

# Second Trimester Anomaly Scan using 3D/4D Ultrasound

<sup>1</sup>Fernando Bonilla-Musoles, <sup>2</sup>Francisco Bonilla Jr, <sup>3</sup>Francisco Raga, <sup>4</sup>Oscar Caballero

<sup>5</sup>Clodoaldo Cadete, <sup>6</sup>Luiz Eduardo Machado

## ABSTRACT

The use of three-dimensional/four-dimensional (3D/4D) ultrasound has become 'universal' in the increasingly precise diagnosis of fetal malformations. The introduction of new ultrasound modes, such as the HDlive or the Radiance System Architecture (RSA), which improve even more the quality of images, makes it easier to examine normal embryos and fetuses with incredible perfection and achieve diagnosis of malformations, increasingly complex and of high clinical importance.

**Keywords:** Three-dimensional/four-dimensional ultrasound, Fetal malformations, HDlive, Radiance system architecture, Second trimester.

**How to cite this article:** Bonilla-Musoles F, Bonilla F Jr, Raga F, Caballero O, Cadete C, Machado LE. Second Trimester Anomaly Scan using 3D/4D Ultrasound. Donald School J Ultrasound Obstet Gynecol 2015;9(4):372-381.

**Source of support:** Nil

**Conflict of interest:** None

## INTRODUCTION

In recent years, the three-dimensional (3D)/four-dimensional (4D) ultrasound has reached a worldwide spread in all of the obstetrics and gynecology fields, and nowadays it takes part of all obstetric-gynecologic diagnostic areas that aim to be comprehended, as it is seen in the current issue of this Donald School Journal of Ultrasound in Obstetrics and Gynecology (DSJUOG). The existing world literature on this subject is so vast that, in our view, a new review is meaningless unless, as we intend, it brings something to improve the image quality to make the diagnosis easier.

The image quality only improved dramatically when we began to use higher sound frequencies and, more recently for the fact of having applied the most modern

ultrasound, such as the 3D/4D and their modes (STIC: spatial temporal image correlation; AVC: Automatic volume calculation; VOCAL: Virtual organ computer-aided analysis and the inverse mode), more recently the HDlive and Radiance System Architecture (RSA). In this chapter, we are going to show normal images and curious cases of malformations that have been observed recently with the use of 3D/4D, HDlive and RAS. They can demonstrate that these new technologies are really useful.

Referring to the 3D/4D bibliography, we have only showed quotations by some authors; among us, the most published ones in this field.<sup>1-32</sup> Concerning the HDlive in obstetrics, the literature, even being poor,<sup>33-61</sup> is enough to show that in fact the HDlive improves the quality of the images<sup>55</sup> whose beauty<sup>56,59</sup> and sharpness are superior to the 3D/4D sonographic ones. These reviews in early and advanced pregnancies include both normal and pathological features,<sup>33-35,39,40,60</sup> images on the fetal development and behavior,<sup>47</sup> isolated cases of singleton<sup>38,41</sup> or normal twin pregnancies,<sup>50</sup> facial expressions<sup>48,49,54</sup> morphological studies of the heart,<sup>48,49,54</sup> and sight of the uvula.<sup>61</sup> Moreover, some specific pathology, such as hygroma colli,<sup>36,42</sup> sirenomelia<sup>37</sup> without skulls/exencephaly,<sup>43</sup> meconium peritonitis,<sup>51</sup> twin reversed arterial perfusion (TRAP) sequence,<sup>53</sup> Turner syndrome<sup>57</sup> or placental abnormalities, such as circumvallate placenta<sup>52</sup> or thrombosed placental varicose vein.<sup>44</sup> Concerning the RSA, there is only a mention, with a small picture, in the case of circumvallate placenta recently described by AboEllail et al.<sup>52</sup>

## NORMAL HDLIVE IMAGE

We started presenting isolated images of normal pregnancies, which were examined with HDlive, and compared with conventional 3D, in order to show the high quality of the obtained images (Figs 1 to 3). If the use of 3D has already been a noticeable improvement, this new technology, which is easily applicable, is exceptional (Figs 1 to 3).

## PATHOLOGICAL IMAGES USING 3D/4D ULTRASOUND AND HDLIVE

We will introduce some other examples of isolated malformations of the first and second quarters, which were studied with 3D/4D ultrasound and HDlive.

<sup>1</sup>Professor and Chairman, <sup>2-6</sup>Professor

<sup>1-3,6</sup>Department of Obstetrics and Gynecology, School of Medicine, University of Valencia, Valencia, Spain

<sup>4</sup>Department of Obstetrics and Gynecology, Estadual University of Southern Western Bahia, Vitoria da Conquista, Bahia, Brazil

<sup>5</sup>Department of Obstetrics and Gynecology, Federal University of Salvador, Bahia, Brazil

**Corresponding Author:** Fernando Bonilla-Musoles, Professor and Chairman, Department of Obstetrics and Gynecology, School of Medicine, University of Valencia, Valencia, Spain, e-mail: profesor.bonillamusoles@hotmail.com



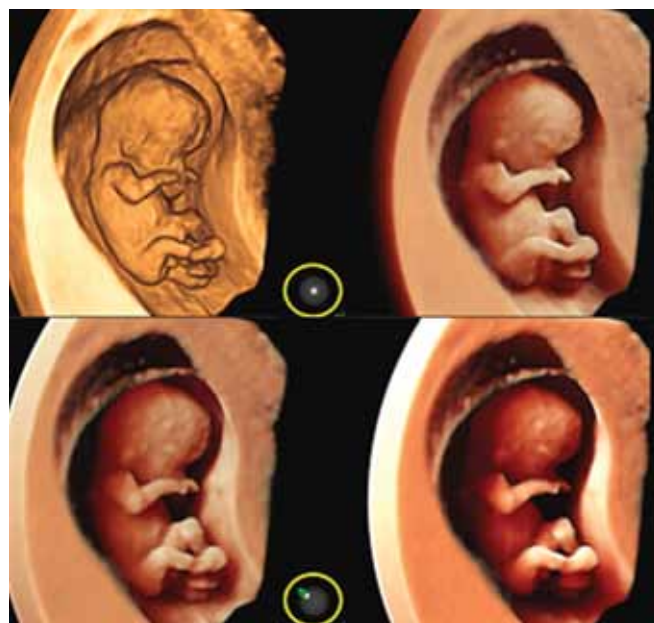
**Fig. 1:** Above, a 9-week pregnancy HDlive shows the embryo profile with the virtual light source from the left. We show the whole embryo and the yolk sac from behind, with maximum luminescence. Besides the very pretty image of the embryo, we can see all the amnion and extraembryonic mesenchyme, which as you know, is not a fluid accumulation, but a mesenchyme with fibrillar part which is clearly seen in the picture. Below, a 14-week gestation, where there is a comparison between the fetal silhouette with lower (on the left) and higher brightness (on the right). The virtual light focus direction is from the left side of the fetus



**Fig. 3:** Variable locations of virtual light source were used to take, with an HDlive, for 36-week facial profiles of the same fetus. The expressions obtained are incredibly beautiful

### Double Yolk Sac

Now we show a 6-week tomographic gestation image of a double yolk sac in AVC, which can be clearly seen in



**Fig. 2:** A complete 13-week gestation that is shown to compare the 3D (up and on the left) with the HDlive, using different light intensities and locations of the virtual light source (yellow circles). The anatomical details, which have been obtained in both the fetus in the amnion and the extracoelomic mesenchyme, are impressive

red and blue. The HDlive allows us to see the embryo anchored to the endometrium, with the amniotic sac and the pathological vesicle (Fig. 4).

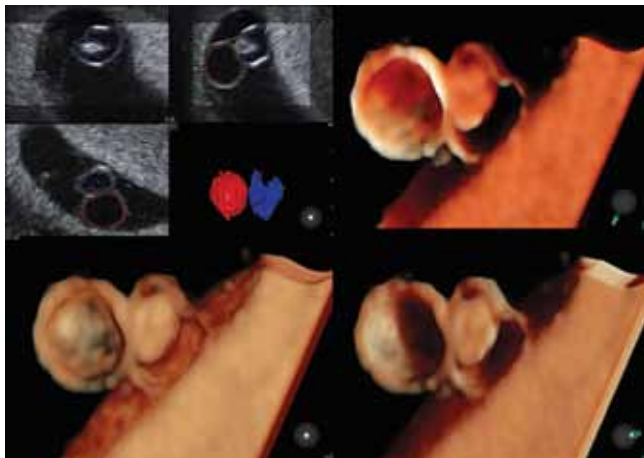
### Hygroma Colli

We show a very typical case at 12 weeks of gestation with 2D, 3D surface and cutting the cephalic pole through a ventricle and the lateral plexuses, and HDlive with maximum brightness. The HDlive image is extremely beautiful, the whole hygroma colli is observed, and the most interesting is how it contains in its interior in addition to an accumulation of fluid, small partitions. These partitions follow the 45 XO karyotypes almost in a pathognomonic way (Fig. 5).

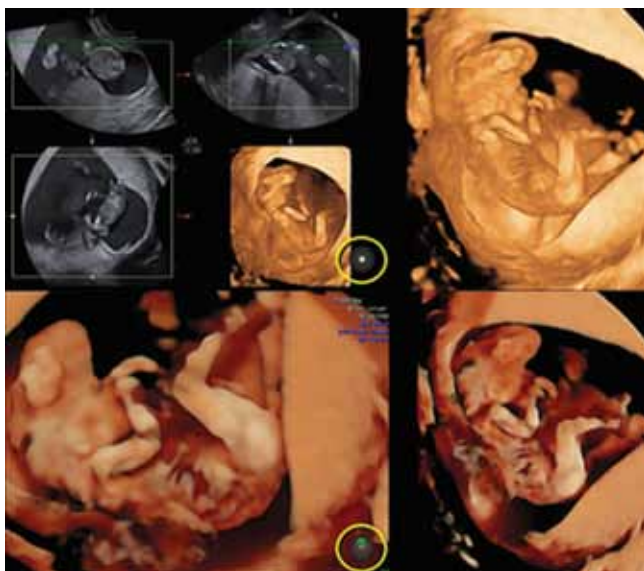
### Anencephaly/Exencephaly/Acrania

This group of malformations has common origin which is the lack or incomplete development of the fetal scalp. Initially, there is a lack of bone development of frontal, temporal and occipital bones, generally the occipital, although it can affect even more skull bones.

In the early stages, the meningeal membranes are preserved, but they usually break in contact with the amniotic fluid. The encephalic mass come into direct contact with the liquid, and expands and dilates outside the cephalic pole (exencephaly). Then, an abacterial encephalitis occurs with atrophy of the brain mass and change into an acrania. Precisely saying about this natural evolution, most of the acrania cases are diagnosed



**Fig. 4:** Six-week gestational image in orthogonal planes with TUI, AVC and HDlive, clearly shows two yolk sacs



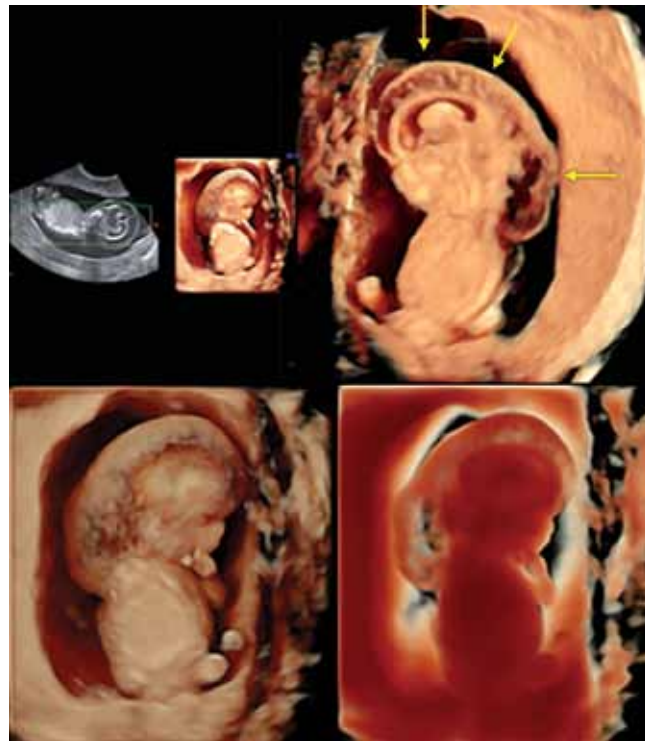
**Fig. 6:** Comparative study of anencephaly/exencephaly. Two-dimensional orthogonal planes (above and on the left), 3D (above and on the right), and HDlive (the two photos below) of a 14-week fetus diagnosed with exencephaly are shown. The definitive diagnosis is obtained in the pathology of the fetal cranial pole. We can see the HDlive image with the 'shadows and the chiaroscuros', which is infinitely superior to 2D/3D ultrasound

during the pregnancy period, except for the exencephaly cases and even fewer anencephaly ones (Figs 6 and 7).

### Encephalocele (Cranium Bifidum)

It is a very rare congenital malformation, in which a diverticulum of the brain tissue, and the meninges protrude through defects in the cranial vault. It is derived from a failure of the closing of neural tube during embryonic development that takes place during the 4th week of gestation. Although its origin is not precisely known, it has been associated with a maternal deficiency in the levels of folic acid during pregnancy as well as consequence of a trauma.

The brain and its coating stay outside the cranial pole, forming a protrusion, generally in occipital but also in the



**Fig. 5:** Hygroma colli. Notice the easy perfect profile in HDlive. In yellow arrows, we have set the thin walls that mold in the magma of hygroma

frontal or sincipital region. If only the ventricle protrudes, we call it as hydroencephalocele. If the meninges also protrude, we call it as meningoencephalocele. The tumor, almost permanently, is located in the occipital bone, from where part of the brain mass outputs (Fig. 8).

### EXTROPHY

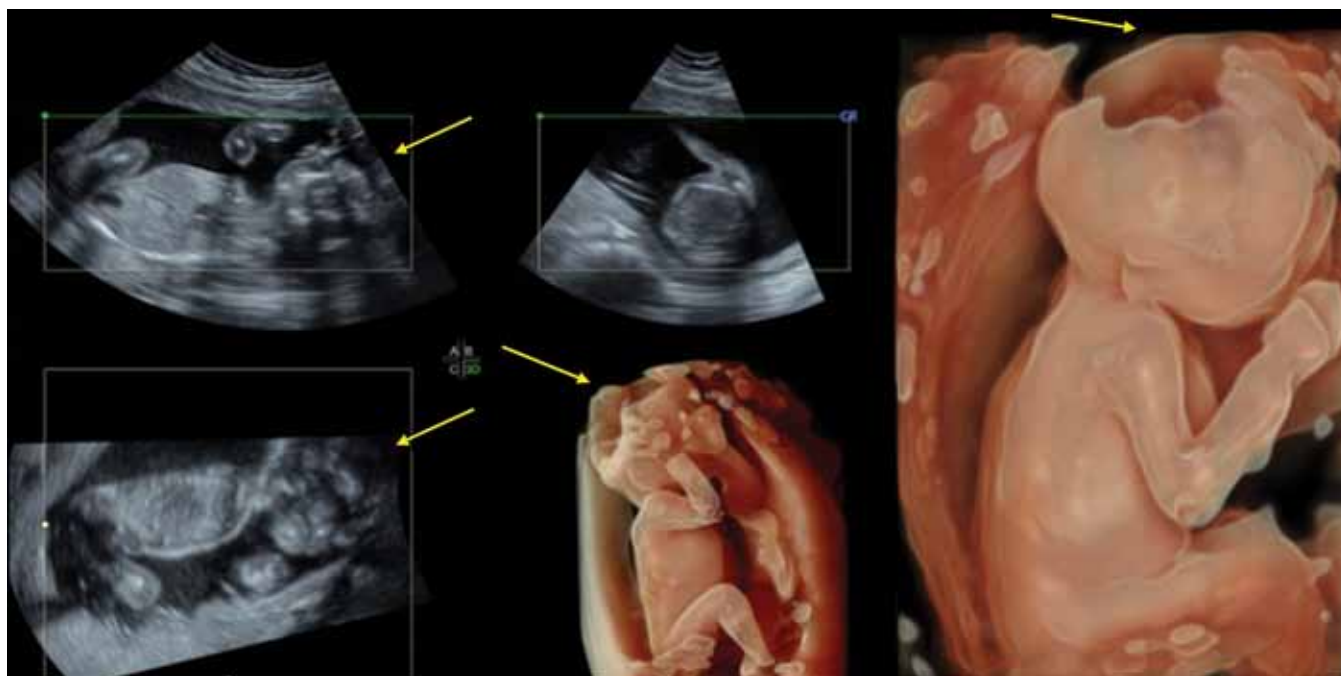
The abdominal wall defects are shown in Table 1. The most common defects are the omphalocele (Fig. 9) and gastroschisis (Fig. 10).

#### Omphalocele

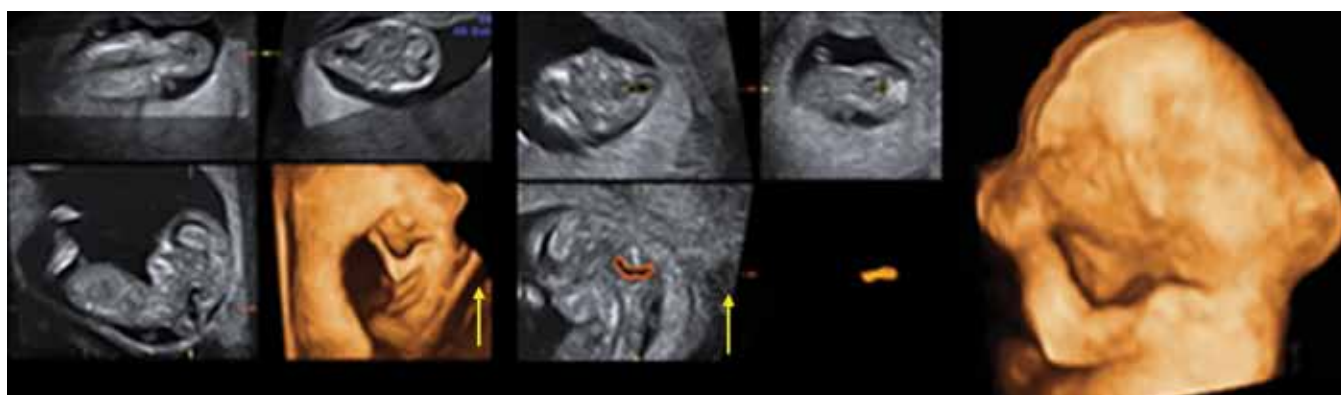
The omphalocele is caused by a closing defect of the two lateral valves. The defect is covered by an amnion membrane, similar to the amnios from where the intestinal loops and/or liver go out. This anomaly almost always accompanies trisomy 18.

#### Gastroschisis

The gastroschisis, however, is an authentic abdominal wall defect, appearing on the left of the umbilicus, generally small, not bigger than 1 cm, and produced by the atresia of one of the umbilical arteries. From the beginning of the intestinal peristalsis, around 14th week, the exit of the intestinal loops to the outside can be produced. They swim freely in the amniotic fluid. Only few exceptionally accompany chromosomopathy (Fig. 10).



**Fig. 7:** Radiance System Architecture image of an acrania case. The yellow arrows show 2D orthogonal planes (on the left) and 3D radiance view of the cranial bone defect. This new technology that defines the edges very well, allows us to see the defect clearly



**Fig. 8:** Encephalocele (arrows). The image using 2D/3D ultrasound shows the occipital tumor

**Table 1:** Malformations of the abdominal wall

- Omphaloceles
- Gastroschisis
- Pentalogy of cantrell
- Extrophies
- Vesical
- Cloacal
- Ectopia cordis
- Limb-body wall complex
- Body stalk complex

**Table 2:** Characteristics of pentalogy of Cantrell

- Defect of the supraumbilical abdominal midline
- Defect of the lower sternum
- Defect of the anterior portion of the diaphragm
- Defect of the diaphragmatic pericardium and
- Intracardiac congenital malformations

## Pentalogy of Cantrell

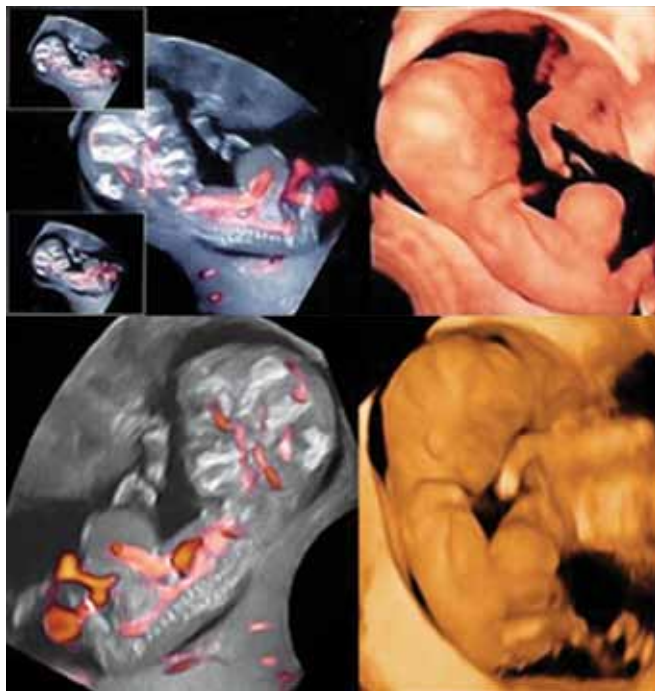
The characteristics of pentalogy of Cantrell are shown in Table 2.

The frequency of the disease (2 in 1,716) is low in autopsies with a reported prevalence of 0.079 per 10,000 live births. The etiology is unknown, but it has been associated with chromosomopathies, such as Turner syndrome and trisomy 18, the teratogen exposure, such as

quinidine, warfarin, thalidomide, infectious agents, such as influenza infection, and even vitamin A deficiency, although generally is considered as multicausal (Fig. 11).

## Prune Belly Syndrome

It is a rare congenital urologic obstructive alteration with a megacystic bladder and visible deformity of the abdominal wall. The sonographic characteristic triad includes: (1) anterior abdominal wall distention with deficiency or absence of abdominal wall musculature, (2) megacystis and (3) pulmonary hypoplasia.



**Fig. 9:** Omphalocele examined on the 16th week, using a 2D glass-body rendering with an angiography (on the left), HDlive (on the right and above) and 3D ultrasound (on the right and below). We can clearly notice the tumor in the abdominal wall, and how the vessels penetrate its interior because the liver occupies the tumor

Typical Prune Belly syndrome has been considered secondary to connective tissue and smooth muscle abnormalities, which cause bladder distention, and result in oligohydramnios. The major features are dilatation of the fetal urinary bladder and proximal urethra with thickening of the bladder wall. The bladder wall hypertrophy is the result of the intravesical pressure generated secondary to obstruction. The urinary bladder fills the pelvis and the abdomen, and does not empty more often. The ureters are usually dilated, and hydronephrosis of variable degrees may be present. A keyhole sign, which is a dilated prostatic urethra, frequently with distention of

the prostatic utricle (utriculus prostaticus) and thickening of the bladder neck, is present (Fig. 12).

### Persistent Urachus with Bladder Prolapse Bladder Extrophy Variety

It is a rare abnormality that occurs in 1/100,000 newborns. Urachal anomalies occur due to the failure of obliteration, resulting in different pathologies, such as its persistence, cysts, sinus or bladder-urachal diverticula. The ultrasound most common feature is the presence of a cystic mass located at the base of the umbilical cord, communicating with the bladder and flanked by the umbilical arteries (Fig. 13). The use of the SonoAVC, allows us to identify and quantify hypoechoic areas, evaluating their absolute dimensions, average diameter and volume (Fig. 13).

### PYELOCALYCEAL ECTASIA

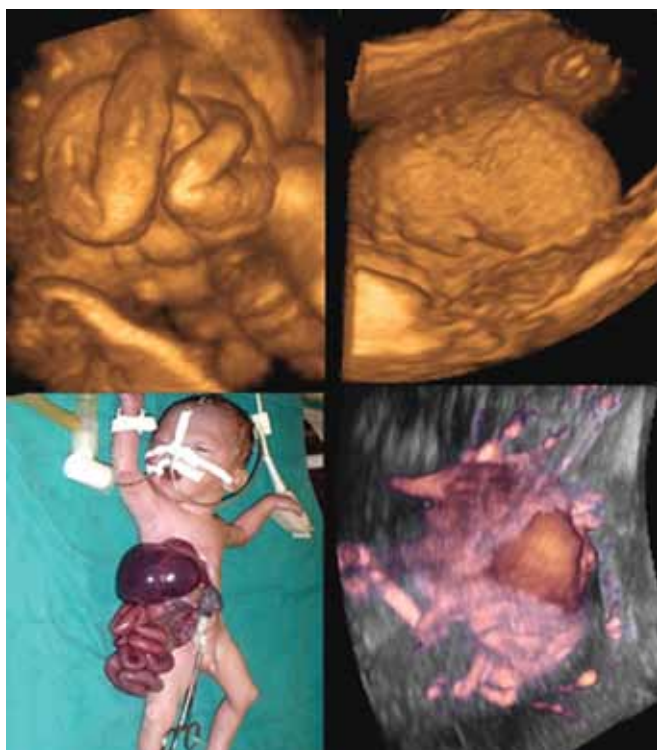
Of all the urinary anomalies, the dilations are the most common, and can affect the pelvis, calices, ureters and bladder. To carry out an evaluation, it is required to take into account:

- *Intensity of dilation level:* The larger, the more likely to be associated with an obstructive process, but the dilation is not synonymous to obstruction.
- *Dilation:* Unilaterality or bilaterality.
- *Characteristics of the renal parenchyma:* The presence of a renal dysplasia is associated with poor prognosis.
- *Fetal renal function:* It is estimated by analyzing the volume of the amniotic fluid and the analytical study of the fetal urine. The appearance of an oligohydramnios or the presence of fetal hypertonic urine indicates kidney malfunction.

The use of 3D/4D ultrasound and their different modes is very useful in the study of internal organic malformations. Figure 14 shows a 30-week fetal kidney studied in 2D, Vocal and HDlive, presenting a remarkable pelvic dilatation.



**Fig. 10:** The image shows a 16-week precocious case of gastroschis (yellow arrows) seen with 3D ultrasound



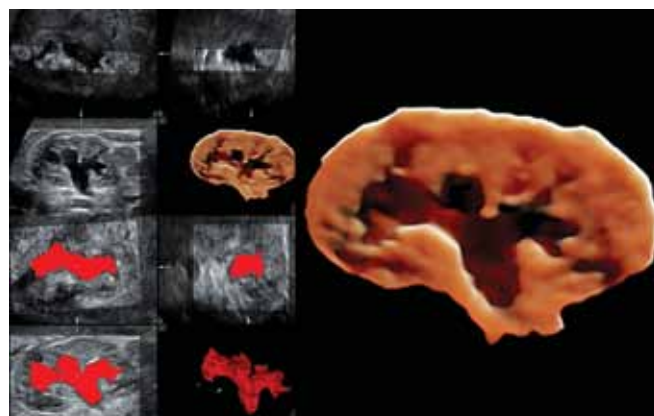
**Fig. 11:** Pentology of Cantrell in 3D ultrasound (above) and 3D Doppler angiography (below right). We can observe the cordis exstrophy, the gastroschisis with liver and intestines protrude due to defect in the diaphragm and abdominal wall, but sternal injury is not shown



**Fig. 12:** Two-dimensional AVC (above on the left) and HDlive of a typical case of Prune Belly syndrome. The bladder distention is clearly observed



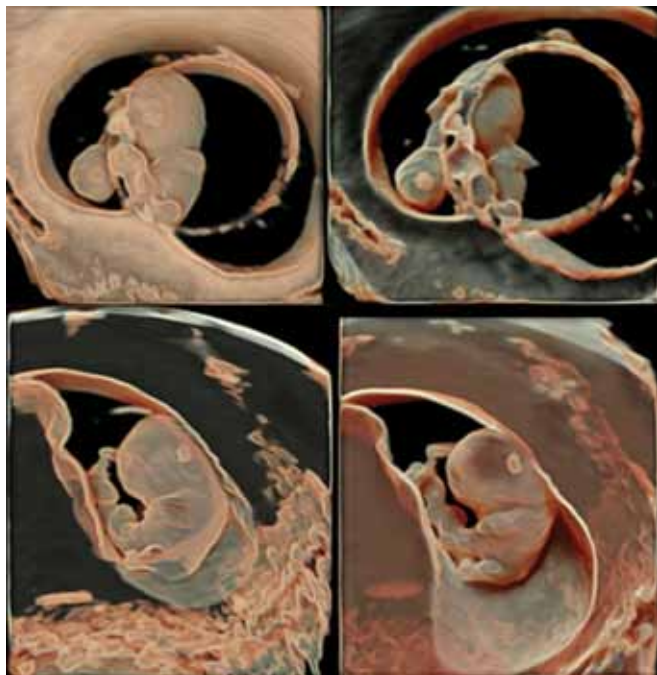
**Fig. 13:** Comparative images in 2D, 3D, Doppler and inversion mode. The 3D image (above on the left) shows the tumor. The 2D image (below on the left) shows the tumor and how it communicates with the bladder (AVC). The inverse mode (above on the right) indicates clearly that these are two communicating cysts. The Doppler shows the vessels around the bladder and of the cyst moving toward the umbilical cord. SonoAVC image and correlation with the birth anomaly found the tumor in the base of the umbilical cord. We can see the vesical prolapse, and its mucosa going outside



**Fig. 14:** Pyelocalyceal dilation studied with 2D sonography, SonoAVC (on the left), and with HDlive (on the right)

## RADIANCE SYSTEM ARCHITECTURE OR SILHOUETTE HDLIVE

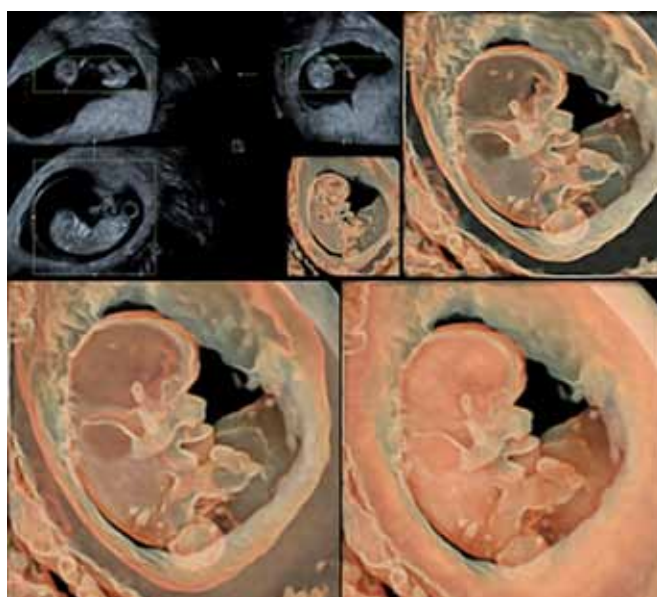
In the literature, there are only a small number of references to this new mode, which has been recently introduced in the Voluson E10 (General Electric Healthcare, Zief, Austria), in a case of circumvallate placenta,<sup>52</sup> a right aortic arch with an aberrant left subclavian artery,<sup>62</sup> a jejunal atresia<sup>63</sup> and an outstanding review of normal embryo and fetuses.<sup>64</sup> We provide a series of the first- and second-trimester normal pregnancy images. So, the readers can have an idea of diagnostic possibilities, which at first sight, seem to revolutionize the results (Figs 15 to 20).



**Fig. 15:** Nine-week gestation with four images with lower and higher 'brightness'. Observe the perfect definition of contours of the fetus, the amnion, the yolk sac and the gestational sac. We are standing in front of a new sonographic view of the gestation



**Fig. 16:** We can see 'radiance' (above), and HDlive (below) pictures of a normal 10-week gestation. It is really amazing the obtained definition of the fetal image. We can clearly observe the delimitation of the hands, cord and physiologic herniation



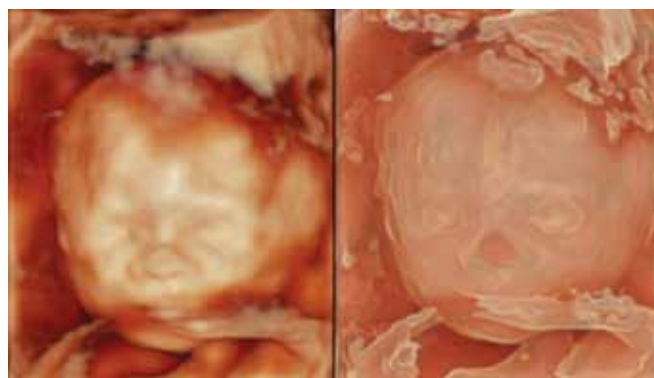
**Fig. 17:** Normal fetal images in 2D orthogonal planes and 'radiance' with less and more 'brightness' at 10 weeks of gestation. We can see all its external and internal structures

## COMMENTS

Despite the remarkable improvement in the image quality that involves the introduction of these new technologies shown in this article, they do not invalidate the entire 'prenatal diagnosis level I and II' of 13 to 14 and 18 to 24 weeks, which will keep on being held by the 2D ultrasound. What these new applications show are the fantastic advance in image quality which supposed, on one hand, the introduction of 3D/4D ultrasound, and on the other hand, more recently, the new HDlive

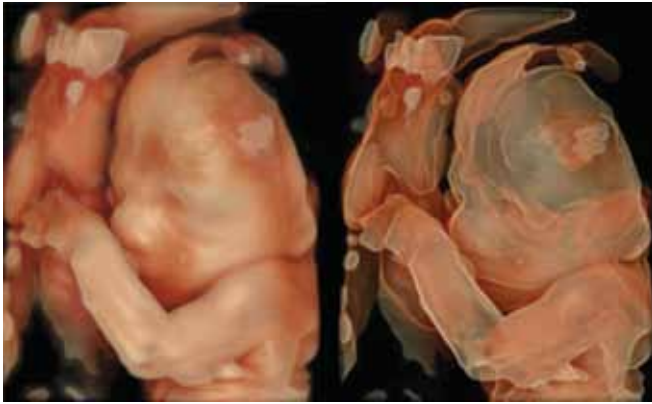


**Fig. 18:** Compare the HDlive (left) and the 'radiance' (right) fetal images at 22 weeks of gestation. The most striking aspect is the perfect delimitation of all the structures, such as the umbilical cord



**Fig. 19:** Two faces of the same 24-week fetus with less (left, HDlive) and more luminous 'brightness' (right, RAS). Highlight for the perfect delimitation of its structures is evident

and 'radiance' modes. We think that the latter two technologies should be used in clinical practice, and



**Fig. 20:** Complete 25-week gestation fetal profile observed with the 'radiance' system which allows us to clearly see all surface delimitation

that they can be arranged in those hospitals with the facilities of specialized 'prenatal diagnosis' units. The 3D/4D ultrasound has already been practically a routine, but not the last two we highlighted and that we think, are going to be essential in the very near future. Any high-level hospital (Level III—Spanish) has obstetrics of such prenatal diagnosis units, therefore, they must adapt.

We focus this work just to show these advances, instead of trying to make a new 'descriptive summary' of existing malformations, and they can be seen with 3D/4D ultrasound. The reason is that it is sufficient to observe the reduced bibliography we have brought (a small sample of the existing one), that we have studied only three authors who have worked hard in this area (Hata, Kurjak, and our group) to show the readers that it is not more accurate and descriptive work malformations, that this is the right direction to follow.

## REFERENCES

1. Kurjak A. A Textbook of Perinatal Medicine. Lancs, England Parthenon Publish; 1998.
2. Kurjak A, Chervenak F. Donal School Textbook of Ultrasound in Obstetrics and Gynecology. II Ed. New York; 2007. p. 978-981.
3. Kurjak A, Chervenak F. Donald School Textbook of Ultrasound in Obstetrics and Gynecology 2008. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd.; 2004. ISBN81-8061-198-1.-8448-202-207. Chapter 42.
4. Kurjak A, Jackson D. An Atlas of Three- and Four-dimensional Sonography in Obstetrics and Gynecology. London: Taylor and Francis; 2004.
5. Kurjark A, Azumendi G. The Fetus in Three-Dimension. Imaging, Embryology and Fetoscopy. Informa Healthcare. England: Abingdon; 2006.
6. Kurjark A, Chervenak FA, Carrera JM. Ian Donald School Atlas of Fetal Malformations. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd.; 2007.
7. Merz E, Abramovicz J, Baba K, Blaas HG, Deng J, Glindes L, Lee W, Platt L, Pretorius D, Schild R, et al. 3D imaging of the fetal face—recommendations from the International 3D Focus Group. *Ultraschall Med* 2012;33(2):175-182.
8. Bonilla-Musoles F, Raga F, Osborne NG. Three-dimensional ultrasound evaluation of the embryo and the early fetus. In: Kurjak A, editor. A Textbook of Perinatal Medicine. Lancs. England: Parthenon Publish; 1998; p. 240-262.
9. Bonilla-Musoles F, Machado LE, Osborne NG, Raga F, Chamusca L, Chagas K, Bonilla F Jr, Cadete C. Ultrasound diagnosis of facial and cephalic pole malformations: Comparative study of different three-dimensional modalities and two-dimensional ultrasound. *Ultrasound Q* 2000;16(2):97-105.
10. Machado LE, Bonilla-Musoles F, Osborne NG. Fetal Limb abnormalities. *Ultrasound Diagnosis. Ultrasound Q* 2000; 16(4):203-219.
11. Bonilla-Machado LE, Bailao LA, Osborne NG. Abdominal wall defects. Two versus three-dimensional ultrasonographic diagnosis. *J Ultrasound Med* 2001;20(4):379-389.
12. Machado LA, Bonilla-Musoles F, Raga F, Bonilla F Jr, Machado LE, Osborne N. Thanatophoric dysplasia, Ultrasound diagnosis. *Ultrasound Q* 2001;17(4):235-243.
13. Bonilla-Musoles F, Machado LE, Osborne N, Muñoz E, Raga F, Blanes J, Bonilla F Jr. Two-and three-dimensional ultrasound in malformations of the medullary canal: report of four cases. *Prenat Diagn* 2001;21(8):622-626.
14. Bonilla-Musoles F, Machado LE, Osborne N, Blanes J, Bonilla F Jr, Raga F, Machado LE. Two-dimensional and three-dimensional sonography of conjoined twins. *J Clin Ultrasound* 2002;30(2):68-75.
15. Bonilla-Musoles F, Machado LE, Osborne N. Multiple congenital contractures (congenital multiple arthrogryposis). *J Perinat Med* 2002;30(1):99-104.
16. Bonilla-Musoles F, Machado L, Osborne N, Raga F, Lima-Coury I, Bonilla F Jr, Torres F. Early diagnosis of congenital anomalies: 1. Cepahlic pole malformations. In: *Controversies in Perinatal Medicine*. Carreras JM, editor. Lancaster: Parthenon Publ; 2003. p. 1-20.
17. Bonilla-Musoles F, Machado L, Osborne N, Lima-Coury I, Bonilla F Jr, Torres F. Early diagnosis of congenital anomalies: 2. Thoracic and abdominal malformations. In: *Controversies in Perinatal Medicine*. Carreras JM, editor. Lancaster: Parthenon Publ; 2003. p. 1-20.
18. Bonilla-Musoles F, Machado LE, Raga F. Three-Dimensional visualization of fetal malformations. Ian Donal School textbook of ultrasound in Obstetrics and Gynecology. Kurjak A, Chervenak F. New Delhi: Jaypee Brothers Medical Publlshers 2004;38:480-499.
19. Bonilla-Musoles F, Machado LE, Raga F. Three- and four-dimensional images of fetal malformations. In: Kurjak A, Jackson D, editors. *An Atlas of Three- and Four-dimensional Sonography in Obstetrics and Gynecology*. London: Taylor and Francis; 2012.
20. Machado LE, Bonilla-Musoles F, Osborne N. Skeletal anomalies. In: Kurjark A, Azumendi G, editors. *Fetus in three-Dimension. Imaging, Embryology and Fetoscopy*. . Abingdon, England: Informa Healthcare 2006;331-349.
21. Bonilla-Musoles F, Machado LE. Gastrointestinal tract and internal abdominal wall. In: Kurjark A, Chervenak FA, Carrera JM. *Ian Donald School Atlas of Fetal Malformations*. New Delhi: Jaypee Brothers Medical Publishers (Pvt) Ltd; 2007. p. 174-194.
22. Sanz-Cortés M, Raga F, Bonilla-Musoles F. 3D sonographic prenatal diagnosis of a lobar holoprosencephaly associated with cebocephaly. Assessment and diagnosis with multipanar reconstruction. *Prenat Diagn* 2007;27(6):585-586.
23. Bonilla-Musoles F, Machado LE, Raga F. 3D Ultrasound in the visualization of fetal Malformations. In: Donald School

- Textbook of Ultrasound in Obstetrics and Gynecology. Kurjak A, Chervenak FK, editors. 2nd ed. New York; 2008, Chapter 42. p. 625-640.
24. Sanz-Cortes M, Raga F, Leon JL, Sniderman A, Bonilla-Musoles F. MRI and multiplanar 3D ultrasound compared in the prenatal assessment of enlarged posterior fossa. *J Perinatal Med* 2007;35(5):422-424.
25. Bonilla-Musoles F, Raga F, Machado LE, Bonilla F Jr. News on 3D-4D Sonographic Applications in the diagnosis of fetal Malformations. In Donald School Textbook of Ultrasound in Obstetrics and Gynecology. 2nd ed. Kurjak A, Chervenak F, editors, 2008. Chapter 42. p. 640-661.
26. Bonilla-Musoles F, Machado LE, Raga F, Castillo JC, Osborne N, Bonilla F Jr. Machado F. 3D/4D US In Fetal Malformations. Part Two: Second Trimester. Cephalic Pole Malformations. Current Topics on Fetal 3D/4D Ultrasound. Hata T, Kurjak A, Kozuma S, editors. Busum Holand: Bentham Science Publishers; 2009;56-86.
27. Bonilla-Musoles F, Machado LE, Raga F, Castillo JC, Osborne N, Bonilla F Jr, Machado F. 3D/4D US In Fetal Malformations. Part Three: Second Trimester. Skeletal Disorders, Thoracic, Abdominal, Kidney and Other Malformations. In: Current Topics on Fetal 3D/4D Ultrasound. Hata T, Kurjak A, Kozuma S, editors. Busum Holand: Bentham Science Publishers; 2009. p. 87-133.
28. Osborne N, Bonilla-Musoles F, Machado L, Raga F, Bonilla F Jr, Ruiz F, Perez-Guardia C, Alhuwalia B. Fetal megacistic (Prune Belly. Differential Diagnosis). *J Ultrasound Med* 2011;30(6):833-841.
29. Austria BS, Hanaoka U, Sato M, Hata T. Three- and four-dimensional sonographic diagnosis of fetal intra-abdominal umbilical vein varix. *J Med Ultrasonics* 2014;41(2):245-246.
30. Hata T, Kurjak A, Kozuma S. Current Topics on Fetal 3D/4D Ultrasound. Busum Holand: Bentham Science Publishers, 2009. p. 56-86.
31. Hata T, Kurjak A. Current Topics on Fetal 3D/4D Ultrasound. Busum Holand: Bentham Science Publishers, 2012.
32. Hata T, Mori N, Tenkumo C, Hanaoka U. Three-dimensional volume-rendered imaging of normal and abnormal fetal fluid-filled structures using inversion mode. *J Obstet Gynecol Res* 2011;37(11):1748-1754.
33. Bonilla-Musoles F, Raga F, Castillo JC, Bonilla F Jr, Climent MT, Caballero O. High definition real time ultrasound (HDlive) of embryonic and fetal malformations before week 16. *DSJUOG*. 2012;7(1):1-8.
34. Bonilla-Musoles F, Raga F, Castillo JC, Bonilla F Jr, Caballero O. Revisión. Alta definición Ecográfica en tiempo real (HDlive US) en Obstetricia y Ginecología. *Rev Peru Ginecol Obstet* 2013;59(1):33-41.
35. Bonilla-Musoles F, Raga F, Osborne N, Bonilla F Jr, Castillo JC, Caballero O. Pictorial review. Multimodality 3D volumetric ultrasound in obstetrics and gynaecology with an emphasis in HDlive technique. *Ultrasound Q* 2013;29(2):189-201.
36. Bonilla-Musoles F, Esquembre MP, Bonilla F Jr, Raga F, Castillo JC, Machado LE, Caballero O. First trimester. *DSJUOG* 2014;8(3):229-233.
37. Bonilla-Musoles F, Caballero O, Castillo JC, Bonilla F Jr, Raga F. HDlive and three-dimensional imaging in prenatal diagnosis of sirenomelia in the first trimester: case report and a brief review of the literature. *DSJUOG* 2015;9(2):1-4.
38. Kagan KO, Pintoffl K, Hoopmann M. First-trimester ultrasound images using HDlive. Picture of the Month. *Ultrasound Obstet Gynecol* 2011;38(5):607.
39. Hata T, Hanaoka U, Tenkumo C, Sato M, Tanaka H, Ishimura M. Three-and four-dimensional HDlive rendering images of normal and abnormal fetuses: pictorial essay. *Arch Gynecol Obstet* 2012;286(6):1431-1435.
40. Hata T, Tenkumo CH, Sato M, Kanenishi K, Ishimura M. Three-dimensional ultrasound HDlive-rendered images of intrauterine abnormalities during pregnancy. *J Med Ultrasonics* 2013;40(2):179-180.
41. Hata T. HDlive rendering image at 6 weeks of gestation. *J Med Ultrasonics* 2013;40(3):495-496.
42. Hata T, Hanaoka U, Tenkumo CH, Ito M, Uketa E, Mori N, Kanenishi K, Tanaka H, Ishimura M. Three-dimensional HDlive rendering image of cystic hygroma. *J Med Ultrasonics* 2013;40(2):297-299.
43. Hata T, Uketa E, Tenkumo C, Hanaoka U, Kanenishi K, Tanaka H. Three- and four-dimensional HDlive rendering image of fetal acrania/exencephaly in early pregnancy. *J Med Ultrasonics* 2013;40(2):271-273.
44. Kanenishi K, Nitta E, Mashima M, Hanaoka U, Koyano K, Tanaka H, Hata T. HDlive imaging of intra-amniotic umbilical vein varix with thrombosis. *Placenta* 2013;34(4):1110-1112.
45. Hata T, Hanaoka U, Mashima M, Ishimura M, Marumo G, Kanenishi K. Four-dimensional HDlive rendering image of fetal facial expression: a pictorial essay. *J Med Ultrasonics* 2013;40(3):441-448.
46. Hata T, Mashima M, Ito M, Uketa E, Mori N, Ishimura M. Three-dimensional HDlive rendering images of the fetal heart. *Ultrasound Med Biol* 2013;39(8):1513-1517.
47. Hata T, Kanenishi K, Hanaoka U, Uematsu R, Marumo G, Tanaka H. HDlive study of fetal development and behavior. *DSJUOG* 2014;8(3):250-265.
48. Hata T, Kanenishi K, Hanaoka U, Tanaka H. HDlive of the fetal heart. *DSJUOG* 2014;8(3):266-272.
49. Hata T, Kanenishi K, Hanaoka U, Marumo G. HDlive and 4D ultrasound in the assessment of fetal facial expressions. *DSJOG* 2015;9(1):44-50.
50. Hata T, Kanenishi K, Hanaoka U, AboEllail MAM, Marumo G. HDlive and 4D ultrasound in the assessment of twin pregnancy. *DSJOG* 2015;9(1):51-60.
51. AboEllail MAM, Tanaka H, Mori N, Tanaka A, Kubo H, Shimono R, Hata T. HDlive imaging of meconium peritonitis. *Ultrasound Obstet Gynecol* 2015;45(4):494-496.
52. AboEllail MAM, Kanenishi K, Mori N, Kurobe A, Hata T. HDlive image of circumvallate placenta. *Ultrasound Obstet Gynecol* 2015;46(4):513-514.
53. Tenkumo C, Tanaka H, Ito T, Uketa E, Mori N, Hanaoka U, Kanenishi K, Ando M, Hata T. Three-dimensional rendering images of the TRAP sequence in the first trimester: reverse end-diastolic umbilical artery velocity in a pump twin with an adverse pregnancy outcome. *J Med Ultrasonics* 2013;40(2):293-296.
54. Merz E. Surface reconstruction of a fetus (28+2 GW) using HDlive technology. *Ultraschall Med* 2012;33(2):211-211.
55. Grigore M, Mares A. The role of HDlive technology in improving the quality of obstetrical images. *Med Ultrasound* 2013;15(3):209-214.
56. Grigore M, Cojocar C, Lazar T. The role of HDlive technology in Obstetrics and Gynecology. Present and Future. *DSJUOG* 2014;8(3):234-238.
57. Grigore M, Vulpoi C, Preda C, Martiniuc V, Vasiliu I, Gorduz V. Using HDlive technology to diagnose Turner syndrome in the first trimester of pregnancy. Case Report. *Acta Endocrinologica (BUC)* 2015;11(1):93-98.

58. Araujo ED Jr, Nardoza MLM, Moron FA. Three-dimensional STIC-HDlive rendering: new technique to assessing of fetal heart. *Rev Brasil Cir Cardiovasc* 2013;28(4):5-7.
59. Araujo Ed Jr, Santana MEF, Nardoza MLM, Moron FA. Assessment of embryo/fetus during pregnancy by three-dimensional ultrasonography using the HDLive software: iconographic essay. *Radiol Brazil* 2015;48(1):52-55.
60. Pooh RK, Kurjak A. Novel applications of three-dimensional HDlive imaging in prenatal diagnosis from the first trimester. *J Perinat Med* 2015;43(2):147-158.
61. Tonni G, Grisolia G. Fetal uvula: navigating and lightening the soft palate using HDlive. *Arch Gynecol Obstet* 2013;288(2): 239-244.
62. AboEllail MAM, Kanenishi K, Tenkumo C, Mori N, Katayama T, Koyano K, Kusaka T, Hata T. 4D power Doppler with HDlive silhouette mode in antenatal diagnosis of right aortic arch with an aberrant left subclavian artery. *J Ultrasound Med* 2015 (In Press).
63. AboEllail MAM, Tanaka H, Mori N, Hanaoka U, Hata T. HDlive silhouette mode in antenatal diagnosis of jejunal atresia. *Ultrasound Obstet Gynecol* 2015 August 2. doi: 10.1002/uog.15753
64. Pooh RK. Brand new technology of HDLive Silhouette and HDlive Flow images. In: Pooh RK, Kurjak A: *Donald School Atlas of Ultrasound in Obstetrics and Gynecology*. Chapter 1. New Delhi: The Health Science Publishers, Jaypee Brothers Medical Publishers (P) Ltd; 2015. p. 1-38.