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Cephalometric analysis of craniofacial growth of a cohort of cleft lip and palate patients

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Ce mémoire intitulé :

Cephalometric analysis of craniofacial growth of
a cohort of cleft lip and palate patients
(Analyse céphalométrique de la croissance craniofaciale
d'une cohorte de patients atteints de fentes labio-palatines)

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Résumé

Chez les patients avec fente labio-palatine (FLP), la fermeture du palais primaire au moment de la labioplastie reste une pratique controversée à cause du risque d'interférer avec la croissance. Nous avons évalué la croissance maxillaire et craniofaciale chez un groupe de patients avec fente labio-palatine unilatérale complète (FLPUC) et nous les avons comparés avec un groupe témoin d'enfants sains ainsi qu'avec des données de la littérature.

Trente-quatre patients (19 M, 15 F) entre les âges de 7 et 20 ans, répartis en deux groupes, rencontraient les critères. Leurs radiographies céphalométriques latérales ont été tracées et analysées selon les méthodologies de Ross (1987) et Demirjian (1968).

Nos résultats montrent que pour les mesures linéaires indiquant les dimensions antéro-postérieures du maxillaire supérieur (PMP-ANS) et le développement vertical du maxillaire supérieur (N-ANS), les patients de notre cohorte sont relativement similaires aux enfants sains pairés par âge et sexe.

Pour les mesures angulaires, les patients de cette cohorte montrent plus de similarités avec des cohortes publiées pour les patients atteints de FLPUC : les valeurs de SNA et ANB indiquent un certain degré de rétrusion maxillaire. Cependant, la position maxillaire antéropostérieure reste comparable à ce qui est observé dans d'autre cohortes d'enfants atteints de FLPUC. On constate un patron de croissance plus verticale que chez les sujets normaux et qui s'accentue avec le temps.

La fermeture du palais primaire au moment de labioplastie ne semble pas avoir influencé négativement la croissance maxillaire chez ces patients lorsque comparés avec d'autres groupes d'enfants avec FLPUC.

Mots-clés : analyse céphalométrique, fermeture du palais primaire, fente labio-palatine unilatérale

Abstract

Closure of the primary palate at the time of early lip repair has remained an area of controversy because of the risk of interfering with growth. We assessed maxillary and craniofacial growth in a group of patients with complete unilateral cleft lip and palate and compared this group with healthy children and with data from the literature.

Thirty four patients (19 M, 15 F) between 7 and 20 years of age met the criteria. Lateral cephalograms were traced and analyzed according to Ross (1987) and Demirjian (1968).

Our results show that for linear measurements indicating anteroposterior maxillary dimensions (PMP-ANS) and vertical development of the maxilla (N-ANS), the patients in the cohort are relatively similar to normal children matched for age and gender.

For angular measurements, patients in this cohort show more similarities with reported cohorts of UCCLP patients: SNA and ANB values indicate some degree of maxillary retrusion. However, maxillary anteroposterior position is comparable to what is observed in other reported UCCLP cohorts. We find that there is a more vertical growth pattern in the UCCLP sample when comparing with normal subjects and that this difference accentuates with time.

Closure of the primary palate at the time of early lip repair did not seem to negatively influence maxillary growth when these patients are compared with other children with clefts.

Keywords: cephalometric analysis, primary palate closure, unilateral cleft lip and palate

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List of abbreviations

ANB	Angle between A point, Nasion and B point
ANS	Anterior Nasal Spine
Ar	Articulare
Ba	Basion
CLP	Cleft lip and palate
Co	Condylion
FH	Frankfort horizontal plane
FLPUC	*Fente labio-palatine unilatérale complète*
FMA	Frankfurt Mandibular plane Angle
Gn	Gnathion
Go	Gonion
ICC	Intra-class correlation coefficient
Me	Menton
MP	Mandibular plane
N	Nasion
NAM	Naso-alveolar molding
Or	Orbitale
P	Porion
Pg	Pogonion
PMP	Posterior maxillary point
PNS	Posterior Nasal Spine
Point A	Subspinale
Point B	Supramentale
PP	Palatal plane
PTM	Pterygomaxillare
S	Sella turcica
SNA	Angle between Sella, Nasion and A point
SNB	Angle between Sella, Nasion and B point
UCCLP	Unilateral complete cleft lip and palate
UCLP	Unilateral cleft lip and palate

Leave no stone unturned

-Euripides

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Chapter 1: Introduction

Cleft lip and palate is the most frequent congenital malformation in the craniofacial area. Numerous controversies surround the treatment of this malformation. In order to establish evidence-based treatment protocols, the study of treatment outcomes becomes essential. Every facet of treatment should be subjected to extensive research.

This study examined treatment outcome for a cohort of patients at Sainte Justine University Hospital Center. We note that our centre is among the few in North America that closes the primary palate at the time of lip repair. After studying data from 538 males with unilateral cleft lip and palate as well as treatment variables, Ross (1987) concluded that early soft tissue alveolus repair causes a deficiency in vertical growth. While Ross does not specifically address primary palate closure, it is still legitimate to ask: does repair of the primary palate at the time of lip repair also affect maxillary growth?

1.1 Specific goals

The aims of the present investigation were the following:

- Compare maxillary and craniofacial growth of UCCLP patients (treated at Sainte Justine University Hospital Center) with a cohort of healthy teenagers and children

- Characterize the growth of our patient sample over time

- Compare this cohort to other published data from the literature.

- Evaluate the outcome of the treatments our patients receive with regards to craniofacial growth by being able to quantify differences.

- Allow for future comparisons between our UCCLP group and other groups around the world.

1.2 Hypotheses

The following hypotheses will be explored in the present work:

- The treatment protocol used at Sainte Justine University Hospital Center (Montréal) which includes closure of the primary palate at the time of lip repair has a similar influence on craniofacial and maxillomandibular growth to other protocols in the world.

- There will be differences in hard tissue growth between the studied UCCLP sample and measurements obtained from lateral cephalograms of healthy French-Canadian subjects. The expected findings and differences are: greater maxillary retrusion, reduced anterior vertical maxillary growth and slightly smaller mandible in the cleft sample.

Chapter 2: Review of literature

2.1 Prenatal growth and development

The unilateral cleft lip and palate finds its origin in the embryological period. It is thus important to explore the causes that explain this intrinsic deformity to be able to distinguish it afterwards from the iatrogenic and functional factors that affect craniofacial morphology in patients with UCCLP.

2.1.1 The branchial apparatus

The branchial arches begin their development during the fourth week *in utero*, as a result of migration cells of the neural crest into the head and neck region. Arches I to VI start to appear in a cephalad to caudal sequence and form branchial clefts externally and branchial pouches internally (Proffit and Fields, 2001). This process is under the control of homeobox genes, which contribute to the position of future structures. These genes are all possible suspects for orofacial clefts

The first branchial arch, which is the mandibular arch, will divide into two separate processes: the maxillary and the mandibular prominences. The maxilla, zygoma and the zygomatic process of the maxilla originate from the maxillary prominence while the mandibular prominence will give rise to Meckel's cartilage. The muscles of mastication as well as the anterior digastric muscle, and the mylohyoid muscles all derive from the first branchial arch (Ranly, 1988).

2.1.2 Development of the skull and cranial base

The skull can be divided into three components: the neurocranium, the chondrocranium (cranial base) and the viscerocranium (facial skeleton).

The primary chondrogenic centers are the basioccipital, orbitotemporal, otic, and ethmoid regions. Endochondral ossification ensues to form the basicranial bones of the sphenoid, petrous temporal, and basioccipital.

The facial skeleton is subdivided into an upper third, predominantly of neurocranial composition and incorporating the orbits; middle third, incorporating the nasal complex, maxillae, zygomata, temporal bones, and ears; and a lower third, composed of the mandible.

Facial bones develop intramembranously from ossification centers in the neural crest mesenchyme of the facial prominences. During the third intrauterine month, centers appear for the frontal, nasal, lacrimal, palatine, zygomatic, and maxillary bones. Separate membranous centers appear for the medial and lateral pterygoid plates, the pterygoid hamulus, and the greater wing of the sphenoid bone. The squamous portion of the temporal bone ossifies intramembranously from a single center (Ranly, 1988).

2.1.3 Development of the face

The fourth and tenth week *in utero* will see substantial development of the human face (Ferguson, 1991; Johnston, 1997). The frontonasal and the right and left maxillary and mandibular prominences, which delimitate the stomodeum, will position themselves in this period. During this period, many processes will undergo fusion. It is a lack of complete fusion that will cause a cleft. Fusion between the facial processes occurs through adhesion of opposing epithelial layers which forms a junction which then degenerates by apoptosis and epitheliomesenchymal transformation (Ferguson, 1988).

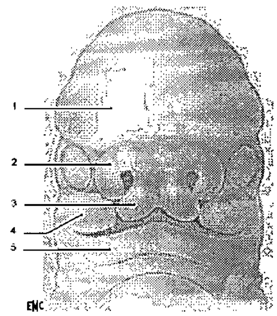

Figure 2-1 : Embryo at 7 weeks. **(1)** Frontal prominence; **(2)** Nasal lateral process; **(3)** Nasal medial process; **(4)** Maxillary prominence; **(5)** Mandibular prominence. (Reproduced with authorization from Pavy B *et al.* 1998)

The ends of the mandibular prominences will fuse to form the future mandible, lower lip and chin (Johnston, 1997). Shortly after, the epithelium layer of the frontonasal prominence forms the nasal placodes which will eventually disappear and form nasal pits (O'Rahilly and Muller, 1987).

Elevation of the lateral nasal prominences creates the alae of the nose. The medial tip of the maxillary prominence is initially separated from the inferior and lateral aspect of the median nasal prominence by an epithelial nasal fin that degenerates, allowing the maxillary mesenchyme to merge with the median nasal mesenchyme (Sperber, 2001).

The median nasal prominences are initially widely separated but they merge in the midline with an involvement of the premaxillary prominence, from which are derived the tip of the nose, the columella, the philtrum, the labial tuberculum of the upper lip, the fraenulum and the entire primary palate. The central premaxillary prominence is overgrown by the two lateral maxillary prominences. The philtrum and Cupid's bow shape of the upper lip form between the third and fourth intrauterine month. (Sperber, 2001)

Between the fourth and eighth weeks, the merging of cells between the medial nasal and maxillary prominence results in a continuous upper jaw and lips (Berkowitz, 2006).

2.1.4 Development of the palate

2.1.4.1 Primary palate

The primary palate or the premaxilla is the portion of the palate located anteriorly to the incisive foramen. Morphogenesis of the human palate depends heavily on a balance of genetic, hormonal, and various growth factors.

At the beginning of the 6th week, prominences extend bilaterally from the lower aspects of the medial nasal processes to form the primary palate (Ranly, 1988). The critical period for the formation of the palate is from the end of the sixth week through the eighth intrauterine week. Once the prominences are in contact, there is an apoptosis of epithelial cells along the contact area and there is a movement of crest-derived mesenchymal cells from one shelf to the other. This process of epithelial degeneration along with bridging between the shelves of mesenchymal cells is called fusion. Inadequate union of the prominence will lead to clefts of the lip with or without cleft palate (Dionisiopoulos and Williams, 1997).

The branchial arches begin their development during the fourth week *in utero*, as a result of the migration cells of the neural crest into the head and neck region. Arches I to VI appear in a cephalad to caudal sequence and form branchial clefts externally and branchial pouches internally (Sperber, 2001).

2.1.4.2 Secondary palate

The three elements that make up the secondary palate, the two lateral maxillary palatal shelves and the primary palate of the frontonasal prominence, are initially widely separated due to the vertical orientation of the lateral shelves on either side of the tongue. During the 8th week post conception, the position of the lateral shelves changes from vertical to horizontal as a prerequisite to their fusion and to division of the oronasal chamber. They fuse in the midline, forming the median palatine raphe above the dorsum of the tongue.

Ferguson (1991) says that the shelves possess an intrinsic elevating force which is substantial enough to be able to displace the tongue. This force is believed to be generated by the hydration of hyaluronan (Ferguson, 1988). At this moment, interferences that will cause a delay in palatal shelf elevation can lead to the formation of a cleft of the secondary palate. Almost simultaneously, growth of Meckel's cartilages promotes the positioning of the tongue in the developing mandible, while the maxilla continues to develop and moves forward. There is a resulting rotation of the future head upwards from the mandible and this further facilitates the retraction of the tongue away from the palatal shelves and allows their future fusion (Diewert, 1983).

2.1.5 Development of the dentition

Development of the dentition does contribute, albeit slightly, to craniofacial growth. It is often observed that edentulous patients have a more concave profile. It is also noted that dental development is often affected in patients with clefts. Teeth are derived from ectoderm and mesoderm (two of the primary germ layers), with a neural crest contribution. The enamel of teeth is derived from oral ectoderm, and neural crest tissue provides material for the dentine, pulp, and cementum. The periodontium is of both neural crest and mesodermal origin (Graber, 1966). Ectomesenchyme derived from the neural crest is the primary material of odontogenesis. A great number of genes associated with signalling molecules and epithelial-mesenchymal interactions are expressed in developing teeth (Sperber, 2001).

2.2 Postnatal growth and development

The principles that govern postnatal growth and development are key to understanding the growth and variations in craniofacial morphology as experienced by patients with UCCLP. In general, craniofacial growth proceeds in a cephalad to caudal sequence which means that the cranial base will attain its final size before the mandible. This has a direct influence on the evolution of the profile, as children will mostly have a convex profile and while they advance in age and their mandible grows, the profile will become less convex (Proffit and Fields, 2000).

2.2.1 Growth of the cranium, cranial base and orbits

The interface between the facial skeleton anteroinferiorly and the calvarial base determines the chondrocranial influence on facial growth. The sites of interface are clearly defined by the pterygomaxillary fissure and the pterygopalatine fossa, between the sphenoid bone of the calvarial base and the maxillary and palatine bones of the posterior aspect of the face. The zygomatic bone is attached to the calvarial skeleton at the temporozygomatic and the frontozygomatic sutures. The maxillary and nasal bones of the anterior aspect are attached to the calvaria at the frontomaxillary and frontonasal sutures. (Ranly, 1988).

2.2.2 Growth of the maxilla and nasal septum

According to the functional matrix theory (Moss and Salentijn, 1969), soft tissues, cavities and their functions all have an influence on growth. The eye, the nasal cavity, the nasal septum, and the external ear, situated along the approximate boundaries of the upper and middle thirds of the face, act as functional matrices to some extent in determining certain aspects of the growth pattern of the face. The tongue, the teeth, and the oromasticatory musculature are similarly interposed between the middle and lower thirds of the face, and their functioning also influences facial skeletal growth.

The nasal cavity and the nasal septum have considerable influence in determining facial form. In the foetus, the septomaxillary ligament awhich arises from the sides and anteroinferior border of the nasal septum and inserts into the anterior nasal spine, is believed to transmit septal growth to the maxilla.

Facial growth is directed downward and forward by the septal cartilage, which expands its vertical length seven times between the 10th and 40th weeks post conception. At birth, the nasal cavity lies almost entirely between the orbits. Growth of the nasal septal cartilage continues at a decreasing rate until the age of 6 years, lowering the nasal cavity floor well below the orbits (Sperber, 2001).

The thrust and pull created by nasal septal growth separate the frontomaxillary, frontonasal, frontozygomatic, and zygomaticomaxillary sutures to varying degrees. The growth potential of the nasal septal cartilage is clearly demonstrated in cases of bilateral cleft lip and palate: the tip of the nose, columella, philtrum, prolabium, and primary palate protrudes anteriorly (Ranly, 1988).

The maxilla grows downward and forward from the cranial base with growth occurring mostly at the interface with adjacent bones, which are the sutures. Remodelling also occurs at its external aspects (Enlow, 1990).

2.2.3 Growth of the mandible

Postnatally, mandibular growth will occur at the condyles and along the posterior and exterior surface of the ramus (Enlow, 1990). Resorption at the interior surface of the ramus and in the anterior edge of it will allow for tridimensionnal growth. As for the body of the mandible, it will exhibit complex remodelling where bone is resorbed in the anterior area (except for the mental area) and deposited in the external aspect (Enlow, 1990).

Growth at the condyles is possible through a different mechanism than in the rest of the mandible because of the presence of secondary cartilage. This allows endochondral conversion of cartilage into bone (Proffit and Fields, 2000). Condylar heads will grow upwards, outwards and backward, which leads to a downward and forward translation of the mandible (Enlow, 1990).

2.3 Classification of cleft lip and palate

Oral clefts may be classified on the basis of aetiology or pathogenesis. In 1922, Davis and Ritchie proposed a classification that divides clefts in three groups: prealveloar clefts, postalveolar clefts and complete clefts. In 1931, Veau proposed a four-category classification where clefts are divided between incomplete clefts of the palate, complete cleft of the palate, complete unilateral cleft lip and palate and complete bilateral cleft lip and palate.

In 1958, Kernahan and Stark proposed that the incisive foramen be used as dividing point between the primary and secondary palate. In 1971, Kernahan introduced the "striped Y logo" (Fig. 2-2). The two arms of the Y are each divided into three sections, representing the lip, alveolus and the primary palate back to the incisive foramen. The single section of the "Y" is also divided into three parts to account for the different degrees of clefting of the hard and soft palate.

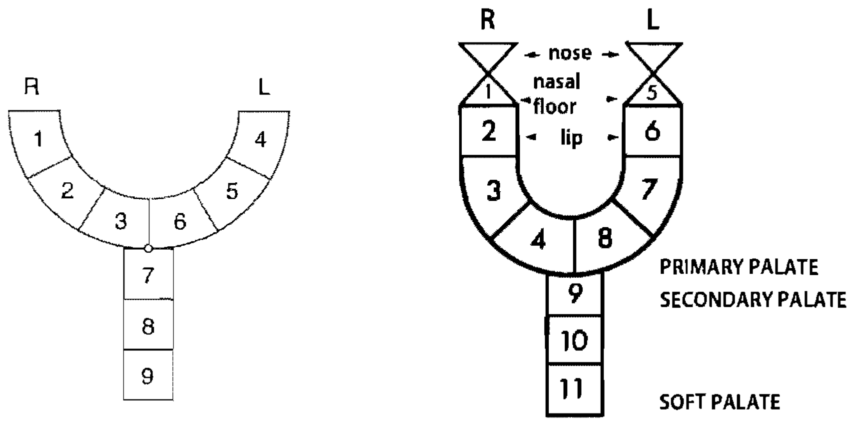

Figure 2-2 : Kernahan's diagram as published in 1971 (left) and as used in the Cleft Lip and Palate Clinic at Sainte Justine University Hospital Center (right).

2.4 Epidemiology of cleft lip and palate

Orofacial clefts (including but not limited to unilateral cleft lip and palate) are amongst the most common congenital malformations as they affect 1 out of every 600 newborn. Approximately 400 to 500 children with orofacial clefts are born in Canada each year (Kohut and Rusen, 2002).

The incidence of cleft lip and palate varies considerably between ethnic and racial groups. In the Caucasian populations, the incidence varies between 1.5 to 2.0 cases per 1000. Asian (Chinese) populations in Canada show a prevalence of 1.7 cases per 1000. Native Canadians have a prevalence of 3.7 cases per 1000.

If a sibling is already affected, the risk of being born with a CLP is 3 to 5 %. If a parent is affected, then the risk becomes 4% and if parents and children are already diagnosed, the risk rises to 10% (Kohut and Rusen, 2002).

2.5 Aetiology of cleft lip and palate

Cleft lip and palate can appear as an isolated defect or in association with other congenital malformations. When it presents in conjunction with a number of other manifestation, it is referred to as syndromic, whereas cleft lip and palate alone is referred to as non-syndromic. The present work will focus on non-syndromic clefts. Studies suggest that around 70% of cases of CLP are non-syndromic (Murray, 2002).

Fraser and Pashayan (1970) suggested that parental facial form might increase the likelihood of having a child with a cleft. However Mossey *et al.* (1998) have found, through a comprehensive review of the topic, that there is a lack of agreement on which specific craniofacial features are more likely to be a risk factor for cleft lip and palate. The merger of embryonic structures in the facial area depends on many developmental events, each of which might fall under the influence of genetic, environmental or a combination of both factors.

Facial shape in relatives of cleft patients
• All studies have found significant craniofacial differences between parents of children with clefts and the general population
• The most common findings are: greater lower facial height, increased interorbital distance, rotated mandibular position
• Many of the features that distinguish parents from controls also distinguish affected individuals from healthy individuals
• These findings support the existence of a multifactorial threshold inheritance in some cases and a purely environmental cause in others

Table I : Facial shape in cleft relatives according to Wyszynski *et al.* (2002).

A wide array of factors have been related to orofacial clefts, among them: smoking, alcohol, caffeine, benzodiazepines, and corticosteroids. There also appears to be an association between maternal smoking and oral clefting (Kallen, 1997). All these relationships need to be supported by further research.

The contribution of maternal nutrition has also been studied in diverse studies. Deficiencies in vitamin A, folate, vitamin B6 or exposure to plant toxins have been examined but these relationships remain unclear (Wyszynski *et al*, 2002).

Primary prevention with periconceptionnal supplementation with folic acid has shown a significant level of risk reduction (Itikala *et al.*, 2001, Tolarova *et al.* 1995, Shaw *et al.* 1995).

Shprintzen (1985) studied a sample of 364 cases of cleft lip and palate. He found that in 54% of cases, the origin was multifactorial, in 13%, it was monogenic (syndromic), in 3% it was teratogenic, in 3% of cases there was an association with a chromosomic anomaly, in 5%, a intrauterine perturbation or deformation and in 22%, the aetiology was totally unknown.

2.6 Treatment of cleft lip and palate

Patients with UCCLP will undergo a number of procedures, mostly surgical but also orthodontic, that will aim at correcting the initial dysmorphology. Cleft lip and cleft palate repair is done by the plastic and reconstructive surgeons. All along childhood, patients are followed to monitor normal physical, dental and psychological development. Speech rehabilitation also plays a central role (Berkowitz, 2006). Table II details the treatment regimen as performed at our Cleft Lip and Palate Clinic in Montreal.

Procedure	Timing
Cleft lip repair, anterior palate closure and nose repair	3-4 months
Cleft palate repair	12 months
Palatal expansion	8-10 years
Alveolar bone graft	8-12 years
Comprehensive orthodontic treatment	12-18 years
Orthognathic surgery	17 years and above

Table II : Treatment regimen performed at our Cleft Lip and Palate Centre.

2.6.1 Plastic and reconstructive surgery: technique used at Sainte Justine

While general surgical techniques are well described in the literature, each cleft centre has their own variations which makes comparative research arduous if one wants to assess a single factor. Our center is among the few centers in North America that closes the primary palate at the time of lip repair. This procedure has generated some controversy as similar procedures like early alveolus repair, periosteoplasty and early bone grafting have been shown to cause disturbance of maxillary growth (Ross, 1987). However, the patients in our cohort have no periosteoplasty, no alveolus repair and no early bone grafting

(Caouette-Laberge, 2007). Primary palate closure simply means that the area superior and posterior to the anterior alveolar ridge, but anterior to the incisive foramen, is closed using soft tissue flaps.

2.6.1.1 Lip repair and nasal correction

Our center uses the Millard rotation advancement lip repair (Millard, 1960, 1964, 1976, 1980) (Fig. 2-3). It is a widely used technique in many cleft centres and it can be easily adapted to narrow or wide clefts.

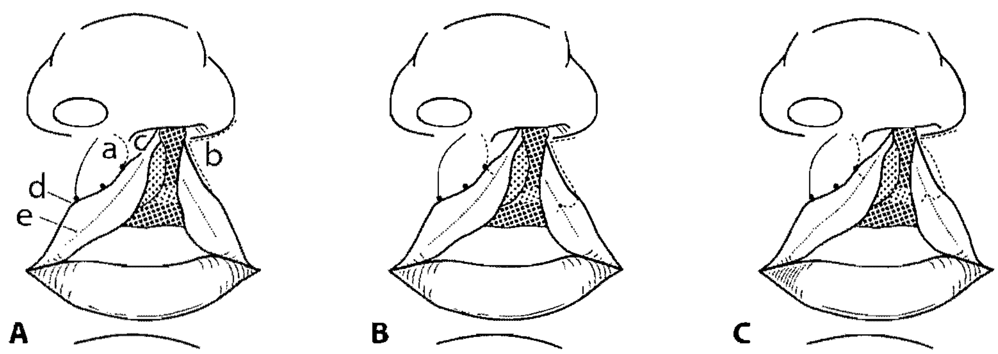

Figure 2-3 : Classic and modified Millard lip repair: **A** Classic Millard drawing with rounded medial rotation flap (a), lateral advancement flap with incision around the alar base (b), columella based flap (c), white skin roll and Cupid's bow (d), and red line (e). **B** Modified Millard drawing with straighter medial rotation flap and shorter incision at the base of the nostril. **C** Modified Millard drawing with straighter medial rotation flap, short back-cut on medial flap, and curved lateral flap with wider tip and short incision at the base of the nostril. (Reproduced with permission from Caouette-Laberge L, 2007)

On the lateral unit, Millard's original technique has also been modified to reduce the length of the incision around the base of the nostril (Fig. 2-3 B and C). The deforming force of the orbicularis oris on the nasal tip (lateral and superior pull on ala) is released by freeing the muscle from the alar base and the periosteum along the pyriform aperture (DeMey *et al.* 1989).

The key to the lip repair is the muscular reconstruction: the abnormal orbicularis muscle insertions on the nostril base, the columella and the maxilla are released and the muscule is realigned, to centralize the columella and lengthen the medial lip.

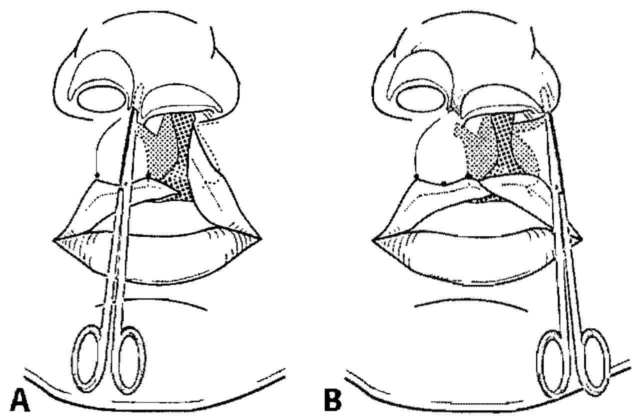

Figure 2-4 : Nasal correction A Subcutaneous dissection of the nasal tip with access through the medial skin incision. B Subcutaneous dissection of the nasal tip with access through the lateral skin incision. (Reproduced with permission from Caouette-Laberge L, 2007)

2.6.1.2 Medial side

A flap is raised from the mucoperichondrium of the nasal septum to close the primary palate (Fig. 2-5). This flap is based inferiorly on the limit of the cleft as originally described by Campbell (1922) and used extensively by Schmid. The width of this flap may vary according to the width of the cleft but does not need to be as wide as the cleft, because it will be sutured to a lateral mucoperiosteal flap reaching medially. When elevating the mucoperiosteum on the premaxilla, the mucosa over the alveolar bone is left intact to preserve the tooth buds and to keep a normal height of alveolar bone and sulcus along the cleft.

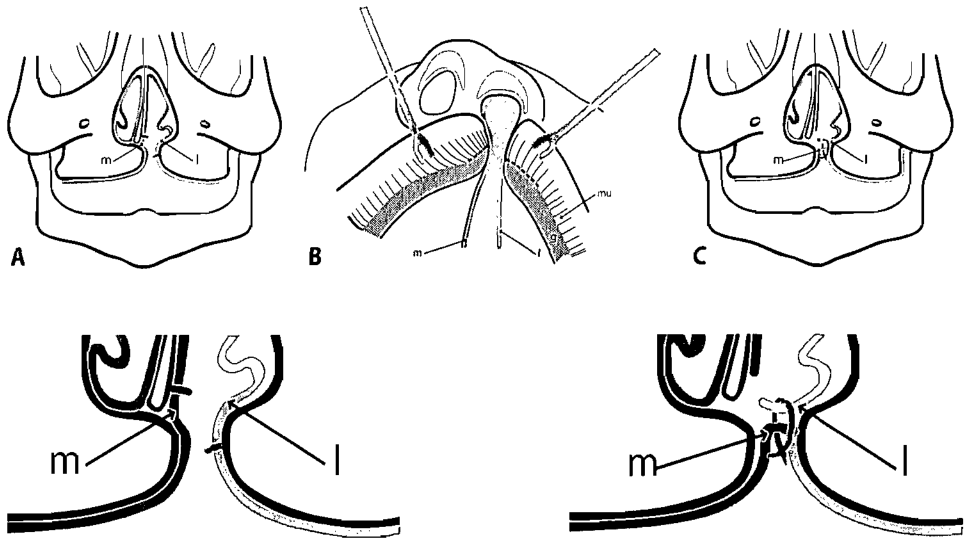

Figure 2-5 : Flap design A Incision of the medial vomer flap (m) on the nasal septum and incision of the lateral flap (l) along the cleft at the junction of the oral and nasal mucosa. B Incision of the medial and lateral mucosa (mu) in the sulcus adjacent to the gingiva (g). C Transposition of the medial (m) and lateral (l) flaps to obtain a two-layer closure of the primary palate (Reproduced with permission from Caouette-Laberge, 2007)

2.6.1.3 Lateral side

The incision of the mucosa and periosteum is continued posteriorly along the delimitation the cleft at the junction of the oral and nasal mucosa. A lateral mucoperiosteal flap (Fig. 2-5), based superiorly, along the pyriform aperture under the lower turbinate in the nasal cavity. This flap is advanced medially to narrow the pyriform aperture to a normal size and to provide a two-layer closure of the floor of the nose as it reaches under the surface of the medial mucoperichondral flap (vomer) (Fig. 2-5).

Subsequently, the pyriform aperture of the nasal cavity and the floor of the nose are closed to provide a stable base for the lip repair and to avoid an oronasal fistula (Figs 2-5). The medial inferiorly based vomer mucoperichondral flap is covered by the lateral superiorly based mucoperiosteal flap that is brought to close the floor of the nose and reach the midline. As opposed to the frequently used Veau technique (1931), in which the vomer flap is raised with a superior base, the Campbell inferiorly based vomer flap provides a two-layer closure of the anterior palate and pyriform aperture. The internal surfaces of the medial and lateral flaps slide, and are facing each other.

As the nostril floor closure reaches the premaxilla, the vomer flap is sutured to the lateral lip mucosa (Fig. 2-6) to provide for complete closure of the sulcus and avoid a vestibulo-nasal fistula.

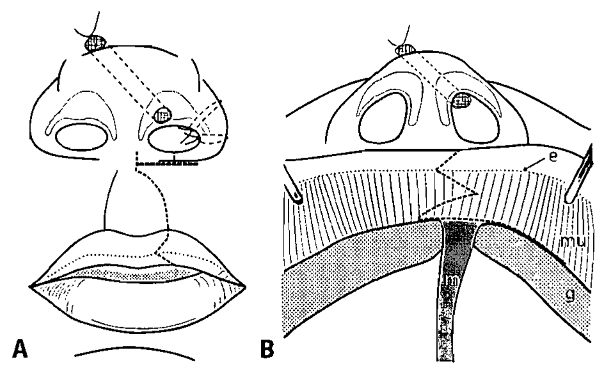

Figure 2-6 : Closure flaps : A Completed lip closure with insertion of the lateral vermilion flap to widen the medial vermilion, and nasal tip correction with traction suture. B Oral view of the closed primary palate and lip with mucosal flaps. e Red line; g Gingiva; m Medial flap; mu Mucosa. (Reproduced with permission from Caouette-Laberge, 2007)

According to Caouette-Laberge (2007), the result obtained at the completion of the procedure remains stable with growth, and, if the structures have been meticulously aligned, revisions are rarely necessary.

The posterior cleft palate is closed later which leaves no anterior fistula. A bone graft is secured in the alveolar cleft during the mixed dentition stage. Because the soft tissues of the primary palate have already been closed at the time of lip repair, the bone graft is simply inserted under the flaps (Caouette-Laberge, 2007).

2.7 Growth and morphology in individuals with cleft lip and palate

All patients affected with unilateral cleft lip and palate (UCLP) have a face that differs from the norm, whether they had corrective surgery or not. Some of the deformity will be caused by intrinsic anomaly which can be very noticeable in treated and untreated populations (Table III).

Before looking at growth and development of cleft lip and palate patients, we will try to identify the initial characteristics present in these individuals and establish how they affect all the components of the craniofacial skeleton. Afterwards, we will look into the effects of therapy on growth.

In terms of soft tissue anomalies in patients with UCCLP, it is found that the fibers of the orbicularis oris are interrupted by the cleft lip and are inserted on the nasal structures (Kernahan *et al.* 1984, DeMey *et al.* 1989). This causes a distortion of the nasal tip. Asymetry in nostrils is therefore invariably present in all patients with UCCLP (Berkowitz, 2006). The cleft palate will affect the soft palate musculature. The divided levator palatini is not able to contribute correctly to speech and velopharyngeal function. These soft tissue deformities directly affect the functional matrices of the craniofacial area which results in altered craniofacial growth because of altered function. Another factor that comes into account is iatrogenic consequences of surgical interventions, especially scarring in the hard palate area which is believed to affect maxillary growth (Ross, 1987, Leenstra *et al.* 1995).

Craniofacial anomalies in patients with UCCLP (Hermann, 2000)
Decreased length of maxilla (ANS-PMP)
Retrusion measured at the premaxilla area (reduced SNA)
Decreased posterior length of the maxilla
Decreased posterior height of the maxilla
Increased width of the maxilla
Increased width of nasal cavity
Decreased length of mandible
Mandibular retrognathia

Table III : Summary of primary anomalies in UCCLP according to Hermann (2000).

2.7.1 Morphology of untreated patients

In order to evaluate the effects of surgical treatment on growth of UCCLP patients, it is necessary to determine the intrinsic characteristics that are directly related to the cleft deformity. This can only be done by assessing unoperated patients. It is a research area that has proved difficult to study and there are still many ongoing controversies (Berkowitz, 2006).

In order to know the effect of the cleft on the final development of the maxilla, it is necessary, according to McCance *et al.* (1990), to examine adult patients with an unoperated cleft lip and palate and compare them with non-cleft controls of the same racial group. They state that many researchers have tried to do so, but that the results of most studies have been compromised by a small sample size, heterogeneity of the sample, and inclusion of partially operated cases along with true unoperated cases. An ideal study should include a sufficiently large sample of patients from the same ethno-racial group who have different types of clefts and have reached maturity without any treatment.

However, data on adult patients with clefts who have not undergone surgery at all is extremely rare. These patients are found only in remote areas where medical care for patients with clefts is not available. Often in these areas, because of harsh living conditions, only some of the individuals born with severe clefts will reach maturity (Mars and Houston, 1990).

An study of unoperated adult patients with clefts was presented by Ortiz-Monasterio *et al.* (1959), from Mexico, whose sample included 18 unoperated adult unilateral cleft lip and palate individuals. They found that the initial embryonic cleft deformity did not interfere with maxillary growth. They concluded that the growth defect often seen in the middle third of the face is definitely caused by surgery. For them, key determinants are: surgery performed too early, repeated surgical procedures and aggressive surgical technique.

In 1959, Law and Fulton presented a study on unoperated patients but their sample was not exclusively unoperated: it also included patients who had previously undergone lip surgery. Only 7 of the 47 patients included in the study did not undergo surgery. The remaining 40 had undergone lip surgery long before the investigation. The results of this study showed normal mandibular and maxillary growth.

Mestre *et al.* (1960) presented a sample of 49 unoperated patients with clefts. However in this study, fully unoperated patients were analyzed together with patients who had undergone lip surgery. In their sample, 27 patients had an unoperated unilateral cleft lip, alveolus and palate. However, 21 of these 27 patients had had an earlier lip repair and only 6 of them had not been operated at all. In fact, 3 groups of patients were combined and analyzed as one entity. They found reduced maxillary length relative to mandibular length.

In 1962, Innis presented a report on 50 patients with cleft lip and alveolus or cleft lip, alveolus and palate, who had reached developmental maturity without having undergone any surgery in infancy or childhood. These patients were studied cephalometrically and the author compared them to a control group taken from the same population and found that only 20% of UCCLP patients had maxillary retrusion.

In another article, Ortiz-Monasterio *et al.* (1974) studied 450 patients with a cleft lip and palate treated in late childhood or in adulthood. It is difficult to say how many truly unoperated individuals with various types of clefts were included in this study. This study found evidence of a protrusive premaxilla and higher SNA.

Bishara *et al.* (1976) performed a study on unoperated adult patients with clefts which were compared to each other and to a matched sample of normal individuals. Twelve individuals with unoperated unilateral clefts of the lip and palate and eight with unoperated unilateral clefts of the lip and alveolus were examined clinically and cephalometrically. All subjects were examined in India. Based on the findings of this investigation, it is suggested that, in general, the cranial base is not affected in individuals with unoperated unilateral clefts of the lip and palate when compared to matched healthy controls. Yet, there were distinct differences in dentoalveolar and skeletal relations as UCCLP patients were found to have a smaller mean SNA angle.

More recently, Mars and Houston (1990) and McCance *et al.* (1990) also presented studies of unoperated adult patients with clefts. McCance *et al.* (1990) considers that the small sample size, the heterogeneity of the population (grouping different cleft types together), the combining of partially operated cases with fully unoperated cases, wide age ranges are substantial weaknesses of most of the studies. However, in the more recent articles, the number of patients analyzed as well as the quality of the analysis and therefore the results of the studies are more reliable than in earlier articles.

Mars and Houston (1990) looked at 60 patients with clefts in Sri Lanka. Twenty-eight were unoperated, 18 had lip but not palate repair, and 14 had both lip and palate repaired. The patients with totally unoperated clefts had a larger SNA angle than noncleft controls, those with repaired lips had angles slightly smaller than normal, but those patients with repaired lips and palates had SNA angles markedly smaller than normal.

In 2006, Shetye *et al.* studied 30 unoperated patients with UCCLP and found that their maxillae were normal in size and slightly prognathic in position. They also noted that their mandibles was smaller in size and posteriorly positioned. It appeared to them that the potential for normal growth of the maxilla existed in patients with UCCLP. They conclude that it is likely that disturbances of maxillary growth in surgically operated patients with clefts are primarily iatrogenic.

In a study of 32 adult patients with unoperated UCLP, Diah *et al.* (2007) showed that they had an intrinsic tissue deficiency. However, their sagittal development was still comparable to that of a normal population. They have also showed that tissue deficiency mostly occurs in the anterior part of the maxilla.

Many studies have shown that craniofacial morphology in children, adolescents and adults with cleft lip and palate deviates from the norm (Dahl *et al.* 1982). Investigations have shown that the morphological anomalies are not limited to the maxillary complex and deviations are also present in the mandible, the calvaria, the cranial base, the orbital region and even as far as the bony naso-pharynx.

2.7.1.1 Naso-maxillary morphology in untreated patients

In cleft lip and palate patients, we observe a deviation of the maxilla, along with the nasal structures in general and the nasal septum. Abnormal muscle insertions of cheek and lip muscles are observed at the base of the nose, causing a rotating force on the larger bony segment during muscle contraction. It is often reinforced by tongue protrusion into the alveolar cleft (Ross and Johnston, 1972). Absence of restriction of nasal septum growth was also believed to be a possible cause of this distortion (Latham and Burston, 1964).

As early as the embryonic stage, Latham (1969) notes that the nose is displaced towards the non-cleft side by muscle function while the alar base on the cleft side is not, resulting in asymmetrical nostrils. In untreated UCLP patients, we also often find a tendency for wide nasal cavities (Atherthon, 1967, Farkas *et al.*, 1993).

The functional disequilibrium results in a visible deviation of the nasal septum. This deviation is directed toward the non-cleft side (Fig. 2-7) and is greater with increasing cleft sizes (Bayerlein *et al.*, 2006). The anterior nasal spine is displaced towards one side as the whole maxillary complex is often asymmetrical but not hypoplastic. Symmetry of the upper arch is also affected as the segments adjacent to the cleft are often misaligned.

Figure 2-7 : Effect of functional forces on cleft lip and palate deformity. Separation in the orbicularis oris, the buccinator and the superior constrictor muscle ring cannot counter the lingual forces and causes the lesser segment and the premaxillary portion of the larger segment to be pushed apart. (Based on a drawing by J.D. Subtelny, reproduced with authorization from Berkowitz S, 2006)

2.7.1.2 Mandibular morphology in untreated patients

According to some authors, the mandible in UCLP patients is retrognathic when compared to the cranial base (Graber, 1954, Dahl, 1970, Hayashi *et al.* 1976, Smahel and Müllerova, 1986, Dahl *et al.*, 1989, Capelozza *et al.*, 1993, da Silva Filho *et al.* 1993, Friede and Lilja, 1994, Han *et al.*, 1995).

Studies that have compared untreated UCLP patients to noncleft subjects found that UCLP patient have a reduced mandibular body and ramus height, mandibular retrusion, and a higher mandibular plane angle (Bishara *et al.*, 1976, Mars and Houston, 1990, Capelozza *et al.*, 1993).

In 1989, Dahl *et al.* suggested that there might be an intrinsic link between retrognathia and a cleft that affects the secondary palate. According to a few studies, UCLP patients present with a retrusion and clockwise rotation of the mandible (Treutlein *et al.*, 2003), even if it is not directly involved in the defect.

An increase of the gonial angle has been reported in a few studies (Dahl, 1970, Capelozza *et al.* 1993, da Silva Filho *et al.* 1993, 1998). According to da Silva Filho *et al.* (1993), clefts that involve the palate result in a downward and backward rotation of the mandible which can be correlated with an increased gonial angle along with shorter mandibular bodies and ramuses.

2.7.1.3 General facial shape in untreated patients

Ross and Coupe (1965) showed that the whole face is slightly wider in children with clefts. Other authors even talk about hypertelorism (Graber, 1949; Psaume, 1957; Ross and

Coupe, 1965; Farkas and Lindsay, 1972). The arch widths seems to be greater as illustrated by measurements of dental casts of the newborn (Harding and Mazaheri, 1972), which is likely to be because of functional factors. A key question that remains unanswered is: Is the face wider because of the presence of a cleft or is there a cleft partly because of the larger facial phenotype?

2.7.1.4 Morphology of the cranial base and calvaria in untreated patients

Ross (1965) found that although the proportions of the cranial base were similar when comparing UCCLP and healthy subjects, the entire cranial base was smaller in UCCLP patients, proportionally to the smaller size of the children studied. Dado and Kernahan (1986) have reported that in unoperated cases, considerable variations in craniofacial morphology are seen in newborn children with clefting. Variation in the dimensions and shape of the cranial base has been described (Horswell and Gallup, 1992). Most studies have concentrated on the cranial base viewed from the lateral aspect. Moreover, the spheno-occipital synchondrosis has been found to be wider in a study of 57 3-month old children with complete clefts of the lip, alveolus and palate compared with 3-month old children with minor incomplete clefts of the lip (Mølsted *et al.*, 1993). In a study of 28 patients, Silva Filho *et al.* (1998) have suggested that both the anterior and posterior cranial base are reduced in unoperated adult UCLP patients.

2.7.1.5 Dental anomalies and malocclusions

Patients with UCLP will often present with dental anomalies such as early or delayed eruption, morphological and dimensional abnormalities, as well as hyperdontia or hypodontia (Bohn, 1963; Kraus *et al.*, 1966; Ranta, 1986). The incidence of dental anomalies varies a lot because it is difficult to distinguish between the congenital and iatrogenic causes of these anomalies. The anomalies tend to be more concentrated along the cleft area (usually the lateral incisor zone). However, in general, all these anomalies are more prevalent in UCLP patients than in the normal population (Berkowitz, 2006).

Often these patients present with dental anomalies starting at birth with a 2.02 % incidence of natal or neonatal teeth incidence, compared with 0.05% for the control group (de Almeida and Gomide, 1996).

Outside of the cleft area, it seems that hypodontia tends to be more prevalent than hyperdontia (Bohn, 1963; Nagai *et al.*, 1965; Fishman, 1970; Ranta, 1986; Suzuki and Takahama, 1992). The incidence of supernumerary teeth is greatest in cases of cleft lip only and decreases as the extent of the cleft increases. For aplasia, its incidence follows an opposite course, increasing with more complex clefts (Brook, 1984).

Dental development is delayed for all teeth except third molars. Asymmetrical development of tooth pairs (with delayed eruption on the side of the cleft) was seen in about half of a group of children with orofacial clefts. This is consistent with other observations that eruption is delayed in both dentitions (Ranta, 1973).

2.7.2 Morphology of treated cleft lip and palate patients

Apart from embryonic distortion, intrinsic growth deficiency and functional adaptations, facial growth in cleft lip and palate patients is likely to be affected as a consequence of surgical repair of the palate and orthodontic treatment (Graber, 1949, Ross, 1987).

There is a considerable discrepancy among studies concerning the group of patients that will present with a maxillary growth deficiency. Levin (1963) reports that this happened in 29.6% of 314 adult patients he studied at his center. Maxillary growth deficiency was defined as SNB being greater than SNA when measuring the anteroposterior length of the maxilla.

The largest studies are a article by Graber (1949) that documented severe three-dimensional maxillary collapse in adult patients with complete clefts following surgical repair of the lip and palate, and a study by Dahl (1970) evaluating the craniofacial morphology of 272 adults operated for different types of clefts. Both reported similar findings. These authors also showed that the affected maxillary growth is likely to influence the physiological growth of the mandible.

Aduss (1971) evaluated 50 males and 21 females with UCLP between the ages of 4 and 14 years. He found that growth in males and females was similar. He found that the gonial angle was larger in the cleft patients and that the mandible was retrognathic.

Hayashi *et al.* (1976) studied craniofacial growth using lateral cephalograms in 135 males and 120 females between the ages of 4 and 18 and found that growth in cleft patients was more vertical, that their cranial base was more flat, that their maxilla was smaller and more posterior and upward and that ramus height was smaller.

Smahel and Müllerova (1986) studied 30 males with UCLP and found that when compared to normal subjects, they had a shorter mandible and a retropositionned maxilla. In 1996, Smahel and Müllerova studied 22 males and 23 females with UCLP and found higher maxillary retrusion and flattening of the face as growth progressed. The difference was more significant in males.

According to Ross (1987), the average individual with a UCLP who underwent surgical treatment had an anteroposterior midface deficiency of 5 to 6 millimetres at the adult age. Data from almost all cephalometric studies support this conclusion (Rygh and

Tinlund, 1996). Most studies note that the anterior maxilla is retrusive and shorter relative to the cranial base, and this finding deteriorates with age (Ross, 1987).

Ross (1987), from the Hospital of Sick Children in Toronto studied a sample of 1,600 cephalometric radiographs of 538 males with complete unilateral cleft lip and palate. These radiographs came from 15 cleft centers around the world. The aims of the study, divided in seven parts, were to determine the effects of treatment protocols on facial growth in children with UCCLP. This article shows that UCCLP patients have a general retrusion of the profile, involving the maxilla and the mandible. They were found to have a shorter mandible, an open mandibular plane angle and lowered chin. In terms of vertical dimensions, they have a decreased vertical height and increased lower face height associated with a more open mandibular plane angle. Depending on where treatment was administered, there were wide variations in outcome. However, even where growth had been excellent, the observed differences with normal patients were essentially the same as those listed above, but to a lesser degree.

Horswell *et al.* (1988) did a follow-up study of skeletal growth in 16 UCLP patients and compared them to normal controls. He found that anterior cranial base, upper and lower face heights, maxillary horizontal length were all smaller in the UCLP group. However he found that mandibular length was normal.

Semb *et al.* (1991) did a serial cephalometric study that involved 76 males and 81 females with UCCLP treated in Oslo. Compared with normal controls, he found that the patients with clefts had skeletal and soft tissue retrusion, elongation of the anterior face, retrusion of the mandible, reduction of the posterior facial height and a slight increase in the angle of the cranial base.

Hermann *et al.* (2000) analyzed and compared the craniofacial morphology of 22-month-old children after the cleft lip and anterior part of the palate had been surgically closed at 2 months of age with cleft lip controls. Comparison of the post-operative craniofacial morphology with the control group indicated that the posterior height of the maxilla was still diminished. The mandible was still short and retrognathic with bimaxillary retrognathia. The lateral segment of the cleft moved toward the mid-sagittal plane resulting in a narrow dental arch at the level of the deciduous canine and the first molar.

Post-operative craniofacial growth in unilateral complete cleft lip and palate was similar to the controls (unilateral incomplete cleft lip), with normal growth potential observed in all craniofacial regions except where the growth had been influenced by surgical intervention. However, the mandible and maxilla showed a more vertical growth pattern than that observed in the control group. This research suggests that individuals with complete cleft lip and palate deviate may be more affected than those with incomplete clefts (Hermann *et al.* 1999).

A few experimental animal studies have shown that cleft repair can result in mandibular growth disturbance in morphology and spatial position (Bardach *et al.*1979, 1980; Bardach *et al*, 1984). Some clinical studies have examined the effect of various treatment regimens on the mandible but the results are not conclusive as far as showing the influence of surgical treatment on the mandible (Ross, 1987, 1995; Brattström *et al.*, 1992; da Silva *et al.*, 1992, 1993, 2001; Smahel and Müllerova, 1994; Capelozza *et al.*, 1996; Trotman *et al.*, 1996).

Besides the underdevelopment of the maxilla, the position of the alveolus and teeth is often inadequate. The dentoalveolar discrepancy is of course most clearly visible in the patients with clefts who have not yet undergone any orthodontic treatment. There is a lateral compression of the alveolar parts of the maxilla resulting in anterior or posterior crossbite, severe crowding of the teeth, especially in the premolar area (Ross, 1987).

As discussed before, the missing teeth frequently observed outside the cleft area accentuate both the retrusion of the maxilla and the relative shortness of the maxillary dental arch (Bohn, 1963; Olin, 1964; Lekkas *et al.*, 2000; Lekkas *et al.*, 2001). Orthodontic has an important role in the prevention and treatment of maxillary arch collapse and in the alignment of the teeth. However, there is a considerable relapse tendency even after successful orthodontic treatment.

In the subsequent pages, the following surgical procedures and their effect on maxillofacial growth and maxillary arch dimensions in UCLP patients will be outlined: primary periosteoplasty, primary bone grafting, lip surgery, palatal surgery, and early secondary bone grafting.

Individuals with a surgically repaired complete unilateral cleft lip and palate have a profile and growth that deviates from the noncleft individual. There is enormous variation in facial growth in children with a repaired cleft lip and palate that can be attributed to the racial and familial genetic background, the type of cleft, and the nature of the surgical and orthodontic management received. Often, adolescents and adults will present with abnormal facial morphology and it seems that the cause is mainly iatrogenic.

2.7.3 Effect of presurgical orthopedics and early orthodontic treatment

Presurgical orthopedics can be divided between active (Latham's) and passive appliances (nasoalveolar molding plates). Although no presurgical infant orthopedic procedures were used in the studied sample, they are used extensively around the world. Three out of the five groups in the Eurocleft study (Brattsröm *et al.* 2005) used this treatment modality. Many publications seem to show that presurgical orthopedics has no lasting effect on facial growth and on the maxillary dental arch (McNeil, 1950; Hotz and Gnoinski, 1979; Ross, 1987; Kramer *et al.*, 1994; Larson *et al.*, 1993; Ross and McNamara, 1994; Ball *et al.*, 1995; Joos, 1995; Winters and Hurwitz, 1995; Kuijpers-Jagtman and Prahl, 1996; Kuijpers-Jagtman and Prahl-Anderson, 1997; Kuijpers-Jagtman and Long, 2000). The orthopedic appliances currently used have not shown that they can accomplish permanent growth modification.

As for early orthodontic treatment in the primary or mixed dentition, it does not seem to offer an added benefit (Ross and Johnston, 1967). Permanent therapeutic growth modification during early treatment seems now to be the exception rather than a predictable outcome (Tindlund, 1989, 1994, Ishikawa *et al.* 2000). Face masks to protract the maxilla have been shown to create a minimal amount of advancement (Sarnäs and Rune, 1987). While some have used this device extensively, with some success (Rygh and Tindlund, 1995) others have found that its benefits are temporary only (Ross, 2001).

2.7.4 Effect of labial and nasal surgical reconstruction

In an attempt to minimize the long-term effects on growth of the maxilla, different approaches have been proposed for the surgical interventions aiming at closing the labial, alveolar and palatal defects. In most if not all centers around the world, the first surgical procedure in the postnatal period is usually the reconstruction of the cleft lip and nose. Its goal is to provide more normal functional forces on the maxilla by establishing continuity of the skin, fascia and muscles.

The influence of lip closure on the growth of the facial skeleton remains controversial. Maxillary retrusion and hypodevelopment is a typical feature of many patients with clefts of the lip and palate. Most patients with unrepaired cleft lip and palate do not have this retrusion. This was confirmed by Mars and Houston (1990) in their study with Sri Lanka unoperated subjects. Many researchers considered that palatal closure is the only reason that explains midfacial retroposition although lip repair may also have an influence on the upper front teeth and the alveolar bone but not on the development of maxilla (Pruzansky, 1955; Mazaheri *et al.*, 1971; Wada and Miyazaki, 1975; Ross, 1987, Kramer *et al.*, 1994; Ball *et al.*, 1995).

However, other researchers like Herfert (1958) and more recently Bardach *et al.* (1984) believe that lip repair has a negative effect on maxillary growth. It is noted that it is difficult to separate the effects of palatal closure and labial closure because both operations are performed during the first 2 years of age, when growth disturbances are not visible until many years after the surgical interventions.

Li *et al.* (2006) studied cephalometric radiographs and photographs of patients with a complete unilateral cleft of lip and palate in whom only the lip had been repaired during infancy. It was thus possible to isolate the impact of the lip repair alone on maxillary growth and development of the facial soft tissue. This team found that there was more maxillary retrusion in the cleft samples and that lip height and projection were reduced.

2.7.5 Effect of early cleft repair and lip repair

Many surgeons think alveolar repair should be performed along with labial repair. The rationale behind this idea is that when closing the alveolar cleft, a favourable relationship between maxillary segments would occur and would improve growth potential. Sameshima *et al.*, (1996) and Smahel *et al.*, (1996, 1998) have published articles that show that this approach has a negative influence on maxillary growth. However, other studies show satisfactory maxillary growth even when primary bone grafts are performed (Rosenstein *et al.* 1982, Nordin *et al.* 1983). Skoog (1965) described a technique for primary repair of the alveolar cleft using a periosteal flap to create bone continuity over the alveolar cleft defect. This technique is usually used at the time of lip repair but can also be delayed until when the patient is between 2 and 10 years. Other studies confirm that outcome for facial growth is less favourable in patients subjected to periosteoplasty at a young age compared with those who had delayed periosteoplasty (Hellquist *et al.*, 1983; Hellquist and Svärdström, 1986).

Smahel and Müllerova (1994, 1995) studied infant periosteoplasty and found that the use of a narrower periosteal flap produced less extensive exposure of the anterior maxilla. However, when evaluated at 15 years of age patients still showed a marked maxillary retrusion with a flattening of the face, a discrepancy of sagittal jaw relationship and a reduction in upper lip prominence (Smahel and Müllerova 1994, 1995).

In order to achieve presurgical approximation of segments, some groups advocate the use of NAM appliances (Cutting and Grayson from New York University) while others are in favour of active appliances (like Matic and Latham from London, Ontario). In recent years, conflicting results on the gingivoperiosteoplasty technique have been reported by Berkowitz (1996), Henkel and Gundlach (1997), Lukash *et al.*, (1998), Santiago *et al.* (1998) and Millard *et al.* (1999) and the debate is still ongoing. Recently, Sato *et al.* (2008) reported that gingivoperiosteoplasty alone or combined with secondary alveolar bone grafting results in superior bone levels when compared with conventional secondary alveolar bone grafting alone. However, this study did not assess maxillary growth *per se.*

2.7.6 Effect of primary bone grafting

Depending on the age at which it is performed, the procedure will be termed primary and secondary bone grafting. Primary bone grafting takes place around the time of lip repair, while secondary bone grafting refers to the filling of the alveolar cleft defect later in the mixed dentition.

Primary bone grafting is performed in some cleft centers in order to prevent relapse or collapse of the maxillary segments and to create the possibility to orthodontically move teeth or place implants into the cleft area.

Primary bone grafting was first used in the late 1950s (Nordin and Johansson, 1955; Schmid, 1955). Many centres started to report midfacial growth inhibition in the 1970s and stopped using primary bone grafting (Friede and Johanson, 1982; Pfeiffer, 1986; Lilja *et al.*, 1996; Smahel *et al.*, 1998). However, a few centers like Kernahan and Rosenstein continued to use this technique and claim that the timing and surgical aspects of the placement of the bone graft are critical to its success (Kernahan and Rosenstein, 1990).

2.7.7 Influence of palatal surgery

Usually, the cleft in the hard and soft palate is closed at an early age, before the child starts its speech development. Some authors (Malek *et al.*, 1986; Witzel *et al.*, 1984) think that early closure is important for optimal speech development. However, a study by Prahl-Anderson and Ross (1997) revealed that delayed palate repair at about age 8 had superior midfacial growth but that this advantage was definitely lost by age 12. According to Ross (1987) the timing of hard palatal repair does not matter within the first decade. Many authors express reservations about delaying surgery past the age of early speech development (Dorf and Curtin, 1982; Witzel *et al.*, 1984; Rohrich *et al.*, 1996).

The operation for closure of the hard palate is generally considered to be the key factor in the development of dentoalveolar and facial growth disturbances. Palatal surgery may have a minor short-term effect on palatal growth but as growth in the posterior region continues until maturity, the restricting effect of palatal surgery on the three-dimensional growth of the maxilla may be considerable. Therefore, in an attempt to minimize the effect of palatal surgery on the growth of the cleft maxilla, surgical closure of the hard palate is postponed as long as possible in some treatment protocols (Schweckendiek, 1951, 1978; Krause, 1976; Friede and Johanson, 1982; Bardach *et al*, 1984 (the Marburg study), Capelozza Filho *et al.*, 1996). Not all authors, however, consider hard palate surgery to be the most important factor in the collapse of the maxillary segments. Da Silva Filho and Capelozza (1989) affirm that the influence of palatal surgery on the dentofacial morphology of the patient is minimal and statistically insignificant whereas the role of lip closure is of paramount importance.

The factors underlying the deficient growth of the maxilla are controversial. Some authors attribute it to the presence of the cleft itself. Others believe that the deficient growth is the result of the primary surgery, resulting in formation of scar tissue at the lip, and soft or hard palate level affecting normal growth of the maxilla (Dahl, 1960; Schweckendiek, 1978; Spauwen *et al.*, 1993). In general, most authors agree that palatal surgery appears to have a significant restrictive influence on the sagittal, vertical, and transversal development of the maxilla.

2.7.8 Effect of palatal expansion and secondary bone grafting

In preparation for secondary bone grafting, palatal expansion pursues the goal of obtaining an adequate transverse dimension by expanding the posterior segments (Åbyholm *et al.* 1981). This may also widen a pre-existing fistula, but not create one *de novo*. A larger expansion widens the defect between the 2 segments and provides for better access during surgery. The secondary bone graft provides the best opportunity to close any remaining fistula in the area. Post-expansion retention is always necessary until the bone graft is well incorporated and stable because the grafted bone is not likely to prevent relapse.

Secondary bone grafting has become a commonly used procedure to repair the alveolar bony defect. This method was introduced by Boyne and Sands (1972) and consists of grafting bone in the cleft area prior to the eruption of the permanent canine. The advantages of restoring the alveolar ridge are numerous: support for the teeth bordering the cleft, which stabilizes the maxillary segment, eliminating the notched aspect of the alveolar ridge, and even supporting the alar bases of the nose (Åbyholm *et al.* 1981, Long, 1995). Results for bone grafting are better before canine eruption, and worse after growth complete as demonstrated by Daskalogiannakis and Ross in 1997.

Ross (1987) found that patients grafted between 4 and 10 years of age showed an important deficiency in anterior upper facial height at 15 years of age when compared to ungrafted patients. In the same study, it appears that grafting between 9 and 13 years of age did not have such an effect. Brattsröm *et al.* (1991) compared 85 patients with UCCLP treated in three different centers using four different protocols. They found that the regimens that included primary or early bone grafting in the alveolar area created inhibition of anterior maxillary growth. Regimens that involved secondary bone grafting resulted in much better outcomes but still less than regimens that involved no bone grafting at all. Semb (1988) found no statistically significant differences in either anteroposterior or vertical maxillary growth when comparing children who had received alveolar bone grafts between 8 and 12 years of age and those who did not. In recent studies, Daskalogiannakis and Ross (1997), and Levitt *et al.* (1999) all present evidence of adequate growth after secondary alveolar bone grafting.

2.7.9 Effect of comprehensive orthodontic treatment

Before they reach the adolescent growth spurt, cleft lip and palate patients usually start comprehensive orthodontic treatment. It is also a moment when pre-existing skeletal discrepancies becomes more accentuated and occlusal relationships often deteriorate. Typically, UCLP patients will have a tendency towards sagittal and sometimes vertical maxillary deficiency and mandibular prognathism (Kuijpers-Jagman and Long, 2000, Will, 2000). Decisions the orthodontist faces are either to attempt to obtain favourable occlusal relationships without surgery or to orient the case towards orthognathic surgery. (Berkowitz, 2006) Sometimes, orthognathic jaw relationships can be obtained by increasing the vertical dimension by rotating the mandible downwards and back. Alterations in the axial inclination of teeth might achieve camouflage in borderline cases. If surgery is required, decompensation will become necessary as both arches have to be corrected to ideal relationships so that the skeletal bases can be displaced.

Chapter 3: Materials and methods

3.1 Research methodology

3.1.1 Design

The primary source of the data for this study were the cephalometric radiographs, all of which had been taken on-site, using the same cephalometric x-ray machine (Siemens, Munich, Germany) located in the dental department of the Sainte Justine University Hospital Center.

This study followed a retrospective design as illustrated in Fig. 3-1.

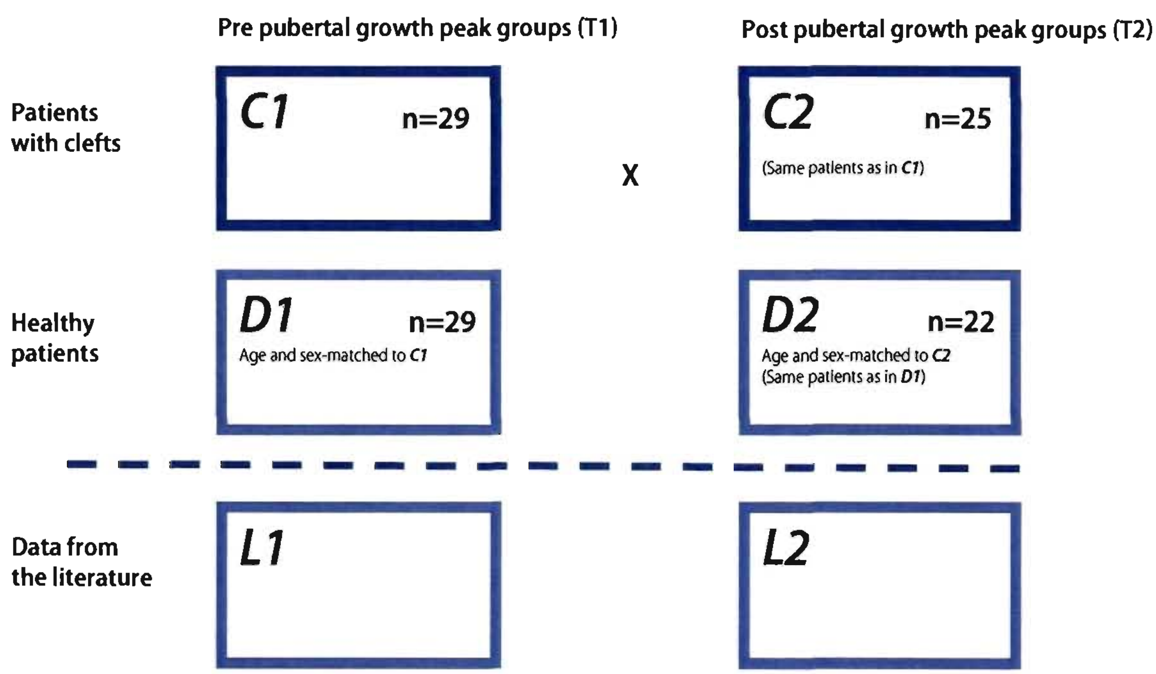

Figure 3-1 : Study design

For each patient, cephalometric radiographs were assessed at the pre-pubertal growth peak period (T1) and at the post-pubertal growth peak period, which corresponds to the end of growth (T2) (Fig. 3-2).

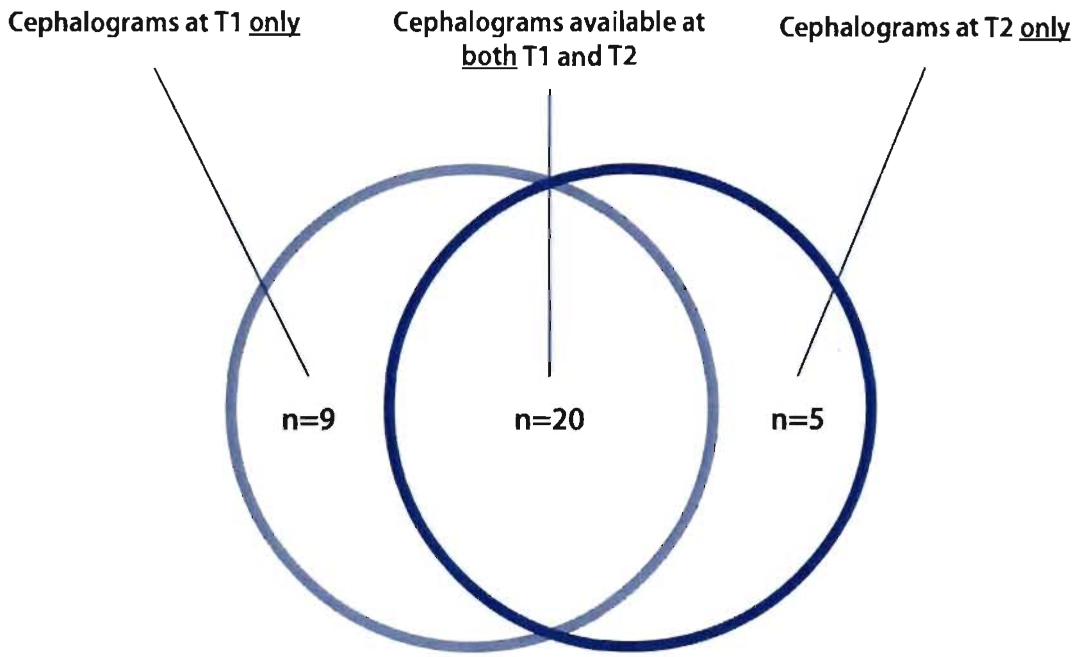

Figure 3-2 : Distribution of cephalometric radiographs for subjects

3.1.2 Research sample

All charts if children born with UCCLP between 1983 and 1989 were reviewed by Louise Caouette-Laberge (LCL). This search resulted in an initial identification of 40 patients born with a cleft lip and palate between 1983 and 1989. When the criteria for inclusion and exclusion from the study were applied, the initial list was reduced to 34 eligible patients (19 females and 15 males).

The following criteria were used to support inclusion in the experimental (UCCLP) group:

1. Presence of a UCCLP with primary palate repair at the time of lip repair,

2. No other congenital anomaly,

3. Patients followed since birth and have been through all treatment phases at the Sainte Justine University Hospital Center,

4. Availability of a cephalometric radiograph at ages ≥15 for females and ≥16 for males (T2) and/or the availability of a cephalometric radiograph between the age of 6 and 10 (T1).

The following criteria were used to support exclusion from the experimental (UCCLP) group:

1. Any patients with a syndromic congenital anomaly;

2. Children diagnosed with UCCLP but whose records lacked cephalometric radiographs as required by the present study

3. Patient whose ethno-racial origin is other than Caucasian

4. Patient who was not followed since birth at Sainte Justine University Hospital Center

Inclusion and exclusion criteria were assessed for each patient using the individual medical chart. Ethno-racial origin was assessed using patient names and surnames as well as photographs.

The records of 20 subjects in the experimental group included an initial cephalometric radiograph (taken at time T1) and a follow-up cephalometric radiograph (taken at time T2). At time T1, the age range of the patients was 6.17 to 10.25 years, with a mean age of 7.97 years and median age of 8.00. The records of 25 of the 39 subjects contained a cephalometric radiograph taken at time point T2. The age range in this case was 16.00 to 20.00 years, with a mean age of 17.18 years and a median age of 17.25 years.

3.1.3 Control group

As a control group, we have used data from the Human Growth Research Centre (*Centre de Recherche sur la Croissance Humaine*), Université de Montréal, Montréal, Québec, Canada. This is one of the largest samples of anthropometric and cephalometric data in North America. This longitudinal sample is derived from a study that spanned over two decades, starting its activities in 1966 and being dismantled in 1986. The sample is drawn from three randomly selected school districts representing the socioeconomic background of the larger population. Within each district, the individuals were chosen at random from 107 randomly selected schools. This mixed-longitudinal sample includes 227 individuals (119 males and 108 females) with untreated normal occlusions and malocclusions. The sample included untreated growing adolescents between 6 and 20 years of age with four French-Canadian grandparents, therefore this sample is very homogenous ethnically.

3.1.4 Comparison groups from the literature

We decided to use the Toronto study (Ross, 1987) and the Eurocleft study (Brattström *et al.* 2005). The Toronto study consisted of 543 individuals with UCCLP from 12 centres. The Eurocleft study was a multicentered project that involved five major European centers. Those two studies were selected because of their large breadth, excellent methodology and patient selection criteria. Both are considered landmark studies.

3.1.5 Cephalometric methodology

Cephalometric tracings were performed by Nabil Ouatik (NO), senior resident in paediatric dentistry at Université de Montréal, Faculty of Dentistry under the guidance of Hicham El-Khatib (HEK), orthodontist and associate professor of orthodontics at the Université de Montréal, Faculty of Dental medicine, and Sainte Justine Hospital Center. All lateral cephalometric radiographs were traced on acetate paper using a 0.5 mm pencil. The mean value was determined for structures that were superimposed on the radiograph. A summary of all landmarks used is given in Fig. 3-3 and Appendix A. Landmarks selected for the present study were all located on hard tissue. With the exception of the two dentoalveolar landmarks (A point and B point) all other dental landmarks were not assessed as the present study aims at studying skeletal growth exclusively.

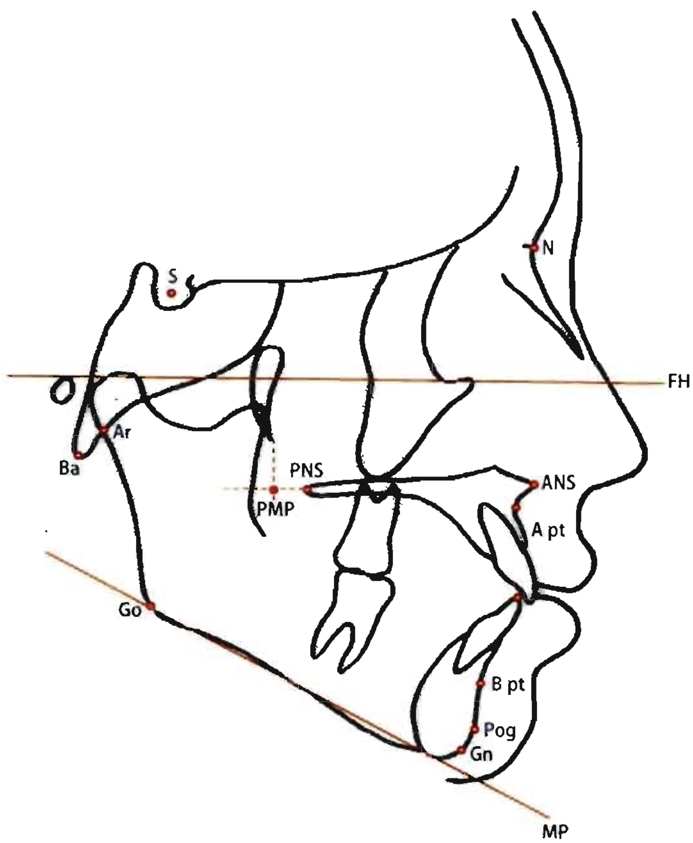

Figure 3-3 : Cephalometric landmarks used in the present study.

Tracings were then digitized using a HP 5590 Scanjet digitizer (Hewlett-Packard, Palo Alto, California, USA). We retraced 25% of cephalograms to ensure intra-examiner reliability and 20% of cephalograms were retraced by an experienced orthodontist (HEK) to do external calibration of the examiner (NO). In the present study, repeat tracings were performed after 2 months to assess the reproducibility of landmark determination and the reliability of variables derived from these landmarks. The time interval ensured point identification clues for specific individuals would not be recalled and influence relocation.

We used the software Viewbox 4.0 for our cephalometric measurements (courtesy of Dr Demetrios Halazonetis, dHAL Software, Kifissia, Greece).

3.1.6 Calibration of the magnification rate in cephalometry

After calibration with a dry skull (Fig. 3-4) which had well defined metal screws implanted at landmarks along the midline area, all our film measurements were adjusted by a factor of 0,92, to correct for the film enlargement that this camera geometry produces. Our measures are therefore true mid-head values.

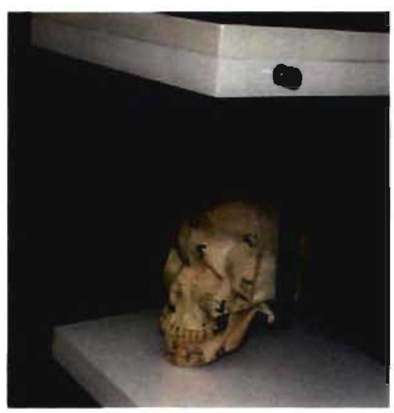

Figure 3-4 : Dry skull used to calibrate the magnification rate on the cephalometric machines at Université de Montréal and Sainte Justine University Hospital Centre.

3.1.7 Variables

Age and sex were recorded for each patient. Age of lip repair, palatal closure and alveolar bone graft were also computed. The following cephalometric variables were used in the present study (Table IV). They reflect the variables used in the Human Growth Research Centre sample (Demirjian, 1968), Toronto Study (Ross, 1987) and Eurocleft study (2005). One can refer to Appendix A for landmark definitions used.

Cranial base	
S-N	Distance from Sella to Nasion (mm), indicates anterior cranial base length
S-Ar	Distance from Sella to Articulare (mm), indicative of posterior cranial base length
Ar-S-N	Angle between Articulare, Sella and Nasion (°), indicates flexion of the cranial base
Ba-S-N	Angle between Basion, Sella and Nasion (°), indicates flexion of the cranial base
Facial profile	
N-A (FH)	Distance from Nasion to A (mm) on FH, indicates anteroposterior position of A
N-B (FH)	Distance from Nasion to B (mm) on FH, indicates anterior cranial base length
N-Pg (FH)	Distance from Nasion to Pg (mm) on FH, indicates anterior cranial base length
A-B (FH)	Distance from A to B (mm) on FH, indicates maxillo-mandibular relation
S-Gn	Distance between Sella and Gnathion, (mm) indicates size of the mandible (Y-Axis)
N-A-Pg	Angle between Nasion, A point and Pogonion (°), indicates flexion of the base
SNA	Angle between Sella, Nasion and A point (°), indicates flexion of the cranial base
SNB	Angle between Sella, Nasion and B point (°), indicates flexion of the cranial base
ANB	Angle between A point, Nasion and B point (°), indicates flexion of the cranial base
Ba-N-ANS	Angle between Ba, Nasion and ANS (°), angulation between maxilla and cranial base
Maxilla and Mandible	
ANS-PNS (FH)	Distance from A to B (mm) on FH, indicates maxillo-mandibular relation
PMP-ANS	Distance from PMP to ANS (mm), indicates anteroposterior maxillary lenght
Ar-Pg (FH)	Distance from Ar to Pg (mm) on FH, indicates anteroposterior mandibular lenght
Go-Ar	Distance from Go to Ar (mm), indicates posterior mandibular height
Go-Pg (MP)	Distance from Go to Pg (mm) on MP, indicates prominence of the chin
B-Pg (MP)	Distance from A to B (mm) on FH, indicates maxillo-mandibular relation
Ar-Go-Me	Angle between Articulation, Gonion and Menton (°), indicates gonial angle
Facial height	
N-ANS (⊥FH)	Distance from N to ANS, perpendicular to FH (mm), indicates upper facial height
ANS-Me (⊥FH)	Distance ANS to Menton, perpendicular to FH (mm), indicates lower facial height
PP-FH	Angle between Palatal plane and FH (°), indicates flexion of the cranial base
MP-FH	Angle between Mandibular plane and FH (°), indicates flexion of the cranial base

Table IV : Cephalometric variables used in present study.

3.1.8 Statistics

Sample size was determined to be sufficient to obtain a reasonable statistical power (α=0.05). In the statistical analysis of the direct measurements, cephalometric variables and comparison data, the following entities were used.

Basic descriptive statistics including arithmetical means and standard deviations were used to summarise the quantitative data.

Standard Student *t*-tests were used to compare all groups. Comparisons in the present study were T1 vs T2 for UCCLP, T1 vs T2 for Controls and then UCCLP vs Controls at T1 and UCCLP vs Controls at T2. Comparison with data from the literature was also done using standard *t*-tests. For comparison with averages, we have used one sample *t*-tests. For the *t*-tests, the level of significance was set at 5%.

Dahlberg's formula was used for method error, intra-examiner reliability and examiner calibration. Bland-Altman's formula and ICC were also used for these calculations.

Chapter 4: Results

4.1 Studied samples

Thirty five patients (19 males, 16 females) were studied at prepubertal and post-pubertal stages. Average age for lip repair was 3.36 month ± 1.2 months and the average age of palatal surgery was 1.2 years ± 1.1 months. For the alveolar bone graft, the average age for the surgery was 10.2 years ± 1.3 years. We calculated that 16% of our patients had to have orthognathic surgery. In total 22 patients were identified as meeting the inclusion criteria when charts that had missing cephalograms were excluded.

The mean age for the cephalometric radiograph at T1 was 8.82 years for the UCCLP group with a range of 6.57 – 10.43 years, and a median at 8.79 years (Fig. 4-1). The Control group had a cephalometric radiograph at T1 at a mean age of 9.00 years, a range of 7.00 – 11.00 years, and a median of 9.00 years. At T2, the controls had cephalometric radiographs with a mean age of 16.86 years, median at 18.00 years, and a range of 15.00 – 18.00 years, whereas the 25 UCCLP subjects had cephalometric radiographs with a mean age of 17.83 years, median at 17.63 years, and a range of 16.11 – 20.36 years. There were slight yet statistically insignificant differences in the age range, median age, and mean age between the subjects in the UCCLP group and those in the Control group. At T2, the difference between the ages of the UCCLP group and the control group was statistically but not clinically significant.

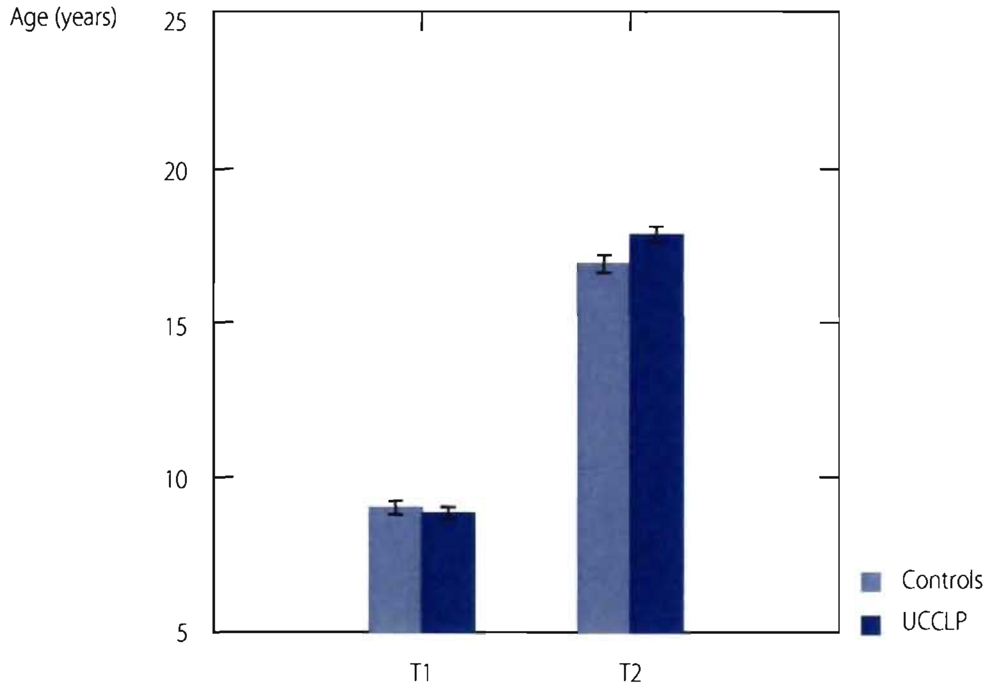

Figure 4-1 : Average ages at T1 and T2

The subjects (UCCLP) and the control groups were comparable in composition and distribution at T1 (Subjects with UCCLP: n = 29; 14 females and 15 males. Controls: n = 29; 14 females, 15 males) and at T2 (subjects with UCCLP: n = 25; 13 females and 12 males. Controls: n = 22; 10 females, 12 males) (Tables V and VI). No statistically significant difference was noted between males and females in either group. At T1, a Fisher's Exact test showed $p = 1.000$, and an odds ratio of 1.000. At T2, a Fisher's Exact test showed $p = 0.773$, and an odds ratio of 0.769.

T1	F	M	Total
Controls	14	15	29
Subjects	14	15	29
Distribution	48.28%	51.72%	100%

Table V : Control and subject distribution by gender (at T1).

T2	F	M	Total
Controls	10	12	22
Subjects	13	12	25
Distribution	48.93%	51.06%	100%

Table VI : Control and subject distribution by gender (at T2).

As mentioned previously, the UCCLP subjects were selected retrospectively from the available records at the Cleft Lip and Palate Clinic of Sainte Justine University Hospital Centre in Montreal. All our subjects were classified as being Caucasian and a large majority of our subjects were of French-Canadian descent.

On average, our subjects had an average age of lip repair of 3.36 month ± 1.2 months and an average age of palatal surgery of 1.2 years ± 1.1 months. For the alveolar bone graft in the mixed dentition stage, the average age for the procedure was 10.2 years ± 1.3 years. We have calculated that 16% of our subjects needed orthognathic surgery (4/25).

4.2 Comparison samples from the literature

As stated previously, we used the Toronto study (Ross, 1987) and the Eurocleft study (Brattström *et al.* 2005) for comparison purposes. These two studies were selected because of their large breadth, excellent methodology and patient selection criteria. Both are considered landmark studies.

From the Toronto study, we used mostly the Toronto Base group. This group comprises 136 individuals and 580 cephalograms and is a heterogeneous group of all the available cases at the University of Toronto with multiple long-term records excluding the group of cases of Dr W.K. Lindsay and a group treated by presurgical orthopedics. Numerous surgeons and numerous surgical techniques were involved, making it a useful group to establish information on the morphology of the facial skeleton following nonspecific treatment. Another group used was the *median repair group* which included cephalograms from centers around the world that close the palate between 12 to 20 months. This other comparison group was where data was not available in the Toronto Base group for specific measurements or ages.

Within the Eurocleft study, we used the five groups for which data was published in 2005 by Brattström *et al.* The Eurocleft study was a multicentre project whose goal was to compare treatment outcomes in various European centers. It was a longitudinal cohort study up to age 17 in individuals with repaired complete unilateral cleft lip and palate in multidisciplinary cleft services in Northern Europe (Table VII).

Age		Centre A	B	D	E	F
9 years	Females	9	9	10	10	13
	Males	14	17	16	20	10
	Total	23	26	26	30	23
	Mean age	9.2	9.6	9.5	9.7	9.3
	SD	0.6	0.8	0.9	0.8	1.1
17 years	Females	9	9	9	10	11
	Males	14	17	16	20	9
	Total	23	26	25	30	20
	Mean age	17.1	17.2	17.4	17.2	17.2
	SD	0.5	0.7	2.2	1.0	0.9

Table VII : Overview of the subjects in the Eurocleft study (2005).

4.3 Examiner calibration

Examiner calibration was performed using Dahlberg's formula and scores ranged between 0.30 and 2.02 (average: 0.9 mm, 1.1°). ICC (intra-class correlation) scores were between 0.872 and 0.997 (average: 0.921), which reflects good agreement between examiner and calibrator.

4.4 Intra-examiner reliability

Intra-examiner reliability was assessed using Dahlberg's formula and scores ranged from 0.27 to 1.92 (average: 0.7 mm, 0.9°) whereas ICC ranged between 0.927 and 0.999 (average: 0.942). An ICC score superior to 0.8 is reflective of a very good agreement.

The design of the present study was based on previously published studies. If we look at the validity of our cephalometric methodology we note that intra-examiner reliability and external calibration were sufficient to guarantee acceptable results. This means that if another individual is trained to retrace our cephalograms according to our methodology, we would expect similar results.

4.5 Cephalometric morphology findings

Results for cephalometric morphology are summarized on Table VIII, showing *p*-values and significant differences between groups at T1 and T2.

	T1				T2			
Variable	UCCLP	Controls	Statistical significance	Clinical significance	UCCLP	Controls	Statistical significance	Clinical significance
Age	**8.82**	**9.00**	*p*=0.528		**17.83**	**16.86**	*p*=0.015*	Not significant
S-N	63.83	62.41	*p*=0.090*	Minimal	68.77	67.40	*p*=0.232	
S-Ar	29.64	28.12	*p*=0.011		34.11	32.94	*p*=0.226	
N-S-Ar	123.92	121.83	*p*=0.103		122.93	122.15	*p*=0.627	
Ba-S-N	130.47	129.65	*p*=0.461		128.47	129.12	*p*=0.659	
N-A (FH)	-0.70	-1.21	*p*=0.528		-6.39	-0.95	*p*<0.001***	**Significant**
N-B (FH)	-7.82	-8.02	*p*=0.858		-11.31	-7.35	*p*=0.055	
N-Pg (FH)	-8.28	-9.74	*p*=0.252		-10.29	-7.73	*p*=0.283	
A-B (FH)	-7.13	-6.69	*p*=0.581		-4.92	-6.41	*p*=0.225	
S-Gn	104.92	101.15	*p*=0.007**	Mild	123.85	116.64	*p*<0.001***	**Significant**
N-A-Pg	8.30	8.50	*p*=0.891		-2.27	6.21	*p*<0.001***	**Significant**
SNA	79.97	81.52	*p*=0.112		76.45	82.01	*p*<0.001***	**Significant**
SNB	75.54	77.27	*p*=0.035*	Mild	76.23	78.38	*p*=0.061	
ANB	4.43	4.16	*p*=0.680		0.22	3.63	*p*=0.035*	**Significant**
ANS-PNS	47.07	44.95	*p*=0.016*	Mild	49.71	49.76	*p*=0.964	
Ar-Pg	89.28	87.98	*p*=0.232		103.56	101.10	*p*=0.180	
Go-Ar	36.91	35.90	*p*=0.206		47.10	43.28	*p*=0.027*	Mild
Go-Pg	62.54	62.32	*p*=0.826		70.07	71.16	*p*=0.419	
B-Pg	4.94	5.03	*p*=0.806		8.34	7.32	*p*=0.174	
Ar-Go-Me	133.33	128.95	*p*=0.003**	**Significant**	131.60	125.35	*p*=0.001***	**Significant**
N-ANS ⊥FH	43.78	42.65	*p*=0.068		50.49	49.62	*p*=0.301	
ANS-Me ⊥FH	57.55	52.14	*p*<0.001***	**Significant**	69.75	60.05	*p*<0.001***	**Significant**
∠PP-FH	-1.65	-0.31	*p*=0.162		-0.89	0.89	*p*=0.129	
∠MP-FH	28.99	28.01	*p*=0.416		31.27	26.21	*p*=0.007**	**Significant**

Table VIII : Significant differences and p-values between groups at T1 and T2.

4.5.1 Craniofacial morphology between 7 and 10 years of age

Craniofacial morphology at the pre-pubertal growth peak period (T1) differs markedly between the control group, the groups from the literature and the UCCLP groups for SNA and ANB (Figs 4-2 and 4-3). For the measures of S-N-Pg (Fig. 4.4), the various groups are very similar. Statistically significant differences are highlighted in red.

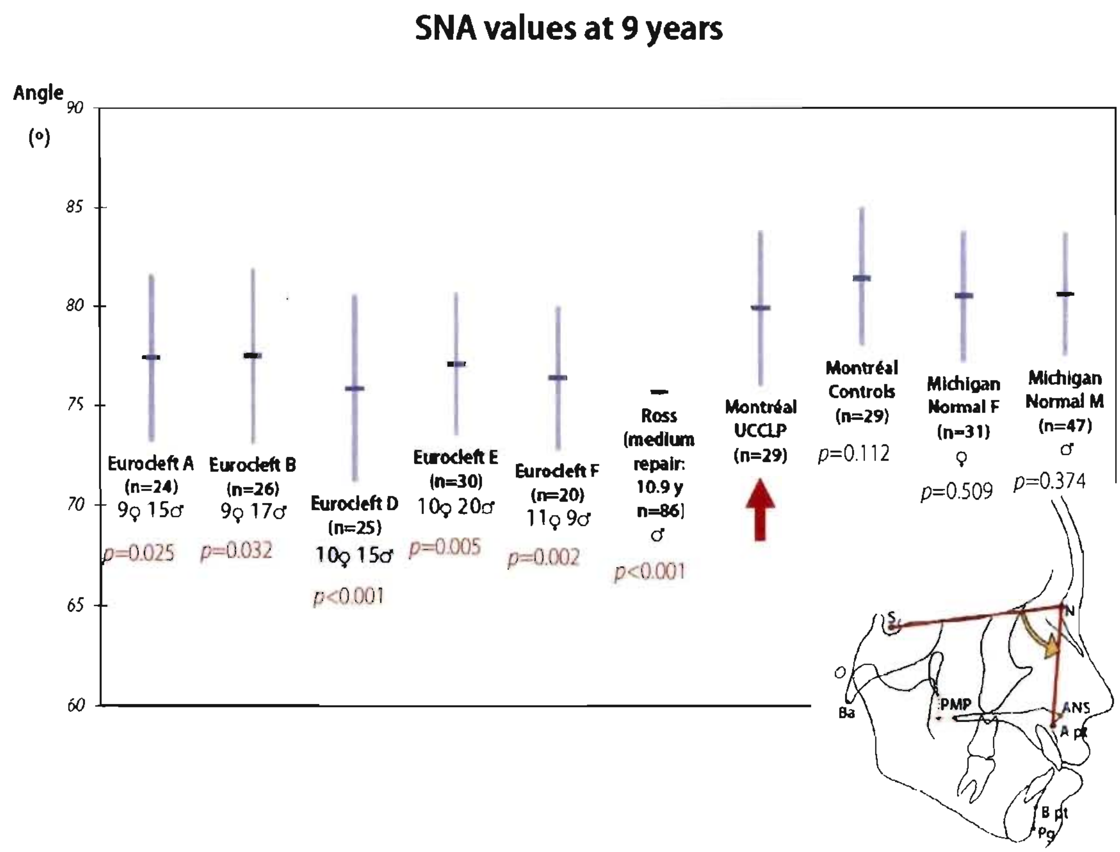

Figure 4-2 : SNA values at age 9.

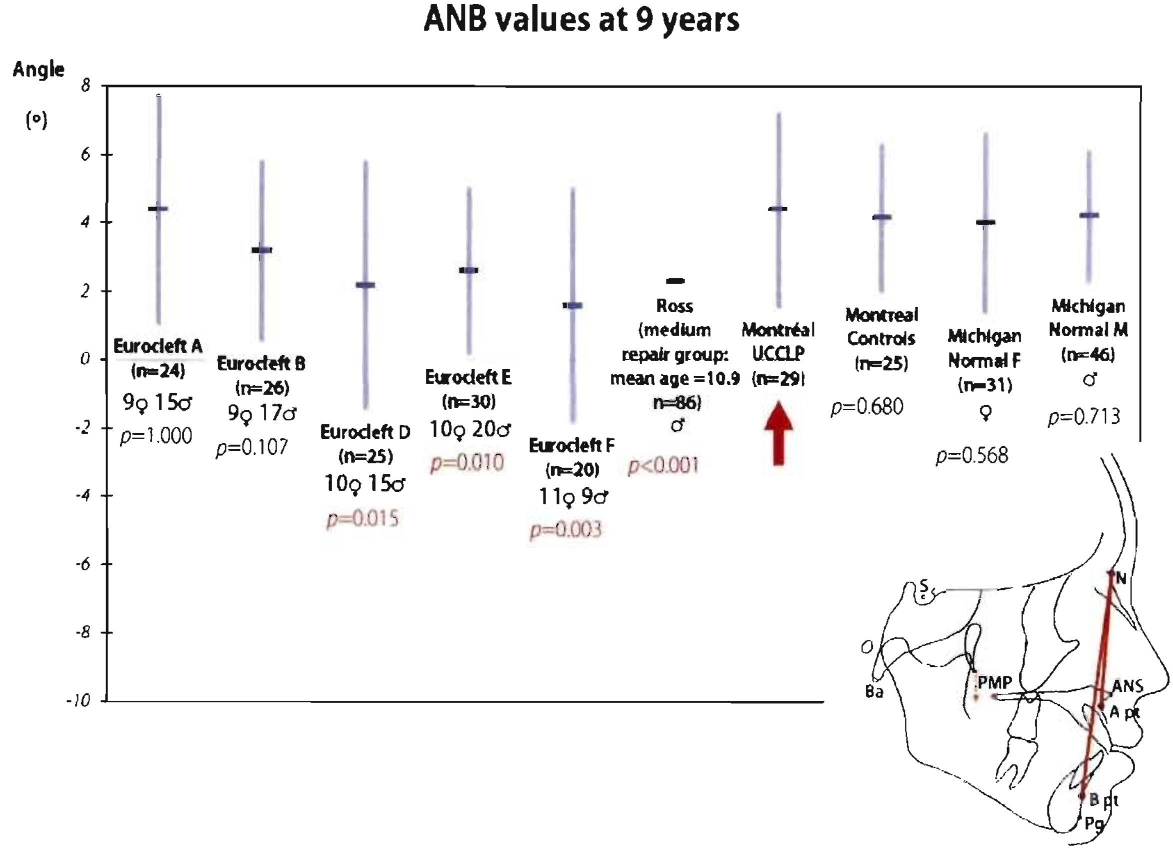

Figure 4-3 : ANB values at age 9.

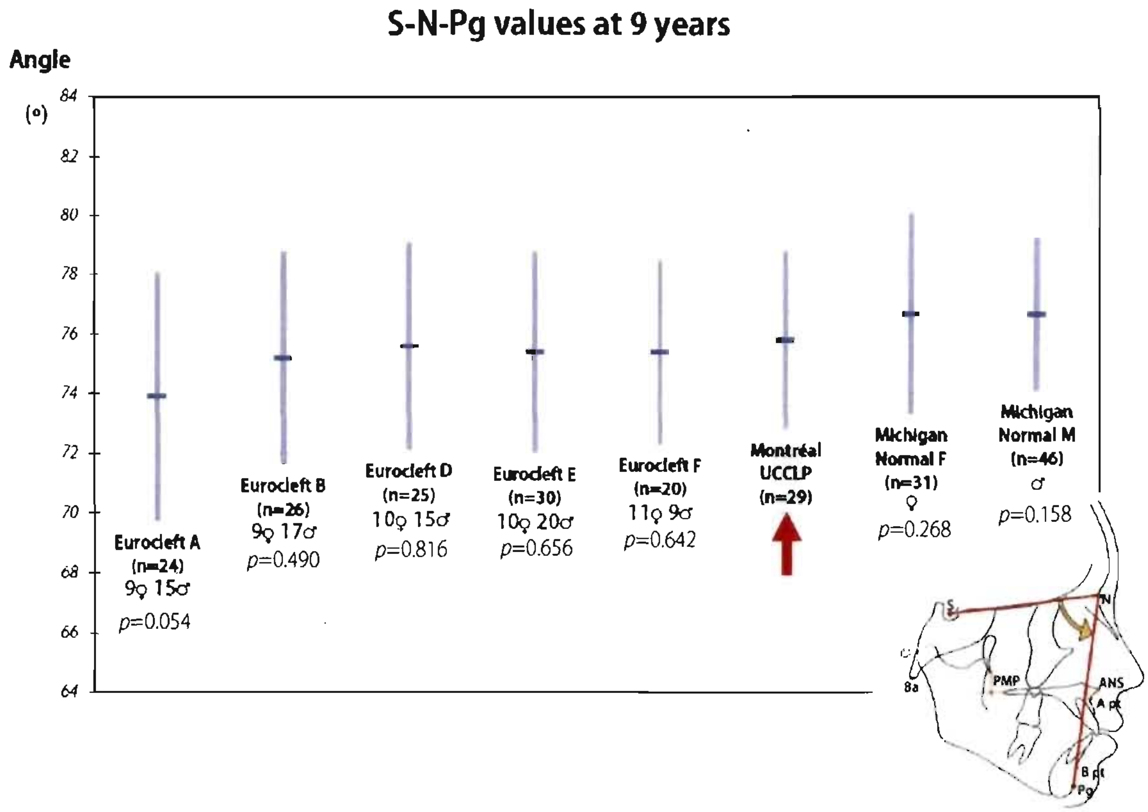

Figure 4-4 : S-N-Pg values at age 9.

4.5.2 Craniofacial morphology between 16 and 20 years of age

Craniofacial morphology at T2 shows that there is an accentuated difference (when comparing to T1) between the control groups, the groups from the literature and the UCCLP groups for SNA and SNB (Figs 4-5 and 4-6).

For S-N-Pg values, there is almost general accordance in values (Fig. 4.7). PMP-ANS and N-ANS values do not show a significant difference when compared to values from the literature (Figs 4.8 and 4.9).

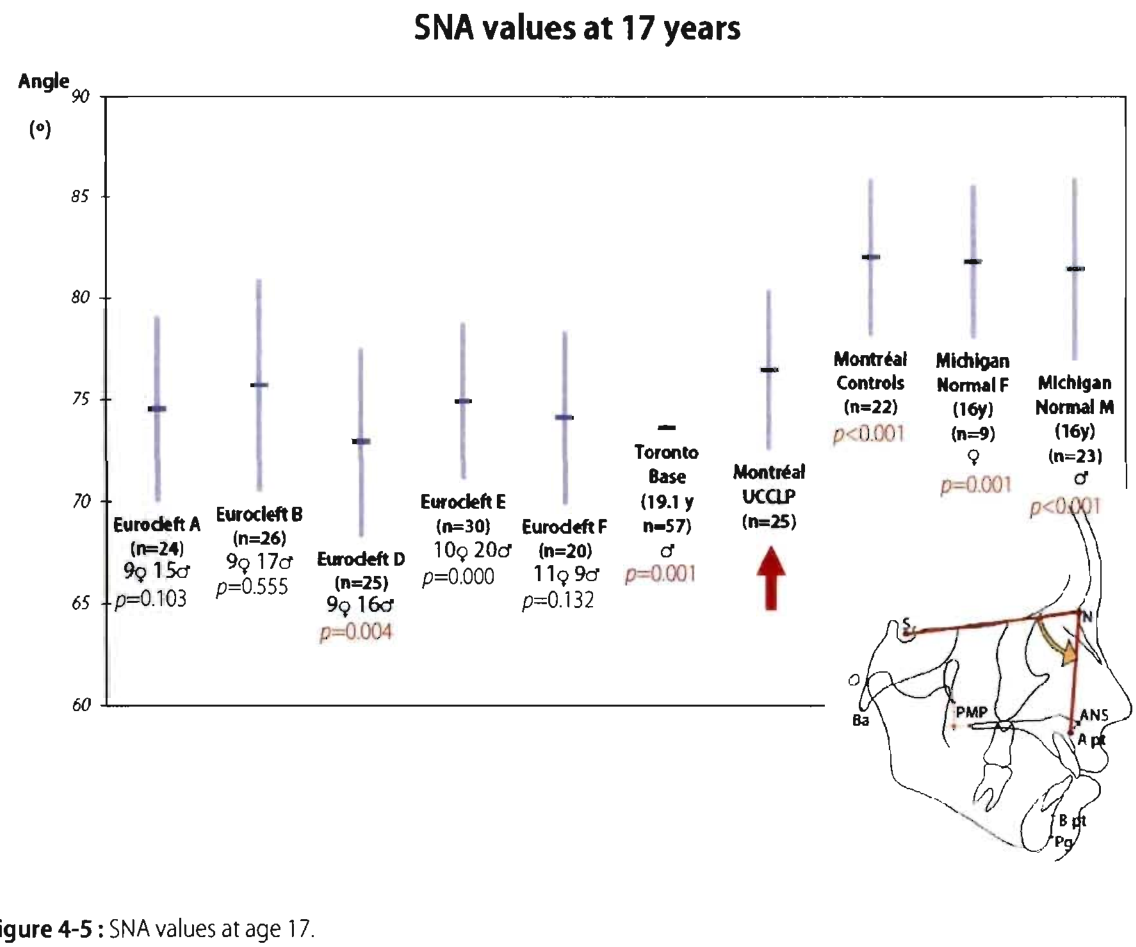

Figure 4-5 : SNA values at age 17.

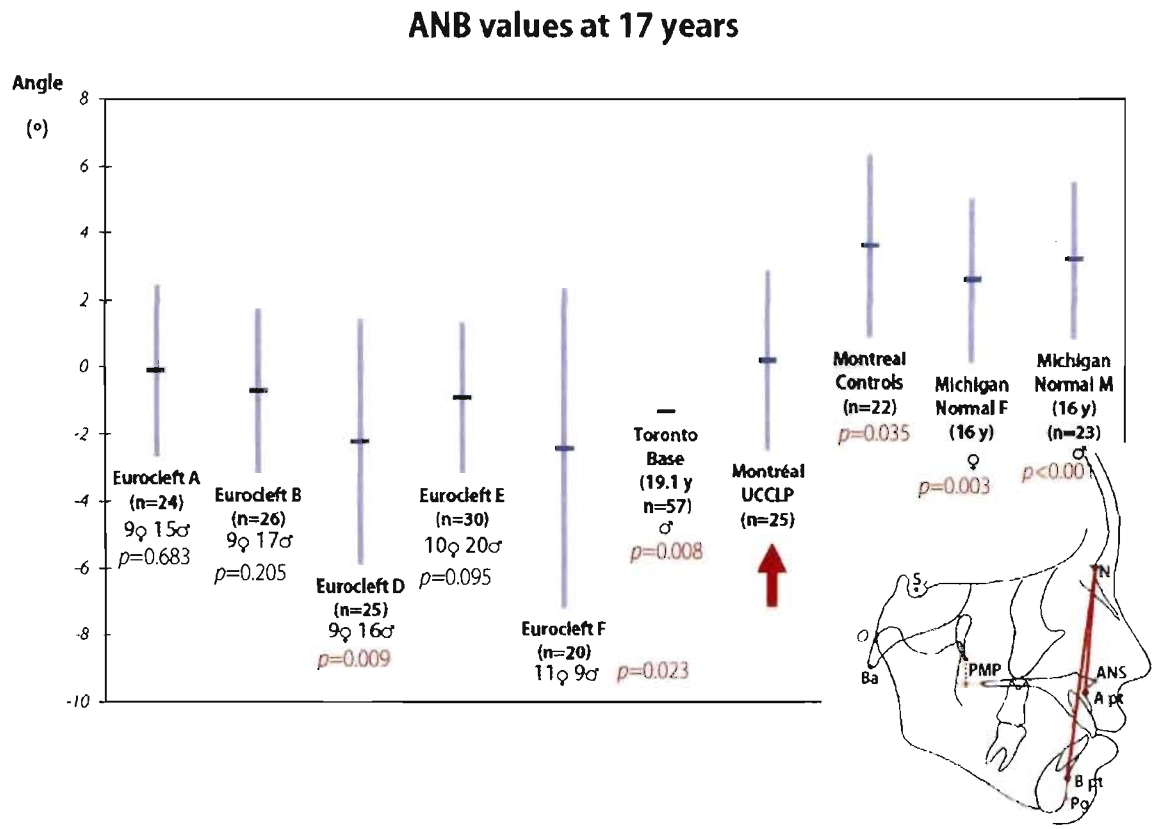

Figure 4-6 : ANB values at age 17.

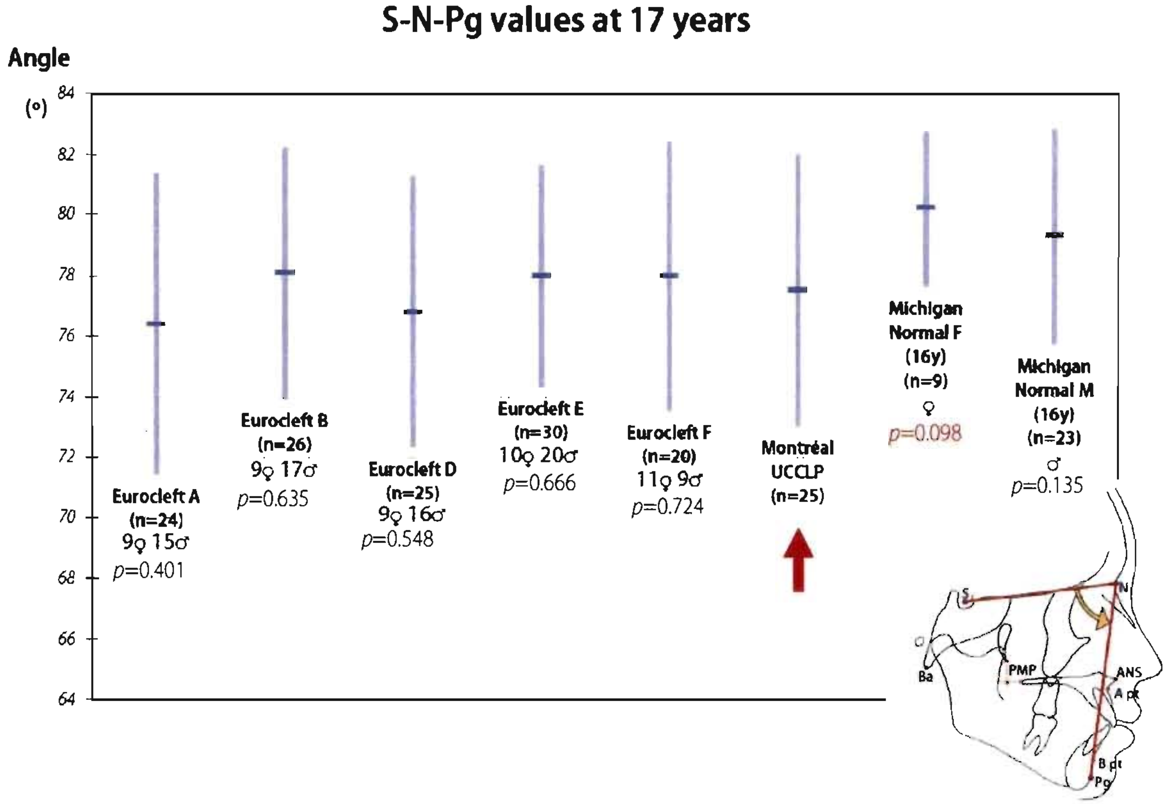

Figure 4-7 : S-N-Pg values at age 17.

Anteroposterior maxillary length (PMP-ANS)

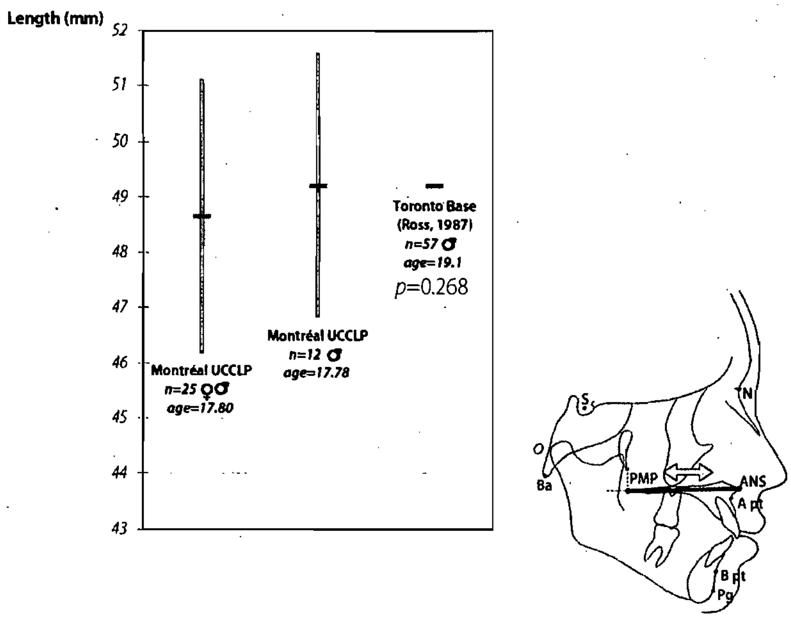

Figure 4-8 : PMP-ANS values at age 17 (Differences are not statistically significant).

Vertical maxillary position (N-ANS)

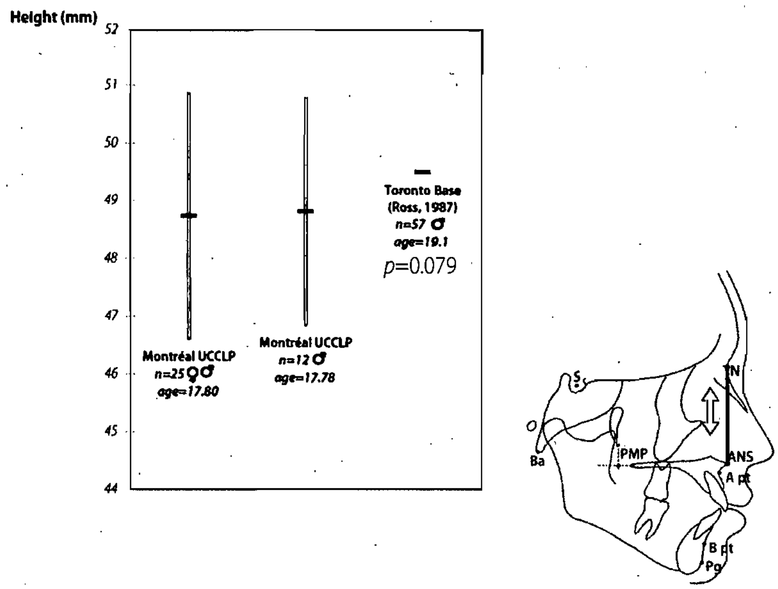

Figure 4-9 : N-ANS values at age 17 (Differences are not statistically significant).

4.5.3 Craniofacial growth

4.5.3.1 Cranial base

The cranial base seems to grow very similarly in the UCCLP and the Control group (Figs 4-11, 4-12, 4-13). One exception is S-N at 9 years, but this difference is not clinically significant (Fig. 4-10).

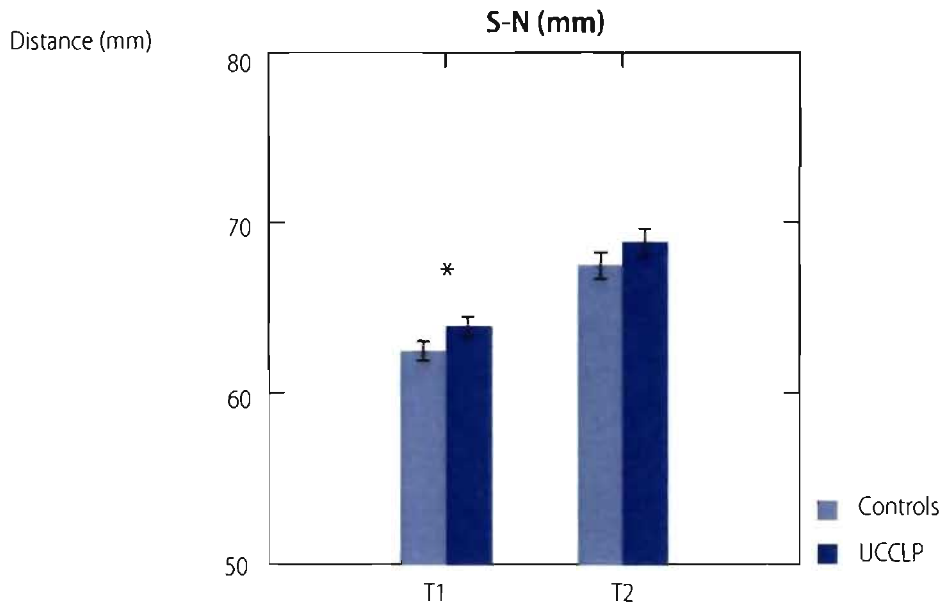

Figure 4-10 : Evolution of S-N distance over time (Difference is significant only at T1: p=0.090).

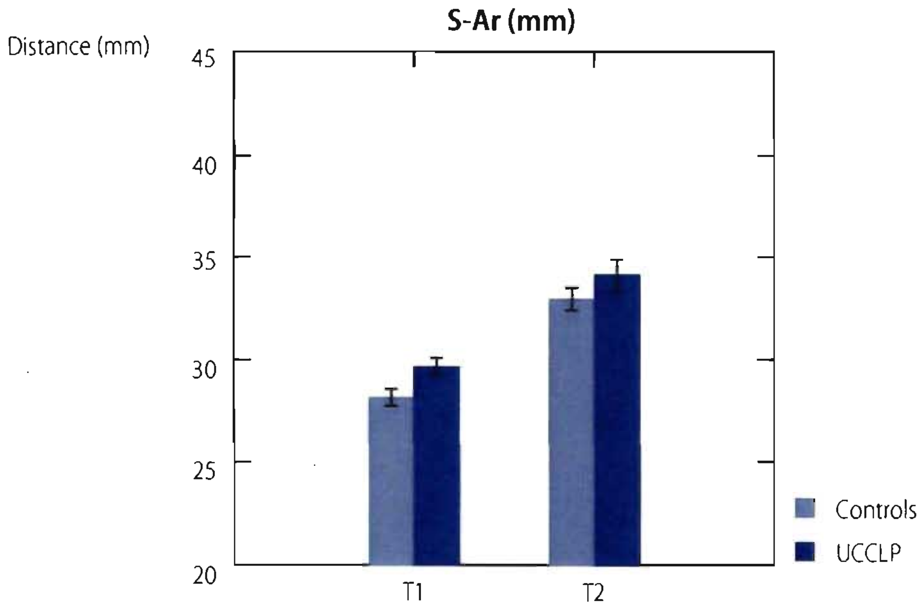

Figure 4-11 : Evolution of S-Ar distance over time (No significant differences).

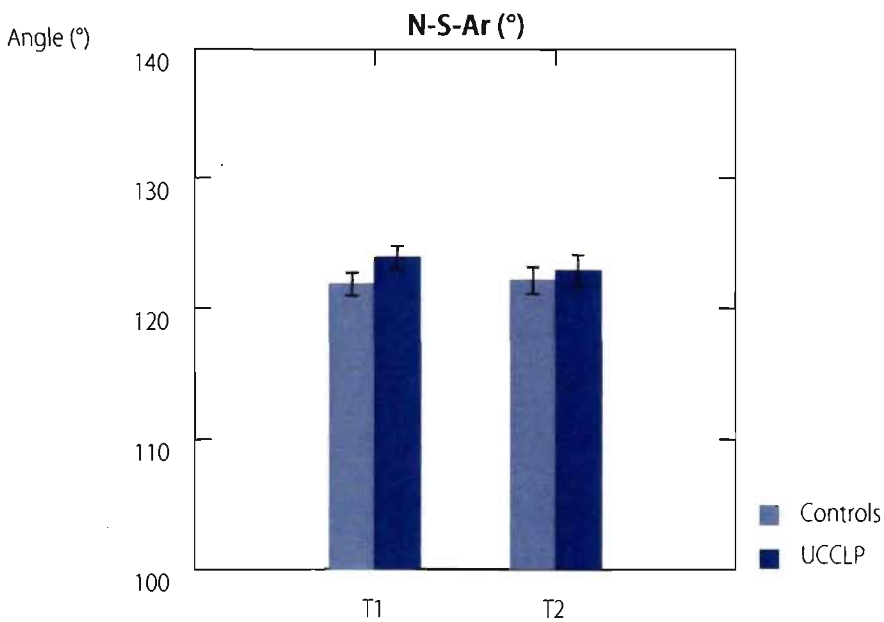

Figure 4-12 : Evolution of N-S-Ar angle over time (No significant differences).

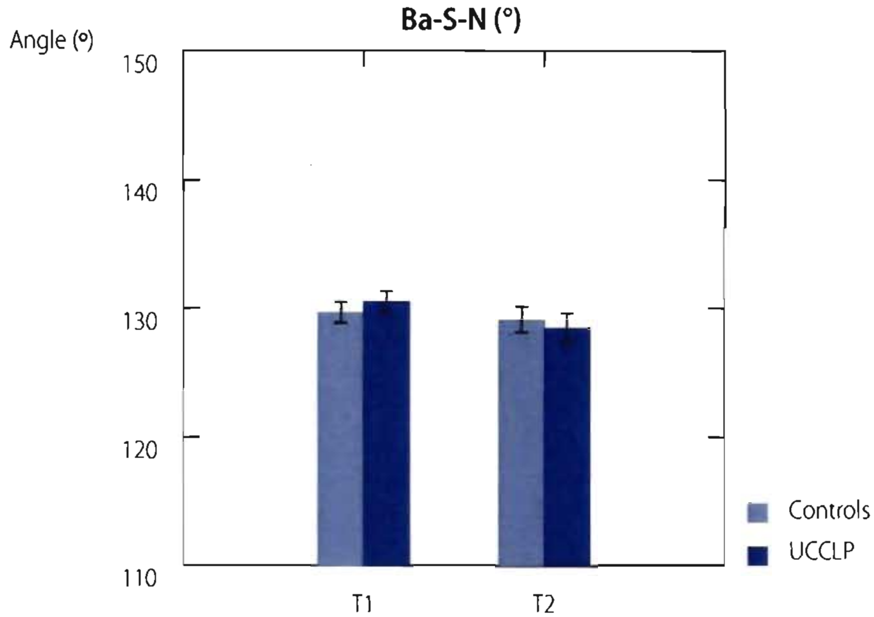

Figure 4-13 : Evolution of Ba-S-N angle over time (No significant differences).

4.5.3.2 Facial profile

The facial profile is significantly affected during growth in patients with UCCLP. Key values (N-A (FH), N-A-Pg, SNA, ANB) (respectively Figs 4-14, 4-19, 4-20, 4-21) show a significant decrease between the ages of 9 and 17 in the cleft group. This is not the case in the control group. There is also a higher S-Gn value at T2 for the group with UCCLP (Fig. 4-18). All other values are not significantly affected during growth (N-B (FH), N-Pg (FH), A-B (FH), SNB) (respectively Figs 4-15, 4-16, 4-27, 4-22).

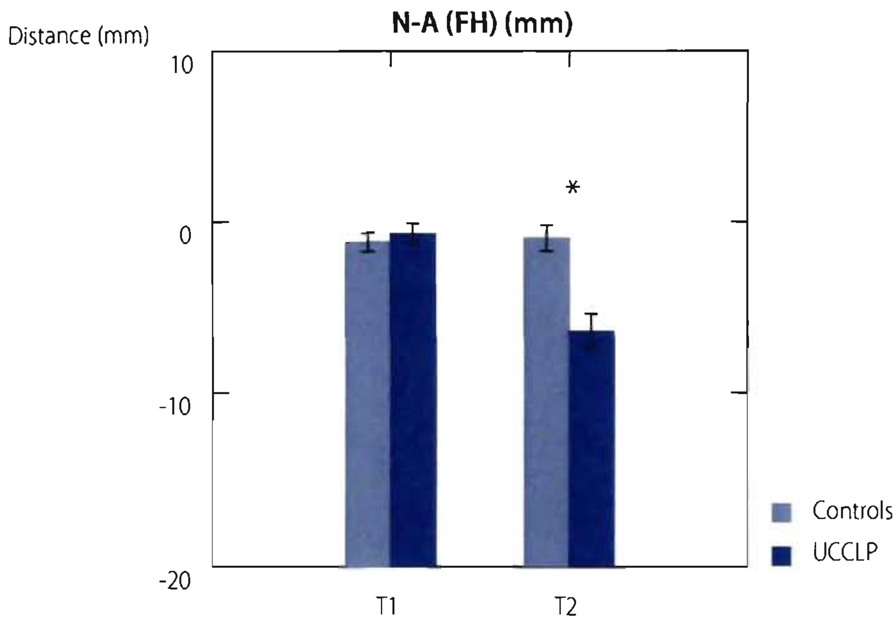

Figure 4-14 : Evolution of N-A (FH) values over time (Significant difference only at T2: $p<0.001$).

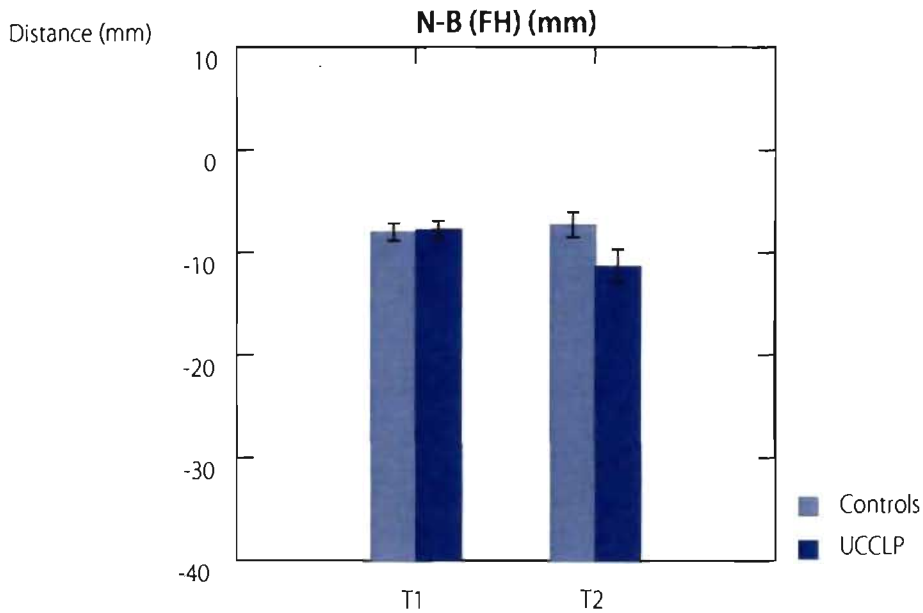

Figure 4-15 : Evolution of N-B (FH) values over time (No significant differences).

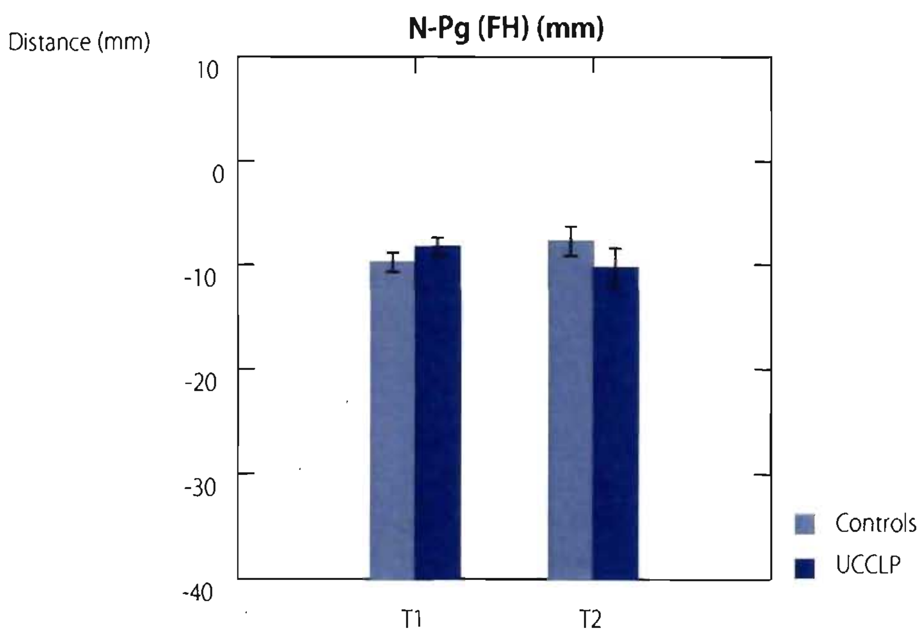

Figure 4-16 : Evolution of N-Pg (FH) over time (No significant differences).

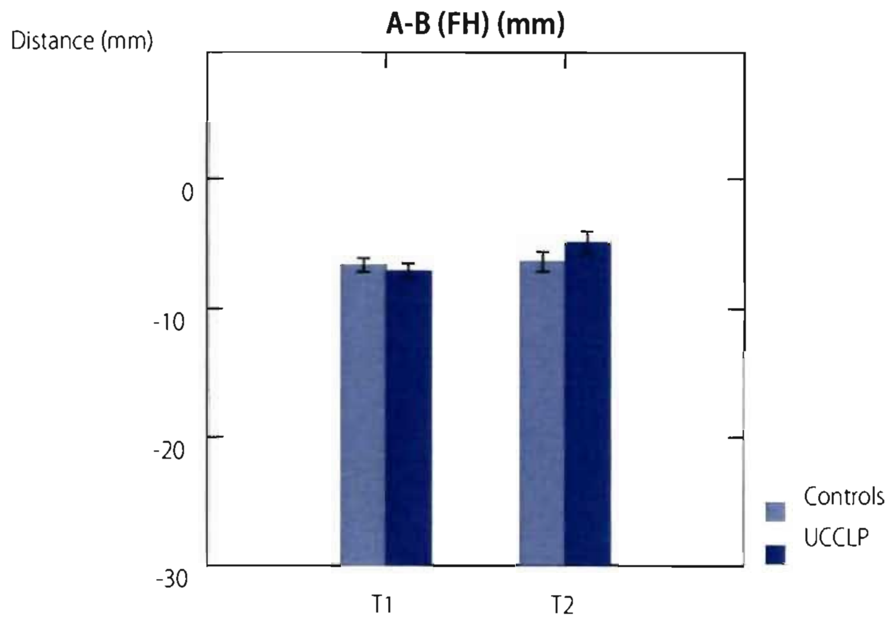

Figure 4-17 : Evolution of A-B (FH) over time (No significant differences).

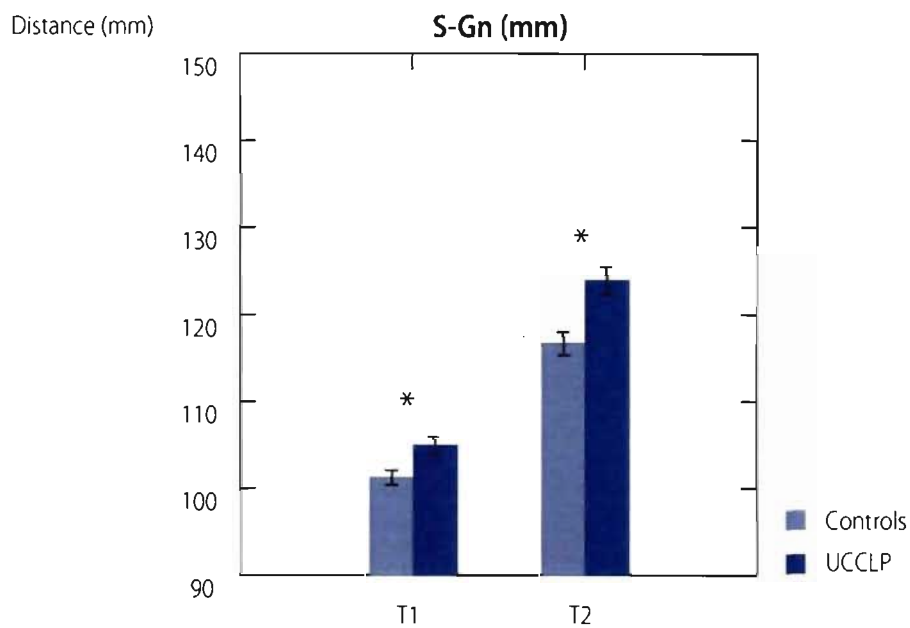

Figure 4-18 : Evolution of S-Gn (Y-axis) over time (Difference is significant at T1: p=0.007 and T2: p<0.001).

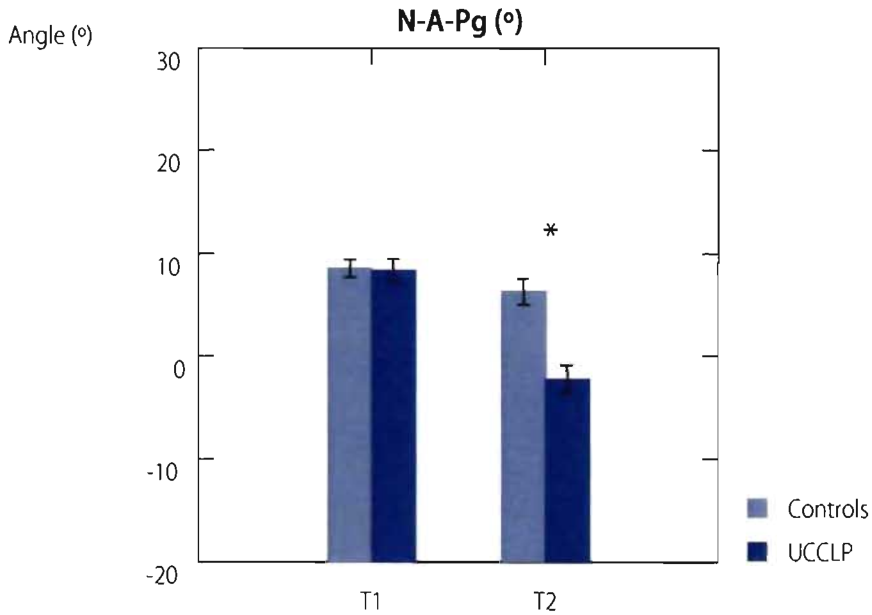

Figure 4-19 : Evolution of N-A-Pg over time (Significant difference only at T2: $p<0.001$).

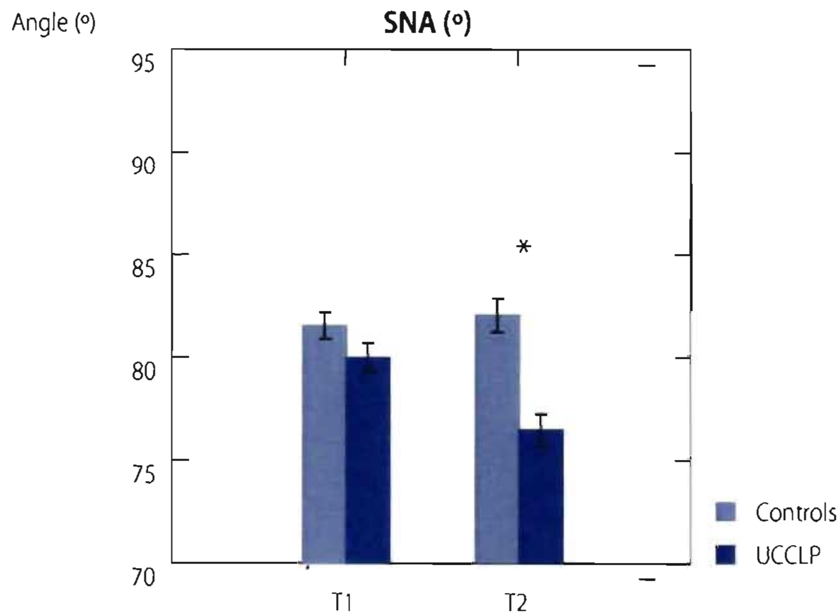

Figure 4-20 : Evolution of SNA angle over time (Significant difference only at T2: $p<0.001$).

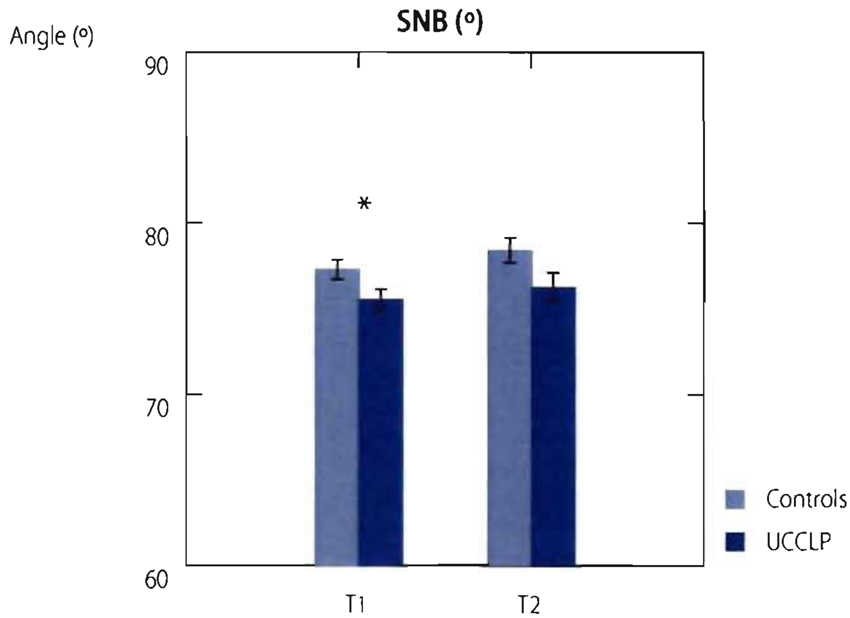

Figure 4-21 : Evolution of SNB angle over time (Significant difference only at T1: p=0.035).

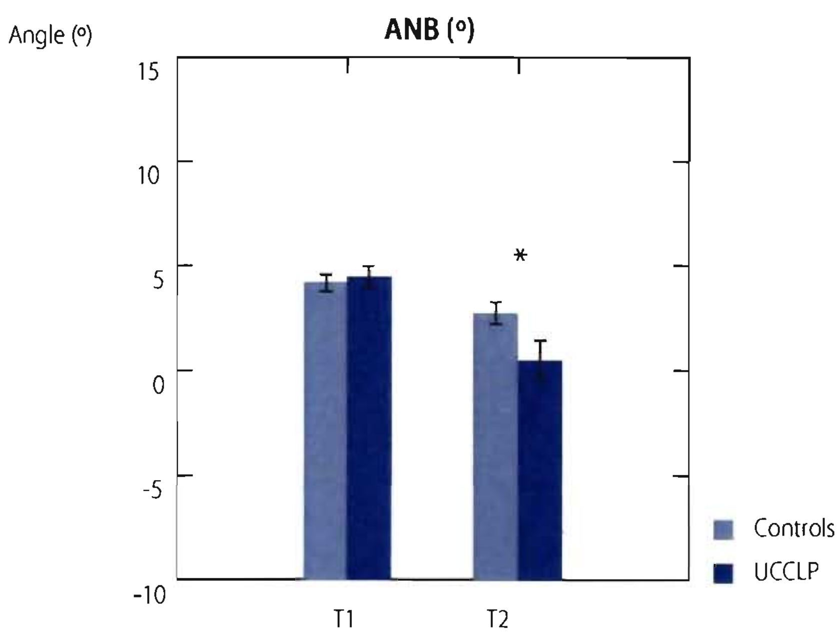

Figure 4-22 : Evolution of ANB angle over time (Significant difference only at T2: p=0.035).

4.5.3.3 Maxilla and mandible

Measurements limited to the mandible and maxilla do not show important differences between patients with UCCLP and Controls. The ANS-PNS distance, initially higher than for Controls at T1, grows slower in patients with UCCLP, yet it is not shorter than for Controls at T2 (Fig. 4-23). Posterior mandibular height becomes larger at T2 for patients with UCCLP (Fig. 4-25) but this has no influence on the vertical growth pattern observed in that group. All other values (Ar-Pg, Go-Pg, B-Pg) are not significantly affected during growth (respectively Figs 4-24, 4-26, 4-27).

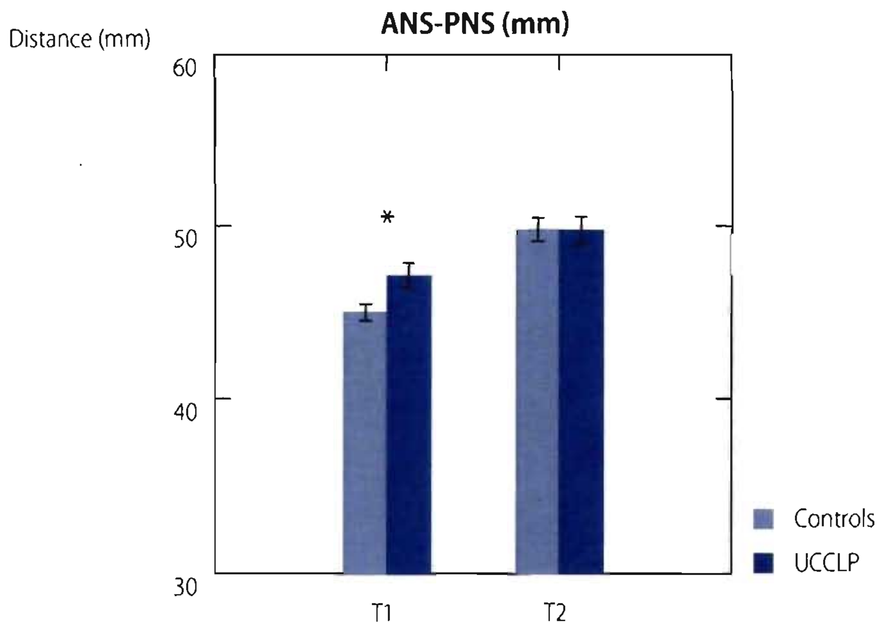

Figure 4-23 : Evolution of ANS-PNS distance over time (Significant difference only at T1: p=0.016).

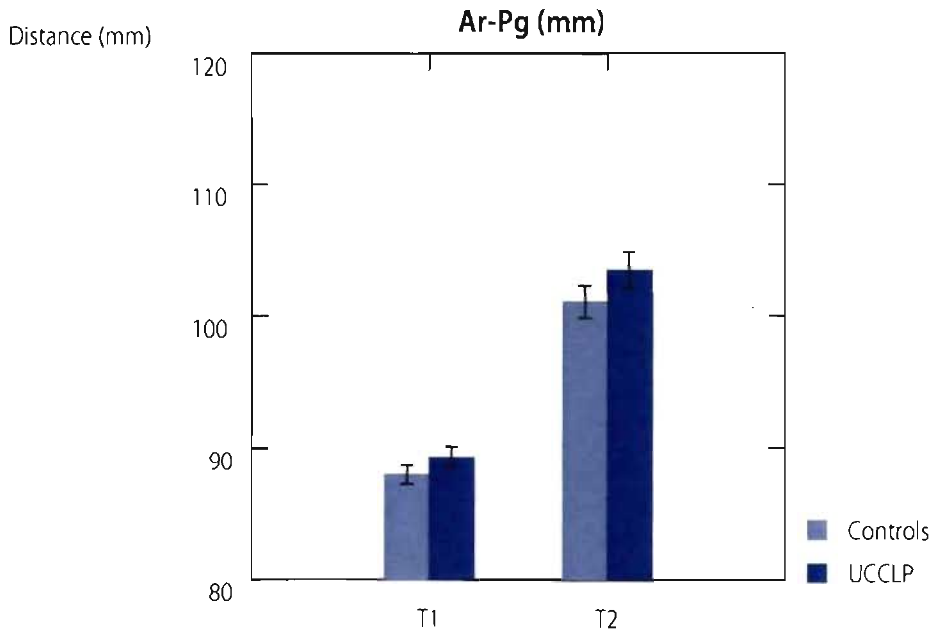

Figure 4-24 : Evolution of Ar-Pg distance over time (No significant differences).

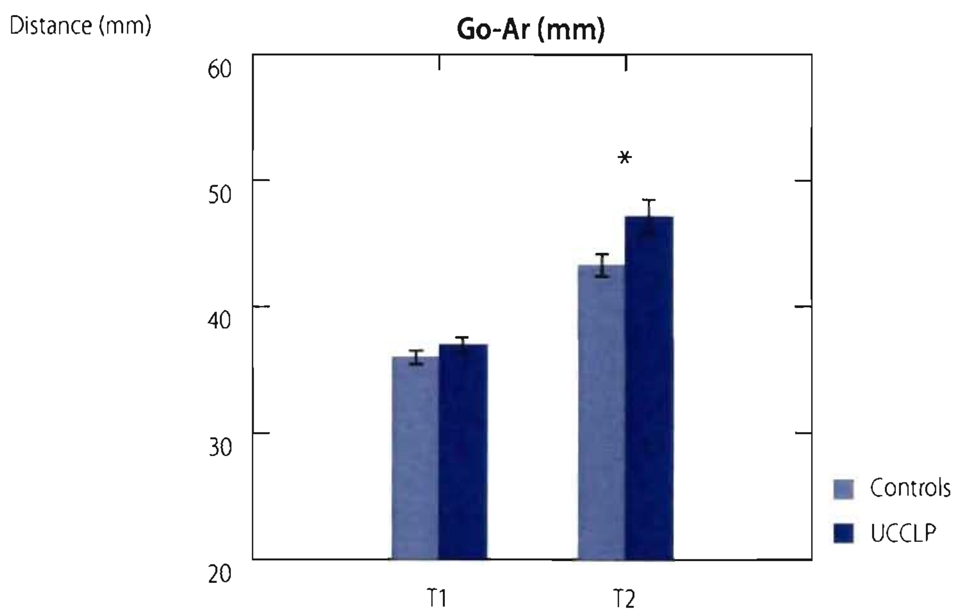

Figure 4-25 : Evolution of Go-Ar distance over time (Significant difference only at T2: p=0.027).

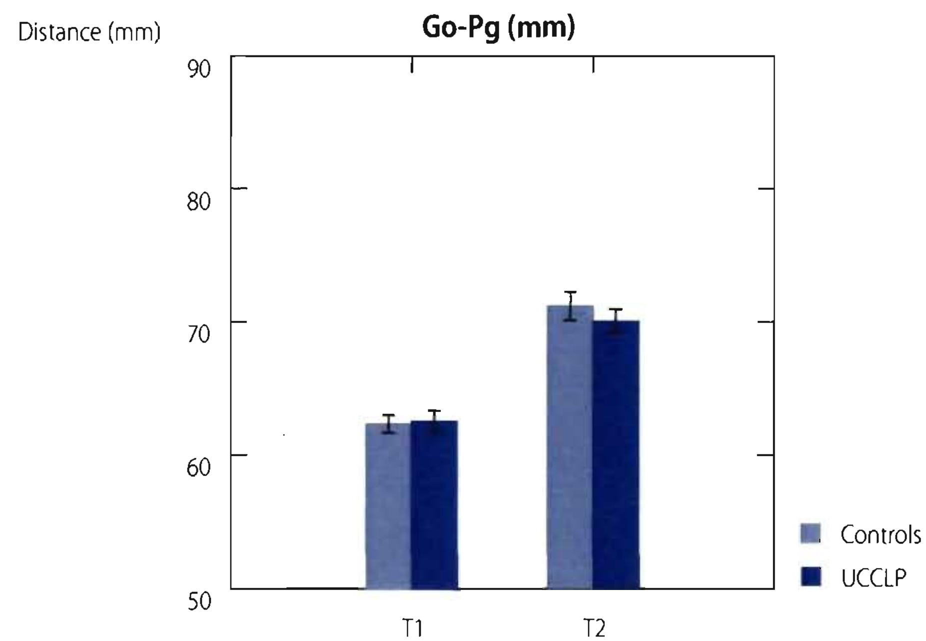

Figure 4-26 : Evolution of Go-Pg distance over time (No significant differences).

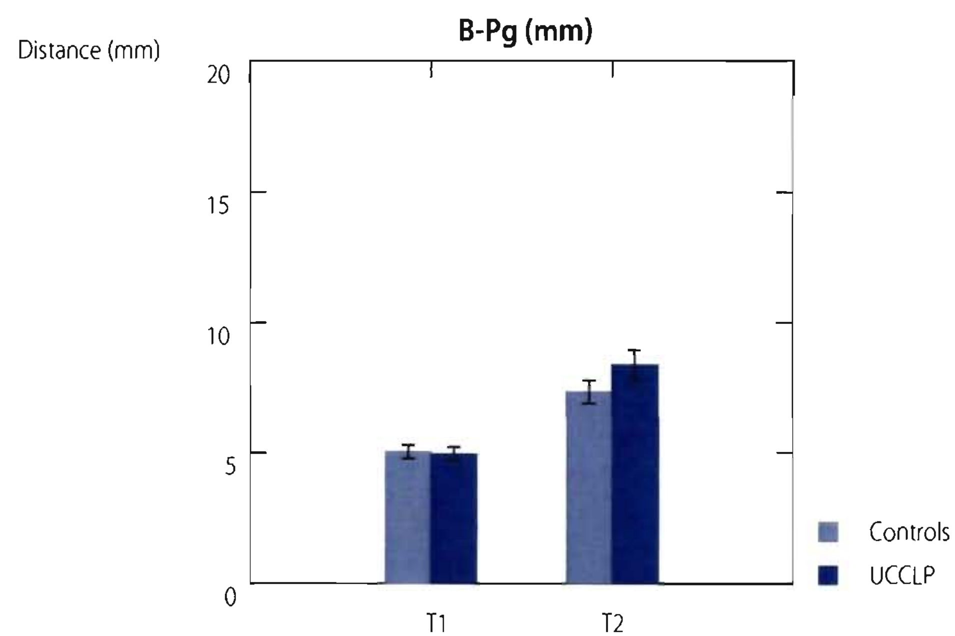

Figure 4-27 : Evolution of B-Pg distance over time (No significant differences).

4.5.3.4 Facial height

Some parameters reflecting higher lower face height like Ar-Go-Me (Fig. 4-28) and ANS-Me ⊥FH (Fig. 4-30) are higher at T1 and T2 for patients with UCCLP. The FMA (∠MP-FH) (Fig. 4-32) becomes higher at T2 in UCCLP patients. Other parameters (N-ANS⊥FH and ∠PP-FH) (Fig. 4-29 and 4-31) do not show different change between the patients with UCCLP and the Controls.

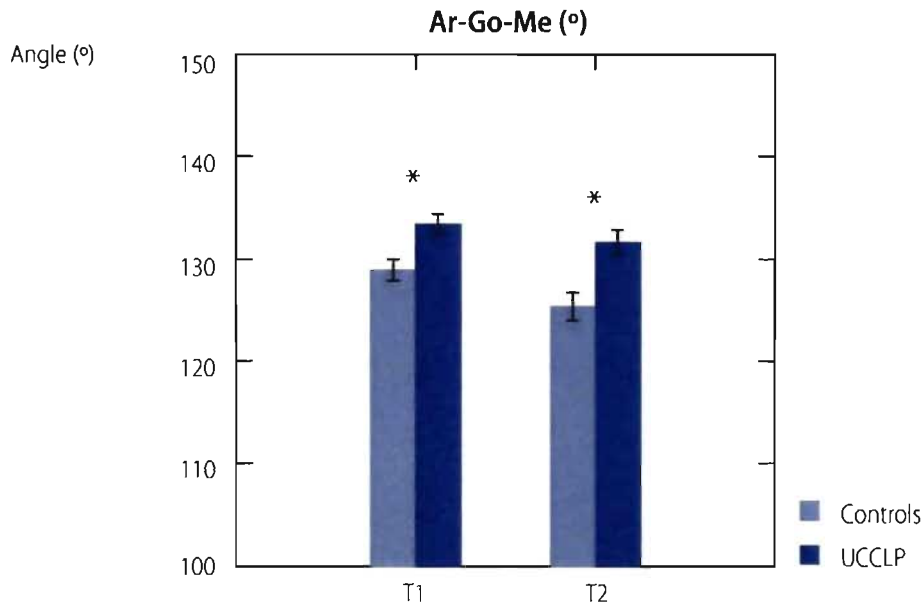

Figure 4-28 : Evolution of Ar-Go-Me angle over time (Difference is significant at T1: p=0.003 and T2: p=0.001).

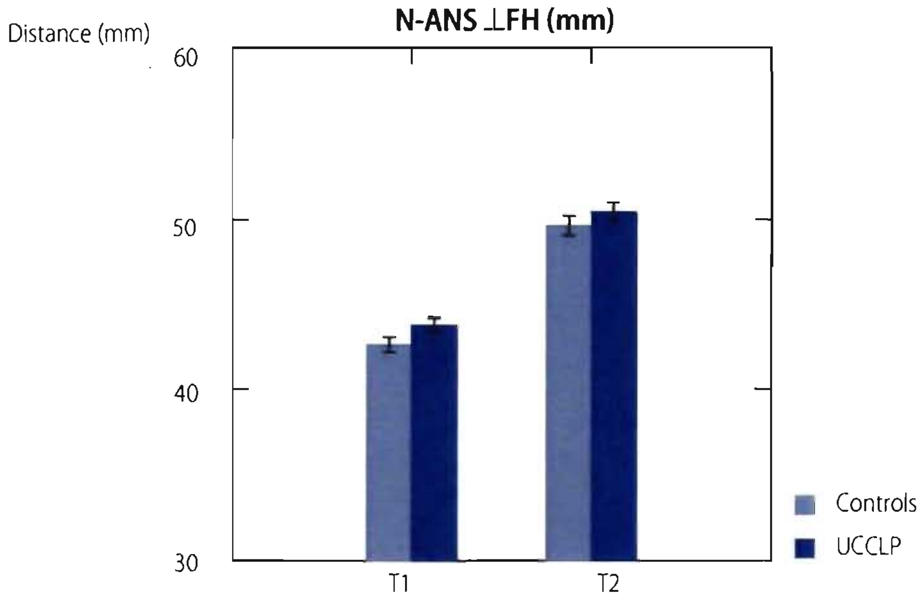

Figure 4-29 : Evolution of N-ANS ⊥FH distance over time (No significant differences).

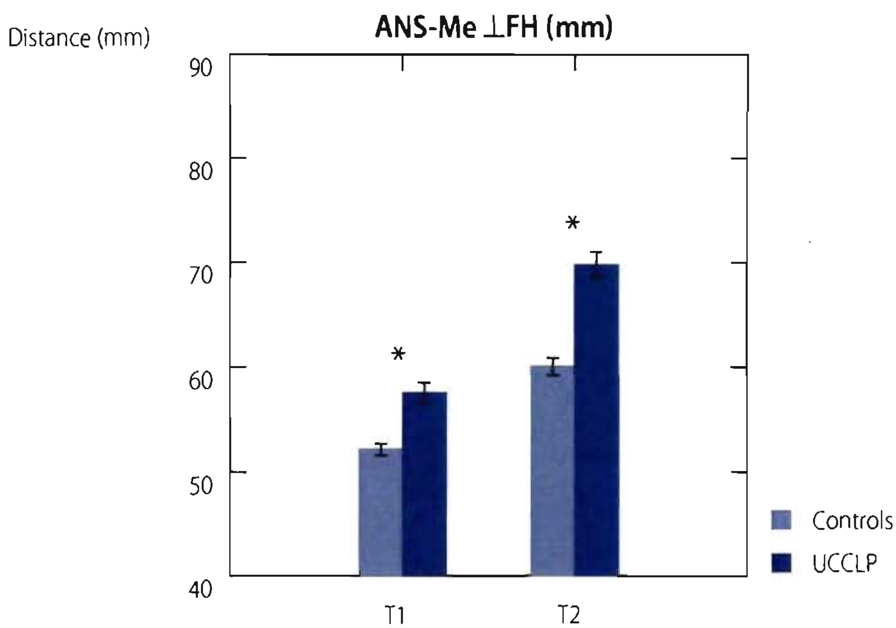

Figure 4-30 : Evolution of ANS-Me ⊥FH distance over time (Difference is significant at T1: $p<0.001$ and T2: $p<0.001$).

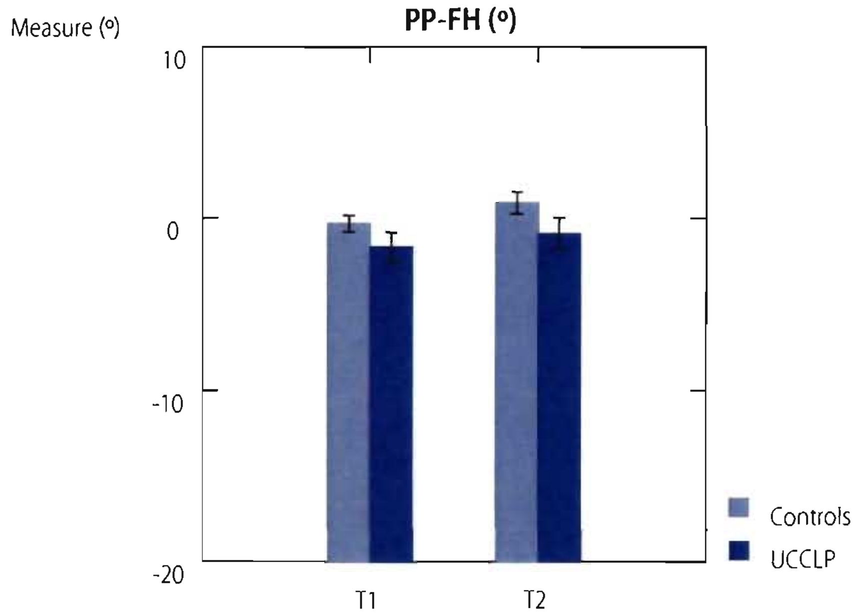

Figure 4-31 : Evolution of Palatal Plane to FH angle over time (No significant differences).

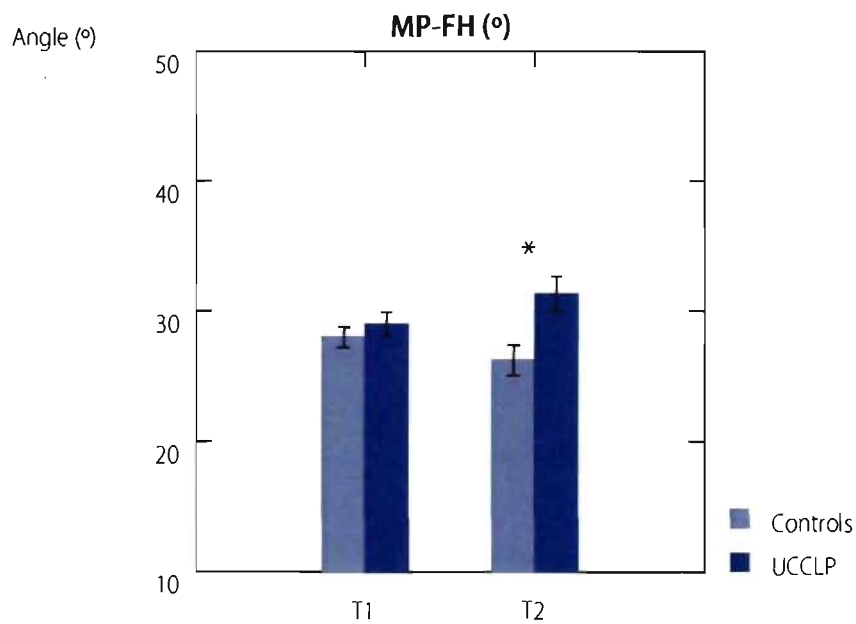

Figure 4-32 : Evolution of MP-FH angle over time (Significant difference only at T2: p=0.007).

Chapter 5: Discussion

5.1 Discussion of cephalometric morphology findings

Our initial goal was to compare maxillary and craniofacial growth of UCCLP patients (treated at Sainte Justine University Hospital Center) with a cohort of healthy teenagers and children.

One might argue that separate analyses for males and for females should have been performed. The reason why this was considered but not done is that this would have halved all our groups and weakened the statistical conclusions. If we look at similar studies, we see that Ross (1987) could afford to use only cephalograms from males in his multicentre study, with 15 centres participating. However, like us, the Eurocleft researchers (Brattström *et al.* 2005) have found it acceptable to have mixed study groups with equal distribution of males and females.

Age distribution between the compared groups was a factor that was closely accounted for. In that regard, the Eurocleft study was an ideal comparison study because patients in it were evaluated at 9 and 17 years of age, which is very similar to our T1 and T2 time points. In the Toronto study (Ross, 1987), we were also able to find groups with comparable ages. If we look at our control and subject groups we find an average age difference of one year at T2. While this is not clinically significant, our statistical analyses showed that this difference was statistically significant. The reason why this difference is deemed to be clinically not significant is because, as highlighted by Baumrind (1999), individual differences are a more significant source of variation than a small age increment.

Although there are many publications reporting on craniofacial growth of patients with UCCLP, no publication has studied a centre where the surgical protocol is significantly close to ours. It seems that we are one of the few centres using early and double layered closure of the primary palate at a distinct time from the posterior palate. As the variations between centres studied in the Eurocleft study show (Fig. 5-1), differences in treatment protocols are so wide that assessment of a single surgical intervention is extremely arduous. Nonetheless, comparisons such as the ones we attempted are useful because they can provide evidence that the final outcome in our patients is comparable to what is obtained in other centers.

	Montréal	Eurocleft A	Eurocleft B	Eurocleft D	Eurocleft E	Eurocleft F	Toronto Base
Birth		Presurgical orthopedics (Hotz)		Presurgical orthopedics (Extra-oral strapping)		Presurgical orthopedics (T-traction)	
3 months	Lip closure and primary palate* closure	Lip closure (Millard, Skoog)	Lip and hard palate† closure (Tennison + vomerplasty)	Lip (Varied methods and timing)	Lip and hard palate† closure (Millard + vomerplasty)		Heterogeneous group. Numerous surgical techniques involved
5 months						Lip closure (Modified Skoog/Tennison -Randall) and bone grafting	
9 months	Hard and soft palate closure	Soft palate closure (von Langenbeck, Perko, Wardill, Kriens)		Hard† and soft palate closure (Varied methods and timing)			
18 months					Soft palate closure (Modified von Langenbeck)	Hard† and soft palate closure (Vean-Wardill-Kilner pushback)	
24 months			Soft palate closure (Wardill pushback)				
8-11 years	Bone grafting	Bone grafting and hard palate† closure	Bone grafting	Bone grafting	Bone grafting		

Figure 5-1 : Variations in surgical protocols within the Eurocleft study (2005). †Hard palate includes primary palate unless otherwise specified (*) (Adapted from Berkowitz S. 2006)

One might ask if conclusions can be drawn as to whether or not the centres that close the primary palate early (like Eurocleft B) have specific characteristics. The answer to this question is that to answer such a specific question, the design of the study needs to be a randomized clinical trial in which all other factors are similar in all groups, with the only difference being early closure of the primary palate. The underlying idea behind our approach was that if primary closure of the primary palate at the time of lip repair was deleterious to maxillary growth, then the differences between our center and the Toronto Base group or the Eurocleft groups would be markedly visible. When looking at the graphical display of data, we see that this is not the case.

5.1.1 Craniofacial morphology between 7 and 10 years of age

It is noteworthy that at age 9, the values that reflect maxillary growth and facial profile (SNA, SNB, N-A-Pg, N-ANS, ANS-PNS and N-A (FH)) are essentially normal. As it was seen when comparing with data from Brattström *et al.* 2005 (Eurocleft), some published samples achieve similar outcome to ours at age 9 (Aduss, 1971) while in other samples, there are already significant differences by age 9 for those variables (Brattström *et al.* 2005). This is consistent with similar findings of wide variations by Aduss (1971), Hayashi *et al.* (1976), Smahel and Brejcha (1983), Ross (1987) and Smahel *et al.* (1998). This might be explained by the fact that surgical protocols vary substantially and that full growth potential has not been fully expressed yet for all craniofacial structures at 9 years of age. We will later see that when all growth has been achieved, the maxilla is literally "left behind".

Other differences are a greater gonial angle, a larger Y-axis value and a higher lower facial height in the UCCLP group. This is consistent with a more vertical growth pattern as described by Ross (1987). This difference was also found at a very young age (22 months) by Hermann (2000). If we review the studies on untreated patients (Dahl, 1970, Capelozza *et al.* 1993, da Silva Filho *et al.* 1993, 1998), we see that this might be a characteristic that is intrinsic to the UCCLP deformity. Some authors have related this to genetics, as relatives of patients with clefts have a higher lower face pattern (Wyszynski, 2002).

We note that the value for S-N is larger for the patients with clefts. The only explanation for this is that our study group is genetically bigger than the control group. The clinical significance of this difference is minimal since the difference is only 1.4 mm. Some studies (Aduss, 1971) found that S-N was shorter while most other studies found that the S-N values were generally normal (Ross, 1987).

Like Horswell *et al.* (1988), we find that mandibular length (Ar-Pg) is normal. We also find that the mandible (Pg) is displaced somehow farther from Sella (S), which might be a contribution of a higher lower facial height. We did not find smaller mandibular length as highlighted in other studies like Hayashi *et al.* (1976), Smahel and Müllerova (1986), Ross (1987) and Dahl *et al.* (1989).

5.1.2 Craniofacial morphology between 16 and 20 years of age

As expected at age 17, because of more complete expression of the growth potential, the differences between groups are more apparent. Interestingly, the difference for S-N is not present anymore. This might be explained by two factors: first the difference was very small initially, second, the individuals at 9 years of age were not all revaluated at 17 years of age. At 17, the differences between the groups can be divided in two: first, the patients with clefts have a deficient maxilla, as expected. Second, on average they show characteristics consistent with a vertical growth pattern.

Parameters that support the conclusion that the maxilla is deficient anteroposteriorly are SNA, ANB, N-A (FH) and N-A-Pg values. While ANS-PNS is similar to that of the Controls, we find a deterioration of this value between the ages of 9 and 17. We find similar results to Smahel and Brejcha, 1983; Ross, 1987; Rygh and Tinlund, 1996 in that the average individual with a UCLP who underwent surgical treatment had an anteroposterior midface deficiency of 5 to 6 millimetres at the adult age.

Interestingly, A-B (FH) is similar between patients with clefts and Controls. This might be explained by the fact that our patients with clefts were treated orthodontically. Even if the maxilla is retrusive, normal A-B (FH) values can be obtained by accentuating the clockwise rotation of the mandible.

We have to take into account that a few patients in the study cohort were being prepared for orthognathic surgery. However, we did not observe differences that we could relate to presurgical orthodontic decompensation. We note that it is one of the reasons why dental measurements were largely ignored in this study.

Values that support a more vertical growth pattern in the studied cohort are Ar-Go-Me, ANS-Me ⊥FH and MP-FH. This finding is reported in the scientific literature even in very young patients (Hermann *et al.* 2000) but the reasons explaining it are largely unknown. Other studies in adult or mature patients also found a vertical growth pattern (Hayashi *et al.* (1976), Smahel and Brejcha (1983), Ross (1987) and Smahel *et al.* (1998)). Some authors attribute mandibular differences to surgical factors, but this was based mostly on animal studies (Bardach *et al.*1979, 1980; Bardach and Mooney, 1984).

Unusually, average Go-Ar (height of the mandibular ramus) was larger in patients with UCCLP. Others in the literature have found lower values for posterior face height (Semb, 1991). Initially, this might seems to contradict the vertical growth pattern finding. However other values measured are supporting a vertical growth pattern and it is possible to have a higher Go-Ar without necessarily contradicting the latter concept. We note that a similar finding was highlighted by Kwon *et al.* (1998) who found an increased posterior facial height in patients with UCCLP.

At age 17, we find that mandibular length (Ar-Pg) is normal while the mandible (Gn) is displaced somehow farther from Sella (S), resulting in a higher S-Gn, which might be a contribution of a higher lower facial height. We did not find smaller mandibular length as highlighted in other studies like Hayashi *et al.* (1976), Smahel and Müllerova (1986), Ross (1987) and Dahl *et al.* (1989). However we note that in some samples (Ross, 1987, Horswell *et al.* 1988), mandibular size was normal. In our case and in other studies, these variations between studies might be explained by the difficulty in obtaining a large sample size.

5.2 Findings related to growth when comparing T1 and T2

We can evaluate growth by evaluating if the difference for any given cephalometric parameter is similar between the UCCLP group and the Control group. Since we have evaluated only two time points, when a statistically significant difference was observed at T1 or T2, this results in a statistically significant difference in growth. For most parameters, growth is similar. The two main exceptions are growth of the maxilla, as expected, and the vertical growth pattern.

For maxillary growth, we find that vertical growth of the maxilla (N-ANS) does not seem to be affected. This is confirmed when comparing with the values from the Toronto Base group (Ross, 1987). Unusually, ANS-PNS is higher for the UCCLP group at age 9. This is not a finding typically reported in the literature. However the difference becomes non-significant at 17 years of age. This deterioration is similar to what has been observed in other cohorts (Dahl, 1970, Ross, 1987, Brattsröm *et al.* 2005).

When comparing our data with data from the literature, it is remarkable that our sample has very high SNA and ANB values when evaluated at age 9, compared to other Eurocleft groups for example (Brattström *et al.* 2005). We note that it is no longer the case at age 17. We do not have a clear explanation for this. One possible cause might be the sample size which is small. There again, there is a deterioration that is similar to what has been observed in other cohorts (Ross, 1987, Brattsröm *et al.* 2005). Maxillary growth in our sample does not seem to be affected by the sole fact that these patients received an early closure of the primary palate at the time of lip repair.

For vertical growth in general, the differences observed at 9 years of age are maintained at 17 years of age. Thus, the values that are higher and remain higher in UCCLP patients are Ar-Go-Me and ANS-Me $\perp$FH. The values that are similar, and remain similar, are N-ANS $\perp$FH and $\angle$PP-FH. The only value that becomes more differentiated is $\angle$MP-FH, showing that our UCCLP patients accentuate their vertical growth tendency. Various explanations can justify this: UCCLP patients have a higher rate of mouth breating, which accentuates vertical growth (Warren *et al.* 1988); all our patients had orthodontic therapy and it is known that all therapies have an extrusive effect on teeth, which can contribute to increasing the vertical dimension (Proffit and Fields, 2001). Our values are similar to what was described by Ross, 1987, Semb *et al.* 1991 and Hermann *et al.* 2000.

Our measures were not focused on measuring mandibular size but for the two variables that give us an approximation on mandibular size (S-Gn and Ar-Pg). In our study, we did not find smaller mandibles as reported by others like Hayashi *et al.* (1976), Smahel and Müllerova (1986), Ross (1987) and Dahl *et al.* (1989). Usually in UCCLP patients, this difference in mandibular size is much smaller than the difference in profile, therefore it is possible that it went undetected. Another possible contributing factor is our sample, which was not selected randomly and its small size. For S-Gn the difference becomes larger, which we explain by the vertical growth pattern of our UCCLP sample. We believe there is a definite contribution of vertical growth of the lower face to the significant difference observed at age 17 for S-Gn: we think that as the mandible rotates counter-clockwise, the Gn point is displaced further from Sella (S).

5.3 Limitations and future studies

Among the limitations of the present study is the relatively small sample size. A larger sample size could have raised the statistical power of the analysis and thus, added more weight to the inferences and conclusions that arise from our data. However, we note that even large scale studies like Eurocleft (Brattström *et al.* 2005) were not able to amass more than 30 subjects per center.

We accept that other factors such as soft tissue profile and dental parameters were not evaluated. However, most studies that have looked at maxillary growth have used skeletal landmarks like the ones we used.

While Mølsted (1992) enumerates the advantages of participating in multicentre studies to advance cleft lip and palate research, practical, administrative and logistical problems often hinder such initiatives. We have faced such obstacles in the present study.

On the other hand, published results from multicentre studies often represent valuable comparison data, which allows any center to assess their outcomes. We note that many studies have used published data from other studies for comparison purposes.

In research, the use of published results becomes a very interesting alternative when a multicentre study is not possible. Future comparisons with other centers in Quebec, in Canada and around the world are encouraged.

Some improvements can be suggested for further studies. We suggest evaluation of plaster orthodontic study casts using the Goslon Yardstick (Mars *et al.* 1987) to determine the quality of the dental arch relationships. The Goslon Yardstick (Great Ormond Street, London and Oslo) is a clinical tool that allows categorization of the dental relationships in the late mixed and or early permanent dentition stage into five discrete categories.

Looking at what is a successful treatment outcome for a patient with a cleft we find soft tissue and photographic analysis would offer a more complete overview of treatment outcome since skeletal deficiencies are sometimes associated with an adequate soft tissue profile. We see that the Eurocleft study has used these parameters.

With the advent of three-dimensional cephalometry, a whole new approach to the study of craniofacial growth can now be imagined. So far very few studies have studied cleft lip and palate in three dimensions (Hermann, 2000).

Not all clefts are created equal. As stated by Berkowitz (2006), the initial size of the cleft is an important factor in determining outcome. It would be a valid approach to document and correlate initial cleft size with cephalometric outcome. Documentation can be photographic or through study casts. Berkowitz (2006) has used digitized casts at regular intervals.

Studies such as ours show the necessity to standardize documentation between centres. This has been attempted by the Eurocleft initiative. Interestingly, there are currently (April 2008) talks to launch an Americleft project for North America.

Chapter 6: Conclusion

When compared to normal children and adolescents, the patients in this cohort demonstrate some of the characteristic craniofacial disturbances observed in patients with cleft lip and palate.

At age 9, when compared to normal subjects, our patients do not have very severe disharmonies with the exception of a more vertical growth pattern.

At age 17, when compared to normal subjects, our patients present with a profile that is more consistent with a skeletal class III and this is mainly due to maxillary retrusion. The lower face height and FMA are both higher.

In terms of growth, our patients present a deterioration of the profile over time. This is similar to what is observed in data published in the literature. They also present with a vertical growth pattern that becomes more pronounced with time.

In general, the subjects from the Montreal sample were found to be similar to the comparison samples published in the literature when assessing maxillary growth. There were variations for some parameters, however, the design of this study does not allow for specific explanatory factors related to treatment protocol to be identified.

This study provides some evidence that the treatment protocol in Montreal achieves similar results than in other centers around the world. Further comparisons are definitely needed to better assess the growth of our patient cohort and the specific contribution of early repair of the primary palate at the time of lip repair.

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Appendix A

Lateral reference points used in the present study

Abbreviation	Name	Definition	Author	Year	Ref.
N	Nasion	The junction of the nasal and frontal bones as seen on the profile of the cephalometric roentgenogram.	T.M. Graber	1975	1
Or	Orbitale	The most inferior point on the lower border of the left orbit.	T.M. Graber	1975	1
PTM	Pterygomaxillare	The contour of the pterygomaxillary fissure formed anteriorly by the retromolar tuberosity of the maxilla and posteriorly by the anterior curve of the pterygoid process of the sphenoid bone. The lowest point of the opening is used. Apex of the teardrop-shaped Pterygomaxillary fissure.	Alex Jacobson Page W. Caufield	1985	8
S	Sella turcica	The center of the pituitary fossa.	T.M. Graber	1975	7
P	Porion	The highest point on the roof of the left external auditory meatus	L.B. Higley	1954	4
Ba	Basion	The most inferior point on the anterior margin of the foramen magnum in the midsagittal plane.	T.M. Graber	1975	9
Point A	Subspinale	The deepest midline point on the premaxilla between the anterior nasal spine and prosthion.	William B. Downs	1948	2
ANS	Anterior Nasal Spine	Most anterior point of the nasal floor; tip of premaxilla on midsagittal plane.	Vicken Sassouni	1971	5
PNS	Posterior Nasal Spine	The bony posterior projection of the horizontal portion of the palatine bone at the midline.	T.M. Graber	1975	7
PMP	Posterior maxillary point	Junction of the palatal plane and a line drawn perpendicular to the plane from the pterygomaxillary fissure.	R.B. Ross	1987	11
Pg	Pogonion	The most anterior point on the symphysis of the mandible.	T.M. Graber	1952	3
Gn	Gnathion	The most anterior inferior point in the lateral shadow of the chin. Best determined by selecting the midpoint between Pogonion and Menton on the contour of the chin.	Robert E. Moyers	1973	6
Me	Menton	The most inferior point on the symphysis of the mandible, as seen on the lateral jaw projection.	T.M. Graber	1975	9
Point B	Supramentale	An arbitrary measure point on the anterior profile curvature from the mandibular anthropometric landmark pogonion to the crest of the alveolar process.	T.M. Graber	1952	3
Go	Gonion	A posterio-inferior point on the ramus. Cephalometric Go is at the intersection of the mandibular plane and the ramus plane.	Robert M. Ricketts	1989	10
Co	Condylion	The most posterior superior point on the condyle of the mandible.	Robert E. Moyers	1988	9
Ar	Articulare	The point of intersection of the dorsal contours of the process articularis mandibulae and os temporale.	T.M. Graber	1975	7

References for lateral reference points used in the present study

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