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The 27 Facial Sutures: Timing and Clinical Consequences of Closure

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Summary

Facial sutures contribute significantly to postnatal facial development, but their potential role in craniofacial pathology is understudied. Since interest in their development and physiology peaked in the mid-20th century, facial sutures have not garnered nearly the same clinical research interest as calvarial sutures or cranial base endochondral articulations. In addition to reinforcing the complex structure of the facial skeleton, facial sutures absorb mechanical stress and generally remain patent into adolescence as they mediate growth and refine the shape of facial bones. However, premature closure of these sites of postnatal osteogenesis leads to disrupted growth vectors and consequent dysmorphologies. While pathology in individual sutures results in isolated facial deformities, we posit that generalized pathology across multiple may be involved in complex craniofacial conditions such as syndromic craniosynostosis. In this work, we comprehensively review 27 key facial sutures, including physiologic maturation and closure, contributions to postnatal facial development, and clinical consequences of premature closure.

Introduction

Facial sutures are overshadowed by their calvarial counterparts in the modern craniofacial literature. As craniosynostosis is the principal context in which sutures are discussed, it is unsurprising that those of the calvarium have dominated the clinical and research spheres. Facial sutures, however, were studied on par with those of the calvarium during the rise of craniofacial biology in the 1950s-60s. Scott, Enlow, Sarnat, and others were deeply interested in both their physiology and the craniofacial defects secondary to their disruption (1-3).

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Craniosynostosis can occur in isolation or as part of a syndrome involving a spectrum of physical manifestations, including profound facial anomalies (4-6). While the etiology of these facial deformities is debated, the current leading theory suggests they are sequelae of aberrant cranial base development (5,7). However, for several decades craniofacial experts and basic scientists have endorsed the alternative hypothesis that premature facial suture synostosis plays a primary role in the development of these deformities (8-13).

To further explore this hypothesis, we sought to comprehensively review the existing literature on facial sutures. This review reveals that beyond their general developmental and physiologic roles, individual human facial sutures have not been rigorously or systematically studied since the mid-20th century. Our current understanding of the maturation course of individual sutures is derived from a select few forensic anthropology and human cadaveric studies, with limited contribution from clinical imaging studies. We herein synthesize all knowledge to-date on the physiology and pathophysiology of 27 prominent facial sutures. Particular attention is paid to their posited contributions to facial deformity in both craniosynostotic and non-craniosynostotic contexts.

Development

The neurocranium (bones encasing the brain) is derived from a combination of head mesoderm and neural crest, while the viscerocranium (bones forming the face) is derived exclusively from neural crest mesenchyme (14,15).

Most craniofacial bony interfaces are true sutures, fibrous joints consisting mainly of type I collagen (16). There are notable histologic distinctions between facial and calvarial sutures early in development (17). Several cranial base articulations are synchondroses (cartilaginous joints with predominantly type II collagen) but often referenced inaccurately as sutures.

Facial sutures are patent at birth and progressively ossify, at variable rates and to variable extents. Generally, the ossification of facial sutures differs from that of calvarial sutures. While calvarial sutures achieve significant closure – involving dense interdigitations with a remnant visible suture line – by age 20-30, most of their facial counterparts remain patent through late adulthood (18-20). Some facial sutures do not form appreciable interdigitations until the 7th to 8th decades of life (20).

Physiologic Roles

Throughout life, facial sutures provide structural support and mechanical stress absorption for deformational forces induced during motion such as in mastication (21). While patent, facial sutures also adjoin the periostea of adjacent bones and serve as centers for osteogenesis (20). Their dual functionality as sites of intramembranous osteogenesis and absorbers of mechanical stress allows them to play an essential transducing role in directing facial development (20).

Recognizing the potential impact of suture pathology on facial development requires understanding sutural growth dynamics, a topic heavily studied in the 1950s-60s. Scott documented the permissive growth theory in 1954, hypothesizing that facial bones grow

at sutures because underlying organs and cartilage – namely, the eyes and nasal septum – increase in size and physically separate adjacent bones, allowing new bone to be deposited at the junction (1). He posited that sutural growth ceases and closure commences when the underlying structures stop growing. Enlow also endorsed this theory, suggesting that in the same way dura mater and brain tissue provide stimuli for new bone formation at expanding calvarial sutures, facial cartilage such as the nasal septum provides signals for bone deposition at their overlying facial sutures (3).

These experts also investigated how postnatal suture growth relates to macroscopic development of the facial skeleton. Scott described three “suture systems”, each mediating facial growth in a particular direction (22). Sarnat characterized how concerted growth at the frontomaxillary, zygomaticomaxillary, and pterygomaxillary sutures translocates the maxilla outward (2). Enlow found that inferolateral displacement of the zygoma requires growth at the frontozygomatic and zygomaticomaxillary sutures (3). Similarly, Björk demonstrated the necessity of frontozygomatic and intermaxillary suture growth in achieving proper maxillary expansion (23,24).

By 1963, sutural growth was widely considered a main catalyst of postnatal facial growth, along with endochondral cranial base ossification, appositional growth at facial bone surfaces, and nasal septal growth (2). In contrast to reactive, intramembranous sutural growth, endochondral osteogenesis at the cranial base synchondroses is active and prolific through early adolescence (25, 26).

Although facial sutures remain patent for a considerable duration, bony growth does not continue indefinitely. Certain aspects of facial growth do persist throughout life, as evidenced by the continuous increase in measurements like the nasion to anterior nasal spine distance and bizygomatic width; however, midfacial growth is typically complete by the mid-teen years, when endochondral growth momentum decelerates with the ossification of cranial base synchondroses (27,28). While additional research is required to quantify the correlation between facial suture patency with sutural growth velocity, it can be extrapolated from calvarial craniosynostosis that early gross ossification appreciated on imaging signifies the restriction of subsequent growth at that suture site.

Anatomy and Terminology

The neurocranium, totaling eight bones, encases the brain and is further divided into the calvarium and cranial base. The viscerocranium, or facial skeleton, totals 14 bones.

The “face” is a colloquial term lacking defined anatomic borders. “Facial sutures” are similarly vaguely defined, referring to various articulations between craniofacial bones. Given these intricacies, we take an anatomically oriented approach to systematically cover the bony articulations supporting the face. We delineate nine facial regions as our framework to discuss 27 articulations (Figure 1, Table 1). For conciseness, only sutures with the most significant clinical findings are discussed in the body of this review (all others can be found in Table 1).

Frontal Region

The metopic suture, often considered a calvarial suture, courses down the frontal bone midline (*M* in Figure 1, Table 1) (29). Closure on CT imaging is detectable as early as 3 months and frequently completes before 1 year (30,31). Synostosis generates the trigonocephalic phenotype, characterized by a triangular forehead with a raised bony midline ridge, a shortened anterior cranial fossa, and hypotelorism. Severe cases have been associated with ethmoidal hypoplasia, neuropsychologic sequelae, and minor cranial base suture involvement (32, 33). While most patients with metopic craniosynostosis are non-syndromic, patients with syndromic craniosynostoses have also been reported to have metopic synostosis (34, 35).

The frontonasal sutures run transversely at the nasion (*FN* in Figure 1, Table 1). Closure occurs in the 5th through 6th decades in cadaveric studies (36,37). A synostotic mouse model found consequent hypertelorism, snout shortening, and midface hypoplasia, suggesting patency is required for normal early midfacial development (38). Similarly, a lagomorph model of stunted frontonasal growth demonstrated midface shortening and secondary growth restrictions at the coronal and internasal sutures (39). Clinically, frontonasal synostosis has been reported in both metopic and coronal craniosynostosis patients. Calandrelli et al. found that most of their 59 pediatric subjects with metopic synostosis actually had synostotic extension into the frontonasal suture (40). In their cohort of 7 patients with the same condition, Udayakumaran et al. reported frontonasal synostosis in all and hypothesized that it contributes to metopic suture angulation (41). Asymmetric frontonasal closure has also been associated with unilateral coronal synostosis (UCS), implicating facial suture synostosis in the characteristic facial twist of UCS patients (42).

The frontomaxillary sutures connect the frontal process of the maxilla to the inferior margin of the frontal bone (*FM* in Figure 1, Table 1). This suture does not start closing until the 7th decade in a cadaveric study (19). Similar to nasofrontal sutures, asymmetric synostosis of the frontomaxillary sutures is increased on the synostotic side in UCS patients (42). A CT study found a 70% prevalence of concomitant frontomaxillary synostosis in non-syndromic metopic synostosis patients and established a significant positive association between frontomaxillary synostosis and severity of the trigonocephalic phenotype (40).

The frontozygomatic is the sole suture of the lateral orbital rim (*FZ* in Figure 1, Table 1). Cadaveric study suggests closure occurs between the 8th and 10th decades (43). Patency enables growth and contributes to increasing bizygomatic width until age 60. Isolated synostosis mimics the fronto-orbital dysplasia of UCS with frontal flattening, small orbit, and shortened lateral orbital rim (44). Synostosis has also been found in UCS and metopic synostosis patients, and contributes to posterior malpositioning of the zygomatic bone frequently seen in the latter (45,46).

Orbital Region

The sphenozygomatic sutures contribute to both the lateral orbital wall and the anterior wall of the temporal fossa (*SZ* in Figure 1, Table 1) (47). Closure occurs between the 5th and 6th decades in a cadaveric study (37). Despite a lack of isolated cases,

sphenozygomatic synostosis occurs concomitantly with other synostoses. Rogers et al. reported synostotic extension into the sphenozygomatic in a frontal plagiocephalic patient with unilateral frontosphenoidal synostosis (48). They thus consider frontal plagiocephaly a phenotypic spectrum with multiple synostotic etiologies, including coronal ring fusions that may extend into adjacent sutures. Genitori et al. found 7% of their metopic synostosis patients had concurrent sphenozygomatic synostosis (46). Within the radiologic literature, simultaneous sphenozygomatic and frontozygomatic synostoses were found in an infant with the phenotypic appearance of UCS in the absence of coronal suture involvement (44).

The frontoethmoidal sutures are found in the medial orbital walls (*FE* in Figure 1, Table 1). Closure occurs between the 5th and 6th decades (37). As basilar continuations of the coronal ring, the frontoethmoidal and frontosphenoidal are frequently closed prematurely in coronal synostosis (49). When basilar synostoses are involved, the classic forehead flattening of UCS is accompanied by a more severely shortened anterior fossa, thickened pterion, and shallowed orbits. Because of cranial base tethering, lateral canthal advancement enhances the treatment of coronal ring synostosis. Artificial coronal and cranial base sutures are created, enabling complete mobilization of the frontal bone. A study of syndromic and non-syndromic trigonocephalic subjects found a 7% prevalence of concomitant frontoethmoidal synostosis (46). In the case of severe trigonocephaly, metopic suture synostosis may extend down the face to affect the frontoethmoidal, causing hypotelorism (50). Frontoethmoidal synostosis has also been observed on CT imaging of Crouzon, Pfeiffer, and Apert subjects (34,35).

Maxillary Region

The zygomaticomaxillary suture is the longest and thickest maxillary suture (*ZM* in Figure 1, Table 1) (51). It is completely patent on CT until age 10-15 and remains incompletely interdigitated through the 7th decade in cadavers (19,52,53). Induced unilateral synostosis in newborn guinea pigs resulted in asymmetry of the nasomaxillary complex due to constrained anteroinferior displacement of the maxilla and zygoma (54). A CT study demonstrated that suture patency enabled greater orthodontic maxillary protraction in malocclusion patients (51). These data suggest that synostosis causes tethering of the maxilla that limits its outward growth potential. The seminal CT study of Calandrelli et al. found that while all other viscerocranial sutures were patent in their syndromic subjects, the zygomaticomaxillary was prematurely closed bilaterally in 5 (26%) of the infants (4 Crouzon and 1 Pfeiffer) (35). These infants demonstrated significant maxillary retrusion, leading the authors to interpret zygomaticomaxillary synostosis as a marker of severe facial deficit and a potential cause of maxillary retrusion.

The pterygomaxillary sutures are located where the maxilla and sphenoid are most closely approximated (*PMx* in Figure 1, Table 1) (55). It appears considerably interdigitated on CT by age 12, and orthodontic maxillary protraction becomes more difficult after this age (56). Synostosis during development is rare, given the neurovascular intricacy of the region. Suture disruption is performed to mobilize the maxilla during midface advancement, a mainstay procedure for correcting syndromic facial deformities (57,58). However, surgical manipulation may prematurely obliterate the suture and consequently disrupt transverse

maxillary growth (58). Growth at this suture also contributes to anterior maxillary growth, which is thought to be limited in cleft patients due to the iatrogenic effects of reconstructive surgeries and therapies compounded on an intrinsic growth disturbance, resulting in higher incidences of maxillary hypoplasia (59,60).

Lateral Region

The zygomaticotemporal suture is the most lateral suture of the face (*ZT* in Figure 1, Table 1). It is one of the last sutures to close, with interdigitation starting in the 7th decade in cadavers (52). An isolated synostosis case presented as "progressive midfacial and orbital asymmetry, angulation of the cranial base, and nasal deviation" (61). The patient also displayed maxillary retrusion and asymmetric calvarial shortening. CT noted a thickened lateral orbital wall and zygomatic body, suggesting compensatory growth. Another report described unilateral midfacial and frontal retrusion and nose and chin deviation (62). The surgeons performed a segmental zygomaticotemporal suturectomy, hypothesizing that release would facilitate normal growth. The effectiveness of this procedure is to be determined.

Nasal Region

The internasal suture runs in the midline of the anterior face (*IN* in Figure 1, Table 1). Closure begins in the 20s and completes in the 30s in cadavers (63). Udayakumaran et al. found all their non-syndromic metopic synostosis subjects had concomitant synostosis of the internasal and frontonasal sutures, hypothesizing that premature nasion sutural complex synostosis leads to severe metopic angulation (41). The internasal suture was surgically released in 3 infants, with improved angulation and hypotelorism.

The nasoethmoidal and septovomerine sutures are deep nasal structures (*NE and SV* in Figure 1, Table 1). The timing of closure for these sutures are not well studied, but bony growth at these sutures contributes significantly to nose and airway development through the mid-teens (64,65). Disruption due to trauma or surgery can cause premature ossification, leading to downstream growth arrest, asymmetric nasal deformities, septal deviation, or airway obstruction (65,66). The effect of the deep nasal sutures on nasal growth is the rationale for delaying surgical manipulation of the septum until skeletal maturity (64,67-69).

Palatal Region

The intermaxillary and midpalatal sutures are contiguous (*IMx and MP* in Figure 1, Table 1). The former is mostly closed by age 18 but variably patent through the late 20s (70). Closure of the latter begins in the teens, with variable progression among individuals influenced by masticatory forces, genetic heterogeneity, and hormonal parameters (71-74). Transverse growth at the intermaxillary suture through the late teens may be the paramount determinant of adult maxillary width (20). Restricted growth across prematurely closed palatal sutures results in transverse maxillary hypoplasia, which can be effectively managed with non-surgical palatal expansion before the teenage years (75). However, the sutures are considerably interdigitated by the late teens, thus requiring surgical release for expansion (76,77).

Basal Region

We briefly mention the sphenooccipital (SOS) and sphenoethmoidal (SES) synchondroses here, as they are well studied with extensive literature on their closure timing and synostotic involvement in syndromic craniosynostosis (*SO and SE* in Figure 1, Table 1) (34,35,78-81). SOS ossification starts and completes in the teens, occurring earlier in females (82-90). SES closure occurs between age 2 and 15 (91). Both are major contributors to midfacial growth through adolescence, mediating anteroposterior lengthening of the cranial base and protrusion of the midface (7,46,82,92,93). Premature ossification, reported in Apert, Crouzon, Pfeiffer, and Saethre-Chotzen patients, is strongly associated with midface retrusion (34,35,78-80,93,94).

Circummeatal Region

The frontosphenoidal sutures (FSS) are the inferomedial extensions of the coronal sutures and joined at the midline by the SES (*FS* in Figure 1, Table 1). The coronal sutures, FSS, and midline SES form the coronal ring. Closure of the FSS on CT occurs between age 5 and 15 (91). With the SES, it facilitates anteroposterior cranial base expansion from birth to age 7 (46). Since Francel et al. first documented frontal plagiocephaly caused by an isolated FSS synostosis, there have been over 20 published cases (95-105). Puente-Espel et al. characterized the phenotype of isolated FSS synostosis as ipsilateral frontal flattening and retrusion, and inferolateral positioning of the ipsilateral orbit with compensatory medial elongation (97). Variation in orbital deformity is the key differentiator between isolated coronal and FSS synostoses (106). FSS synostosis occurs more often with UCS than as an isolated synostosis. There is also a high likelihood of FSS synostosis in syndromic craniosynostosis. Early studies identified extension of coronal synostosis to the FSS as a likely contributor to brachycephaly in Apert and Crouzon patients (107-109). Recent CT studies have documented synostosis in Pfeiffer and Saethre-Chotzen patients as well (34,35).

The sphenoparietal sutures are short sutures on the lateral skull at the pterion (*SP* in Figure 1, Table 1). On CT, closure starts before age 7 and is complete by the teens (110). In addition to sagittal synostosis, premature closures of the sphenoparietal and sphenosquamosal may occur in scaphocephaly (111). The sphenoparietal may also be synostosed in Apert because of the frontal bone's shortened orbital plate (112). Synostosis results in retrusion and elevation of the supraorbital wings, a fronto-orbital defect with cutaneous manifestations like disrupted eyebrows and excessive forehead skin wrinkling. Synostosis is also observed in Crouzon, Pfeiffer, and Saethre-Chotzen patients (34,35).

Discussion

Facial sutures are an essential yet presently under-studied element of craniofacial anatomy. Aside from maintaining structural integrity and absorbing mechanical stress, they mediate fine-tuned postnatal growth for the facial skeleton (1-3,17,22,23). Early studies demonstrated that multiple growth processes required to achieve a normal adult midface necessitate precise facial sutural growth (2,3,23,24).

The focus on neurocranial articulations in the craniosynostosis literature has contributed to the current paucity of systematic studies on facial sutures. We hereby present the first comprehensive review of the numerous facial sutures of the human craniofacial skeleton with discussion of the maturation, physiology, and pathophysiology of each respective suture.

Despite the notoriety of syndromic craniosynostosis facial deformities, the pathogenesis thereof has yet to be solidly understood. The current majority opinion considers premature ossification of cranial base growth centers the primary culprit (7,78-81,113). Although cranial base tethering may play an overarching role, the severity and multifocal nature of syndromic facial deformities suggest multiple factors are at play.

Sarnat elucidated endochondral, appositional, and sutural growth as the key modalities of postnatal facial development (2). Because suture growth is inherently permissive and reactive to stimuli, it is finely controlled along defined vectors rather than rapidly expansionary (20). Therefore, while endochondral pathology could stunt cranial base lengthening and thereby explain maxillary retrusion, it may be unable to completely explain the characteristic morphologic and dimensional aberrations of individual facial bones in syndromic craniosynostosis (92). Rather, the tightly regulated nature of sutural growth may make suture synostosis a more compatible explanation for these granular abnormalities with significant macroscopic consequences. The last decade has seen an increase in reports of facial suture synostosis, both in isolated cases and in the context of craniosynostosis (35,42,103).

Our synthesis of the literature demonstrates multifaceted ways in which facial suture synostosis is detrimental to craniofacial development. Discrete patterns of suture pathology can exacerbate facial deformities in non-syndromic craniosynostosis, generate focal abnormalities in isolated synostosis cases, and disrupt downstream growth vectors. Asymmetric frontonasal and frontomaxillary synostoses augment the facial twist phenotype in UCS (42). Frontonasal, internasal, and frontoethmoidal synostoses intensify the metopic angulation and hypotelorism seen in severe, non-syndromic trigonocephaly (40,41,46). Premature closures of the midpalatal and intermaxillary sutures result in transverse maxillary deficiency by limiting lateral growth (20,75). Furthermore, frontonasal synostosis restricts growth at the coronal and internasal sutures, zygomaticomaxillary synostosis tethers the maxilla posteriorly and prevents its outward growth, and traumatic premature ossification of the nasoethmoidal and septovomerine sutures predisposes to septal deviation and airway obstruction by stunting nasal complex growth (39,51,54,65,66).

Despite these exciting insights, exploration of facial suture involvement in human syndromic craniosynostosis is still in its nascency. The recent imaging studies of Runyan et al. and Calandrelli et al. have begun to elucidate patterns of orbital and circummeatal region suture synostoses in infants with various craniosynostosis syndromes (34,35). The latter study – as the only thus far to evaluate sutures located primarily within the viscerocranium – also reported zygomaticomaxillary involvement in a small subset of patients, preliminarily suggesting a potential contributory role to midface retrusion and airway hypoplasia (35). While these studies are novel, their limitations and dearth of related research leave further

questions yet to be answered. Aside from small sample sizes, Runyan et al. focused on minor calvarial and cranial base sutures with a peri-facial location and did not assess sutures located primarily within the viscerocranium, and Calandrelli et al. evaluated young infants at a single timepoint likely too early for the effects of facial suture synostosis to manifest.

The gap in the literature may be addressed with multi-institutional, *in vivo* imaging studies that comprehensively and longitudinally evaluate facial osteology in patients with various craniosynostosis syndromes, from birth through adolescence. While ambitious, such a study would answer key questions regarding the magnitude of facial suture synostosis as a pathology in syndromic craniosynostosis and the mechanisms by which suture pathology contributes to the development of syndromic facial deformities. By quantifying the extents of both cranial base ossification and facial suture synostosis over time and correlating these findings with the developing craniofacial phenotype, this study could test our hypothesis that endochondral and sutural pathology produce disparate aspects of facial deformity in syndromic patients. Ultimately, we hope that further research in this realm generates a more complete understanding of syndromic facial deformities and their pathoetiology, with the objective of optimizing outcomes.

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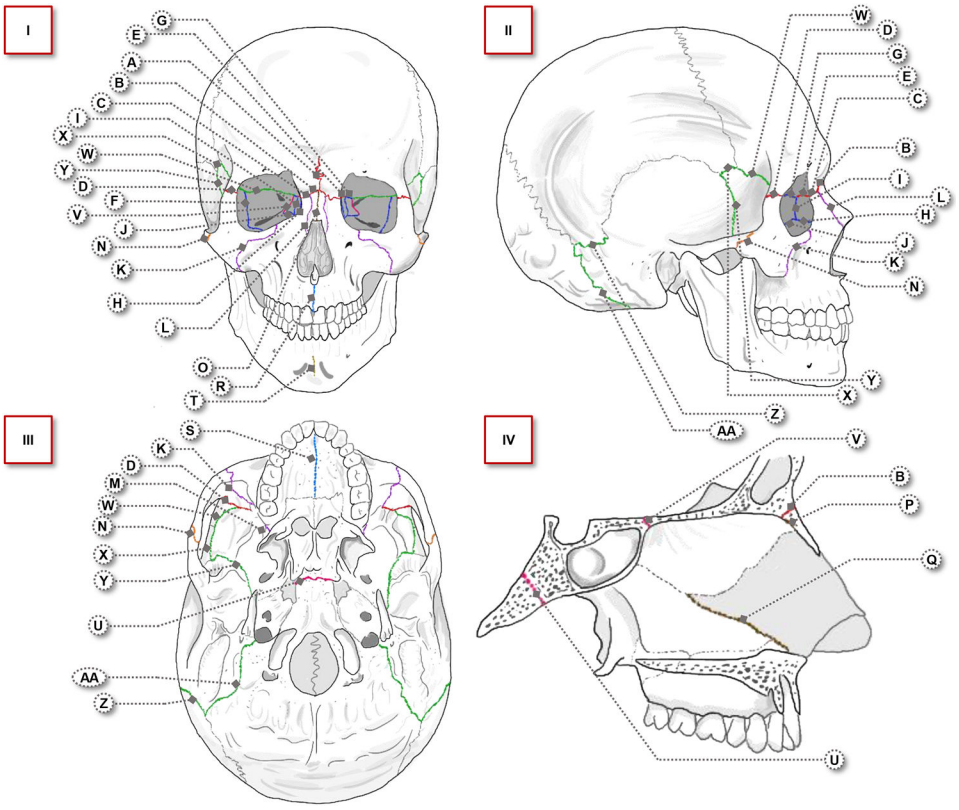

Figure 1.

Four views of the craniofacial skeleton, with 27 labeled facial sutures. Suture labels correspond to those in Table 1. Sutures are color-coded by facial region (frontal: red, orbital: dark blue, maxillary: purple, lateral: orange, nasal: brown, palatal: light blue, mandibular: gold, basal: magenta, circummeatal: green). *I)* Anterior view, *II)* lateral view, *III)* inferior view, *IV)* midline sagittal view, with focus on the basal and nasal regions.

Table 1

egion. Abbreviations of the articulations correspond to the labels in Figure 1. Includes timing of closure, nted cases of premature closure in the literature. Abbreviations are as follows: *M* = metopic, *FN* = frontonasal, atic, *FL* = frontolacrimal, *SZ* = sphenozygomatic, *FE* = frontoethmoidal, *LM* = lacrimomaxillary, *EL* = ary, *ZM* = zygomaticomaxillary, *NM* = nasomaxillary, *PMx* = pterygomaxillary, *ZT* = zygomaticotemporal, *IN* septovomerine, *IMx* = intermaxillary, *MP* = midpalatal, *IM* = intermandibular, *SO* = sphenooccipital, *SE* = *SP* = sphenoparietal, *SS* = sphenosquamosal, *PM* = parietomastoid, *OM* = occipitomastoid, *CT* = computed

on		Timing of closure			Clinical Consequences of Premature Closure in Humans			
					In humans			
ndrosis	Symphysis	In humans	In Animal (*if limited human studies)*	Notable functions of suture growth	Cases of isolated synostosis	Involvement in non-syndromic craniosynostosis	Involvement in syndromic craniosynostosis	Animal models of isolated synostosis
		CT: Starts at 3 months, completes by 9 months		Transverse frontal bone growth, across supraorbital ridge	Non-syndromic trigonocephaly (raised midline ridge, hypotelorism, possible neuropsychologic disturbances)			
		Cadaveric: Starts in 40s, completes in 50s		Protrusion of the nasal complex		• *Calandrelli et al.:* Synostosed in 78% of trigonocephaly subjects • *Udayakumaran et al.:* Synostosedin 100% of trigonocephaly subjects. Contributes to metopic angulation • *Miri et al.:* Contributes to facial twist in unilateral coronal synostosis		• *Nelson & Williams:* Hypertelorism, snout shortening, midface hypoplasia (mice) • *Babler et al.:* Midface shortening (rabbits)
		Cadaveric: Does not start until 7th-8th decade		Protrusion of the maxilla		• *Calandrelli et al.:* Synostosed in 70% of trigonocephaly subjects. Synostosis		

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on		Timing of closure			Clinical Consequences of Premature Closure in Humans			
					In humans			
ndrosis	Symphysis	In humans	In Animal (*if limited human studies)*	Notable functions of suture growth	Cases of isolated synostosis	Involvement in non-syndromic craniosynostosis	Involvement in syndromic craniosynostosis	Animal models of isolated synostosis
						predicts trigonocephaly severity		
						• *Miri et al.:* Contributes to facial twist in unilateral coronal synostosis		
		Cadaveric: Starts in 8th decade, completes in 10th		Inferolateral displacement of the zygoma	*Currarino:* Frontal flattening, small/round orbit, broadened/shortened lateral orbital rim	• *Barrabé et al.:* Synostosed in some unilateral coronal synostosis cases		
						• *Genitori et al.:* Synostosed in some trigonocephaly cases. May contribute to posterior mispositioning of the zygoma		
		Prolonged patency	*Ateles* monkeys: Closes late in adult life					
		Cadaveric: Starts in 5th decade, completes in 6th			*Currarino:* One case of synostosis concomitant with frontozygomatic synostosis. Contributes to lateral orbital wall broadening/shortening	• *Rogers et al.:* Can be synostosed in unilateral frontosphenoidal synostosis. Contributes to plagiocephaly (frontal flattening, orbital rim recession)	• *Kreiborg & Bjork:* Synostosed in postmortem Crouzon skull. Laterally deviated lateral orbital walls	
						• *Genitori et al.:* Synostosed in 7% of		

on		Timing of closure			Clinical Consequences of Premature Closure in Humans			
					In humans			
ndrosis	Symphysis	In humans	In Animal (*if limited human studies)*	Notable functions of suture growth	Cases of isolated synostosis	Involvement in non-syndromic craniosynostosis	Involvement in syndromic craniosynostosis	Animal models of isolated synostosis
						trigonocephaly subjects		
		Cadaveric: Starts in 40s, completes by early 50s				• *Hoffman & Mohr:* If involved in unilateral coronal synostosis, more severe anterior fossa shortening, pterion thickening, orbital shallowing • *Genitori et al.:* Synostosed in severe trigonocephaly subjects, contributing to hypotelorism	• *Francel et al.:* Synostosed in Apert and Crouzon • *Runyan et al.:* Synostosed in 100% of Pfeiffer and Apert subjects, 33% of Crouzon • *Calandrelli et al.:* Synostosed in 50% of Apert subjects, 78% of Crouzon, 67% of Pfeiffer. Anterior/ middle cranial fossa shortening	
		Prolonged patency	• *Ateles* monkeys: Closes late in adult life • *Presbytis* monkeys: Does not close					

on		Timing of closure			Clinical Consequences of Premature Closure in Humans			
					In humans			
ndrosis	Symphysis	In humans	In Animal (*if limited human studies)*	Notable functions of suture growth	Cases of isolated synostosis	Involvement in non-syndromic craniosynostosis	Involvement in syndromic craniosynostosis	Animal models of isolated synostosis
		Cadaveric: Starts in mid 30s, completes by age 50						
		Cadaveric: Starts and completes in late 40s to 50s						
		• *CT:* Starts age 10-15 • *Cadaveric:* Some patency through 7th decade		• Protrusion of maxilla • Inferolateral displacement of the zygoma			*Calandrelli et al.:* Synostosedin 26% of syndromic infants (4 Crouzon, 1 Pfeiffer). Severe maxillary retrusion and reduced SNA angle. Involvement indicates higher severity facial skeletal deficit, exacerbates maxillary retrusion	*Thimaporn et al.:* Nasomaxillary complex asymmetry, constrained downward/ forward displacement of the maxilla/ zygoma (guinea pigs)
		Cadaveric: Does not begin until 60s-70s				*Miri et al.:* Synostosed in 62% of unilateral coronal synostosis subjects. Contributes to facial twist		
		CT: Starts in mid teens		Protrusion of maxilla				
		Cadaveric: Significant closure does not start until 7th decade			• *Rogers et al.:* Delayed progressive midface/ orbital asymmetry, cranial base angulation, nasal deviation. Maxillary retrusion, thickened lateral orbital wall/ zygomatic body (compensatory growth)		*Kreiborg & Bjork:* Synostosed in postmortem Crouzon skull	

on		Timing of closure			Clinical Consequences of Premature Closure in Humans			
					In humans			
ndrosis	Symphysis	In humans	In Animal (*if limited human studies)*	Notable functions of suture growth	Cases of isolated synostosis	Involvement in non-syndromic craniosynostosis	Involvement in syndromic craniosynostosis	Animal models of isolated synostosis
					• *Sullivan et al.:* Progressive unilateral midfacial and frontal retrusion. Nose/chin deviated toward fused suture. Shortening of zygomatic arch, greater sphenoid wing, temporal bone, and frontal bone			
		Cadaveric: Starts in 20s, completes after age 30				• *Udayakumaran et al.:* Synostosed in all trigonocephaly subjects. Contributes to metopic angulation and hypotelorism • *Calandrelli et al.:* Synostosed in 78% of metopic synostosis subjects		
		Patent through mid-teens at least (based on critical growth roles through adolescence)		• Nose and nasal airway development through the mid-teens • Septovomerine may also contribute to	*Haug & Foss:* Deep facial trauma can cause premature ossification of the septovomerine and consequent midface growth disruption. Also asymmetric			

on		Timing of closure			Clinical Consequences of Premature Closure in Humans			
					In humans			
ndrosis	Symphysis	In humans	In Animal (*if limited human studies)*	Notable functions of suture growth	Cases of isolated synostosis	Involvement in non-syndromic craniosynostosis	Involvement in syndromic craniosynostosis	Animal models of isolated synostosis
				maxillary protrusion	nasal deformity, septal deviation, obstructed airway			
		Cadaveric: Mostly closed by age 18, variable patency in 20s		Transverse maxillary growth	Transverse maxillary hypoplasia, possible severe malocclusion			
		CT and cadaveric: Starts in teens, completion varies considerably					*Kreiborg & Bjork:* Synostosed in postmortem Crouzon skull. Hypoplastic maxilla in vertical and transverse dimensions	
	✓	*Cadaveric:* Ossifies by 7-8 months, completely closed by 12 months						*Wang et al.:* Narrowed mandible with missing mandibular teeth (mice exposed to all-trans retinoic acid)
		• *CT:* Starts at age ~12, completes at ~15 in females • *CT:* Starts at ~13, completes at ~17 in males		Midfacial growth, cranial base lengthening			• *Goldstein et al.:* Significantly premature closure in Apert, Crouzon, and Pfeiffer patients (average of fusion is 3.5 years) • *Tahiri et al.:* Premature closure in Crouzon. Midface deficit • *McGrath et al.:* Significantly premature closure in Apert. Not premature in Muenke	*Rosenberg et al.:* Severe midface retrusion (rabbit)
	✓							

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on		Timing of closure			Clinical Consequences of Premature Closure in Humans			
					In humans			
ndrosis	Symphysis	In humans	In Animal (*if limited human studies)*	Notable functions of suture growth	Cases of isolated synostosis	Involvement in non-syndromic craniosynostosis	Involvement in syndromic craniosynostosis	Animal models of isolated synostosis
		CT: Starts at age 2, completes by age 15			*Burdi et al.:* Isolated fusion in warfarin-exposed fetus. Severe exorbitism	*Rogers et al.:* Involved in one case of unilateral frontosphenoidal synostosis. Frontal flattening, orbital rim depression/recession	• *Runyan et al.:* Synostosed in 75% of Pfeiffer subjects, 50% of Apert subjects. Not synostosed in Crouzon • *Calandrelli et al.:* Synostosed in 50% of Apert subjects, 11% of Crouzon, 67% of Saethre-Chotzen. Variable middle cranial fossa shortening. Not synostosed in Pfeiffer	
		CT: Starts at age 5, completes by age 15		Anteroposterior lengthening of cranial base from birth to age 7	• *Francel et al:* Frontal plagiocephaly phenotype • *Rogers et al.:* Ipsilateral flattening, contralateral bossing, orbital rim depression/ recession • *Puente-Espel et al.:* Ipsilateral	*Showalter et al.:* If synostosis occurs in unilateral coronal synostosis, it blunts the harlequin orbital deformity and can delay diagnosis	• *Kreiborg et al.:* Bilateral synostosis in Apert skull. May contribute to cranial base shortening • *Kreiborg & Bjork:* Synostosed in Crouzon skull • *Seeger & Gabrielsen:*	

on		Timing of closure			Clinical Consequences of Premature Closure in Humans			
					In humans			
ndrosis	Symphysis	In humans	In Animal (*if limited human studies)*	Notable functions of suture growth	Cases of isolated synostosis	Involvement in non-syndromic craniosynostosis	Involvement in syndromic craniosynostosis	Animal models of isolated synostosis
							frontal flattening/ retrusion, inferolateral positioning of ipsilateral orbit with compensatory medial elongation	In Apert and Crouzon. Frontal shortening, anterior cranial fossa shortening, orbital shallowing • *Runyan et al.:* Synostosed in 50% of Pfeiffer and Apert subjects. Not synostosed in Crouzon • *Calandrelli et al.:* Synostosed in 100% of Apert and Saethre-Chotzen subjects, 44% of Crouzon, 33% of Pfeiffer. Variable middle cranial fossa shortening
		CT: Starts before age 7, completes during teen				*Lambert & Wineski:* Can be involved in scaphocephaly with sagittal synostosis	• *Cohen & Kreiborg:* In Apert, retrusion/ elevation of the supraorbital wings. Disrupted eyebrows, forehead	

on		Timing of closure			Clinical Consequences of Premature Closure in Humans			
					In humans			
ndrosis	Symphysis	In humans	In Animal (*if limited human studies)*	Notable functions of suture growth	Cases of isolated synostosis	Involvement in non-syndromic craniosynostosis	Involvement in syndromic craniosynostosis	Animal models of isolated synostosis
							skin wrinkling • *Runyan et al.:* Synostosed in 100% of Pfeiffer subjects, 33% of Crouzon, and 50% of Apert • *Calandrelli et al.:* Synostosed in 50% of Apert subjects, 56% of Crouzon, and 67% of Pfeiffer and Saethre-Chotzen. Variable anterior/ middle cranial base shortening	
		CT: Starts at age 2, completes by age 6				*Sakamoto et al.:* Suture growth is arrested in unilateral coronal synostosis. Shortened sphenoid greater wing and temporal bone	• *Kreiborg & Bjork:* Synostosed in Crouzon skull. Laterally deviated lateral orbital walls • *Runyan et al.:* Synostosed in 100% of Pfeiffer subjects, 67% of	

on		Timing of closure			Clinical Consequences of Premature Closure in Humans			
					In humans			
ndrosis	Symphysis	In humans	In Animal (*if limited human studies)*	Notable functions of suture growth	Cases of isolated synostosis	Involvement in non-syndromic craniosynostosis	Involvement in syndromic craniosynostosis	Animal models of isolated synostosis
							Crouzon, and 50% of Apert • *Calandrelli et al.:* Synostosed in 50% of Apert subjects, 78% of Crouzon, and 67% of Pfeiffer. Variable anterior/ middle cranial base shortening	
		CT: Starts in 40s-50s, completes after age 70				*Jimenez et al.:* Unilateral posterior plagiocephaly without lambdoid synostosis, but with parietomastoid and occipitomastoid synostosis. Anterior displacement of ear. Compensatory frontal bossing, malar protrusion	• *Runyan et al.:* Synostosed in 100% of Pfeiffer subjects, 67% of Crouzon, and 50% of Apert • *Calandrelli et al.:* Synostosed in 100% of Apert and Crouzon subjects, 67% of Saethre-Chotzen, and 33% of Pfeiffer. Variable anterior/ middle cranial base shortening	

		Timing of closure			Clinical Consequences of Premature Closure in Humans			
					In humans			
Sagittal	Symphysis	In humans	In Animal (*if limited human studies*)	Notable functions of suture growth	Cases of isolated synostosis	Involvement in non-syndromic craniosynostosis	Involvement in syndromic craniosynostosis	Animal models of isolated synostosis
		CT: Partially patent through late teens					• *Coll et al.:* Synostosis in Crouzon starting at age 2 • *Runyan et al.:* Synostosed in 75% of Pfeiffer subjects, 67% of Crouzon, and 50% of Apert • *Calandrelli et al.:* Synostosed in 50% of Apert subjects, 67% of Crouzon, and 33% of Pfeiffer. Variable anterior cranial base shortening	