CARLOS EDUARDO GOMES DO COUTO FILHO

ACCURACY IN THE DIAGNOSIS OF THE ANTERIOR LOOP OF THE MENTAL NERVE BETWEEN PANORAMIC RADIOGRAPHY AND CONE BEAM COMPUTED TOMOGRAPHY: IS CLINICALLY RELEVANT?

ACURÁCIA NO DIAGNÓSTICO DA ALÇA ANTERIOR DO NERVO MENTUAL ATRAVÉS DE RADIOGRAFIAS PANORÂMICAS DIGITAIS E TOMOGRAFIA COMPUTADORIZADA DE FEIXE CÔNICO

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Tese de Doutorado apresentada à Faculdade de Odontologia de Piracicaba - Unicamp para obtenção do Título de Doutor em Clínica Odontológica, na Área de Cirurgia e Traumatologia Buco-Maxilo-Faciais.

Thesis presentes to the Piracicaba Dentistry School of the University of Campinas in partial fulfillment of the requirements of degree of Doctor in Clinical Dentistry, in Oral and Maxillofacial Surgery area.

Orientador: Prof. Dr. José Ricardo de Albergaria Barbosa

Este exemplar corresponde à versão final da Tese defendida pelo Aluno Carlos Eduardo Gomes do Couto Filho e Orientada pelo Prof. Dr. José Ricardo de Albergaria Barbosa

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ABSTRACT

Oral rehabilitation with dental implants has revolutionized dentistry. However, both anatomical and technical knowledge are essential to provide an appropriate treatment. Thus, the rehabilitation by installing dental implants at interforaminal region (mental foramina) has become common in total mandibular rehabilitation. Consequently, a large number of sensory disorders has been described and related to the anterior loop of mental nerve. The division of the mandibular canal into mental nerve, responsible for innervation of soft tissues (buccal mucosa, bottom of buccal sulcus, labial mucosa of the lower lip, skin of the chin and lower lip), and incisive branch, which may be located in the incisive canal and is responsible for the innervation of the lower anterior region (teeth and periodontal tissues) should be considered during the planning of interventions in this region. Injury to the loop of the mental nerve of the mandibular canal and to the incisive branch will likely bring disorders such as loss of sensitivity, swelling, hematoma and failure of osseointegration. Although considered a safe area for surgery, it is very neglected in the planning of such procedures. The association of anatomical knowledge, both clinical and of images, makes the procedure more predictable due to anatomical variations, making the imaging examinations necessary, which are essential in the control of accidents related to intraforaminal implant procedures. As one of the most widely used imaging examinations in dental implants, panoramic radiograph presents questionable diagnostic accuracy. Therefore, we verified the accuracy of panoramic radiograph in comparison with cone-beam computed tomography in the diagnosis of the anterior loop of the mental nerve.

Keywords: panoramic radiography, cone-beam computed tomography, anterior loop length, mental nerve

RESUMO

A reabilitação bucal com implantes dentários revolucionou a odontologia. No entanto, conhecimentos anatômicos como também técnicos são essenciais para a realização de um adequado tratamento. Desta forma, a reabilitação através da instalação de implantes dentários na região interforaminal (forames mentuais) tornou-se comum em reabilitações totais mandibulares. Em consequência disto, um grande número de transtornos sensoriais tem sido descritos e relacionados a alças anteriores do nervo mentual. A divisão do canal mandibular em nervo mentual, responsável pela inervação de tecidos moles (mucosa vestibular, fundo de sulco vestibular, mucosa labial do lábio inferior, pele do mento e lábio inferior), e feixe incisivo, que pode localizar-se no canal incisivo e é responsável pela inervação da região ântero-inferior (dentes e tecidos periodontais) deve ser considerada no planejamento de intervenções nesta região. A injúria a alça do nervo mentual do canal mandibular e ao feixe incisivo poderá trazer transtornos como perda de sensibilidade, edema, hematoma e falha na osseointegração. Apesar de ser considerada uma área segura para cirurgias ela é muito negligenciada no planejamento de tais procedimentos. A associação do conhecimento anatômico, tanto clínico quanto de imagens, torna o procedimento mais previsível devido às variações anatômicas, fazendo-se necessários exames de imagens, essenciais no controle de acidentes relacionados aos procedimentos de implantes intraforaminais. Como um dos exames de imagem mais utilizado em implantes dentais, a radiografia panorâmica apresenta precisão diagnóstica questionável. Portanto, verificamos a precisão da radiografia panorâmica quando comparada com a tomografia computadorizada cone-beam no diagnóstico da alça anterior do nervo mentual.

Palavras chave: radiografia panorâmica, tomografia computadorizada de feixe cônico, alça anterior do nervo mentual

SUMÁRIO

DEDICATÓRIA

“Simplesmente à vida, por me permitir experimentar e viver.

Através de Débora, minha parceira e porto e Alexandre, meu norte e porto, dedico a todos que de alguma maneira me fazem sorrir.“

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"Quando alguém lhe provocar irritações,
pegue um copo de água,
beba um pouco e conserve o resto na boca.
Não a ponha fora, nem a engula.
Enquanto durar a tentação de responder,
deixe a água banhando a língua.
Esta é a água da paz."

Chico Xavier

INTRODUÇÃO

A reabilitação implantosuportada proposta por Branemårk, revolucionou a reabilitação oral e passou a ser utilizada de maneira rotineira por vários profissionais. Entretanto, o adequado planejamento protético/cirúrgico torna-se imprescindível ao sucesso do tratamento.

A reabilitação através da colocação de implantes na região interforaminal (forames mentuais) tornou-se comum e, em consequência disto, um grande número de transtornos sensoriais foram descritos e relacionados a alças anteriores do nervo mentual e feixe incisivo. A divisão do nervo alveolar inferior em nervo mentual, responsável pela inervação de tecidos moles (mucosa vestibular, fundo de sulco vestibular, mucosa labial do lábio inferior pele do mento e lábio inferior) e feixe incisivo, que pode localizar-se no canal incisivo e sendo responsável pela inervação da região ântero-inferior (dentes e tecidos periodontais) deve ser considerada no planejamento de intervenções cirúrgicas nesta região. A injúria a alça do feixe vásculo nervoso mentual do canal mandibular e ao feixe incisivo poderá trazer complicações como perda de sensibilidade, edema e hematoma e falha na osseointegração.

Apesar de ser considerada uma área com baixo risco de complicações para cirurgias ela é muito negligenciada no planejamento de tais procedimentos (MARDINGER, et al. 2000). A associação do conhecimento anatômico, tanto clínico quanto de imagens torna o procedimento mais previsível. A anatomia do canal mandibular apresenta um grande número de variações anatômicas que tornam o planejamento ainda mais necessário, e a utilização dos exames de imagens cada vez mais importantes no controle de acidentes relacionados a estas variações uma vez que vários procedimentos cirúrgicos, tanto relacionados aos implantes quanto às cirurgias ortognáticas podem causar danos a estruturas nobres. Um dos requisitos para o sucesso das cirurgias nesta região está diretamente ligado ao conhecimento anatômico da região, o que ainda necessita de muito estudo e documentação, o que ainda é fator gerador dúvidas quanto as intercorrências possíveis.

Rotineiramente, o cirurgião dentista utiliza a radiografia panorâmica como principal exame de imagens no planejamento de cirurgias invasivas, como a colocação de implantes osseointegráveis. Além das limitações de localização no sentido de profundidade, a qualidade da imagem nem sempre permite uma localização precisa dos acidentes anatômicos.

As tomografias computadorizadas de feixe cônico mostram, de forma mais precisa, os detalhes anatômicos das áreas a serem operadas, minimizando a chance de acidentes trans-operatórios, além de baixas doses de radiação e melhor qualidade de imagens, tendo grandes vantagens em relação às imagens bidimensionais por mostrar de melhor maneira os acidentes anatômicos da região.

Salvador, J.F. et al (2010), verificaram as variações anatômicas do canal mandibular e a visualização do forame mentual, de acordo com a classificação de Nortjé (1977), e a presença de canais bífidos de acordo com a classificação de Langlais (1985) e demonstraram não haver diferenças significantes quanto ao gênero ou etnia na posição do forame e que o forame mentual não foi observado em 0,4% da amostra do sexo masculino.

Na classificação de Langlais (1985) não houve diferenças significantes entre homens e mulheres e a maior prevalência foi para canais sem bifurcação. Observaram, ainda, que a curva mesial do canal mandibular está presente na maioria dos casos.

Uchida et al (2007), mediram a distância anterior da alça anterior do canal mentual em cadáveres e verificaram que existe uma grande variação tanto na distância quanto no diâmetro do canal incisivo, não assumindo uma medida segura em relação mesial ao forame mentual e recomendaram que o exame pré-operatório das estruturas nobres é indispensável para uma segura instalação de implantes na região interforaminal da mandíbula.

CAPÍTULO 1

Accuracy in the diagnosis of the anterior loop of the mental nerve between panoramic radiography and cone beam computed tomography: is clinically relevant?

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Keywords: panoramic radiography, cone-beam computed tomography, anterior loop length, mental nerve

ABSTRACT

Oral rehabilitation with dental implants has revolutionized dentistry. However, both anatomical and technical knowledge are essential to provide an appropriate treatment. Thus, the rehabilitation by installing dental implants at intraforaminal region (mental foramina) has become common in total mandibular rehabilitation. Consequently, a large number of sensory disorders has been described and related to the anterior loop of mental nerve. The division of the mandibular canal into mental nerve, responsible for innervation of soft tissues (buccal mucosa, bottom of buccal sulcus, labial mucosa of the lower lip, skin of the chin and lower lip), and incisive branch, which may be located in the incisive canal and is responsible for the innervation of the lower anterior region (teeth and periodontal tissues) should be considered during the planning of interventions in this region. Injury to the loop of the mental nerve of the mandibular canal and to the incisive branch will likely bring disorders such as loss of sensitivity, swelling, hematoma and failure of osseointegration. Although considered a safe area for surgery, it is very neglected in the planning of such procedures. The association of anatomical knowledge, both clinical and of images, makes the procedure more predictable due to anatomical variations, making the imaging examinations necessary, which are essential in the control of accidents related to intraforaminal implant procedures. As one of the most widely used imaging examinations in dental implants, panoramic radiograph presents questionable diagnostic accuracy. Therefore, we verified the accuracy of panoramic radiograph in comparison with cone-beam computed tomography in the diagnosis of the anterior loop of the mental nerve.

INTRODUCTION

The mental nerve (MN) is a general somatic afferent nerve that provides sensation to the lip, chin, and gingival. It is the terminal branch of the mandibular nerve, which is the third division of the trigeminal nerve. MN exits the mandible through the mental foramen, divides into 3 branches deep to the depressor anguli oris muscle, and supplies the skin and mucous membrane of the lower lip, the skin of the chin, and the vestibular gingiva of the mandibular incisor.[1,2] Historically, anatomical literature has described the interforaminal region of the mandible as possessing a mental nerve with a path that creates an anterior loop (AL) before entering the mental foramina. The AL is described as an extension of the mental nerve that is mesial to the mental foramen[3].

Treatment planning for dental implant patients is often complicated by the unknown extent of the anterior loop of the mental neurovascular bundle. Sensory disturbances of the mental nerve region may arise after endosseous implants are installed in the mandibular interforaminal. A relatively common problem is the use of an inappropriate attachment depth or path during the insertion of dental implant fixtures, which may damage the inferior alveolar nerve (IAN) and MN. The incidence of permanent sensory disturbance to the lower lip after dental implant insertion in the mental foramen area is reportedly 7% to 10%.[4,5] Complications such as loss of lip and chin sensation may result in lip biting, impaired speech, and diminished salivary retention, deficits that have a significant impact on a patient's activities of daily living.[6,7].

Preoperative radiographic examination is essential for selecting the sites for the installation of an optimum number of implants of optimal size. The potential location and angulations for each implant must be carefully determined and the operator must be familiar with the dimensions and shape of the jaws and the location of anatomical structures. Panoramic radiographs provide 2-dimensional information, while three-dimensional determination requires tomography. Panoramic radiographs have severe limitations for the evaluation of anatomical structures and available bone for implants. Preoperative tomography, is preferable, but is not always performed. Therefore, bone dimensions are usually assessed only by panoramic radiographic examinations.

Therefore, the aim of this study was to determine the correlation between the visual interpretation of the panoramic radiographs (PR) and the cone beam computed tomography (CBCT) for the detection of the AL as well as the clinical relevance for planning the installation of dental implants.

MATERIAL AND METHODS

Measurement Procedure

The objective was to evaluate the presence of the anterior extension (AE) of the mandibular canal and to measure its length. This study was divided into 2 steps: firstly panoramic radiography was performed for subjective evaluation of the trajectory of curvilinear AE, thus classified as present or absent (rectilinear) only on a total of 94 hemimandibles. In the second step, for each cross-sectional imaging on CBCT, the hemimandibles were evaluated regarding the presence of the AE, which was classified as rectilinear or curvilinear, and the measurement of its length was obtained (Oliveira-Santos, 2011). The lenght was obtained by the linear distance between the most anterior border of the mental foramen to the most anterior margin of the anterior loop and was defined as the ALL. Slice thickness of panoramic reconstructions were 25 mm, so that the entire course of the canal could be visualized, including the mental foramen, without impairing image superimposition. For the cross-sections, the anterior loop was determined by counting the number of sequential 1 mm slices displaying two round hypodense images (corresponding to the upper and lower segments of the mandibular canal, typically ending in an “8-like” shape anteriorly), from the anterior-most image of the mental foramen and start point of the incisive canal. The number of parasagittal cuts containing the ALL was counted and multiplied by 0.25, thus achieving the ALL measurement.

The occlusal plane served as the reference for the cross-sections since the slices were reconstructed following the occlusal plane. Before starting the evaluation of parasagittal cuts, the occlusal plane was aligned, avoiding inclination and rotation of the image due the inclinations of the head during image acquisition. Thus centralized parabolic curve (axial), leading the points up dental crowns. (Figure 1)

One oral and maxillofacial radiologist with experience in manipulation and interpretation of CBCT images performed the measurements.

Reliability was assessed using replicate measurements and intraobserver reliability was estimated based on 2 measurements performed at the right and left sides of the mandible with a 20-day interval to avoid dilution of error. The final mean values of each measurement resulted from the average of the 2 measurements.

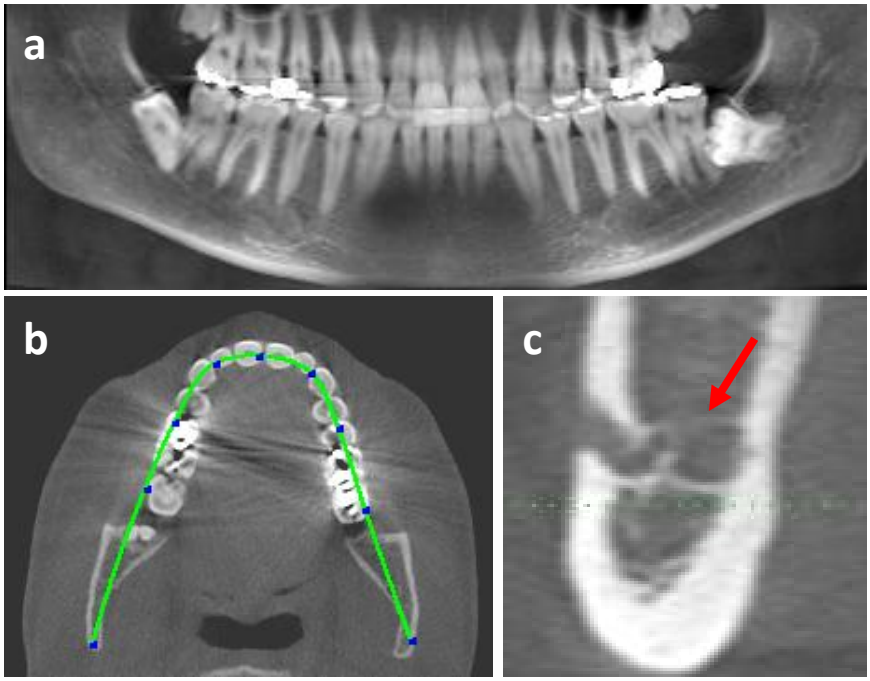

Figure 1. a Panoramic reconstruction, **b** axial slice, and **c** cross-sectional image. The AL of the mental nerve can be seen at the slice C (*arrow*).

RESULTS

The frequencies of the AL identified throught PR and CBCT were different. In PR the loop was identified in 42.6% of cases, and only 12.8% were bilateral (Table 1). In contrast, the loop was detect in 29.8% of the samples using CBCT, with 6.4%being bilateral (Table 2).

Table 1. Frequency distribution of the presence of the AL of the mental nerve in panoramic images, bilaterally

Side	Presence
	N(%)
Absent	27 (57.4%)
Right	9 (19.2%)
Left	5 (10.6%)
Both	6 (12.8%)
Total	47 (100.0%)

Out of the 47 patients studied, 14 (29.8%) presented the AL: three were bilateral, seven unilateral right and four unilateral left. Making calculations based hemimandibles study, 94, out of which 17 (18.1%) out of the loop anterior mental nerve was bilateral and 35.3%, 41.2% and 23.5% unilateral right-sided left.

Table 2. Frequency distribution of the presence of AL on CBCT images, bilaterally

Side	Presence
	N(%)
Absent	33 (70.2%)
Right	7 (14.9%)
Left	4 (8.5%)
Both	3 (6.4%)
Total	47 (100.0%)

Table 3. Frequency distribution of the presence of AL on PR X CBCT images, bilaterally

Side	Presence	
	N(%)	
	PR	TCCB
Absent	27 (57.4%)	33 (70.2%)
Right	9 (19.2%)	7 (14.9%)
Left	5 (10.6%)	4 (8.5%)
Both	6 (12.8%)	3 (6.4%)
Total	47 (100.0%)	

Statistical comparison between PR and CBCT showed that the PR led to false-positive diagnostics of the loop in the samples. (Table 4).

Table 4. Correlation between panoramic (PR) and cone beam computed tomography (CBCT) evaluation for the detection of the anterior loop of the mental nerve.

Side	PR	CBCT		Kappa	IC95%
		Presence	Absence		
Rigth	Presence	3 (6.4%)	12 (25.5%)	-0.02	-0.29;0.25
	Absence	7 (14.9%)	25 (53.2%)		
Left	Presence	2 (4.3%)	9 (19.2%)	0.05	-0.24;0.34
	Absence	5 (10.6%)	31 (66.0%)		

Despite the moderate agreement between the two methods of examination, the Kappa coefficient calculated presented poor, can not we use this way with confidence diagnosis of panoramic radiography for the presence of AL.

Table 5. Comparison for directed measurement of the anterior loop length

Authors	Methods	Sample	Length of Loop (mm) Incidence (%)	Mean _SD (Range)
Bavitz *et al*[27] (1993)	Cadavers	24	11	
		Dentate group n=24		0.2 _ 0.3 (0.0–1.0)
		Edentulous group n=23		0.0 _ 0.0 (0.0–0.0)
Solar *et al*[28] (1994)	Cadavers	37	60	1.0 _ 1.2 (0.0–5.0)
Rosenquist[29] (1996)	Patients	58	26	0.15 (0.0–1.0)
Mardinger *et al*[13] (2000)	Cadavers	46 hemimandibles	28	1.05 _ 0.47 (0.4–2.19)
Kuzmmanovic *et al*[9] (2003)	Cadavers	22 (44 hemimandibles)		1.2 _ 0.9 (0.11–3.31)
	Caucasian descent			
Neiva *et al*[24] (2004)	Caucasian skulls	22	88	4.13 _ 2.04 (1.0–11.0)
Hwang *et al*[30] (2005)	Cadavers	30 fresh hemimandibles		5.0(1.9)
	Korean	50 dry hemimandibles		
Uchida *et al*[17] (2007)	Cadavers			
	Japanese	38 (75 hemimandibles)	62.7	1.5 _ 1.4 (0.0–6.0)
Uchida *et al*[18] (2009)	Cadavers	71(140 hemimandibles)	71	2.2 (0.8)
	Japanese			

Table 6. Average length of the anterior loop and confidence interval depending on the side of the CBCT images

Side	Length mm
Right	3.00 (2.5-3.25)
Left	4.00 (2.70-3.25)

Despite of the prevalence of AL varies widely in the literature, our results are in agreement with numerous other studies, are to anatomical bodies, use of panoramic radiography and in CBCT[9,13,17,22,23]. On panoramic radiographs, we obtained a value of 42.6,% while the presence of AL in CBCT was only 29.8%.

DISCUSSION

Methodology of Measurement

For more than a century dental radiographs have been the dominant source for diagnostic information on the maxillofacial complex[8]. However, other study has shown that the reliability of the panoramic radiographs, when planning for implant placement in the interforaminal region of the mandible, may be limited[9]. One of the disadvantages of panoramic images is the geometric distortion of the anatomical structures[10]. Distortions of the panoramic images in the horizontal and vertical planes, especially in the anterior region, depend on the anatomical variations between arch curvatures - focal plane shape - and operator error in patient positioning affects the utility of panoramic images to provide accurate measurements[11,12].

Our results are in agreement with Kuzmanovic et al.[9] regarding the limitation of using panoramic radiographs, when planning for implant placement in the interforaminal region of the mandible. The interpretation of the panoramic radiograph showed subjective (Table 1) did not show accuracy in diagnosis of the presence of AL, as well as inferred the underestimation or overestimation of the size of the AL when compared with the CBCT. Thus, panoramic radiography is unreliable in identifying the AL (Table 3), which is in agreement with other studies that use exclusively in implant planning in the region is questionable interforaminal[9,13,14].

The picture quality and contrast between adjacent structures are important factors in the task of identifying various anatomical structures and possible injuries. CBCT has been proven as reliable imaging technique for the maxillofacial region[15-18], extremely useful in evaluating bone, once it provides images with high contrast without overlapping images and displays real action.

The use of CBCT for oral and maxillofacial imaging holds the promise of overcoming these obstacles while providing more accurate craniometrical and diagnostic information than conventional radiographic techniques[19].

Thus, to obtain accurate measurements and diagnosis, the CBCT was evaluated. Furthermore, computed tomography is the best method to obtain minimally invasive and correct preoperative measurement of the AL in living patients[20,21].

Despite of the prevalence of AL varies considerably in the literature, our results are in agreement with others modalities of study such as: anatomic cadavers studies; use of panoramic radiographs as well as in CBCT[9,13,17,22,23]. Using panoramic radiographs, AL was detected in 42.6% of the cases, while using CBCT it was found in only 29.8% of them.

The method used to measure the extent of previous AL is relevant. Conventional radiography does not seem to show the true anatomical shape and extent of the AL. Confirming the reliability of CBCT as a tool to determine the extent of previous AL, differences of less than 0,1mm between anatomical measurements performed on cadavers and CBCT images were found[9,13,18]. Our results ranged from 2.5mm to 3.25mm lengh which is consistent with other studies (Table 4).

Anatomical Considerations

The length of AL ranging from 0 mm to 9 mm has been reported[9,13,17,18,22] and the longest loop reported in the literature was 11 mm[24].

Although some potential influence of ethnic-geographic variability[25], methodological differences and lack of clear definitions for AL are recurrent in the literature and may yield differences in prevalence findings and measures. The term AL refers to the curvature of the nerve chin in a "loop", which surpass the earlier level of mental foramen returns toward the right in the upper, lateral and distal. A measure of the extent of previous AL is a feature that should be viewed cautiously. Extensions of AL greater than 2mm are clinically relevant, especially for installation of surgical implants[26]. Where such values corroborate our results, when the AL present, the minimum length of 2.5 mm found already to be considered when planning surgery. (Table 5)

Surgical Considerations

Clinically, if an implant was placed in contact with the anterior loop of the mental nerve, the implant would likely fail because of increased edema and a lack of supportive hard tissue together with increasing soft tissue in the area.

Injury to the mental nerve or inferior alveolar nerve should be carefully considered when placing an implant in this area.

Fixed distances above the mental foramen, supposedly safe, were recommended in the past[9]. However, the results of this study in accordance with the results of other studies[17,18] show that beyond the limitation of radiographic conventional anatomic variability cannot be neglected. Therefore, sectional tests, such as CBCT should be used for evaluation of AL. Thus, the surgeons must familiarize themselves with anatomic information obtained by measuring the length of the previous loop on a case-by-case basis once the recommendations of fixed distances to the anatomical landmarks of the AL are unreliable.

Although it is known that the linear measurements obtained in CBCT images represent real values, an important aspect to be considered is the transfer of these measures for clinical practice. Ideally, measurements should be easily reproduced during surgery. However, the plan used as a reference for the implementation of measures is often overlooked.

However, if a significant anterior loop of the mental nerve is discovered, it should be classified as more of an anomaly than a historically common structure. According to the results of this study, the frequency of AL was too low. Thus, it can be assumed that it is a rare condition in the population studied, and considering that LA has a range of 0 to 11mm[9,13,17,18,24,27-30], it becomes extremely relevant when present.

CONCLUSION

The limitations of PR show the need for three-dimensional tests (CBCT) for preoperative assessment and AL becomes extremely clinically relevant when present in planning for dental implants.

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CONCLUSÃO

1 – A tomografia computadorizada de feixe cônico apresentou-se como a melhor opção, em relação à radiografia panorâmica, a diagnósticar com precisão a presença e extensão da alça anterior no nervo mentual.

2 – Quando a alça anterior do nervo mentual estiver presente, torna-se extremamente relevante, do ponto de vista clínico, devido a sua grande variabilidade anatômica.

3 – Não se deve considerar um valor de referência fixo, como margem de segurança, para as intervenções cirúrgicas na região pré forame mentual.

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ANEXO

COMITÊ DE ÉTICA EM PESQUISA

FACULDADE DE ODONTOLOGIA DE PIRACICABA
UNIVERSIDADE ESTADUAL DE CAMPINAS

CERTIFICADO

O Comitê de Ética em Pesquisa da FOP-UNICAMP certifica que o projeto de pesquisa "**Qualidade óssea do complexo maxilomandibular através das imagens da radiografia panorâmica digital e da tomografia computadorizada de feixe cônico: Validação da classificação de Klemetti**", protocolo nº **138/2009**, dos pesquisadores **MARIA BEATRIZ CARRAZZONE CAL ALONSO e PLAUTO CHRISTOPHER ARANHA WATANABE**, satisfaz as exigências do Conselho Nacional de Saúde – Ministério da Saúde para as pesquisas em seres humanos e foi aprovado por este comitê em 28/10/2009.

The Ethics Committee in Research of the School of Dentistry of Piracicaba - State University of Campinas, certify that the project "**Bone quality of maxillomandibular complex using images of panoramic radiographs and cone beam computed tomography: Validating of Klemetti index**", register number **138/2009**, of **MARIA BEATRIZ CARRAZZONE CAL ALONSO and PLAUTO CHRISTOPHER ARANHA WATANABE**, comply with the recommendations of the National Health Council – Ministry of Health of Brazil for research in human subjects and therefore was approved by this committee at 28/10/2009.

Prof. Pablo Agustín Vargas
Secretário
CEP/FOP/UNICAMP

Prof. Jacks Jorge Júnior
Coordenador
CEP/FOP/UNICAMP

Nota: O título do protocolo aparece como fornecido pelos pesquisadores, sem qualquer edição.
Notice: The title of the project appears as provided by the authors, without editing.