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ANDRÉ WEISSHEIMER

MÉTODOS DE AVALIAÇÃO TRIDIMENSIONAL DO COMPLEXO CRANIOFACIAL EM TOMOGRAFIA CONE BEAM

Profa. Dra. Luciane Macedo de Menezes.
Orientadora

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Tese apresentada ao Programa de Pós-graduação em Odontologia da Faculdade de Odontologia da Pontifícia Universidade Católica do Rio Grande do Sul como requisito final para obtenção do título de Doutor em Odontologia, na Área de Concentração Ortodontia e Ortopedia Facial.

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ANDRÉ WEISSHEIMER

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Esta Tese foi julgada adequada para obtenção do Título de "Doutor em Odontologia" e aprovada em sua forma final pelo Programa de Pós-Graduação em Odontologia da Faculdade de Odontologia da Pontifícia Universidade Católica do Rio Grande do Sul.

Porto Alegre, 28 de novembro de 2013.

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"Na vida, o difícil se faz imediatamente, e o impossível, logo em seguida..."

Dedico essa tese a Deus e a minha família.

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Resumo

Introdução: o objetivo desta tese foi avaliar a acurácia de programas para análises 3D do complexo maxilofacial em tomografia computadorizada cone beam (TCCB). Com esse propósito, dois estudos foram realizados. O primeiro estudo avaliou a precisão e acurácia de 6 programas para avaliação do volume da via aérea superior em TCCB. O segundo estudo objetivou validar um método rápido de superposição 3D de TCCB. **Método:** no estudo 1, a amostra consistiu de 33 pacientes e 1 *Phantom* de acrílico da orofaringe (PAO), escaneados com o tomógrafo iCAT. O volume conhecido do PAO foi utilizado com "padrão ouro". Segmentação semiautomática da orofaringe dos pacientes (OP) e do PAO foi realizada com os programas Mimics, ITK-Snap, OsiriX, Dolphin3D, InVivo Dental e Ondemand3D. No estudo 2, a amostra consistiu de TCCB de 18 pacientes. Em 10 pacientes, como padrão de comparação, a TCCB pré-tratamento foi reorientada espacialmente, salva como TCCB reorientada, e então superposta na imagem original. Em 8 pacientes, sendo 4 sem crescimento e 4 em crescimento, foram superpostas as TCCB e pós-tratamento. A acurácia da superposição foi avaliada através de inspeção visual e mensurada através do programa CFM com mapas coloridos. **Resultados:** no estudo 1, as segmentações com o Mimics, Dolphin3D, OsiriX e ITK-Snap mostraram menos de 2% de erro no volume do PAO em comparação ao "padrão ouro". O Ondemand3D e o InVivo Dental apresentaram mais de 5% de erro no volume do PAO em comparação ao "padrão ouro". As segmentações da OP com o ITK-Snap, Mimics, OsiriX e Dolphin3D foram estatisticamente diferentes (P<.05) em comparação ao InVivo Dental. Não houve diferença estatisticamente significante (P>.05) entre os programas InVivo Dental e o OnDemand3D. No estudo 2, o erro da superposição das TCCB reorientadas, medidas através dos mapas coloridos foi menor que 0,5mm. O erro da superposição das TCCB pré-tratamento e pós-tratamento para pacientes com e sem crescimento, na região da base do crânio, foi menor que 0,5 mm e considerado aceitável e clinicamente insignificante. **Conclusão:** no estudo 1, todos os 6 programas foram precisos, mas apresentaram erros no volume da segmentação da OP. Mimics, Dolphin3D, ITK-Snap e OsiriX foram considerados similares e mais acurados em comparação ao InVivo Dental e Ondemand3D. No estudo 2, o método de superposição baseado em voxel avaliado foi reproduzível em diferentes condições clínicas, rápido e potencialmente aplicável para pesquisa e prática clínica.

Palavras chave: Tomografia computadorizada cone beam, Superposição 3D, Craniofacial, Via aérea superior e Programa de visualização de imagem.

Abstract

Introduction: this thesis aimed to evaluate the software accuracy for 3D analysis of craniofacial complex in cone beam computed tomography (CBCT). With this purpose, two studies were performed. The first study evaluated the precision and accuracy of 6 imaging software programs for measuring the upper airway volume in CBCT. The second study aimed to validate a fast method for 3D superimposition of CBCT. **Methods:** in study 1, the sample consisted of 33 growing patients and 1 oropharynx acrylic phantom (OAP), scanned with iCAT scanner. The known OAP volume was used as gold standard (GS). Semi-automatic segmentations of the patients´ oropharynx (OP) and OAP was performed using Mimics, ITK-Snap, OsiriX, Dolphin3D, InVivo Dental and Ondemand3D software programs. In study 2, the sample consisted of CBCT scans of 18 patients. For 10 patients as a gold standard, the spatial position of the pretreatment CBCT volume was reoriented, saved as a reoriented volume, and then superimposed to the original image. For 8 patients, 4 non-growing and 4 growing patients, pre and post-treatment scans were superimposed. Superimposition accuracy was assessed by visual inspection and measured by using the CMF application and expressed via color maps. **Results:** in study 1, the OAP segmentations with Mimics, Dolphin3D, OsiriX and ITK-Snap showed less than 2% error in volume compared to the GS. Ondemand3D and InVivo Dental showed more than 5% error compared to the GS. In the OP segmentation, ITK-Snap, Mimics, OsiriX and Dolphin3D were statistically significantly different ($P<.05$) from InVivo Dental. No statistical difference ($P>.05$) was found between InVivo Dental and OnDemand3D. In study 2, Superimposition error of the spatial reorientation as measured by the color-coded surface distances was less than 0.5mm. Superimposition error of pre and post treatment scans for both growing and non-growing patients at the cranial base were smaller than 0.5 mm, which was considered acceptable and clinically insignificant. **Conclusion:** in study 1, all 6 imaging software programs were reliable but showed errors in the volume segmentation of OP. Mimics, Dolphin3D, ITK-Snap and OsiriX were similar and more accurate than InVivo Dental and Ondemand3D. In study 2, the voxel-based superimposition method evaluated was reproducible in different clinical conditions, time-efficient and potentially applicable for both research and clinical practice.

Keywords: Cone-Beam Computed Tomography, 3D superimposition, Craniofacial, Upper airway and Imaging software.

Sumário

1. Introdução

A Ortodontia é o ramo da ciência especializada no diagnóstico, prevenção e correção das irregularidades dento-faciais. O diagnóstico ortodôntico constitui a base fundamental da especialidade, sendo indispensável na busca dos objetivos do tratamento ortodôntico. As radiografias convencionais representam parte da documentação ortodôntica e ainda são utilizadas para o diagnóstico, análise do crescimento e desenvolvimento craniofacial e avaliação dos resultados do tratamento. As radiografias são representações bidimensionais (2D) de estruturas tridimensionais (3D), provendo informações diagnósticas limitadas. Além do mais, possuem magnificação da imagem, distorções geométricas e sobreposição de estruturas anatômicas. A introdução da tomografia computadorizada (TC) pelo Engenheiro Inglês Godfrey Hounsfield juntamente com o físico norte-americano Allan Comark, lhes valeu o prémio Nobel de Medicina de 1979 e possibilitou a inclusão da terceira dimensão no diagnóstico por imagem. Apesar de utilizada rotineiramente na medicina, o emprego da TC na Odontologia era limitado em função do alto custo financeiro e dose de radiação. Essas desvantagens foram superadas pela introdução da tomografia computadorizada de feixe cônico ou cone beam (TCCB). Avanços em termos de custo financeiro, dose de radiação e acurácia vêm contribuindo para a consolidação da TCCB na Odontologia, especialmente nas áreas da ortodontia e cirurgia buco-maxilo-facial.

A avaliação morfológica do complexo craniofacial, utilizando TCCB, pode ser realizada de diversas maneiras, dentre as quais, destaca-se a técnica de segmentação. A segmentação pode ser definida como o processo de construção de modelos virtuais 3D (chamados de segmentações) de uma determinada estrutura. Significa separar um elemento específico, através da remoção de outras estruturas de não interesse, para melhor visualização e análise. Modelos virtuais 3D de estruturas esqueléticas, tecidos moles e vias aéreas podem ser construídos por meio de segmentação, servindo como base para análises quantitativas e qualitativas do complexo craniofacial. A qualidade final da segmentação depende de aspectos relacionados à qualidade da imagem e da capacidade dos algoritmos em identificar e preencher as estruturas anatômicas de interesse. O problema é que, em teoria, programas com algoritmos distintos podem gerar segmentações diferentes, comprometendo o controle de qualidade das análises tridimensionais. Uma recente revisão sistemática da literatura relatou 18 diferentes programas contendo módulos destinados à visualização, mensuração e análise das vias aéreas superiores.[1] Um único estudo de validação comparou a acurácia e precisão de 3 programas para avaliação das vias aéreas superiores.[2] Isso significa que a grande maioria dos programas está sendo comercializados sem estudos de validação. Essa falta de controle na qualidade dos programas para diagnóstico 3D em TCCB pode ter implicações sérias, especialmente nos casos de apneia obstrutiva do sono. Por isso, é imprescindível a realização de estudos para validação de programas destinados ao diagnostico 3D das vias aéreas superiores.

Além do diagnóstico das vias aéreas, a TCCB vem modificando a maneira como ortodontistas e cirurgiões avaliam os resultados dos tratamentos ortodôntico-cirúrgicos. A superposição de radiografias cefalométricas, embora ainda utilizada, esta sendo substituída gradativamente pela superposição de TCCB, em função dos avanços nos algoritmos para registro de imagens. Atualmente, a superposição tridimensional de TCCB, com registro na base do crânio, é considerada o método mais avançado para avaliação 3D dos efeitos do tratamento ortodôntico-cirúrgico. Dentre os métodos utilizados para superposição de TCCB, os mais acurados são os que utilizam os valores dos tons de cinza ou densidade dos voxels (voxel-based). Cevidanes et al, em 2005, introduziu na Odontologia o primeiro método automático para superposição de TCCB, com base nos tons de cinza dos voxels da base do crânio.[3] Esse método é baseado na teoria da informação mútua, e foi descrito por Maes et al, em 1997.[4] No método original descrito por Cevidanes et al, dois programas são requeridos. O primeiro é utilizado para construir modelos virtuais 3D da base do crânio e o segundo programa para realizar a superposição das tomografias através da transformação rígida (rotação e translação). Esse método tem sido utilizado em varias pesquisas e é considerado o método mais avançado para superposição de TCCB e avaliação 3D dos tratamentos.[3,5-9] Embora esse método utilize programas gratuitos, desenvolvidos pelo departamento de ciências da computação da *University of North Caroline (UNC)*, a complexidade no manuseio dos programas e a necessidade de arquivos específicos (pipelines) não disponibilizados, tornam a utilização deste método de superposição restrita a alguns centros de pesquisa. Outra desvantagem é o longo tempo dispendido (45 a 60 minutos para um usuário treinado) para completar o processo de superposição das tomografias (segmentação + superposição). Essas limitações dificultam a popularização e aplicação desse método na prática clínica diária por ortodontistas e cirurgiões.

Em 2010, os pesquisadores Jeong-Ho Choi, da *Seul National University*, e James Mah, da *University of Southern California (USC)*, desenvolveram um novo método de superposição automática de TCCB com base nos tons de cinza dos voxels (voxel-based).[10] Esse método de superposição também é baseado na teoria da informação mútua e está presente no programa Ondemand3D (Cybermed, Seoul, Korea), disponível comercialmente. A superposição dos volumes de TCCB é realizada de forma rápida (10 a 15 segundos) com apenas um programa e sem a necessidade de segmentação prévia como no método descrito por Cevidanes et al. Esse método tem um grande potencial para aplicação na prática diária em função da rapidez e facilidade do processo superposição. Embora esse método tenha sido apresentado por Choi e Mah,[10] e ter sido utilizado em algumas pesquisas recentes,[11-13] estudos de validação científica para testar a sua acurácia são necessários.

2. Proposição

2.1 Objetivo geral

Avaliar a acurácia de programas para avaliação tridimensional da região craniofacial em tomografia computadorizada cone beam.

2.2 Objetivos específicos

2.2.1 Avaliar e comparar a precisão e acurácia de 6 programas para avaliação do volume da via aérea orofaríngea em tomografia computadorizada cone beam (Artigo 1).

2.2.2 Avaliar a acurácia de um método rápido de superposição tridimensional de tomografia computadorizada cone beam (Artigo 2).

3. Artigo 1

Titulo: *Imaging software accuracy for 3-dimensional analysis of the upper airway*

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ORIGINAL ARTICLE

AJO-DO

Imaging software accuracy for 3-dimensional analysis of the upper airway

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Introduction: The aim of this study was to compare the precision and accuracy of 6 imaging software programs for measuring upper airway volumes in cone-beam computed tomography data. **Methods:** The sample consisted of 33 growing patients and an oropharynx acrylic phantom, scanned with an i-CAT scanner (Imaging Sciences International, Hatfield, Pa). The known oropharynx acrylic phantom volume was used as the gold standard. Semi-automatic segmentations with interactive and fixed threshold protocols of the patients' oropharynx and oropharynx acrylic phantom were performed by using Mimics (Materialise, Leuven, Belgium), ITK-Snap (www.itksnap.org), OsiriX (Pixmeo, Geneva, Switzerland), Dolphin3D (Dolphin Imaging & Management Solutions, Chatsworth, Calif), InVivo Dental (Anatomage, San Jose, Calif), and Ondemand3D (CyberMed, Seoul, Korea) software programs. The intraclass correlation coefficient was used for the reliability tests. A repeated measurements analysis of variance (ANOVA) test and post-hoc tests (Bonferroni) were used to compare the software programs. **Results:** The reliability was high for all programs. With the interactive threshold protocol, the oropharynx acrylic phantom segmentations with Mimics, Dolphin3D, OsiriX, and ITK-Snap showed less than 2% errors in volumes compared with the gold standard. Ondemand3D and InVivo Dental had more than 5% errors compared with the gold standard. With the fixed threshold protocol, the volume errors were similar (–11.1% to –11.7%) among the programs. In the oropharynx segmentation with the interactive protocol, ITK-Snap, Mimics, OsiriX, and Dolphin3D were statistically significantly different ($P < 0.05$) from InVivo Dental. No statistical difference ($P > 0.05$) was found between InVivo Dental and OnDemand3D. **Conclusions:** All 6 imaging software programs were reliable but had errors in the volume segmentations of the oropharynx. Mimics, Dolphin3D, ITK-Snap, and OsiriX were similar and more accurate than InVivo Dental and Ondemand3D for upper airway assessment. (Am J Orthod Dentofacial Orthop 2012;142:801-13)

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For the last century, the gold standard method for analysis of craniofacial development was cephalometry, with linear and angular measurements performed on lateral headfilms. However, as a 2-dimensional representation of 3-dimensional (3D) structures, lateral headfilms offer limited information about the airways.[1] Information regarding axial cross-sectional areas and overall volumes can only be determined by 3D imaging modalities.[2-9] Medical computed tomography is a 3D imaging modality used in medicine but not as a routine method for airway analysis because of its high cost both financially and in terms of radiation. These drawbacks were overcome with the introduction of cone-beam computed tomography (CBCT). CBCT is becoming a popular diagnostic method for visualizing and analyzing upper airways. Since its introduction in 1998, CBCT technology has been improved, with lower costs, less radiation exposure to patients, and better accuracy in identifying the boundaries of soft tissues and empty spaces (air).[7] Furthermore, CBCT allows for the assessment of axial cross-sectional areas and volumes of the upper airways. The accuracy and reliability of CBCT for upper airway evaluation have been validated in previous studies,[2,6,8,10-12] and the use of CBCT for airway evaluation has been reported in a systematic review of the literature.[1]

The evaluation of the size, shape, and volume of the upper airway starts by defining the volume corresponding to the airway passages, a process called segmentation. In medical imaging, segmentation is defined as the construction of 3D virtual surface models (called *segmentations*) to match the volumetric data.[13] In other words, it means to separate a specific element (eg, upper airway) and remove all other structures of noninterest for better visualization and analysis. Upper airway segmentation can be either manual or semiautomatic. In the manual approach, the segmentation is performed slice by slice by the user. The software then combines all slices to form a 3D volume. This method is time-consuming and almost impractical for clinical application. In contrast, semiautomatic segmentation of the airway is significantly faster than manual segmentation.[14] In the semiautomatic approach, the computer automatically differentiates the air and the surrounding soft tissues by using the differences in density values (grey levels) of these structures. In some programs, the semiautomatic segmentation includes 2 user-guided interactive steps: placement of initial seed regions in the axial, coronal, and sagittal slices, and selection of an initial threshold.

Image thresholding is the basis for segmentation. When the user determines a threshold interval, it means that all voxels with grey levels inside that interval will be selected to construct the 3D model (segmentation). Lenza et al[7] reported the use of a single threshold value to segment the airway in each patient's CBCT scan. This approach can generate errors, especially in volume analysis, but it is certainly more reproducible than the use of a dynamic threshold. However, there are few studies comparing the results of threshold filtering with different imaging software programs for airway assessment.

A growing number of software programs to manage and analyze digital imaging communications in medicine (DICOM) files are introduced in the market every year. Many of these have incorporated tools to segment and measure the airway. A systematic review of the literature reported 18 imaging software programs for viewing and analyzing the upper airway in CBCT.[1] However, validation studies with a clear study design were performed in only 4 software programs.[10,14] The systematic review suggested that studies assessing the accuracy and reliability of current and new software programs must be conducted before these imaging software programs can be implemented for airway analysis.[1]

The aim of this study was to compare the precision and accuracy of 6 imaging software programs for measuring the oropharynx volume in CBCT images. The primary null hypothesis, that there are no significant differences in airway volume measurements among the 6 imaging software programs, was tested.

MATERIAL AND METHODS

This study was approved by the ethical committee of Pontifical Catholic University of Rio Grande do Sul in Brazil. The records we used were obtained from the patient database of the Department of Orthodontics and consisted of the pretreatment CBCT scans of a preexisting rapid maxillary expansion sample.[15] The sample included 33 growing patients (mean chronologic age, 10.7 years; range, 7.2-14.5 years) with transverse maxillary deficiency and no congenital malformations. Additionally, a custom-made oropharynx acrylic phantom with a known volume was used as the gold standard (Fig 1). The oropharynx acrylic phantom consisted of an air-filled plastic rectangular prism surrounded by water. Water was the medium of choice because it has a similar attenuation value to soft tissue. The dimensions of the outer surface of the phantom were created to simulate the dimensions of a growing patient's neck, and the rectangular prism to simulate the dimensions of the oropharynx. The oropharynx acrylic phantom's dimensions were measured to the nearest 0.01 mm by using digital calipers (model 727; Starret, Itú, São Paulo, Brazil), and the volume was calculated multiplying the base area by the height. Additionally, the oropharynx acrylic phantom's volume was confirmed by using the water weight equivalent. The oropharynx acrylic phantom was filled with distilled water, at 20°C, and the water weight was determined by using a digital scientific scale (model BG1000; Gehaka, São Paulo, São Paulo, Brazil).

Patients and the phantom were scanned with the i-CAT scanner (Imaging Sciences International, Hatfield, Pa) set at 120 kVp, 8 mA, scan time of 40 seconds, and 0.3-mm voxel dimension. The images were reconstructed with a 0.3-mm slice thickness and exported as DICOM files. Any CBCT scans with artifacts distorting the airway borders were excluded from this study. CBCT scans were imported into OsiriX software (version 4.0; Pixmeo, Geneva, Switzerland) for head orientation and definition of the oropharynx's region of interest. The head orientation was performed by using the palatal plane as a reference (ANS-PNS parallel to the global horizontal plane in the sagittal view and perpendicular to the global horizontal plane in the axial view). After head orientation, a tool in OsiriX (Vol cutter) was used

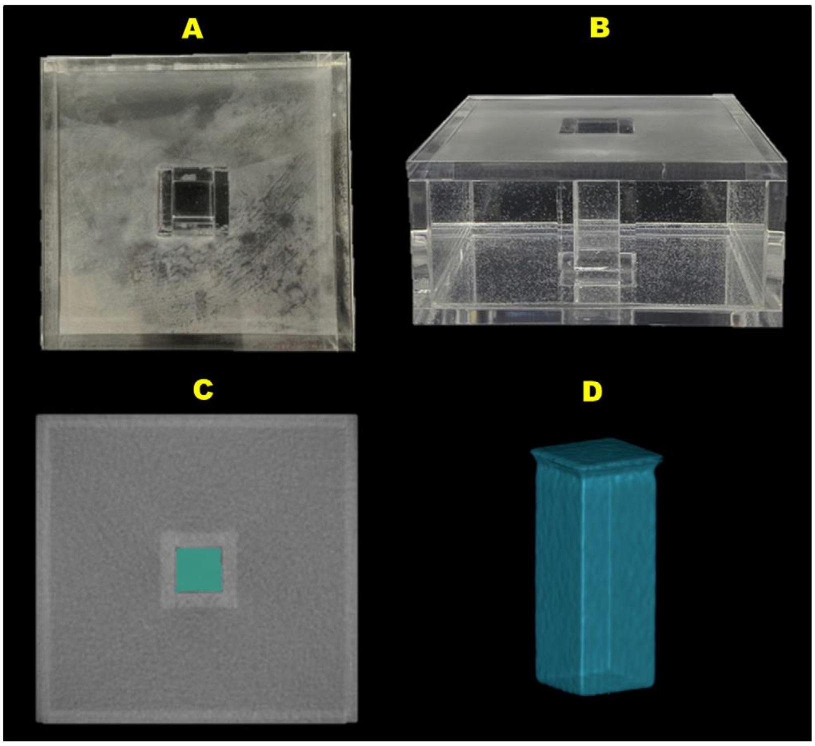

Fig 1. **A** and **B**, Oropharynx acrylic phantom used as the gold standard; **C**, CBCT image of the oropharynx acrylic phantom in the axial view, with the inner part (prism) containing air as the region of interest for segmentation; **D**, example of a 3D model generated from oropharynx acrylic phantom segmentation.

to select and crop the oropharynx, according to the following references: superior limit, extension of the palatal plane (ANS-PNS) to the posterior wall of the pharynx; inferior limit, a plane parallel to the palatal plane that passes through the most anteroinferior point of the second cervical vertebrae[14]; anterior limit, a perpendicular plane to palatal plane that passes through the posterior nasal spine; posterior limit, posteriorly to the posterior wall of pharynx (Fig 2, *A* and *B*). The regions of noninterest were excluded, and the new volume, containing only the oropharynx region, was exported as the new DICOM file, with the same voxel resolution but a smaller file size (Fig 2, *C*).

Six imaging software programs were used to segment and compute volumes from the CBCT images of the patients' oropharynx and the oropharynx acrylic phantom (Figs 3 and 4). The specifications of each software program are shown in Table I. The oropharynx and the oropharynx acrylic phantom segmentations were performed according to each software manufacturer's recommendations,[16-21] with 2 techniques for semiautomatic segmentation: (1) interactive threshold interval, as used in a previous study,[14] and (2) fixed threshold interval. In the interactive thresholding, the operator selected the best threshold interval based on a visual analysis of the anatomic boundaries of the oropharynx and the oropharynx acrylic phantom in the axial, sagittal, and coronal slices. In the fixed threshold, the threshold interval was fixed (−1000 to −587 grey levels) to test the variability among the software programs. The segmentations with interactive thresholding were performed with Mimics (version 14.12; Materialise, Leuven, Belgium), Dolphin3D (version 11.7; Dolphin Imaging & Management Solutions, Chatsworth, Calif), Ondemand3D (version 1.0.9.1451; CyberMed, Seoul, Korea), OsiriX (version 4.0; Pixmeo), and ITK-Snap (version 2.2.0; www.itksnap.org) (except InVivo Dental [version 5.0; Anatomage, San Jose, Calif]), and those with

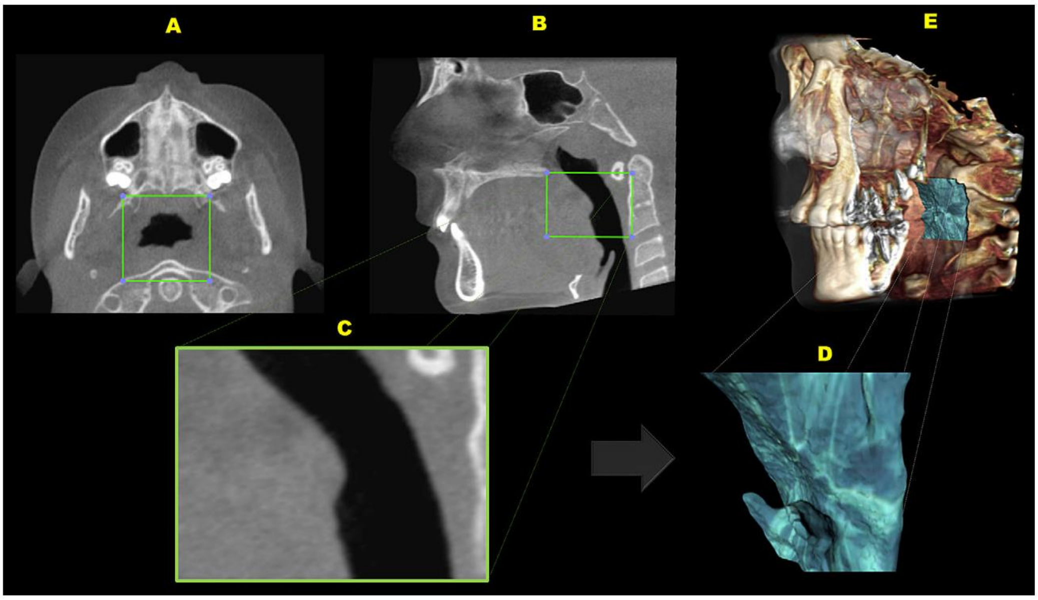

Fig 2. **A** and **B**, CBCT images after head reorientation with OsiriX software, in the axial and sagittal views, respectively, with the oropharynx's region of interest delimited (*green box*) in the axial and sagittal images; **C**, 3D volume exported as a new DICOM file; **D**, from this new volume, the segmentation was performed and the oropharynx's 3D model obtained for volume analysis; **E**, location of the oropharynx's region of interest in the patient's head.

fixed thresholding were InVivo Dental, Mimics, Ondemand3D, OsiriX, and ITK-Snap (except Dolphin3D).

Statistical analysis

The oropharynx and the oropharynx acrylic phantom segmentations and the volume analyses were performed by 1 investigator (A.W.). All measurements were made again 2 weeks later. The reliability of the first and second measurements was evaluated by intraclass correlation coefficient. A total of 680 segmentations were performed with the 6 imaging software programs. Values were imported into an Excel spreadsheet (Microsoft, Redmond, Wash).

The oropharynx acrylic phantom measurements with the 6 imaging software programs failed the Kolmogorov-Smirnov test for normality, so nonparametric tests were used. The oropharynx acrylic phantom segmentations were compared with the gold standard by using the Wilcoxon signed rank test for related samples. The oropharynx volume measurements of the 33 patients, with the 6 imaging software programs and the 2 threshold protocols (interactive and fixed), were normally distributed. Not all imaging software programs offered both interactive and fixed thresholds. A repeated measurements analysis of variance (ANOVA) test was used to compare the Mimics, Dolphin3D, Ondemand3D, OsiriX, and ITK-Snap software programs with the interactive threshold, and a second repeated measurements ANOVA test was used to compare the InVivo Dental, Mimics, Ondemand3D, OsiriX, and ITK-Snap software programs supporting a fixed threshold capability. The Mauchly's test of sphericity showed that the assumption of sphericity was violated; the Greenhouse-Geisser correction was used to complement the ANOVA test. Additionally, post-hoc tests with the Bonferroni correction were used to compare the volume measurements between 2 imaging software programs. Statistical significance was established at $\alpha = 0.05$. The statistical analysis was performed with SPSS software (version 12.0 for Windows; SPSS, Chicago, Ill).

RESULTS

The oropharynx acrylic phantom was used as the gold standard by comparing the actual physical volume with the segmentation volume in the CBCT images. The oropharynx acrylic phantom's physical volume was

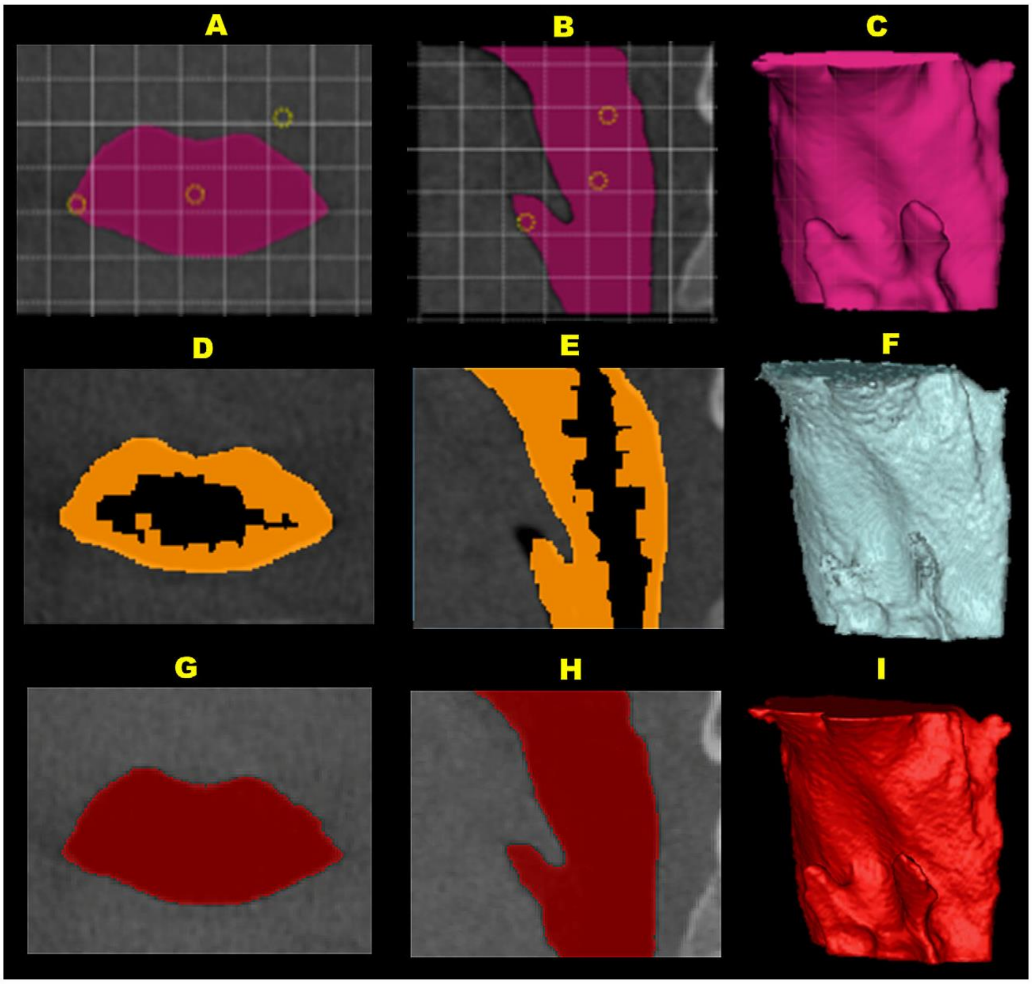

Fig 3. Examples of the oropharynx segmentation process with 3 imaging software programs: **A**, **D**, and **G**, axial views and **B**, **E**, and **H**, sagittal views of the oropharynx segmentation processes in the CBCT images; **C**, **F**, and **I**, 3D models of a patient's oropharynx obtained from segmentations. **A-C**, Segmentation process with Dolphin3D (*pink*) was based on addition and growth of seeds (*yellow circles*) that spread, matched, and filled the oropharynx airway. **D-F**, Segmentation with Ondemand3D (*orange*) showing, in the axial and sagittal views, empty spaces (*black*) without segmentation in some areas and overflowed in other regions. **G-I**, Segmentation with ITK-Snap (*red*). The segmentation matched precisely the oropharynx in the axial and sagittal views.

computed as 9.405 cm^3 with the formula: base area (235.13 mm^2) × height (40 mm). Additionally, the oropharynx acrylic phantom's volume was measured by the water-weight technique. Considering the weight measured (9.40 g) and the standard density of water at 20°C (1 cm^3 of water, 0.9982 g), the volume calculated by the rule of 3 (volume = 9.4/0.9982) was 9.410 cm^3. By using the average of the 2 methods, the oropharynx acrylic phantom's actual physical volume (gold standard) was 9.407 cm^3.

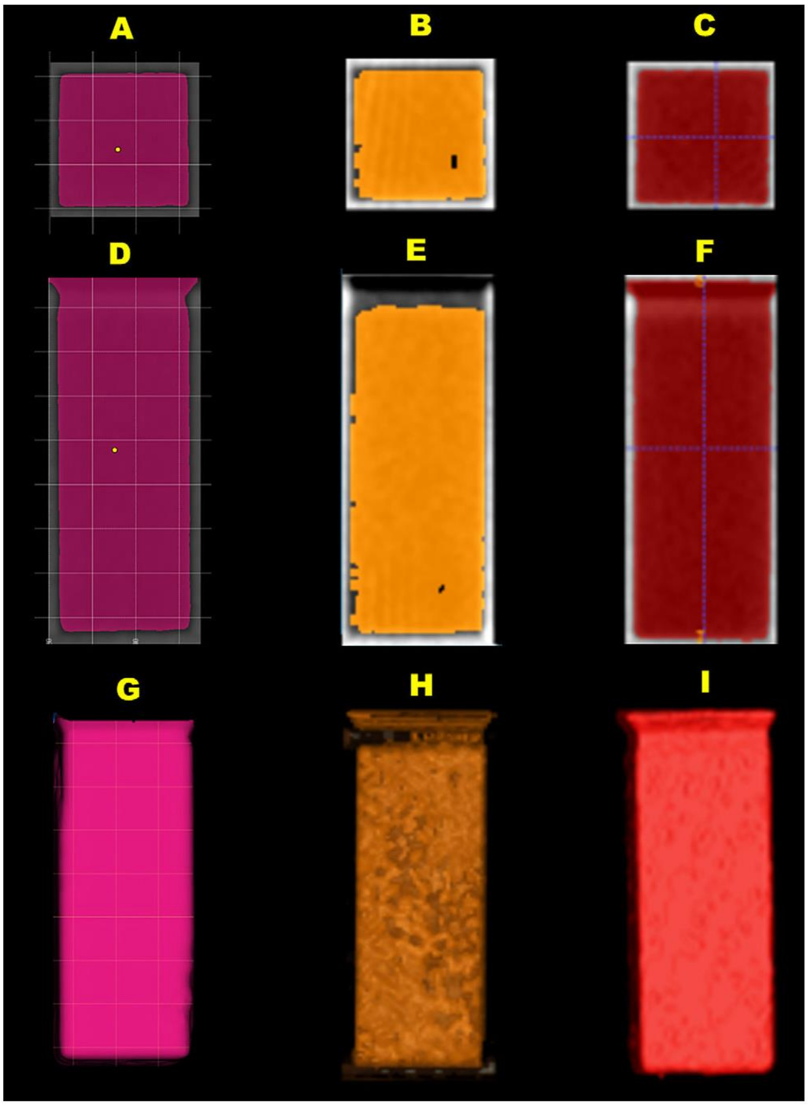

Fig 4. Examples of the oropharynx acrylic phantom segmentation process with 3 imaging software programs: **A-C,** axial views and **D-F,** sagittal views of the oropharynx acrylic phantom segmentation processes in CBCT images; **G-I,** 3D models of the oropharynx acrylic phantom obtained from segmentations. **A**, **D**, and **G**, Segmentation with Dolphin3D (*pink*). **B**, **E**, and **H**, Segmentation with Ondemand3D (*orange*) showing, in the axial and sagittal views, empty spaces (*black*) without segmentation in some areas and overflowed in other regions. **C**, **F**, and **I**, Segmentation with ITK-Snap (*red*). The segmentation matched precisely the oropharynx acrylic phantom in the axial and sagittal views.

Table I. CBCT imaging software compared in this study

Software	*Description*	*Operational system*	
Dolphin3D	Version 11.7; Dolphin Imaging & Management Solutions, Chatsworth, Calif	Windows	Not free
InVivo Dental	Version 5.0; Anatomage, San Jose, Calif	Windows	Not free
Ondemand3D	Version 1.0.9.1451; CyberMed, Seoul, Korea	Windows	Not free
Mimics	Version 14.12; Materialise, Leuven, Belgium	Windows	Not free
OsiriX	Version 4.0; Pixmeo, Geneva, Switzerland	Mac OS X	Free open source
ITK-Snap	Version 2.2.0; www.itksnap.org	Windows Mac OS X Linux	Free open source

Table II. Descriptive statistics of oropharynx acrylic phantom volume segmentation with the 6 imaging software programs

Software program	*Segmentation volume mean (mm^3)*	*Gold standard volume (mm^3)*	*Difference (mm^3)*	*Difference (%)*
Mimics	9392	9407	−15	−0.2
Dolphin3D	9315	9407	−92	−1.0
OsiriX	9289	9407	−118	−1.3
ITK-Snap	9236	9407	−172	−1.8
OnDemand3D	8809	9407	−598	−6.4
InVivo Dental	8366	9407	−1041	−11.1
Mimics FT	8340	9407	−1067	−11.3
OnDemand3D FT	8344	9407	−1063	−11.3
ITK-Snap FT	8328	9407	−1079	−11.5
OsiriX FT	8310	9407	−1097	−11.7

Programs designated *FT* (fixed threshold protocol) were used with a different segmentation protocol of −1000 to −587 grey levels.

The method repeatability for oropharynx acrylic phantom segmentations was excellent. The intraclass correlation coefficient between the first and second measurements (mean volume) was 0.999. The Wilcoxon signed rank test showed statistically significant differences ($P = 0.005$) between the medians of all 10 oropharynx acrylic phantom segmentation volumes and the gold standard. All 6 imaging software programs, with both interactive and fixed threshold protocols, underestimated the gold standard volume (Table II). When the interactive thresholding technique was used, Mimics, Dolphin3D, OsiriX, and ITK-Snap showed less than 2% error differences (underestimated) in volume calculation compared with the gold standard, whereas Ondemand3D and InVivo Dental showed more than a 5% errors compared with the gold standard (Table II). When the fixed threshold interval technique was used (−1000 to −587 grey levels), the software programs (InVivo Dental, Mimics, Ondemand3D, OsiriX, and ITK-Snap) had similar errors and underestimated the phantom volume by 11% compared with the gold standard (Table II).

The method repeatability for the patients' oropharynx measurements was high (ICC >0.94) for all imaging software programs (Table III). When oropharynx segmentations were performed with interactive thresholding, the volume measurements with the 6 imaging softwares were statistically different (repeated measures ANOVA with the Greenhouse-Geisser correction: $F = 8.3$; $P = 0.006$). The descriptive statistical analysis showed higher oropharynx mean volumes for ITK-Snap (7174 mm^3), Mimics (7163 mm^3), OsiriX (7086 mm^3), and Dolphin3D (7071 mm^3), and lower mean volumes for InVivo Dental (6661 mm^3) and Ondemand3D (6061 mm^3) (Table III). According to the Bonferroni post-hoc paired comparisons, there were no statistically significant differences ($P > 0.05$) among ITK-Snap, Mimics, OsiriX, Dolphin3D, and Ondemand3D. However, the oropharynx volume segmentations with ITK-Snap, Mimics, OsiriX, and Dolphin3D were statistically significantly different from InVivo Dental. The comparison between InVivo Dental and OnDemand3D showed no significant difference (Table IV). When the fixed threshold technique was used, the ANOVA analysis with the Greenhouse-Geisser correction showed overall statistically significant differences ($F = 30.7$; $P < 0.001$) in the oropharynx volume segmentation among all imaging software programs tested (InVivo Dental, Mimics, Ondemand3D, OsiriX, and ITK-Snap). The post-hoc paired comparisons also showed significant differences

Table III. Descriptive analysis of 33 patients' oropharynx volumes with the 6 imaging software programs

Software	*Volume measurement 1 (mm³)*	*Volume measurement 2 (mm³)*	*ICC*	*Mean volume (mm³)*	*SD (mm³)*	*95% CI (lower and upper bounds)*
ITK-Snap	7271	7077	0.99	7174	607	5938, 8409
Mimics	7206	7119	0.99	7163	594	5952, 8373
OsiriX	7093	7079	0.99	7086	593	5878, 7086
Dolphin3D	7121	7021	0.99	7071	585	5879, 8263
InVivo Dental	6679	6644	0.99	6661	587	5465, 7858
OnDemand3D	6198	5924	0.94	6061	349	5350, 6772
Mimics FT	6753	6753	1.00	6753	583	5566, 7940
ITK-Snap FT	6616	6627	1.00	6622	577	5445, 7797
OsiriX FT	6646	6645	1.00	6645	575	5475, 7817
OnDemand3D FT	6881	6881	1.00	6881	585	5688, 8075

Programs designated *FT* (fixed threshold protocol) were used with a different segmentation protocol of −1000 to −587 grey levels.
CI, Confidence interval; *ICC*, intraclass correlation coefficient.

for most software pairs, with the exception of InVivo Dental, which had no significant difference compared with ITK-Snap, Mimics, and OsiriX with the fixed threshold technique. Also, there was no significant difference between ITK-Snap and OsiriX (Table V).

DISCUSSION

Currently, several imaging software programs are available for upper airway assessment. A previous systematic review reported 18 imaging software programs for viewing, measuring, and analyzing the upper airway in CBCT images.[1] Only 1 study compared the accuracy and reliability of the imaging software programs for upper airway assessment in CBCT.[14] However, only Dolphin3D, InVivo Dental, and Ondemand3D software were compared; these programs were compatible only with the Windows operating system (Microsoft).[14] In our study, 6 imaging softwares were compared to test the accuracy of oropharynx segmentation (Table I). These programs are compatible not only with the Windows operating system, but also with Macintosh operating system X (Apple, Cupertino, Calif) and Linux operating system. A custom-made oropharynx acrylic phantom with a known volume was used as the gold standard. Dolphin3D, Ondemand3D, and InVivo Dental software were selected in this study because of their popularity among orthodontists and maxillofacial surgeons in the United States. Mimics software was chosen because of its wide use in biomedical engineering. OsiriX and ITK-Snap software were chosen because they are free, open-source softwares commonly used in medicine. Thus, the results of this study can be used as the basis for future airway studies with CBCT in both dentistry and medicine.

In this study, the method's design addressed some important aspects regarding the region of the upper airway analyzed. According to El and Palomo,[14] nasopharynx morphology is complex, and its volume measurement has less reliability than does oropharynx volume measurement. Because of this, to reduce the variability in measurements because of the structural complexity during software comparisons, only the oropharynx was evaluated. After head reorientation, the oropharynx was defined and exported as a new DICOM file maintaining the original 0.3-mm-voxel resolution. This image-processing step allows for standardized upper and lower oropharynx limits, eliminating variability introduced by using different imaging software programs to define the oropharyngeal airway. Furthermore, removing areas of noninterest created smaller files, reducing computing time.

The upper airway volume assessment depends on segmentation accuracy, image quality, and threshold interval selection. The CBCT image quality is impacted by several factors, such as the CBCT device's settings, patient positioning and management, volume reconstruction, and DICOM export.[22] When scanning is performed with high settings (small voxel size, longer scan time), the CBCT images are obtained with better spatial resolution.[23] In this study, both the oropharynx acrylic phantom and the patient's oropharynx were scanned with an i-CAT scanner, with high settings (0.3-mm voxel, 40-second scan time).[14] However, even with these settings, the patient's movement during the scan (40 seconds) might have produced motion-related artifacts, which could have some influence on the segmentation accuracy. Additionally, noise and artifacts also might have affected the contrast of the images. This could affect the discrimination between densities during the thresholding filter process and, consequently, the segmentation accuracy.

The upper airway segmentation and volume measurement are also influenced by the threshold interval selection. Interactive thresholding is a technique where

Table IV. Results of the post-hoc pairwise comparisons (with Bonferroni adjustment for multiple testing) for oropharynx segmentation with interactive thresholding

					95% CI for difference†	
Software (I)	*Software (J)*	*Mean difference (I − J) (mm³)*	*SE (mm³)*	*Significance*†	*Lower bound*	*Upper bound*
InVivo	ITK-Snap	−512*	53	.000	−682	−343
	Dolphin3D	−410*	51	.000	−573	−247
	OsiriX	−425*	46	.000	−570	−279
	Ondemand3D	600	364	1.000	−555	1755
	Mimics	−501*	43	.000	−638	−364
ITK-Snap	InVivo	512*	53	.000	343	682
	Dolphin3D	102	57	1.000	−78	283
	OsiriX	88	53	1.000	−82	258
	Ondemand3D	1113	378	.090	−86	2311
	Mimics	11	44	1.000	−128	151
Dolphin3D	InVivo	410*	51	.000	247	573
	ITK-Snap	−102	57	1.000	−283	78
	OsiriX	−15	46	1.000	−159	130
	Ondemand3D	1010	365	.139	−146	2167
	Mimics	−91	41	.517	−222	40
OsiriX	InVivo	425*	46	.000	279	570
	ITK-Snap	−88	53	1.000	−258	82
	Dolphin3D	15	46	1.000	−130	159
	Ondemand3D	1025	363	.122	−126	2176
	Mimics	−76	29	.183	−167	15
Ondemand3D	InVivo	−600	364	1.000	−1755	555
	ITK-Snap	−1113	378	.090	−2311	86
	Dolphin3D	−1010	365	.139	−2167	146
	OsiriX	−1025	363	.122	−2176	126
	Mimics	−1101	365	.075	−2259	56
Mimics	InVivo	501*	43	.000	364	638
	ITK-Snap	−11	44	1.000	−151	128
	Dolphin3D	91	41	.517	−40	222
	OsiriX	76	29	.183	−15	167
	Ondemand3D	1101	365	.075	−56	2259

Based on estimated marginal means. Because the mean difference could have positive or negative values, the letters *I* and *J* show that the mean difference (*I* − *J*) was obtained by subtracting the first-column program (*I*) from the second-column program (*J*).
CI, Confidence interval.
*Statistically significant at $P < 0.05$; †Bonferroni adjustment for multiple comparisons.

the threshold interval is determined by the operator's visual discrimination. When an interactive thresholding technique was used, although the reliability of the measurements was considered high, all imaging softwares produced different segmentations and volumes for both the oropharynx acrylic phantom and the patient's oropharynx. All programs underestimated the oropharynx acrylic phantom segmentation compared with the gold standard. These findings indicate that giving the operator freedom to determine the threshold interval based on visual analysis influences the upper airway segmentation accuracy. El and Palomo[14] demonstrated similar results, with Dolphin3D, InVivo Dental, and Ondemand3D software used to segment the upper airway. Also, they concluded that the airway segmentation using interactive thresholding showed high reliability but poor accuracy. This is because interactive thresholding is based on the operator's visual discrimination of the airway boundaries, and human vision is subject to a host of factors: eg, lighting conditions, fatigue, gray-scale ability, and visual acuity.[24] Fixed thresholding eliminates operator subjectivity in boundary selection. When fixed thresholding was used for oropharynx acrylic phantom segmentation, all imaging softwares produced similar segmentation and volume results. This further confirms that the operator's influence in threshold selection affects the final segmentation, and that the thresholding scale is compatible between the programs when a noncomplex structure, such as our oropharynx acrylic phantom, is segmented. However, when the oropharynx was segmented by using the same patient and the same threshold interval via the fixed threshold technique, most imaging software programs produced different segmentation and volume measurements. This could

Table V. Results of the post-hoc pairwise comparisons (with Bonferroni adjustment for multiple testing) for oropharynx segmentation with the fixed threshold interval, −1000 to −587 grey levels

Software (I)	*Software (J)*	*Mean difference (I − J) (mm³)*	*SE (mm³)*	*Significance*†	*95% CI for difference*† *Lower bound*	*Upper bound*
Ondemand3D FT	ITK-Snap FT	260*	28	.000	175	345
	OsiriX FT	236*	28	.000	152	319
	InVivo	220*	37	.000	107	332
	Mimics FT	128*	23	.000	59	197
ITK-Snap FT	Ondemand3D FT	−260*	28	.000	−345	−175
	OsiriX FT	−24	11	.388	−58	10
	InVivo	−40	36	1.000	−149	68
	Mimics FT	−132*	14	.000	−173	−90
OsiriX FT	Ondemand3D FT	−236*	28	.000	−319	−152
	ITK-Snap FT	24	11	.388	−10	58
	InVivo	−16	35	1.000	−122	90
	Mimics FT	−108*	11	.000	−141	−75
InVivo	Ondemand3D FT	−220*	37	.000	−332	−107
	ITK-Snap FT	40	36	1.000	−68	149
	OsiriX FT	16	35	1.000	−90	122
	Mimics FT	−92	31	.060	−186	2
Mimics FT	Ondemand3D FT	−128*	23	.000	−197	−59
	ITK-Snap FT	132*	14	.000	90	173
	OsiriX FT	108*	11	.000	75	141
	InVivo	92	31	.060	−2	186

Based on estimated marginal means. Because the mean difference could have positive or negative values, the letters *I* and *J* show that the mean difference (*I* − *J*) was obtained by subtracting the first-column program (*I*) from the second-column program (*J*). Programs designated *FT* (fixed threshold protocol) were used with a different segmentation protocol of −1000 to −587 grey levels.
*The mean difference is significant at the .05 level; †Bonferroni adjustment for multiple comparisons.

be explained by the fact that, even with the oropharynx's less complex morphology compared with the nasopharynx, there are still small areas in the oropharynx where the software's segmentation algorithms differ in identifying, matching, and filling.

Although all programs underestimated the oropharynx acrylic phantom's physical volume, Mimics (0.2% error), Dolphin3D (1% error), OsiriX (1.3% error), and ITK-Snap (1.8% error) showed better accuracy than did Ondemand3D (6.4% error) and InVivo Dental (11.1% error) (Table II). Similar results were obtained for patients' oropharynx segmentations, in which the mean volumes with Mimics, Dolphin3D, OsiriX, and ITK-Snap were similar (Table III). Even though the Bonferroni post-hoc correction did not show significant differences between Ondemand3D and the other imaging software programs, both Ondemand3D and InVivo Dental underestimated the phantom's volume the most and produced the greatest mean differences between pairs of software measurements of the oropharynx (Tables III and IV). A possible explanation could be related to differences in the softwares' segmentation algorithms to identify, match, and fill the upper airway. With Ondemand3D software, both segmentation control (capability to allow a fine threshold interval adjustment) and sensitivity (capability to identify and segment all voxels with the grey levels compatible with air) were deficient, especially when small spaces of the oropharynx had to be filled and segmented. After segmentation, empty spaces were frequently observed in the axial, coronal, and sagittal slices, explaining the underestimated volumes (Fig 3, *D* and *E*). A similar problem with Ondemand3D was demonstrated in a previous study.[14] With InVivo Dental software, the user can only adjust the threshold interval in the 3D mode of view, not in the axial, coronal, or sagittal slices as traditionally found in all other software programs, so the user cannot accurately check the segmentation of the upper airway. Because of this program limitation, we used the standard threshold interval given by InVivo (−1000 to −587 grey levels), which seems to underestimate the oropharynx acrylic phantom's actual physical volume. Based on our findings, new updates and improvements in the airway modules for InVivo Dental and Ondemand3D are recommended.

Because of the limitation of the InVivo Dental software program, the standard threshold interval given by InVivo Dental (−1000 to −587 grey levels) was chosen as a control threshold interval. This control threshold interval was then applied to the fixed threshold protocol

Table VI. Main advantages and disadvantages of the 6 imaging softwares used in this study

Software	*Advantages*	*Disadvantages*
Dolphin3D	• User friendly • Quick upper airway segmentation • Good segmentation sensitivity (Figs 3, *A-C*; and 4, *A*, *D*, and *G*) • Segmentation can be checked in 2D slices (axial, coronal, and sagittal) • Minimal cross-sectional area analysis	• Not free • Lacks tools to adjust or correct segmentation in 2D slices (in spite of good segmentation sensitivity, in small regions with complex morphology, the segmentation algorithm fills empty space in some areas and overflows in other areas; this requires correction before volume rendering) • Threshold interval units (grey levels) not compatible with other imaging software
InVivo Dental	• User friendly • Quick upper airway segmentation • Threshold interval units (grey levels) compatible with other imaging software	• Not free • Threshold selection performed only in 3D mode of view (lack of parameter to check whether the segmentation matches the airway anatomy correctly in axial, coronal, and sagittal slices)
Ondemand3D	• Quick airway segmentation • Segmentation can be checked in 2D slices (axial, coronal, and sagittal) • Threshold interval units (grey levels) compatible with other imaging software	• Not free • Deficient segmentation control and sensitivity • Failed to render large areas of oropharynx, especially those with complex morphology (Figs 3, *D-F*; and 4, *B*, *E*, and *H*) • Lacks tools to adjust or correct segmentation in 2D slices
Mimics	• User friendly • Quick and easy airway segmentation • Best segmentation control and sensitivity • Segmentation can be checked in 2D slices • Tools to correct segmentation in 2D slices • Threshold interval units (grey levels) compatible with other imaging software	• Not free • Designed for biomedical engineering • Not as user friendly as Dolphin3D and InVivo
OsiriX	• Free and open source • Quick airway segmentation • Good segmentation sensitivity • Segmentation can be checked in 2D slices • Tools to correct segmentation in 2D slices • Threshold interval units (grey levels) compatible with other imaging software	• Designed for use in medicine • Not as user friendly as Dolphin3D and InVivo
ITK-Snap	• Free and open source • Good segmentation control and sensitivity (Figs 3, *G-I*; and 4, *C*, *F*, and *I*) • Segmentation can be checked in 2D slices • Tools to correct segmentation in 2D slices • Threshold interval units (grey levels) compatible with other imaging software	• Designed for use in medicine • Not as user friendly as Dolphin3D and InVivo

for the other programs. However, using this method resulted in underestimation of the oropharynx acrylic phantom for all softwares in our study. An improvement on our method would have been to adjust the threshold interval in InVivo Dental until the oropharynx acrylic phantom segmentation volume reached the actual physical volume of the oropharynx acrylic phantom, and then use this adjusted threshold interval as the control threshold interval for the other programs.

Although all 6 programs perform semiautomatic segmentations, they have different tools and ways to segment the upper airway. The main advantages and disadvantages of each imaging software program are described in Table VI.

In this study, we compared the precision and accuracy of 6 imaging software programs to segment and compute the volume of a phantom representing the oropharynx and the oropharynx airways of 33 patients. The influence of the threshold selection was addressed, and the advantages and disadvantages of each program were described, including some suggestions for future updates. Currently, there are only a few studies about the reliability and accuracy of imaging software programs for the upper airway.[1,10,14] Further research regarding CBCT imaging of the airway is needed to ensure the validity of the upper airway diagnosis.

CONCLUSIONS

1. All 6 imaging software programs were reliable in the volume segmentation of the oropharynx acrylic phantom but underestimated the values compared with the gold standard.
2. Mimics, Dolphin3D, ITK-Snap, and OsiriX values were similar and considerably more accurate than InVivo Dental and Ondemand3D for upper airway assessment.
3. The final segmentation volume depends on the threshold interval selection, the imaging software's segmentation algorithms, and the complexity of airway morphology.
4. Upper airway volume assessment depends on segmentation accuracy; the 6 imaging software programs used different segmentation engines. Contrary to popular belief, there is no established protocol or algorithm for processing DICOM images to produce an assessment of airway volume, and there are differences among the methods that are currently available commercially.

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4. Artigo 2

Fast 3-dimensional superimposition of CBCT volumes: validation study

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Abstract

Objectives: Our aim was to test and validate a method for fast 3D superimposition of CBCT volumes in growing patients and adults. **Methods:** The sample consisted of CBCT scans of 18 patients. For 10 patients as a gold standard, the spatial position of the pretreatment CBCT volume was reoriented, saved as a reoriented volume, and then superimposed to the original image. For 8 patients, 4 non-growing and 4 growing patients, pre and post-treatment scans were superimposed. Fully automated voxel-based superimposition was performed, with registration at the anterior cranial base using the Ondemand3D program. The registration process took 10-15s. The fit of the cranial base superimposition was verified by visual inspection of all corresponding anatomic structures in all semi-transparent multi-planar cross-sectional slices and by semi-transparent overlays of the surface models. Virtual 3D surface models of the skull were generated via a standardized segmentation protocol by using ITKSNAP program. Superimposition errors in the reoriented models and result of treatment for the treated cases were evaluated with 3D surface distances in color-coded maps. **Results:** Superimposition error of the spatial reorientation as measured by the color-coded surface distances was less than 0.5mm. Superimposition error of pre and post treatment scans for both growing and non-growing patients included small segmentation errors and surface distances at the cranial base were smaller than 0.5 mm, which was considered acceptable and clinically insignificant. **Conclusion:** The voxel-based superimposition method evaluated was reproducible in different clinical conditions, time-efficient and potentially applicable for both research and clinical practice.

Introduction

Cone beam computed tomography (CBCT) has become a well-established diagnostic tool in dentistry.[1-9] In Orthodontics and Oromaxillofacial Surgery, CBCT now allows clinicians to better identify and distinguish treatment outcomes. While 2D cephalometric superimposition is the conventional method used to evaluate growth and treatment outcomes, improvements in image registration algorithms have made the superimposition of CBCT volumes the state-of-the-art technique for treatment outcome assessments.

In medical imaging, the process of spatially superimposing three-dimensional (3D) images obtained from different imaging modalities is also called image registration, or, fusion.[10] Superimposition of CBCT volumes in the three-dimensional space when changes in shape and position of the craniofacial components have occurred with time and treatment is challenging and requires knowledge of the different types of superimposition. The three basic types of superimposition algorithms are: (1) *point-landmark based, (2) surface based* and *(3) voxel based*.[11] Point-landmark based methods are done through the superimposition of corresponding or homologous points that are manually input by the user. The precision of this method is highly user dependent and most anatomic surfaces do not present well-defined landmarks in the 3 planes of the space. Surface-based methods require construction of 3D surface models from corresponding CBCT volumes, and surface segmentation algorithms depend on the software determination of quality of the scan and software dependent. *Voxel-based superimposition* methods use an optimized function that measures the similarity of all geometrically corresponding voxels pairs for a user-defined anatomic region.[11] This method compares voxel by voxel of non-changing reference structures in volumetric data, does not depend on landmark identification, as in point-landmark based methods, and is not limited by segmentation errors, as in surface based methods.

Cevidanes et al[12] were the first to introduce into dentistry the voxel-based method for fully automated 3D superimposition of CBCT volumes. The method proposed in that study was based on mutual information theory[11] and required construction of surface models of the reference structure prior to the registration steps. Application of those methods for both growing and non-growing subjects has been described in the literature. The main difference between the growing and non–growing patient algorithms in those studies was that the growing patients algorithm took changes in scale (growth and/or response to treatment) into account without applying it, while the non-growing algorithm performed a rigid transformation with 6 degrees of freedom (x, y, z of translation and rotation) to superimpose the CBCT volumes.[5-7,12-14] The main drawback of that method was that the registration process was time consuming (45 to 60min), and lacked a clinician friendly user-interface and visualization tool.

In 2010, Choi and Mah[15] introduced a new method for cranial base superimposition method that does not require construction of 3D surface models prior to the registration process. Choi et al also added volume and slice visualization capabilities, providing a clinician friendly user interface. This method also uses the principle of mutual information for image registration.[11] The result was a new, commercially available, software program (Fusion module of Ondemand3D, Cybermed, Seoul, Korea) that performs CBCT volume superimpositions faster (10 to 15s) and while requiring fewer steps. While some research studies,[16-18] have applied the superimposition method introduced by Choi and Mah,[15] in the Ondemand3D software, there has been no previous validation study of this method for fast CBCT volume superimposition in growing patients and adults.

The aim of this study was to evaluate the fast 3D superimposition of CBCT volumes present in the fusion module of Ondemand3D software program. Specifically first, this study tested whether there are differences when the same CBCT volumes, with different spatial orientations, are superimposed at the anterior cranial base. Second, this study tested whether there are differences in the cranial base when longitudinal CBCT volumes of growing patients and adults, which also present maxilla-mandibular changes due to growth and/or treatment response, are superimposed at the anterior cranial base.

Method

This study was approved by the ethical committee of Pontifical Catholic University of Rio Grande do Sul (PUCRS) in Brazil. The sample consisted of CBCT scans of 18 patients. For 10 patients as a gold standard, the spatial position of the pretreatment CBCT volume was reoriented, saved as a reoriented volume, and then superimposed to the original image. For 8 patients, 4 non-growing and 4 growing patients, pre and post-treatment scans were superimposed. The 10 pre-treatment scans had mean age of 11.4 ±1 years. The 4 non-growing adult patients (mean age 26.3 ± 5.7 years) had CBCT scans taken pre and 1 year post- surgery. The 4 growing patients (mean age 9.5 ± 1.8 years) had CBCT scans taken pre and post-treatment with rapid maxillary expansion (RME). The CBCT scans were available from datasets obtained for clinical purpose using the i-CAT scanner (Imaging Sciences International, Hatfield, Pa) set at 120 kVp, 8 mA, large field of view, and scan time of 40 seconds. The images were reconstructed with 0.25-mm slice thickness and exported as Digital Imaging and Communications in Medicine (DICOM) files.[19]

Creating CBCT volumes with different spatial orientation

The DICOM files, corresponding to pre-treatment CBCT scans of 10 growing patients, were imported into Ondemand3D software program (version 1.0.9.1451; Cybermed, Seoul, Korea) and organized in the database management module. Each CBCT volume was opened, the patient head was reoriented in the space (translation and rotation) to a different spatial position and exported as a new DICOM file. Thus, for each original CBCT volume a second CBCT volume was created, with the same voxel size but with different head orientation (Figure 1A, B and C). This procedure was performed for all 10 pre-treatment CBCT volumes, creating 10 additional CBCT volumes with different head orientation.

CBCT volumes superimposition

For the fully automatic voxel-wise rigid registration, we used the fusion module in Ondemand3D software program. Axial, sagittal and coronal slice views of the volumes were used to select the anatomic structures of the anterior cranial base in the registration of the original and reoriented CBCT volumes (Figure 1A and B) and the registration of the longitudinal scans. Next, the Ondemand3D automated registration tool was used to perform the rigid registration (translation and rotation) that optimally aligned the reoriented CBCT volume to the original CBCT volume, using the intensity of the grey levels for each voxel in the anterior cranial base of the 2 CBCT volumes (Figure 1C and D). The superimposition process took a total of 10-15 seconds to complete.

Superimposition assessment

The precision of the superimposition was verified by using two methods: (1) by qualitative visualization, by a single observer A.W., of the semi-transparent axial, sagittal and coronal cross-sectional slices of all corresponding anatomic structures between original and reoriented scans, and between the two time point scans. (Figures 1D, 5A e 6A) and (2) by quantification of the surface distances using closest point color maps on 3D surface models (Figures 1E, 4, 5B and 6B).[20,21] To measure the outcomes of the registration, after the registration process, the superimposed CBCT volumes were exported as DICOM files and imported into ITK-SNAP software program (www.itksnap.org) for segmentation.[22] Automatic segmentation was performed, by a single observer L.K.D., for each CBCT volume in 4 different steps: mandible, maxilla, frontal bone/anterior cranial fossa and middle cranial fossa. The segmentation was then exported as a stereo lithography file (STL) and converted to an Open Inventor file (IV) using STL to SGI Inventor 2.0 Utility Beta (developed by Reuben Reyes, hitechmax@austin.rr.com). The surface models were then opened in the Cranio-MaxilloFacial application software (CMFapp, developed at the M. E. Müller Institute for Surgical Technology and Biomechanics, University of Bern, Bern, Switzerland)[23] that calculates the closest point surface distance between thousands of surface triangles in the 3D surface models and the color-coded surface distance maps allow quantification of the registration errors (Figure 1E, 4, 5 , 6 and 7).

Results

The superimposition results for the original and reoriented CBCT scans of 10 growing patients are shown in Figures 1 to 4. The visualization of the semi-transparent axial, sagittal and coronal cross-sectional slices of all corresponding anatomic structures confirmed the adequate registration of the cranial base structures in all axial, sagittal and coronal slices (Figure 1 to 3). The quantification of the superimposition errors by color-coded surface distances revealed that the error was less than 0.25mm (Figure 1 to 4).

The superimposition results for longitudinal scans of growing patients and adults are shown in Figures 5, 6 and 7. The visualization of the semi-transparent axial, sagittal and coronal cross-sectional slices of all corresponding anatomic structures confirmed the adequate registration of the extremely complex cranial base structures, such as the ethmoidal air cells. The quantification of the superimposition errors by color-coded surface distances revealed that distances in the cranial base between registered surface models were less than 0.5mm for most regions (Figures 5B, 6B and 7).

Discussion

CBCT is currently a well-established diagnostic tool for 3-dimensional evaluation of patients, especially in orthodontic-surgical cases. This study is the first to validate a method for fast CBCT volume superimposition in growing patients and adults.

Improvements in image registration algorithms have led to the development of new methods for CBCT volume superimposition. McCance et al proposed a method for cranial base superimposition with CT scan using 5 landmarks on areas not affected by surgery in non-growing patients.[24] Kawamata et al suggested a similar method, rotating semi-transparent pre- and post-surgery models aiming to overlap then in the same structure.[25] These point landmark-based methods for CBCT superimposition are also used in the current versions of Dolphin3D (Dolphin imaging & Management Solutions, Chatsworth, Calif) and InVivo Dental (Anatomage, San Jose, Calif) software programs. However, point landmark-based methods are observer dependent. The method introduced by Cevidanes et al was observer independent and did not rely on specific landmarks.[12] However, it was time consuming and lacked a clinician friendly user-interface and visualization tool.

This study validated the superimposition method introduced by Choi and Mah for voxel-based registration using Ondemand3D software.[15] This study method for superimposition of longitudinal CBCT volumes in growing patients and adults has advantages over previously used voxel-based methods. [5-7,12,14] The advantages include time efficiency (takes about 10 to 15 seconds), and user-friendly software interface suitable for clinical application. As demonstrated in our study, the CBCT volume superimpositions are fast even with small voxel sizes (0.25mm) and higher spatial resolution. Another advantage is that the registration process does not require previous segmentation to designate the area of superimposition (i.e. cranial base). Ondemand3D software also enables CBCT volume superimpositions with registration at areas outside the cranial base that can be potentially applied for regional superimpositions not tested in this study. Park et al have recently used regional superimpositions with Ondemand3D software to evaluate the condylar head remodeling after bi-maxillary surgery by using rigid registration at the condylar neck and posterior ramal area of pre and post-operative CBCT images.[16]

In this validation study, the construction of standardized 3D surface models and part-comparison analysis with color maps confirmed the accuracy of this voxel-based superimposition method. The differences observed in the color-coded surface distance maps for the 10 pre-treatment CBCT scans were minimal, less than 0.25 mm (Figures 1-4). However, superimposition of the same CBCT volumes, with different spatial orientation, should be evaluated with caution because they have the same grey level intensity and no modifications by growth and/or treatment. The challenge for image registration is to superimpose CBCT volumes of patients with craniofacial modifications due to the normal growth and/or treatment response in different time points. In these situations, the CBCT volumes may have different grey level intensity, field of view, and dental/skeletal components modified by growth and/or treatments, making the registration process difficult and prone to fail. Additionally, CBCT scans obtained with different scanners may have different grey levels,[26] which could affect the superimposition process. For these reasons, this study tested superimpositions of longitudinal CBCT volumes with one-year interval of growing patients treated with RME and adult patients treated with orthognathic surgery. The green color-code (0mm surface distances) in most part of the anterior cranial base shows the adequate superimposition for both growing patients and adults. Some areas of larger surface distances, as shown in black, red and blue color-coded areas that are displayed in the superior view of the cranial base (Figures 5B, 6B and 7), do not represent superimposition errors, as confirmed by the visualization of semi-transparent multi-planar cross-sectional slices and by semi-transparent overlays of the surface models (Figure 7). Since the CBCT obtained at different time points have differences in the grey level for the same anatomical structures (i.e. cranial base), the automatic segmentation was not performed by using the same threshold interval. This variation introduced by the user input to define the properties of 3D surface model creation leads to small surface variations in the cranial base. Additionally, areas with low gray-scale contrast such as the ethmoidal air cells are not included automatically in the segmentation. In these situations, manual editing were necessary and produced slightly different outlining of surface boundaries, during the segmentation, introducing manual errors that explaining the black, red and blue areas observed in the internal surface of the cranial base.

For some scans, the registration of the two CBCT volumes failed, requiring 2 or 3 repeated procedures. In these cases, it was necessary to resize the selection area for registration (anterior cranial base) in both primary and secondary volumes in order to obtain an adequate superimposition. In a previous study, Alexandroni et al[18] also reported similar failed attempts using the same superimposition method to evaluate orthognathic surgery skeletal prediction in 44 patients. Those authors used only visual inspection to verify adequate CBCT volume superimpositions. The registrations that required repeated procedures in this study could be due to the small area used for CBCT volume registration in our study (anterior cranial base) in comparison to the global anatomic structure of the dry skull used by Lee et al.[27] In addition, the amount of the misalignment between the CBCT volumes may have some influence in the superimposition process. According to Pluim, et al, when using registration methods based in mutual information theory, results may be suboptimal, or may even fail, if the initial misalignment of the two images is large or if the overlay region of the two images is relatively small.[28] For this reason, we recommend to perform a quick manual superimposition (manual registration tool) previously to the automated superimposition. Lee, et al[27] evaluated the accuracy of CBCT image registration with Ondemand3D by using a dry skull with titanium markers, simulating different head orientations, although their research did not evaluate the accuracy of longitudinal CBCT superimposition. The location of titanium markers were assessed by two examiners and the distance between the markers were calculated using the 3D coordinates in the Ondemand3D software program. The superimposition mean error was 0.39mm (±0.142mm) and there were no significant differences in the dry skull superimpositions.

A potential limitation of the Ondemand3D software used in this study is that it is only available commercially, whereas the method previously proposed by Cevidanes et al can be done using readily available open-source software programs. Nada, et al[29] have tested the reliability of another commercial voxel based method using the Maxilim software (Medicim, Mechelen, Belgium) for CBCT volumes superimposition on the anterior cranial base and zygomatic arch of 16 surgical orthodontic patients. The authors reported small average superimposition errors, however the closest-point color-coded maps used for quantification of errors do not allow local quantification of surface errors and minimize surface differences.

The current study showed that Ondemand3D software performs a reliable, automated and fast superimposition of CBCT volumes. However, the Ondemand3D software tools for construction of surface models and quantification of treatment outcomes are limited, and other multiple software packages performed these image analysis steps in this study. Quantification of topographic bone remodeling and displacement requires construction of surface models that can be still time consuming. For quantification of changes overtime even though most commercial and open-source software use closest point surface distance, recently, a new method for 3D evaluation of topographic changes, shape correspondence, has been introduced. The shape correspondence method provides the magnitude and direction of the displacement and can be used to identify and quantify the morphological changes in patients with temporomandibular joint osteoarthritis,[9,30] asymmetry assessments[8] and for evaluation of orthopedic or orthognathic surgery outcomes.[31]

In summary, this study was the first to test and validate a voxel-based method for fast CBCT volumes superimposition. Several software packages have been introduced in the market every year, many of them with 3D image superimposition modules. However, there is no established protocol or algorithms for fast and precise 3D image registration used in orthodontics and maxillofacial fields.

Conclusion

Ondemand3D voxel based superimposition method was precise and not time-consuming. The fast 3D superimposition method of CBCT volumes validated in this study may be applied for longitudinal assessment of growing patients and adults and is suitable for both research and clinical routine, in the orthodontic and maxillofacial surgery fields.

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Figures

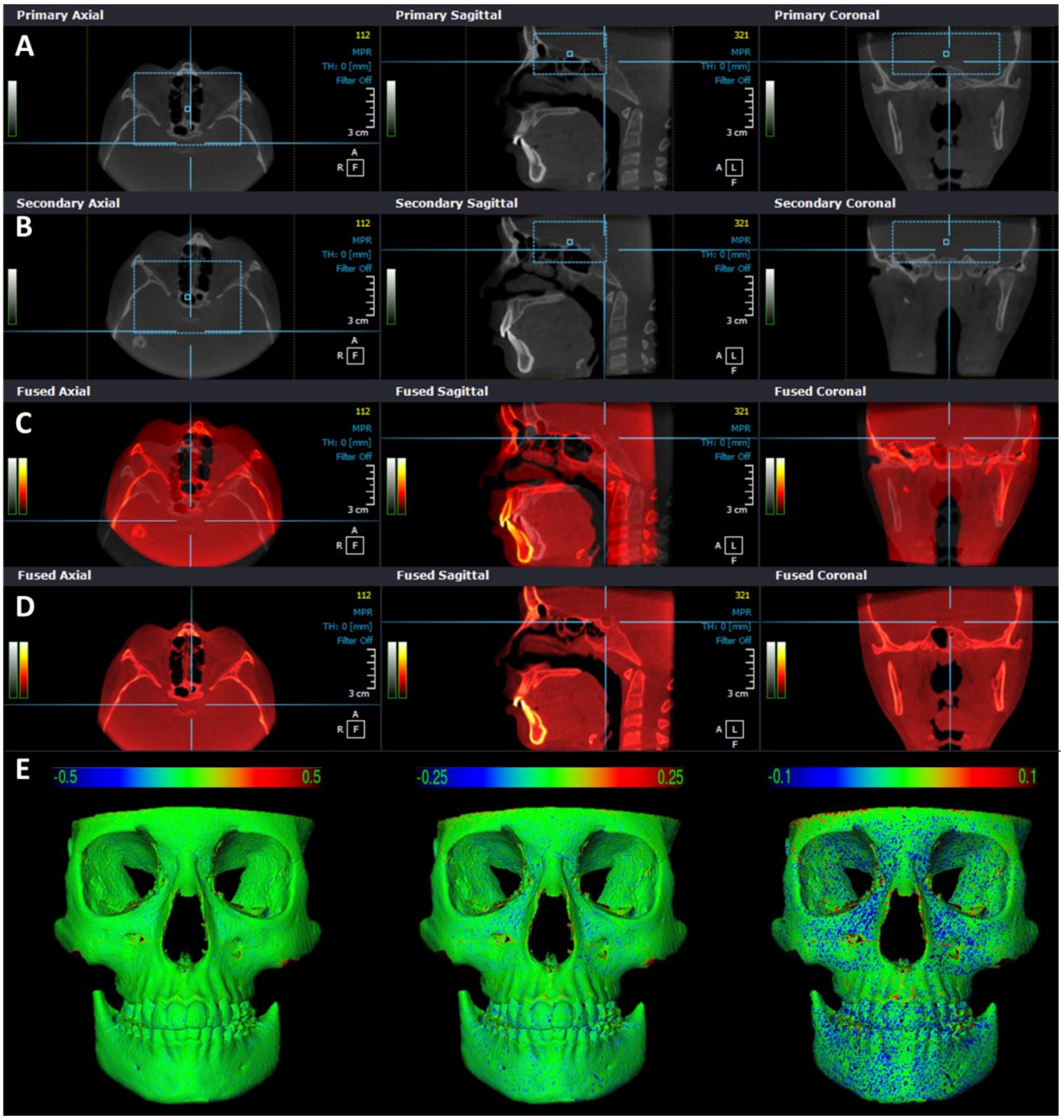

Figure 1 – (A) multiplanar slices of original CBCT and (B) reoriented CBCT files, of patient 1, in Ondemand3D. The anterior cranial base was selected (blue rectangle) for superimposition. (C) slices view of CBCT files before cranial base superimposition and (D) after cranial base superimposition. (E) Skull models after superimposition showing 3D displacements (registration error) via color maps with scale of 0.5mm, 0.25mm and 0.01mm. Positive and negative values indicate outward (red) and inward (blue) changes, respectively (CMF application software).

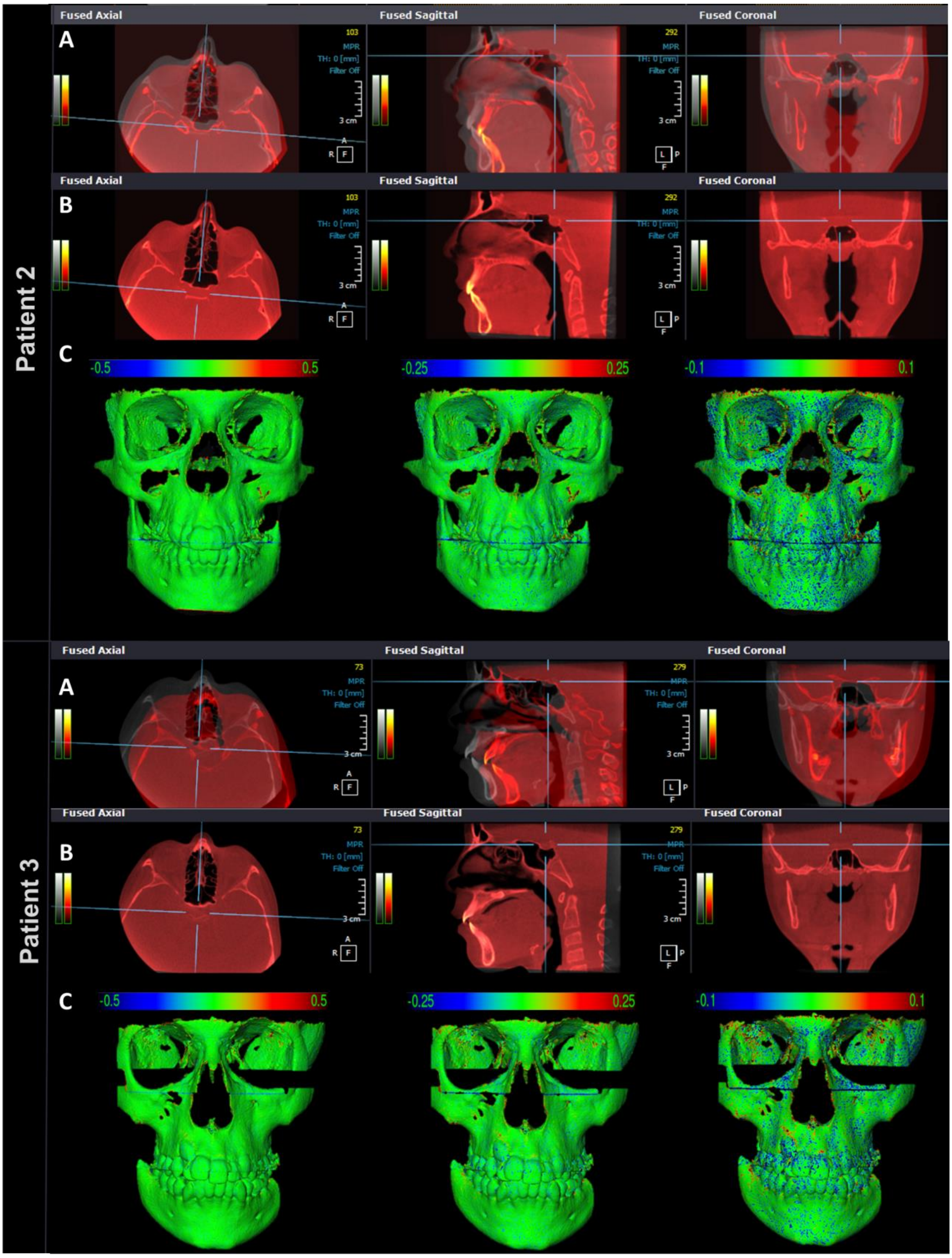

Figure 2 - Patients 2 and 3, (A) multiplanar slices of CBCT volumes before cranial base superimposition and (B) after cranial base superimposition, in Ondemand3D, showing the complete correspondence of registration in all areas (C) Skull models after superimposition showing 3D displacements (registration error) via color maps with scale of 0.5mm, 0.25mm and 0.01mm. Positive and negative values indicate outward (red) and inward (blue) changes, respectively. Note the error was less than 0.25mm (CMF application software).

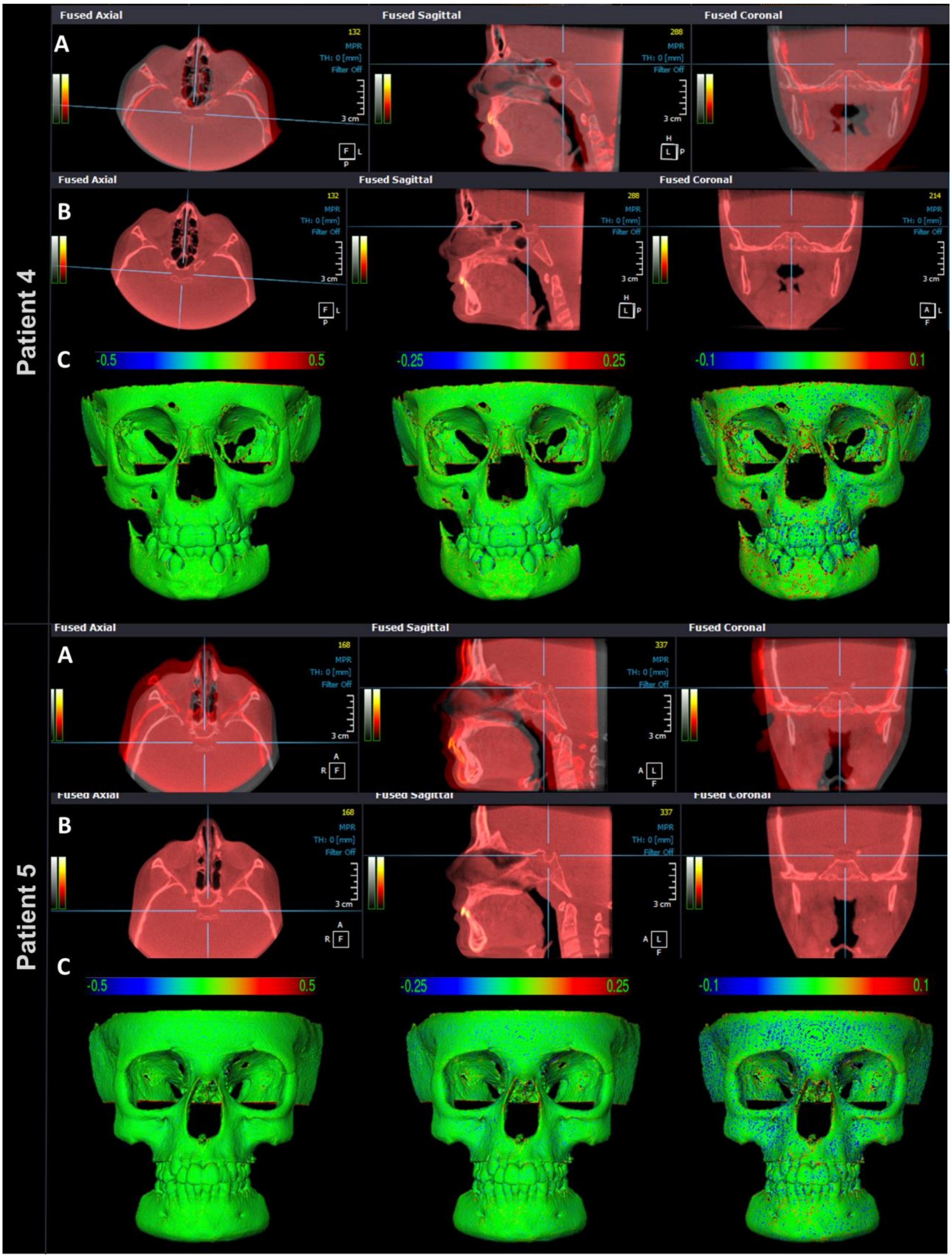

Figure 3 - Patients 4 and 5, (A) multiplanar slices of CBCT volumes before cranial base superimposition and (B) after cranial base superimposition, in Ondemand3D, showing the complete correspondence of registration in all areas (C) Skull models after superimposition showing 3D displacements (registration error) via color maps with scale of 0.5mm, 0.25mm and 0.01mm. Positive and negative values indicate outward (red) and inward (blue) changes, respectively. Note the error was less than 0.25mm (CMF application software).

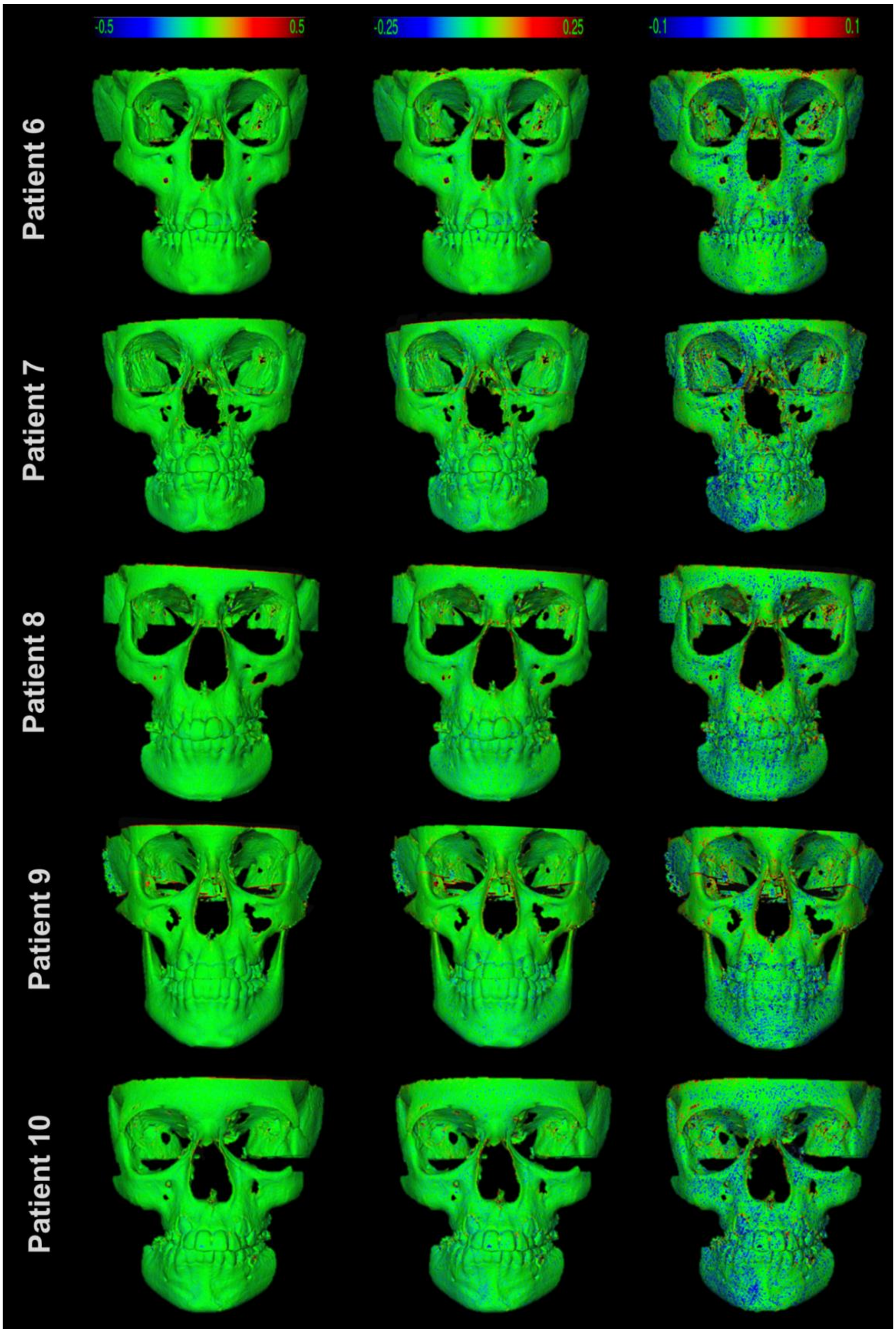

Figure 4 - Patients 6 to 10 - 3D models after superimposition. Each row contains images from the same patient. Skull models after anterior cranial base superimposition showing 3D displacements (registration error via color maps with scale of 0.5mm, 0.25mm and 0.01mm. Positive and negative values indicate outward (red) and inward (blue) changes, respectively. Note the error was less than 0.25mm (CMF application software).

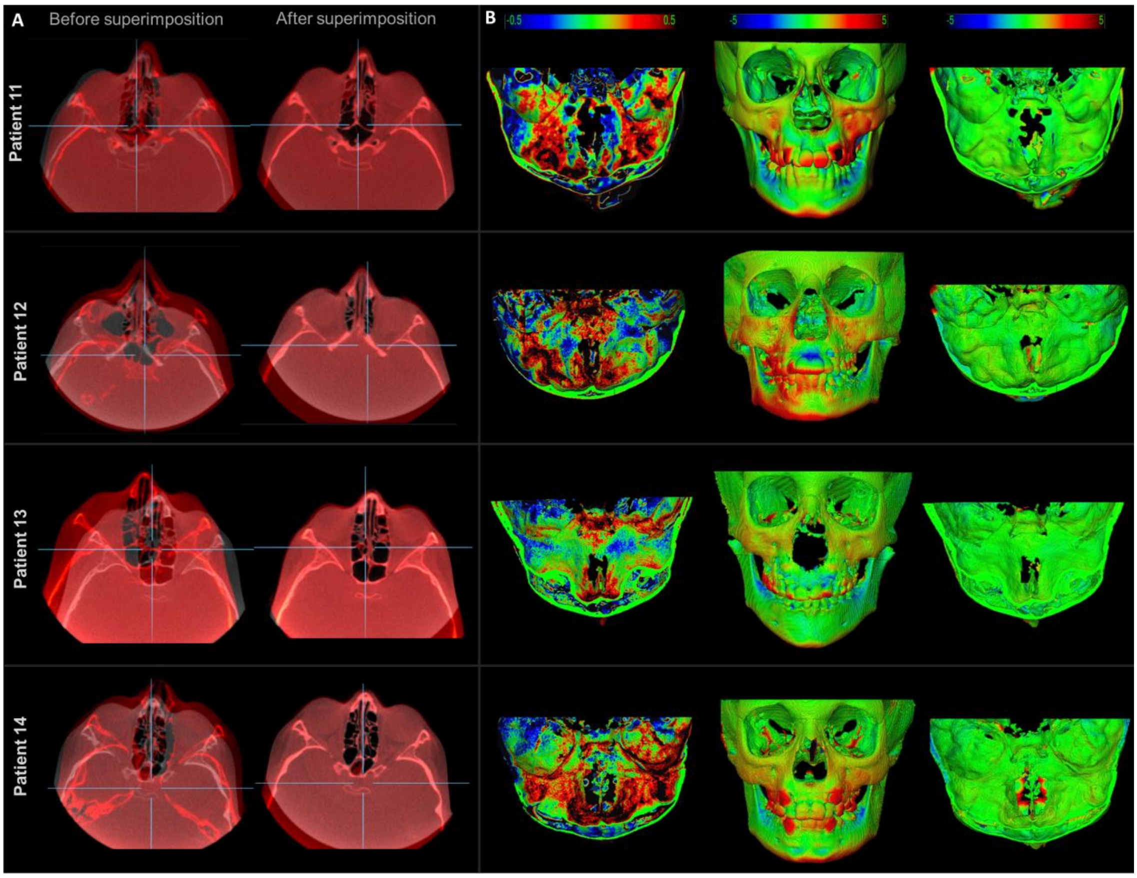

Figure 5. CBCT superimposition of growing patients subjected to RME with 1-year follow-up. (A) axial slices view before and after anterior cranial base superimposition in Ondemand3D. (B) 3D models after superimposition showing 3D displacements via color maps. In the 0.5mm color map, the black areas represent changes of 0.5 mm, blue/red areas represent changes less than 0.5mm and green areas represents no changes. The 5mm color map, the areas in black, red and blue are due to the RME and normal growth. The changes at the cranial base were minimal as shown in green color (CMF application software).

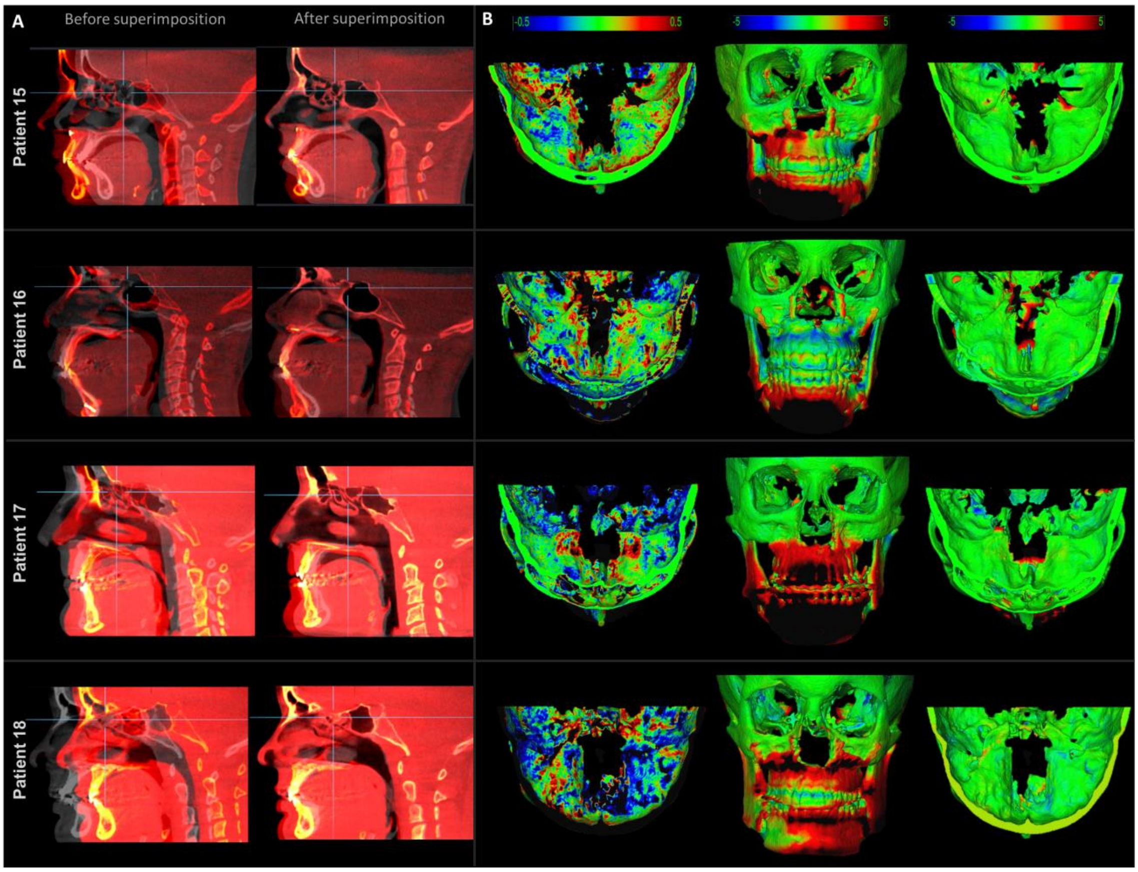

Figure 6. CBCT superimposition of non-growing patients subjected to orthognathic surgery with 1-year follow-up. (A) Sagittal slices view before and after cranial base superimposition in Ondemand3D. (B) 3D models after superimposition showing 3D displacements via color maps. In the 0.5mm color map, the black areas represent changes of 0.5 mm, blue/red areas represent changes less than 0.5mm and green areas represents no changes. The 5mm color map, the areas in black, red and blue are changes due to the surgical treatment. The changes at the cranial base were minimal (green) (CMF application software).

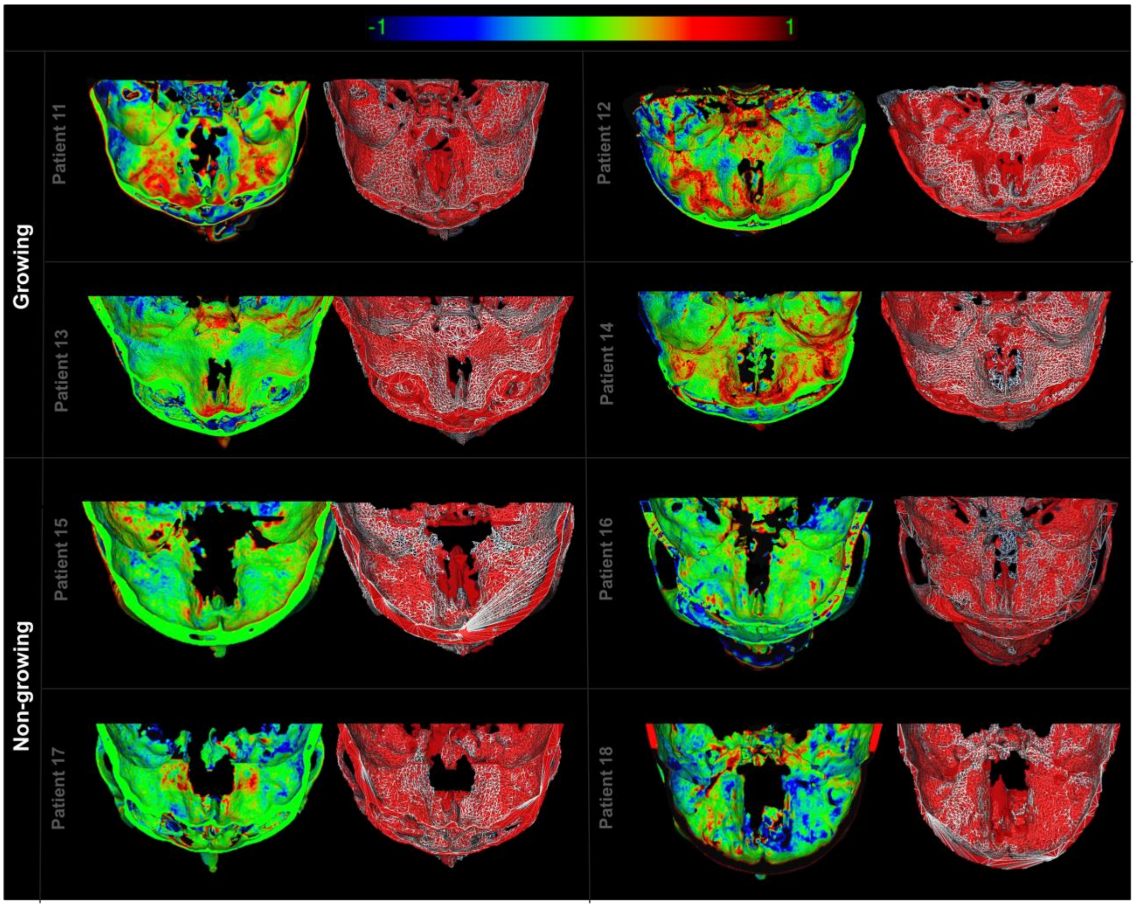

Figure 7. Cranial base superimposition assessment for growing and non-growing patients subjected to RME and to orthognathic surgery, respectively, with 1-year follow-up. In the 1mm color-coded surface distance maps, the black areas represent changes of 1mm, blue/red areas represent changes less than 1mm and green areas represents no changes. The semi-transparent overlays of the pre-treatment (red) and post-treatment (transparent) surface models show adequate superimposition of the anterior cranial bases.

5. Discussão complementar

O objetivo final do processo de elaboração e execução de uma pesquisa científica é sua publicação em um periódico de qualidade, contribuindo como evidência cientifica que suporte a tomada de decisões na prática clínica. Entretanto, as publicações seguem diretrizes e normatização de formatação, sendo cada vez mais compacta e priorizando as informações mais relevantes. Com isso, aspectos secundários, porém importantes, acabam sendo omitidos das publicações. O objetivo dos próximos parágrafos foi discutir alguns desses aspectos secundários, porém, considerados importantes.

Atualmente, a TCCB é uma ferramenta de diagnóstico 3D bem estabelecida e popularizada na Odontologia. Isso aumentou a demanda por programas para arquivos DICOM com módulos específicos para mensuração e análise do complexo craniofacial. Inúmeras empresas iniciaram o desenvolvimento e comercialização de programas para suprir o emergente mercado das análises 3D. Através de estratégias de marketing, grandes empresas atraem os profissionais utilizando imagens tridimensionais sofisticadas, porém, com valor diagnóstico limitado e sem validação científica. Por isso, pesquisas bem conduzida são imprescindíveis para garantir a qualidade do diagnóstico 3D.

Em uma recente revisão sistemática da literatura, foram encontrados 18 programas para visualização, mensuração e análise das vias aéreas superiores. Apenas um estudo testou a precisão e acurácia de somente 3 programas, sendo todos para o sistema operacional Windows (Microsoft). A necessidade de pesquisas de validação de programas destinados à avaliação das vias aéreas nos levou a desenvolver o estudo descrito no Artigo 1. Os programas aqui estudados, além de serem populares na Odontologia, Medicina e Engenharia Biomédica, são compatíveis com os sistemas operacionais Windows (Microsoft), Macintosh OS X (Apple) e Linux. Esses programas foram testados, comparados e a evidência científica produzida poderá servir como base para futuros estudos que utilizem segmentação das vias aéreas superiores.

No artigo 1 (Páginas 14-27), seis diferentes programas foram utilizados para avaliar o volume da orofaringe por meio de segmentação e construção de modelos virtuais 3D. Embora os seis programas utilizem segmentação semiautomática, eles possuem diferentes ferramentas e mecanismos para segmentar as vias aéreas. As principais vantagens e desvantagens de cada programa são descritas a seguir:

(1) Dolphin3D: A segmentação das vias aéreas é realizada de forma simples e rápida. Além disso, permite a identificação da área de menor secção transversal da orofaringe, informação essencial no diagnóstico das vias aéreas superiores. O processo de segmentação é baseado na adição de sementes (pontos inicias de segmentação) as

quais se espalham e se difundem através das áreas (*voxels*) pré-estabelecidas pelo intervalo da escala de cinzas (Figura 1A). A ferramenta que controla o intervalo da escala de cinza permite um ajuste preciso das áreas a serem segmentadas. Entretanto, uma vez determinado o intervalo da escala de cinzas, ele se aplica a todos os cortes axiais, sagitais e coronais das vias aéreas. Com isso, a segmentação preenche espaços vazios em certas áreas e ultrapassa os limites das vias aéreas em outras regiões, especialmente nos casos em que as vias aéreas possuem morfologia complexa. Além disso, o intervalo da escala de cinzas é exibido em unidades próprias do Dolphin3D sendo incompatível com os programas que utilizam a unidade Hounsfield (Figura 1). Seria recomendada a atualização desse programa incluindo ferramentas para ajuste e correção da segmentação em cada imagem 2D (axial, sagital e coronal), quando necessário. Outra melhoria seria a utilização de unidades da escala de cinza compatíveis com outros programas. Dentre todos os programas avaliados, foi o que apresentou maior facilidade para avaliação das vias aéreas superiores.

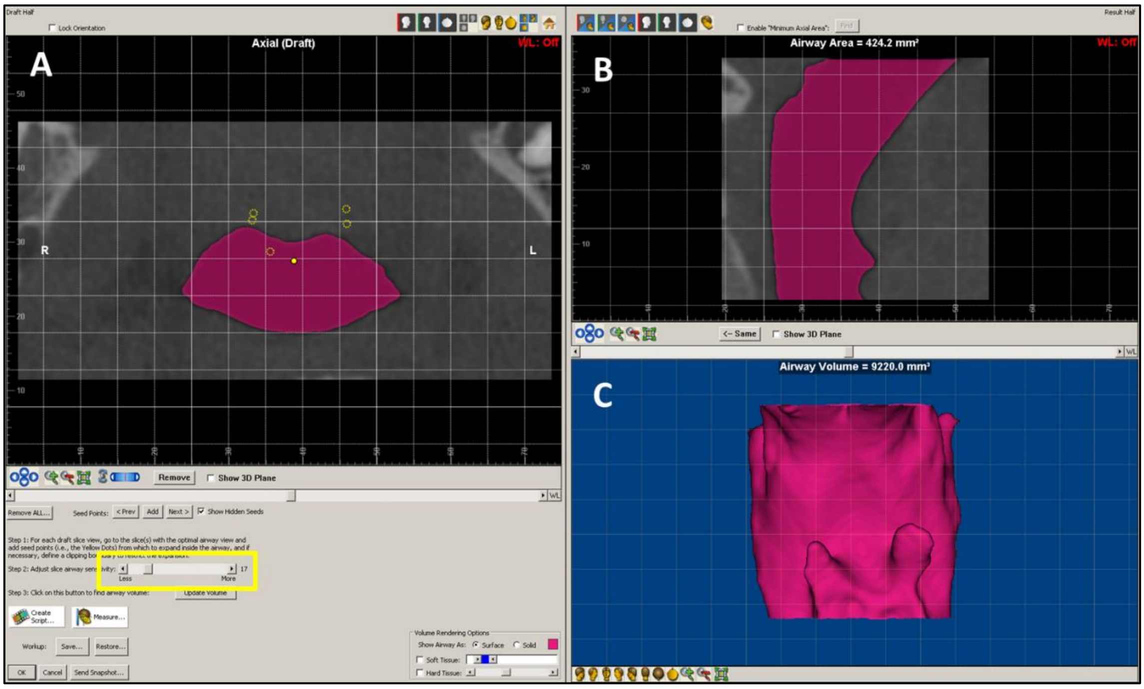

Figura 1. Segmentação no programa Dolphin3D. Em (A) imagem axial e (B) sagital mostrando a orofaringe corretamente preenchida pela segmentação. (C) modelo virtual 3D da orofaringe. O retângulo amarelo mostra a ferramenta para ajustar o intervalo da escala de cinza, o qual é representado por unidades incompatíveis com outros programas.

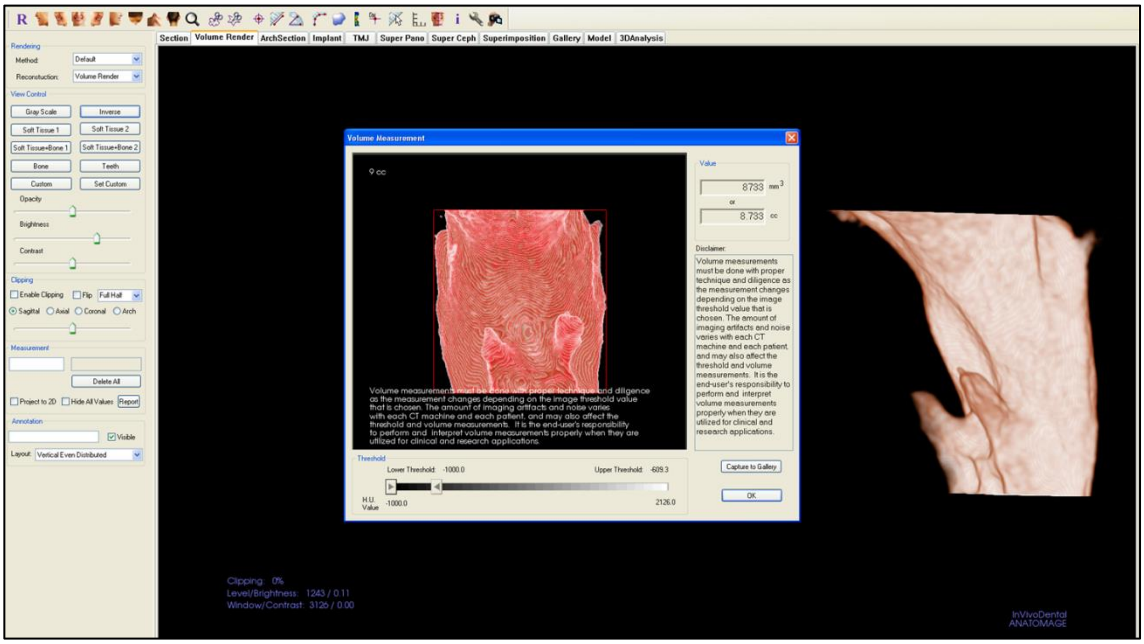

Figura 2. Segmentação da orofaringe no programa InVivo Dental. A segmentação é realizada apenas do modo de visualização 3D. Não há parâmetros em imagens axiais, sagitais e coronais para conferir a acurácia da segmentação previamente a construção do modelo 3D a análise do volume.

(2) InVivo Dental: a avaliação das vias aéreas superiores pode ser realizada de forma rápida e fácil. Após a renderizacão das vias aéreas, a delimitação da região de interesse (orofaringe) é realizada através da seleção do intervalo de escala de cinzas em um modo de visualização exclusivamente em 3D (Figura 2). Isso constitui uma limitação, pois não permite a inspeção visual dos limites anatômicos das vias aéreas e impossibilita a conferência da acurácia da segmentação. A impossibilidade de realizar e visualizar a segmentação nas imagens 2D (axiais, sagitais e coronais) constitui uma importante desvantagem desta versão do programa InVivo Dental. Por ser um programa disponível apenas comercialmente, o seu módulo de avaliação das vias aéreas superiores deixa a desejar e necessita de atualização.

(3) Ondemand3D: a segmentação das vias aéreas é realizada de forma rápida, através da inserção de sementes (pontos iniciais de segmentação) diretamente nas imagens bidimensionais (axial, sagital e coronal). A seguir, a densidade tecidual das vias aéreas é detectada automaticamente, delineando a área a ser segmentada. Entretanto, existe a necessidade de ajuste do intervalo da escala de cinza (*threshold interval*) para

refinamento e obtenção de uma segmentação mais acurada. O problema é que o Ondemand3D não permite um ajuste fino do intervalo de escala de cinza, produzindo alterações grosseiras das áreas delineadas para segmentação. A ausência de um controle preciso do processo de segmentação, ou ajuste fino, faz com que mínimas mudanças no intervalo da escala de cinza selecionado produzam grandes alterações no volume 3D gerado. Além do mais, o algoritmo do módulo de segmentação do Ondemand3D é deficiente em detectar precisamente os limites anatômicos das vias aéreas. O resultado é uma segmentação com falhas tanto na região interna como nos limites anatômicos das vias aéreas superiores (Figura 3).

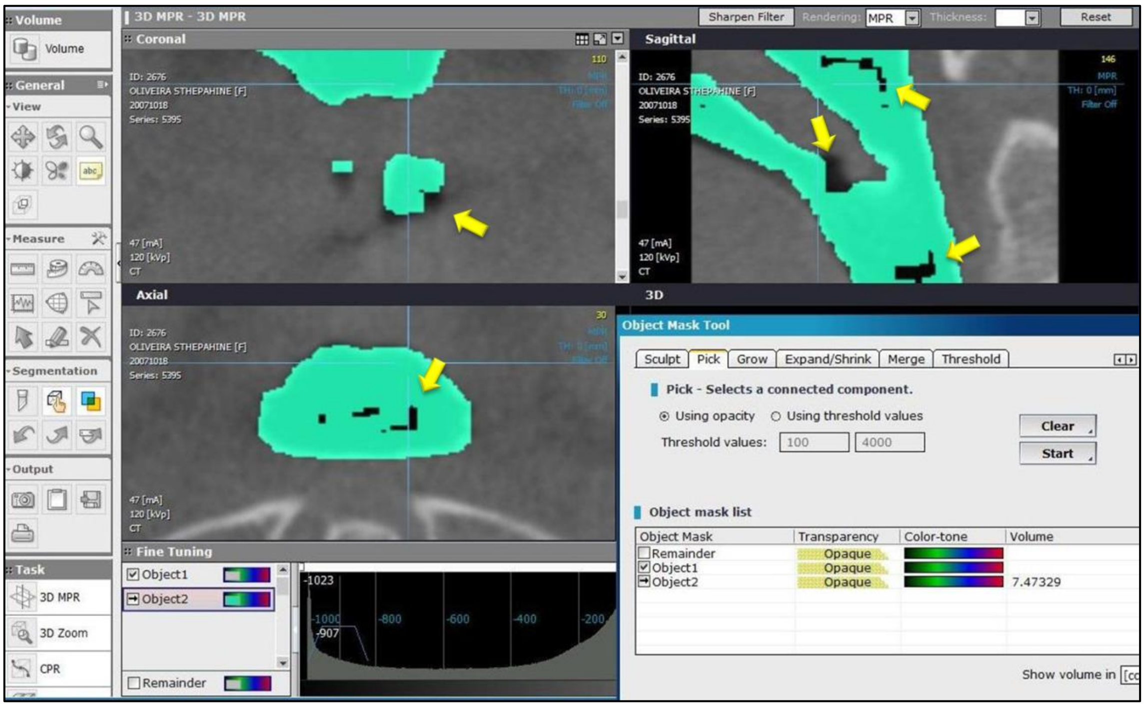

Figura 3. Segmentação da orofaringe no programa Ondemand3D. As setas amarelas mostram falhas da segmentação nas regiões internas e nos limites anatômicos da orofaringe.

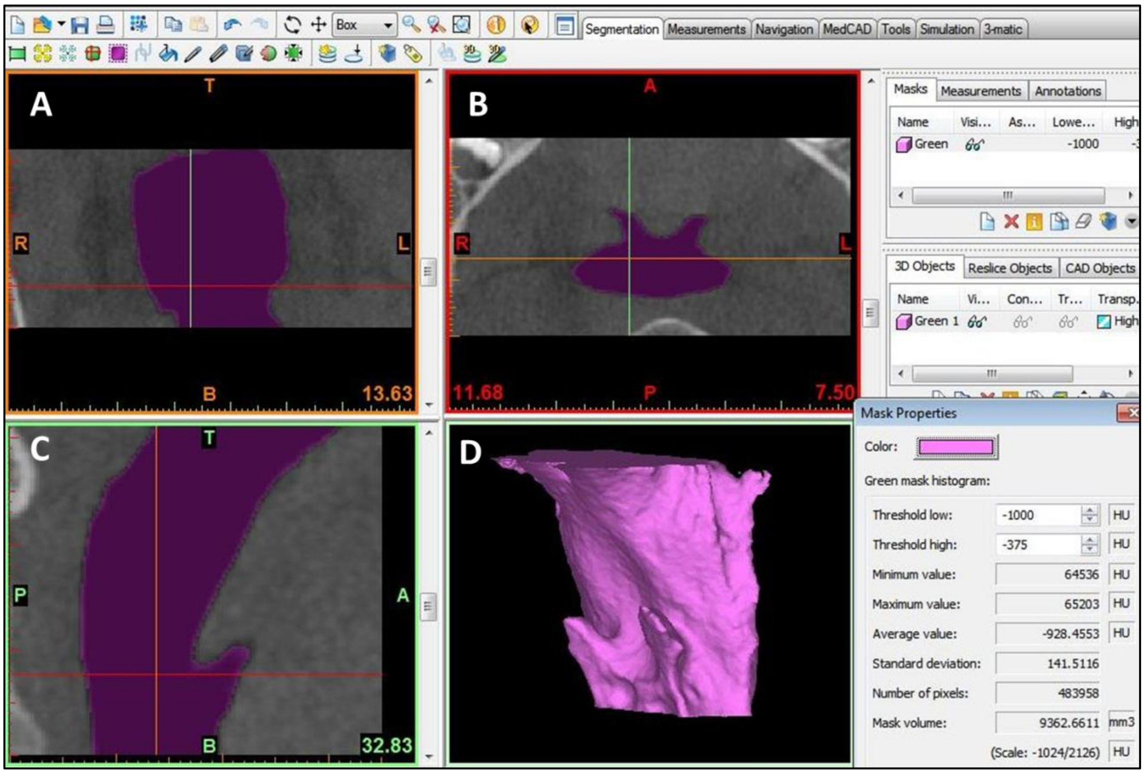

Figura 4. Segmentação da orofaringe no programa Mimics. Em (A) imagem coronal, (B) axial e (C) sagital mostrando a orofaringe corretamente preenchida pela segmentação. Em (D) modelo virtual 3D da orofaringe a partir qual foi computado o volume.

(4) Mimics: é um programa utilizado na engenharia biomédica que permite a realização de segmentações de maneira rápida e fácil. A segmentação das vias aéreas pode ser realizada através da seleção do intervalo de escala de cinza compatível com o ar ou do filtro específico para as vias aéreas superiores. A acurácia da segmentação pode ser conferida nas imagens 2D (Figura 4A, 4B e 4C) e, se necessário, o intervalo da escala de cinza pode ser ajustado facilmente para que se obtenha uma segmentação fiel das vias aéreas superiores. Possui ferramentas para edição da segmentação, alta sensibilidade e controle do processo segmentação. As principais desvantagens são o custo elevado e a dificuldade de manuseio em comparação aos programas Dolphin3D e o InVivo.

(5) OsiriX: realiza segmentações de maneira rápida e precisa, porém, o manuseio não é tão fácil quanto os programas Dolphin3D e o InVivo dental. A segmentação semiautomática se dá pela seleção de um ponto qualquer nas vias aéreas para determinação da densidade tecidual e delineamento da área a ser segmentada. Após conferência da segmentação nas imagens 2D, o modelo 3D da orofaringe é gerado e o

seu volume computado (Figura 5). O programa possui ferramentas para ajuste do intervalo da escala de cinza e edição da segmentação. A detecção dos limites anatômicos da orofaringe é excelente. Como vantagem adicional, permite que um volume específico seja selecionado dentro do volume total da TCCB e exportado como arquivo DICOM. Tal procedimento viabiliza a avaliação de regiões especificas do complexo maxilofacial utilizando imagens de alta resolução em arquivos pequenos, o que reduz a demanda computacional e acelera o processamento dos dados.

(6) ITK-Snap: é um programa disponível gratuitamente, porém, de difícil manuseio em comparação aos programas Dolphin3D e InVivo Dental. É excelente para segmentação e construção de modelos virtuais 3D das vias aéreas. O processo de segmentação semiautomático inclui a seleção do intervalo da escala de cinza e inserção de sementes nas imagens 2D. A segmentação se dá pelo crescimento e difusão dessas sementes através das áreas (*voxels*) pré-estabelecidas pelo intervalo da escala de cinzas (Figura 6, página 51). Apresenta boa sensibilidade, preenchendo pequenas e complexas áreas da orofaringe. Possui ferramentas para edição e correção da segmentação tanto nas imagens 2D e 3D. A segmentação com o ITK-Snap foi descrita, validada e testada em relação a sua acurácia, sendo considerada superior ao método de segmentação manual realizado corte por corte.[14]

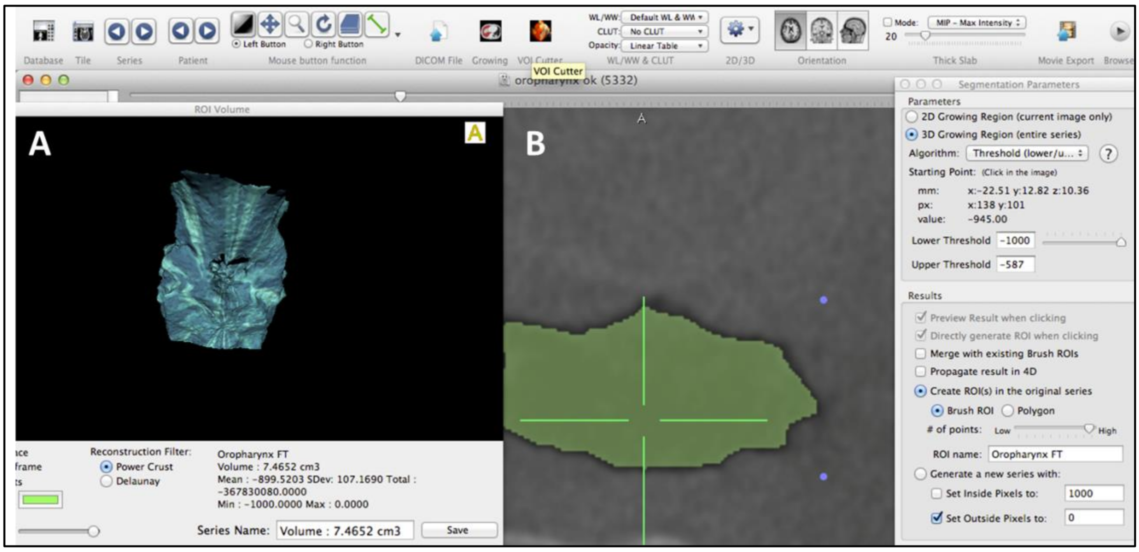

Figura 5. Segmentação da orofaringe no programa OsiriX. Em (A) modelo virtual 3D da orofaringe a partir do qual foi computado o volume. Em (B) imagen axial mostrando segmentação adequada da orofaringe.

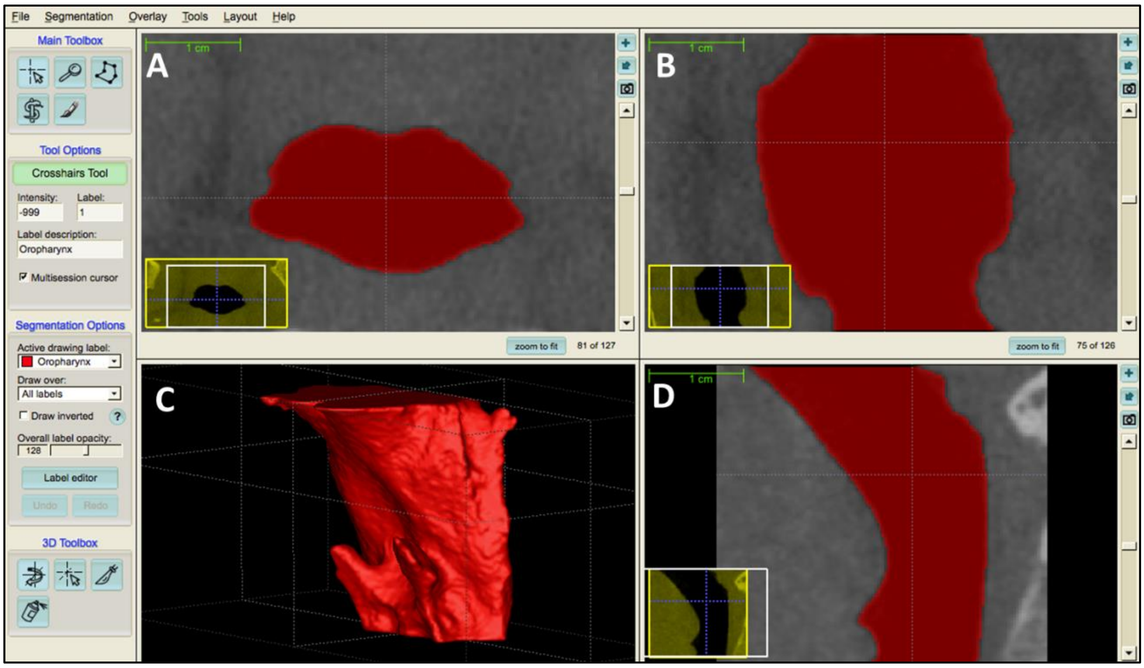

Figure 6. Segmentação da orofaringe no programa ITK-Snap. (A) imagem axial, (B) sagital e (D) coronal mostrando a orofaringe corretamente preenchida pela segmentação. Em (C) modelo virtual 3D da orofaringe a partir do qual foi computado o volume.

Algumas considerações importantes em relação as limitação da análise do volume das vias aéreas superiores em TCCB são necessárias. A avaliação do volume das vias aéreas superiores é diretamente dependente da acurácia da segmentação. Esta, por sua vez, depende da qualidade da imagem da TCCB, da seleção do intervalo de escala de cinza (*threshold interval*) e do algoritmo utilizado para segmentação, o qual pode variar em cada programa. A qualidade da imagem da TCCB, representada pela resolução espacial, é interdependente de fatores como configuração do tomógrafo durante a aquisição da imagem, posição do paciente, volume da reconstrução, tamanho do voxel e do modo como os arquivos DICOM são exportados. Outros fatores intrínsecos da aquisição da TCCB, como média de densidade do voxels, ruído e presença de artefatos também podem afetar a qualidade da imagem. A influência dos artefatos na densidade tecidual dos voxels (*grey values*) tem sido relatada em alguns estudos. [15-17] O problema é que mesmo utilizando imagens com alta resolução espacial (voxel pequeno e tempo de escaneamento longo) a presença dos artefatos, especialmente aqueles relacionados à movimentação do paciente, podem afetar a densidade tecidual dos voxels, tornando os limites anatômicos das vias aéreas pouco definidos. Isso dificulta a determinação do intervalo de escala de cinza e prejudica a diferenciação dos voxels pelos algoritmos dos programas durante o processo de segmentação (Figura 7).

No artigo 1 (Páginas 14-27), foram testados os algoritmos de segmentação presentes em 6 diferentes programas, por meio de dois protocolos de utilização do intervalo escala de cinza (threshold interval), utilizando sempre um mesmo volume de TCCB (*Phantom* de acrílico e orofaringe de 33 pacientes). Portanto, o fator qualidade da imagem foi o mesmo para evitar viés e possibilitar melhor comparação entre os programa e protocolo de segmentação. Entretanto, avaliações das vias aéreas antes e após tratamentos, através de segmentação e construção de modelos virtuais 3D, devem ser analisadas com cautela. Além do viés impostos pela influência da posição da cabeça e fases do ciclo respiratório na morfologia das vias aéreas superiores, existem as alterações na densidade tecidual dos voxels em função dos artefatos e que podem afetar a segmentação e construção de modelos virtuais 3D.

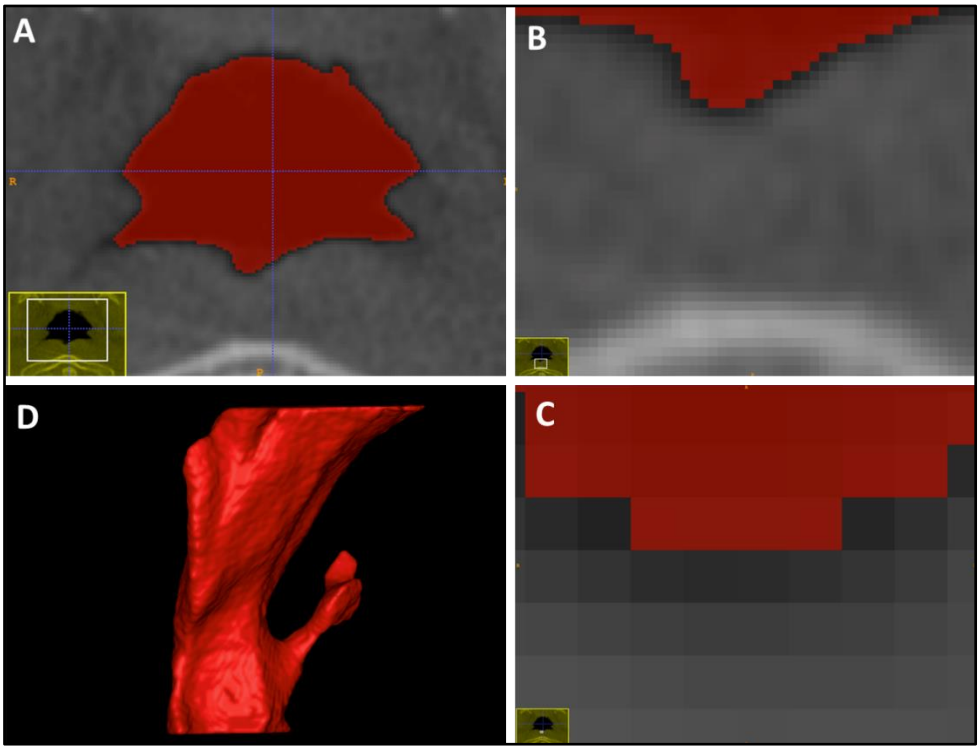

Figura 7. (A) imagem axial mostrando uma segmentação padrão da orofaringe, considerada adequada. Em (B), ampliação da imagem mostrando o limite anatômico da orofaringe pouco definido, em função da provável alteração da densidade dos voxels pelos artefatos da TCCB. Em (C), ampliação da imagem, ao nível dos pixels, mostrando a dificuldade para determinar os limites da orofaringe durante o processo de segmentação. Em (D) modelo 3D da orofaringe gerado a partir da segmentação.

Com base nos achados do artigo 1 e discussão adicional, ficaram evidentes as limitações de alguns programas e a necessidade de atualização e avaliação dos módulos para análises das vias aéreas. Além do mais, existe a necessidade de se estabelecer um protocolo universal de utilização dos tipos de algoritmos e técnicas de segmentação a fim de padronizar a avaliação tridimensional das vias aéreas superiores.

A consolidação da TCCB na Odontologia e os avanços nos algoritmos para registro de imagens vêm transformando a maneira de avaliação realizada por ortodontistas e cirurgiões. A superposição tridimensional de TCCB com registro na base do crânio vem sendo considerada o método de eleição para avaliações 3D dos efeitos do tratamento ortodôntico-cirúrgico. A superposição automática de TCCB baseada em voxel foi introduzida na Odontologia por Cevidanes et al,[3] em 2005. Esse método vem sendo utilizado em diversas pesquisas e é considerado o método mais avançado para avaliação do complexo craniofacial em TCCB.[3,5-9] Embora os programas utilizados sejam gratuitos, existem limitações impostas pela dificuldade de manuseio e longo tempo necessário para realizar o processo completo de superposição, que restringem uma maior utilização desse método de superposição. Tais limitações privam a maioria dos profissionais de realizar avaliações 3D acuradas dos seus tratamentos. Isso levou algumas empresas a desenvolverem e comercializarem programas para superposição de TCCB. O problema é que a maioria desses programas utiliza métodos não acurados (*point landmark based*) ou não possuiu estudos de validação científica. Isso nos levou a realizar o artigo 2, no qual foi estudado e validado um método rápido e fácil de superposição 3D de TCCB, com potencial para utilização em pesquisas e na prática clínica diária.

Como as imagens axiais, sagitais e coronais da superposição da TCCB dos pacientes 6, 7, 8, 9 e 10 não foram incluídas no artigo 2 devido ao número excessivo de figuras, as mesmas são apresentadas e comentadas a seguir:

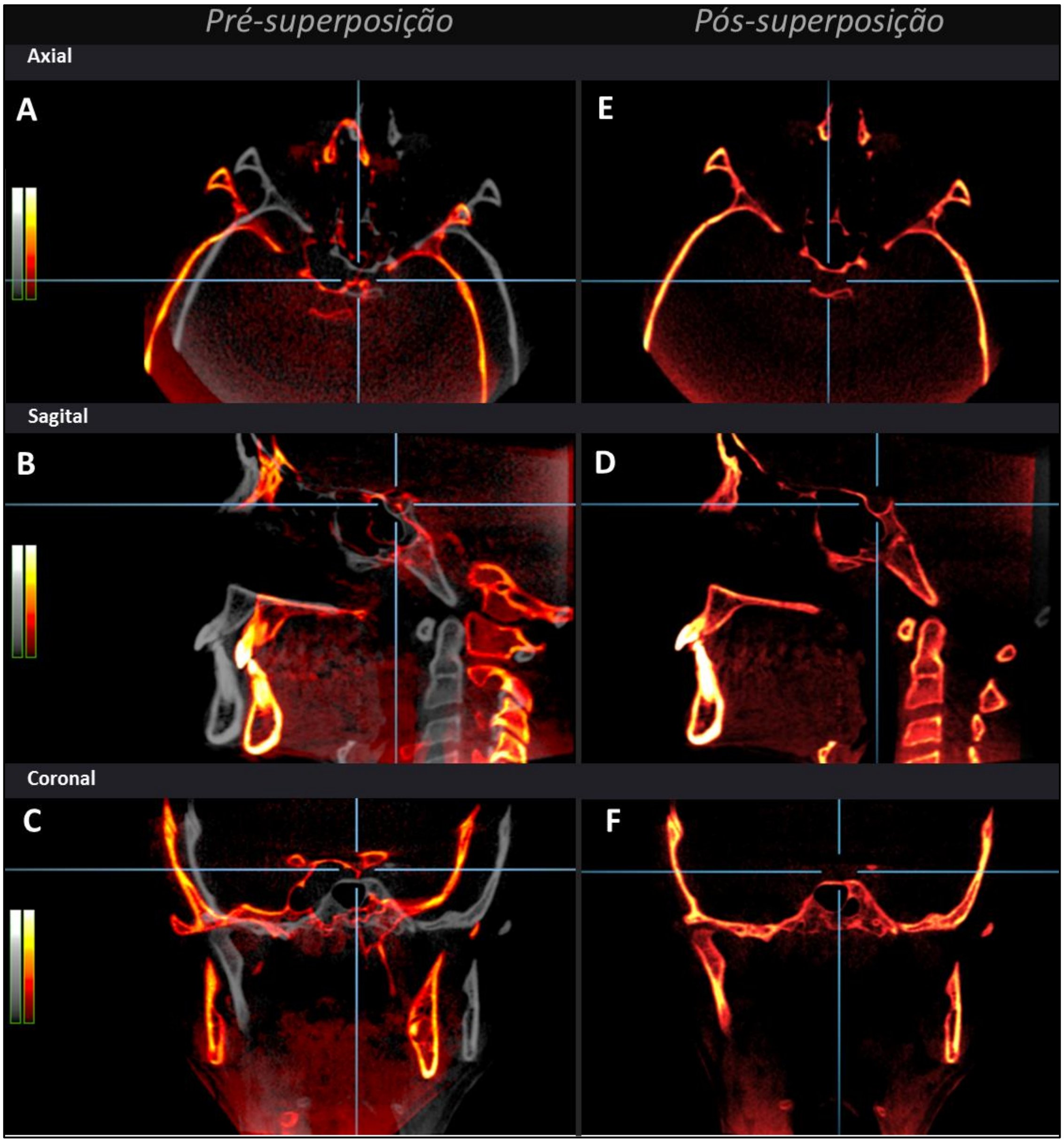

Figura 8. Paciente 6. Superposição tridimensional, baseada em voxel, com registro na base anterior do crânio. Em (A) imagem axial, (B) sagital e (C) coronal mostrando a TCCB original (cor cinza) e TCCB reorientada (cor laranja) antes da superposição. Em (E) imagem axial, (D) sagital e (F) coronal, após a superposição da TCCB original com a TCCB reorientada. Notar a perfeita superposição de todas as estruturas anatômicas.

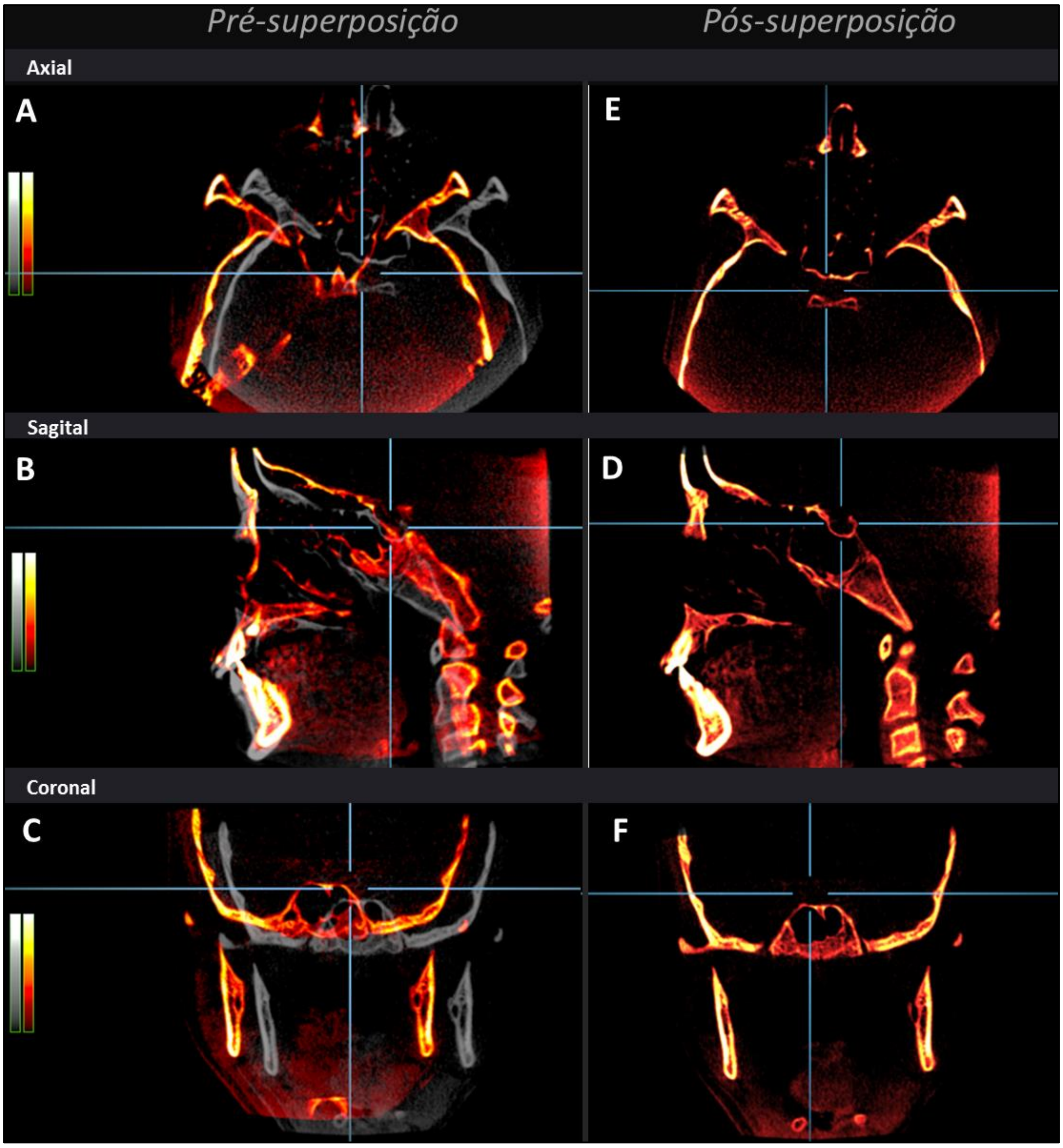

Figura 9. Paciente 7. Superposição tridimensional, baseada em voxel, com registro na base anterior do crânio. Em (A) imagem axial, (B) sagital e (C) coronal mostrando a TCCB original (cor cinza) e TCCB reorientada (cor laranja) antes da superposição. Em (E) imagem axial, (D) sagital e (F) coronal, após a superposição da TCCB original com a TCCB reorientada. Notar a perfeita superposição de todas as estruturas anatômicas.

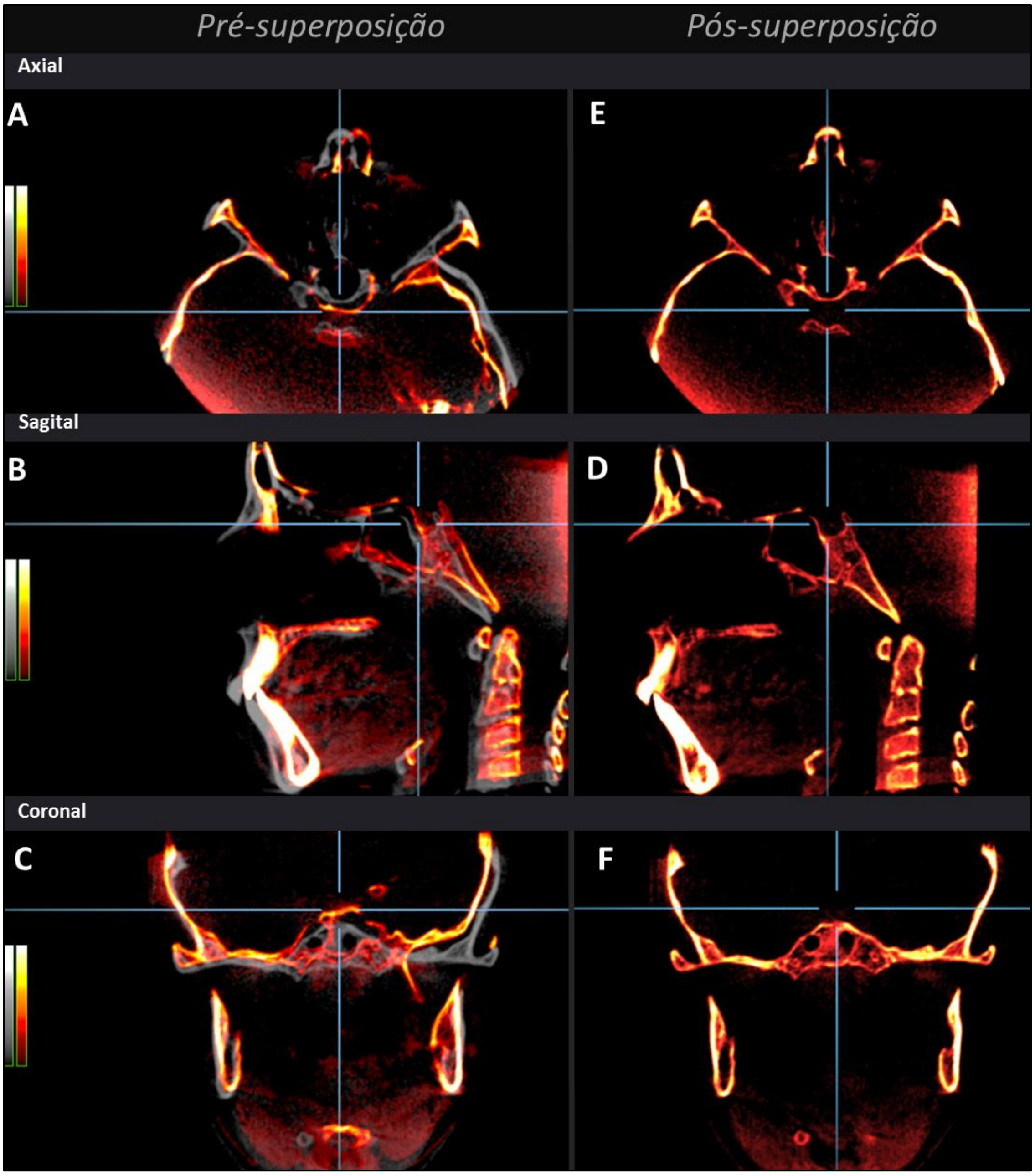

Figura 10. Paciente 8. Superposição tridimensional, baseada em voxel, com registro na base anterior do crânio. Em (A) imagem axial, (B) sagital e (C) coronal mostrando a TCCB original (cor cinza) e TCCB reorientada (cor laranja) antes da superposição. Em (E) imagem axial, (D) sagital e (F) coronal, após a superposição da TCCB original com a TCCB reorientada. Notar a perfeita superposição de todas as estruturas anatômicas.

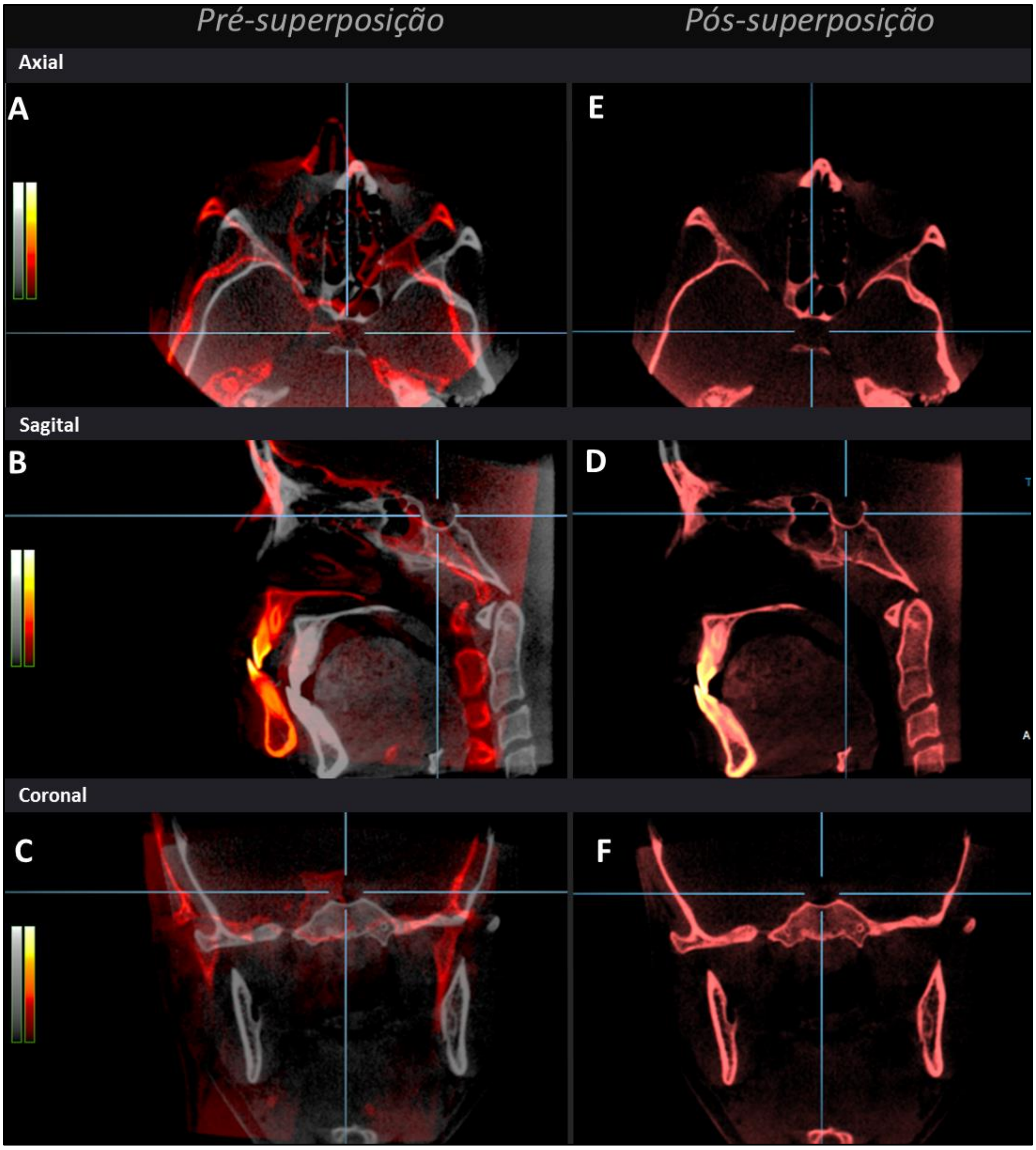

Figura 11. Paciente 9. Superposição tridimensional, baseada em voxel, com registro na base anterior do crânio. Em (A) imagem axial, (B) sagital e (C) coronal mostrando a TCCB original (cor cinza) e TCCB reorientada (cor laranja) antes da superposição. Em (E) imagem axial, (D) sagital e (F) coronal, após a superposição da TCCB original com a TCCB reorientada. Notar a perfeita superposição de todas as estruturas anatômicas.

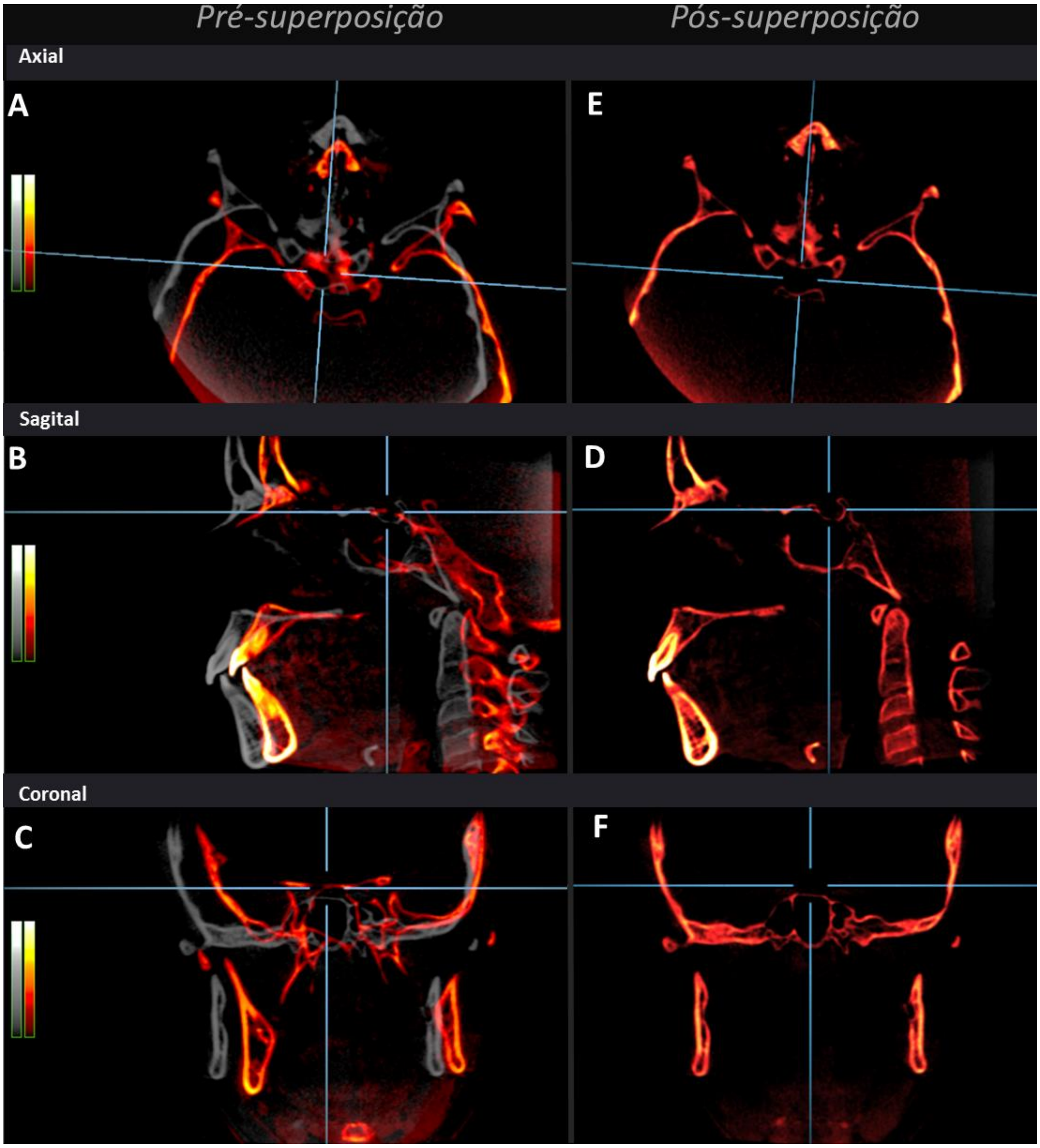

Figura 12. Paciente 10. Superposição tridimensional, baseada em voxel, com registro na base anterior do crânio. Em (A) imagem axial, (B) sagital e (C) coronal mostrando a TCCB original (cor cinza) e TCCB reorientada (cor laranja) antes da superposição. Em (E) imagem axial, (D) sagital e (F) coronal, após a superposição da TCCB original com a TCCB reorientada. Notar a perfeita superposição de todas as estruturas anatômicas.

6. Conclusão

6.1 Conclusão geral

Os seis programas foram precisos na avaliação tridimensional do volume da orofaringe, porém, apresentaram graus variados de acurácia. Em relação à superposição rápida de volumes de TCCB, o programa avaliado foi considerado acurado e validado cientificamente.

6.2 Conclusões específicas

Artigo 1 *(Imaging software accuracy for 3-dimensional analysis of the upper airway)*

- Os seis programas foram precisos na avaliação do volume da orofaringe, porém, subestimaram o volume do *Phantom* acrílico da orofaringe (padrão ouro).
- Em relação à segmentação da via aérea orofaríngea, os programas Mimics, Dolphin3D, ITK-Snap e OsiriX foram considerados similares entre si e mais acurados em comparação aos programas InVivo Dental e Ondemand3D.
- A segmentação final depende da seleção do intervalo da escala de cinza (threshold interval), do algoritmo de segmentação do programa e da complexidade morfológica das vias aéreas. Os seis programas utilizam mecanismos de segmentação diferentes, não havendo padronização na utilização de algoritmos para segmentação e análise das vias aéreas superiores.

Artigo 2 *(Fast 3-dimensional superimposition of CBCT volumes: validation study)*

- O método de superposição tridimensional rápida de volumes de TCCB do programa Ondemand3D foi validado, sendo considerado rápido e preciso. Esse método tem potencial para aplicações na prática clínica diária e em pesquisas, possibilitando avaliações longitudinais tridimensionais de pacientes em crescimento e adultos submetidos a tratamentos ortodônticos e/ou cirúrgicos.

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8. Anexos

Anexo A – Aprovação do projeto de tese pela Comissão Científica e de Ética da Faculdade de Odontologia da PUCRS.

Comissão Científica e de Ética
Faculdade da Odontologia da PUCRS

Porto Alegre 12 de Janeiro de 2011

O Projeto de: Tese

Protocolado sob nº: 0006/10

Intitulado: Alterações morfológicas do complexo naso-maxilar decorrentes da expansão rápida da maxila, em tomografia computadorizada cone beam

Pesquisador Responsável: Profa. Dra. Luciane Macedo de Menezes

Pesquisadores Associados André Weissheimer

Nível: Tese / Doutorado

Foi ***aprovado*** pela Comissão Científica e de Ética da Faculdade de Odontologia da PUCRS em *12 de Janeiro de 2011.*

Este projeto deverá ser imediatamente encaminhado ao CEP/PUCRS

Profa. Dra. Ana Maria Spohr
Presidente da Comissão Científica e de Ética da Faculdade de Odontologia da PUCRS

Av. Ipiranga, 6681, Prédio 06 sala 210
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Anexo B – Aprovação do projeto de tese pelo Comitê de Ética em Pesquisa da PUCRS.

Pontifícia Universidade Católica do Rio Grande do Sul
PRÓ-REITORIA DE PESQUISA E PÓS-GRADUAÇÃO
COMITÊ DE ÉTICA EM PESQUISA

OF. CEP-886/11

Porto Alegre, 27 de maio de 2011.

Senhora Pesquisadora,

O Comitê de Ética em Pesquisa da PUCRS apreciou e aprovou seu protocolo de pesquisa registro CEP 11/05370 intitulado **"Alterações morfológicas do complexo naso-maxilar decorrentes da expansão rápida da maxila em tomografia computadorizada cone beam"**.

Salientamos que seu estudo pode ser iniciado a partir desta data.

Os relatórios parciais e final deverão ser encaminhados a este CEP.

Atenciosamente,

Prof. Dr. Rodolfo Herberto Schneider
Coordenador do CEP-PUCRS

Profª Dr. Virgínia Minghelli Schmitt
Coordenadora Substituta
Comitê de Ética em Pesquisa da PUCRS
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Anexo C– Aprovação da modificação do projeto de tese pelo Comitê de Ética em Pesquisa da PUCRS.

Pontifícia Universidade Católica do Rio Grande do Sul
PRÓ-REITORIA DE PESQUISA E PÓS-GRADUAÇÃO
COMITÊ DE ÉTICA EM PESQUISA

OF.CEP-1468/11

Porto Alegre, 26 de setembro de 2011.

Senhora Pesquisadora,

O Comitê de Ética em Pesquisa da PUCRS apreciou e aprovou sua solicitação de inclusão de uma mensuração adicional, datada em 13 de setembro de 2011, referente ao seu protocolo de pesquisa intitulado **"Alterações morfológicas do complexo naso-maxilar decorrentes da expansão rápida da maxila em tomografia computadorizada cone beam"**.

Atenciosamente,

Profa. Dr. Virgínia Minghelli Schmitt
Coordenadora Substituta do CEP-PUCRS

Ilma. Sra.
Profa. Luciane Macedo de Menezes
FO
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