer on computed tomography. **Pediatric Radiology** 2013 **43:6**, v. 43, n. 6, p. 728–742, 2 maio 2013.
- BLASER, SI *et al.* Skull base development and craniosynostosis. **Pediatric radiology**, v. 45 Suppl 3, p. 485–496, 13 set. 2015.
- BRANSON, Helen M.; SHROFF, Manohar M. Craniosynostosis and 3-Dimensional Computed Tomography. **Seminars in Ultrasound, CT and MRI**, v. 32, n. 6, p. 569–577, 1 dez. 2011.
- CARINCI, Francesco *et al.* Apert and Crouzon syndromes: Clinical findings, genes and extracellular matrix. **Journal of Craniofacial Surgery**, v. 16, n. 3, p. 361–368, maio 2005.
- CATTANEO, Paolo M. *et al.* Comparison between conventional and cone-beam computed tomography-generated cephalograms. **American Journal of Orthodontics and Dentofacial Orthopedics**, v. 134, n. 6, p. 798–802, dez. 2008.
- COHEN, M. M. **Craniosynostosis : diagnosis, evaluation, and management.** [S.l.]: OUP USA, 2000.
- CROSSLEY, Beate M. *et al.* Guidelines for Sanger sequencing and molecular assay monitoring. **Journal of veterinary diagnostic investigation : official publication of the American Association of Veterinary Laboratory Diagnosticians, Inc**, v. 32, n. 6, p. 767–775, 1 nov. 2020.
- DELASHAW, Johnny B. *et al.* Cranial vault growth in craniosynostosis. **Journal of Neurosurgery**, v. 70, n. 2, p. 159–165, fev. 1989.
- DESAI, Vela; PRIYADARSHINI, Smita R.; SHARMA, Rajeev. Copper Beaten Skull! Can It be a Usual Appearance? **International Journal of Clinical Pediatric Dentistry**, v. 7, n. 1, p. 47, 1 abr. 2014.
- GOODRICH, James Tait. FOCUS SESSION Skull base growth in craniosynostosis. **Childs Nerv Syst**, v. 21, p. 871–879, 2005.
- GREENWAY, Kyle; CAMPOS, Arlene; KNIPE, Henry. Hounsfield Unit. **Radiopaedia.org**, 6 mar. 2023.
- HARIRI, F. *et al.* Midface hypoplasia in syndromic craniosynostosis: predicting craniofacial growth via a novel regression model from anatomical morphometric analysis. **International Journal of Oral and Maxillofacial Surgery**, v. 53, n. 4, p. 293–300, 1 abr. 2024.
- KATSUMATA, Akitoshi *et al.* Effects of image artifacts on gray-value density in limited-volume cone-beam computerized tomography. **Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology**, v. 104, n. 6, p. 829–836, 1 dez. 2007.

- KATZEN, J. Timothy; MCCARTHY, Joseph G. Syndromes Involving Craniosynostosis and Midface Hypoplasia. **Otolaryngologic Clinics of North America**, v. 33, n. 6, p. 1257–1284, 1 dez. 2000.
- KIM, So Young *et al.* Reliable manifestations of increased intracranial pressure in patients with syndromic craniosynostosis. **Journal of Cranio-Maxillofacial Surgery**, v. 47, n. 1, p. 158–164, 1 jan. 2019.
- MICOVIC, Mirko *et al.* Imaging Modalities in Craniosynostosis: A Systematic Review and Proposal of the ARCANA Protocol for Multimodal Radiation-Free Assessment. **Diagnostics**, v. 15, n. 20, p. 2632, 1 out. 2025.
- PAUWELS, Ruben *et al.* Variability of dental cone beam CT grey values for density estimations. **The British journal of radiology**, v. 86, n. 1021, 1 jan. 2013.
- PROTZENKO, M. *et al.* Contributing Factors for Angle’s Class III Phenotype in Crouzon Syndrome. **European journal of paediatric dentistry**, v. 27, n. 1, p. 59–64, mar. 2026.
- RENIER, D. *et al.* Management of craniosynostoses. **Child’s Nervous System**, v. 16, n. 10–11, p. 645–658, 2000.
- RÜHLI, Frank J.; NICKLISCH, Nicole; ALT, Kurt W. A historical case of beaten-copper cranium. **Journal of neurosurgery**, v. 106, n. 1 Suppl, p. 71–73, 2007.
- TAYLOR, W. J. *et al.* Enigma of raised intracranial pressure in patients with complex craniosynostosis: The role of abnormal intracranial venous drainage. **Journal of Neurosurgery**, v. 94, n. 3, p. 377–385, 2001.
- TNG, Tony T. H. *et al.* Effect of head posture on cephalometric sagittal angular measures. **American Journal of Orthodontics and Dentofacial Orthopedics**, v. 104, n. 4, p. 337–341, 1993.
- VARGHESE, S. *et al.* Evaluation of the accuracy of linear measurements on spiral computed tomography-derived three-dimensional images and its comparison with digital cephalometric radiography. **Dentomaxillofac Radiol**, v. 39, n. 4, p. 216–223, 28 jan. 2014.
- ZAMORA, Natalia *et al.* A study on the reproducibility of cephalometric landmarks when undertaking a three-dimensional (3D) cephalometric analysis. **Medicina oral, patologia oral y cirugia bucal**, v. 17, n. 4, jul. 2012.