

IMAGING

Three- and four-dimensional ultrasonography for the structural and functional evaluation of the fetal face

Asim Kurjak, MD, PhD; Guillermo Azumendi, MD; Wiku Andonotopo, MD, PhD; Aida Salihagic-Kadic, MD, PhD

The development of the face and its related structures (eg, nose and palate) takes place during the embryonic period. By the end of the sixth week, there is visual evidence of development, and by the end of the eighth week, the face has characteristics that allows its identification as human.^{1,2}

Even though the embryologic development of the face has been well characterized by embryologists, clear visualization of the embryonic face is not currently possible by ultrasound (Figure 1).¹⁻³ During the fetal period, examination of the face by ultrasound is facilitated by the presence of surrounding fluid.⁴ Most experts perform a qualitative evaluation of the fetal face by using 2-dimensional ultrasonography (2DUS) and manipulate the probe to visualize the following: (1) a coronal view for visualization of soft tissues, bones and symmetry; (2) a transverse view for visualization of the mandible, maxilla and palate, tooth buds, and orbits; and (3) a sagittal view for evaluation of the forehead, the nasal bridge, and the mandible.

Ultrasonographic examination of the fetal face can provide information that may lead to the diagnosis of anomalies in other organs or systems. Thus, the fetal face represents a "diagnostic window" for fetal diseases and syndromes. Three-dimensional ultrasonography (3DUS) improves the evaluation of anatomic fetal facial anomalies over what is possible by 2-dimensional ultrasonography (2DUS). Four-dimensional ultrasonography (4DUS), by adding the temporal component to the examination, allows visualization of facial expressions that might be useful in the study of fetal behavior and maternal-fetal bonding. In this article, we evaluate the potential of 3D/4DUS for the study of structural and functional development of the fetal face.

Key words: three-dimensional ultrasound, four-dimensional ultrasound, fetal face, fetal behavior

Cite this article as: Kurjack A, Azumendi G, Andonotopo W, et al. Three- and four-dimensional ultrasonography of the fetal face. *Am J Obstet Gynecol* 2007;196:16-28.

Using this approach, a detailed study of the facial anatomy can be carried out.⁴

The incorporation of 3-dimensional ultrasound (3DUS) technology into clinical practice has resulted in remarkable progress in visualization and anatomic examination of the fetal face. Four-dimen-

sional ultrasonography (4DUS), in turn, provided for the first time an opportunity to evaluate subtle fetal facial expressions, which can be used to understand fetal behavior.⁵⁻¹⁰ Because of its curvature and small anatomic details, the fetal face can be visualized and analyzed only to a limited

FIGURE 1

Embryonic and human facial development depicted in utero by 3DUS surface rendering during the first trimester



Department of Obstetrics and Gynecology, Medical School University of Zagreb, Sveti Duh Hospital, Zagreb, Croatia (Drs Kurjak and Andonotopo); Centro Gutenberg Clinic, Malaga, Spain (Dr Azumendi); Department of Health, Ministry of Health, Republic of Indonesia, Jakarta, Indonesia (Dr Andonotopo); Department of Physiology, Medical School University of Zagreb, Zagreb, Croatia (Dr Salihagic-Kadic)

Received May 19, 2006; revised June 11, 2006; accepted June 27, 2006

Reprints: Wiku Andonotopo, MD, PhD, Department of Obstetrics and Gynecology, Sveti Duh Hospital, Sveti Duh 64, Zagreb, HR 10000, Croatia. drwiku@yahoo.com

0002-9378/\$32.00

© 2007 Mosby, Inc. All rights reserved.

doi: 10.1016/j.ajog.2006.06.090

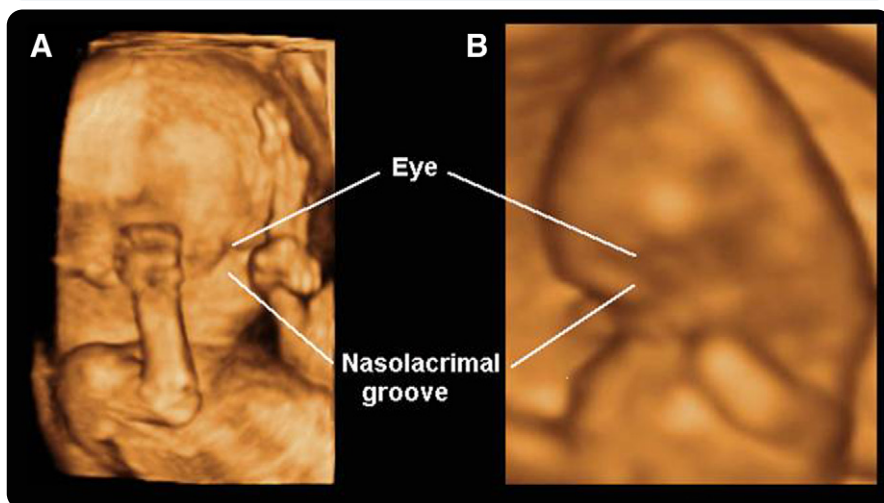
FIGURE 2

Depiction of some fetal facial images obtained by 3DUS surface rendering. The data can be saved and rebuilt off-line anytime with great quality



FIGURE 3

Comparison of the development of the nasolacrimal groove that separated initially the maxillary prominence and the lateral nasal prominence



At: **A**, 13 weeks' fetus and **B**, 7 weeks' embryo

extent with 2DUS.⁴ 3DUS has the capability of demonstrating planes of section that cannot be obtained with 2DUS and, thus, allows for a comprehensive evaluation of facial anatomy.¹¹⁻¹⁵ The standardized image display helps sonologists to understand fetal anatomy better and to communicate complex observations to both parents and less-experienced observers. The entire face cannot be seen on a single 2DUS image. 3DUS allows spatial reconstruction of the fetal face and simultaneous visualization of all facial structures such as the fetal nose, eyebrows, mouth, and eyelids (Figure 2). It is the purpose of this review to illustrate the potential of 3D/4D sonography in the study of the structural and functional development of fetal face.

All 3D and 4D examinations in this study were performed by experienced operators with the use of Voluson 730 Expert (GE Medical System, Zipf, Austria) and Sonoline Antares (Siemens AG, Issaquah, WA) with transvaginal 8-MHz transducer for examination in the first trimester and transabdominal 5-MHz transducer for examination during the second and third trimesters.

NORMAL FACIAL DEVELOPMENT

The human face is unique in that each individual has distinct, individually rec-

ognizable features. Formation of the face is embryologically complex, and continuous growth and remodeling is not complete until postpuberty.¹

At the end of week 4, the stomodeum forms the center of the face and is surrounded by 5 facial prominences. The maxillary prominences are lateral to the stomodeum and the mandibular prominences caudal to the stomodeum. Both develop from neural crest derived mesenchyme from the first pharyngeal arch. The fifth prominence, the frontonasal prominence, develops from proliferating mesenchyme ventral to the brain vesicles and is located above (cranial to) the stomodeum.¹⁻³

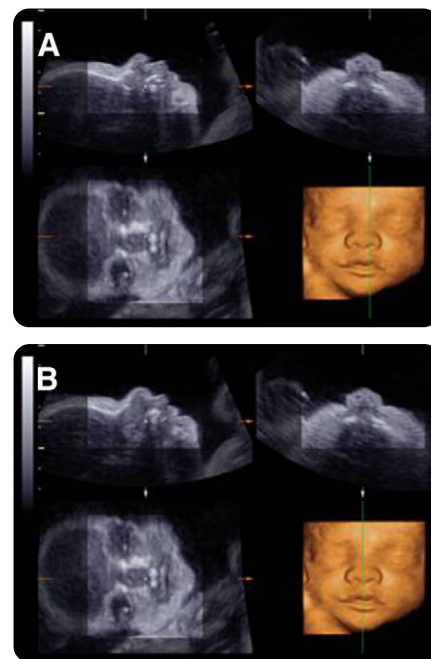
On both sides of frontonasal prominence, 2 thickenings can be observed—the nasal placodes. During week 5, the nasal placodes invaginate to form nasal pits, creating a ridge of tissue surrounding each pit, forming the medial and lateral nasal prominences. During the next 2 weeks, the maxillary prominences enlarge and grow medially, compressing the medial nasal prominence toward the midline. The cleft between the maxillary and medial nasal prominence is lost and the 2 fuse forming the upper lip. The lateral nasal prominence does not take part in the formation of the lip. The lower lip and jaw are formed by the mandibular prominence.¹⁻³

Initially the maxillary and the lateral nasal prominences are separated by a groove, the nasolacrimal groove (Figure 3). The ectoderm in the floor of the groove forms a solid epithelial cord and detaches from the overlying ectoderm. It canalizes to form the nasolacrimal duct. After detachment of the cord, the maxillary and lateral nasal prominences merge with each other. The maxillary prominences then enlarge to form the cheeks and maxillae.¹⁻³

During week 6 the nasal pits deepen considerably because of growth of secondary prominences and penetration of the underlying mesenchyme. At first the oronasal membrane separates the pits from the primitive oral cavity by way of

FIGURES 4

3DUS is used to ensure that the fetal face contour was placed exactly on the midline



A, Whether the profile on plane A may seem correct, the reference green line superimposed on the rendered image demonstrates that such profile does not belong to the midline, but it is slightly off center to the left side of the fetal face. **B**, By using appropriate movement of translation, it becomes easy to move the line to the middle of the face, ensuring that the profile displayed on the plane A was placed exactly in the midsagittal plane.

FIGURES 5

Calculation of the inferior facial angle



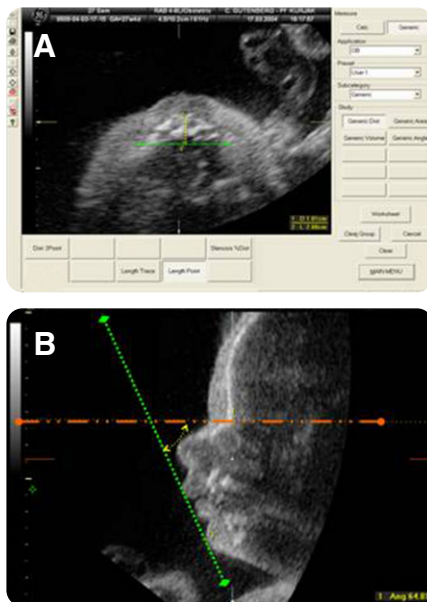
A, Demonstration of off-line analysis that uses computer software to assess multiplanar navigation through the sagittal plane; **B**, Calculation of the inferior facial angle on midsagittal view, by the crossing of: (1) the line orthogonal to the vertical part of the forehead at the level of the synostosis of the nasal bones (reference line in orange); (2) the line joining the tip of the mentum and the anterior border of the more protruding lip (profile line in green). The cut off value for the inferior facial angle is 49.2 degrees (mean -2 SDs). Any value below was defined as retrognathism.

newly formed foramina, the primitive choanae (just behind the primary palate). With the formation of the secondary palate and further development of the primitive nasal chambers, the definitive choanae lie at the junction of the nasal cavity and the pharynx.¹⁻³

From the sixth week onward, embryonic anatomy can be assessed by transvaginal 3D sonography.^{8,10,11} At 6 weeks, the embryo is characterized by a rounded, bulky head (prominent because of the developing cerebral vesicles-prosencephalon, mesencephalon, and rhombencephalon) and a thinner body. At 7 weeks, the head is strongly flexed anteriorly, in contact with the chest, which complicates the assessment of

FIGURE 6

Calculation of the mandible to maxilla width ratio on axial views obtained at the alveolar level



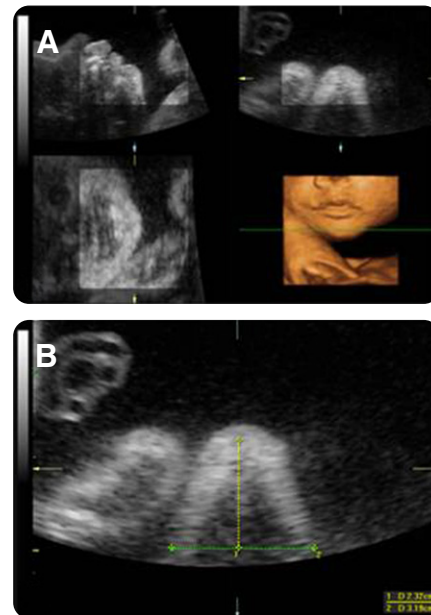
A, Maxilla and **B**, mandible widths were measured 10 mm posteriorly to the anterior osteous border (approximately at the level of the canines). The mean value of the mandible to maxilla width ratio during 18th and 28th gestational week interval was 1.017 (SD \pm 0.116). A mandible to maxilla width ratio $<$ 0.785 defined as micrognathism.

viscerocranial structures (Figure 1). Around 8 weeks, the shape of the face becomes apparent but the flexion of the cranial pole still makes it difficult to view the face entirely. From 9 weeks, the head is clearly divided from the body by the neck (Figure 1). Finally, at 11 to 12 weeks, facial structures, such as nose, orbits, maxilla, and mandible, as well as eyes and mouth, are visible (Figure 1).¹¹

For 3D visualization of the fetal face, the surface mode is generally used. From weeks 13 to 14, facial structures have reached an adequate degree of development to start studying them for diagnostic purposes.⁴ However, images of the fetal face during the first trimester, may appear strange to parents and caution is advised while showing those images, so that a distorted mental image of their child is not created, which may affect affective bonds

FIGURE 7

Demonstration of the assessment of the jaw index

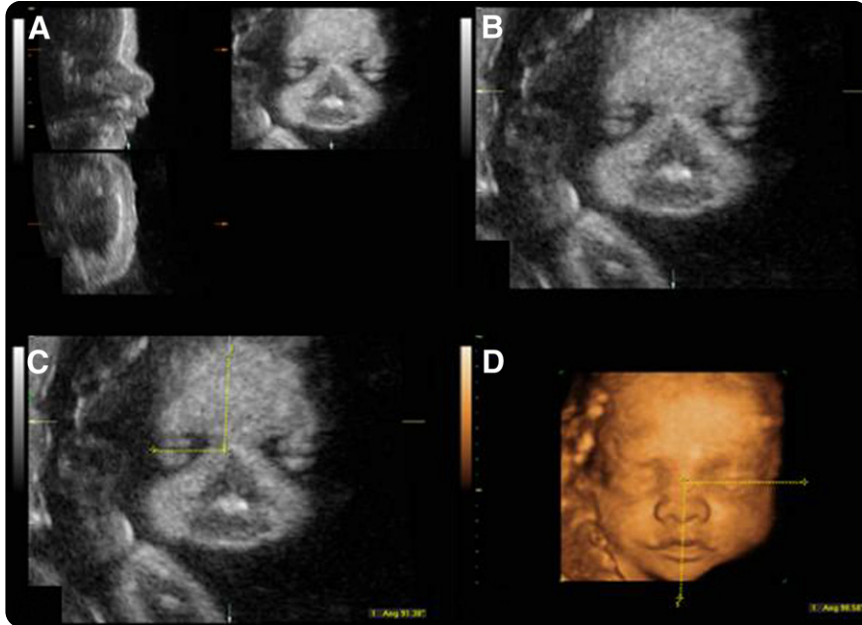


The mandible is measured on an axial plane at the base of the cranium caudal to the lower dental arch, where the whole horseshoe mandible is visualized. Anteroposterior and laterolateral diameters are measured as follows: the laterolateral diameter is traced joining the bases of the 2 rami; the anteroposterior diameter from the symphysis mentis to the middle of the laterolateral diameter. Care must be taken to achieve the correct plane and to avoid inadvertent partial inclusion of the rami within the calipers. The jaw index is then calculated as follows: anteroposterior mandibular diameter/BPD \times 100. BPD, biparietal diameter.

or create inadvertent anxiety. From 18 to 19 weeks until 35 to 36 weeks, 3D reconstruction of the fetal face is possible in a high percentage of cases. In our opinion, the most favorable gestational ages for 3D scanning of the fetal face range from weeks 23 until 30. During this period of gestation (Figure 2), we have successfully visualized the face in a high percentage of the cases, without extending the length of the prenatal 2DUS scan.⁴

ASSESSMENT OF FACIAL ANOMALIES

3DUS improves and facilitates the identification of anomalies in planes that

FIGURE 8**Evaluation of the palpebral fissure shape**

A and B, Achievement of the coronal plane of the fetal face at the level of palpebral fissures by translations movements. Measurement of the sloping angle of the palpebral fissure shape related to the middle line of the face, **C**, in the coronal plane or even easier, **D**, in the surface rendering mode.

cannot be obtained by conventional 2DUS. Several authors have reported improvement in the visualization of the fetal face and neck in high-risk pregnancies, dysmorphic syndromes due to exposure of teratogens (ie, phenytoin), fetal alcohol syndrome, and chromosomal abnormalities.¹²⁻¹⁴ Cleft lip, microgna-

thia, malformed ears, and frontal bossing have all been reported to be better displayed and analyzed by 3DUS.¹⁵⁻²²

Multiplanar navigation provides a valuable modality for reevaluation of the 3D volume in the three orthogonal planes and to visualize facial structures from multiple perspectives. This can be

useful in cases of suboptimal fetal position, which may prevent the sonologist from obtaining suitable planes of section and evaluate subtle abnormalities by 2DUS. Multiplanar imaging and the ability to navigate through the volume dataset has improved the study of certain morphologic abnormalities.^{18,23-25}

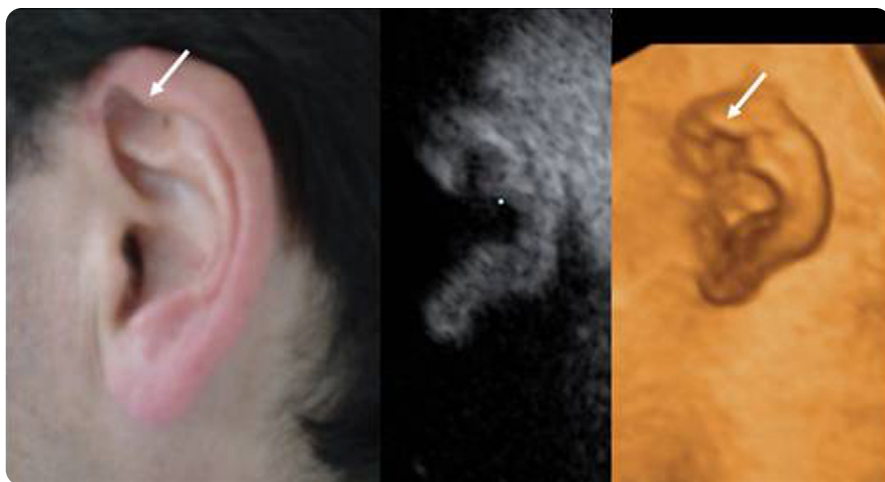
One of the most important advantages of 3DUS is its ability to display a true midsagittal plane of the fetal face (Figures 4, A and 3, B).²⁶ Merz et al¹² analyzed the effect of 3D facial profile reconstruction on 125 fetuses. In their study, 30.4% of the facial profiles were rotated 3 degrees to 20 degrees from the original position. Therefore, only in 69.6% of the cases was the true profile obtained by 2DUS. The relevance of this finding has to be considered because if a true middle plane is not identified, anomalies may be either missed or overdiagnosed. For example, the assessment of the maxilla and mandible for the diagnosis of micrognathia and retrognathia requires a true sagittal plane.²⁶ Evaluation of the mandible is very important because of several anomalies that commonly encounter fetal facial defects as part of more than 100 genetic syndromes such as Pierre Robin sequence or Treacher Collins syndrome, and various chromosomal anomalies such as trisomies 18 and 13, triploidy, and those involving gene deletions or translocations.²⁷⁻²⁹ Fetuses with mandibular anomalies are at risk of acute neonatal respiratory distress syndrome because the tongue may obstruct the upper airway. There is no strict parallelism between the severity of the anatomic defect and the impairment of respiratory function at birth. It is very important to recognize even mild cases of mandible anomalies antenatally to allow the neonatologist to be present in the delivery room to provide immediate care for the infant and prepare everything for the ex utero intrapartum treatment.

Mandibular anomalies are usually diagnosed subjectively as a prominent upper lip and small chin or a subjective impression of a small jaw or posterior displacement of the mandible. Although there have been some attempts to define biometric parameters that would allow objective distinctions between normal

FIGURE 9**Clear visualization of ear morphology by 3D surface rendering mode**

The appropriate position of the ear is easy to check having all the reference points on the same image.

FIGURE 10

Assessment of a subtle auricular dysmorphism by 3DUS

The image on the left depicts the father's ear of this fetus. His previous children also presented with this auricular morphology. The 2D visualization on the central image offered enough quality to evaluate the auricular morphology broadly, but such dysmorphism could not be appreciated, something that became evident by the 3D surface rendering mode (right image).

FIGURES 11

Visualization of severe facial malformations

Visualization of severe facial malformations in a realistic way by 3DUS (upper images) and subtle dysmorphologies (lower images) such as small skin tags or persistent tongue protrusion that lead us to the diagnosis of macroglossia.

and abnormal mandibles,³⁰ it is still difficult to differentiate between retrognathia (abnormal recession of the chin) and micrognathia (insufficient size of the mandible). Trying to use objective measurements that allow distinguishing between these 2 entities, Rotten et al²⁷ defined 2 indices, the inferior facial angle for assessment of the posterior displacement (retrognathia) and the mandible to maxilla width ratio for assessment of the restriction in size (micrognathia) (Figures 5 and 6).⁷ In another study, Paladini et al³¹ described the measurement of the anteroposterior and laterolateral diameters of the mandible for the calculation of the jaw index in diagnosing micrognathia (Figure 7).

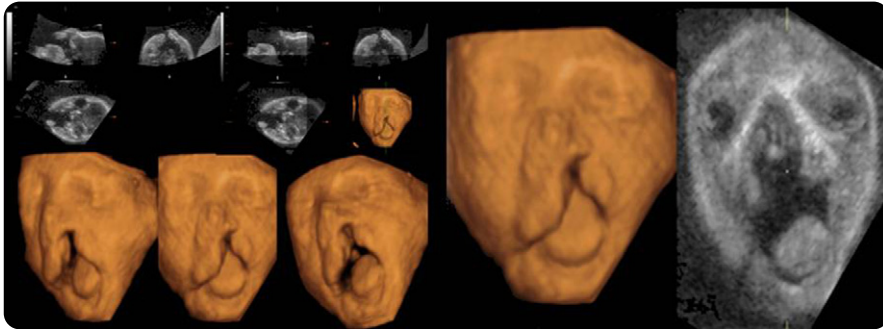
Another possibility offered by the multiplanar navigation in the study of fetal face is scroll movement or translation in the coronal plane for angle evaluation of the palpebral fissure shape. This assessment is very difficult to obtain with 2DUS, whereas the 3D multiplanar navigation it is easily performed (Figure 8 A through D).

Some authors have shown that 3DUS is helpful in depicting the morphological detail, location, and orientation of the fetal ear.²² Accurate depiction of the fetal ear is important, because ear anomalies may be associated with complex congenital syndromes. All the reference points needed for ear evaluation can be obtained by using 3D surface rendering, which is impossible to achieve with 2DUS because of the curvature of the face (Figure 9). Although rarely decisive, 3DUS is of interest when attempting to precisely describe craniofacial dysmorphisms and the study of fetal ears.³² According to Merz et al,³³ 3DUS might depict facial dysmorphology with greater accuracy and clarity, particularly in case of subtle abnormalities (Figures 10 and 11).

ASSESSMENT OF OTHER FACIAL FEATURES AND FETAL ANOMALIES SUCH AS CLEFT LIP AND PALATE

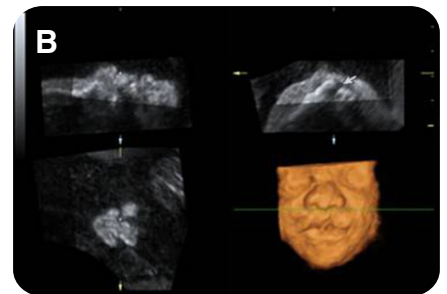
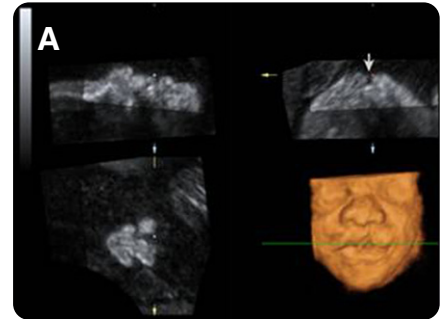
Several authors have found that 3DUS is useful for identifying the location and level of facial anomalies. The value of

FIGURE 12
Multiplanar imaging in severe unilateral cleft lip and palate



Multiplanar images assist in establishing the location and extent of the anomaly. The surface-rendering modes, apart from being a reference for the multiplanar navigation, also allow obtaining realistic images, helping the parents as well as the practitioners to make decisions.

FIGURE 13
Detection of the small cleft lip by multiplanar imaging



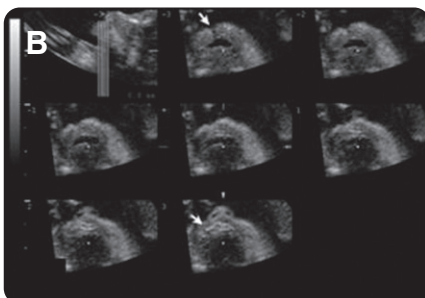
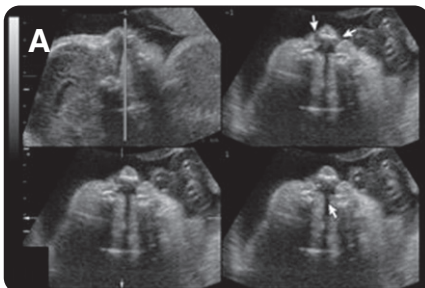
A, The green line was scrolled through the surface location of the upper lip in the axial plane. Note the small unilateral cleft lip is appreciated (*arrow*); **B**, In this case, the green line was moved up to the maxilla in the axial plane. Note the existence of a small cleft in the alveolar ridge (*arrow*).

3DUS compared with 2DUS for the detection of cleft lip and palate has been studied extensively.³⁴⁻⁴⁰ Experts have shown that 3D multiplanar imaging and magnetic resonance imaging (MRI) could be used to evaluate the extent of clefting into the anterior alveolar ridge

or even a cleft of the soft palate.⁴¹ Rendered images provide landmarks for the planar images and assist the family and the consulting surgeon in explaining the abnormality (Figures 12 and 13).

Johnson et al⁴⁰ found that 3DUS has an impact on diagnosis and clinical management in detecting the associated cleft palate as can be demonstrated in the new modality Multi-Slice View (Medison, Seoul, Korea) or Tomographic Ultrasound Imaging technique (GE Medical System, Zipf, Austria).⁴² By using both techniques, facial structures can be dis-

FIGURE 14
Bilateral cleft lip and cleft palate detection by TUI



A, Tomographic ultrasound imaging (TUI) display of a bilateral cleft lip and cleft palate (*arrows*); **B**, The defect and the integrity of the palate can be visualized on the same screen by TUI.

FIGURE 15
3D reverse face view can be obtained easily by rotating the rendered image through 180 degrees in the vertical axis

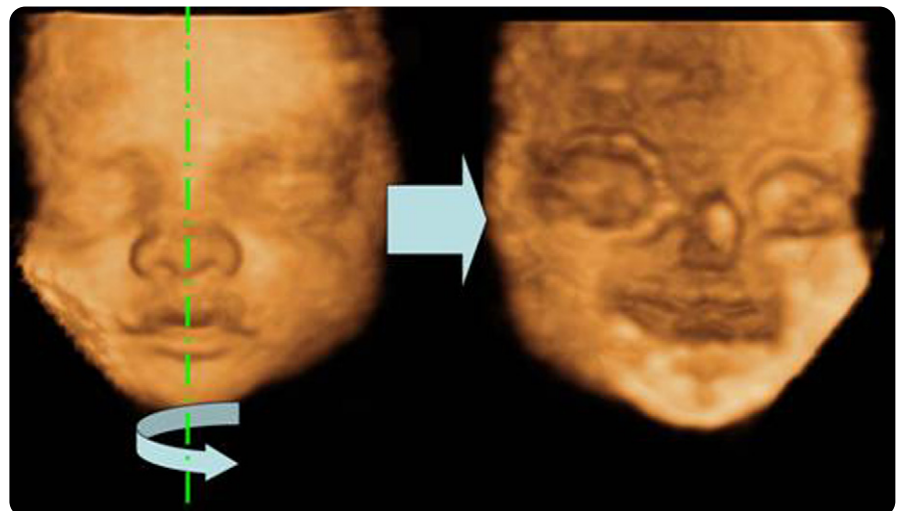
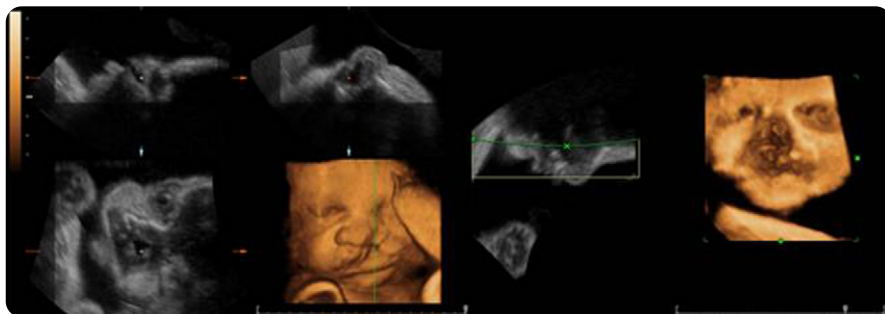


FIGURE 16
3D reverse face view for the visualization of the cleft palate



played easier for analysis and documenting of the defect (Figure 14).

Another possibility is “3D reverse face view” which rotated the surface rendered through 180 degrees on the vertical axis (Figure 15). Campbell et al published interesting results using this approach in the antenatal categorization of facial clefting and in particular clefting of the hard palate. However, in our opinion, the frequent interposition of structures like the tongue for instance, facilitates the appearance of many artifacts diminishing the reproducibility of this technique (Figures 16 and 17).

FIGURE 17
Possibility of simultaneous 3D imaging of several features



Simultaneous visualization of several facial and head features. In this image, at the same moment, the location and morphology of the ear, cranial suture, and both hands can be observed distinctly.

IMPROVED VISUALIZATION OF BONY STRUCTURES

Fetal head bones can be visualized with the transparent maximum rendering. The threshold level can also be modified to enable visualization of facial surface as well as bones (Figure 18).

Abnormal development of the sutures has been associated with dysmorphic syndromes and metabolic disturbances. 3DUS offers clearer visualization of cranial structures, bone plates and enhanced illustration of the subsequent de-

velopment of the metopic suture during prenatal life, offering improvement for assessment of cranial anatomy.⁴³ With 3DUS, visualization of the “overlapping” sutures in fetal death and in craniosynostosis or abnormal cranial contours such as cloverleaf skull can be clearly seen.⁴³ This possibility is also very helpful in the evaluation of nasal bones as described by several authors.⁴⁴⁻⁴⁷

FUNCTIONAL STUDY OF FETAL FACIAL EXPRESSION

4DUS has additional advantages in studying fetal activity in the surface rendered mode and is particularly superior for fast fetal movements.⁴⁸ With 2DUS, fetal movements such as yawning, swallowing and eyelid movements cannot be displayed simultaneously, whereas with 4DUS, the simultaneous facial movements can be clearly depicted.⁴⁹

The qualitative and quantitative aspects of behavioral patterns expand rapidly as the pregnancy progresses, and the random movements of the fetal body, which are the earliest signs of fe-

FIGURE 18
Threshold level modification for visualization of bony structures



(A) Numerous possibilities can be offered by 3DUS technology as seen in these images; (B) By modifying the threshold level, we can shift from the facial surface onto the underlying skeleton.

FIGURE 19

Precise evaluation of fetal behavioral expressions

3D/4DUS provides clear depiction of dynamic changes of fetal facial expression allowing study of fetal behavior from early pregnancy onward.

tal activity, change into the well-organized behavioral patterns, observed later in gestation. Analysis of the dynamics of fetal behavior has led to the conclusion that fetal behavioral patterns directly reflect developmental and maturational processes of the fetal central nervous system (CNS). With 4D sonography, it is now possible to produce measurable parameters for the assessment of normal neurobehavioral development.

There are several types of jaw movement patterns, such as isolated jaw movement, sucking, and swallowing, which can be observed by 2DUS.⁴⁹ The possibility of observing facial expressions in detail may be of both scientific

and diagnostic value, opening up an entire new field of investigation with many unanswered questions.^{50,51} Two examples of questions that remain to be answered are as follows: (1) when do facial expressions start; and (2) which facial expression predominates in fetal life and at what gestational age can it be first observed? An important diagnostic aim of the observation of facial expression is prenatal diagnosis of facial paresis. The criterion for the diagnosis is asymmetric facial movement and detection of the movements limited to only 1 side of the face. Unfortunately, during the relaxed phase it is not possible to evaluate the status of the facial nerve. Therefore, during the active

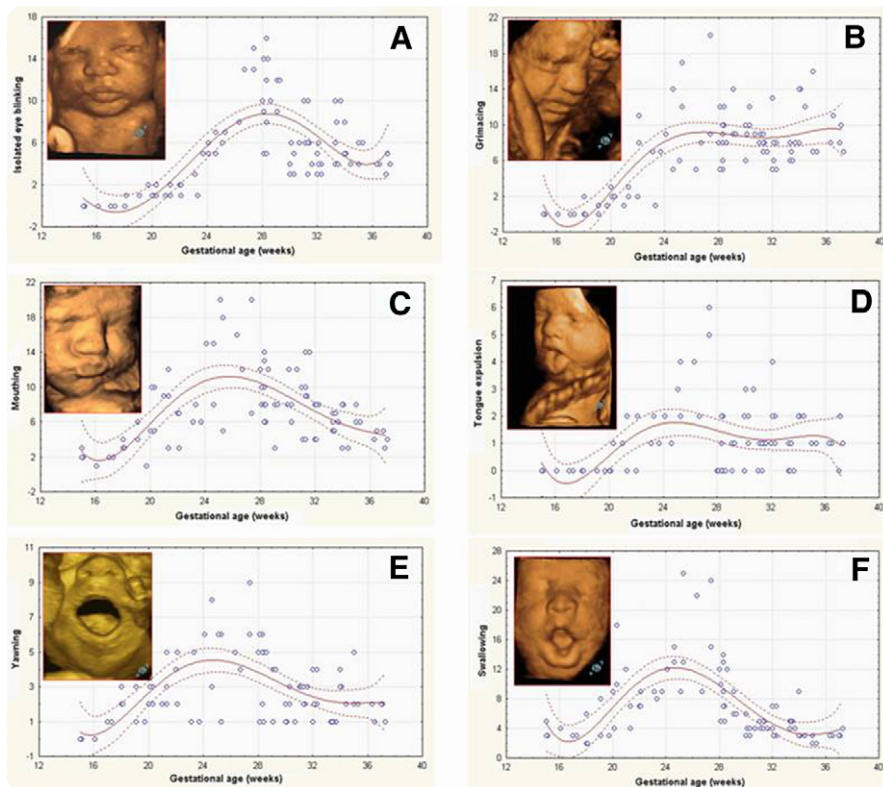
phase, the fetus should be scanned by 4DUS.

Because the origin of facial expression can be influenced by external forces, before the final diagnosis, examiners should be aware of this pitfall. For example, force of the fetal hand can alter the facial expression on 1 side of the face, causing asymmetry. This kind of asymmetry, however, should be differentiated from pathologic features such as unilateral facial paresis.⁴

2DUS and 4DUS are complementary methods used for the evaluation of fetal movements. However, the quality of each fetal movement can be visualized and evaluated more precisely by 4DUS (Figure 19).⁸⁻¹⁰ Fetal behavioral

FIGURE 20

Frequency of observed facial expression versus gestational age



Normal parameters of several facial expressions studied by 4DUS during the second through the third trimester of pregnancy.

patterns in the third trimester between 30th to 33rd weeks of gestation and the continuity between fetal and neonatal behavior have been recently evaluated.^{6,52}

In the second and third trimesters, all facial movements can be visualized by 4DUS. Furthermore, 4DUS opened, for the first time, the possibility of visualizing the full range of facial expressions, including subtle grimaces similar to emotional expressions in adults.⁹ The most frequent facial movement patterns in the second trimester were isolated eye blinking, grimacing, suckling, and swallowing, whereas mouthing, yawning, tongue expulsion (Figure 20), and smiling could be seen less frequently.¹⁰ We noted a tendency toward decreased frequency of observed facial expressions with increasing gestational age. At the beginning of the second trimester, the fetuses began to display a tendency toward increased frequency of observed fetal fa-

cial expression to the end of second trimester. An oscillation and dispersion of the incidence of all facial expressions, as seen in the polynomial regression diagram are shown in Figure 20. All types of facial expression patterns display the peak frequency at the end of second trimester, except in isolated eye blinking which began to increase at the beginning of 24 weeks of gestation because the fetuses cannot open the eyelids before this period. During the third trimester, the fetuses began to display decreasing incidence or paucity of fetal facial expression.¹⁰

The systematic investigations of fetal facial expressions confirmed that all components of the fetal yawning pattern, prolonged jaw opening, followed by a quick closure and accompanied by head flexion and elevation of arms, can easily be recognized by 4DUS in this period (Figure 21 B).⁵³ Furthermore, when the fetal yawning in the third trimester

was compared with the yawning in the neonates during the first week of life, no differences were found in the frequencies of this reflex. The frequency of yawning gradually increased between 15th and 24th week when a short plateau was observed from 24th to 26th week and was followed by a slight decrease toward the term (Figure 20, E).¹⁰ A clear gestational age-related trend in the frequency of yawning could be interpreted as the maturation of the brain stem and possibly the acquisition of control of more cranial structures over yawning pattern. These findings have provided new information about the course of neurodevelopment of this interesting, but poorly understood reflex. Whether this is altered in cases of neurodevelopmental disturbances and whether such alterations can give us insight into the function of fetal nervous system in high-risk pregnancies, remains to be determined.

Fetal yawning is still quite a mysterious phenomenon, and its possible relation to the pathologic conditions, particularly those affecting fetal CNS has not been investigated so far, despite the clearly altered incidence of yawning in a wide specter of CNS disorders, observed in adults. The early reports of yawning movements in the 20-week-old fetus indicated that 4DUS might facilitate the investigation of this infrequent movement pattern.⁵³

This impressive finding, however, raises a number of questions, many of which are yet to be answered. First, precise criteria to distinguish between these facial expressions in the fetus should be established. The exact onset of facial expressions has not been determined and it is still unclear whether their appearance is gestational age related. The maturation of midbrain also begins in the second trimester. It consists of the dopamine-producing substantia nigra, the inferior-auditory and superior-visual colliculus, and cranial nerves III and IV, which, together with the medial longitudinal fasciculus and the VI cranial nerve, control eye movements.⁵² This explains the delayed onset of eye movements, which cannot be registered before 16th postconceptional week. The maturation of the me-

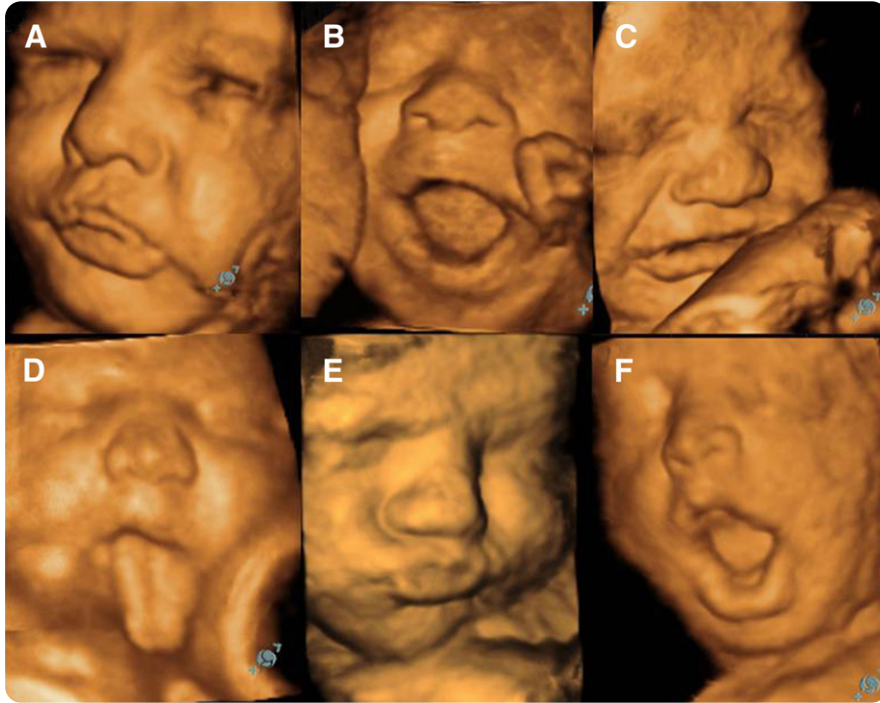
FIGURE 21**All components of facial expression can easily be recognized**

Illustration of several facial expressions which can be studied quantitatively by 4DUS. (A) Isolated eye blinking; (B) yawning; (C) grimacing; (D) tongue expulsion; (E) mouthing; and (F) swallowing

dulla oblongata is also revealed by the appearance of the breathing movements as well as the swallowing movements, hiccups, yawning and jaw opening, visible between 9th and 11th week.⁵⁴ Facial movements, which are also controlled by V and VII cranial nerves, appear around 10 and 11 weeks, whereas delayed onset of more specific functions, such as the selective response to sounds and vibration, can be explained by the prolonged pontine maturation. The nuclei of the facial nerve, a structure that controls these motor patterns, are developed by the end of first trimester, indicating that some facial grimaces could appear rather early in gestation.⁵⁴ The possibility of studying such subtle movements certainly opens a completely new area of investigation. One potential value of such observations could be the detection of facial nerve paresis in utero. It remains to be determined to what extent are the facial motoric patterns related to the function and integrity of the CNS.

Nevertheless, the fact that even in the embryonic period, the same inductive forces that cause growth and reshaping of the neural tube influence the development of facial structures, and that many genetic disorders affecting the CNS are also characterized by dysmorphism and dysfunction of facial structures, emphasize the importance of these investigations. Obviously, the story of fetal intrauterine activity is far from being complete; the development of new recording techniques should enrich the perspective of intrauterine life.

IMPROVED MATERNAL-FETAL BONDING

Several authors have studied the effects of 3D/4DUS on maternal or paternal antenatal attachment.^{55,56} Steiner et al⁵⁵ reported that many parents thought that 2DUS images were abstract, whereas on the 3D images, they recognize the fetal

facial features as being normal or not, and they can feel more attached to them.

Maier et al⁵⁶ evaluated the influences of 3DUS on women with high-risk pregnancies. They offered 3DUS to 20 high-risk women at 24 to 32 weeks of pregnancy. After receiving 3DUS rendered images of their fetuses, 15 of 20 women thought that 3DUS had a positive influence on their perception of the fetus. The mothers reported more motivation to endure pregnancy-related difficulties, reduced anxiety, and improved capacity to cope.

Rustico et al⁵⁷ published a study in which the addition of 4DUS does not change significantly the perception that women have of their infant nor their antenatal emotional attachment compared with conventional 2DUS. In that study, the quality of the 3D acquired images is not considered and lacks a valid initial approach because a patient can be as satisfied with an isolated 2D examination as that of a woman undergoing a 4D additional exploration. Rustico et al⁵⁷ admitted that facial expressions and hand-to-mouth movements were twice as likely to be seen with 4DUS, although this difference was not significant.

We currently started to research this aspect in our department. After the 3DUS examination, a survey was given to the patient and the relatives attending the exploration. Several questions were made to find out the emotional aspects and the level of satisfaction. Most of the patients find positive aspects with the 4D rather than the 2D exploration, such as a stronger feeling of emotion with the 4D image than with the 2D image, providing easier interpretation of the images and tightening of the affective bonds with their future child (Figure 22). Currently, this study is being extended with several additional parameters in which we will try to compare the level of satisfaction with the quality of the images perceived by the patient in comparison with the 1 referred by the practitioner or the auxiliary staff in our clinic. We also intend to correlate these data with the level of experience the doctor has in 3DUS and the time spent in the acquisition of good images.

FIGURE 22

One of the positive aspects with 4D imaging during prenatal ultrasound examination



A clear 3DUS-like "kissing twins" imaging can provide a positive effect in maternal-fetal bonding between the parents and their future children.

We believe that the positive aspect represented by the 3D/4DUS in the maternal-fetal bonding must not be underestimated because it becomes one of the occasions when we feel closer to our patients from a human point of view.

CONCLUSION

3DUS expands our diagnostic abilities in obstetric imaging and provides additional information about the face in complementary ways to conventional 2DUS. It is not only a useful tool in appreciating the severity of a fetal defect, but also provides more convincing evidence of a normal fetus than does conventional 2DUS in recurrent surface malformation cases. This technique does not replace conventional real-time 2DUS imaging, but rather supplements it. 3DUS requires an investment of additional time in each case; therefore, it is predominately used, presently in conjunction with 2DUS, as a problem-solving tool. As this relatively new technology becomes easier to use and more widely available, recognition of its advantages and clinical use will likely expand.³³ ■

REFERENCES

- Evans DJ, Francis-West PH. Craniofacial development: making faces. *J Anat* 2005;207:435-6.
- Nuckolls GH, Shum L, Slavkin HC. Progress toward understanding craniofacial malformations. *Cleft Palate Craniofac J* 1999;36:12-26.
- Rice DP. Craniofacial anomalies: from development to molecular pathogenesis. *Curr Mol Med* 2005;5:699-722.
- Azumendi G, Kurjak A. Three-dimensional and four-dimensional sonography in the study of the fetal face. *Ultrasound Rev Obstet Gynecol* 2003;3:160-9.
- Kurjak A, Azumendi G, Vecek N, Kupesic S, Solak M, Varga D, et al. Fetal hand movements and facial expression in normal pregnancy studied by four-dimensional sonography. *J Perinat Med* 2003;31:496-508.
- Kurjak A, Stanojevic M, Andonotopo W, Salihagic-Kadic A, Carrera JM, Azumendi G. Behavioural pattern continuity from prenatal to postnatal life—a study by four-dimensional (4D) ultrasonography. *J Perinat Med* 2004;32:346-53.
- Andonotopo W, Kurjak A, Kosuta MI. Behaviour of an anencephalic fetus studied by 4D sonography. *J Matern Fetal Neonatal Med* 2005;17:165-8.
- Andonotopo W, Medic M, Salihagic-Kadic A, Milenkovic D, Maiz M, Scazzocchio E. The assessment of fetal behaviour in early pregnancy: comparison between 2D and 4D sonographic scanning. *J Perinat Med* 2005;33:406-14.
- Kurjak A, Stanojevic M, Andonotopo W, Scazzocchio-Duenas E, Azumendi G, Carrera JM. Fetal behaviour assessed in all three trimesters of normal pregnancy by four-dimensional ultrasonography. *Croat Med J* 2005;46:772-80.
- Kurjak A, Andonotopo W, Hafner T, Salihagic-Kadic A, Stanojevic M, Azumendi G, et al. Normal standards for fetal neurobehavioural developments—longitudinal quantification by four-dimensional sonography. *J Perinat Med* 2006;34:56-65.
- Kurjak A, Pooch RK, Merce LT, Carrera JM, Salihagic-Kadic A, Andonotopo W. Structural and functional early human development assessed by three-dimensional and four-dimensional sonography. *Fertil Steril* 2005;84:1285-99.
- Merz E, Weber G, Bahlmann F, Miric-Tesanic D. Application of transvaginal and abdominal three-dimensional ultrasound for the detection or exclusion of malformations of the fetal face. *Ultrasound Obstet Gynecol* 1997;9:237-43.
- Stoll C, Clementi M. Prenatal diagnosis of dysmorphic syndromes by routine fetal ultrasound examination across Europe. *Ultrasound Obstet Gynecol* 2003;21:543-51.
- Matthews L, Marais AS, Kay HH, Viljoen DL. Possible ultrasound markers for fetal alcohol syndrome: assessment of the fetal face and brain. *Ultrasound Obstet Gynecol* 2004;24:264.
- Hull AD, Pretorius DH. Fetal face: what we can see using two-dimensional and three-dimensional ultrasound imaging. *Semin Roentgenol* 1998;33:369-74.
- Pretorius DH, Nelson TR. Fetal face visualization using three-dimensional ultrasonography. *J Ultrasound Med* 1995;14:349-56.
- Lee A, Deutinger J, Bernaschek G. Three dimensional ultrasound: abnormalities of the fetal face in surface and volume rendering mode. *BJOG* 1995;102:302-6.
- Gonçalves LF, Lee W, Espinoza J, Romero R. Three- and four-dimensional ultrasound in obstetric practice: does It Help? *J Ultrasound Med* 2005; 24:1599-624.
- Johnson DD, Pretorius DH, Budorick NE, Jones MC, Lou KV, James GM, et al. Fetal lip and primary palate: three-dimensional versus two-dimensional US. *Radiology* 2000;217:236-9.
- Pretorius DH, House M, Nelson TR, Hollenbach KA. Evaluation of normal and abnormal lips in fetuses: comparison between three- and two-dimensional sonography. *AJR Am J Roentgenol* 1995;165:1233-7.
- Pretorius DH, Nelson TR. Prenatal visualization of cranial sutures and fontanelles with three-dimensional ultrasonography. *Ultrasound Obstet Gynecol* 1995;5:219-21.
- Shih JC, Shyu MK, Lee CN, Wu CH, Lin GJ, Hsieh FJ. Antenatal depiction of the fetal ear with three-dimensional ultrasonography. *Obstet Gynecol* 1998;91:500-5.
- Chen ML, Chang CH, Yu CH, Cheng YC, Chang FM. Prenatal diagnosis of cleft palate by three-dimensional ultrasound. *Ultrasound Med Biol* 2001;27:1017-23.
- Chmait R, Pretorius D, Jones M, Hull A, James G, Nelson T, et al. Prenatal evaluation of facial clefts with two-dimensional and adjunctive three-dimensional ultrasonography: a prospective trial. *Am J Obstet Gynecol* 2002;187:946-9.
- Ulm MR, Kratochwil A, Ulm B, Lee A, Bettelheim D, Bernaschek G. Three-dimensional ultrasonographic imaging of fetal tooth buds for characterization of facial clefts. *Early Hum Dev* 1999;55:67-75.
- Lee W, McNie B, Chaiworapongsa T, Conoscenti G, Kalache KD, Vettraino IM, et al. Three-dimensional ultrasonographic presentation of micrognathia. *J Ultrasound Med* 2002;21:775-8.
- Rotten D, Levailant JM, Martinez H, Ducou le Pointe H, Vicaud E. The fetal mandible: a 2D and 3D sonographic approach to the diagnosis of retrognathia and micrognathia. *Ultrasound Obstet Gynecol* 2002;19:122-30.
- Nicolaiades KH, Salvesen DR, Snijders RJM, Gosden CM. Fetal facial defects: associated

malformations and chromosomal abnormalities. *Fetal Diagn Ther* 1993;8:1-9.

29. Turner GM, Twining P. The facial profile in the diagnosis of fetal abnormalities. *Clin Radiol* 1993;47:389-95.

30. Otto C, Platt LD. The fetal mandible measurement: and objective determination of fetal jaw size. *Ultrasound Obstet Gynecol* 1991;1:12-7.

31. 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;93:382-6.

32. Mangione R, Lacombe D, Carles D, Guyon F, Saura R, Horovitz J. Craniofacial dysmorphism and three-dimensional ultrasound: a prospective study on practicability for prenatal diagnosis. *Prenat Diagn* 2003;23:810-8.

33. Merz E, Welter C. 2D and 3D Ultrasound in the evaluation of normal and abnormal fetal anatomy in the second and third trimesters in a level III center. *Ultraschall Med* 2005;26:9-16.

34. Pretorius DH, Johnson DD, Budorick NE, Jones MC, Lou KV, Nelson TR. Three-dimensional ultrasound of the fetal lip and palate. *Radiology* 1997;205(P)(suppl):245.

35. Rotten D, Levallant JM. Two- and three-dimensional sonographic assessment of the fetal face: 2— analysis of cleft lip, alveolus and palate. *Ultrasound Obstet Gynecol* 2004;24:402-11.

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

37. 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;25:12-8.

38. Johnson DD, Pretorius DH, Budorick NE, Jones MC, Lou KV, James GM, et al. Fetal lip and primary palate: three-dimensional versus two-dimensional US. *Radiology* 2000;217:236-9.

39. Benacerraf BR, Sadow PM, Barnewolt CE, Estroff JA, Benson C. Cleft of the secondary palate without cleft lip diagnosed with three-dimensional ultrasound and magnetic reso-

nance imaging in a fetus with Fryns' syndrome. *Ultrasound Obstet Gynecol* 2006;27:566-70.

40. Leung KY, Ngai CS, Chan BC, Leung WC, Lee CP, Tang MH. Three-dimensional extended imaging: a new display modality for three-dimensional ultrasound examination. *Ultrasound Obstet Gynecol* 2005;26:244-51.

41. 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;26:618-21.

42. Benoit B, Chaoui R. Three-dimensional ultrasound with maximal mode rendering: a novel technique for the diagnosis of bilateral or unilateral absence or hypoplasia of nasal bones in second-trimester screening for Down syndrome. *Ultrasound Obstet Gynecol* 2005;25:19-24.

43. Gonçalves LF, Espinoza J, Lee W, Schoen ML, Devers P, Mazor M, et al. Phenotypic characteristics of absent and hypoplastic nasal bones in fetuses with Down syndrome: description by 3-dimensional ultrasonography and clinical significance. *J Ultrasound Med* 2004;23:1619-27.

44. Peralta CF, Falcon O, Wegrzyn P, Faro C, Nicolaides KH. Assessment of the gap between the fetal nasal bones at 11 to 13 + 6 weeks of gestation by three-dimensional ultrasound. *Ultrasound Obstet Gynecol* 2005;25:464-7.

45. Rembouskos G, Cicero S, Longo D, Vandecruys H, Nicolaides K. Assessment of the fetal nasal bone at 11-14 weeks' gestation by three-dimensional ultrasound. *Ultrasound Obstet Gynecol* 2004;23:232-6.

46. Lee A. Four-dimensional ultrasound in prenatal diagnosis; leading edge in imaging technology. *Ultrasound Rev Obstet Gynecol* 2001;1:194-8.

47. Kozuma S, Baba K, Okai T, Taketani .Y. Dynamic observation of the fetal face by three-dimensional ultrasound. *Ultrasound Obstet Gynecol* 1999;13:283-4.

48. Hata T, Kanenishi K, Akiyama M, Tanaka H, Kimura K. Real-time 3-D sonographic observation of fetal facial expression. *J Obstet Gynaecol Res* 2005;31:337-40.

49. Kuno A, Akiyama M, Yamashiro C, Tanaka H, Yamagihara T, Hata T. Three-dimensional sonographic assessment of fetal behaviour in the early second trimester of pregnancy. *J Ultrasound Med* 2001;20:1271-5.

50. Kurjak A, Stanojevic M, Azumendi G, Carrera JM. The potential of four-dimensional (4D) ultrasonography in the assessment of fetal awareness. *J Perinat Med* 2005;33:46-53.

51. Walusinski O, Kurjak A, Andonotopo W, Azumendi G. Fetal yawning assessed by 3D and 4D sonography. *Ultrasound Rev Obstet Gynecol* 2005;5:210-7.

52. Salihagic-Kadic A, Kurjak A, Medic M, Andonotopo W, Azumendi G. New data about embryonic and fetal neurodevelopment and behaviour obtained by 3D and 4D sonography. *J Perinat Med* 2005;33:478-90.

53. Ji EK, Pretorius DH, Newton R, Uyan K, Hull AD, Hollenbach K, et al. Effects of ultrasound on maternal-fetal bonding: a comparison of two- and three-dimensional imaging. *Ultrasound Obstet Gynecol* 2005;25:473-7.

54. Righetti PI, Dell'Avanzo M, Grigio M, Nicolini U. Maternal/paternal antenatal attachment and fourth- dimensional ultrasound technique: a preliminary report. *Br J Psychol* 2005;96:129-37.

55. Steiner H, Staudach A, Spitzer D, Schaffer H. Three-dimensional ultrasound in obstetrics and gynaecology: technique, possibilities and limitations. *Hum Reprod* 1994;9:1773-8.

56. Maier B, Steiner H, Wienerroither H, Staudach A. The psychological impact of three-dimensional fetal imaging on the fetomaternal relationship. In: Baba K, Jurkovic D, editors: *Three-dimensional ultrasound in obstetrics and gynecology*. New York: Parthenon; 1997: p. 67-74.

57. Rustico MA, Mastromatteo C, Grigio M, Maggioni C, Gregori D, Nicolini U. Two-dimensional vs. two- plus four-dimensional ultrasound in pregnancy and the effect on maternal emotional status: a randomized study. *Ultrasound Obstet Gynecol* 2005;25:468-72.