

# An Overview of Craniosynostosis Craniofacial Syndromes for Combined Orthodontic and Surgical Management



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## KEYWORDS

- Craniosynostosis • Maxillary distraction osteogenesis • Craniofacial syndromes • Apert syndrome
- Pfeiffer syndrome • Crouzon syndrome

## KEY POINTS

- Patients with craniosynostosis syndromes require comprehensive multidisciplinary care.
- Common presenting clinical features include maxillary hypoplasia, class III malocclusions, anterior openbites.
- Excellent outcomes can be achieved with good teamwork.

## OVERVIEW OF CRANIOSYNOSTOSIS

Craniosynostosis, defined as the premature fusion of 1 or more cranial sutures, occurs in 1 in 2000 to 2500 live births and is one of the most common congenital craniofacial anomalies.<sup>1–3</sup> Lack of growth perpendicular to the fused sutures and compensatory growth at normal ones result<sup>4–6</sup> in patients presenting with a distorted head shape. Most cases of craniosynostosis are isolated or nonsyndromic, but 9% to 40% of patients have a syndromic form with more than 130 syndromes associated with craniosynostosis.<sup>6–9</sup> Patients with

syndromic craniosynostosis may also have associated abnormalities of the face, trunk, and extremities that vary in presentation, severity, and cause.<sup>3,4,6–9</sup> Early diagnosis and treatment of craniosynostosis is important to ensure that brain growth is not restricted by insufficient cranial volume and to minimize distortion of the cranium. In severe cases, affected patients may have increased intracranial pressure (ICP) and experience functional problems (eg, breathing difficulty, choking or vomiting with feeding), exorbitism, irritability, developmental delays, and even death.<sup>4,10,11</sup>

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## EPIDEMIOLOGY

Several studies have investigated the incidence and prevalence of craniosynostosis across different regions.<sup>1,3</sup> In Western Australia, prevalence of craniosynostosis between the years of 1980 and 1994 was 5.06 per 10,000 births, similar to the prevalence of 4.3 per 10,000 in the metro-Atlanta area from 1989 to 2003.<sup>1,3</sup> The Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project Kids Inpatient Database estimates prevalence of craniosynostosis at 3.5 to 4.5 per 10,000 births between 1997 and 2006.<sup>12</sup> These values are lower than those from other studies in regions such as Colorado (14.1 per 10,000), New South Wales (8.1 per 10,000), and Israel (6.0 per 10,000) for a coincident time period.<sup>1,13,14</sup> The same study in Australia showed an increase in lambdoid synostosis of 15.7% per year linearly and did not distinguish a particular cause or explanation.<sup>1</sup> In contrast, its metro-Atlanta counterpart discovered a decrease in prevalence of lambdoid synostosis and attributed this to a possible misclassification of deformational posterior plagiocephaly in these patients.<sup>3</sup>

## SYNDROMIC VERSUS NONSYNDROMIC CRANIOSYNOSTOSIS

The diagnosis of, risk factors associated with, and management of nonsyndromic or syndromic craniosynostosis syndromes differ markedly. Among the nonsyndromic population, sagittal synostosis is the most common, followed by synostosis of the lambdoid suture, whereas coronal suture involvement is more characteristic of syndromic craniosynostosis.<sup>1</sup> Boulet and colleagues<sup>3</sup> found that 39% of nonsyndromic cases had sagittal synostosis and that this was more common in boys, whereas coronal synostosis was more common in girls. Being male is also a risk factor for lambdoid synostosis. Although less severe, other major birth defects were still noted in 11.2% of nonsyndromic patients.<sup>1</sup> Syndromic craniosynostosis is more complex, harder to care for, and necessitates multidisciplinary treatment. It is also associated with an increased risk of increased ICP caused by intracranial venous congestion, hydrocephalus, and upper airway obstruction.<sup>9</sup> Syndromic patients are at the greatest risk for perioperative complications.<sup>15</sup> Diagnosis of a syndrome is based primarily on dysmorphic presentation and genetic testing, and, according to Singer and colleagues,<sup>1</sup> 25.3% of patients with craniosynostosis are seen by a geneticist.<sup>10</sup>

## GENETICS

Johnson and Wilkie<sup>8</sup> reported that 21% of patients with craniosynostosis had a genetic diagnosis of single-gene mutations or chromosomal abnormalities. Craniosynostosis is mostly autosomal dominant and is more likely to be associated with multiple-suture synostosis and extracranial complications. The most common mutations are in the FGFR2, FGFR3, TWIST1, and EFNB1 genes.<sup>8</sup> Crouzon, Apert, and Pfeiffer syndromes are caused by mutation to the FGFR-2 gene, Saethre-Chotzen is caused by the TWIST-1 gene mutation, and Muenke is unique in that there is a mutation in the FGFR-3 gene.<sup>9,16-19</sup> In a study by Timberlake and Persing,<sup>20</sup> exome sequencing was completed in 384 families and a new genetic testing protocol was established. It had been previously determined that syndromic craniosynostoses are associated with mutations in the FGF/Ras/ERK, BMP, Wnt, ephrin, hedgehog, and STAT genes, as well as resultant deficits in the retinoic acid signaling pathways.<sup>21</sup> Similarly, nonsyndromic craniosynostosis was found to be associated with a nonmendelian inheritance pattern but also frequently involves mutations in the Wnt, BMP, and Ras/ERK pathways.<sup>20</sup> Another study by Wilkie and colleagues<sup>22</sup> used targeted molecular genetics and cytogenetic testing for 326 children born between 1993 and 2002 who required craniosynostosis repair, and they discovered that a genetic diagnosis was achievable in 21% of cases and was associated with an increased risk of complications. Therefore, genetic work-ups are integral to the management of patients with craniosynostosis and contribute to both risk assessment and overall prognosis.<sup>8,20,22</sup>

## OROFACIAL FEATURES OF COMMON CRANIOSYNOSTOSIS SYNDROMES

There are pathognomonic features found in the 4 most common craniosynostosis syndromes (Muenke, Crouzon, Pfeiffer, and Apert).<sup>10,16-19</sup> Muenke syndrome is an autosomal dominant disorder with an estimated incidence of 1 in 30,000 live births.<sup>3,16,22</sup> It is characterized by either unicoronal or bicoronal synostosis.<sup>16</sup> Patients with Muenke syndrome present with macrocephaly, midface hypoplasia, and developmental delay. Occlusal findings are typical of a class III skeletal pattern, including anterior crossbite, class III molar and canine relationship, and a concave profile.

Crouzon syndrome is an autosomal dominant disorder and is estimated to affect 1 in 25,000 live births.<sup>9,17</sup> Patients with Crouzon syndrome

present most commonly with bicoronal synostosis, brachycephaly, shallow orbits with ocular proptosis, hypertelorism, midface hypoplasia, and relative mandibular prognathism.<sup>17</sup> Those with Crouzon syndrome show maxillary deficiency in the vertical, transverse, and sagittal dimensions and typically present with anterior open bite, posterior and anterior crossbites, and severe crowding of the maxillary arch.<sup>17,23,24</sup> Frequently, teeth become impacted (usually canines) or erupt labially/palatally because of severe teeth-to-arch size discrepancies. Those with severe midface hypoplasia may have lip incompetence and localized areas of gingival inflammation.

Although most cases of Apert syndrome are sporadic, an autosomal dominant inheritance pattern has been reported.<sup>18</sup> It affects 1 in 100,000 live births.<sup>9,18</sup> It is similar in presentation to Crouzon syndrome but with more severe midface hypoplasia, and with syndactyly of the fingers and toes. Apert syndrome is characterized by 1-year to 2-year delay in dental development as well as delayed eruption of the teeth, crowding of upper teeth, and skeletal discrepancy between the maxilla and mandible.<sup>25</sup> Boulet and colleagues<sup>3</sup> estimate that 40% of patients with syndromic craniosynostosis have Apert syndrome. Those with Apert syndrome present with hypoplastic maxillary growth and airway restriction resulting in mouth breathing and anterior open bites, and therefore orthodontic intervention during growth could play a pivotal role in reducing the impact of the developing dentofacial deformity.<sup>26</sup> A distinctive feature in those with Apert syndrome is the presence of bulbous lateral palatal swellings that give the appearance of a pseudocleft. Retention of food and inflammation of surrounding tissues are common findings in such cases.<sup>25–28</sup> Presence of syndactyly frequently precludes patients from following adequate oral hygiene protocols, resulting in poor oral hygiene, increased risk of caries, and gingivitis.<sup>25–28</sup>

Pfeiffer syndrome is autosomal dominant and occurs in 1 in 100,000 live births.<sup>19,29</sup> Pfeiffer syndrome is divided into 3 subtypes: type I Pfeiffer syndrome is the classic manifestation presenting with midface hypoplasia, brachydactyly, and variable syndactyly.<sup>19,29</sup> Cloverleaf skull along with Pfeiffer hands/feet and ankyloses of elbows is the typical presentation of type II. Type III presents with all the features of type II with the exception of Cloverleaf skull. Patients with type III also present with severe ocular proptosis, very short anterior cranial base, and visceral malformations.<sup>19,29</sup>

## SURGICAL MANAGEMENT DURING EARLY YEARS

Management of patients with craniosynostosis requires multidisciplinary care teams that include a pediatric neurologist, geneticist, plastic surgeon, oral and maxillofacial surgeon, neurosurgeon, pediatric dentist, and other specialists ideally in a tertiary health care center. During the first few years of life, treatment mainly involves surgical intervention to relieve the fused sutures. The goal is to reduce the risk of increased ICP, improve the head shape, and allow normal brain development.<sup>4,8–12</sup> Commonly performed surgical procedures include fronto-orbital advancement, open cranial vault remodeling, extended strip craniectomy, endoscopic strip craniectomy, spring-assisted cranial expansion, and cranial vault distraction. Although techniques for initial cranial vault expansion and reshaping depend on the location and extent of the deformity, variability in surgical practice patterns and surgeon experience has been reported in a recent national survey of craniofacial surgeons in the United States.<sup>11</sup> Complication rates also vary widely across different centers, ranging from 10% to 39%.<sup>30–35</sup>

## COMBINED ORTHODONTIC AND SURGICAL TREATMENT PROTOCOLS AND TIMING WITH CASE EXAMPLES

Dentists play a pivotal role in the continuum of care for patients with craniosynostosis.<sup>36</sup> It is recommended that oral health providers conduct a clinical examination following the early surgical management of craniosynostosis. Photographs, diagnostic models, and imaging records should be obtained at periodic intervals to assess growth and eruption of teeth. **Table 1** summarizes the key dental interventions at different time periods.

### Midface Advancement

Much controversy exists on the timing of midface advancement. Some craniofacial teams recommend doing the midface advancement (either with distraction or standard Le Fort III osteotomy procedures) early in life to ameliorate sleep apnea and as an alternative to tracheostomy.<sup>36</sup> Indications for early midface advancement (before growth of midface is complete) include obstructive sleep apnea, globe protection, and psychosocial reasons. It is generally recommended that midface advancement be accomplished between 7 and 12 years of age so as to minimize repeat surgical procedures. There will not be much forward growth of the midface following the surgical

**Table 1**  
**Key dental interventions**

Age (y)	Dentition Stage	Interventions	Providers Involved
<1	Primary dentition	Establish dental home	Pediatric dentist
1–6	Primary dentition	<ul style="list-style-type: none"> <li>• Periodic oral examinations</li> <li>• Assessments for growth</li> <li>• Supervised oral hygiene practices/aids</li> <li>• Maxillary expansion when possible to facilitate incisor and molar eruption</li> </ul>	Pediatric dentist, orthodontist, and oral and maxillofacial surgeon
7–12	Mixed dentition	<ul style="list-style-type: none"> <li>• Oral hygiene assessments and prophylaxis as needed</li> <li>• Phase I orthodontic treatment (eg, maxillary expansion to correct posterior crossbites, limited maxillary arch orthodontic treatment to correct anterior crossbites, limited orthodontic treatment to facilitate eruption of permanent dentition, and reverse-pull headgear treatment)</li> <li>• Sequential extractions of primary teeth to facilitate eruption of permanent teeth</li> <li>• Midface advancement (as needed)</li> </ul>	Pediatric dentist, periodontist, orthodontist, and oral and maxillofacial surgeon
13–21	Permanent dentition	<ul style="list-style-type: none"> <li>• Periodic oral examinations, hygiene assessments, and prophylaxis</li> <li>• Comprehensive phase of orthodontic treatment with or without orthognathic surgery (depending on degree of skeletal imbalance)</li> <li>• Restorative treatment (eg, implants, crowns, veneers) following completion of comprehensive phase of orthodontic treatment</li> </ul>	Orthodontist, oral and maxillofacial surgeon, periodontist, and prosthodontist
>21	Permanent dentition	<ul style="list-style-type: none"> <li>• Retention checks</li> <li>• Periodic observations to assess long-term stability of surgical corrections</li> <li>• Periodic oral hygiene visits</li> </ul>	Orthodontist, oral and maxillofacial surgeon, and periodontist

procedure and hence these procedures should be done close to when growth is complete.<sup>24,37</sup>

### **Case example for Midface Advancement Using Distraction**

Patients with syndromic craniosynostosis present with severe midface hypoplasia. Many have sleep apnea as a result of retropalatal airway collapse.<sup>38,39</sup> When obstructive sleep apnea is present and is not adequately treated with nonoperative maneuvers and tonsillectomy/adenoidectomy, an early midface advancement is recommended. This article presents the case of a female patient, 7 years 2 months old, with Pfeiffer syndrome (type 1) who presented with severe obstructive sleep apnea, concave profile, mixed dentition stage, constricted maxillary arch,

posterior and anterior crossbites, anterior open bite, and class III molar relationship (Figs. 1–3).

The treatment objectives at this time were to correct the obstructive sleep apnea and improve the profile. To accomplish these objectives, the patient had a midface advancement using distraction osteogenesis. Le Fort III osteotomies were completed and a rigid external distraction device was applied with fixation to the midface using bone-anchored miniplates (Fig. 4). At the time of surgery, 3 mm of distraction was performed. Thereafter, 1 mm of distraction per day was done for a total of 10 days followed by 0.5 mm of distraction per day for 2 days. The amount of distraction to be done was decided by airway improvement and polysomnography. A reverse-pull headgear was used for retention for 1 year



**Fig. 1.** Lateral cephalometric radiograph (at time of presentation).



**Fig. 2.** Panoramic radiograph (at time of initial presentation).

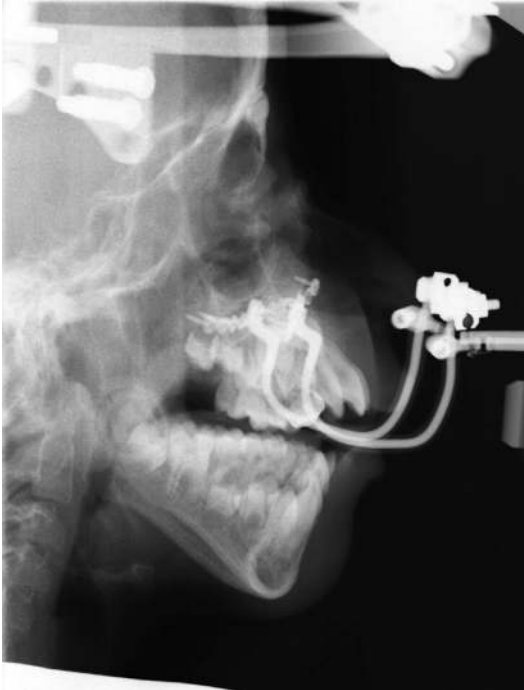
following distraction. The 1-year postdistraction intraoral pictures and lateral cephalometric radiograph are presented in **Figs. 5** and **6** respectively.

### ***Phase I Orthodontic Treatment***

Phase I orthodontic treatment usually involves maxillary expansion. Patients with syndromic craniosynostosis present with severely constricted maxillary arches that manifest as posterior crossbites and incompatible arch forms. It is critical that the maxillary arch form be established early, including correction of posterior crossbites to minimize facial asymmetry and eliminate traumatic occlusion. Depending on the severity of maxillary arch constriction, several rounds of expansion may be required. It is best to use a 4-banded expansion appliance if adequate anterior (primary first molars or primary canines) and posterior abutments (permanent first molars) are present, and overexpansion (by about 30%) should be achieved to account for expected relapse. The expansion appliance (usually hyrax, W arch, or quad helix) should be in place for at least 3 months and a fixed transpalatal arch with mesial extension arms should be placed at the time of device removal. Hawley appliances (with acrylic covering of the palate) can also be used, but these need to be periodically adjusted as the primary teeth exfoliate and permanent teeth emerge. It is most efficient to correct transverse maxillary deficiency during the mixed dentition phase when the circum-maxillary and palatal sutures are patent. As the patient ages, the palatal suture becomes fused and there is a considerable amount of resistance from the circum-maxillary sutures to maxillary expansion. In such situations, a surgically assisted maxillary expansion may be required.



**Fig. 3.** Intraoral views (at time of initial presentation).



**Fig. 4.** Lateral cephalometric radiograph after completion of midfacial distraction.

Occasionally, a limited phase of orthodontic treatment is recommended in the maxillary arch to align and level the arch in preparation for a maxillary advancement operation. Limited orthodontic treatment is also recommended to facilitate eruption of permanent teeth into an ideal position in the arch and for treating impacted teeth. It is best that this phase of treatment not be beyond 6 to 9 months to prevent patient burnout.



**Fig. 6.** Lateral cephalometric radiograph 1 year postdistraction.

#### ***Case example for Surgically Assisted Maxillary Expansion and Limited Orthodontic Treatment***

A 16-year-old male patient presented with severe constriction of the maxillary arch, anterior open bite, and severe crowding of both maxillary and mandibular arches (**Fig. 7**). Treatment objectives were to relieve the crowding in both arches, expand the maxillary arch and make it compatible with the mandibular arch, and align/level both arches with a limited phase of orthodontic treatment. A surgically assisted maxillary expansion was done along with extractions of maxillary and mandibular permanent canines, which had



**Fig. 5.** Intraoral views 1 year postdistraction.



Fig. 7. Initial presentation.



Fig. 8. Maxillary expansion and limited phase of orthodontic treatment.



Fig. 9. Completion of maxillary expansion.



Fig. 10. Intraoral views at initial presentation.



Fig. 11. Lateral cephalometric radiograph at initial presentation.

erupted labially because of severe teeth material/arch length discrepancy. Considering the severely constricted maxillary arch form, 3 rounds of expansions were conducted with a modified maxillary expander (Figs. 8 and 9). Comprehensive



Fig. 12. Panoramic radiograph at initial presentation.

orthodontic treatment in conjunction with orthognathic surgery is planned for the future.

### ***Comprehensive Orthodontics with Orthognathic Surgery***

Most patients with syndromic craniosynostosis present with severe maxillary/mandibular skeletal imbalances and malocclusions that require comprehensive orthodontic treatment in conjunction with orthognathic surgery during the late teen years. Treatment is rendered in 3 stages: pre-surgical orthodontics, orthognathic surgery, and postsurgical orthodontics. The treatment objectives of these stages are discussed here.

#### ***Presurgical orthodontics***

The objectives of this stage are to align and level both maxillary and mandibular arches, obtain compatible arch forms, remove dental compensations (may need extractions of permanent teeth to accomplish this), and resolve crowding/spacing issues.

#### ***Orthognathic surgery***

The objectives of this stage are to correct anterior/posterior, transverse, and vertical maxillary/mandibular discrepancies with single jaw or bimaxillary surgery.

#### ***Postsurgical orthodontics***

During this stage, the final detailing and settling of occlusion are accomplished.

### ***Case Example 1 of Comprehensive Orthodontic Treatment with Orthognathic Surgery***

A male patient with Apert syndrome presented during the early teen years with a concave profile,





**Fig. 13.** Lateral cephalometric radiograph during midface advancement by distraction.



**Fig. 14.** Lateral cephalometric radiograph 1 year postdistraction.

multiple missing teeth in the maxillary arch, anterior open bite, and anterior crossbite (Figs. 10–12). Considering the severity of the anterior/posterior imbalance between the maxillary and mandibular arches and severe midface hypoplasia, the treatment was planned in 2 phases. During the initial phase, the patient had midface distraction (Figs. 13–15). During the late teen years, the patient underwent a comprehensive phase of orthodontic treatment along with orthognathic surgery (Figs. 16–18).

#### ***Case Example 2 of Comprehensive Orthodontic Treatment with Orthognathic Surgery***

A male patient with a diagnosis of Apert syndrome presented during the early mixed dentition stage with an impacted maxillary left central incisor (Fig. 19). A limited phase of orthodontic treatment was done with the objective of facilitating eruption of the impacted tooth into the arch (Figs. 20 and 21). Space was created for the impacted tooth, a surgical exposure was



**Fig. 15.** Intraoral views 1 year postdistraction.



**Fig. 16.** Intraoral views during comprehensive phase of orthodontic treatment (3 years postdistraction).



**Fig. 17.** Intraoral views before orthognathic surgery.

done, and orthodontic traction was placed to erupt the impacted tooth into the arch. At 14 years, the patient presented with concave profile, severe maxillary hypoplasia, anterior openbite, negative overjet, posterior crossbite, and class III malocclusion (Figs. 22 and 23). A distraction osteogenesis procedure was done

using Le Fort III osteotomies (Fig. 24) at age 14 years. During the late teen years, the patient had a comprehensive phase of orthodontic treatment along with orthognathic surgery (Le Fort I and genioplasty). Following the comprehensive phase of treatment, an excellent outcome was achieved (Figs. 25–28).



**Fig. 18.** Intraoral views after Le Fort I osteotomy procedure and after debond.



**Fig. 19.** Panoramic radiograph showing impacted maxillary left central incisor.



**Fig. 21.** Panoramic radiograph during limited phase of orthodontic treatment.



**Fig. 20.** Intraoral views during limited phase of orthodontic treatment.



**Fig. 22.** Intraoral views at 14 years of age before distraction osteogenesis.

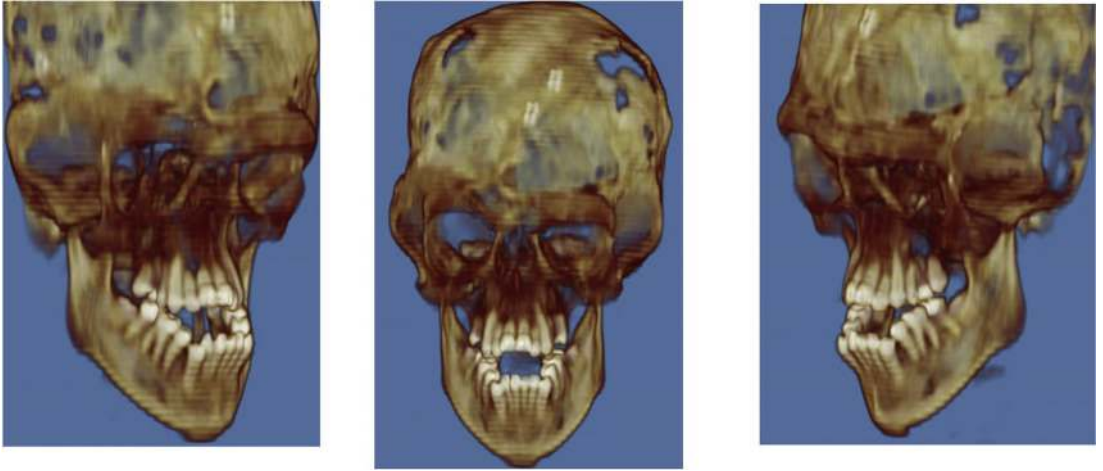


Fig. 23. Cone beam computed tomography (CBCT) images before maxillary distraction osteogenesis.

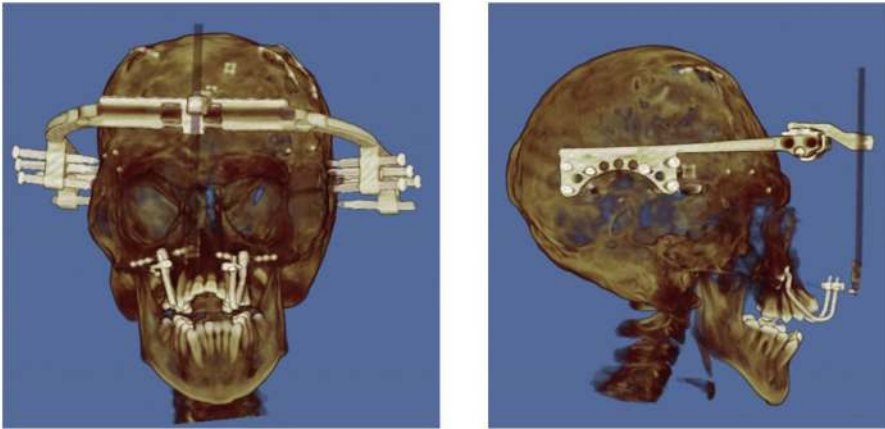


Fig. 24. CBCT images during distraction osteogenesis procedure.



Fig. 25. Intraoral views before initiation of comprehensive phase of orthodontic treatment.



Fig. 26. Intraoral views before Le Fort I and genioplasty procedures.



Fig. 27. Intraoral views following completion of comprehensive phase of orthodontic treatment.



Fig. 28. Lateral cephalometric radiograph following completion of comprehensive phase of orthodontic treatment.

## SUMMARY

As shown by the case examples, orthodontic management of syndromic craniosynostosis requires an interdisciplinary approach to treatment, a willingness to understand the limitations inherent (eg, ectopic teeth, impacted teeth, severe maxillary constriction, malformed teeth), and a creative but determined craniofacial orthodontist. Maxillary expansion when done early may reduce but cannot eliminate the occurrence of impaction and the eventual need to extract maxillary permanent teeth, creating the need to design an occlusion providing good function and esthetics. This outcome requires the providers to work together to minimize the amount of intervention (implants, prostheses, phases of orthodontia) needed so as to decrease the overall morbidity of treatment and to reduce the financial and psychological burden on the patient and family.

## DISCLOSURE

The authors have nothing to disclose.

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