GE Healthcare

Three dimensional ultrasound of cranio-facial anomalies

Gianluigi PILU

Associate Professor of Obstetrics and Gynecology
University of Bologna, Italy

Craniofacial anomalies include a wide spectrum of malformations. They may be clinically relevant in themselves, and may also be associated with other congenital anomalies, or be a part of a syndrome. Evaluation of the face is indeed an important part of the clinical genetic examinations that are performed postnatally.

Prenatal sonographic diagnosis of cranio-facial anomalies is possible from early gestation and has been described in many publications. However, a meticulous scanning technique is required that can hardly be applied in all examinations. Most national guidelines for the standard examination of fetal anatomy include only a few views of the fetal face, mostly demonstration of orbits and eyes, but do not consider feasible an examination of nose, lips and chin. The accuracy of referral centers in the investigation of high risk patients is universally reported to be very high. Conversely, the sensitivity of standard examinations in a low the sensitivity is extremely variable in the different studies, but tends to be low, in the range of 20%-40%, with a general tendency to recognize facial malformations associated with other anomalies and to miss the isolated ones. Part of the difficulty in the diagnosis of craniofacial anomalies with standard two-dimensional sonography lies in the need to reconstruct the complex tridimensional anatomy of the face from tomographic planes.

The use of three-dimensional (3D) ultrasound for the evaluation of the fetal face is well established. The advantages over standard 2D ultrasound include the visualization of scanning planes that are physically impossible or very difficult to obtain, the demonstration of the surface of the face, and the possibility of having panoramic views. The limitations of the technique are the same as for 2D sonograms. If the fetal face is not accessible or there is not a pocket of amniotic fluid separating the face from the surrounding structures, 3D will be of little help. However, in expert hands, a satisfying exam is possible in the majority of cases in the second to early third trimester. The relative value of 2D over 3D ultrasound has been debated. In expert hands, 2D ultrasound is precise in the identification and categorization of cranio-facial malformations. Although 3D ultrasound does not seem to offer overt diagnostic advantage, it has other potential benefits, such as offering the parents a realistic and understandable image of the fetal anomaly, and allowing better communication with the specialists involved in the management of the infant. With the expanding use of 3D ultrasound and the decrease in costs of the instrumentation, this technique is becoming a standard of care in obstetric sonograms.

Most of the experience with 3D ultrasound has been derived from referral centers. The impact of this technique in standard examinations has yet to be assessed. In general, 3D ultrasound is complex and probably beyond the scope of a basic evaluation of fetal anatomy in low risk pregnancies. It is however possible that real time 3D (4D) ultrasound that allows a rapid and accurate visualization of the external surface of the fetus will prove useful for assessment of facial anatomy in such settings. The scope of this chapter is to review the technique of 3D and 4D ultrasound examination of the fetal face and the diagnosis of anomalies.

Technique of 3D ultrasound of the fetal face

The following discussion applies mostly to the midtrimester fetus. However, many details of facial anatomy can be identified as early as 11 weeks, particularly by using transvaginal sonography. In the third trimester of gestation, the examination will frequently fail because of intrauterine crowding and unfavorable fetal position. One necessary prerequisite of sonography of the fetal face is that this is accessible and there is a pocket of fluid in front of it. With two-dimensional (2D) a combination of planes must be used to assess facial anomalies (Figure 1).

Static 3D ultrasound and 4D have a similar approach. Both techniques begin with the acquisition of a sonographic volume containing the fetal face. Although the approach will vary from case to case depending upon the position of the fetus, there are two fundamental possibilities. The fetal face can be insonated frontally or from one side (Figure 1). Frontal insonation is ideal for evaluating the nose, lips and the symmetry of the face. Lateral insonation allows the demonstration of only one side of the face, but it has several advantages in the assessment of the ears and mandible.

Once an ultrasound volume has been acquired, it can be studied with a variety of approaches. Thus far, three modes have been reported to be useful in the diagnosis of cranio-facial anomalies. The multiplanar mode consists in the simultaneous demonstration of three orthogonal planes whose direction is chosen by the operator. Typically the volume is obtained with a frontal approach, from the profile view of the fetus, which is displayed on the upper left corner of the screen, while the two perpendicular planes are demonstrated in the upper right and low quadrants (Figure 2). The advantage of 3D ultrasound in comparison with 2D ultrasound is that it may be difficult at times to obtain the exact plane in a moving fetus. The multiplanar mode can also be used to reconstruct a profile view of the face when the fetus is lying on one side (Figure 3)

The surface mode allows one to visualize the external surface of the fetal face when this is surrounded by fluid. To obtain it, the region of interest (ROI) is positioned inside the volume in such a way that the fetal face is observed from the amniotic fluid layer (Figure 4). The surface view of the face is probably the most significant view for the diagnosis of many facial malformations (Figure 5,6).

One limitation of 2D ultrasound is the difficulty of demonstrating clearly the posterior portion of the palate, due to shadowing artifacts arising from the anterior palate. 3D sonography could however overcome this difficulty. One approach is the so called 'reverse view of the face', that is, once the volume has been acquired, to view the face in surface mode from the back instead from the front (Figure 7). Another approach consists of insonating the face at an angle to demonstrate the palate (Figure 8,9).

Eventually, the maximum or transparent mode allows one to demonstrate the brightest echoes within the volume and it can be used to visualize the skull and the fontanelles and sutures (Figure 10).

The advantage of 4D ultrasound with regard to static 3D is that the images are obtained faster and this virtually eliminates movement artifacts. Although originally 4D had low resolution, modern apparatuses allow an excellent quality of the images that compares favorably even with static 3D (Figure 11).

The approach is similar to the one described for static 3D. The transducer is placed in such a way that a pocket of fluid is interposed between the uterine wall and the fetal face, with a frontal or lateral approach.

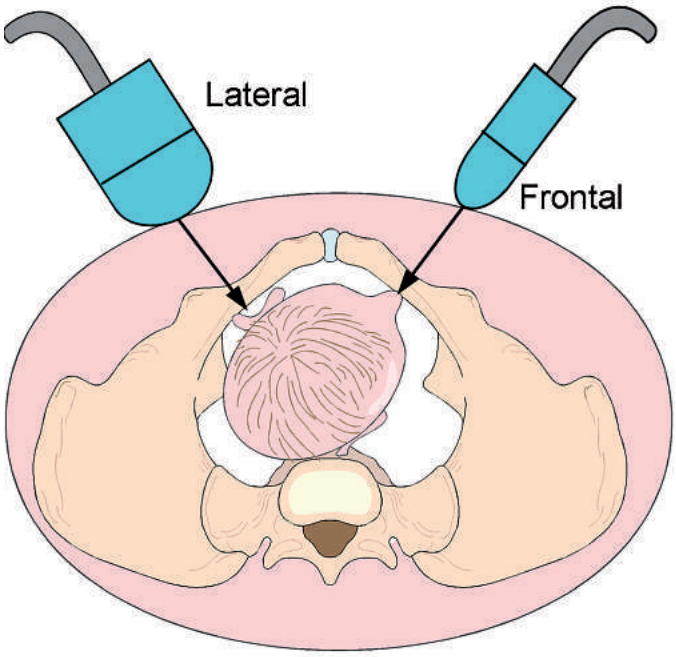

Figure 1: Schematic demonstration of the approach to the 3D ultrasound evaluation of the fetal face. The transducer can be aligned either frontally or laterally to the fetal face.

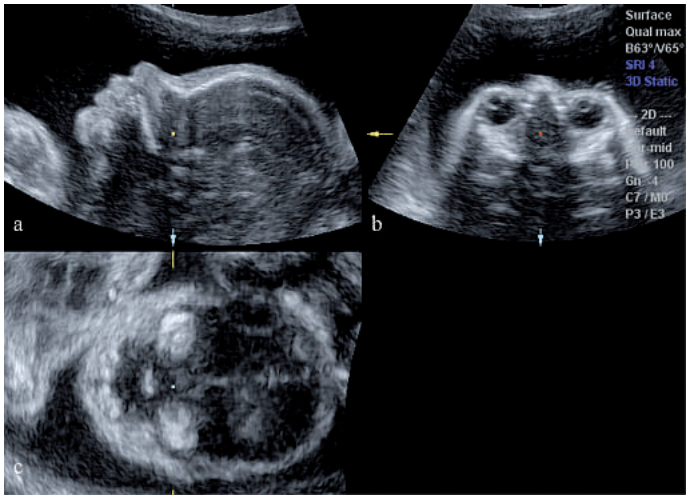

Figure 2: Three dimensional ultrasound: multiplanar analysis of the fetal face from a frontal approach. To obtain the volume the transducer was originally aligned with the profile of the fetus (a); the two orthogonal planes, axial (b) and coronal (c) are simultaneously displayed. From this position it is possible to navigate into the volume to demonstrate different anatomical details.

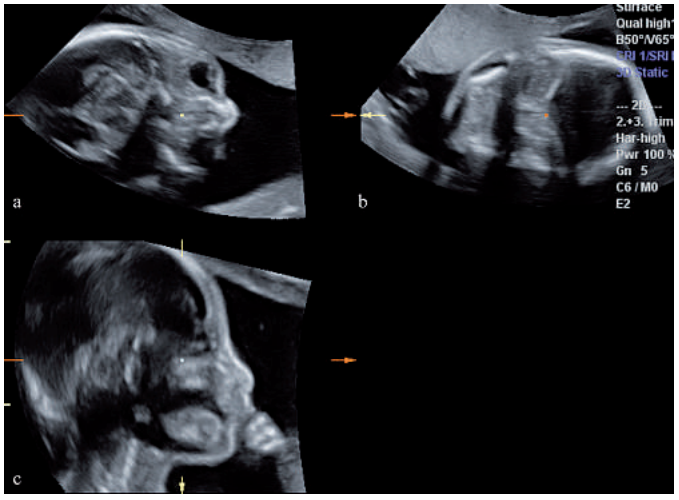

Figure 3: Three dimensional ultrasound multiplanar analysis of the fetal face from a lateral approach. In this case, the fetus was lying on one side and the transducer was aligned with an axial view of the face (a); the reconstructed coronal plane (c) allows clear visualization of the fetal profile, that due to the position of the fetus was physically impossible to obtain with standard two dimensional ultrasound.

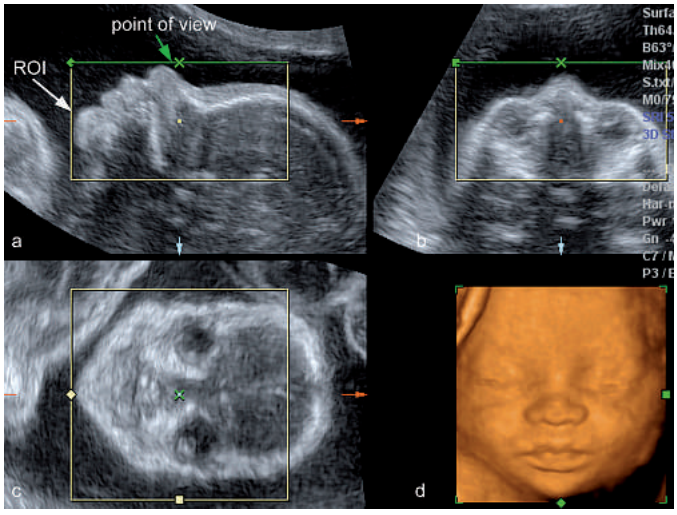

Figure 4: Surface rendering of the fetal face in the same case of Figure 2. The region of interest (ROI) has been positioned into the amniotic fluid to include the relevant detail of the fetal face. The green line indicates the point of view. In this example the fetal face is demonstrated as seen from above. The display conventionally demonstrates the three orthogonal planes in a,b,c and the rendering in the lower right corner (d).

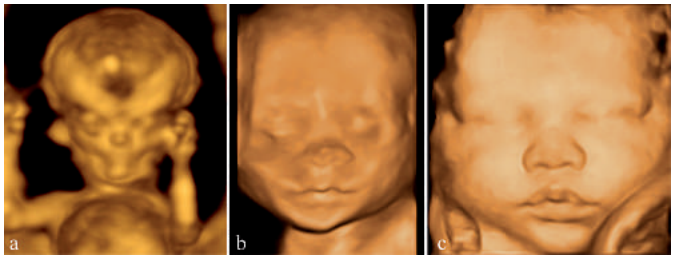

Figure 5: Surface rendering of the fetal face from a frontal approach at 11 weeks (a), 19 weeks (b) and 37 weeks (c).

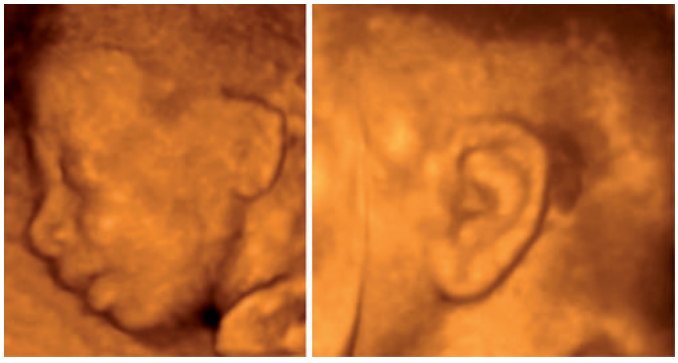

Figure 6: Surface renedering of the fetal face using a lateral approach. Only one side of the face is demonstrated. However, this approach is valuable to assess, among other details, the position and morphology of the ears and maxilla.

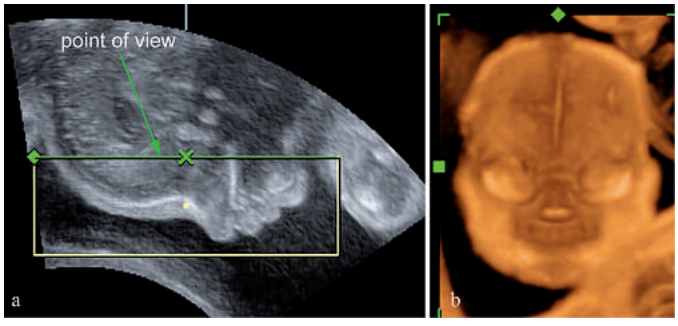

Figure 7: Reverse view of the fetal face. This is the same volume as figure 4. The point of view has been changed and the face is seen from inside the skull. This demonstrates the alveolar ridge of the palate.

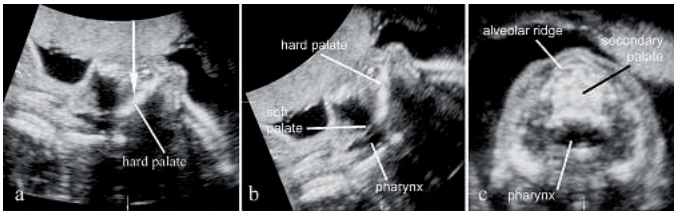

Figure 8: Three dimensional ultraound: angled approach to visualize the fetal palate.
a) to overcome acoustiuc shadowing from the alveolar ridge a midsagittal view of the fetal face is obtained and the transducer is angled to insonate the secondary palate with a angle of about 45 degrees;
b) a static 3D volume is obtained and rotated to bring the secondary palate in a vertical position;
c) reslicing the volume in multiplanar mode, an axial view displaying both the alveolar ridge and secondary palate is obtained. The soft palate can be appreciated in the sagittal section. However, it lies at an angle to the secondary palate and is not demonstrate in the axial view.

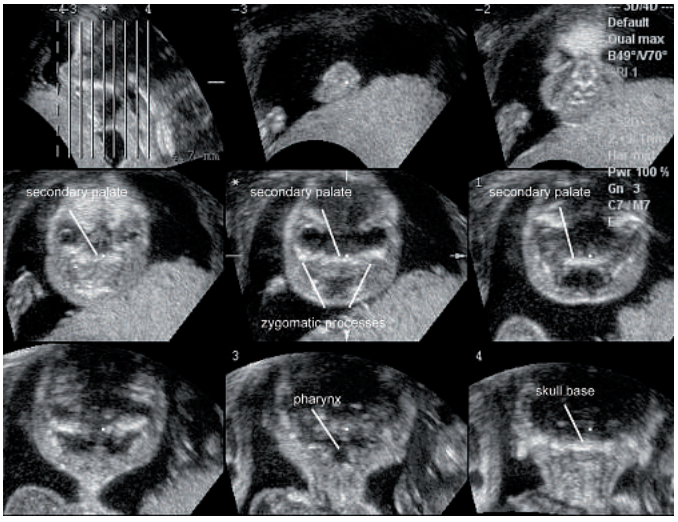

Figure 9: Three dimensional ultrasound: TUI (multiple slices) of the fetal palate visualized with an angeld approach. Comparing the reference midsagittal view with the coronal slices, the entire secondary palate is clearly demonstrated.

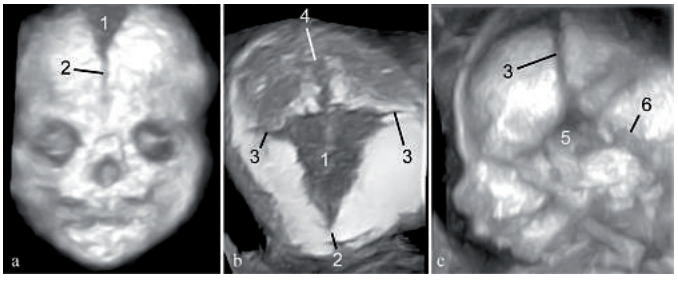

Figure 10: Three dimensional ultrasound: the skeleton of the face and skull is clearly demonstrated with the maximum or transparent mode. The different sutures and fontanelles are depicted in the coronal (a), superior (b) and lateral view (c) of the skull: 1. bregmatic fontanelle; 2. frontal or metopic suture; 3. coronal suture; 4. parietal suture; 5. sphenoid fontanelle; 6. mastoid suture.

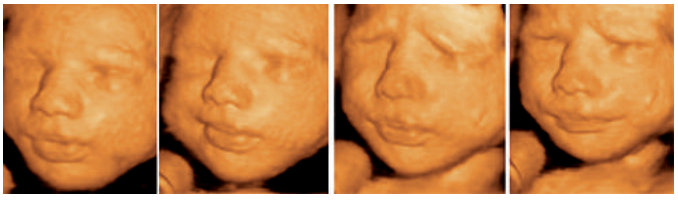

Figure 11: Visualization of the fetal face with 4D ultrasound. Despite the rapid turnover of ultrasound volumes (in this case, 4 per seconds) there is sufficient resolution to demonstrate not only anatomic details but also facial expressions.

CRANIO-FACIAL ANOMALIES

Typical facial clefts

Facial clefts are the most frequent craniofacial anomalies and the second most common congenital malformation, accounting for 13 percent of all anomalies. The incidence is about 1.4 cases per 1000 births. Clefts can occur in any part of the face, but typically involve the ideal line running between each of the nostrils and the central part of the posterior palate. Atypical types of facial clefts differ in the etiology, clinical implications as well as in the diagnostic approach and therefore will be discussed separately.

Typical facial clefts are commonly referred to as cleft lip (CL) and cleft palatae (CP). CL may be associated with cleft palate (CL-CP). The term cleft palate (CP) refers to a defect of the posterior portion of the palate in the presence of a normal upper lip and anterior palate. The anatomy and pathogenesis of these defects can be better understood in light of the embryological development. The fetal splanchnocranium derives from outgrowths of mesenchyma that surround the primitive oral cavity or stomodeum. These outgrowths (frontonasal prominence, maxillary prominence, and mandibular prominence) are separated by grooves that eventually undergo fusion and obliteration. The palate originates from the fusion of three palatine processes. The median originates from the medial nasal prominences, and the two lateral ones originate from the maxillary processes. The palatine processes also fuse with the nasal septum, which divides the nasal cavities. The palate is commonly divided in three parts: the anterior or primary palate, the posterior or secondary palate, and the soft palate (Figure 8). Typical facial clefts presumably arise from failure of fusion of the different bony structures and overlying soft tissues, with persistence of the embryological grooves (Figure 9).

CL+/-CP and isolated CP are two different anomalies. With exceedingly rare exceptions, recurrences are type specific. If the index case has CL+/-CP, there is no increased risk for isolated CP, and vice versa. Roughly, of all cases with typical facial clefts, 25% have CL, 50% CL-CP and 25% CP.

In the vast majority of cases, typical facial clefts have a multifactorial etiology. The empiric risks of recurrence for these cases are reported in Table 1. In some cases, however, facial clefts are a part of well-established genetic and nongenetic syndromes. The claimed risk associated with diazepam and steroidal agents intake has not been confirmed in carefully controlled studies. Chromosomal abnormalities are rare in postnatal series but rather frequent in the prenatal ones. The discrepancy may be due to a high rate of intrauterine selection of aneuploid fetuses, as well as to the inclusion of an excess of atypical clefts.

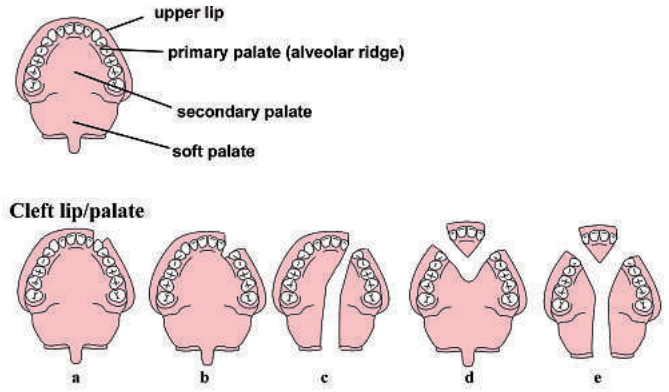

Figure 12: Schematic representation of the normal and cleft lip and palate: a) unilateral cleft lip (the defect may also be bilateral); b) cleft lip-palate with a defect limited to the primary palate (or alveolar ridge); c) cleft lip-palate with a defect extending to the secondary palate (in this case involving also the soft palate); d) bilateral cleft lip-palate limited to the primaty palate; note the anterior displacement of the central portion of the maxilla; e) bilateral cleft lip-palate extending to the posterior palate.

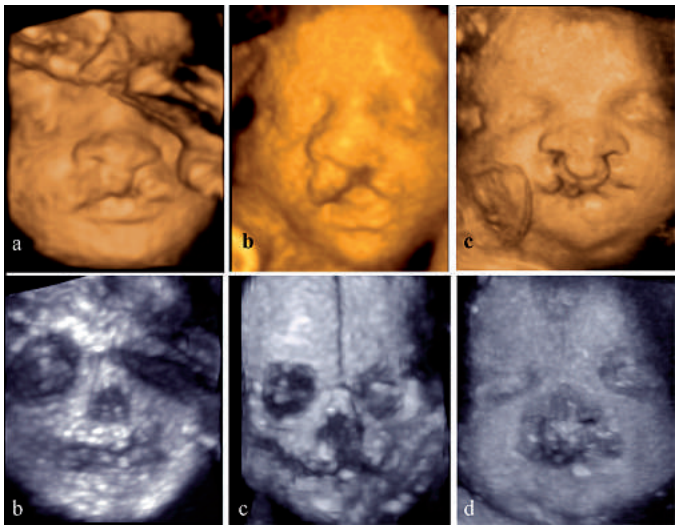

Figure 13: Three dimensional ultrasound of cleft lip in surface mode (a,b,c) and maximum mode (d,e,f). a,b) unilateral cleft lip; b,e) unilateral cleft lip and palate; c,f) bilateral cleft lip and palate.

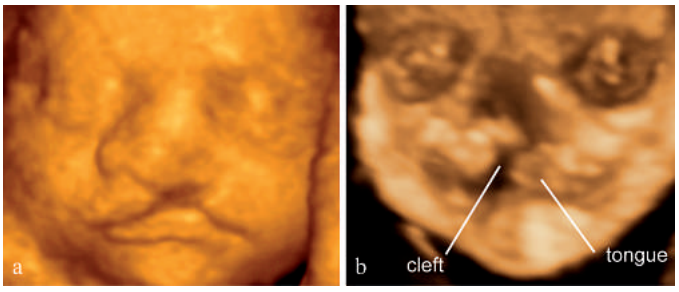

Figure 14: Unilateral cleft lip-palate; in the left panel, a) an anterior view of the face in surface mode; b) reverse view of the face demonstrating that the defect extends to the posterior palate; as it frequently happens, the tongue is apposed to the defect

Facial clefts encompass a broad spectrum of severity. The typical CL will appear as a linear defect extending from one side of the lip into the nostril. CL-CP may extend through the alveolar ridge and hard palate, reaching the floor of the nasal cavity or even the floor of the orbit. CP may include defects of the hard palate, the soft palate, or both or the submucosal tissue (Figure 12).

Associated anomalies are found in 50 percent of patients with isolated CP and in only 13 percent of those with CL-CP. An incidence of 60 percent has been found in embryos and fetuses with facial clefting. In the majority of patients, the associated anomalies do not conform to an established syndrome. In cases of either isolated CL or CP, the most frequent anomaly is clubfoot, whereas in cases of CL-CP, it is polydactyly. Of particular importance is the association with congenital heart disease. No specific pattern could be identified. Specific associations with well-described syndromes are shown in Table 2.

If a satisfying ultrasound volume can be acquired, the diagnosis of cleft lip is easy. The surface mode will demonstrate the defect of the lip, as well as the associated facial deformations, that typically include a distortion of the nose. The maximum mode can be used to demonstrate whether the palate is involved or not (Figure 13). With a standard approach, however, the most anterior portion of the palate, the primary palate or alveolar ridges cast an acoustic shadow that does not allow one to visualize the degree of extension of the defect into the posterior or secondary palate. To overcome this difficulty, the reverse fetal face (Figure 14) and the angled insonation of the palate can be used (Figure 15).

In all typical clefts with bilateral CL-CP, there is a protrusion of the central portion of the palate and lip that is commonly referred to as the 'maxillary pseudomass' (Figure 16). With bilateral CL-CP there is a major distortion of facial anatomy and the pseudomass is a more obvious and reliable finding than the visualization of the clefts which is sometimes difficult. Conversely, with unilateral CL+/-CP or bilateral CL the profile view is always unremarkable.

The prognosis of facial clefts depends primarily on the presence and type of associated anomalies. Mild clefts, such as lineal indentations of the lips or submucosal cleft of the soft palate may not require surgical correction. Larger defects cause cosmetic, swallowing, and respiratory problems. Recent advances in surgical technique have produced good cosmetic and functional results. Cases that are associated with a defect in the posterior palate represent the greatest challenge for surgical correction, as the soft palate is involved in the process of swallowing and vocalizing. Furthermore, tubal disorders may lead in time to acoustic problems and deafness.

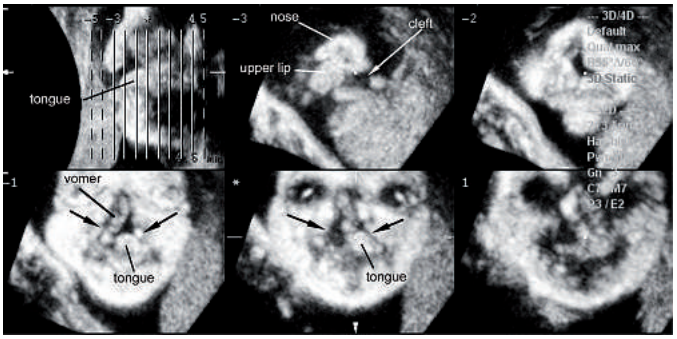

Figure 15: Three dimensional ultrasound of unilateral cleft lip and palate: TUI (multiple slices) of a volume obtained with angled insonation of the fetal palate. A comparison between the reference sagittal view and the coronal slices allows to identify the defect extending into the secondary palate. (arrowheads).

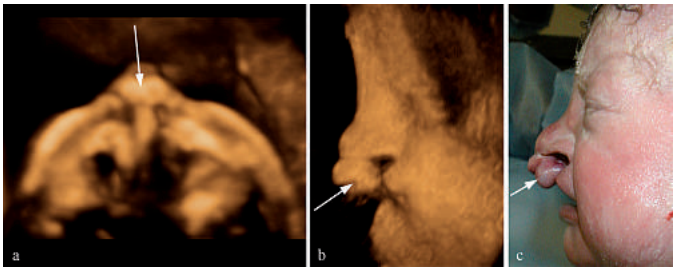

Figure 16: Typical premaxillary protrusion in a fetus with bilateral clet lip-palate.

Atypical facial clefts

In about 3% of cases clefts occur in portions of the face different from the line joining the nostrils to the posterior palate. The prevalence is much higher in prenatal studies due to both the high intrauterine fatality rate that is associated with some of these conditions and probably the higher detection rate due to the frequency of associated malformations.
The atypical cleft that has been reported by far most frequently in prenatal diagnosis series is the median cleft or Tessier cleft number 0. This is a quadrangular defect in the central portion of the upper lip and palate, usually associated with a flattened nose. It accounts for less than 1% all cases of cleft lip. It is considered to represent the consequence of underdevelopment of the frontonasal prominence, which normally joins the two maxillary prominences. Development of the midface is induced by the prechordal mesenchyma, which is also responsible for the differentiation of the midline structures of the brain. This explains the frequent association of median clefts with alobar or semilobar holoprosencephaly. The typical combination of findings in these cases include hypotelorism, flat nose and median cleft lip (Figure 17).

Median cleft lip may also occur in association with hypertelorism (increased orbital distance), a combination that is pathognomonic of the "median cleft face syndrome" or "frontonasal dysplasia". The pathogenesis is much different in these cases. The premaxilla is present, as well as the nose that is usually bifid, and the brain is normal in most cases. The diagnosis relies on the demonstration of a wide central defect involving both the upper lip and the palate in axial or coronal scans.

The prognosis of a median cleft depends entirely on the association with other anomalies. Median cleft face syndrome is usually associated with normal intelligence. Radical cosmetic surgery may be required. Alobar and semilobar holoprosencephaly both have a very severe prognosis.

Severe holoprosencephaly is also associated with other craniofacial anomalies due to underdevelopment of the midface that includes a combination of hypotelorism/cyclopia, absence of a nose, presence of a proboscis. Bilateral CLCP is usually associated with anterior displacement of the premaxilla. In a minority of cases it may occur without protrusion and a flat facial profile. This is a different and more extreme anomaly than typical CLCP, which is probably pathophysiologically connected to median cleft lip, and usually associated with multiple anomalies and chromosomal aberrations, trisomy 18 in particular (Figure 18).

The most common atypical cleft found at birth is the lateral one (or Tessier number 7), which has an estimated incidence of one in 3000–5600 live births and may be either unilateral (more frequently on the left side) or bilateral. It is probably due to defective development of the branchial arches and is characterized by a variable degree of widening of the oral commissure (macrostomia) associated with hypoplasia of the lateral skeleton of the face (maxilla, zygomatic bone, ascending branch of the mandible) and external ear. A handful of cases have been diagnosed antenatally. Sonographic findings include unusual deepening of the corners of the mouth and asymmetry between the two sides of the face. 3D ultrasound is particularly valuable for recognizing lateral clefts (Figure 19). The central portion of the face, nose, lips and alveolar ridge is well visualized with a standard 2D scan. However, the lateral part of the fetal face is not equally accessible. A panoramic view of the entire face in surface mode is certainly the best approach for the diagnosis.

Lateral clefts of the face are usually isolated malformations. Surgical correction is possible but is extremely challenging due to the association with underlying skeletal abnormalities involving the mandible. Ear abnormalities are also frequent.

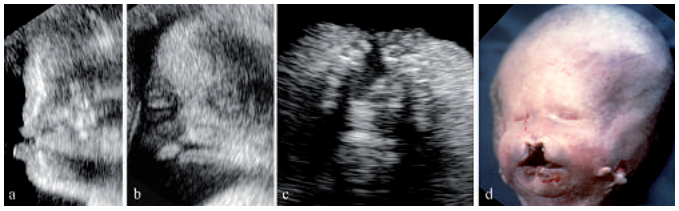

Figure 17: Median cleft lip-palate in a fetus with alobar holoprosencephaly.

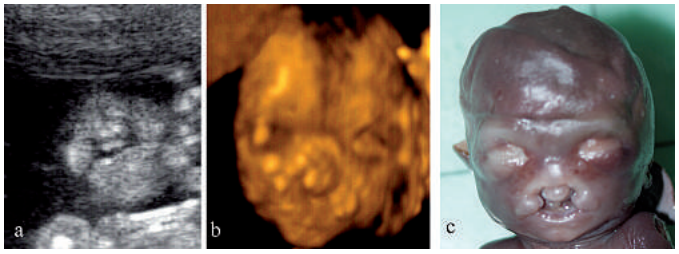

Figure 18: Bilateral cleft lip and palate with flat face in 14 weeks' fetus with trisomy 18: a) coronal view of the upper lip demonstrating bilateral cleft; b) surface mode at 14 weeks; c) postnatal image.

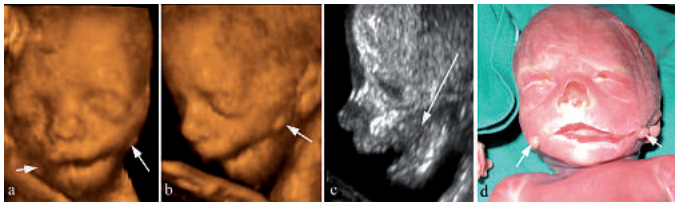

Figure 19: Lateral cleft of the fetal face: a, b) surface mode demonstrates a lateral cleft associated with a typically sunken cheek; c) lateral view of the face in maximum mode demonstrating hypoplasia of the zygomatic process and ascending branch of the mandible (long arrow); d) postnatal image; the arrowhead indicate skin tags.

Micrognathia and retrognathia

The mandible forms the floor of the oral cavity and contains the tongue. If the mandible is severely hypoplastic (micrognathia) or posteriorly displaced (retrognathia) a typical malformative sequence occurs: the tongue is displaced superiorly and posteriorly, leading to both abnormal closure of the palatine process, which results in either a cleft palate or a high arched palate, and glossoptosis which may cause suffocation at birth. This sequence is frequently referred to as the Robin anomalad, which may be a sporadic isolated finding (in about 40% of cases) or may be associated with other anomalies or with recognized genetic and non-genetic syndromes including Treacher Collins, Robin and Robert syndromes, Cornelia de Lange syndrome, chromosomal abnormalities (mainly trisomy 18 and triploidy) and teratogen exposure. Micrognathia/retrognathia encompass a wide spectrum of severity and in all likelihood most mild cases cannot be recognized in utero. Conversely, severe forms can be identified from early gestation and different approaches have been suggested from time to time. Probably, the simplest one is the profile view to demonstrate that the midportion of the mandible is not aligned with the maxilla (Figure 20). In this view, the upper lip is usually very prominent and the chin is receding. This is however a subjective observation, and at times is associated with many uncertainties. The index of suspicion increases when the tongue appears displaced posteriorly and superiorly. Measurement of the mandible has also been proposed. Distinguishing micrognathia from retrognathia is not simple, and the two conditions frequently coexist. Intrauterine development of micrognathia, limiting early prenatal diagnosis has been suggested. With 3D ultrasound in maximum mode the entire mandible can be visualized and this may increase diagnostic precision (Figure 20).

Severe micrognathia can be a neonatal emergency due to airway obstruction by the tongue in the small oral cavity. If prenatal diagnosis is made a pediatrician should be present in the delivery room and be prepared to intubate the infant. The prognosis however depends mostly on the presence of associated anomalies. In all probability, only the most severe cases and those with associated malformations are detected in utero, and this may explain the poor outcome of most neonatal series.

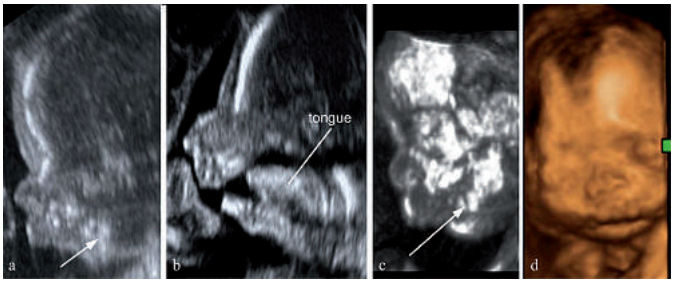

Figure 20: Severe micrognathia in a fetus with Cornelia de Lange syndrome a) sagittal view of the fetal face demonstrating protruding upper lip and small chin (arrow); b) note the unusual posterior displacement of the tongue that occupies the hypopharynx; c) three-dimensional ultrasound, maximum mode demonstrating the small mandible; postnatal radiograph; 4) three-dimensional ultrasound, surface mode, demonstrating abnormal face with hypertelorism, proptosis, downward slanting of the eyelids and small chin.

Facial dysmorphism

Modern high-resolution ultrasound allows detailed evaluation of the fetal face and an expert sonologist can perform on a living fetus in early gestation an anatomical examination that in many ways is similar the clinical evaluation that can be performed on a live infant. Facial dysmorphism is now amenable to antenatal detection and 3D is certainly valuable in these settings (Figure 21). The detection of even subtle facial findings has been useful in diagnosing or corroborating the diagnosis of syndromes in pregnancies at increased risk. Typical facial features of common syndromes such as Noonan's, Costello's and Wolf-Hirschhorn have also been described. However, some caution is necessary because facial features may demonstrate extreme variations in normal individuals. Among the facial dysmorphisms that can be reliably identified, one is Binder syndrome or maxillonasal dysplasia that is characterized by the association of an extremely small and flat nose, a convex upper lip, and malocclusion. Antenatally, the profile view is particularly striking, with an extremely small and flat nose that does not form an angle with the forehead (Figure 22). This condition does not seem to affect neurological development an d surgical treatment is available. An association with chondrodysplasia punctata has however been described.

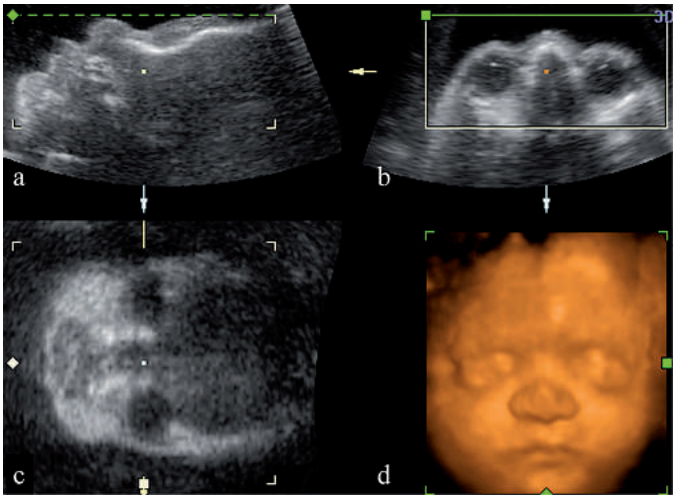

Figure 21: This fetus had increased nuchal transluciency in the late first trimester, and a thick nuchal fold and polyhydramnios in the second trimester. Although the bidimensional examination of the fetal face (a,b,c) is negative, the surface mode reveals unusual facies with antimongoloid slanting of the eyelids. Noonan syndrome was diagnosed after birth.

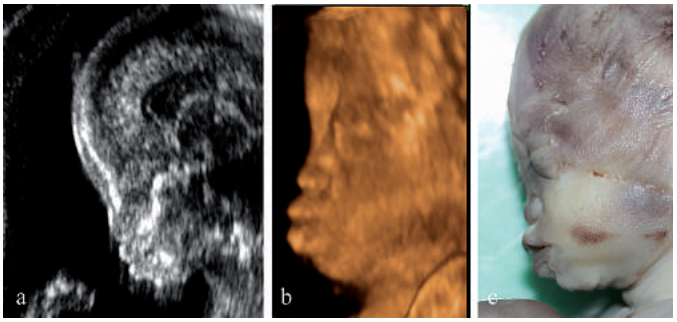

Figure 22: Binder syndrome: a) sagittal view of the face: b) fetal profile in three dimensional surface mode ultrasound; c) postnatal image. Note the small and flat nose with absence of any angle between forehead and nose.

Craniosynostosis

Premature ossification and closure of the cranial sutures results in abnormal shape and size of the skull. In severe cases, this condition can also cause compression on cranial nerves and increased pressure on the growing brain. The final result depends upon the sutures that are involved and the time the closure takes place. Craniosynostosis (or craniostenosis) occurs in about 1 of 2500 births. In most cases, only one suture is affected and the condition is isolated and sporadic. However, in a minority of cases, closure of multiple sutures is possible and associated anomalies are present (Figure 23). Craniosynostosis is a part of many genetic syndromes. The genetic defect underlying some of these syndromes has been identified. Most frequently this is a mutation in the genes encoding the fibroblast growth factor receptors (FGFR) 1, 2 and 3.

The most frequent craniosynostosis is due to closure of the sagittal suture which is responsible for about half of the cases, resulting in an elongated head (scaphocephaly). The second most frequent type is due to closure of the coronal suture that results in a very flat, recessed forehead (brachicephaly). Crouzon and Apert syndromes are the most common of the craniosynostosis syndromes. The main findings include premature closure of the coronal suture, hypoplasia of the midface, exopthalmus, and ploydactyly/syndactaly of the hands and feet. Crouzon Syndrome occurs in approximately 1 in 25,000 births. It may be transmitted as an autosomal dominant genetic condition or appear as a fresh mutation. The appearance of an infant with Crouzons can vary in severity from a mild presentation with subtle midface characteristics to severe forms with multiple cranial sutures fused and marked midface and ocular problems. The incidence of Apert syndrome is approximately 1 in 100,000 births and most cases are fresh mutations. The general features of a child with Apert syndrome are similar to those in Crouzon syndrome (Figure 23) however there is not as much variability between cases and the degree of presentation is more severe. Other types of craniosynostosis syndromes that have been diagnosed in utero include Pfeiffer syndrome which is characterized by closure of all sutures with a cloverleaf skull, and trigonocephaly which is due to closure of the metopic suture that results in a triangular forehead (Figure 23).

The experience with prenatal diagnosis of craniosynostosis is limited and consists mostly of case reports and small series of severe types. Most likely, the majority of cases are missed antenatally. We are aware of many infants that were diagnosed after birth with craniosynostosis and had completely unremarkable prenatal sonograms. Dolicocephaly due to compression is a frequent finding during fetal life and we expect that differentiation from the most frequent type of craniosynostosis, closure of the sagittal suture, would be impossible in most cases. Even severe forms may only be associated with subtle findings, particularly in early gestation.

Craniosynostosis should be suspected in the presence of an abnormal skull shape Failure to visualize the sutures that are normally seen as linear interruptions of the echogenic calvarium increases the index of suspicion. Recent reports on 3D ultrasound suggest that this technique may be valuable in the diagnosis of craniosynostosis.

Apart from the demonstration of panoramic views of the cranium using the standard surface mode (Figure 24), the transparent or maximum mode allows one to better visualize the sutures, something that is particularlty useful for demonstrating the abnormal compensatory opening of the patent sutures that occurs when there is craniostenosis. With premature closure of the coronal sutures, for example, there is a typical enlargement of the metopic one (Figure 25).

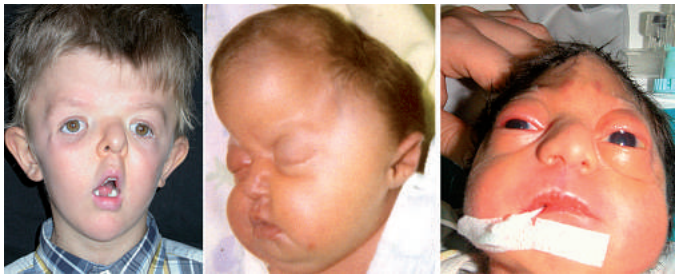

Figure 23: Craniosynostosis syndromes: a) Apert syndrome; b) Pfeiffer syndrome, lethal variety (cloverleaf skull); c) trigonocephaly

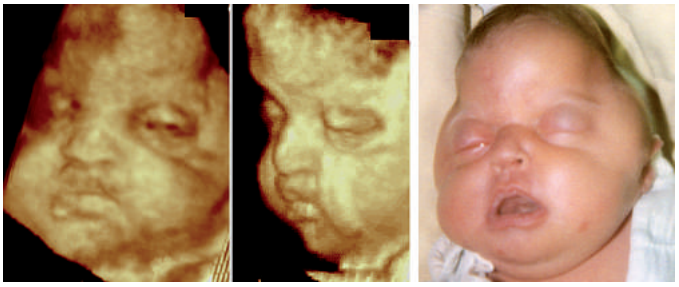

Figure 24: Pfeiffer syndrome, lethal variety: three dimensional surface mode (a,b) compared with a postnatal image.

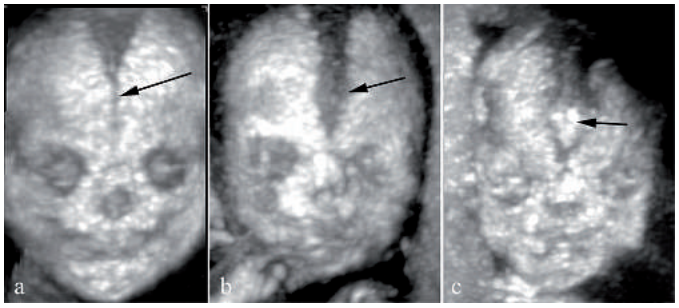

Figure 25: The metopic suture (arrow) in a normal fetus (a) and in two fetuses with cranosynostosis multiple anomalies (b,c). Note the presence of a wormiam bone in (c).

REFERENCES

1. Benacerraf BR, Frigoletto FD, Jr., Bieber FR. The fetal face: ultrasound examination. Radiology 1984;153(2):495-7.

2. Nyberg DA, Sickler GK, Hegge FN, Kramer DJ, Kropp RJ. Fetal cleft lip with and without cleft palate: US classification and correlation with outcome. Radiology 1995;195(3):677-84.

3. Pilu G, Reece EA, Romero R, Bovicelli L, Hobbins JC. Prenatal diagnosis of craniofacial malformations with ultrasonography. Am J Obstet Gynecol 1986;155(1):45-50.

4. Rotten D, Levaillant JM. Two- and three-dimensional sonographic assessment of the fetal face. 2. Analysis of cleft lip, alveolus and palate. Ultrasound Obstet Gynecol 2004;24(4):402-11.

5. Rotten D, Levaillant JM, Martinez H, Ducou le Pointe H, Vicaut E. The fetal mandible: a 2D and 3D sonographic approach to the diagnosis of retrognathia and micrognathia. Ultrasound Obstet Gynecol 2002;19(2):122-30.

6. Ghi T, Perolo A, Banzi C, Contratti G, Valeri B, Savelli L, Morselli GP, Bovicelli L, Pilu G. Two-dimensional ultrasound is accurate in the diagnosis of fetal craniofacial malformation. Ultrasound Obstet Gynecol 2002;19(6):543-51.

7. Jones MC. Prenatal diagnosis of cleft lip and palate: detection rates, accuracy of ultrasonography, associated anomalies, and strategies for counseling. Cleft Palate Craniofac J 2002;39(2):169-73.

8. Stoll C, Dott B, Alembik Y, Roth M. Evaluation of prenatal diagnosis of cleft lip/palate by foetal ultrasonographic examination. Ann Genet 2000;43(1):11-4.

9. Sohan K, Freer M, Mercer N, Soothill P, Kyle P. Prenatal detection of facial clefts. Fetal Diagn Ther 2001;16(4):196-9.

10. Wayne C, Cook K, Sairam S, Hollis B, Thilaganathan B. Sensitivity and accuracy of routine antenatal ultrasound screening for isolated facial clefts. Br J Radiol 2002;75(895):584-9.

11. Campbell S, Lees C, Moscoso G, Hall P. Ultrasound antenatal diagnosis of cleft palate by a new technique: the 3D "reverse face" view. Ultrasound Obstet Gynecol 2005;25(1):12-8.

12. Campbell S, Lees CC. The three-dimensional reverse face (3D RF) view for the diagnosis of cleft palate. Ultrasound Obstet Gynecol 2003;22(5):552-4.

13. Pilu G, Segata M. submitted for publication.

14. Bellis TH, Wohlgemuth B. The incidence of cleft lip and palate deformities in the south-east of Scotland (1971-1990). Br J Orthod 1999;26(2):121-5.

15. Berge SJ, Plath H, Van de Vondel PT, Appel T, Niederhagen B, Von Lindern JJ, Reich RH, Hansmann M. Fetal cleft lip and palate: sonographic diagnosis, chromosomal abnormalities, associated anomalies and postnatal outcome in 70 fetuses. Ultrasound Obstet Gynecol 2001;18(5):422-31.

16. Nicolaides KH, Salvesen DR, Snijders RJ, Gosden CM. Fetal facial defects: associated malformations and chromosomal abnormalities. Fetal Diagn Ther 1993;8(1):1-9.

17. Nyberg DA, Hegge FN, Kramer D, Mahony BS, Kropp RJ. Premaxillary protrusion: a sonographic clue to bilateral cleft lip and palate. J Ultrasound Med 1993;12(6):331-5.

18. Pilu G, Romero R, Rizzo N, Jeanty P, Bovicelli L, Hobbins JC. Criteria for the prenatal diagnosis of holoprosencephaly. Am J Perinatol 1987;4(1):41-9.

19. Blaas HG, Eriksson AG, Salvesen KA, Isaksen CV, Christensen B, Mollerlokken G, Eik-Nes SH. Brains and faces in holoprosencephaly: pre- and postnatal description of 30 cases. Ultrasound Obstet Gynecol 2002;19(1):24-38.

20. Martinelli P, Russo R, Agangi A, Paladini D. Prenatal ultrasound diagnosis of frontonasal dysplasia. Prenat Diagn 2002;22(5):375-9.

21. Presti F, Celentano C, Marcazzo L, Dolcetta G, Prefumo F. Ultrasound prenatal diagnosis of a lateral facial cleft (Tessier number 7). Ultrasound Obstet Gynecol 2004;23(6):606-8.

22. Pilu G, Visentin A, Ambrosini G, D'Antona D, Andrisani A. Three-dimensional sonography of unilateral Tessier number 7 cleft in a mid-trimester fetus. Ultrasound Obstet Gynecol 2005;26(1):98-9.

23. Hsieh YY, Chang CC, Tsai HD, Yang TC, Lee CC, Tsai CH. The prenatal diagnosis of Pierre-Robin sequence. Prenat Diagn 1999;19(6):567-9.

24. Pilu G, Romero R, Reece EA, Jeanty P, Hobbins JC. The prenatal diagnosis of Robin anomalad. Am J Obstet Gynecol 1986;154(3):630-2.

25. Bronshtein M, Blazer S, Zalel Y, Zimmer EZ. Ultrasonographic diagnosis of glossoptosis in fetuses with Pierre Robin sequence in early and mid pregnancy. Am J Obstet Gynecol 2005;193(4):1561-4.

26. Paladini D, Morra T, Teodoro A, Lamberti A, Tremolaterra F, Martinelli P. Objective diagnosis of micrognathia in the fetus: the jaw index. Obstet Gynecol 1999;93(3):382-6.

27. Paladini D, Tartaglione A, Lamberti A, Lapadula C, Martinelli P. Prenatal ultrasound diagnosis of Nager syndrome. Ultrasound Obstet Gynecol 2003;21(2):195-7.

28. Lee W, McNie B, Chaiworapongsa T, Conoscenti G, Kalache KD, Vettraino IM, Romero R, Comstock CH. Three-dimensional ultrasonographic presentation of micrognathia. J Ultrasound Med 2002;21(7):775-81.

29. van den Elzen AP, Semmekrot BA, Bongers EM, Huygen PL, Marres HA. Diagnosis and treatment of the Pierre Robin sequence: results of a retrospective clinical study and review of the literature. Eur J Pediatr 2001;160(1):47-53.

30. Vettraino IM, Lee W, Bronsteen RA, Harper CE, Aughton D, Comstock CH. Clinical outcome of fetuses with sonographic diagnosis of isolated micrognathia. Obstet Gynecol 2003;102(4):801-5.

31. Cohen J, Ghezzi F, Goncalves L, Fuentes JD, Paulyson KJ, Sherer DM. Prenatal sonographic diagnosis of Treacher Collins syndrome: a case and review of the literature. Am J Perinatol 1995;12(6):416-9.

32. Cook K, Prefumo F, Presti F, Homfray T, Campbell S. The prenatal diagnosis of Binder syndrome before 24 weeks of gestation: case report. Ultrasound Obstet Gynecol 2000;16(6):578-81.

33. Cuillier F, Cartault F, Lemaire P, Alessandri JL. Maxillo-nasal dysplasia (binder syndrome): antenatal discovery and implications. Fetal Diagn Ther 2005;20(4):301-5.

34. Drolshagen LF, Durmon G, Berumen M, Burks DD. Prenatal ultrasonographic appearance of "Cornelia de Lange" syndrome. J Clin Ultrasound 1992;20(7):470-4.

35. Hansen WF, Rijhsinghani A, Grant S, Yankowitz J. Prenatal diagnosis of Apert syndrome. Fetal Diagn Ther 2004;19(2):127-30.

36. Leo MV, Suslak L, Ganesh VL, Adhate A, Apuzzio JJ. Crouzon syndrome: prenatal ultrasound diagnosis by binocular diameters. Obstet Gynecol 1991;78(5 Pt 2):906-8.

37. Levaillant JM, Gerard-Blanluet M, Holder-Espinasse M, Valat-Rigot AS, Devisme L, Cave H, Manouvrier-Hanu S. Prenatal phenotypic overlap of Costello syndrome and severe Noonan syndrome by tri-dimensional ultrasonography. Prenat Diagn 2006;26(4):340-4.

38. Menashe Y, Ben Baruch G, Rabinovitch O, Shalev Y, Katzenlson MB, Shalev E. Exophthalmus--prenatal ultrasonic features for diagnosis of Crouzon syndrome. Prenat Diagn 1989;9(11):805-8.

39. Paladini D, D'Armiento M, Ardovino I, Martinelli P. Prenatal diagnosis of the cerebro-oculo-facio-skeletal (COFS) syndrome. Ultrasound Obstet Gynecol 2000;16(1):91-3.

40. Roy S, Sinsky A, Williams B, Desilets V, Patenaude YG. Congenital epulis: prenatal imaging with MRI and ultrasound. Pediatr Radiol 2003;33(11):800-3.

41. Urban M, Hartung J. Ultrasonographic and clinical appearance of a 22-week-old fetus with Brachmann-de Lange syndrome. Am J Med Genet 2001;102(1):73-5.

42. Volpe P, Gentile M. Three-dimensional diagnosis of Goldenhar syndrome. Ultrasound Obstet Gynecol 2004;24(7):798-800.

43. Levaillant JM, Touboul C, Sinico M, Vergnaud A, Serero S, Druart L, Blondeau JR, Abd Alsamad I, Haddad B, Gerard-Blanluet M. Prenatal forehead edema in 4p- deletion: the 'Greek warrior helmet' profile revisited. Prenat Diagn 2005;25(12):1150-5.

44. Munro IR, Sinclair WJ, Rudd NL. Maxillonasal dysplasia (Binder's syndrome). Plast Reconstr Surg 1979;63(5):657-63.

45. Benacerraf BR, Spiro R, Mitchell AG. Using three-dimensional ultrasound to detect craniosynostosis in a fetus with Pfeiffer syndrome. Ultrasound Obstet Gynecol 2000;16(4):391-4.

46. Delahaye S, Bernard JP, Renier D, Ville Y. Prenatal ultrasound diagnosis of fetal craniosynostosis. Ultrasound Obstet Gynecol 2003;21(4):347-53.

47. Esser T, Rogalla P, Bamberg C, Kalache KD. Application of the three-dimensional maximum mode in prenatal diagnosis of Apert syndrome. Am J Obstet Gynecol 2005;193(5):1743-5.

48. Faro C, Chaoui R, Wegrzyn P, Levaillant JM, Benoit B, Nicolaides KH. Metopic suture in fetuses with Apert syndrome at 22-27 weeks of gestation. Ultrasound Obstet Gynecol 2006;27(1):28-33.

49. Gollin YG, Abuhamad AZ, Inati MN, Shaffer WK, Copel JA, Hobbins JC. Sonographic appearance of craniofacial dysostosis (Crouzon syndrome) in the second trimester. J Ultrasound Med 1993;12(10):625-8.

50. Hill LM, Grzybek PC. Sonographic findings with Pfeiffer syndrome. Prenat Diagn 1994;14(1):47-9.

51. Hill LM, Thomas ML, Peterson CS. The ultrasonic detection of Apert syndrome. J Ultrasound Med 1987;6(10):601-4.

52. Martinelli P, Paladini D, D'Armiento M, Scarano G. Prenatal diagnosis of cloverleaf skull in the subtype 2 Pfeiffer syndrome. Clin Dysmorphol 1997;6(1):89-90.

53. Faro C, Benoit B, Wegrzyn P, Chaoui R, Nicolaides KH. Three-dimensional sonographic description of the fetal frontal bones and metopic suture. Ultrasound Obstet Gynecol 2005;26(6):618-21.

TABLES

Table 1: Risk of recurrent cleft lip/cleft palate in subsequent offspring.

Variable	Cleft lip/palate (%)
Unaffected parent	
No affected offspring	0.1
No affected offspring plus 1 affected first cousin	0.4
One affected offspring	4.0
Two affected offspring	9.0
One affected offspring plus one affected relative	4.0
Affected parents	
One parent plus no affected offspring	4.0
One parent plus one affected offspring	10-17
Two parents plus one affected offspring	60.0

Table 2: Most frequent syndromes associated with facial clefts

Chromosomal aberrations
Deletion 4p (Wolf-Hirschhorn syndrome)
Trisomy 10
Trisomy 13
Trisomy 18
Trisomy 22
Trisomy 9
Malformations and sequences
Amniotic bands
Arthrogryposis
Camptomelic dysplasia
Caudal regression syndrome/syrenomelia
CHARGE association
Diastrophic dysplasia
Ectrodactyly, ectodermal dysplasia, clefting
Holoprosencephaly
Hydrolethalus
Majewski (short rib-polydactyly syndrome, type II)
Median cleft face (frontonasal dysplasia)
Syndromes
Crouzon
Femoral hypoplasia, unusual facies
Fryns
Goldenhar
Gorlin
Klippel-Feil
Larsen
Marfan
Meckel-Gruber
Multiple pterigiums
MURCS association
Nager
Neu-Laxova
Oral-facial-digital (Mohr)
Pena Shokeir
Pierre Robin
Roberts
Shprintzen
Smith-Lemli-Opitz
Treacher Collins
Van der Woude
Alker-Warburg

Conclusion

Facial anomalies are frequent malformations. The sonographic evaluation of the fetal face is difficult and these malformations are frequently missed in standard examinations. In expert hands an accurate diagnosis is possible from early gestation. 3D and 4D ultrasound are useful adjuncts to the standard 2D examination. Specific application of 3D and 4D ultrasound

GE Medical Systems Ultrasound – United Kingdom
Fax: (+44) 1234 266261, Tel: (+44) 1234 340881

GE Medical Systems – America:
Milwaukee, WI, USA - Fax: (+1) 262 544-3384

GE Medical Systems – Asia:
Tokyo, Japan – Fax: (+81) 3-3223-8524
Shanghai, China – Fax:(+86) 21-5208 0582

Visit us online at: www.gehealthcare.com

Healthcare Re-imagined

GE is dedicated to helping you transform healthcare delivery by driving critical breakthroughs in biology and technology. Our expertise in medical imaging and information technologies, medical diagnostics, patient monitoring systems, drug discovery, and biopharmaceutical manufacturing technologies is enabling healthcare professionals around the world discover new ways to predict, diagnose and treat disease earlier. We call this model of care "Early Health." The goal: to help clinicians detect disease earlier, access more information and intervene earlier with more targeted treatments, so they can help their patients live their lives to the fullest. Re-think, Re-discover, Re-invent, Re-imagine.

GE Ultraschall Deutschland GmbH & Co. KG
Beethovenstr. 239, D-42655 Solingen

Fax: (+49) 212-28 02 28
Tel: (+49) 212-28 02-0

www.gehealthcare.com

GE imagination at work

Printed in Austria - 300-06-U024E