UNESP - Universidade Estadual Paulista

“Júlio de Mesquita Filho”

Faculdade de Odontologia de Araraquara

Doutorado em Ciências Odontológicas

FERNANDA BRASIL DAURA JORGE BOOS LIMA

AVALIAÇÃO DA ALTERAÇÃO DA VIA AÉREA SUPERIOR E DA ESTABILIDADE ÓSSEA EM PACIENTES SUBMETIDOS À OSTEOTOMIA LE FORT III MODIFICADA ASSOCIADA À OSTEOTOMIA LE FORT I PARA TRATAMENTO DA HIPOPLASIA DO TERÇO MÉDIO DA FACE

Araraquara

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Tese apresentada ao Programa de Pós-Graduação em Ciência Odontológicas Área de Diagnóstico e Cirurgia, da Faculdade de Odontologia de Araraquara, da Universidade Estadual Paulista “Júlio de Mesquita Filho” para Título de Doutor em Ciências Odontológicas, Área de Concentração: Diagnóstico e Cirurgia.

Orientador: Prof. Dr. Eduardo Hochuli Vieira

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“A tarefa não é ver aquilo que ninguém viu, mas pensar o que ninguém ainda pensou sobre aquilo que todo mundo vê.” (Arthur Schopenhauer)

Lima FBDJB. Avaliação da alteração da via aérea superior e da estabilidade óssea em pacientes submetidos à osteotomia Le Fort III modificada associada à osteotomia Le Fort I para tratamento da hipoplasia do terço médio da face [Tese de Doutorado]. Araraquara: Faculdade de Odontologia da UNESP; 2016.

RESUMO

A hipoplasia maxilar geralmente resulta em uma maloclusão Classe III de Angle, podendo, em alguns casos, apresentar mordida aberta anterior. O grau de deficiência de crescimento orbital, maxilar e ao nível oclusal raramente é uniforme nos três planos. Para corrigir discrepâncias severas e atingir uma relação intermaxilar adequada, com oclusão estável, a osteotomia Le Fort III está indicada para tratamento de pacientes sindrômicos e não sindrômicos. A técnica segue um desenho semelhante a uma fratura Le Fort III, descrita por René Le Fort. Devido à mobilização de todo segmento esquelético do terço médio, apresenta resultados estéticos mais favoráveis em comparação com avanço apenas do segmento maxilar. Este trabalho tem o propósito de avaliar comparativamente, por meio de análise tomográfica retrospectiva, a alteração das vias aéreas superiores e a estabilidade óssea em pacientes não sindrômicos submetidos à osteotomia Le Fort III modificada associada à osteotomia Le Fort I para tratamento da hipoplasia do terço médio da face.

PALAVRAS CHAVES: Cirurgia ortognática. Osteotomia maxilar. Tomografia.

Lima FBDJB. Evaluation of the change of the superior airway and the stability of the bone advancement in non-syndromic patients who underwent modified Le Fort III osteotomy associated with the Le Fort I osteotomy for treatment of midface hypoplasia [Tese de Doutorado]. Araraquara: Faculdade de Odontologia da UNESP; 2016.

ABSTRACT

The maxillary hypoplasia generally results in an Angle Class III malocclusion, and may in some cases produce anterior open bite. The level of orbital, maxillary and occlusal growth deficiency is rarely uniform in all three planes. To correct severe discrepancies and achieve adequate intermaxillary relation, with stable occlusion, Le Fort III osteotomy is indicated for the treatment of syndromic and non-syndromic patients. The technique is similar to a Le Fort III fracture, described by René Le Fort. Due to the mobilization of the entire skeletal segment of the facial middle third, presents more favorable cosmetic results compared to advancement of only the maxillary segment. This retrospective work aims to compare, using computed tomography, the change of the superior airway and the stability of the bone advancement in non-syndromic patients who underwent modified Le Fort III osteotomy associated with the Le Fort I osteotomy for treatment of midface hypoplasia.

KEY WORDS: Orthognathic Surgery. Maxillary Osteotomy. Tomography.

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1 INTRODUÇÃO

Segundo Angle[1] (1899), Nout[16] (2008) e Cheung[3] (2010), a hipoplasia do terço médio da face caracteriza-se por um hipodesenvolvimento do complexo naso-maxilo-zigomático podendo ocasionar deficiência nasolabial, ângulo nasolabial obtuso, proptose, Síndrome da Apnéia Obstrutiva do Sono (SAOS), maloclusão Classe III de Angle, mordida aberta anterior e dislalia. O grau de deficiência de crescimento orbital, maxilar e ao nível oclusal raramente é uniforme nos três planos.

De acordo com Nout[16] (2008), para corrigir esta discrepância e atingir uma relação intermaxilar adequada, com oclusão estável, podem ser realizadas três modalidades de tratamento: instalação de próteses associada à osteotomia Le Fort (LF) I; distração osteogênica do terço médio associada à LF I ou osteotomia LF III associada à osteotomia LF I.

A osteotomia LF III é indicada para correção da hipoplasia severa do terço médio de face, em pacientes sindrômicos e não sindrômicos. A técnica inicialmente descrita por Gillies[8], em 1950, e popularizada por Paul Tessier[22], em 1967, segue um desenho semelhante a de uma fratura LF III, descrita por René Le Fort[11], em 1901. Devido à mobilização de todo segmento esquelético do terço médio, apresenta resultados estéticos mais favoráveis em comparação com a técnica de avanço apenas do segmento maxilar.

Seu trajeto anatômico percorre os ossos nasais, processo ascendente da maxila, porção superior dos ossos lacrimais, parede medial das órbitas, células etmoidais e caminha para o canal óptico, sem atingi-lo. Passa pela parede lateral da órbita, passando pelo esfenóide ou mesmo o frontal, separando o frontal do zigoma, ao nível da sutura frontozigomática. Inferior e posteriormente, há separação ao nível da fissura pterigomaxilar. A fratura atinge ainda o arco zigomático e o septo nasal próximo a lâmina cribiforme.

Segundo Nout[16] (2008), Obwegeser[17] (1969), Freihofer[7] (1973), Cheung[4] (1998) e Schmitz[20] (1995), devido à morbidade, grande quantidade de complicações e recidiva do movimento realizado, modificações foram propostas para melhorar os resultados dessa osteotomia. Em 1969, Obwegeser[17] (1969) publicou uma modificação da LF III em que a osteotomia nasal não foi incluída e adicionou a LF I ao procedimento. Em 1971, Converse[5] publicou a osteotomia “tripartite”, ampliando as possibilidades de movimentação do terço médio para obter melhores resultados estéticos. Tessier[23,24] também em 1971, propôs a osteotomia oblíqua no corpo do zigoma. Em 2010, Cheung[3] propôs a osteotomia LF III associada à LF I segmentada.

Atualmente, após estas modificações, a osteotomia LF III modificada ou subcranial é realizada por meio de acesso coronal para exposição da região frontotemporal, região orbital lateral, nariz, arco zigomático e corpo do zigoma. A superfície anterior da maxila pode ser abordada por meio de acesso intrabucal. São realizadas osteotomias deslizantes no corpo do zigoma, assoalho da órbita e osso nasal utilizando uma serra reciprocante. Em seguida,

por via intrabucal é separada a maxila dos processos pterigóides. Um cinzel de septo nasal é usado para separar o etmóide do crânio e fórceps de Rowe são então utilizados para mobilizar a LF III.

Devido ao design deslizante da osteotomia não se criam gaps e por isso, não há necessidade de enxertia óssea ou malhas de titânio para o assoalho orbital. As malhas são utilizadas apenas em casos de fratura indesejada do assoalho orbital durante a disjunção craniofacial. Com o avanço do terço médio observa-se um pequeno degrau nos ossos nasais, o qual é corrigido com brocas de desgaste.

A fixação do zigoma é feita por meio de duas placas orbitais de quatro furos de cada lado. O osso nasal é fixado com uma placa em “Y” e a maxila é fixada da maneira tradicional com placas em “L”, no pilar canino e zigomático, bilateralmente.

Atualmente, a técnica da osteotomia e fixação da LF III já estão bem estabelecidas, porém algumas variações ainda vêm sendo publicadas. De acordo com Epker[6] (1976), Freihofer[7] (1973), Kaban[10] (1984), Kaban[9] (1986), McCarthy[12] (1990), Meazzini[15] (2005) e Phillips[18] (2006) a osteotomia LF III apresenta um pós-operatório com posição relativamente estável do terço médio da face. Recidiva, quando ocorre, pode ser atribuída à fixação pós-operatória inadequada levando a rotação posterior do terço médio da face ao nível das órbitas ou 'pseudorecidiva', definida como uma alteração no plano oclusal devido ao crescimento mandibular normal, combinado com a diminuição do

crescimento maxilar. Pseudorecidiva é observada em pacientes que foram operados na infância e podem ser tratados com sucesso por meio de uma LF I após a maturidade esquelética. A nossa amostra difere das outras já publicadas, pois acrescenta o uso de uma placa em “Y” no osso nasal, visando maior estabilidade e neutralização de fulcro nesta região.

2 PROPOSIÇÃO

Este trabalho tem o propósito de avaliar comparativamente, por meio de análise tomográfica retrospectiva, a alteração das vias aéreas superiores e a estabilidade óssea, em pacientes não sindrômicos, submetidos à osteotomia LF III modificada associada à osteotomia LF I para tratamento da hipoplasia do terço médio da face.

3 MATERIAL E MÉTODO

Este estudo foi realizado de acordo com os Princípios Éticos para a Experimentação em Humanos, após ter sido submetido e aprovado pelo Comitê de Ética em Experimentação Humana (Plataforma Brasil) sob número 56390815.5.0000.5416 (ANEXO C) e todos os voluntários assinaram um Termo de Consentimento Livre e Esclarecido junto aos autores da pesquisa (ANEXO A) ou consentimento pós-informação (ANEXO B).

Para o presente estudo foi realizada uma análise retrospectiva das tomografias computadorizadas de 11 pacientes submetidos à osteotomia LF III modificada associada à osteotomia LF I para tratamento de hipoplasia do terço médio da face.

Segundo a análise cefalométrica de Mcnamara, considera-se normal o paciente que apresenta o ponto A (ponto localizado na maior concavidade da porção anterior da maxila) posicionado 1mm à frente em relação ao N-PERP [linha que passa em N (Nasio) e perpendicular ao plano horizontal de Frankfurt (Po-Or)] e comprimento efetivo da maxila [do ponto Condílio (Co) até o ponto A] de 94mm para mulheres e de 100mm para homens. Segundo a análise de Steiner o ângulo SNA ideal é de 82º +/- 2º. Segundo a análise de Rickets a profundidade maxilar (ângulo formado pelo Plano de Frankfurt com a linha N-A) ideal é em média 90º +/- 3º. Não existem relatos de padrões cefalométricos em pacientes apresentando hipoplasia de terço médio, nem tampouco do valor

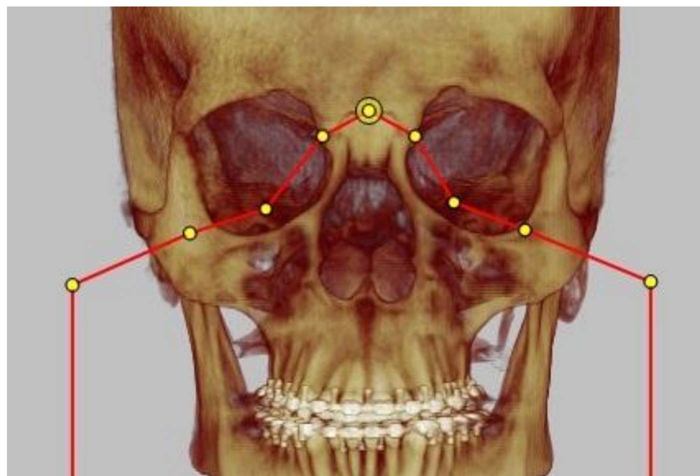
ideal do ponto Orbital, em vista disso como critério para definir a hipoplasia utilizamos como referência valores abaixo das medidas normais da posição maxilar assim como ângulos mais agudos e predominantemente a análise facial.

Todos os pacientes foram submetidos à osteotomia LF III modificada associada à osteotomia LF I e osteotomia sagital bilateral do ramo mandibular para correção da deformidade dentofacial, sendo em todos os casos realizado o planejamento virtual e a confecção de guias cirúrgicos prototipados para transferência precisa do planejamento. (Figuras 1, 2 e 3)

Foram considerados critérios de inclusão: 1. Pacientes adultos; 2. Pacientes com discrepância dental ≥ 10mm e 3. Presença de hipoplasia do terço médio da face.

Foram excluídos da amostra: 1. Pacientes que apresentavam doenças ósseas; 2. Pacientes em uso de medicações que alteram o metabolismo ósseo; 3. Pacientes portadores de fissura lábio palatina; 4. Pacientes que haviam realizado cirurgia prévia nas vias aéreas e 5. Pacientes sindrômicos.

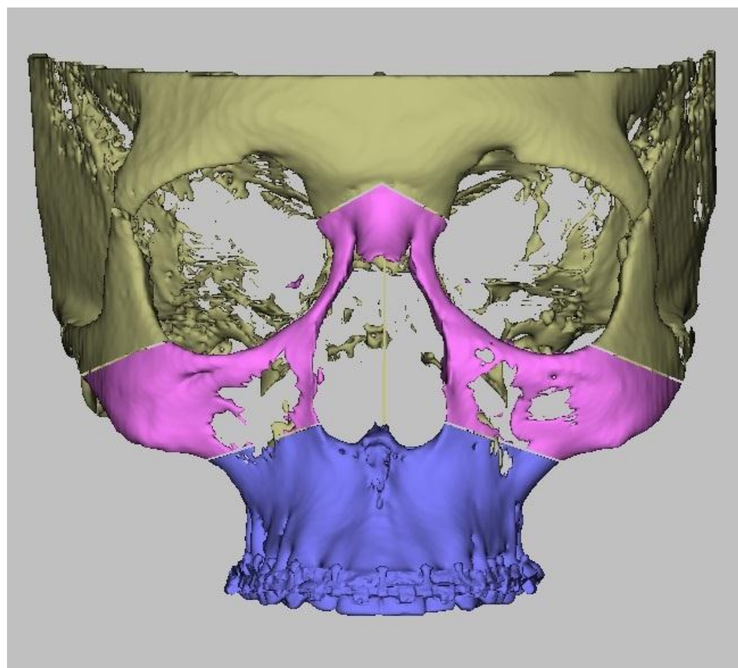
Figura 1 - Desenho da osteotomia LF III modificada no planejamento virtual com o software Dolphin Imaging 11.07



Autor: Fernanda Brasil Daura Jorge Boos Lima

Fonte: Arquivo pessoal do autor

Figura 2 - Planejamento da osteotomia LF III modificada e da osteotomia LF I no planejamento virtual com o software Dolphin Imaging 11.07



Autor: Fernanda Brasil Daura Jorge Boos Lima

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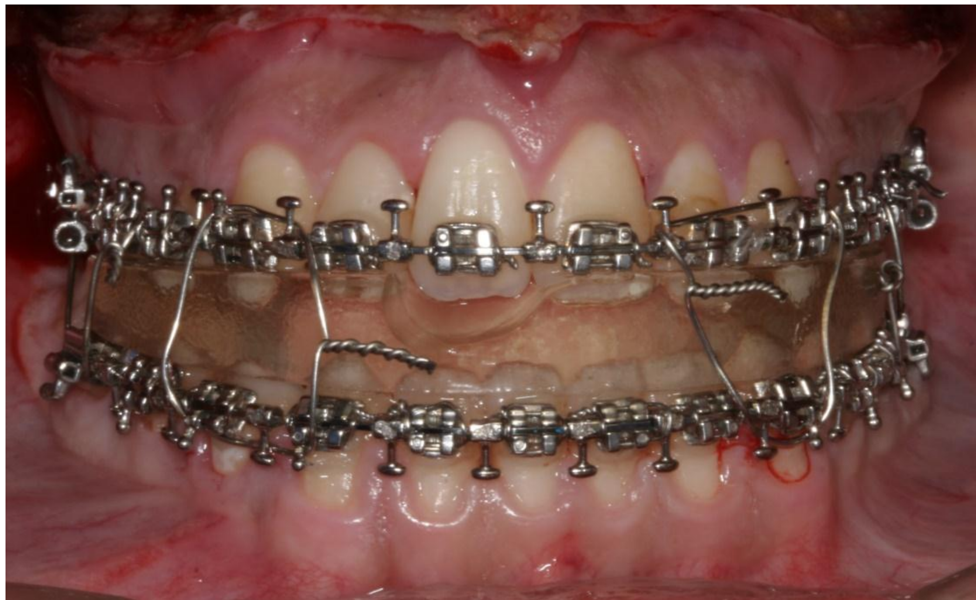
Figura 3 - Guia cirúrgico prototipado para transferência precisa do planejamento



Autor: Fernanda Brasil Daura Jorge Boos Lima

Fonte: Arquivo pessoal do autor

Os arquivos, salvos em DICOM (Digital Imaging and Communications in Medicine), foram avaliados nos softwares Dolphin Imaging 11.07 (Dolphin Imaging Management Solutions, Chatsworth, California, Estados Unidos) e Mimics (Materialise, Leuven, Bélgica).

As tomografias computadorizadas foram analisadas em três tempos:

1. Tomografia pré-operatória (T0);
2. Tomografia pós-operatória imediata (T1);
3. Tomografia pós-operatória de 18 meses (T2).

A partir das tomografias foram realizadas:

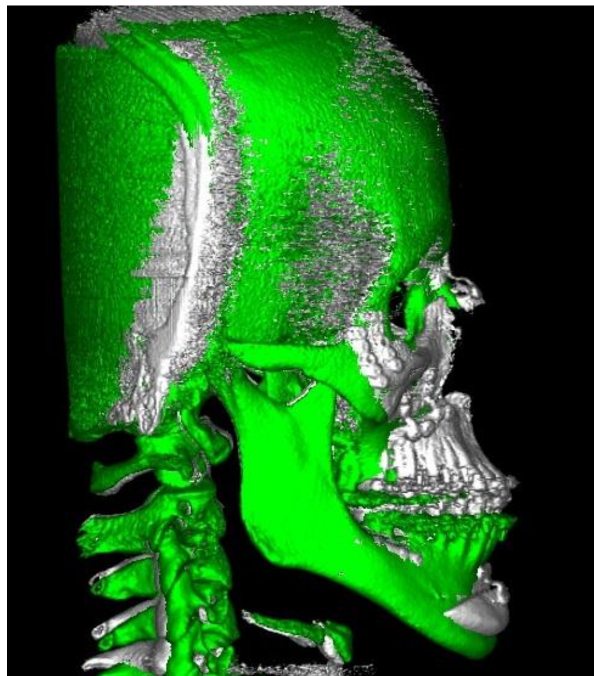
1. Sobreposição tridimensional da tomografia pré e pós-operatória imediata e comparação do avanço do terço médio pós cirurgia (T1 – T0);

2. Comparação da posição do terço médio no pós-operatório imediato e no pós-operatório de 18 meses e análise da estabilidade óssea (T2 – T1);

3. Análise da alteração da via aérea superior pós cirurgia (T1 – T0 e T2 – T0).

Para sobreposição tridimensional e posterior medição, os arquivos DICOM foram importados para os softwares. Foi calibrada a posição da cabeça, a linha média da face e do rebordo infraorbitário. (Figuras 4 e 5)

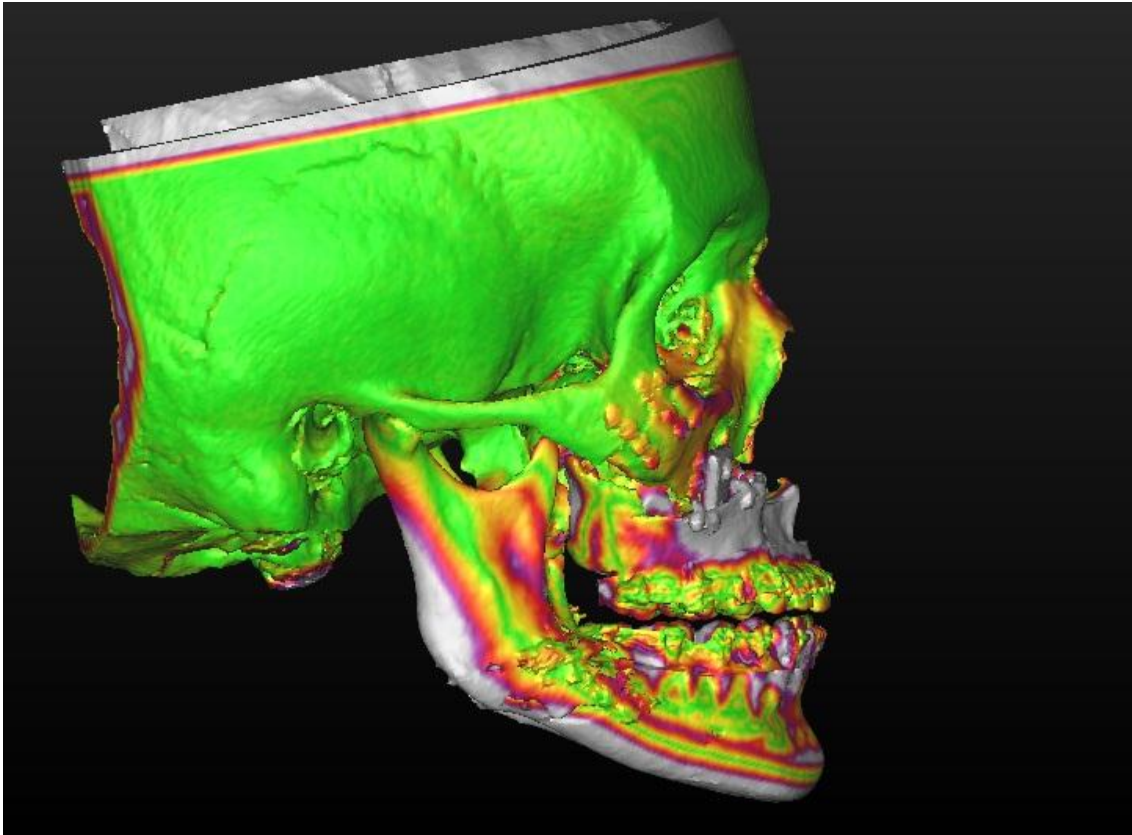
Figura 4 - Vista lateral da sobreposição 3D da tomografia pré-operatória e pós-operatória imediata no software Dolphin Imaging 11.07. Em verde a tomografia pré-operatória e em cinza a tomografia pós-operatória imediata



Autor: Fernanda Brasil Daura Jorge Boos Lima

Fonte: Arquivo pessoal do autor

Figura 5 - Vista lateral da sobreposição 3D da tomografia pré-operatória e pós-operatória imediata no software Mimics. Em verde a tomografia pré-operatória e em cinza a tomografia pós-operatória imediata



Autor: Fernanda Brasil Daura Jorge Boos Lima

Fonte: Arquivo pessoal do autor

Foram considerados pontos de referência para sobreposição:

- Ponto Pórion (Po);
- Ponto Glabella (G);
- Ponto Zygion (Zy);
- Sutura fronto-zigomática;
- Crista galli.

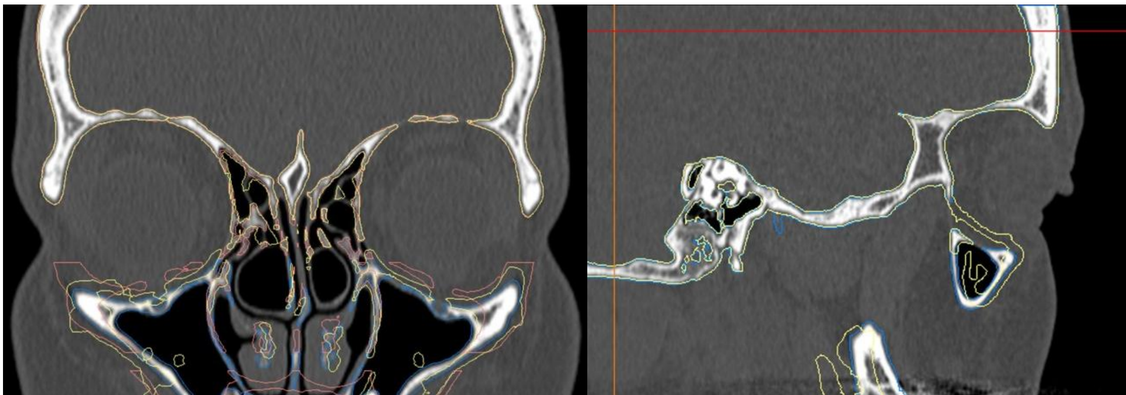
Após a sobreposição, foram utilizados o osso frontal, em corte sagital, e o osso esfenóide, em corte coronal, para conferência da exatidão da sobreposição. (Figura 6)

Foram considerados pontos de referência para analisar a alteração da posição do terço médio:

- Ponto Orbitário Inferior (ORD e ORE);
- Ponto Subespinhal (A);
- Incisal do Incisivo Superior (IIS);
- Espinha Nasal Posterior (ENP).

As medidas foram feitas em cortes sagitais sobrepostos, em plano cartesiano, no sentido horizontal e vertical, a fim de se avaliar o movimento ântero-posterior e vertical, respectivamente. As medidas verticais foram feitas em relação ao Plano de Frankfurt e as medidas horizontais foram feitas em relação ao Plano Perpendicular ao Plano de Frankfurt. (Figura 7) As medições foram feitas em três tempos, por um único examinador, com intervalo mínimo de 15 dias entre elas, sendo utilizada a média destas três medidas, e os resultados foram analisados estatisticamente.

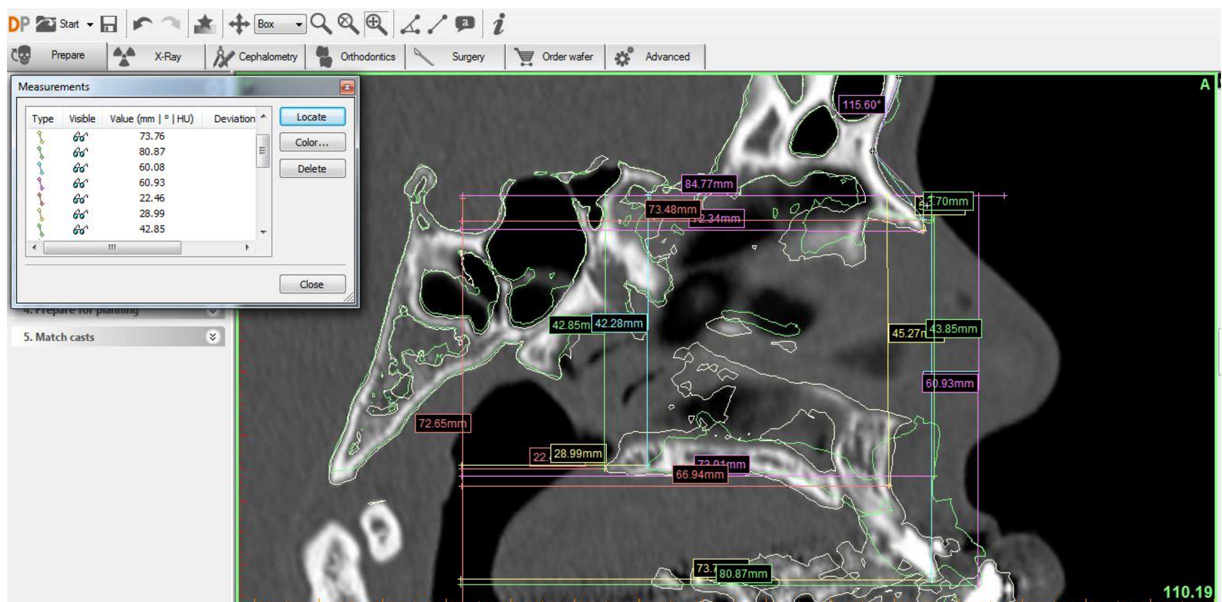
Figura 6 - O osso esfenóide, em corte coronal, e osso frontal, em corte sagital, foram utilizados para conferência da exatidão da sobreposição



Autor: Fernanda Brasil Daura Jorge Boos Lima

Fonte: Arquivo pessoal do autor

Figura 7 - Sobreposição sagital no software Mimics para medições horizontais e verticais



Autor: Fernanda Brasil Daura Jorge Boos Lima

Fonte: Arquivo pessoal do autor

Para análise da via aérea superior, a partir das imagens tomográficas no software Dolphin Imaging 11.07, planos foram formados utilizando-se referências anatômicas, determinando-se assim, os limites da via aérea superior e possibilitando, desta forma, a quantificação do volume que foi obtido.

Os limites da nasofaringe utilizados foram:

Anterior: Limite anatômico: plano frontal perpendicular ao Plano de Frankfurt passando pela espinha nasal posterior;

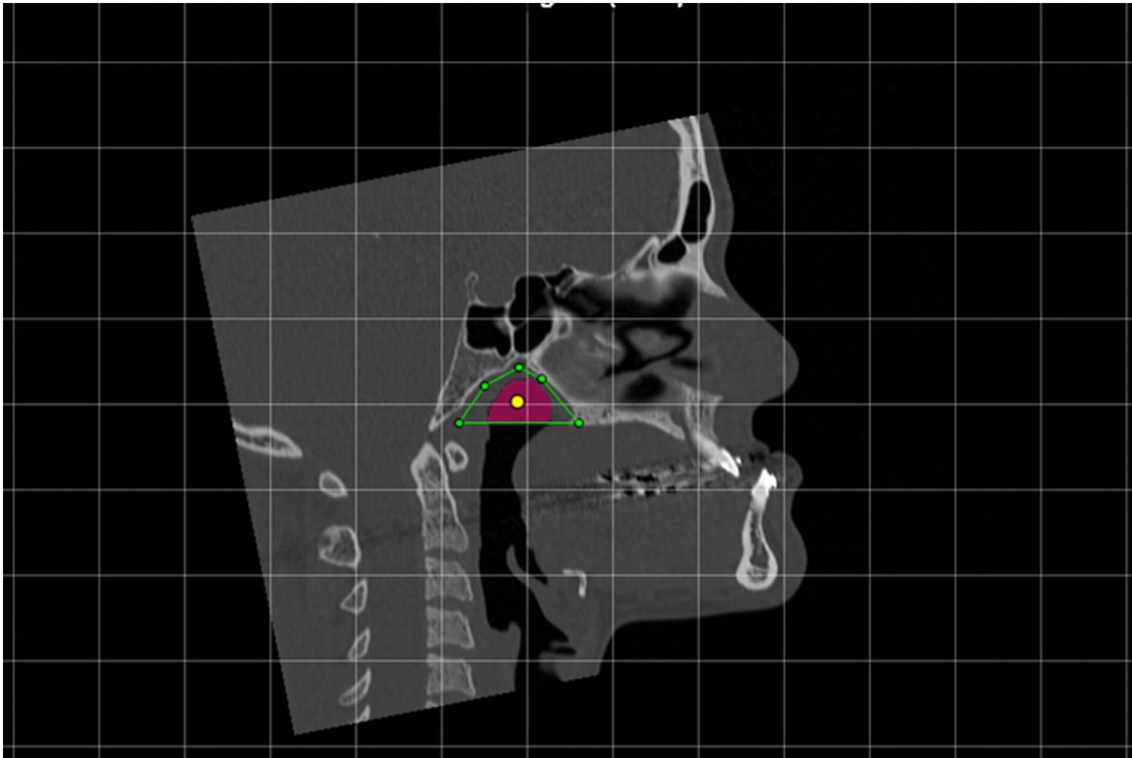
Posterior: Limite anatômico: contorno dos tecidos moles da parede da faringe. Limite técnico: plano frontal perpendicular ao Plano de Frankfurt passando por C2sp (Ponto médio entre os pontos mais superior e posterior da segunda vértebra cervical);

Superior: Limite anatômico: contorno dos tecidos moles da parede da faringe. Limite técnico: plano transversal paralelo ao Plano de Frankfurt passando pela da raiz do clívus;

Inferior: Limite anatômico: plano paralelo ao Plano de Frankfurt passando pela espinha nasal posterior e estendendo para a parede posterior da faringe;

Lateral: Limite anatômico: contorno dos tecidos moles das paredes laterais da faringe. Limite técnico: plano sagital perpendicular ao Plano de Frankfurt passando pelas paredes laterais do seio maxilar. (Figura 8)

Figura 8 - Análise volumétrica da nasofaringe no software Dolphin Imaging 11.07



Autor: Fernanda Brasil Daura Jorge Boos Lima

Fonte: Arquivo pessoal do autor

Os limites da orofaringe utilizados foram:

Anterior: Limite anatômico: plano frontal perpendicular ao Plano de Frankfurt passando pela espinha nasal posterior;

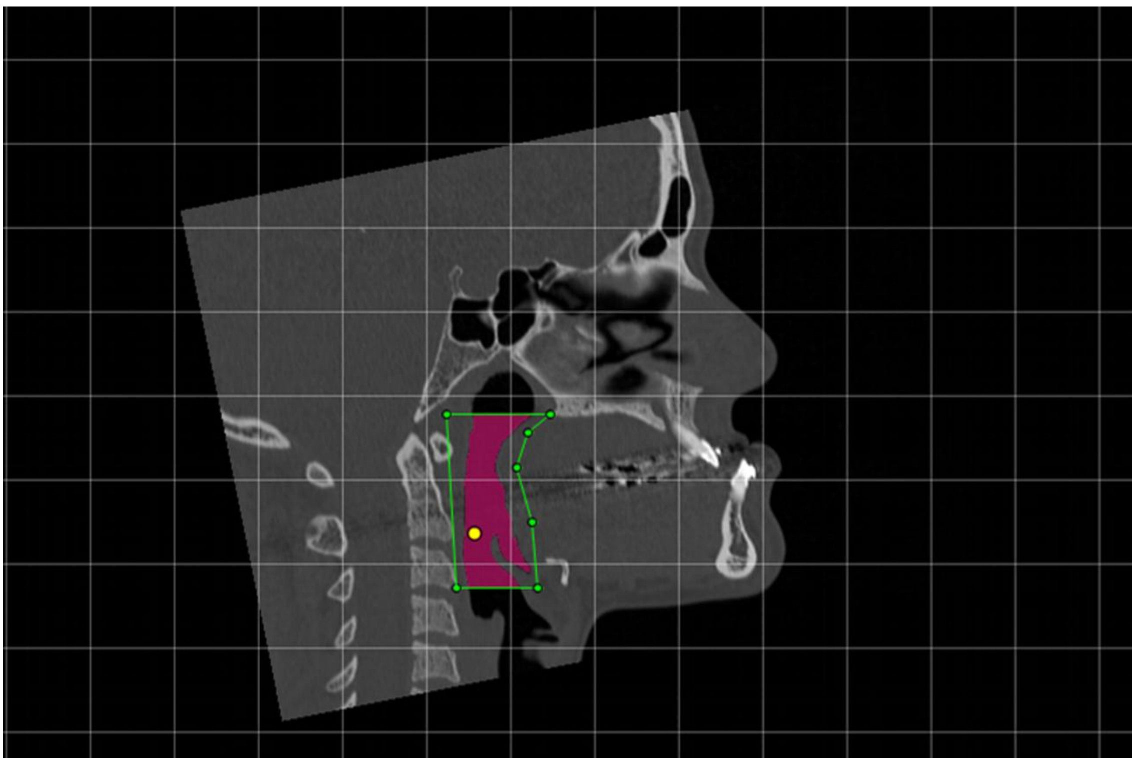
Posterior: Limite anatômico: contorno dos tecidos moles da parede da faringe. Limite técnico: plano frontal perpendicular ao Plano de Frankfurt passando por C2sp;

Superior: Limite anatômico: plano paralelo ao Plano de Frankfurt passando pela espinha nasal posterior e estendendo para a parede posterior da faringe;

Inferior: Limite anatômico: plano paralelo ao Plano de Frankfurt passando por C3ai (Ponto mais anterior e inferior da terceira vértebra cervical)

Lateral: Limite anatômico: contorno dos tecidos moles da parede lateral da faringe. Limite técnico: plano sagital perpendicular ao Plano de Frankfurt passando pelas paredes laterais do seio maxilar (Figura 9).

Figura 9 - Análise volumétrica da orofaringe no software Dolphin Imaging 11.07



Autor: Fernanda Brasil Daura Jorge Boos Lima

Fonte: Arquivo pessoal do autor

Os limites da hipofaringe utilizados foram:

Anterior: Limite anatômico: plano frontal perpendicular ao Plano de Frankfurt passando pela espinha nasal posterior;

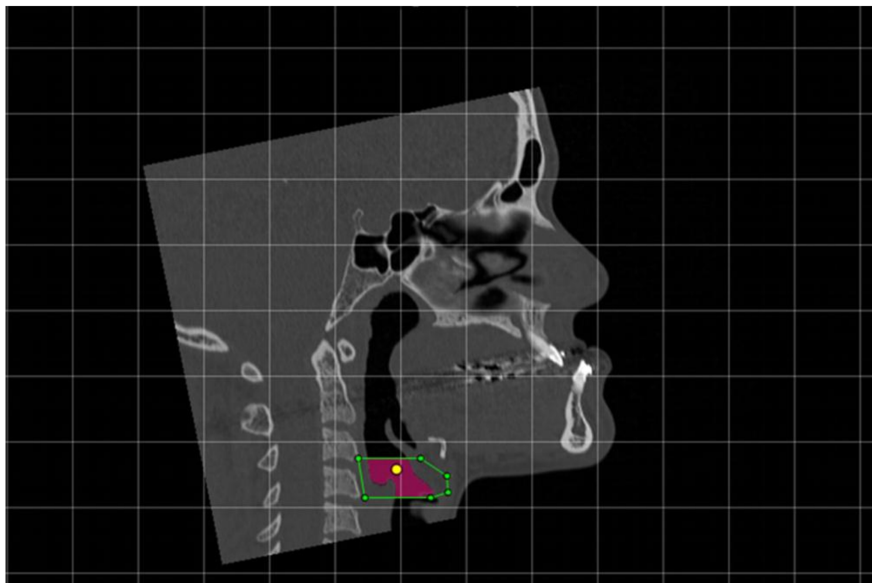
Posterior: Limite anatômico: contorno dos tecidos moles da parede da faringe. Limite técnico: plano frontal perpendicular ao Plano de Frankfurt passando por C2sp;

Superior: Limite anatômico: plano paralelo ao Plano de Frankfurt passando por C3ai;

Inferior: Limite anatômico: plano paralelo ao Plano de Frankfurt conectando a base da epiglote com a entrada do esôfago. Limite técnico: plano paralelo ao Plano de Frankfurt conectando a base da epiglote com C4ai (Ponto mais anterior e inferior da quarta vértebra cervical);

Lateral: Limite anatômico: contorno dos tecidos moles da parede lateral da faringe, Limite técnico: plano sagital perpendicular ao Plano de Frankfurt passando pelas paredes laterais do seio maxilar (Figura 10).

Figura 10 - Análise volumétrica da hipofaringe no software Dolphin Imaging 11.07



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Fonte: Arquivo pessoal do autor

Foram analisadas as alterações (T2 – T1 e T1 – T0) da nasofaringe, orofaringe e hipofaringe e os resultados foram analisados estatisticamente.

4 PUBLICAÇÃO 1

TECHNICAL NOTE

TITLE PAGE

A TECHNICAL NOTE ON THE IMPORTANCE OF THE DESIGN OF THE SUBCRANIAL LE FORT III OSTEOTOMY *

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Key Words: Orthognathic Surgery, Maxillary Osteotomy, Midface osteotomy, Le Fort III, Midface Hypoplasia.

ABSTRACT

Midface hypoplasia is a naso-maxillary-zygomatic hypodevelopment and usually presents severe Angle Class III malocclusion, leading to psychosocial problems. Currently, in order to correct severe discrepancies and achieve adequate intermaxillary relationship, with stable occlusion, subcranial Le Fort III osteotomy in association with Le Fort I osteotomy is indicated for the treatment of syndromic and non-syndromic patients. The purpose of this article is to describe details of the design of the subcranial LF III, in a series of eleven patients, which were not completely discussed in the literature, and elucidate points that are important to help surgeons improve results with less morbidity. The following topics were discussed: the design of the osteotomy and its importance to increase bone contact; adequate fixation aiming stability and the correct time during surgery to vertical reposition the upper incisor. The functional and esthetic outcomes suggests that subcranial Le Fort III osteotomy should be incorporated as an option for non-syndromic patients with large maxillo-mandibular discrepancies associated with midface hypoplasia.

INTRODUCTION

One of the most challenging topics in orthognathic surgery is the midface hypoplasia. Midface hypoplasia is a naso-maxillary-zygomatic hypo development with depressed nasolabial area, obtuse nasolabial angle, deficient projection of the malar and infraorbital regions and usually presents exorbitism, severe Angle Class III malocclusion, open bite, everted lower lip, flat labiomental fold, airway obstruction, speech articulation errors and facial distortion, leading to psychosocial problems[1-3].

Classically, the Le Fort III (LF III) osteotomy was classified and derived from Tessier's reports[4,5]. Over time, several authors described the procedure virtually addressed for syndromic patients, with several forms of craniofacial dysostosis, due to the physiological and functional problems associated[6,7]. Currently, in order to correct severe discrepancies and achieve adequate intermaxillary relationship, with stable occlusion, subcranial LF III osteotomy in association with Le Fort I (LF I) osteotomy is indicated for the treatment of syndromic and non-syndromic patients presenting with severe class III malocclusion and 10mm or more of reverse overjet[1,7]. Details of the design of the subcranial LF III, which were not completely elucidated in the literature, are discussed and are important to help surgeons to improve results with less morbidity.

Surgical Technique

A standardized coronal flap is raised from the vertex region. Hemostasis is achieved with scalp clips on the skin edges and with bipolar cautery. Bilateral endoaural extension of the coronal incision is done to completely expose the zygomatic arch during dissection. The dissection goes under the periosteum to expose the supraorbital rims, nasal bones, lateral orbital rims, zygomatic arch and zygoma body. The supraorbital neurovascular bundles are released from their foramen bilaterally. On the lateral orbital rims, the tissue reflection is extended as far down and medially as possible along the infraorbital rim, until the orbital floor is completely visible. On the medial orbital rims, only the anterior limb of the medial canthus is detached, exposing the lacrimal sac, which is reflected to expose the lacrimal groove, dissecting along the infraorbital rim as laterally as possible. It is possible to communicate the periosteal tunnels created by this dissection. Once all the tissues are dissected from the midfacial skeleton, an external reference point is measured to correct the vertical dimension of the face during surgery.

The osteotomy begins at the body of the zygoma (Fig. 1). An oblique cut made with reciprocating saw or piezoelectric device is done from a point as far as down and posterior as possible at the zygoma body to the lateral orbital rim, bellow the lateral orbital tendon attachment. These bone cuts are made bilaterally and it is important that they are parallel and as the most horizontal as possible.

The orbital floor is approached through the coronal approach. Orbital floor is then separated from the skull using a piezoelectric device (Fig. 2). This cut is made from the end of the lateral orbital rim osteotomy, 03mm behind the orbital rim, extending medially until it stops behind the nasolacrimal duct.

The third osteotomy separates the nasal bones from the skull. Care must be taken to cut the nose bellow the cribriform plate. A plane osteotomy, preferably parallel to the osteotomies of the zygoma body, is done in order to help the adaption of the cuts after advancement.

The next osteotomy aims to separate the medial orbital wall. This cut should also be done with piezoelectric tips. This osteotomy begins at the end of the nasal bone osteotomy and continues in an inferior direction behind the lacrimal apparatus and medial tendon of the orbit until it reaches the orbital floor osteotomy.

Then a vestibular maxillary incision is done intraorally and a standard dissection is done to expose the midface, similarly to a LF I osteotomy surgery. Pterigomaxillary disjunction is performed using curved chisels followed by an osteotomy from the end of the zygoma body osteotomy until the pterygoid plates.

The separation of the nasal septum from the skull base is done with a septal osteotome. The septal osteotome must be inserted at the nasofrontal osteotomy and directed inferiorly and posteriorly, remaining anterior to the

cranial base. A pair of Smith spreaders is placed at the zygoma osteotomies to help moving down the midface while separating the nasal septum.

With the Smith spreaders in place a downward force is done to completely move down and mobilize the miface. Downward, anterior, and rotary motion can be now done with the Rowe forceps to completely downfracture the midfacial skeleton. Adequate mobilization of the facial skeleton is mandatory for success and all the osteotomy sites must move symmetrically.

With adequate mobilization, a surgical occlusal splint with the predetermined middle third advanced position planned is placed, and temporary intermaxillary fixation (IMF) is done. There must be very good contact at the zygoma bodies and nasal osteotomies. Two plates are placed bilaterally in the zygomatic bones and one plate in “Y” design achieves stabilization of the nasal bones.

A conventional LF I osteotomy follows the LF III osteotomy (Fig. 3). The LF I can be advanced and is used to correct oclusal plane alterations. It should be kept in mind that the final vertical position of the upper incisor is obtained using the external reference at this moment. No attempt should be done to correct vertical deficiencies during LF III osteotomies. After applying fixation at the maxilla, mandible sagittal splits osteotomies are performed to obtain final occlusion and fixed using the hybrid technique. The patient is usually discharged from hospital after 5 days of hospitalization (Fig. 4).

DISCUSSION

Modifications and combinations of midface osteotomies exist to correct midface deformations, but only subcranial LF III osteotomy addresses the nose, orbits, cheeks and maxilla[8]. Although functional, LF III osteotomy also improves facial esthetics.

Performing a horizontal osteotomy at the body of the zygoma and nasal bones during LF III, the surgeon will achieve a large surface on which the midface will slide forward and in upper direction under the skull of the patient. There are a number of studies that concluded that the standard LF III procedure provides a relatively stable postoperative position of the midface, making this technique reliable and applicable for treating patients with midface hypoplasia[9,10]. First described by Cheung et al[3], the sliding osteotomy that is done on the zygomatic bone bilaterally, in the LF III osteotomy, permits the maintenance of bone contact between the bone segments. These bone contact generate two great advantages on the technique: there is no need for bone graft in the midface advancement and the bone contact improves the stability of the LF III osteotomy, making relapse less probable to occur.

Also regarding the design of the zygoma body osteotomies, they should be parallel to each other. By failing in doing so, after advancement, a differential contact may be created between both sides, creating gaps and different heights

of the zygoma, thus creating an asymmetry and the necessity of grafting one side of the osteotomy to fill the gap created.

The orbit is approached through the coronal incision. In rare cases, a transconjuctival incision is done. Extending the coronal incision until the tragus cartilage by using an endoaural approach will mask the incision and allow complete exposure of the zygomatic arch, zygoma body and the floor of the orbit. This approach will allow surgeons to perform the orbital floor osteotomy just after the orbital rim without the necessity of an eyelid incision. This approach will also allow the insertion of a mesh at the orbital floor in cases of orbital floor fractures or in cases where the orbital floor is elongated after the advancement. Executing the orbital floor osteotomy just after the orbital rim (03mm) is better, because this area has more cortical bone. During downfracture of the midface, the chances of an undesired orbital floor fractures decreases considerably.

The authors use a standard external reference technique to control the final vertical position of the upper incisor during LF III osteotomy. It is important to note that no attempt of correcting the vertical facial height should be done during the LF III. If a surgeon fails to do this, one may elongate the nose and the midface, possibly with deleterious effects on the esthetical result. Therefore, the maxilla should be used to correct the final position of the upper incisor. If a gap is created between the downfractured maxilla and the midface, it should be grafted according to the surgeon’s experience. To the best of our knowledge, this is the first paper that reports the use of the Kirschner wire or screws to

control and maintain the vertical maxillary position in the desired surgical plan involving simultaneous LF III and LF I osteotomies. The Kirschner wire is fixed in the frontal bone and is maintained during surgery as the external reference point to control vertical maxillary position.

Compared to Cheung subcranial sliding LF III technique[3], a difference in our surgical protocol is the fixation on the nasal osteotomy. Fixating the nasal bones helps avoiding the rotation of the midface complex, favoring long term stability. This anti clockwise rotation is one the main causes of relapse in the midface osteotomy[9]. Another difference comparing Cheung's description is the choice of the mandibular ramus osteotomy technique. We adopt the sagittal ramus split osteotomy instead of the vertical ramus osteotomy. Using the bilateral sagittal ramus osteotomy, we avoid a long period of intermaxillary fixation. This will reflect directly in the patient overall functional recovery, as we allow a better airway flow, chewing and an improved oral hygiene.

In conclusion, this paper describes the details of the surgical technique of a subcranial LF III osteotomy for the correction of midface hypoplasia in a series of eleven non-syndromic patients. Advancement of the bones of the midfacial skeleton with the LF III osteotomy benefits and improves functional and aesthetic outcomes. Increased bone contact with adequate fixation will lead to superior results in respect to stability. Our results, regarding functional and esthetic outcomes, associated with low complication rate, suggests that this surgical technique should be incorporated as an option for non-syndromic

patients with large maxillo-mandibular discrepancies associated with midface hypoplasia.

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FIGURES

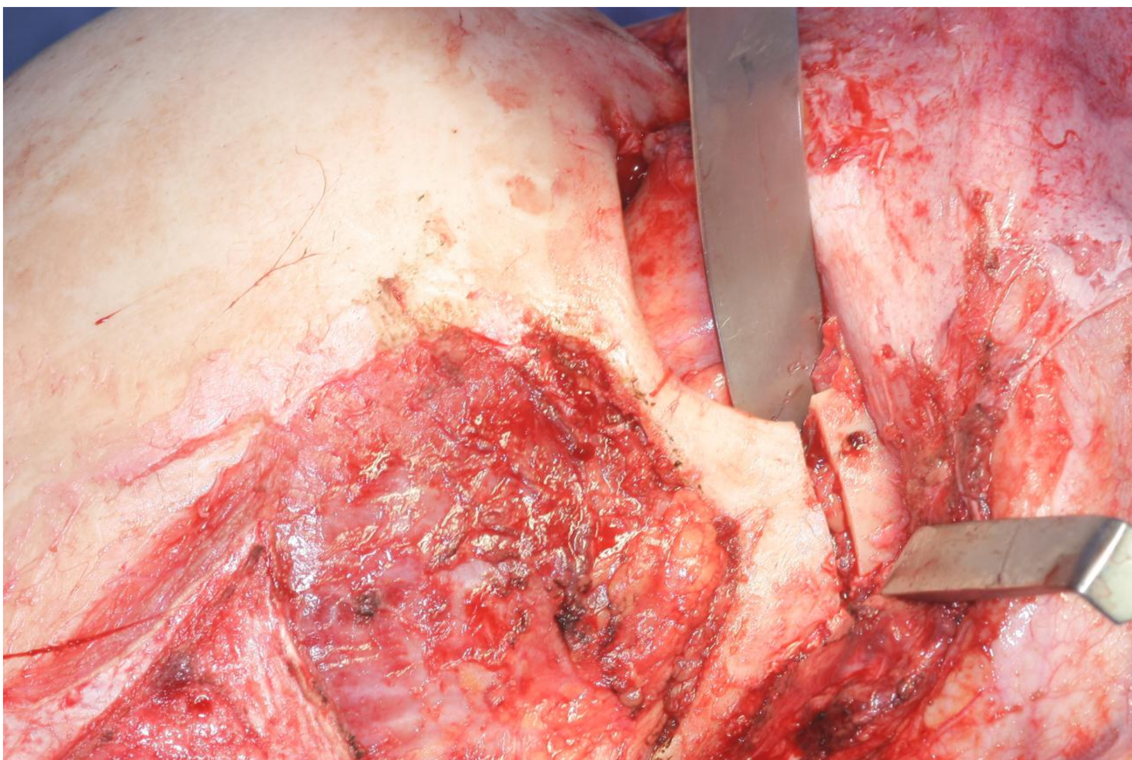

Figure 1.

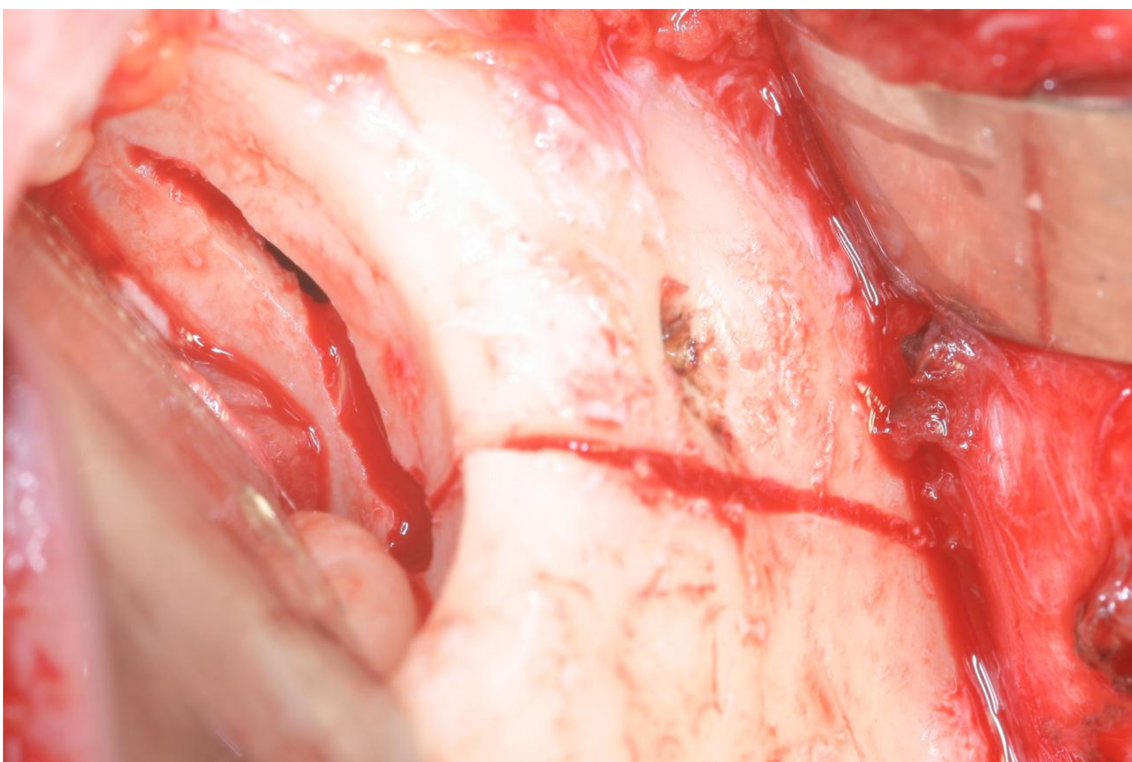

Figure 2.

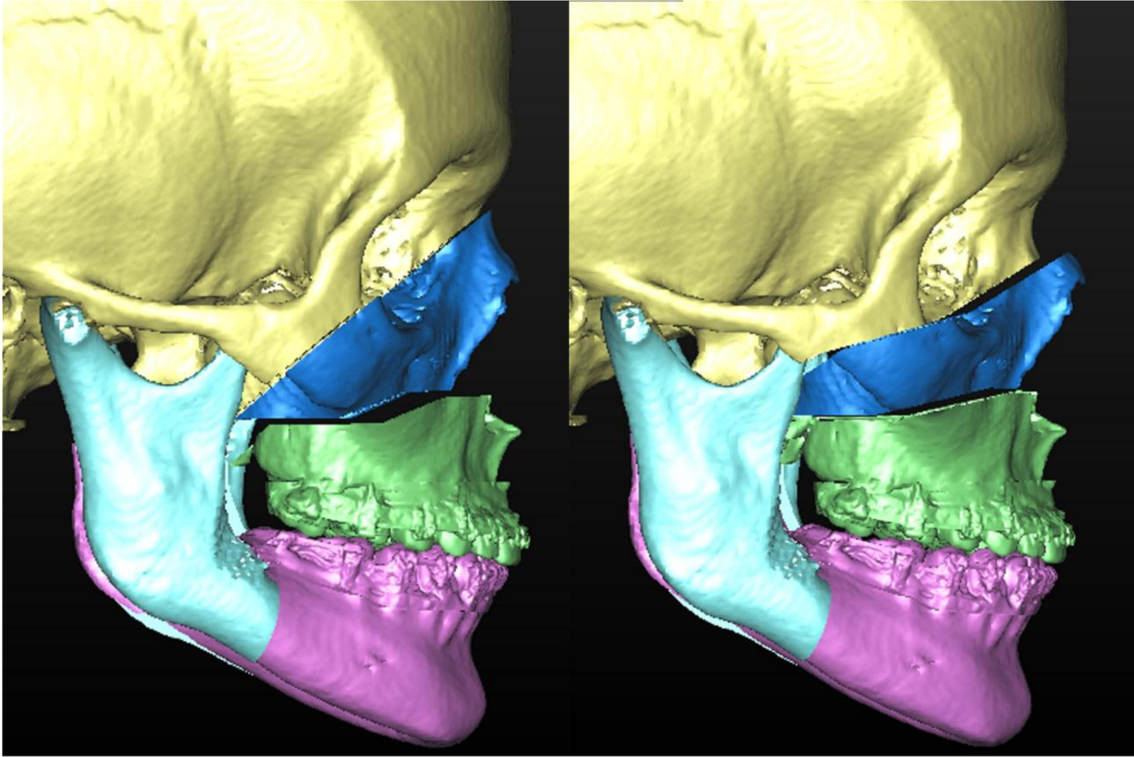

Figure 3.

Figure 4.

LEGENDS

Figure 1. The osteotomy of the zygoma finishes inside orbit, bellow the lateral tendon. The left osteotomy should be parallel to the right one.

Figure 2. Osteotomy of the orbital floor through the coronal incision. It should be done 3 mm posterior to the orbital rim to avoid unwanted fractures of the thin orbital floor.

Figure 3. Design of the LF III osteotomy in software. Note that osteotomies should be parallell and as the most horizontal as possible to allow an advance without the need of bone grafts. Gaps are smaller at the right simulation

Figure 4. Pre and postoperative long term profile view of a patient submitted to LF III, LF I and Sagittal osteotomies.

5 PUBLICAÇÃO 2

RESEARCH PAPER

TITLE PAGE

THREE-DIMENSIONAL AIRWAY CHANGES AFTER SUBCRANIAL LE FORT III OSTEOTOMY COMBINED WITH LE FORT I OSTEOTOMY.*

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Key Words: Orthognathic Surgery, Maxillary Osteotomy, Hypoplasia, Airway Obstruction, Tomography, Three-dimensional Image.

ABSTRACT

The purpose of this report was to describe changes of airway volume in non-syndromic patients after simultaneous subcranial Le Fort III and Le Fort I osteotomy for midface advancement associated with bilateral sagittal split osteotomy. Eleven consecutive patients were studied comparing the airway volume, area and minimum cross-sectional area by using Dolphin Software, before, immediately after and 18 months after surgery. The airway space was divided in nasopharynx, oropharynx and hypopharynx. There was an increase in the three variables analyzed, but statistical differences were observed only in the increase of the minimal cross-sectional area after surgery. There were no differences between male and female patients. In conclusion, the posterior airway space must be carefully examined before midface advancement. Although mandible setback should be avoided because it has a negative effect on the airway, the midface advancement compensates this narrowing by maintaining or increasing the airway volume. Linear midface and maxillary advancement will have positive effects on the airway volume and patency.

INTRODUCTION

The upper airway space has 3 major functions: ventilation, swallowing, and speech. During ventilation, the upper airway must remain patent, but during swallowing or speech, it must be narrow or close. Integration of these functions in 1 single anatomic region is critical. In addition, the nose and the mouth are sources of large volumes of secretions that must be cleared through the pharynx (the lower airway space). Consequently, the patency of the pharynx is vital for respiratory function[1].

Treatment of dentoskeletal deformities with jaw osteotomies has an effect on the morphology of the pharynx. Several bone structures and soft tissues such as the soft palate, uvula, palatoglossal arch, the base of tongue and all the suprahyoid muscles, hyoid bone and epiglottis may be directly or indirectly moved using this technique. Anatomically, these structures are closely related to the superior posterior airway space and their movements lead to alterations in this region[2].

Midface hypoplasia is a naso-maxillary-zigomatic hypodevelopment with depressed nasolabial area, obtuse nasolabial angle and poor projection of the malar and infraorbital region[2-7]. This midface hypoplasia may give rise to obstructive sleep apnea, ocular proptosis, and class III malocclusion including a transverse maxillary hypoplasia and aesthetic facial disharmony[2-4].

Consequently, maxillomandibular advancement has been used successfully in the treatment of obstructive sleep apnea (OSA) with an increase of the pharyngeal airway space (PAS). Moreover, mandibular setback has been associated with a decrease in the PAS postoperatively and in some cases a potential for the development of OSA[8-15].

Non-syndromic patients with class III occlusion had the airway studied using lateral cephalograms [8-11]. With the purpose of investigate airway volume following surgery more precisely, segmentation of the airway using computed tomographic data can be performed, and three-dimensional airway volumes can be obtained using proper threshold values in commercially available software[16].

From the literature, the number of studies reporting the airway modifications in a group of patients who underwent Le Fort III (LF III) osteotomy or its modifications in correcting non-syndromic midface hypoplasia is small[1,2,17]. This report describes changes of airway volume in non-syndromic patients after simultaneous subcranial LF III and Le Fort I (LF I) osteotomy associated with bilateral sagittal split osteotomy by analyzing preoperative and postoperative computed tomography scans with an airway volume segmentation technique.

MATERIALS AND METHODS

Surgical Technique

A standardized coronal flap is raised from the vertex region. The dissection goes under the periosteum to expose the supraorbital rims, nasal bones, lateral orbital rims and zygomatic arch and zygoma body. On the lateral orbital rims, the tissue reflection is extended as far down and medially as possible along the infraorbital rim, until the orbital floor is completely visible. On the medial orbital rims, only the anterior limb of the medial canthus is detached, exposing the lacrimal sac, which is reflected to expose the lacrimal groove, dissecting along the infraorbital rim as laterally as possible. It is possible to communicate the periosteal tunnels created by this dissection. Once all the tissues are dissected from the midfacial skeleton, an external reference point is measured to correct the vertical dimension of the face during surgery.

An oblique cut is done from a point as far as down and posterior as possible at the zygoma body to the lateral orbital rim, bellow the lateral orbital tendon attachment. The orbital floor is approached through the coronal approach. Orbital floor is the separated from the skull using a piezoelectric device. The third osteotomy was to separate the nasal bones from the skull. Care must be taken to cut the nose bellow the cribriform plate. The next osteotomy aims to separate the medial orbital wall. This osteotomy begins at the end of the nasal bone osteotomy and continues in an inferior direction

behind the lacrimal apparatus and medial tendon of the orbit until it reaches the orbital floor osteotomy. Pterigomaxillary disjunction was performed using curved chisels followed by an osteotomy from the end of the zygoma body osteotomy until the pterygoid plates. The separation of the nasal septum from the skull base is done with a septal osteotome.

With adequate mobilization, a surgical occlusal splint with the predetermined middle third advanced position planned is placed, and temporary intermaxillary fixation (IMF) is done. There must be very good contact at the zygoma bodies and nasal osteotomies. Two plates are placed bilaterally in the zygomatic bones and one plate in “Y” design achieves stabilization of the nasal bones.

A conventional Le Fort I osteotomy follows the Le Fort III osteotomy. The Le Fort I can be advanced and is used to correct oclusal plane alterations. After applying fixation at the maxilla, mandible sagittal splits osteotomies are performed to obtain final occlusion and fixed using the hybrid technique.

Data Acquisition

The study protocol obtained local ethics review board approval under the number 56390815.5.0000.5416. The present study was designed as a retrospective study. Multi-slice computed tomography (CT) scans were obtained from 11 consecutive patients who underwent subcranial Le Fort III osteotomy,

Le Fort I osteotomy and Sagittal Split osteotomy to correct a severe class III malocclusion associated with a naso-maxillary-zygomatic deficiency. Inclusion criteria were the following: age between 18 and 30 years; angle Class III molar relationship with a minimum negative overjet of 10mm; presence of midface hypoplasia; normal body mass index (BMI). Syndromic individuals or prior surgery in the head and neck were excluded from the evaluation.

The multi-slice scans were obtained in three different times: one week prior to surgery (T0). This scan was used to virtually plan the surgery and create intermediate splints. Immediately after surgery an immediate postoperative scan was performed (T1) and after 18 months (T2) a second postoperative scan was performed.

Multi-slice scans were made using a standardized scanning protocol, with a slice increment of 0.625 mm, in a field of 17 mm, at 120 Kv and 160.60 mA (GE Healthcare Optima CT660 128-slice). All patients were asked to occlude teeth and rest the tong in a relaxed position, breathe lightly and avoid motor reaction. All scans were performed with the patients in supine position, with a headgear to hold the head. The DICOM (Digital Imaging and Communications in Medicine) data were processed using commercially available third-party software (Dolphin Imaging1, version 11.0, Chatsworth, California, United States).

Prior to stability evaluation, all 33 databases were assessed in order to determine the most appropriate threshold value for upper airway analysis in this

study. The automatically fixed threshold value was manually increased for each dataset until the nasopharyngeal airway was adequately depicted. The average threshold value of all the patients thus defined was 70 (range 48–81) and was established as the reference threshold for this study (Fig. 1).

Patient's skull were reoriented to the Frankfort horizontal (FH) using the following guidelines:

(1) frontal view, the mid-sagittal plane was fixed through the center of the midsagittal maxillary suture and the axial plane was constructed through both infraorbitale skeletal landmarks;

(2) right sagittal view, the axial plane was placed through the right porion and right infraorbitale landmarks;

(3) transversal view (patient facing down or endocranial view), the mid-sagittal plane was constructed through crista galli and basion. In the opposite transversal view (patient facing up or exocranial view), it was ensured that no 'yaw' of the mandible or the zygomatic arches was present (Fig. 2). A similar methodology for airway study was published elsewhere[16].

In the sagittal view, the cranial base angle and cranio-cervical inclination were also measured. The cranial base angle of the analysed population sample was used for descriptive purposes; the cranio-cervical inclination was evaluated in order to test the homogeneity of head inclination during scanning, and hence the effectiveness of our head positioning protocol. The cranial base angle was measured between the points nasion, sella and basion, as described by Enlow (Fig. 3). The cranio-cervical inclination (Fig. 4) was measured as the angle

between the line formed by connecting C2od (tangent point at the most superior–posterior point of the odontoid process of C2) and C2ip (the most inferior–posterior point of the body of C2) and the SN line (sella–nasion).

The anatomical and technical limits of the upper airway were divided in nasopharynx, oropharynx and hypopharynx. Each division of the pharynx was limited in anterior, posterior, upper, lower, lateral limits. Technical limits were also used to limit each division and were described below.

The nasopharynx limits were: 1) Anterior: Anatomical - Frontal plane perpendicular to FH passing through PNS. 2) Posterior: Anatomical - Soft tissue contour of the pharyngeal wall. Technical - Frontal plane perpendicular to FH passing through C2sp. 3) Upper: Anatomical - Soft tissue contour of the pharyngeal wall. Technical - Transversal plane parallel to FH passing through the root of the clivus. 4) Lower: Anatomical - Plane parallel to FH passing through PNS and extended to the posterior wall of the pharynx. 5) Lateral: Anatomical - Soft tissue contour of the pharyngeal lateral walls. Technical - Sagittal plane perpendicular to FH passing through the lateral walls of the maxillary sinus.

The oropharynx limits were: 1) Anterior: Anatomical - Frontal plane perpendicular to FH passing through PNS. 2) Posterior: Anatomical - Soft tissue contour of the pharyngeal wall. Technical - Frontal plane perpendicular to FH passing through C2sp. 3) Upper: Anatomical - Plane parallel to FH passing through PNS and extended to the posterior wall of the pharynx. 4) Lower:

Anatomical - Plane parallel to FH plane passing through C3ai. 5) Lateral: Anatomical - Soft tissue contour of the pharyngeal lateral walls. Technical - Sagittal plane perpendicular to FH passing through the lateral walls of the maxillary sinus.

The hypopharynx limits were: 1) Anterior: Anatomical - Frontal plane perpendicular to FH passing through PNS. 2) Posterior: Anatomical - Soft tissue contour of the pharyngeal wall. Technical - Frontal plane perpendicular to FH passing through C2sp. 3) Upper: Anatomical - Plane parallel to FH plane passing through C3ai. 4) Lower: Anatomical - Plane parallel to FH connecting the base of the epiglottis to the entrance to the esophagus. Technical - Plane parallel to FH connecting the base of the epiglottis to C4ai. 5) Lateral: Anatomical - Soft tissue contour of the pharyngeal lateral walls. Technical - Sagittal plane perpendicular to FH passing through the lateral walls of the maxillary sinus.

The airway area, airway volume and minimum axial area of each division of the pharynx were studied in three different times (T0, T1, T2). (Fig. 5).The statistical analysis was performed using Biostat for Windows, version 5.0 (Marimauá institute, Brazil). A descriptive analysis was used to obtain preliminary normative data for the sample as a whole and also when stratified by gender. After corroborating the normal distribution of the sample with the D'agostino's test, a Student's t-test for independent samples was used to compare the sex groups. Repeated measures analysis of variance (ANOVA) was used to compare the three subregions of the upper airway in three different

times (T0, T1 and T2). Tukey's test was used to stratify this analysis. Statistical significance was fixed at a = 0.05.

RESULTS

Table 1 shows the descriptive variables for the whole sample and for males and females separately. When analyzing sexual dimorphism with the Student's t-test for independent samples, there were no significant differences between males and females in any of the three regions of the pharynx. In addition, the minimum cross-sectional area for the oropharynx was significantly greater in males than in females (P = 0.011)

Considering no differences between groups, the sample was analyzed as a hole, as shown in table 2. Significant differences were observed at the minimum cross-sectional area between T1 and T0 at the nasopharynx and between T2 and T1 at the oropharynx. There were no differences between the final volume of the pharynx, in the three regions studied, between T2, T1 and T0.

Figure 6 shows the mean differences between T1 minus T0 and between T2 minus T0. The volume of oropharynx had the greatest variation, although not statistically significant. A slightly increase of the hypopharynx volume was also observed, and it was not statistically significant.

DISCUSSION

This study used the method validated by Guijarro-Martínez & Swennen[16], which is simple and very useful. Differences were on the data acquisition. Those authors described the data acquisition using cone-beam tomography, while our study obtained from multi-slice tomography in a supine position. Although many studies try to correlate the upper airway and its physiologic functions with the head is its natural position, the most problems of obstructive sleep apnea occurs when patients are sleeping in supine position. Furthermore, polysomnography is also performed during supine position. Therefore, simulating supine position to get images should give more realist results than getting images from “seated” patients.

Xu et al[17] studied the therapeutic effects of LF III osteotomy and midfacial distraction osteogenesis in upper airway stenosis in 11 patients. The authors reported a 64.3% mean increase in upper airway volume and concluded that the LF III osteotomy and midfacial distraction osteogenesis can efficiently relieve the symptoms of upper-airway stenosis in severe midfacial dysostosis.

Nout et al[2] investigated the changes of upper airway volume in 19 syndromic craniosynostosis patients following LF III advancement using CT scans. The authors reported a significant improvement of the upper airway after LF III advancement in syndromic craniosynostosis.

Iannetti et al[1] reported the volumetric measurements of the airway space after LF III advancement using computed tomographic (CT) scans. The authors reported that the airway space volume was significantly increased after surgery and concluded that LF III advancement increases the upper airway space.

Maxillary advancements usually show changes at the level of the oropharynx and nasopharynx. Greco et al[10] evaluated patients with Class III deformity who underwent maxillary advancement surgery and concluded that there was an increase in the PAS in the region of the nasopharynx and hypopharynx, and that the increase was stable in long-term evaluations. Pereira-Filho et al[18] reported similar results, also emphasizing the stability of the airway in long-term evaluations. Samman also reported similar results in patients submitted to maxillary advancement[19].

Patients treated with bimaxillary surgery usually show changes of the airway space at all 3 levels of the pharynx. In their cephalometric study of the changes of the airway space in Class III patients, Pereira-Filho et al[18] concluded that patients who underwent bimaxillary surgery, upper jaw advancement compensated for changes of the PAS brought about by the mandibular setback. Mehra et al[20] evaluated 20 patients undergoing bimaxillary surgery and counterclockwise rotation of the oclusal plane and found a decrease in the oropharynx and hypopharynx. In 35 patients undergoing bimaxillary surgery, Cakarne et al[21] observed an increase occurred in the nasopharynx, without changes in the regions of the oropharynx and hypopharynx.

The results of our study are in accordance with those reported by Pereira-Filho et al[18]. Other studies reported divergent results, with an increase of the upper airway after bimaxillary advancement[2,8,9,10]. The jaws, tongue base, hyoid bone, and pharyngeal walls are intimately connected by muscles and tendons. The tongue with its muscles and ligaments is related to the hyoid bone and mandible. When the mandible is posteriorly repositioned, the tongue assumes a more posterior position, narrowing the PAS[10,11,14,18,22,23]. Such variations may arise from the quantity and variation of surgical repositioning performed in different studies and from individual variation in the initial size of the PAS.

In conclusion, the posterior airway space must be carefully examined before midface advancement. Although mandible setback should be avoided because it has a negative effect on the airway, the midface advancement compensates this narrowing by maintaining or increasing the airway volume. Linear midface and maxillary advancement will have positive effects on the airway volume and patency.

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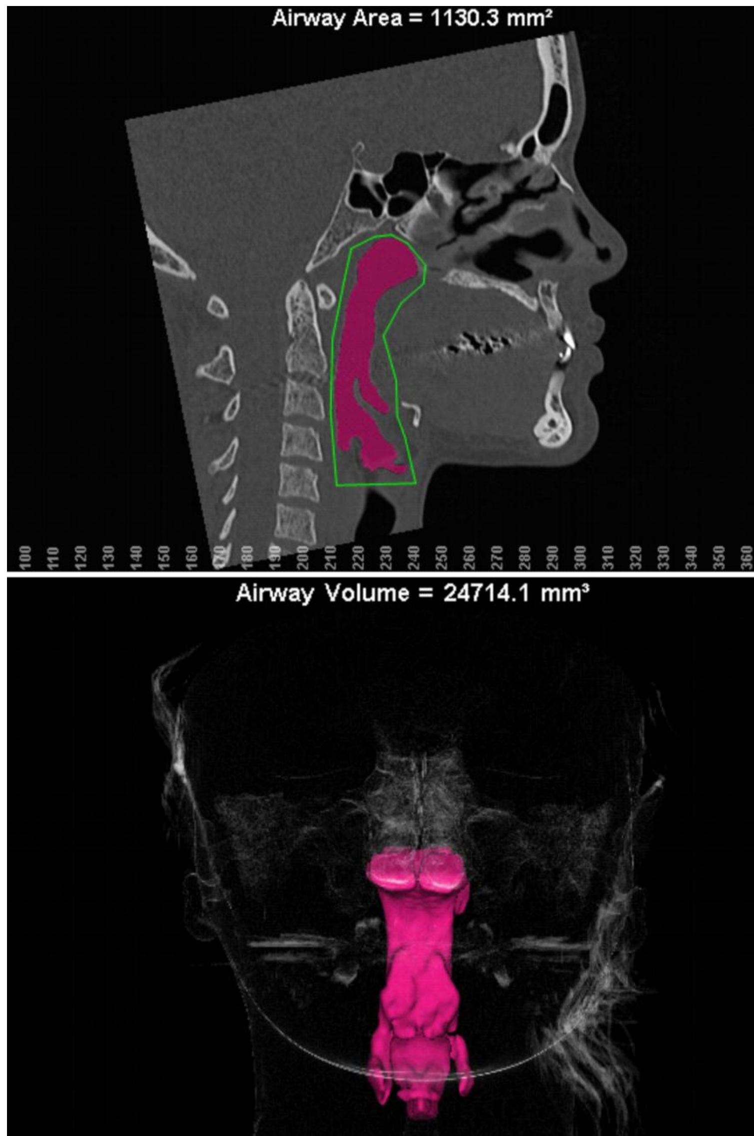
FIGURES



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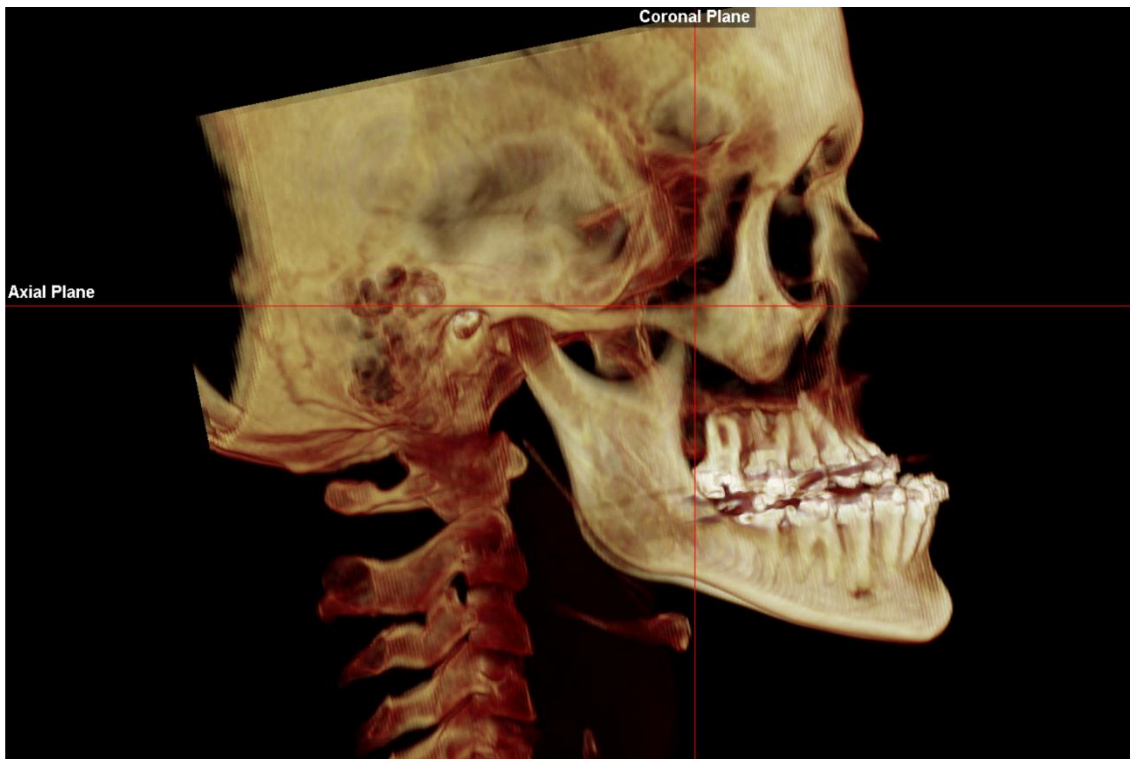

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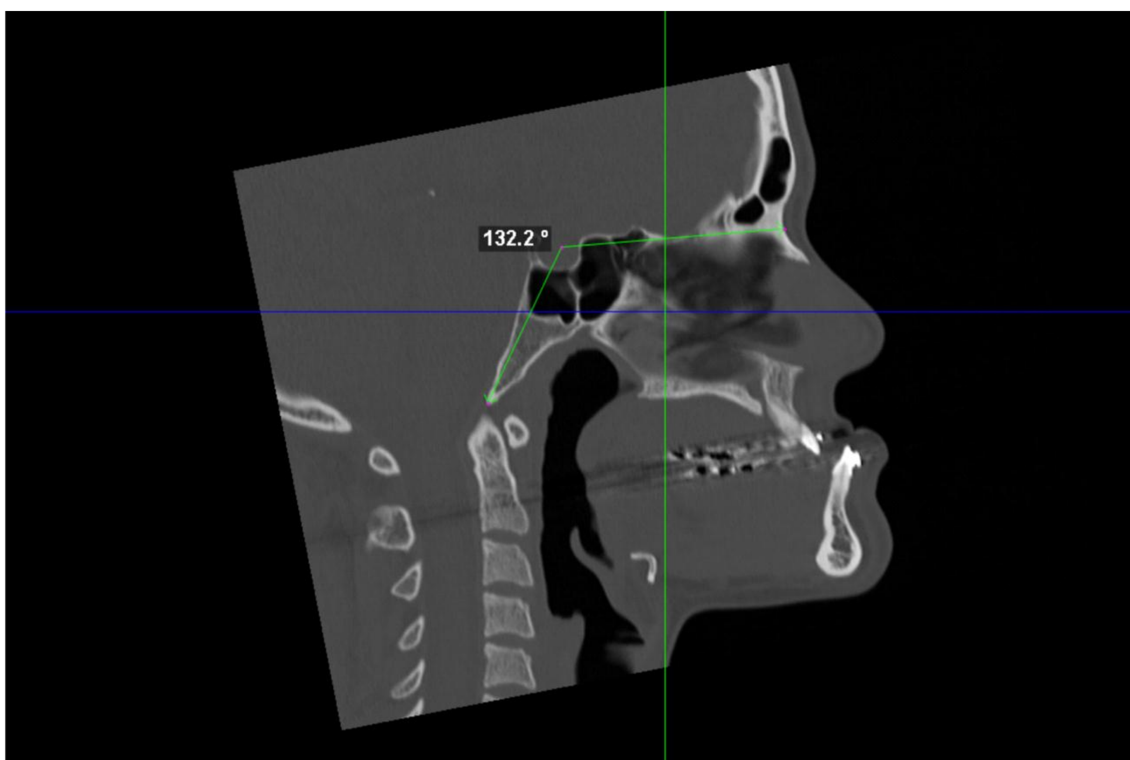

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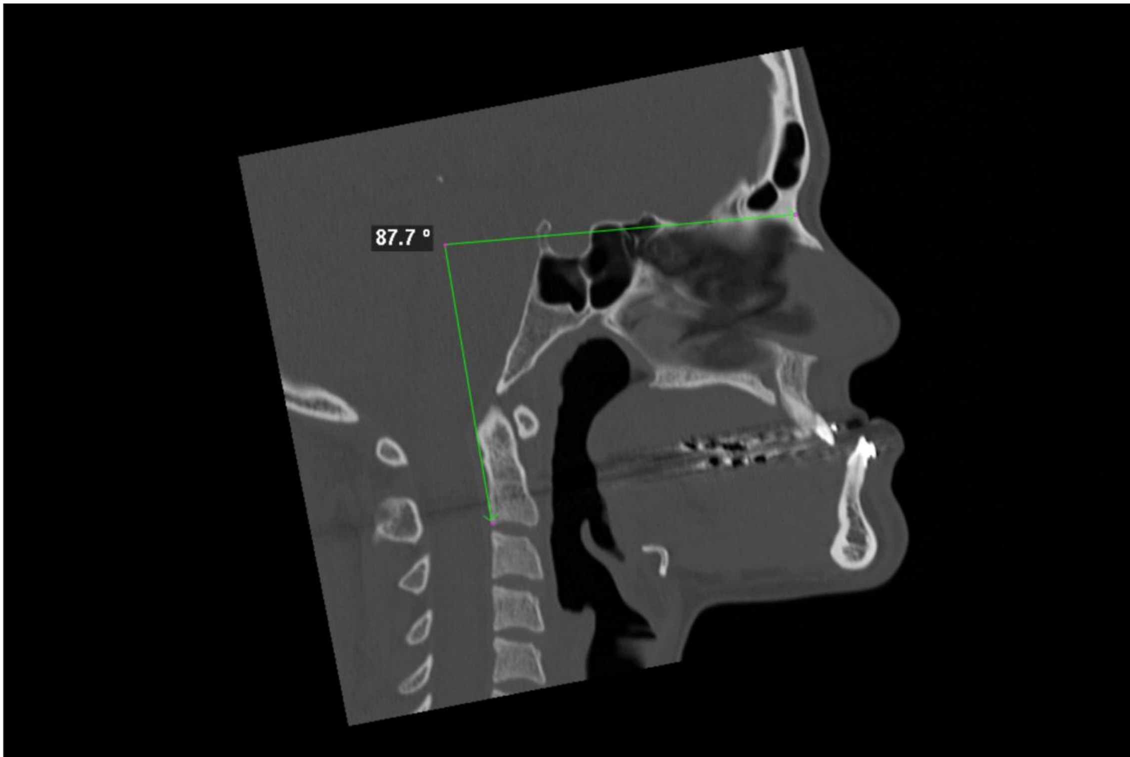

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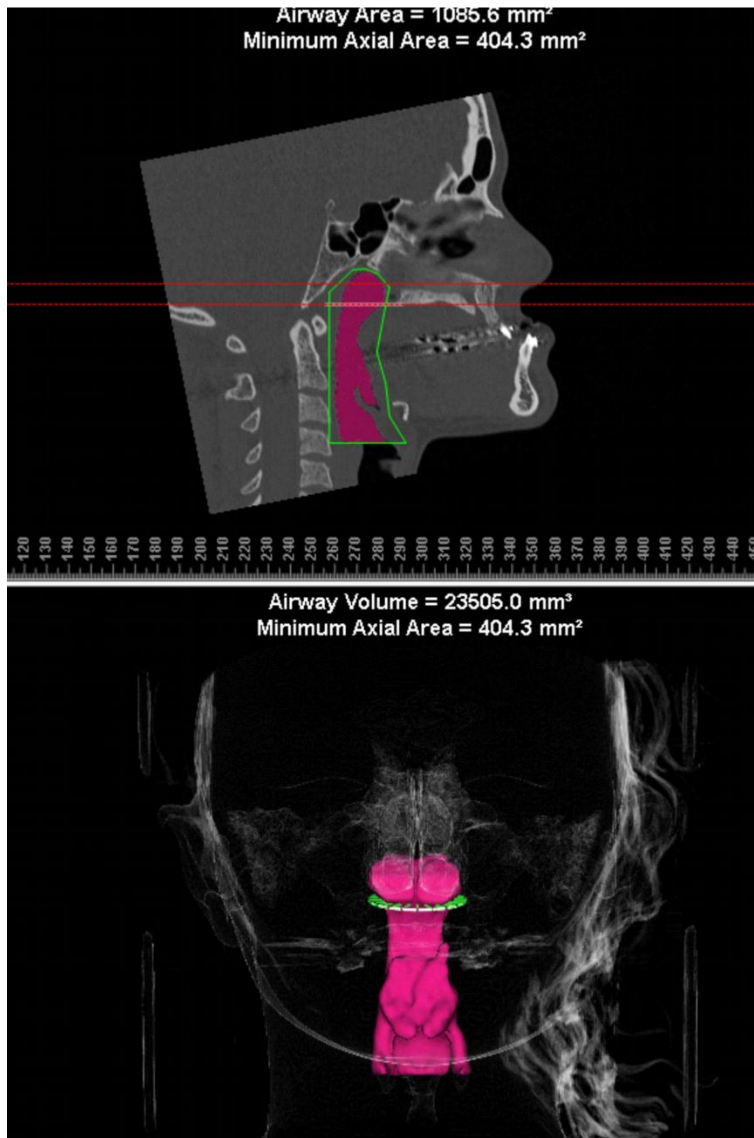

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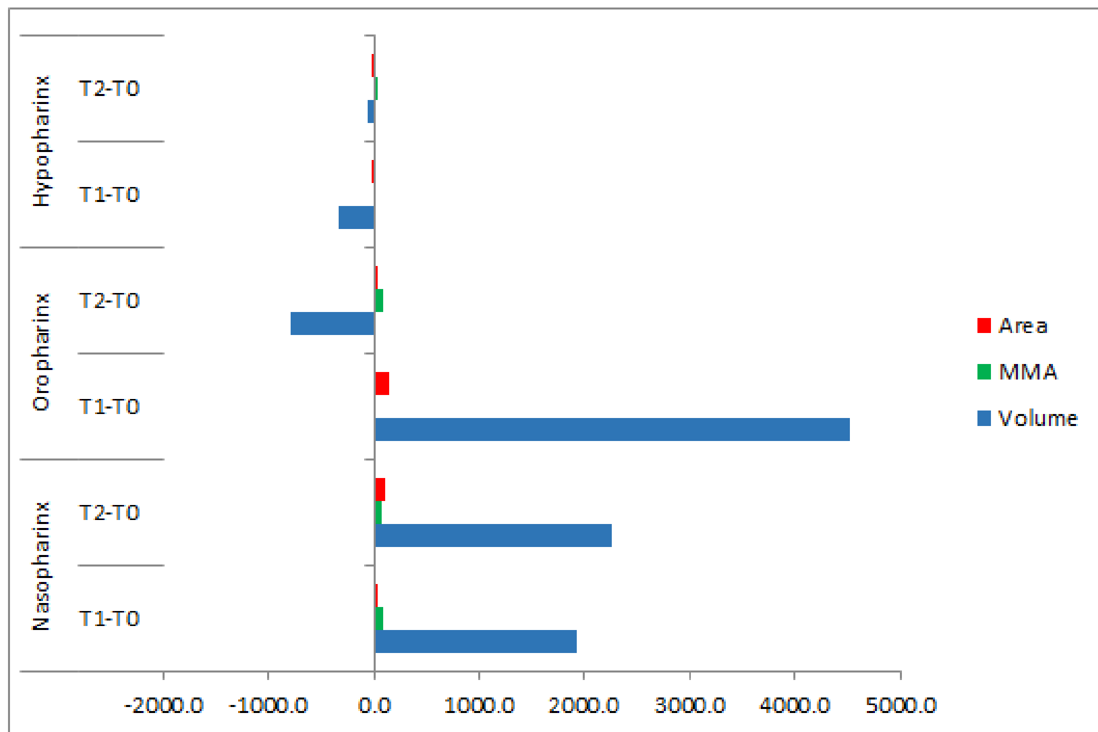

Figure 6.

LEGENDS

Figure 1. Delimitation of the airway space after in sagittal and 3D images.

Figure 2. Profile 3D scan after head orientation. Note the Frankfurt horizontal plane crossing the skull.

Figure 3. Cranial base angle.

Figure 4. Cranio-cervical inclination.

Figure 5. Method used to obtain data from Dolphin.

Figure 6. Mean differences between T1 minus T0 and between T2 minus T0.

Table 01. Descriptive and sexual dimorphism analysis.

		T0					T1					T2				
		Male (n=6)		Female (n=5)			Male (n=6)		Female (n=5)			Male (n=6)		Female (n=5)		
		Mean	SD	Mean	SD	P-value	Mean	SD	Mean	SD	P-value	Mean	SD	Mean	SD	P-value
Nasopharynx	Volume (mm^3)	5342.83	2325.98	5825.25	454.88	0.7971	7718.13	4250.68	6855.20	4.38	0.7119	8085.72	2193.71	7095.30	2234.03	0.6312
	Miminum Cross Sectional area (mm^2)	106.08	10.75	129.60	22.20	0.1339	195.15	70.97	208.85	25.67	0.8135	157.35	84.37	218.40	56.99	0.4195
	Total area (mm^2)	199.90	79.26	212.50	11.88	0.8431	242.78	143.24	226.55	5.02	0.8873	316.07	91.18	290.30	87.26	0.7580
Oropharynx	Volume (mm^3)	16821.55	12990.77	15347.75	1389.54	0.8873	21367.15	10699.71	19837.55	5258.26	0.8634	16255.29	7834.53	14106.60	1683.62	0.7350
	Miminum Cross Sectional area (mm^2)	62.05	47.20	95.85	31.89	0.4239	91.88	78.07	75.05	9.26	0.7886	163.39	31.68	143.80	16.97	0.4747
	Total area (mm^2)	637.70	212.90	678.80	38.75	0.8106	769.40	193.38	830.05	43.63	0.6996	686.31	59.39	677.40	82.59	0.8837
Hypopharynx	Volume (mm^3)	5633.88	3474.99	5908.75	259.15	0.9212	5304.00	2085.09	5579.80	106.91	0.8686	6447.07	1550.93	4123.90	1234.18	0.1437
	Miminum Cross Sectional area (mm^2)	92.00	20.88	78.15	13.08	0.4523	92.10	31.76	93.80	24.47	0.9511	136.20	57.76	116.10	60.25	0.7113
	Total area (mm^2)	240.98	132.72	253.60	11.88	0.9053	228.33	73.61	262.35	26.23	0.5786	246.51	61.74	217.50	42.99	0.5924
CBA		129.35	7.59	131.05	1.63	0.7818	128.68	10.51	135.95	1.20	0.4092	141.85	8.36	145.25	13.65	0.7132
CCI		87.60	11.37	87.65	0.07	0.9935	90.70	5.99	97.80	22.49	0.5441	80.56	4.65	92.20	10.47	0.1110

CBA, Cranial base angle; CCI, Cranio-cervical inclination; n, sample size; SD, standard deviation; Independent Student T-test for comparisons in the sample;
[a] Volumes are expressed in mm^3 and areas in mm^2.

Table 02. Comparison between the three anatomical subregions.[a]

	n		T0		T1		T2		
			Mean	SD	Mean	SD	Mean	SD	P-value
Nasopharynx	11	Volume (mm^3)	5503.63	1830.18	7430.48	3322.58	7755.58	2036.47	0.2677
	11	Miminum Cross Sectional area (mm^2)	113.92	17.76	199.72	56.61	177.70	76.90	< 0.05 (t)
	11	Total area (mm^2)	204.10	61.97	237.37	111.29	307.48	81.78	0.1454
Oropharynx	11	Volume (mm^3)	16330.28	10110.46	20857.28	8651.25	15539.06	6214.98	0.522
	11	Miminum Cross Sectional area (mm^2)	73.32	42.95	86.27	61.23	156.86	27.61	< 0.05 (t)
	11	Total area (mm^2)	651.40	167.17	789.62	154.27	683.34	59.17	0.214
Hypopharynx	11	Volume (mm^3)	5725.50	2697.94	5395.93	1622.07	5672.68	1785.24	0.9582
	11	Miminum Cross Sectional area (mm^2)	87.38	18.63	92.67	26.94	129.50	53.25	0.1211
	11	Total area (mm^2)	245.18	103.15	239.67	60.81	236.84	53.68	0.9823
CBA	11		129.92	5.99	131.10	8.98	142.98	9.07	< 0.05 (t)
CCI	11		87.62	8.81	93.07	11.67	84.44	8.43	0.3275

CBA, Cranial base angle; CCI, Cranio-cervical inclination; n, sample size; SD, standard deviation; t, tukey test for ANOVA for comparisons in total sample;
[a] Volumes are expressed in mm^3 and areas in mm^2.

6 PUBLICAÇÃO 3

RESEARCH PAPER

TITLE PAGE

POST-TREATMENT STABILITY OF THE SUBCRANIAL LE FORT III OSTEOTOMY COMBINED WITH LE FORT I OSTEOTOMY: 3D ANALYSIS.

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Key Words: Orthognathic Surgery, Maxillary Osteotomy, Hypoplasia.

ABSTRACT

The purpose of this retrospective study was to evaluate the long-term stability of a series of non-syndromic patients who underwent subcranial Le Fort III (LF III) osteotomy in association with Le Fort I (LF I) osteotomy. Computed tomography scans were obtained from 11 consecutive patients who underwent subcranial LF III, LF I and sagittal split osteotomy to correct a severe class III malocclusion associated with a naso-maxillary-zygomatic deficiency. The scans were obtained in three different times: one week prior to surgery (T0); immediately after surgery (T1) and after 18 months (T2). The 3D images were constructed using Dolphin (group 01) and Mimics (group 02) and superimposed. The following points were measured for horizontal and vertical changes: the tip of the upper incisor (UI), the A-point, the posterior nasal spine (PNS), the right orbitale inferior (IO-R) and the left orbitale inferior (IO-L). This study supports that subcranial LF III midface advancement combined with Le Fort I as an effective surgical technique to correct malocclusion and midface hypoplasia with post-surgical stability. There was minimal anteroposterior and vertical changes in all of the landmarks of the midface. Both softwares showed similar results and proved to be an efficient clinical tool to study stability.

INTRODUCTION

The underdevelopment of the midface hypoplasia usually causes severe exorbitism, obstructive sleep apnea, distorted facial appearance and class III malocclusion[1]. The treatment of the severe hypo developed midface is a Le Fort III (LF III) osteotomy or an osteogenic distraction by means of a LF III osteotomy. The conventional LF III osteotomy constitutes a one-step technique in which the midfacial segment is osteotomized, advanced, and fixed in the desired position with bone grafts. The subcranial LF III osteotomy is a technique designed to advance the midface without the need of bone grafts[2] to improve stability, since there is great contact between segments, in opposite to the classic technique, where a higher osteotomy and grafts are need at the orbit and zygoma. A Le Fort I (LF I) osteotomy is performed at the same surgical time to obtain a larger advancement of the upper incisor and correct the occlusal plane.

There are many reports in the literature discussing the stability of LF III osteotomy[3-10]. The LF III advancement is stable, but there are differences in the techniques used, being recommended bone grafts and stable fixation in most of the studies. To the best of our knowledge, there was only one study discussing the stability of a subcranial LF III osteotomy, reporting that the degree of horizontal stability and the forward direction of postoperative skeletal changes are consistent with previously published results of Le Fort III osteotomies[11].

The LF III osteotomy was first indicated to treat syndromic patients, but this indication has been expanded to non-syndromic presenting with naso-maxillary-zygomatic hypo development and large class III overjet. Treating large class III non-syndromic patients by other methods than a LF III osteotomy in association with a LF I osteotomy may present several problems which are inherent in performing single segment midface surgery as patients will occasionally present with large anteroposterior dental discrepancies and request advancements of more than 10mm. The advancement of the midface is limited to 8 mm due to the soft tissue restrictions.

It is import to understand the stability of a given surgery, how much changes can be seen in such big advancements and how the results will change in time. LF III osteotomies, although widely accepted, are not widely performed. Therefore, long-term results are an important contribution to guide treatment and indicate such procedures.

The purpose of this study was to evaluate the long-term stability of a series of non-syndromic patients who underwent subcranial LF III osteotomy in association with LF I osteotomy for improvement of midface deficiency by means of superimposition of computed tomography images at the preoperative, immediate postoperative and 18 months after surgery.

MATERIAL AND METHODS

Surgical Technique

A standardized coronal flap is raised from the vertex region. The dissection goes under the periosteum to expose the supraorbital rims, nasal bones, lateral orbital rims and zygomatic arch and zygoma body. On the lateral orbital rims, the tissue reflection is extended as far down and medially as possible along the infraorbital rim, until the orbital floor is completely visible. On the medial orbital rims, only the anterior limb of the medial canthus is detached, exposing the lacrimal sac, which is reflected to expose the lacrimal groove, dissecting along the infraorbital rim as laterally as possible. It is possible to communicate the periosteal tunnels created by this dissection. Once all the tissues are dissected from the midfacial skeleton, an external reference point is measured to correct the vertical dimension of the face during surgery. An oblique cut from a point as far as down and posterior as possible at the zygoma body to the lateral orbital rim, bellow the lateral orbital tendon attachment. The orbital floor is approached through the coronal approach. Orbital floor is the separated from the skull using a piezoelectric device. The third osteotomy was to separate the nasal bones from the skull. Care must be taken to cut the nose bellow the cribriform plate. The next osteotomy aims to separate the medial orbital wall. This osteotomy begins at the end of the nasal bone osteotomy and continues in an inferior direction behind the lacrimal apparatus and medial tendon of the orbit until it reaches the orbital floor osteotomy. Pterigomaxillary

disjunction was performed using curved chisels followed by an osteotomy from the end of the zygoma body osteotomy until the pterygoid plates. The separation of the nasal septum from the skull base is done with a septal osteotome. With adequate mobilization, a surgical occlusal splint with the predetermined middle third advanced position planned is placed, and temporary intermaxillary fixation (IMF) is done. There must be very good contact at the zygoma bodies and nasal osteotomies. Two plates are placed bilaterally in the zygomatic bones and one plate in “Y” design achieves stabilization of the nasal bones. A conventional Le Fort I osteotomy follows the Le Fort III osteotomy. The Le Fort I can be advanced and is used to correct oclusal plane alterations. After applying fixation at the maxilla, mandible sagittal splits osteotomies are performed to obtain final occlusion and fixed using the hybrid technique.

Data Acquisition

The study protocol obtained local ethics review board approval under the number 56390815.5.0000.5416. The present study was designed as a retrospective study. Multi-slice computed tomography (CT) scans were obtained from 11 consecutive patients who underwent subcranial LF III osteotomy, LF I osteotomy and sagittal split osteotomy to correct a severe class III malocclusion associated with a naso-maxillary-zygomatic deficiency. (Figure 1) Exclusion criteria were patients supporting facial clefts or growing patients. The multi-slice scans were obtained in three different times: one week prior to surgery (T0) - this scan was used to virtually plan the surgery and create intermediate splints;

immediately after surgery an immediate postoperative scan was performed (T1) and after 18 months a second postoperative scan was performed (T2).

Multi-slice scans were made using a standardized scanning protocol, with a slice increment of 0.625 mm, in a field of 17 mm, at 120 Kv and 160.60 mA (GE Healthcare Optima CT660 128-slice). All patients were asked to occlude teeth and rest the tong in a relaxed position, breathe lightly and avoid motor reaction. All scans were performed with the patients in supine position, with a headgear to hold the head. The DICOM (Digital Imaging and Communications in Medicine) data were processed using two different commercially available third-party software (Dolphin Imaging1, version 11.0, Chatsworth, California, United States and Mimics, version 16.0, Materialise, Leuven, Belgium).

Prior to stability evaluation, all 33 databases were assessed and the patient's skull were reoriented to the Frankfort horizontal (FH) using the following guidelines: (1) frontal view, the mid-sagittal plane was fixed through the center of the midsagittal maxillary suture and the axial plane was constructed through both infraorbitale skeletal landmarks; (2) right sagittal view, the axial plane was placed through the right porion and right infraorbitale landmarks; (3) transversal view (patient facing down or endocranial view), the mid-sagittal plane was constructed through crista galli and basion. In the opposite transversal view (patient facing up or exocranial view), it was ensured that no 'yaw' of the mandible or the zygomatic arches was present. A similar methodology for airway study was published elsewhere[12].

The 3D images were constructed using Dolphin (group 01) and Mimics (group 02) and superimposed using at least 03 points of superimposition: crista galli, the fronto-zygomatic sutures bilaterally and, if necessary, the cephalometric point zygion, at the zygomatic arch, the glabella point and the porion. None of these points had variation before and after surgery. Both softwares had the tools for registration and superimposition. The result of superimposition was verified by the correct overlay of the 3D skulls of the sphenoid bone at coronal slices (Fig. 2), and frontal bone at axial and sagittal images.

In the sagittal view, at midline, a plane parallel to FH, passing through the sella point was used as horizontal reference to measure linear vertical changes. A perpendicular plane to FH, passing through sella point was used as a vertical reference to measure horizontal changes. The following points were measured at the three different times (T0, T1 and T2) for horizontal and vertical changes: the tip of the upper incisor (UI), the A-point, the posterior nasal spine (PNS), the right inferior orbitale (IO-R) and the left inferior orbitale (IO-L). All the measures were made by a single examiner three times each with a minimum interval of 15 days between each one and used the mean values. Figure 3 show the superimposition using dolphin software and figure 4 shows the superimposition using Mimics software.

The results were expressed in differences between different times for each point. The statistical analysis was performed using Biostat for Windows,

version 5.0 (Marimauá Institute, Brazil). After corroborating the normal distribution of the sample with the D'agostino test, a paired Student's t-test was used to compare the intragroup changes between T1 and T2. Independent Student's t-test was used to compare the same measures between the two groups. Statistical significance was fixed at $\alpha = 0.05$.

RESULTS

Demographic and pretreatment characteristics of the sample are shown in Table 1. The sample consisted of 05 females and 06 males with a mean negative overjet of 13.5 mm with a mean age of 23 years. The intragroup analysis was performed to analyze differences between T1 and T2 subsequently the initial comparison between softwares.

Mean and standard deviations for changes in landmark positions and dimensions from immediate postoperative scan (T1) to 18 months after surgery (T2), comparing the two groups are shown in Figures 5 and 6. Mean and standard deviations for changes in landmark positions and dimensions from immediate postoperative scan (T1) to 18 months after surgery (T2) in the two groups are shown in Table 2.

No statistical differences were observed between Dolphin and Mimics for horizontal measures. All the patients had a horizontal backward movement

smaller than 02 mm at the A-point, PNS, IO-R and IO-L after 18 months of surgery. The upper incisor had a slightly forward movement (Fig. 5).

No statistical differences were observed between Dolphin and Mimics for vertical measures. A difference was noted on the direction of the changes between T1 and T2. Although visible in figure 6, these differences were smaller than 01 mm.

Statistically significant differences in horizontal landmark positions were noted only for PNS at Mimics groups, but the real mean difference in millimeters between T2 and T1 was 1.16 mm. The overall mean values for horizontal and vertical relapse were not statistically neither clinically significant.

DISCUSSION

Gillies[13] presented the follow-up of a patient who had the first reported LF III surgery and observed that the position of the incisor was stable after seven years. Freihofer[14] reported the first cephalometric results of nine patients after LF III osteotomies, two of them underwent simultaneous LF III and Le Fort I osteotomies. Osteotomized segments were stabilized with bone grafts and intermaxillary fixation. The two patients with simultaneous LF III / LF I osteotomies had 3mm and 4mm of vertical maxillary relapse at soft tissue

nasion. The maxilla was relatively stable in the horizontal plane with one patient experiencing 3mm of inferior relapse.

The skeletal and occlusal relapse with middle-third facial osteotomies was also discussed by Epker and Wolford[15]. Their cases were stabilized using wires and bone grafts and the occlusion was overcorrected in all cases. Additionally, intermaxillary fixation was employed.

Many other studies concluded that the standard LF III procedure provides a relatively stable postoperative position of the midface, making this technique reliable and applicable for treating patients with midface hypoplasia[1-11]. First described by Cheung et al[2], the sliding subcranial Le Fort III permits the maintenance of bone contact between the bone segments. These bone contact generate two great advantages on the technique. There is no need for bone graft in the midface advancement and the bone contact improves the stability of the LF III osteotomy, making relapse less plausible to occur.

Proffit, et al.[16] consider changes smaller than 2 mm within the range of method error and clinically insignificant; 2-4 mm outside the range of method error and potentially clinically significant; and >4 mm as often beyond the range of orthodontic compensation and clinically highly significant. The results presented in this study showed stability at a long follow-up, within less than 2.0 mm of variance after 18 months of treatment. Although the PNS Mimics groups showed a statistical difference, clinically, the mean difference is in the range of

method error and clinically insignificant. Also clinically insignificant are the vertical results, within a range of 1 mm or less in different directions.

One may ask why the LF III in association with the LF I is so stable for larger horizontal movements while the LF I osteotomy has proven not to show this stability. A sound hypothesis is that, after a high pterigomaxillary disjunction, midface advancement will move forward all muscles that insert at the maxilla and will secure the skin in an advanced position. Therefore, after LF III advancement, the muscles that will hold the maxilla in a backward position are not yet stretched. Consequently, the maxilla - LF I osteotomy - may be advanced more 6 to 8 millimeters, in addition to midface advancement, until the muscles and skin get stretched. The bone contact and the use of stable internal fixation will also improve stability.

During using the tools of linear measure of the two softwares, Dolphin showed a tendency to round the numbers within one decimal of millimeters, while Mimics tend to show two decimals of millimeters during measures. The two software used in this study showed very much closed results, with a range of mean difference smaller than 1 mm. An advantage of Mimics is that it produces a 3D color superimposition associating colors with changes in millimeters. This 3D color map was created for all superimpositions and the result is seen on Figure 7, showing the significant stability of LF III advancement in association with Le Fort I osteotomy.

This study supports that subcranial LF III midface advancement combined with LF I is an effective surgical technique to correct malocclusion and midface hypoplasia with post-surgical stability. There was minimal anteroposterior and vertical changes in all of the landmarks of the midface. Both softwares showed similar results and proved to be an efficient clinical tool to study stability.

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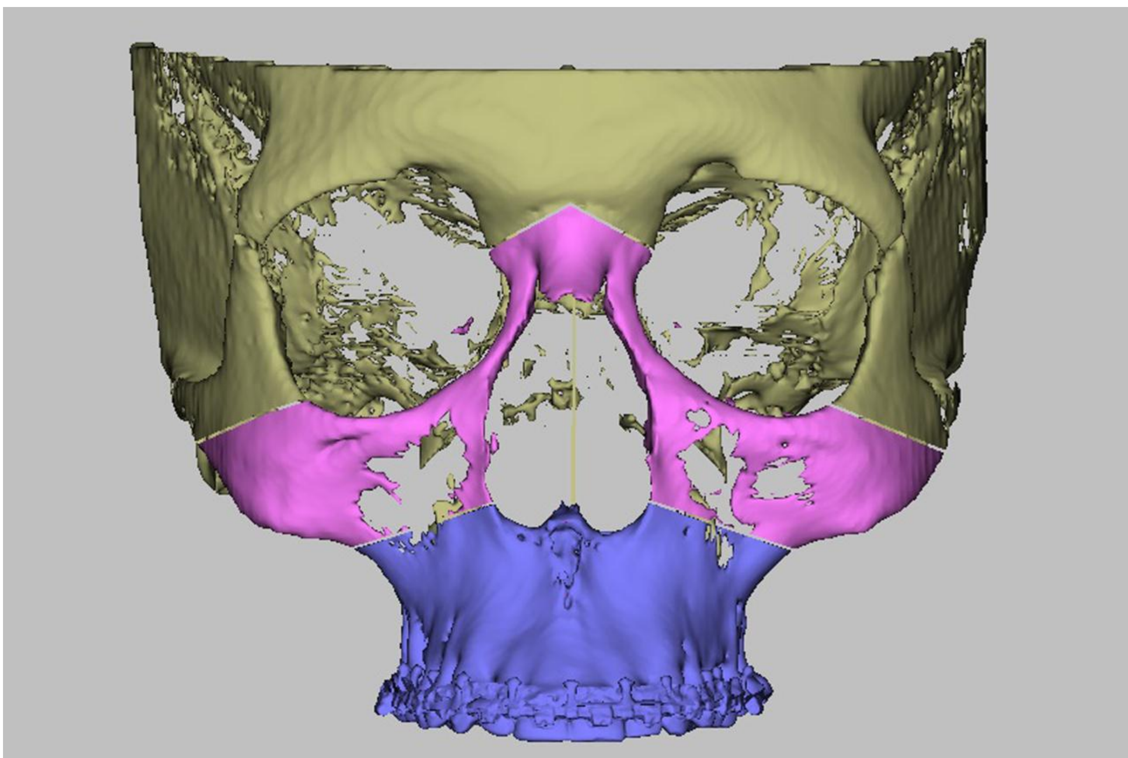
FIGURES



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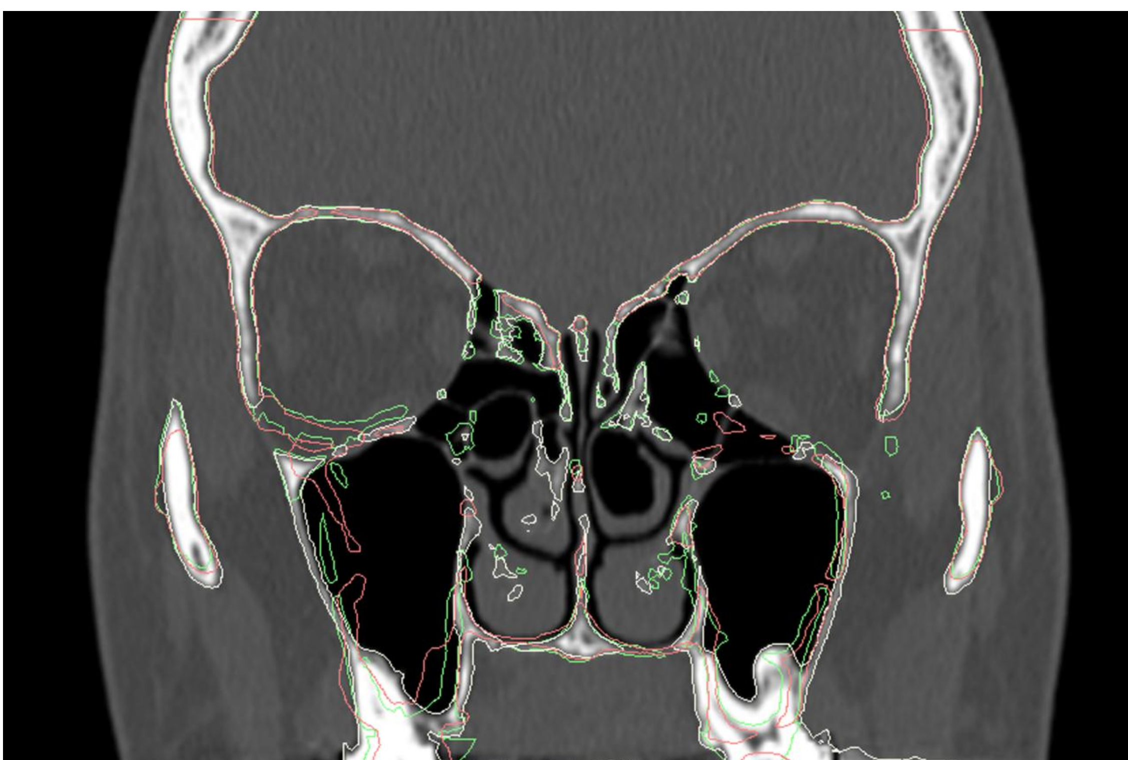

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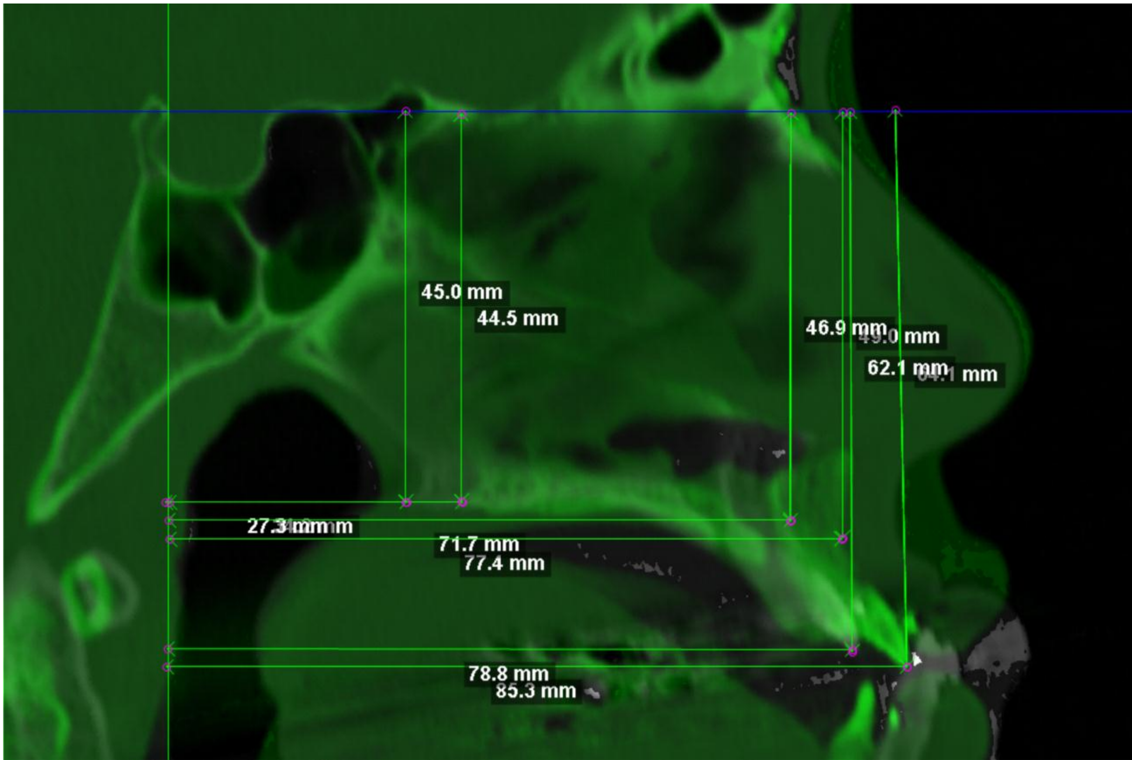

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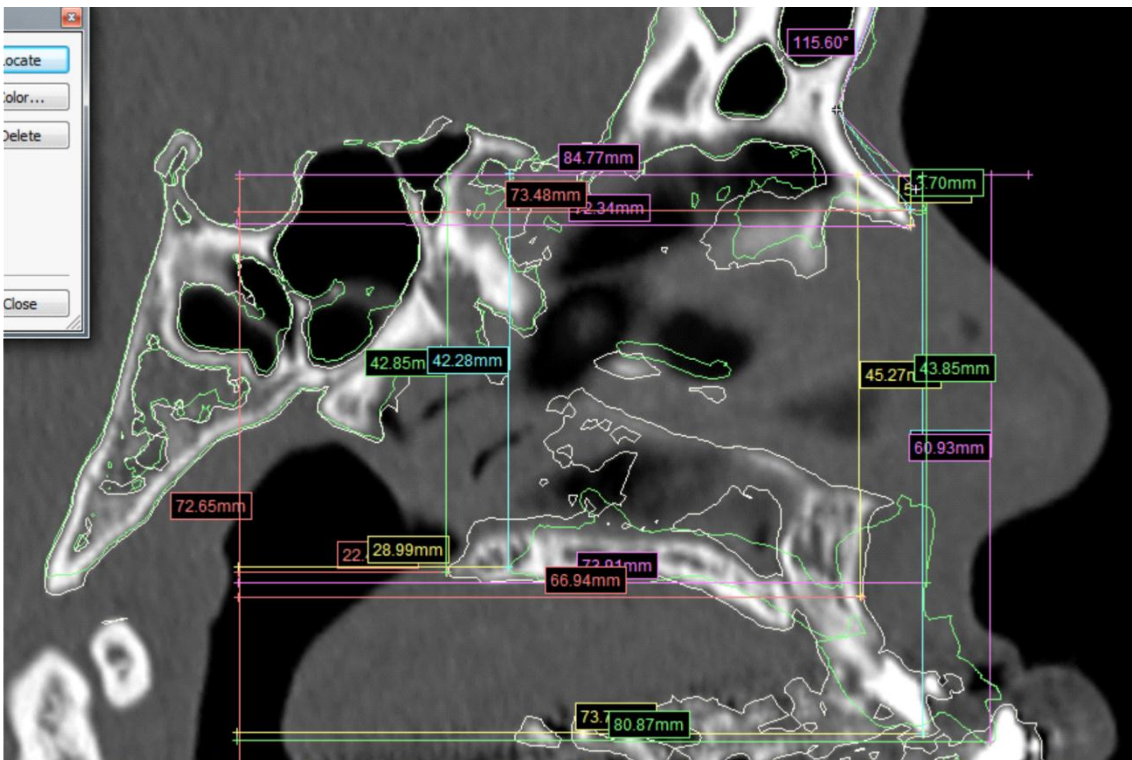

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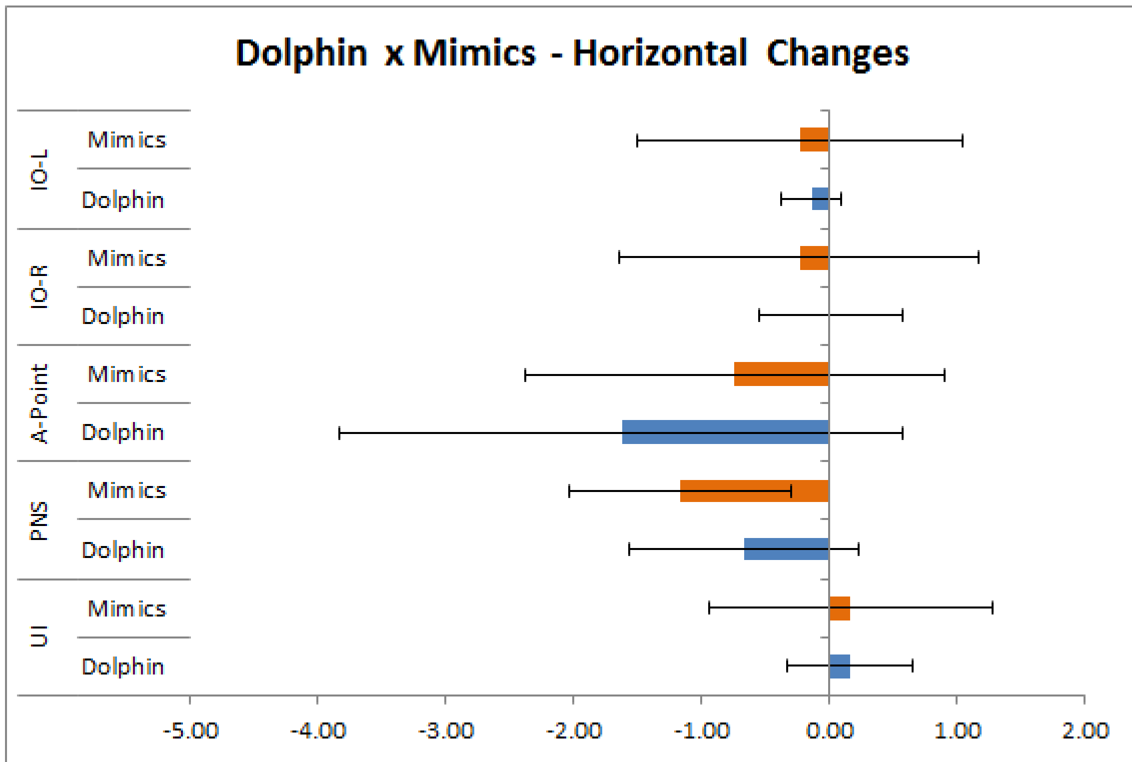

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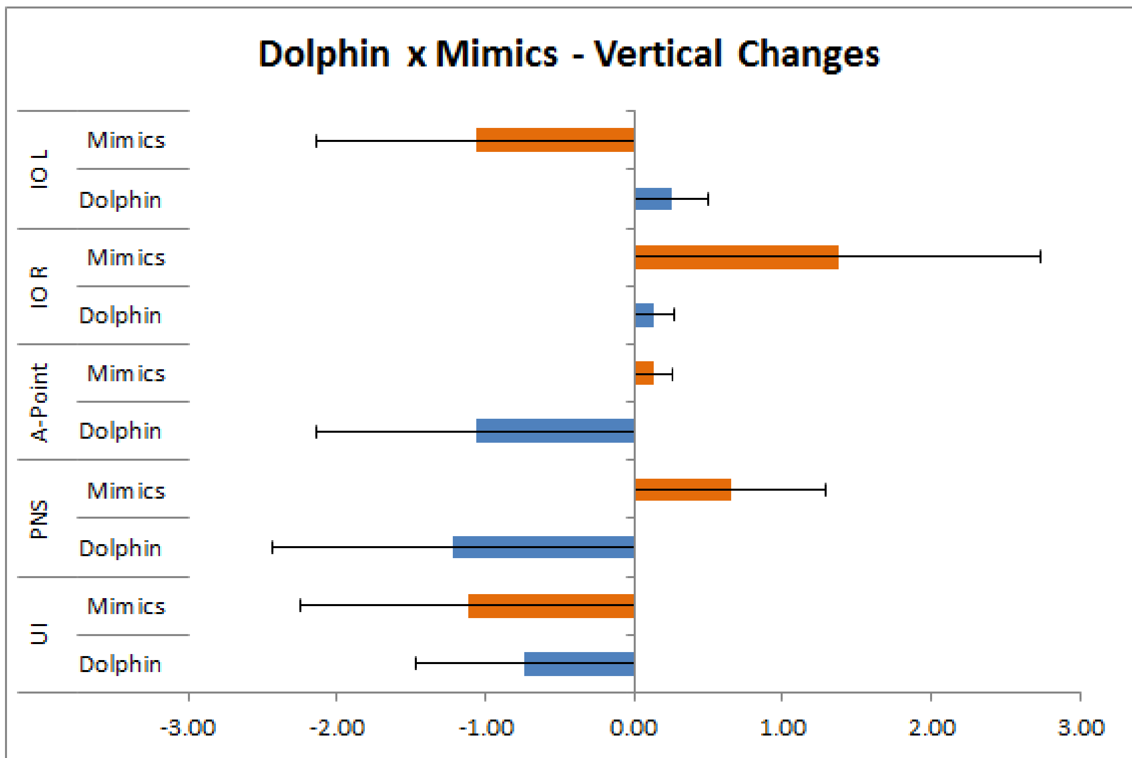

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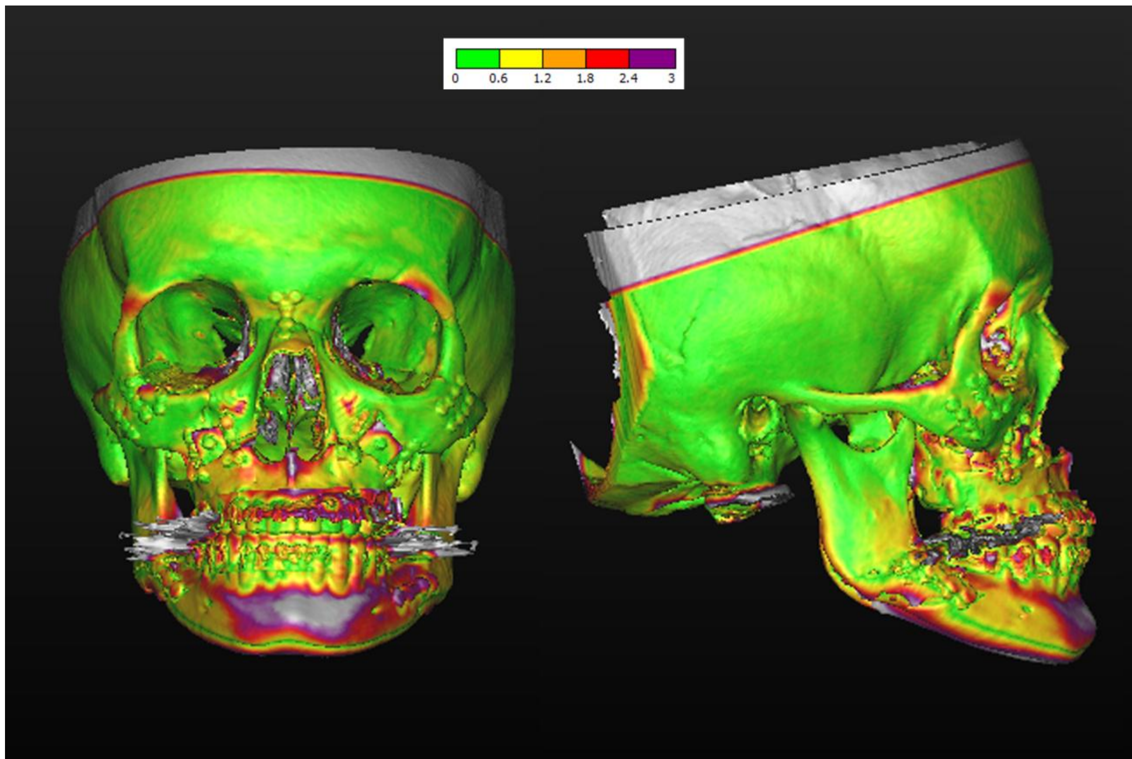

Figure 7.

LEGENDS

Figure 1. Design of the subcranial Le Fort III osteotomy in association with Le Fort I osteotomy.

Figure 2. Coronal slice of Mimics software after registration and superimposition of the 3D skull during T0, T1 and T2.

Figure 3. Linear horizontal and vertical measures after registration and superimposition at Dolphin software.

Figure 4. Linear horizontal and vertical measures after registration and superimposition at Mimics software.

Figure 5. Horizontal changes (T2 minus T1) measured at Dolphin and Mimics software. No statistical difference was observed between groups. UI, tip of the upper incisor; PNS, posterior nasal spine; IO-R, right orbitale inferior; IO-L, left orbitale inferior.

Figure 6. Vertical changes (T2 minus T1) measured at Dolphin and Mimics software. No statistical difference was observed between groups. UI, tip of the upper incisor; PNS, posterior nasal spine; IO-R, right orbitale inferior; IO-L, left orbitale inferior.

Figure 7. Color map of the superimposition between T1 and T2, showing the stability of the Le Fort III osteotomy.

Table 01. Demographic and pre-treatment characteristics.

Characteristic		n
Gender		
	Male	6
	Female	5
Pre-treatment		
	Overjet Pre-Surgery	13.5 mm
Surgery type		
	LF III + LF I + BSSO	7
	LF III + LF I + BSSO +Chin	4
Age at surgery (mean)		
		23
Surgery changes		
Upper Incisor (mean)		
	Horizontal	10.55 mm
	Vertical	0.28 mm
Infra-Orbital Right (mean)		
	Horizontal	4.45 mm
	Vertical	0.8 mm
Infra-Orbital Left (mean)		
	Horizontal	2.28 mm
	Vertical	0.10 mm
B-Point (mean)		-3.96
Lower Incisor (mean)		-0.63
Follow up (months)		18

LF III, Le Fort III osteotomy; LF I, Le Fort I osteotomy; BSSO, Bilateral Sagittal Split Osteotomy

Table 2. Horizontal and vertical changes during immediate postoperative and post-treatment times.

	Dolphin					Mimics				
	T1-T0		T2-T0			T1-T0		T2-T0		
	Mean	SD	Mean	SD	P-value	Mean	SD	Mean	SD	P-value
Horizontal										
Upper Incisor - Right	9.88	2.44	10.05	2.37	0.1922	10.01	1.92	10.18	2.35	0.7203
PNS	10.37	1.60	9.70	2.37	0.1286	10.51	2.06	9.35	2.05	0.0216
A-point	11.25	3.14	9.63	2.91	0.1314	10.14	2.50	9.41	2.44	0.3216
Infra-Orbital - Right	4.43	1.48	4.45	1.65	0.9451	4.23	1.59	4.00	1.85	0.7069
Infra-Orbital - Left	2.25	3.13	2.12	2.96	0.2212	3.86	2.04	3.63	1.44	0.6882
Vertical										
Upper Incisor - Right	0.45	4.23	0.28	2.30	0.5825	0.36	4.07	0.76	3.98	0.1505
PNS	0.07	3.25	1.28	2.94	0.1727	1.76	3.66	1.12	3.27	0.3516
A-point	0.37	5.06	1.43	3.64	0.3818	0.37	2.80	0.24	2.64	0.8498
Infra-Orbital - Right	0.93	2.34	0.80	2.65	0.8318	0.91	1.36	0.46	2.97	0.8318
Infra-Orbital - Left	0.15	1.67	0.10	1.66	0.6228	0.17	3.03	0.89	2.35	0.1352

T1, Immediate post-operative time; T2, post treatment time; PNS, Posterior nasal spine.

Values in mm.

7 CONCLUSÃO

Esta série de estudos conclui que a osteotomia subcranial LF III combinada com a osteotomia LF I é uma técnica cirúrgica eficaz para corrigir a má oclusão e a hipoplasia terço médio da face com estabilidade pós-cirúrgica. Observaram-se mínimas alterações ântero-posteriores e verticais em todos os pontos de referência do terço médio da face, contudo sem significância clínica. Ambos os softwares apresentaram resultados semelhantes e provaram serem ferramentas clínicas eficientes para estudar a estabilidade óssea. Com relação à via aérea superior, embora o recuo da mandíbula ocasione um estreitamento da via aérea, o avanço do terço médio combinado com o avanço da maxila tende a manter ou aumentar o volume da via aérea.

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ANEXO A

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Convidamos o (a) Sr. (Sra.) para participar da Pesquisa **"Avaliação da Alteração da Via Aérea Superior e da Estabilidade Óssea em Pacientes Submetidos à Osteotomia Le Fort III Modificada Associada à Osteotomia Le Fort I para Tratamento da Hipoplasia do Terço Médio da Face."**, sob a responsabilidade do pesquisador Prof. Dr. Eduardo Hochuli Vieira, a qual pretende avaliar comparativamente, por meio de análise tomográfica retrospectiva, a estabilidade óssea e a alteração das vias aéreas superiores em pacientes não sindrômicos submetidos à osteotomia Le Fort III modificada associada à osteotomia Le Fort I para tratamento da hipoplasia do terço médio da face

Sua participação é voluntária e se dará por meio de análise das tomografias computadorizadas já realizadas durante o seu tratamento cirúrgico.

Se depois de consentir em sua participação o Sr. (Sra.) desistir de continuar participando, tem o direito e a liberdade de retirar seu consentimento em qualquer fase da pesquisa, seja antes ou depois da coleta dos dados, independente do motivo e sem nenhum prejuízo a sua pessoa.

O (a) Sr. (Sra.) não terá nenhuma despesa e também não receberá nenhuma remuneração. Os resultados da pesquisa serão analisados e publicados, mas sua identidade não será divulgada, sendo guardada em sigilo.

Para qualquer outra informação, o (a) Sr (a) poderá entrar em contato com o pesquisador no endereço: Faculdade de Odontologia de Araraquara (FOAr UNESP), Rua Humaitá, 1.680, 2º andar, Centro – Araraquara - São Paulo - Brasil.

Fernanda Brasil Daura Jorge Boos Lima
Doutoranda

Prof. Dr. Eduardo Hochuli Vieira
Orientador

ANEXO B

CONSENTIMENTO PÓS–INFORMAÇÃO

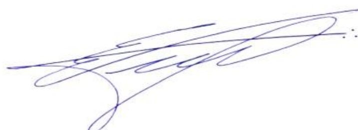
Eu,____

_______________________________________, fui informado (a) sobre o que o pesquisador quer fazer, porque precisa da minha colaboração e entendi a explicação. Por isso, eu concordo em participar do projeto, sabendo que não vou ganhar nada e que posso sair quando quiser. Este documento é emitido em três vias que serão assinadas por mim e pelo pesquisador, ficando uma via comigo, outra arquivada no prontuário e uma com o pesquisador.

Data: ______/ ______/ ______

____

Assinatura do participante



____

Prof. Dr. Eduardo Hochuli Vieira

Pesquisador Responsável

ANEXO C

APROVAÇÃO DO COMITÊ DE ÉTICA

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Avaliação da Alteração da Via Aérea Posterior e da Estabilidade dos Movimentos em Pacientes Submetidos à Osteotomia LeFort III Modificada Associada à Osteotomia Le Fort I para Tratamento da Hipoplasia do Terço Médio da Face.

Pesquisador: Eduardo Hochuli Vieira

Área Temática:

Versão: 2

CAAE: 56390815.5.0000.5416

Instituição Proponente: Faculdade de Odontologia de Araraquara - UNESP

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 1.610.415

Apresentação do Projeto:

Avaliação da Alteração da Via Aérea Posterior e da Estabilidade dos Movimentos em Pacientes Submetidos à Osteotomia LeFort III Modificada Associada à Osteotomia Le Fort I para Tratamento da Hipoplasia do Terço Médio da Face.

Objetivo da Pesquisa:

Este trabalho tem o propósito de avaliar comparativamente, por meio de análise tomográfica retrospectiva, a estabilidade dos movimentos e a alteração das vias aéreas posteriores em pacientes não sindrômicos submetidos à osteotomia LF III modificada associada à osteotomia LF I para tratamento da hipoplasia do terço médio da face.

Avaliação dos Riscos e Benefícios:

RISCOS: o pesquisador relata que não há riscos, visto que é uma análise retrospectiva.

BENEFÍCIOS: Esclarecer a técnica mais eficaz e estável para tratamento da hipoplasia do terço médio da face.

Comentários e Considerações sobre a Pesquisa:

O projeto trará excelente contribuição para a área de Cirurgia Ortognática.

Considerações sobre os Termos de apresentação obrigatória:

Todos os termos e documentos foram apresentados.

Conclusões ou Pendências e Lista de Inadequações:

Todas as solicitações foram devidamente atendidas.

Considerações Finais a critério do CEP:

Atendidas pendências de reunião, considero APROVADO o protocolo.

O pesquisador deverá encaminhar relatórios parciais a cada 01 (um) ano até o prazo final da pesquisa, quando deverá encaminhar o relatório final.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_587173.pdf	28/06/2016 10:39:02		Aceito
Recurso Anexado pelo Pesquisador	Recurso.pdf	20/05/2016 17:55:05	Eduardo Hochuli Vieira	Aceito
Orçamento	Orcamento.pdf	20/05/2016 17:54:55	Eduardo Hochuli Vieira	Aceito
Declaração do Patrocinador	Declaracaopatrocinador.pdf	20/05/2016 17:54:46	Eduardo Hochuli Vieira	Aceito
Declaração de Pesquisadores	Declaracaopesquisadores.pdf	20/05/2016 17:54:34	Eduardo Hochuli Vieira	Aceito
Declaração de Manuseio Material Biológico / Biorepositório / Biobanco	Declaracaomaterialbiologico.pdf	20/05/2016 17:54:24	Eduardo Hochuli Vieira	Aceito
Declaração de Instituição e Infraestrutura	Declaracaoinstituicao.pdf	20/05/2016 17:54:11	Eduardo Hochuli Vieira	Aceito
Cronograma	Cronograma.pdf	20/05/2016 17:54:00	Eduardo Hochuli Vieira	Aceito
Brochura Pesquisa	Brochurapesquisa.pdf	20/05/2016 17:52:07	Eduardo Hochuli Vieira	Aceito
Folha de Rosto	folhaderostoeduardo.pdf	15/09/2015 13:35:03	Eduardo Hochuli Vieira	Aceito
Projeto Detalhado / Brochura	ProjetoDoutorado.pdf	08/09/2015 16:34:17	Eduardo Hochuli Vieira	Aceito

Investigador	ProjetoDoutorado.pdf	08/09/2015 16:34:17	Eduardo Hochuli Vieira	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	Termo.pdf	08/09/2015 16:33:19	Eduardo Hochuli Vieira	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

ARARAQUARA, 28 de Junho de 2016

Assinado por:
Lígia Antunes Pereira Pinelli
(Coordenador)