OUTCOME ASSESSMENT ON SKELETAL STABILITY AFTER RIGID EXTERNAL DISTRACTION OSTEOGENESIS IN CLEFT LIP AND PALATE PATIENTS

by

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ABSTRACT

Purpose: Distraction osteogenesis (DO) using an external distraction device in the correction of maxillary hypoplasia (MH) in cleft lip and palate patients has been shown to be an effective and stable technique. The purpose of this study is to determine the outcome of skeletal stability for this procedure using the Rigid External Distraction (RED) System in patients with cleft lip and palate (CLP).

Materials and methods: Twenty CLP patients with moderate to severe maxillary hypoplasia were treated between June 2000 and June 2006. Their average age at the time of the surgery was 12.6 years. DO was started after a latency period of 5 to 7 days, after a high Le Fort I osteotomy at a rate of 0.5 mm twice a day for an average of 13.4 days. All patients use the RED, which was left in place for an additional period, averaging 3.8 weeks, to allow bony consolidation after the completion of DO. Once this was accomplished, the patient was placed on an orthodontic face mask with elastic traction for several weeks. Orthodontic treatment was then continued. The follow-up period averaged 24.8 months. The statistical analysis utilized in this study was a chi square test and t-test (for the means) with a p value < 0.05.

Results: An average distraction of 12.0 mm was achieved for the time period from before to after distraction (T1-T2). A mean of 4.6 mm was lost in the period that correspond from after distraction to the last follow-up (T2-T3) and correspond to after DO to the last follow-up (mean 25 months). The net maxillary advancement from (T1 – T3) was 7.5
mm, corresponding to before DO to the last follow-up. The resulting relapse rate was 30 percent.

**Conclusions:** Several factors may affect the results of the procedure, severity MH, type of cleft, speed of distraction, length of consolidation, length and use of face mask after RED removal, compliance of patients. Maxillary distraction osteogenesis using the RED has shown in several studies that is an effective and stable procedure in the correction of moderate to severe maxillary hypoplasia in cleft lip and palate patients when followed by further orthodontic night retention with facial mask for several weeks. It appears that greater anterior overcorrection of the hypoplastic maxilla is necessary to compensate for a partial relapse and growth deficit.
DEDICATION

This thesis is dedicated to my family, especially my mother Lucrecia, my aunt Adriana, my brother Mario, my sister Gabriela for their support, sacrifice, love and dedication through all these years of Graduate School and Oral and Maxillofacial Surgery Residency. To Dallas-Shea for all the understanding, love and patience. To all my friends, especially Maria, Francisco, Jack, Jason, and Sofía for all their support.

Esta tesis esta dedicada a mi familia, especialmente a mi mamá Lucrecia, mi tía Adriana, mis hermanos Mario y Gabriela por su apoyo, sacrificio, amor y dedicación durante estos años de Postgrado y del programa de Cirugía Oral y Maxilofacial. A Dallas-Shea por toda su comprensión, amor y paciencia. A todos mis amigos, en especial a Maria, Francisco, Jack, Jason y Sofía por todo el apoyo que me han brindado.
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INTRODUCTION
Cleft Lip and Palate

Facial development defects are the result of a multiplicity of etiologic factors, where some are genetic but most are unknown. It can be categorized in malformations genetically determined, deformations environmentally influenced and disruptions of metabolic, vascular, and/or teratogenic origin. Malformations will develop in the embryonic period and are not self-correcting. Deformations and disruptions occur in the fetal period and may correct themselves. The range of these abnormalities is enormous and produces some degree of disfigurement resulting, to some degree, in the impairment of function.

Cleft lip and palate are congenital (present from before birth) abnormalities that affect the upper lip and the hard and soft palate of the mouth. Severity of the abnormalities may range from a small notch in the lip to a complete fissure (groove) extending into the roof of the mouth and nose. These features may occur separately or together. Cleft lips and palates not associated with a syndrome are caused by a combination of genetic and environmental factors. Inheritance caused by such a combination is called multifactorial. CL(P) has been associated with defect in the genetic loci for growth and transcription factors transforming growth factor-alpha (TGF-α), TGF-β2, TGF-β3, interferon regulatory factor 6 (van der Woude syndrome), T-Box 22 (X-linked cleft palate with ankyloglossia), P63 (ectodermal dysplasia syndromes), Msx1,
and goosecoid transcription factor; for vasoactive peptide endothelin-1 (22q deletion syndromes); for retinoic acid receptor-alpha and fibroblast growth factor receptor-1 (Kallman syndrome); for cell adhesion molecule nectin-1 (ectodermal dysplasia syndromes). CP has been associated with defects in the genetic loci for TGF-α, TGF-β3, T-BOX 22 and P63 (limb mammary syndrome); for polarizing factor sonic hedgehog (holoprosencephaly); and extracellular matrix proteins collagen type II and pro-collagen type XI (Stickler syndrome). Single gene disorders are believed to cause only 15% of clefts. Cigarette smoking during pregnancy seems to be correlated with clefting. Multivitamins play a role in the etiology of clefting. Natsume et al. found a lower risk of having a CL(P) child in mothers who ate foods rich in beta-carotene than those who ate little or no food rich in vitamins. Currently, the role of epigenetic influences are being investigated, such as maternal smoking, maternal alcohol use, folate deficiency or disordered metabolism, steroid and statin use, and retinoid exposure. There are many causes, problems with genes passed down from one or both parents, drugs, viruses, or other toxins can all cause such birth defects. Cleft lip and palate may occur along with other syndromes or birth defects.

The face derives from five prominences (Figure 1) that surround a central depression, the stomodeum, which constitutes the future mouth. These are: the single median frontonasal and the paired maxillary and mandibular prominence that are derivatives of the first pair of six pharyngeal arches. The frontonasal prominence surrounds the forebrain, which sprouts lateral optic diverticula that form the eyes. The frontal portion of the prominence between the eyes forms the forehead; at the inferolateral corners, thickened ectodermal nasal placodes arise and become the olfactory
epithelium and develop the olfactory nerves, then they invaginate by the elevation of the medial and lateral nasal prominences, surrounding each nasal pit, that are the precursors of the anterior nares. The union of the facial prominences occurs by merging of the frontonasal, maxillary, and mandibular prominences or fusion of the central maxillonasal components. Between the 6th and 12th weeks of fetal gestation, the left and right sides of the face and facial skeleton fuse in the middle. When they fail to do so, the result is a craniofacial cleft. Various types of clefts may occur as an isolated condition or as a part of a syndrome.

Figure 1: The face derives from five prominences, the frontonasal prominence and the paired maxillary and mandibular prominences, between weeks 6 and 12.
Incidence

Cleft lip with or without cleft palate [CL(P)] occurs in approximately 1/1000 white births (range 0.7-1.3). Data may differ from study to study in various parts of Europe and the United States, depending on source of information (birth records, birth certificates, pregnancy follow up data, surgical records, hospital records, and multiple sources), whether the data were obtained retrospectively or prospectively, and whether stillbirths or syndromal disorders were included.

A marked racial predilection has been noted. The frequency of CL(P) in Native Americans appears to be the highest of any group in the world (over 3.6/1000 live births). In Japan it is also high (approximately 2.1/1000 births) and in China (approximately 1.4/1000 births) in contrast, it is lower among blacks (approximately 0.3/1000 births) and Maori. In general the more severe the defect, the greater the proportion of males affected. In CL(P) the ratio is 2M:1F, in cleft lip [CL] 1.5M:1F. Isolated CL may be unilateral in 80% or bilateral 25%. However, when only cleft lip is involved, bilateral cases account for approximately 10% and when CL is combined with CP, approximately 25% are bilateral. Unilateral clefts are more common on the left side (approximately 70%). About 85% of cases of bilateral CL and 70% of unilateral CL are associated with cleft palate. CL is not always complete, in approximately 10% to 30%, is associated with skin bridges (Simonart’s bands).

In isolated cleft palate (CP), the frequency in whites and blacks appears to be approximately 0.4/1000 births and is more common in females. Cleft palate among Maori of New Zealand is approximately 1.9/1000 births. There is a 2:1 female
predilection for complete cleft of the hard and soft palate, but the ratio approaches to 1:1 for clefts of the soft palate only.  

**History of Cleft Lip and Palate Repair**

Early evidence of clefting has been found in several cultures: an Egyptian mummy dating from 2400 to 1300 BC, a 2000 years old ceramic statue of a king with a cleft reported from Colombia, and on the description of an African mask showing cleft lip and palate. Hippocrates (400 BC) and Galen (150 AD) mention cleft lip, but not cleft palate in their writings. The first documented cleft lip and palate repair was performed by a Chinese physician in 390 AD. Ambroise Pare is credited with the first diagrammatic representation of cleft lip repair and cleft palate obturator use during the 14th century. In 1766, the first documented successful cleft soft palate repair was performed by a French dentist, Le Monnier. The first closure of the hard palate was performed in 1834 by oral surgeon, Dieffenbach. During the 1950s, Asensio, a Guatemalan oral surgeon, developed a novel technique for cleft lip repair. In the mid 1950s, Ralph Millard, oral surgeon, described his classic rotational advancement technique, and his concepts changed the cleft repair forever.

**Distraction Osteogenesis**

Distraction osteogenesis is a technique in which bone can be lengthened by *de novo* bone formation as part of the normal healing process that occurs between surgically osteotomized bone segments fixed to a mechanical device that undergo gradual,
controlled traction. The ability of the soft tissue envelope (the skin, muscle, and neurovascular structures) to accommodate the gradual expansion of the underlying skeletal framework that contributes to the stability of the reconstruction is unique to distraction. It is the ability to reconstruct combined deficiencies in bone and soft tissue that makes this process unique and invaluable to all types of reconstructive surgeons.

Distraction osteogenesis has become a widely accepted technique for the treatment of skeletal craniofacial deformities and since its first application by McCarthy et al, the technique has been expanded to almost every part of the craniofacial complex and it is applied to nearly all classic approaches to craniofacial reconstruction.

Distraction can be divided into: 1) Elongation DO, where a foreshortened bone is increased in length, and 2) Transport DO, where a segmental defect is repaired within a bone that is otherwise of normal length. It can also be categorized into: monofocal, bifocal, trifocal types (Figures 2), depending on the number of foci where osteogenesis occurs. Monofocal elongation DO represent most of the clinical applications in the craniofacial skeleton.

Figure 2: Categories of DO. a. Distraction osteogenesis. b. Transport or bi-focal osteogenesis. c. Tri-focal distraction osteogenesis.
History of Distraction Osteogenesis

This technique was pioneered by orthopedic surgeons in the late 1880s, and was first described by an Italian physician Codivilla in 1905, for the treatment of limb length discrepancies. Then in 1954, Gavriel Ilizarov, a Russian orthopedic surgeon, popularized the technique through his scientific studies as a method for enhancing bone regeneration in clinical orthopedics\textsuperscript{21} (Figure 3). Distraction osteogenesis applied to the maxillofacial complex was initially described by an orthodontist and his group, Cleall et al.\textsuperscript{22} in 1965 that successfully performed an expansion of the midpalatal suture using juvenile rhesus monkeys. In 1972, Snyder et al.\textsuperscript{23} a plastic surgeon used an external fixation device to lengthen a canine mandible. The first description of distraction osteogenesis of the human mandible was made by McCarthy et al.\textsuperscript{24} in 1992. Later Cohen et al.\textsuperscript{25} described the use of a miniature distraction system for maxillary and midfacial advancement in children with cleft lip and palate or craniofacial syndromes. In 1997, Polley and Figueroa\textsuperscript{26} developed and described the application of a rigid external distractor to cleft lip and palate patients to correct their maxillary deficiency (Figure 4).

\textbf{Figure 3:} The Ilizarov apparatus illustrates the Ilizarov apparatus treatment procedure for a fractured limb.
Physiology of Distraction Osteogenesis

Ilizarov\textsuperscript{27} demonstrate the physiologic factors and variables of the “tension-stress” model for the mechanically induced growth of new tissue, “slow, steady traction of tissues causes them to become metabolically activated, resulting in an increase in the proliferative and biosynthetic functions.”

Distraction osteogenesis has three distinct phases: latency, activation, and consolidation. The latency phase is the period of time between the creation of the osteotomy and the initiation of mechanical distraction, last about 5 to 7 days. Biological events and histological changes are similar to the ones happening during the initial phases of fracture healing. Starting with a hematoma, followed by an invasion of inflammatory cells and evidence of bony necrosis at the fracture site, followed by the appearance of osteoprogenitor cells and neovascularization. Starting the formation of a soft callus with
the deposition of fibroblast and associated collagen. The activation phase corresponds
to the entire time that mechanically induced tensile stress is applied across the
osteotomized bone segments. Without the longitudinal tension-stress of distraction
osteogenesis, the osteotomy site would transition from soft to hard callus while
ossification, trabecular formation, and calcification is taking place to end up in final
remodeling. The activation phase interrupts this sequence, inducing the creation of three
distinct zones of activity that manifest after 5 to 10 days of activation. At the middle of
the distraction gap a fibrous interzone (FZ), which is a radiolucent region with a high
metabolic activity consisting of spindlelike fibroblasts and collagen bundles that align
along the axis of distraction. Fibrous and primitive cartilaginous tissue in the FZ
suggests that membranous and endochondral bone formation contributes, regardless of
bone of origin. At each border of the FZ, connecting to the cut ends of the distraction
bone fragments, mineralization zones (MZ) can be found. Neovascular activity is vital in
the MZ, osteoid formation with histologic and radiographic evidence of the formation of
trabecular bone, speculation and microtubule formation while osteoid differentiates into
maturing bony architecture.

The rate of the distraction is very important for the clinical result. If is too slow
(<0.5-1.0 mm/day) it may result in premature consolidation of the regenerate and very
difficult to continue the distraction with potentially injuring the regenerate or damage of
the distraction device. A too aggressive rate (>1.5-2.0 mm/day) may outstrip the ability
of the regenerate to form new bone, creating a fibrous non-union that may require
reoperation.
Consolidation phase begins when application of continuous tensile force ceases and ends at the removal of the distraction device. It characterizes by the maturation of soft callus, ossification of the FZ, and formation of neocortex, evidenced on radiographs. In this period a gradual increase of physiologic stress on the regenerate, like mastication, is allowed. In the craniofacial area, consolidation period usually last two to four times the activation phase length. After the removal of the DO device, additional remodeling of the new bone will continue for up to a year\(^{31}\).

The volume and architecture of new bone are comparable to the adjacent bones; animal studies have shown that mineral content and readiodensity are less, while the tensile strength of the regenerate segment is approximately 75% of the native bone\(^{32}\).

Beside the bony changes there are effects on the adjacent soft tissues that occur in response to osseous distraction\(^{33}\). Muscle and soft tissue mass increase via distraction histiogenesis, which is an advantage to various types of craniofacial anomalies that have soft tissue hypoplasia in addition to the bony deficiency. Neurovascular elements will also be stimulated to elongate.

**General Background and Problem**

Cleft lip and palate is one of the most common congenital deformities, and the treatment of clefts and associated maxillofacial deformities still present a challenge for the treating physician, and can be very difficult for the treating physician. Patients often present moderate to severe underdevelopment of the maxilla in a sagittal, vertical and transverse direction, with a flattened middle third of the face and a class III malocclusion, partial or total anterior and posterior cross bite. 25% to 60% of all patients born with
CLP will require maxillary advancement to correct their maxillary hypoplasia and improve their facial esthetic proportions\textsuperscript{34}. Traditional treatments had consisted of a combination of orthodontic and surgical procedures essentially after growth completion. The results have been often suboptimal and limited, accompanied by instability that compromised the aesthetics and functionality. Severe class III patients often required mandibular set back, even in the absent of mandibular hyperplasia. The scar tissue in the orofacial skin and mucous membrane it is believe to be a crucial factor affecting the stability of the maxilla after conventional orthognatic surgery in subjects with cleft lip and palate\textsuperscript{35}. The success in the treatment of cleft lip and palate involves different specialist in the various stages of treatment, each carrying different responsibilities.

Children born with facial clefts and other craniofacial conditions often face multiple, complex health problems. These complex issues can best be managed by an interdisciplinary team of specialists who work together, and with the family, to create and update the child’s health care plan. Depending on individual needs, these specialists may include:

1. A surgeon (such as a plastic surgeon, an oral and maxillofacial surgeon, craniofacial surgeon, and/or neurosurgeon).
2. An audiologist (who assesses hearing).
3. A pediatric dentist or other dental specialist (such as a prosthodontist, who makes prosthetic devices for the mouth).
4. An orthodontist (who straightens the teeth and aligns the jaws).
5. A geneticist (who screens patients for craniofacial syndromes and helps
   parent and adult patients understand the chances of having more children
   with these conditions).

6. A nurse (who helps with feeding problems and provides ongoing
   supervision of the child’s health).

7. An otolaryngologist (ENT).

8. A pediatrician (to monitor overall health and development).

9. A psychologist or other mental health specialist (to support the family and
   assess any adjustment problems).

10. A speech-language pathologist (who assesses not only speech but also
    feeding problems).

11. Other necessary specialists who treat specific aspects of complex
    craniofacial anomalies.

12. Volunteers, volunteers, volunteers…

This team is a group of experienced and qualified professionals from medical,
surgical, dental, and allied health disciplines working in an interdisciplinary and
coordinated system, representing many of the following disciplines: anesthesiology,
audiology, diagnostic medical imaging/radiology, genetic counseling, genetics,
dysmorphology, neurology, neurosurgery, nursing, ophthalmology, oral and maxillofacial
surgery, orthodontics, otolaryngology, pediatric dentistry, general pediatrics, pediatric
and neonatal intensive care, physical anthropology, plastic surgery, prosthodontics,
psychology, social work, and speech-language pathology. The type of patient the team evaluates and treats will further determine the additional disciplines needed on the team.

Interdisciplinary team care begins shortly after birth and continues until the physical growth of an individual has been completed. Since skeletal changes continue throughout childhood and soft tissue growth is influenced by the changes, evaluation throughout the maturation process is recommended. Psychosocial adaptation should also continue to be monitored until maturity.

Primary cleft lip and palate repair is a procedure that performed during infancy and early childhood can improve facial appearance, speech, and deglutition, but the long-term negative effect is the impairment of maxillary growth resulting in secondary jaw deformities and malocclusion. Approximately 25% of patients with unilateral cleft lip and palate developed maxillary hypoplasia and do not respond to orthodontic treatment alone. Some authors feel that it is greater than 25%, in these patients the maxilla is difficult to mobilize due to scarring from previous surgeries. The tendency for relapse is greater in cleft patients than noncleft patients with maxillary hypoplasia, and this may adversely affect final surgical results. In cleft patients treatment of severe maxillary hypoplasia with the traditional Le Fort I osteotomy for maxillary advancement, has shown an unstable outcome. Reported rates of relapse ranged between 5% and 80%.

Distraction osteogenesis is an effective method used for bone regeneration, where a gradual formation of new bone by progressive lengthening has widely been applied in the orofacial region to overcome the drawbacks of so-called ‘one step’ orthognatic surgery such as Le Fort I osteotomy (Figure 5).
Figure 5. Patient undergoing maxillary advancement with a rigid external distraction device. A, Frontal view; B, Lateral view.

Distraction osteogenesis (DO) treatment can be performed much earlier in life than orthognatic surgery, thereby improving facial occlusion and social image.

DO is an alternative technique used to correct maxillary deficiencies with predictable and stable results, by gradual bone distraction, allowing the surrounding soft tissues to better adapt to the structural changes. The advantage is that it generates new bone without the need of hardware and bone grafting, DO gradually lengthen the soft tissues permitting unrestricted motion and decreases the postoperative relapse. The Rigid External Distraction (RED) Device, provides treatment for patients with severe maxillary hypoplasia, at any age, patients with severe skeletal deficiencies in whom result could be compromised with the traditional technique, provides with the ability to focus treatment on only the affected region, with minimal morbidity and more controlled and predictable results. It provides a better control of the distraction vector, by allowing vertical,
horizontal, and rotational changes in the distraction, at any time without much discomfort for the patient.

The device is activated after a latency period of 5 to 7 days, at a rate of 0.5 to 1.0 mm/day until an adequate maxillo-mandibular relationship is achieved (class I or II). The length of the consolidation phase recommended for the craniofacial skeleton ranges between four to twelve weeks. There are no studies on the consolidation time for cleft patients, some clinicians use a shorter consolidation period, although a general rule states that the consolidation period should be at least twice the duration of the distraction phase. It is often recommended that patients be followed by further orthodontic night retention with facial mask for the following weeks (Figure 6).

Figure 6. Patient with the protraction face mask. A, Frontal view; B, Lateral view.
Usually patient’s and family #1 question is “how long do I need to wear the device?” we have notice that patients’ dissatisfaction is greater with a lengthy consolidation period than with a shorter one. Ayoub et al. found in their study about patients and family response to DO by extraoral DO, that all the patients experienced problems during their treatment, but were able to cope with the difficulties and complete the treatment successfully. Recreational activities and school attendance were affected during treatment. Eating and speech and sleep were also affected by the device, but patients and their families found ways to adapt. Maintaining oral hygiene was another difficult. The treatment puts a strain on parents who have to activate the device and also clean the distraction pins, maintain oral hygiene, and cope with a restless child who is unable to attend to school, play with friends or realize their hobbies or activities. All patients noticed a change in their appearance as treatment progressed and said that they would recommend DO to others.
OBJECTIVES

The primary objectives of these studies were:

1. To evaluate the stability, relapse and advancement of the hypoplastic maxilla after DO.
2. To compare/correlate consolation phase with relapse.
3. To determine if short consolidation phase could be stabilized by orthodontic protraction face mask.
4. To describe our experience using an external distractor device for the correction of the maxillary hypoplasia in cleft lip and palate patients.
5. To determinate how much advancement in mm has been achieved (with cephalometric evaluation) in our series of patients.
6. To present the clinical and cephalometric results in our series of 20 consecutives patients.
HYPOTHESES

There is no difference of the skeletal stability in the amount of advancement (mm) for T2 (post-distraction period) and T3 (most recent follow-up period).
MATERIALS AND METHODS

Population studied

Only cleft patients were included in this study that underwent rigid external distraction osteogenesis to correct their maxillary hypoplasia by means of a high Le Fort I osteotomy with gradual advancement using the Rigid External Distraction (RED II) System (KLS-MARTIN, Jacksonville, FL, USA). All patients were referred to the University of Alabama at Birmingham Department of Oral and Maxillofacial Surgery for surgical treatment between June 2000 and June 2006. The clinical series included 28 consecutive cleft patients with maxillary hypoplasia, eight of them were lost during follow-ups; of the twenty included, there were thirteen males and seven females with ages ranging from 10.0 years old to 16.2 years (mean 12.6 years). 11 patients had bilateral cleft lip and palate, 8 patients had unilateral cleft lip and palate, and one patient present isolated cleft palate. All of them presented moderate to severe degree of maxillary hypoplasia. Preoperatively, an intraoral splint was fixed to the teeth in all the patients by the treating orthodontist (Figure 7. A and B).
Figure 7. Clinical pictures: A. Lateral view of intraoral splint. B. Frontal view of intraoral splint.
**Data collection method**

The data collection was obtained by reviewing clinical chart of the patients, where lateral cephalograms have been evaluated retrospectively regarding linear and angular measurements; a cephalometric analysis had been made to analyze:

a. **T1** = pre-operatory lateral ceph without the RED.

b. **T2** = post activation lateral ceph with RED on, where there is a different head position noted due to the device).

c. **T3** = long term post-op lateral ceph (mean 25 months) post RED removal, that correspond to the most recent follow-up.

**Surgical Technique**

The procedure was performed under general anesthesia; the patients were intubated via oral endotracheal tube. After infiltration of local anesthesia (1% lidocaine with 1:100,000 epinephrine) a vestibular incision was made extending from the area of the maxillary right 2\textsuperscript{nd} molar to the area of the maxillary left 2\textsuperscript{nd} molar. The mucoperiosteum flap was then deflected; the piriform rims and the anterior and lateral walls of the maxilla were exposed between the canine roots and the infraorbital nerves. The nasal mucosa was gently elevated off the floor of the nose and on the lateral sides, a high Le Fort I osteotomy was performed using a reciprocating saw; septal disjunction and separation of the pterygomaxillary junction were done to complete the down-fracture of the maxilla. Immediate mobilization of the maxilla is important to prove that there is sufficient mobility of the midface and to control the direction of the distraction. An incomplete movement of the bone may indicate inadequate separation. The incision was
closed and the activation of the device expected to start after 5 to 7 days at a rate of 0.5mm twice a day (Figure 8 A-D).

![Image](image1.png)

**Figure 8. Le Fort I osteotomy surgical pictures:**

A. Separation of the pterigomaxillary junction.  
B. Elevation of the nasal mucosa.  
C. Septal disjunction.  
D. Separation of the lateral maxillary wall.

The rigid external head frame (halo) was then secured using 4 or 5 titanium scalp monocortical screws per side. The halo was then secured to the head parallel to the Frankfort horizontal plane. The carbon rod and the distractor segment were then placed.
A 24 gauge wire, twisted around the advancement pins, was used to attach the distraction device to the intraoral splint. The torque wrench was used to confirm the tightness of the pins. Local anesthetic (1% lidocaine with 1:100,000 epinephrine) was applied to the pins areas for pain control. Merocel nasal packs were applied to both nares. The patient was awakened from anesthesia and extubated. All patients spent the night at the hospital for pain control and were discharged the next day (Figure 9 A-D).

Figure 9. Surgical Pictures: A. Securing the RED frame (halo). B. Confirming tightness of pins with torque wrench. C. Lateral view of RED in place. D. Frontal view of RED in place.
Cephalometric Analysis

Lateral cephalometric x-rays were used for the analysis. A pre-operatory x-ray (T1), two follow up x-rays at different time periods after distraction osteogenesis, (T2) post activation period, (T3) long-term post op period that correspond to the most recent follow-up, were evaluated, and compared. The mean follow-up was 24.9 months. All radiographs were digitized and analyzed using the Dolphin image software version 10. Cephalometric landmarks were digitized by single operator (E.T.) in a darkened room using Dolphin Imaging Manager computer software (version 10) (Dolphin Inc., Westwood, CA) on a desktop computer (Dell computer).

Several dentoskeletal anatomical landmarks were identified: sella (S), nasion (N), point (A), point (B), pogonion (Pog), anterior nasal spine (ANS), posterior nasal spine (PNS), upper incisor edge (U1), lower incisor edge (L1). For linear measurements a horizontal plane was created. The Frankfort plane was used as the x-axis, and a line perpendicular to this plane through the nasion was used as the y-axis. The displacement became evident when the values of these landmarks before and after distraction were subtracted. Skeletal changes were evaluated by the skeletal measurements: SNA (degrees), Maxillary skeletal (A – Na perp) (mm), and maxillary length (Co – A) (mm). By subtracting the values of these landmarks before surgery and during follow-ups angular and longitudinal displacement was calculated.

Errors of the Method

To assess the systematic and random errors of the method the operator was calibrated by several digitizing exercises. The reliability and reproducibility of the
cephalometric analyses was established using Kappa statistic test to determine intra-examiner reliability. Intra-examiner reliability was 0.79, an acceptable value.

**Statistical Analysis**

All data were entered into an Excel spreadsheet format and converted to Statistical Product and Software Solution (SPSS®, 13.0 Windows, SPSS International, Chicago, IL). The statistical analyses were done for the pre-operative and post-operative values with a chi-square test and t-test (for the means), comparing the values of each patient pre-operative cephalometric x-ray (T1) and post-operative cephalometric x-ray that correspond with the last lateral cephalometric x-ray (T3), and between the two post-operative follow-up lateral cephalometric (T2) corresponding to the follow-up lateral cephalometric x-ray after distraction osteogenesis and (T3) corresponding to the most recent follow-up lateral cephalometric x-ray, to identify if there are any statistically significant differences. P< 0.05. Kappa statistic test was used to determine intra-examiner reliability. Intra-examiner reliability was 0.79, an acceptable value.
RESULTS

All twenty patients in this study had the diagnosis of cleft lip and palate (11 bilateral, 8 unilateral and 1 cleft palate), showing a moderate to severe class III malocclusion. Information regarding patient’s gender, cleft lip and palate deformity, age of patients at the time of the surgery, surgical procedure and follow-up, are tabulated in Table 1. All were treated with distraction osteogenesis using a rigid external distractor device for the correction of the maxillary hypoplasia (Figures 4 and 10).

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<th>Case No.</th>
<th>Sex (male/female)</th>
<th>Diagnosis</th>
<th>Age (years)</th>
<th>Procedure</th>
<th>Follow-up (months)</th>
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M = male; F = female; CLP = cleft lip and palate.
All the patients completed the course of treatment successfully and clinical examination showed satisfactory advancement of the maxilla. Figures 9 and 13 are for two of the patients in this study. The planned maxillary advancement was achieved, resulting in clinical and radiographic improvement in their facial profile, changing from concave to convex (Figures 4, 5, and 9) and (Figures 10, 11, and 13). The anterior crossbite was greatly improved; dental relationship was acceptable in all cases, showing great improvement in the occlusion (Figure 6, 7, and 8). All patients were overcorrected for anticipation of relapse.

There were few complications during the course of distraction, one of the patients lost the halo in a pillow fight during the retention period, and had to be removed a little earlier than planned, but was placed on protraction face mask by orthodontist. For another patient, the intraoral splint broke and had to be repaired by orthodontist. There was no infection that required antibiotic treatment. Routine oral hygiene had to be reinforced to patients and their families repetitively. None to mild degree of pain was experienced by patients, no analgesic medication was required.

In all patients of this group the activation/distraction period lasted an average of 13.5 days, ranging from 5 to 26 days. The retention/consolidation period lasted and average of 26.7 days ranging from 11 to 68 days. The follow-up period lasted an average of 25 months, ranging from 3.2 to 59.3 months (Table 2).

The RED was well tolerated by all patients; the external hooks of the intraoral splint produce small injuries to the corner of the mouth and swelling of the lips in some of the patients. Protraction face masks used to stabilize the results and further growth is
difficult to predict\textsuperscript{50}. The masks should be worn at night for several weeks (Figures 5 and 11).

Figure 10. Case 1: Clinical photographs. Predistraction (11 years 6 months). Note the anterior crossbite with a posterior crossbite.
Figure 11. Case 1: Clinical pictures. Postdistraction (12 years 4 months). Note the correction of the anterior crossbite.
Figure 12. Case 1: Clinical pictures. Follow-up (15 years 8 months). Closing the bite.
Table 2. Shows patient’s age at day of surgery (years), activation (days), advancement (mm), retention (days), follow-up (months), face mask use (months)

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<th>Ret. (days)</th>
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Cephalometric analysis at the removal of RED revealed a mean effective advancement at point A of 12 mm (SD 3.66) forward and parallel to the Frankfort horizontal plane, (Figs. 3 and 4). However, after a mean follow-up of 25 months the group shows a backward horizontal relapse with a mean of 7.5 mm (SD 3.4) at point A. The horizontal relapse rate was 30% (Table 3). The SNA revealed an average increase of 11.3 degrees (SD 4.8). After a mean follow-up of 25 months it shows an average decrease of 4.7 degrees (SD 3.5). A total increase of an average of 7 degrees (SD 4.0 degrees) after the mean follow-up of 25 months was observed.
There is a significant statistical difference of maxillary skeletal, maxillary length and SNA, when compared all the values of T1 and T2. When comparing the values of T2 and T3, as a group there is no statistical difference of maxillary skeletal, maxillary length and SNA values. There are some subjects that respond poorly to treatment and individual analysis to explain these values are necessary (Tables 3, 4, and 5).

Table 3. Maxillary skeletal (A-Na perp) (mm).

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<th>T3 (mm)</th>
<th>T1 (mm)</th>
<th>T3 (mm)</th>
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| Mean     | 12      | 4.5     | 7.5     | 31.3    |         |           |

T1 – T2 = correspond to the maxillary advancement in mm after DO.
T2 – T3 = correspond to the relapse in mm from the most recent follow-up to the post activation phase.
T1 – T3 = correspond to the net advancement in mm after the relapse.
Table 4. SNA (degrees).

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<td>7.0</td>
<td>8.5</td>
<td>3.7</td>
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T1 – T2 = correspond to the increase in degrees of SNA after DO.
T2 – T3 = correspond to the relapse in degrees from the most recent follow-up to the post activation phase.
T1 – T3 = correspond to the net increase in degrees of SNA after the relapse.

When correlating the advancement (mm) with the rate of relapse (%), it was noted that larger the advancement correlates with higher relapse rate. Subjects 1, 4, 5, 8, 12, and 20 shown to be poor responders with a relapse higher than 50%. Subjects 6, 7, 10, 11, 16, and 18 shown to be poor responders with a mean relapse of 30%. Subjects 2, 3, 9, 13, 14, 15, 17, and 19 shown to be good responders with a mean relapse of 9%.

When correlating the retention (weeks) with the rate of relapse (%), it was noted that for a retention time up to four weeks, subjects 4, 5, 8, and 12 were poor responders with a relapse rate higher than 50%. Subjects 6, 7, 10, and 16 were poor responders with
a mean relapse of 27.8%. Subjects 2, 3, 9, 13, 14, and 17 were good responders with a mean relapse of 8.7%. For a retention time longer than five weeks, it was noted that subjects 1 and 20 were poor responders with a relapse rate higher than 50%. Subjects 11 and 18 were poor responders with a mean relapse rate of 37%. Subjects 15 and 19 were good responders with a mean relapse rate of 12%. We found that the retention time doesn’t correlate with the relapse rate.

Table 5. Maxillary length (Co-A) (mm).

<table>
<thead>
<tr>
<th>Case No.</th>
<th>T1 (mm)</th>
<th>T2 (mm)</th>
<th>T3 (mm)</th>
<th>T1 (mm)</th>
<th>T3 (mm)</th>
<th>% RELAPSE</th>
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</table>

T1 – T2 = correspond to the maxillary advancement in mm after DO.  
T2 – T3 = correspond to the relapse in mm from the most recent follow-up to the post activation phase.  
T1 – T3 = correspond to the net advancement in mm after the relapse.
DISCUSSION

Maxillary advancement by mean of maxillary distraction osteogenesis with rigid external distraction clinically improved the facial profile by reducing the facial concavity. Maxillary advancement through DO is different from the traditional Le Fort I maxillary advancement. The advancement is gradual and less traumatic.

In this study, nineteen patients with severe cleft maxillary hypoplasia and alveolar cleft underwent iliac bone grafting one year before distraction in order to create a stable maxillary arch, which make easier to control as a unit, the vector and the level of distraction.

The cleft palate repair at age 9 to 12 months optimizes speech development. The palatal repair that denude bone heal with scar contracture can result in midfacial growth retardation, resulting in a concave profile (see Figures 10 A and 10 A).

Maxillary advancement with Le Fort I osteotomies and rigid fixation has shown to have a high rate of relapse reported between 5% and 80%. To prevent surgical relapse in cleft lip and palate patients following Le Fort I osteotomy, postoperative protraction face mask have been used51. Distraction osteogenesis of the maxilla is associated with a reduced relapse rate due to its ability of combining new bone deposition with bone remodeling and maxillary advancement. Distraction devices with skeletal anchorage are believed to be superior to tooth-borne devices in that the tooth anchored devices result in greater dental than skeletal movement52,53.
In some of the studies, the changes in the facial skeleton are analyzed by superimposing cephalograms, but errors may occur when analyzing different films taken at different times\(^5^4\). The absence of stable natural reference points within the jaws made complicated the quantification of skeletal changes\(^5^5\) or to measure the orthodontic treatment effects. Bjork et al\(^5^6\) demonstrated a measurement method using metallic implants. The discrepancies between measurements of the implant displacement and the anatomical “best fit” superimposition have been reported\(^5^7,5^8\).
The variability of the reported results can be explained based on different cephalometric analyses, different patient samples (cleft and noncleft), treatment methods (orthodontic, orthopedic, or surgery), surgical technique, and age at intervention\textsuperscript{59}.

The anterior shift of the incisal edge detected after the completion of treatment is highly suggestive of bodily movement of the upper incisors, and the cause of the unwanted movement is the tooth-borne intra-oral distraction component\textsuperscript{60}. This effect on the upper incisor teeth may be avoided if the intra-oral component of the distractor is attached to the skeleton rather than to the anterior teeth\textsuperscript{61}. 

CONCLUSIONS

The following are our conclusions:

- Maxillary and midfacial distraction osteogenesis with rigid external distraction allows for the correction of the midfacial deficiency, including both the skeletal and soft-tissue deficiencies via constantly working tensile forces.

- Advancement of the hypoplastic maxilla in CLP patients can be achieved with either conventional osteotomy, distraction osteogenesis, or a combination of both.

- Early maxillary advancement with rigid external osteogenesis offers a promising option for young patients with maxillary hypoplasia.

- Close follow-up is important due to the difficulty of prediction of growth rate and estimation of relapse in cases with facial clefts.

- Additional distraction osteogenesis procedures or conventional osteotomies may be necessary.

- The supporting orthodontic treatment including the protraction face mask is important in order to avoid an early relapse.

- The use of metallic implants offers a successful method for measuring the changes in facial skeleton.

- DO appear to be more useful for severe anomalies in which there is a need of larger advancement allowing intervention at an earlier age.
• DO can be a clear and standardized procedure, but one have to individualize each case taking in consideration individual risks, specially the unpredictability of further growth.

• Patient cooperation and family support is important for the final outcome of the treatment.

• Patients’ motivation and the full understanding of the family of what to expect is key for successful completion of the treatment.
FUTURE STUDIES

With technologic advancements, distraction devices have become smaller and more sophisticated than early versions. In the horizon several new developments are visualize in the field of craniofacial DO. A combination of endoscopic techniques to create the different osteotomies and insert distraction devices can locate DO into the field of minimally invasive surgery. New work using bioresorbable materials may lead to the implementation of devices that do not require a second surgical procedure to remove them and following resorption leaving no trace of they ever been inserted. The use of microprocessors and miniature motorized distraction devices may provide the ability to insert submerged appliances capable of auto-distraction according to preprogrammed data or via remote monitoring and control of automated device-in-patient by the treatment surgeon. New sophisticated devices and approaches may provide the surgeon, patients and their families with easily placed, user-friendly, easy-to-manage devices that reduce operative time, pain and scarring.

Most probably in a not to far future the care of patients with clefting may change significantly due to all the advancements in fields like tissue engineering (like large-scale culturing of human or animal cells—including skin, muscle, cartilage, bone, marrow, endothelial and stem cells, and provide substitutes to replace damaged components in humans), genetics and fetal surgery. Research in molecular developmental biology may
increase the understanding of the interactions of biomolecules involved in tissue healing and craniofacial development, guiding the application of tissue engineering techniques for the correction of the malformation associated with clefting in utero, and the facilitating of care of patients with cleft lip and palate. As the knowledge of the human genome progresses and several of the genes involved in clefting are being identified, in utero therapy may become feasible. A better comprehension of the environmental factors effect on gene expression may lead to improvements in prenatal care and subsequently reduce the incidence of clefting. Fetal surgery may be exciting and promising prospect for children who have craniofacial anomalies, with the advantages of scarless wound healing when performed at midgestation and normalization of facial growth. Several animal model studies have demonstrated fetal cleft lip and CP repair in utero, but fetal surgery poses significant risk for premature labor, even with the endoscopic techniques. Therefore theses risks make in utero cleft repair ethically unjustifiable at this time.
LIST OF REFERENCES


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14 LeMesurier AB. *Method of cutting and suturing lip in complete unilateral cleft lip*. Plast Reconstr Surg 1949;4:1


APENDIX A

FIGURES
Figure 14. Pt. 1. A. Preoperative lateral cephalometric. B. Post activation (consolidation phase) lateral cephalometric. C. Most recent follow-up (mean 7.6 months) lateral cephalometric.
Figure 15. Pt. 2.  

A. Preoperative lateral cephalogram. 

B. Post activation (consolidation phase) lateral cephalogram. 

C. Most recent follow-up (mean 4.6 months) lateral cephalogram.
Figure 16. Pt. 3.  
A. Preoperatory lateral ceph.  
B. Post activation (consolidation phase) lateral ceph.  
C. Most recent follow-up (mean 8.4 months) lateral ceph.
Figure 17. Pt. 4.  A. Preoperative lateral ceph.  B. Post activation (consolidation phase) lateral ceph.  C. Most recent follow-up (mean 8.7 months) lateral ceph.
Figure 18. Pt. 5.  
A. Preoperative lateral ceph.  
B. Post activation (consolidation phase) lateral ceph.  
C. Most recent follow-up (mean 11.6 months) lateral ceph.
Figure 19. Pt. 6.  

A. Preoperative lateral ceph.  

B. Post activation (consolidation phase) lateral ceph.  

C. Most recent follow-up (mean 10.1 months) lateral ceph.
Figure 20. Pt. 7. A. Preoperatory lateral ceph. B. Post activation (consolidation phase) lateral ceph. C. Most recent follow-up (mean 3.2 months) lateral ceph.
**Figure 21.**  
**A.** Preoperative lateral cephalometric radiograph.  
**B.** Post activation (consolidation phase) lateral cephalometric radiograph.  
**C.** Most recent follow-up (mean 48.6 months) lateral cephalometric radiograph.
**Figure 22.** Pt. 9.  
A. Preoperative lateral cephalogram.  
B. Post activation (consolidation phase) lateral cephalogram.  
C. Most recent follow-up (mean 23.9 months) lateral cephalogram.
Figure 23. Pt. 10. A. Preoperative lateral cephalometry. B. Post activation (consolidation phase) lateral cephalometry. C. Most recent follow-up (mean 33.5 months) lateral cephalometry.
Figure 24. Pt. 11.  
A. Preoperatory lateral ceph.  
B. Post activation (consolidation phase) lateral ceph.  
C. Most recent follow-up (mean 17.3 months) lateral ceph.
Figure 25. Pt. 12.  

A. Preoperatory lateral cephalometric radiograph.  
B. Post activation (consolidation phase) lateral cephalometric radiograph.  
C. Most recent follow-up (mean 56.3 months) lateral cephalometric radiograph.
Figure 26. Pt. 13.  
A. Preoperatory lateral ceph.  
B. Post activation (consolidation phase) lateral ceph.  
C. Most recent follow-up (mean 59.3 months) lateral ceph.
Figure 27. Pt. 14.  

A. Preoperatory lateral cephalometric image.  
B. Post-activation (consolidation phase) lateral cephalometric image.  
C. Most recent follow-up (mean 50.1 months) lateral cephalometric image.
**Figure 28.** Pt. 15.  

**A.** Preoperative lateral cephalogram.  

**B.** Post-activation (consolidation phase) lateral cephalogram.  

**C.** Most recent follow-up (mean 34.7 months) lateral cephalogram.
Figure 29. **A.** Preoperatory lateral cephalometric. **B.** Post activation (consolidation phase) lateral cephalometric. **C.** Most recent follow-up (mean 47.4 months) lateral cephalometric.
Figure 30. Pt. 17.  A. Preoperative lateral cephalometric radiograph.  B. Post activation (consolidation phase) lateral cephalometric radiograph.  C. Most recent follow-up (mean 27.5 months) lateral cephalometric radiograph.
Figure 31. Pt. 18.  
A. Preoperatory lateral cephalometry.  
B. Post activation (consolidation phase) lateral cephalometry.  
C. Most recent follow-up (mean 20.6 months) lateral cephalometry.
Figure 32. Pt. 19.  

A. Preoperative lateral ceph.  

B. Post activation (consolidation phase) lateral ceph.  

C. Most recent follow-up (mean 19.2 months) lateral ceph.
Figure 33. Pt. 20.  
A. Preoperatory lateral ceph.  
B. Post activation (consolidation phase) lateral ceph.  
C. Most recent follow-up (mean 4.0 months) lateral ceph.
APENDIX B

IRB APPROVAL
Form 4: IRB Approval Form
Identification and Certification of Research
Projects Involving Human Subjects

UAB’s Institutional Review Boards for Human Use (IRBs) have an approved Federalwide Assurance with the Office for Human Research Protections (OHRP). The UAB IRBs are also in compliance with 21 CFR Parts 50 and 56 and ICH GCP Guidelines. The Assurance became effective on November 24, 2003 and expires on February 14, 2009. The Assurance number is FWA00005960.

Principal Investigator: TABARINI, J ENRIQUE
Co-Investigator(s): 
Protocol Number: X050419004
Protocol Title: Outcome Assessment on Skeletal Stability After Rigid External Distraction Osteogenesis in Cleft Lip and Palate Patients

The IRB reviewed and approved the above named project on 08/16/07. The review was conducted in accordance with UAB’s Assurance of Compliance approved by the Department of Health and Human Services. This Project will be subject to Annual continuing review as provided in that Assurance.

This project received EXPEDITED review.
IRB Approval Date: 08/16/07
Date IRB Approval Issued: 08/16/07
HIPAA Waiver Approves?: Yes

Marilyn Hess, M.A.
Vice Chair of the Institutional Review Board for Human Use (IRB)

Investigators please note:
The IRB approved consent form used in the study must contain the IRB approval date and expiration date.
IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.
Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.
Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.
UAB IRB Approval of Waiver of Informed Consent and/or Waiver of Patient Authorization

Approval of Waiver of Informed Consent to Participate in Research. The IRB reviewed the proposed research and granted the request for waiver of informed consent to participate in research, based on the following findings:
1. The research involves no more than minimal risk to the subjects.
2. The research cannot practicably be carried out without the waiver.
3. The waiver will not adversely affect the rights and welfare of the subjects.
4. When appropriate, the subjects will be provided with additional pertinent information after participation.

Check one:  ✔ Waiver of Authorization (below)
          or Waiver of Authorization (below)
          Waiver of Authorization not applicable

Approval of Waiver of Patient Authorization to Use PHI in Research. The IRB reviewed the proposed research and granted the request for waiver of patient authorization to use PHI in research, based on the following findings:
1. Use/disclosure of PHI involves no more than minimal risk to the privacy of individuals
   i. There is an adequate plan to protect the identifiers from improper use and disclosure.
   ii. There is an adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention that is otherwise required by law.
   iii. There is an assurance that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of PHI would be permitted.
2. The research cannot practicably be conducted without access to and use of the PHI.

Full Review
The IRB reviewed the proposed research at a convened meeting at which a majority of the IRB was present, including one member who is not affiliated with any entity conducting or sponsoring the research, and not related to any person who is affiliated with any of such entities. The partial waiver of authorization for screening was approved by the majority of the IRB members present at the meeting.

Date of Meeting

Signature of Chair, Vice-Chair or Designee

Date

Expeditied Review
The IRB used an expedited review procedure because the research involves no more than minimal risk to the privacy of the individuals who are the subject of the PHI for which use or disclosure is being sought. The review and approval of the partial waiver of authorization for screening was carried out by the Chair of the IRB, or by one of the Vice-Chairs of the IRB as designated by the Chair of the IRB.

Date of Expedited Review

Signature of Chair, Vice-Chair or Designee

Date