The craniofacial growth pattern in Pierre Robin Sequence from childhood to adulthood

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Abstract

The purpose of this retrospective longitudinal cephalometric study was to find out if there was a difference between the craniofacial growth pattern between patients with Pierre Robin sequence (PRS) and isolated cleft palate (ICP). The study group comprised 23 children with diagnosis PRS which were compared cephalometrically with 22 age matched patients with a history of ICP. Cephalometric measurements were recorded at the age of 5, 8, 11, 14, 17, 19 years in both groups. However, the initial number of the patients at the age of 5 was reduced in the follow up period. All cephalograms were digitised by a computerized cephalometric software. Significant differences were found between the 2 groups. The mandibular length and protrusion was obviously shorter in the PRS group during the entire observation period. The conclusion of this study was that the expected catch up of the mandibular growth in patients with diagnosis PRS did not occur in the same extent as in the ICP group. Furthermore the PRS patients had a significantly shorter mandible as compared with the ICP group.
Keywords

Pierre Robin Sequence, Isolated cleft palate, cephalometry, craniofacial growth, retrognathia,
Introduction

The Pierre Robin sequence (PRS) has been described to present with micrognathia, glossoptosis (backward falling of the tongue into the pharynx) and cleft palate in the new-born (Rinatala et al. 1984, Shprintzen 1989, Lilius 1992a). According to the literature reviewed, the prevalence varies from one in 8500 births (Bush and Williams 1983) to one in 20,000 (Tolarova and Cervenka 1998).

The aetiology of the Pierre Robin sequence is heterogenic (Cohen 1976). For this reason the name anomalad or sequence is suggested to be used instead of syndrome (Gorlin 1990). Gorlin et al (1990) proposed the PRS to be developed due to the mechanically constrained position of the mandible at the time of palatal closure. If this theory is accurate, it would appear logical to expect some rebound growth of the mandible shortly after birth, reducing the facial convexity and perhaps allowing the mandible to catch up with the maxilla.

The clinical picture of children with PRS at birth has been described by Caouette-Laberge et al. (1994). They recognised three groups of new-born: the first had mild clinical distress only; the second had adequate respiration when prone but feeding difficulties that required gavage; the third comprised children with severe respiratory problems that required endotracheal intubation, tongue-lip adhesion or release of the musculature of the floor of the mouth.
Other authors have suggested types of management including mandibular traction and advancement appliances.

**History**

In 1822 St. Hailaire recognized the classical triad of the anomaly: mandibular hypoplasia, glossoptosis and a U-formed cleft palate. (Randal 1965). Fairbairn (1846) described the same condition dealing with newborn micrognathia. In 1923 the French stomatologist, Pierre Robin, first published on the association of newborn with the upper way obstruction caused by glossoptosis. In 1929 Robin published a monograph on the condition, that later was to bear his name. He continued with the subject until 1934, writing 17 articles on the problems of glossoptosis (Randal 1965). He also treated the condition with a monobloc to restore the normal relationship between the upper and lower jaw. Robin also described the failure of these infants to gain weight because of feeding problems. Subsequently the sequence has been discussed by many authors, listed by Dennison (1965) and Randall et al. (1965).

**Aetiology and Pathogenesis**

Satokaka and Mass (1994) could show that the msx 1 homeobox gene deficient mice were found to exhibit a cleft of the secondary palate, an abnormally short mandible and the absence of the tooth buds which is similar in its expression to the isolated nonsyndromic cleft palate (ICP) and also to PRS. Transforming growth factors α (TGFα) (Shiang et al. 1993)
and β3 (TGF β3) (Proetzel et al. 1995) are also regarded as possible candidates involved in the cleft palate aetiology. The Pierre Robin sequence is not a syndrome with a single identifiable pathogenesis, but is a non-specific sequence of findings with aetiological heterogeneity resulting in the same phenotype (Cohen 1981). Also Oligohydraminiosis with decreased amniotic fluid can result in compression of the chin against the sternum causing restricted downward-forward growth of the mandible. Neurogenic hypotonia leading to restricted mouth opening due to lack of exercise can present a similar phenotype. Growth deficiency as a symptom of a chromosomal syndrome can lead to mandibular hypoplasia, which can be caused also by connective tissue disorders. Three major theories concerning PRS have been proposed over the years (1) mechanical (Harris 1964, Poswillo 1966, 1968), (2) metabolic (Edwards and Newall 1985), and (3) genetic (Rintala et al. 1984, Gorlin et al 1990, Satokaka and Mass 1994).

Since the oral cavity is small in an infant with PRS, a massively swollen tongue can continue to occlusion of the oropharynx posteriorly and decrease the airway causing severe respiratory distress (Lee 1985, Sher 1992).

Takagi and Bosma (1960) suggested that the rapidly progressive change in oral-pharyngeal function in infants with PRS which occurs in the few postnatal weeks may be related to neurologic development. The theme of aetiology was further discussed by Rintala et al. (1984) leaving a question
of whether the growth disturbance in both the maxilla and the mandible due to organogenetic differences leads to diverse end results, micrognathia and cleft palate. Since the expression of the PRS and ICP varies widely from mild to severe, the origin of the pathogenesis can still have different sources unsolved (Ferguson 1994). Current research has moved more to the basis on the regulator and signalling genes affecting structures derived from the neural crest.

Associated Syndromes and Anomalies

The syndromes are variably present in 25-38% of all PRS cases (Hanson and Smith 1975, Sheffield et al. 1987). Another 35% have multiple anomalies, while the remaining can be instanced as isolated PRS (Hanson and Smith 1975). It has been estimated (Herrman and Opitz 1975) and presented that one-third of all PRS patients have Stickler syndrome (Cohen 1981, Shprintzen 1988). The syndrome is diagnosed by the presence of skeletal abnormalities and eye symptoms.

Obstructive sleep apnoea syndrome (OSAS) is also seen in connection with PRS. Some patients with anatomic causes of upper airway obstruction (micrognathia, nasal obstruction, enlarged adenoids and tonsils, laryngeal stenosis) as well as some patients without anatomic obstruction, may have similar cardio respiratory problems caused by frequent episodes of central and / or obstructive apnoea during sleep (Cozzi and Pierro 1985). The so called acquired glossoptosis in PRS infants with the clinical picture of
enlarged adenoids most frequently cause the OSAS (Brouillette et al. 1982). According to Cozzi and Pierro (1985) glossoptotic pharyngeal obstructions in PRS infants occur in 72% of them while the infants are awake.

**Postnatal Craniofacial Growth in PRS**

Pruzansky (1955) described the spontaneous narrowing of the palatal cleft in PRS infants within the first 14 months after birth. Since mandibular position and size have been the mean focus of investigations on PRS patients, the earlier reports did not reveal any substantial information about the maxillary size or the maxillary relationship to the anterior cranial base. Marcovic (1972) stated that out of 15 PRS patients 9 had SNA angles smaller than normal indicating that maxillary retrognathia is common in PRS. In addition the SNA angle decreased in 10 out of 15 cases during the growth periods examined. The maxillary retrusion in relation to the anterior cranial base was found to be similar in PRS and ICP subjects (Ranta et al 1985), but the maxilla was anteriorly more downward inclined in PRS patients.

A number of cephalometric studies have attempted to investigate an eventual mandibular catch-up growth issue. Pruzansky (1969) found the facial profiles of 21 patients with PRS to be nearly identical to those of patients with ICP by the age of 10,5 years, although they had been much more convex at infancy. Hots and Gnoinski (1982) reported that by the age
of 5 years no difference in mandibular length existed between a small number of patients with PRS and patients with ICP. Figueroa et al (1991) followed 17 infants with PRS between 3 months and 2 years of age and compared them with 26 infants with ICP and 23 healthy infants of similar age. Their findings of increased rate of growth in the PRS group, as compared with the 2 other groups, were interpreted as partial mandibular catch-up growth, because the mandibular length in the PRS sample still remained significantly shorter at the end of the observation period.

In a study by Laitinen et al (1997) the craniofacial morphology of 30 young adults with the PRS, aged 17-27 years, was analysed and compared with the craniofacial morphology of 116 young adults with isolated cleft palate, aged 16-20 years and they found that the mandible was more retruded and more posteriorly rotated, and the soft tissue profile more convex in PRS patients. Daskalogiannakis et al (2001) followed 96 patients with a history of Pierre Robin sequence between 5 and 17 years of age and compared them with a control group of 50 patients with a history of isolated clefting of the palate. They concluded that patients with Pierre Robin sequence have a significantly smaller mandible as compared with patients with isolated cleft palate and the difference did not change after the age of 5 years.

**Treatment Regimes**

**Early Treatment**

The initial treatment purpose in PRS is to keep the airways free from any obstruction, usually caused by micrognathia and glossoptosis. The
continuous prone position has historically been recommended to control mild airway obstruction. In moderate cases a tongue-lip adhesion could be helpful to keep away the tongue base. Most paediatric airway surgeons have abandoned this technique because of aspiration, feeding abnormalities, increased airway obstruction, and lack of effectiveness (Myer et al. 1998). In the most severe cases tracheotomy has been an effective method. Long term tracheotomy in children has a significant associated morbidity and mortality. The mortality is 0.5% to 4% in various studies (Arola 1981, Wetmore et al. 1982, Puhakka et al. 1992). The morbidity includes recurrent airway infections, airway bleeding, stomal problems, interference with speech development, and feeding and swallowing problems. In addition, there is the issue of socialisation of children with long-term tracheotomies. As an alternative to tracheotomy, distraction of the mandible has been used in recent years with so far good results and stability. Briefly the definition of distraction osteogenesis is the regeneration of the bone between vascularized bone surfaces that are separated by gradual distraction (Aronson 1994). The bone is most commonly separated by an osteotomy or corticotomy and stabilised by external or intraoral fixation. From the historic point of view, Ilizarov began working with these principles after World War II to treat patients with fractures and nonunion of the long bones of the extremities. The principle that Ilizarov emphasized included increased fixator stability and maximum preservation of periosteum, with a
minimal disruption of the central medullary bone using a low-energy corticotomy that only divides the bone cortex (Ilizarov 1989). Distraction forces applied to bone also create tension in the surrounding soft tissues, initiating a sequence of adaptive changes termed distraction histogenesis (Samchukov et al 1998). After osteotomy or corticotomy, the bone segments are held in position for a predetermined latency period of 5 to 7 days, after which the distraction device is gradually lengthened at a specified rate of 1 mm per day. Once the desired lengthening is achieved, the distraction device is used as an external fixator during a period of consolidation (2 weeks) in which mineralization of the new bone occurs. (McCarthy et al 1992, Molina and Ortiz-Monasterio, 1995).

*Mixed and Permanent Dentition*

In the mixed and permanent dentition has following traditional treatment regimes been proposed in the literature:

- Removable appliance in the mixed dentition, with advancement of the mandible, bite plane etc.
- Fixed appliance in the permanent dentition
- In the late adulthood and in the adults orthognathic surgery has been recommended in cases with a severe retrognathia to correct the mandibular retrognathi with a sagittal split of the ramus mandibulae, probably in some cases also combined with correction of the maxilla.
The Aim of the study

The purpose of this retrospective longitudinal cephalometric study was to evaluate the difference between the craniofacial growth pattern from childhood to adulthood in patients with Pierre Robin Sequence (PRS) compared with Isolated Cleft Palate (ICP), with special interest to evaluate if the catch up of mandibular growth was the same in both groups.
Material och methods

Data were collected from the cleft patient files at the Cleft Palate Centre University Hospital Uppsala, Sweden diagnosed in infants as PRS between 1980-1997. The diagnostic features of PRS were retrognathia or micrognathia, glossoptosis, respiratory obstruction and a cleft palate. Children with various syndromes identified, were not included in the present study. This retrospective follow-up study consisted of 23 children, 10 females and 13 males, born between 1980-1997 all with the diagnosis Pierre Robin Sequence (PRS). A comparison was made with 22 aged matched children, 12 females and 10 males all with isolated cleft palate (ICP). 8 patients with PRS were followed from 5 until 17 to 19 years and 10 ICP patients within this same age range (Table 1). Approximately 40% of the children in the PRS group were treated by some kind of orthodontic appliance and among the children in the ICP group, nearly 50% had experienced orthodontic treatment. All Children have been treated at the Cleft lip and Palate Centre at the University Hospital Uppsala, Sweden. The majority of the children with PRS in the present study were included in a previously published study by T.G. Henriksson and V.T. Skoog (2001). The cephalometric recordings of the patients were performed between 5-19 years of age. All the patients were operated by a two-stage repair technique when needed. The reconstruction of the soft palate took place at the age of 1½ year from 1979 until 1984. During 1984 the same operation was done at the age of 1 year, and from 1985 at the age of 6 months. The residual cleft
was closed at 2-4 years of age. In the present study the cephalometric radiographs were available at the ages of 5, 8, 11, 14, 17 and 19. All radiographs have been traced and digitised using the Dentofacial Planner cephalometric software. A total of 68 points were digitised per tracing. Superimposition of individual series of tracings has been performed in each individual to illustrate the growth pattern.

**Measurements**

The anteroposterior and vertical skeletal jaw relationships were analysed in lateral cephalometric radiographs taken with the mandible in intercuspal position and the patient’s head fixed in a cephalostat. Cephalometric measurements were carried out using reference points and lines according to Steiner (1959) and McNamara (1983). Angular and linear variables were calculated to the nearest half a degree. The names and definitions of the reference points, lines and angular measurements used in the analysis are listed below and shown in Figure 1.

**Reference points**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong></td>
<td>Subspinale. The deepest point in the concavity of the anterior maxilla between the anterior nasal spine and the alveolar crest.</td>
</tr>
<tr>
<td><strong>ANS</strong></td>
<td>Anterior Nasal Spine, the tip of the anterior nasal spine.</td>
</tr>
<tr>
<td><strong>Ar</strong></td>
<td>Articulare. The intersection between the external contour of the cranial base and the dorsal contour of mandible.</td>
</tr>
<tr>
<td><strong>B</strong></td>
<td>Supramentale. The deepest point in the concavity of the anterior mandible between the alveolar crest and Pogonion.</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Ba</td>
<td>Basion. The most inferior point on the anterior margin of the foramen magnum.</td>
</tr>
<tr>
<td>Co</td>
<td>Condylion. The most postero-superior point of the mid-planed contour of the mandibular condyle.</td>
</tr>
<tr>
<td>Gn</td>
<td>Gnathion. The most antero-inferior point on the bony chin, located by bisecting mandibular and facial planes.</td>
</tr>
<tr>
<td>Go</td>
<td>Gonion. A mid-planed point at the gonial angle of the mandible located by bisecting the posterior and inferior borders of the mandible.</td>
</tr>
<tr>
<td>Me (M)</td>
<td>Menton. The lowest point on the lower border of the mandibular symphysis.</td>
</tr>
<tr>
<td>N</td>
<td>Nasion. The junction of the frontal and nasal bones at the naso-frontal suture.</td>
</tr>
<tr>
<td>Pg</td>
<td>Pogonion. The most anterior part on the mandibular symphysis.</td>
</tr>
<tr>
<td>Pm</td>
<td>Pterygomaxillare. The inferior junction at the junction of the anterior and posterior borders of the pterygo-maxillare fissure.</td>
</tr>
<tr>
<td>PNS</td>
<td>The tip of the Posterior Nasal Spine.</td>
</tr>
<tr>
<td>S</td>
<td>Sella. The centre of sella turcica.</td>
</tr>
</tbody>
</table>

**Reference lines**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ML</td>
<td>Mandibular Line. The tangent to the lower border of mandible through Me.</td>
</tr>
<tr>
<td>Mand.L</td>
<td>Mandibular Length. The line through points Co and Gn.</td>
</tr>
<tr>
<td>NL</td>
<td>Nasal line. The line points ANS and Pm.</td>
</tr>
<tr>
<td>NSL</td>
<td>Nasion-Sella line. The line through points N and S.</td>
</tr>
<tr>
<td>RL</td>
<td>Ramus line. The tangent to the mandibular ramus through point Ar.</td>
</tr>
</tbody>
</table>
Definition of the angular measurements

SNA  The angle is an expression of the anteroposterior position of point A in relation to the anterior base of the skull.

SNB  The SNB angle describes the anteroposterior position of the mandible in relation to the anterior cranial base.

ANB  This represents the difference between the SNA and SNB angles and defines the mutual relationship, in the sagittal plane, of the maxillary and mandibular bases.

SNpg  As with the SNB angle, the SNpg angle provides an indication of the sagittal position of the mandible.

SNBa  This angle describes the relation of the clivus to the anterior cranial base.

NSL/NL  This expresses the degree of inclination of the maxilla in relation the anterior cranial base.

NSL/ML  This angle expresses the inclination of the mandible in relation to the anterior cranial base.

NL/ML  This angle expresses the degree of inclination of the mandible in relation to the maxillary base.

ML/RL  Gonial angle. This angle is an expression of the form of the mandible relating the body and the ramus.

11/NL  This angle describes the position of the upper incisors as well as the amount of protrusion.

41/ML  This angle describes the axial position and protrusion of the lower incisors.
Figure 1. Cephalometric reference points and lines according to Steiner (1959) and McNamara (1983) used in the study.
**Statistical Analysis**

For each patient a constant growth rate was assumed for the linear and angular measurements. Assuming that individuals start at different levels at age 5 (baseline) a linear mixed-effects model was formulated to describe the growth over time (Pinheiro and Bates 2002). The model account for the design of repeated measurements by assuming a (constant) correlation between all measurements for each patient. Individual intercepts were modelled as random effects while group (PRS vs. ICP) and time were modelled as fixed effects. Differences as regards mean levels and growth rates between the groups (Table 3) were then extracted from the fitted model. In the process of fitting the model we saw that, for most angular and linear measurements, there were no statistical differences between the PRS and ICP groups regarding the rate of change per year. This can also be seen in the figures. Because of this we chose to assume the same rate of change for the two groups in order to achieve estimates with higher precision. This simplifies the model in respect to interpretability and also, as a positive side effect, estimate the average differences between the two groups also with higher precision.

**Reproducibility of recordings**

The intra-examiner reproducibility of the cephalometric measurements were determined from randomised duplicate recordings, approximately 3 months apart from 10 of the study subjects. The intra-class correlation coefficient (ICC) was calculated as a measure of agreement (Bland and
Altman 1986). The ICC varied from 0,79 to 0,99. The ICC variation was within acceptance. (Table 2).
Results

Table 3 and figures 2-5 show the average difference of the cephalometric angular and linear measurements for the PRS group compared with the ICP group and the rate of growth change per year during the observation period 5-19 years.

**Anteroposterior jaw relations**

The average difference of the SNA angle showed that the maxillary protrusion tended to be at a lower mean level in the PRS group during the entire observation period from 5-19 years of age (Table 3). The pattern of change was the same in both groups (Table 3, Fig.2).

The SNB angle increased slightly in both groups (P=0.114) but the mean level in the PRS group was statistically significantly (P=0.001) lower than the mean level of the ICP group during the observation period (Table 3, Fig.2).

In the PRS and ICP group, the rate of the change of the SNpg angle per year showed an increase, but the SNpg angle was 2,83° degrees smaller in the PRS group throughout the years (Table 3, Fig.2).

**Vertical jaw relations**

The average difference of NSL/ML, ML/RL and NL/ML angle was significant between the PRS and ICP group during the study period. However, the rate of change per year showed a reduction in the PRS and ICP group (Table 3, Fig.3).
The Mandibular Length

The length of the mandible increased significantly in both groups. The rate of change per year of the mandibular length was statistically significantly higher in boys compared with girls in both groups (Table 3, Fig.4). The PRS group, boys and girls combined, showed a smaller mandibular length than the ICP group already at the age of 5 years. This same pattern remained throughout the observation period (Table 3, Fig.5).

Incisor position

The proclination of the upper incisors 11/NL varied within and between the groups (Table 3). The 41/ML angle, which expresses the inclination of the lower incisors showed a significant increase in both groups (Table 3).
Discussion

The results of the present study revealed that the patients with the diagnosis of PRS had a shorter mandibular length than those with ICP during the entire observation period, 5-19 years of age. In a similar study by Daskalogiannakis et al (2001) the mandibular length was measured from the point Condylion (Co) to Gnathion (Gn) as in the present study. They did also find that patients with Pierre Robin sequence had a significantly shorter mandible compared with patients with isolated cleft palate and the difference between the groups did not change after the age of 5 until 17.

The vertical relationship of the jaws was also studied and the mandible was found to be more posteriorly rotated and the NL/ML angle was taller in the PRS than in the ICP group. Laitinen et al (1997) found in their study including 30 young adults with PRS, that the mandible was more retruded and more posteriorly rotated in the PRS patients which results also are in agreement with that of the present study. The maxilla tended to be more retruded in the PRS patients than in the ICP and this finding was in agreement with the results of Marcovic (1972). Marcovic reported that out of 15 PRS patients 9 had SNA angles smaller than normal describing the commonly found feature of maxillary retrognathia in the PRS. In the results of Ranta et al (1985) they reported that the maxilla was anteriorly more downward inclined in the PRS patients. These features cannot be clearly described in the present study.

Thilander et al (1982) presented a material which comprised a number of Swedish children and young adults who fulfilled special criteria of normal
occlusion and harmonious skeletal relations and in whom roentogencephalometric data were collected. These children were then compared with previous Scandinavian normative data. In a comparison with the material of Thilander et al. and the present study it was found that the mean level of the cephalometric measurements of the mandible and maxilla in the PRS group were below the mean level of the normal population. Even the mean level of rotation of the mandible was higher in the PRS group than the normal material.

Despite the fact that conventional orthodontic treatment with functional or fixed appliances or with orthognatic surgery and craniofacial reconstruction have experienced widespread success, several limitations are associated with these treatment modalities (Traumer R, and Obwegeser H. 1957, Converse JM. and Horowits SL. 1969, Cassidy et al 1993). One of these limitations is the inability of the muscles to be acutely stretched without the inherent risk of relapse (Schendel et al 1980, Blair VP. 1907, Babcock WW. 1909, Ellis E. III, Carlsson DS. 1983). Moreover many of the congenital deformities require such large musculoskeletal movements that the soft tissues simply will not accommodate the change, leading to relapse or compromised function and aesthetics unless additional soft tissue procedures are performed (Caldwell et al 1968, Longaker MT and Siebert JW 1996, Vargervik et al 1986).

Mandibular elongation and remodelling by distraction osteogenesis proceeds parallel to an expansion of all soft tissues of the face and upper
neck (skin, muscles, vessels, and nerves), achieving aesthetic results much superior to those obtained by skeletal surgery, by soft-tissue surgery done independently, or by a combination of both (Molina, F., and Ortiz-Monasterio, F. 1995) Distraction osteogenesis can be applied at an earlier age than the traditional orthognathic surgery because the technique is relatively simple and bone grafts are not required for augmentation of the hypoplastic craniofacial skeleton (Grayson BH., and Santiago PE. 1999). This treatment procedure may subsequently improve the condition of the glossoptosis and obstruction of the airways. Feeding difficulties is another problem that these patients may thus be helped with. Tracheotomy is performed when the airway obstruction is severe and refractory to other less invasive interventions, tracheotomy is associated with significant morbidity (Judge B et al 1999). In selected Pierre Robin sequence patients with tongue base airway obstruction, mandibular distraction osteogenesis can successfully avoid the need for and the associated mortality and morbidity of indwelling tracheotomy (Denny A, Kalantarian B. 2002).

The number of patients with PRS who ultimately need lengthening of the mandibular hypoplastic bone by distraction osteogenesis will certainly not be dominating. The continued growth may compensate the discrepancy enough to please the patients subjective and functional needs. However, future studies are needed to better evaluate and predict the strategies of treatment modalities.
Conclusion

The conclusion of this study was that the expected catch up of mandibular growth in patients with diagnosis PRS did not occur in the same extent as in the ICP group. However the growth pattern of madibular length and mandibular protrusion was the same in both groups though leaving the PRS group on a lower mean level from childhood to adulthood.
Acknowledgements

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References


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Pruzansky S. Not all dwarfed mandibles are alike. Birth Defects 1969; 5: 120- 129.


Table 1. The numbers of children at the age of 5, 8, 11, 14, 17 and 19 years in the PRS and ICP group.

<table>
<thead>
<tr>
<th>Group</th>
<th>5 YEARS</th>
<th>8 YEARS</th>
<th>11 YEARS</th>
<th>14 YEARS</th>
<th>17 YEARS</th>
<th>19 YEARS</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRS</td>
<td>N = 23</td>
<td>N = 15</td>
<td>N = 13</td>
<td>N = 5</td>
<td>N = 5</td>
<td>N = 3</td>
</tr>
<tr>
<td></td>
<td>13 male</td>
<td>9 male</td>
<td>8 male</td>
<td>3 male</td>
<td>3 male</td>
<td>1 male</td>
</tr>
<tr>
<td></td>
<td>10 female</td>
<td>6 female</td>
<td>5 female</td>
<td>2 female</td>
<td>2 female</td>
<td>2 female</td>
</tr>
<tr>
<td>ICP</td>
<td>N = 22</td>
<td>N = 20</td>
<td>N = 19</td>
<td>N = 10</td>
<td>N = 8</td>
<td>N = 2</td>
</tr>
<tr>
<td></td>
<td>10 male</td>
<td>8 male</td>
<td>9 male</td>
<td>4 male</td>
<td>2 male</td>
<td>0 male</td>
</tr>
<tr>
<td></td>
<td>12 female</td>
<td>12 female</td>
<td>10 female</td>
<td>6 female</td>
<td>6 female</td>
<td>2 female</td>
</tr>
</tbody>
</table>

N= Number of patients.

Table 2. Reproducibility. Intra Class Correlation (ICC), coefficients of the cephalometric measurements.

<table>
<thead>
<tr>
<th>Variable</th>
<th>SNA°</th>
<th>SNB°</th>
<th>SNBa°</th>
<th>NSL/ML°</th>
<th>NL/ML°</th>
<th>ML/RL°</th>
<th>11/NL°</th>
<th>41/ML°</th>
<th>MAND.LENGTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICC</td>
<td>0.88</td>
<td>0.95</td>
<td>0.79</td>
<td>0.88</td>
<td>0.92</td>
<td>0.98</td>
<td>0.95</td>
<td>0.98</td>
<td>0.99</td>
</tr>
</tbody>
</table>
Degrees
Figure 2. The individual growth change of the cephalometric angular measurements of SNA, SNB and SNPG between 5-19 years of age in the ICP and PRS group.

Table 3. The average difference of the cephalometric angular and linear measurements between the PRS and the ICP group and rate of change for both groups combined per year during the observation period 5-19 years of age.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Average diff. between PRS and ICP groups</th>
<th>P.value</th>
<th>Rate of change per year for the ICP and PRS groups</th>
<th>P.value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNA °</td>
<td>-1.48</td>
<td>0.131</td>
<td>-0.03</td>
<td>0.505</td>
</tr>
<tr>
<td>SNB °</td>
<td>-2.95</td>
<td>0.001</td>
<td>0.08</td>
<td>0.114</td>
</tr>
<tr>
<td>ANB °</td>
<td>1.11</td>
<td>0.133</td>
<td>-0.12</td>
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mm.
Degrees
Figure 3. The individual growth change of the vertical angular measurements of the mandible during 5-19 years of age in the ICP and PRS group.
Figure 4. The growth pattern of mandibular length in girls (F) and boys (M) in the PRS and the ICP groups.
Figure 5. The growth pattern of mandibular length for boys and girls combined in the ICP and PRS group during the observation period.