

# High Definition Real-Time Ultrasound (HDLive) of Embryonic and Fetal Malformations before Week 16

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## ABSTRACT

High definition real-time ultrasound (HDLive US) incorporates software that calculates the propagation of light through surface structures in relation to the light direction.

This light source can be freely positioned in order to illuminate the desired area of interest allowing a better image quality, a better sensation of deepness and easier visualization of fetal surfaces.

Cases of normal embryos, fetuses and common fetal malformations are shown.

The full potential of this new technology is still to be revealed. HDLive represents, in our opinion, an innovative tool and a step toward an even more realistic anatomical visualization of normal and malformed fetuses.

**Keywords:** Fetal malformations, High definition real-time ultrasound, Anatomical visualization of fetuses.

**How to cite this article:** 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. *Donald School J Ultrasound Obstet Gynecol* 2013;7(1):1-8.

**Source of support:** Nil

**Conflict of interest:** None declared

## INTRODUCTION

Image quality is extremely important to define origin, nature and extension in cases of early diagnosis of embryonic and fetal malformations.

This quality can be improved by: (i) Using higher frequencies. (ii) increasing the amplitude of the sonic wave. The larger the amplitude, the greater the intensity of color closest to white on the gray scale. (iii) Using three-dimensional (3D) US in orthogonal planes, X-ray, VOCAL and AVC modes. (iv) By changing the color. Some machines allow for a global change in color of the image on the screen. The images are more colorful in monochromatic color, but with no added details. In summary, there is no image improvement. (v) High definition real-time ultrasound (HDLive US): This new mode incorporates a movable virtual adjustable light source and a software that calculates the propagation of light through surface structures in relation to the light direction (Fig. 1).<sup>1</sup>

As it goes deep, the virtual light source produces selective illumination with the respective shadows that are produced by the structures where the light is reflected. The combination of lights and shadows results in spectacular

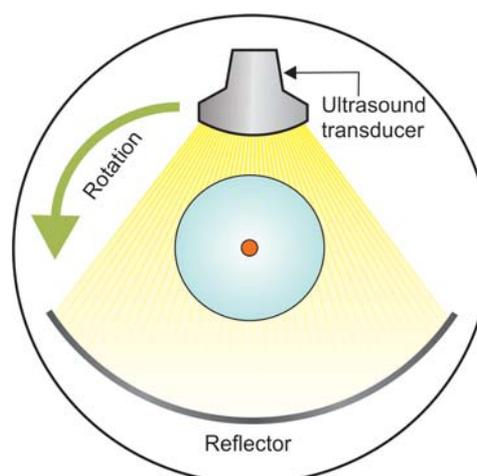


Fig. 1: Sound speed measurement (From 1)

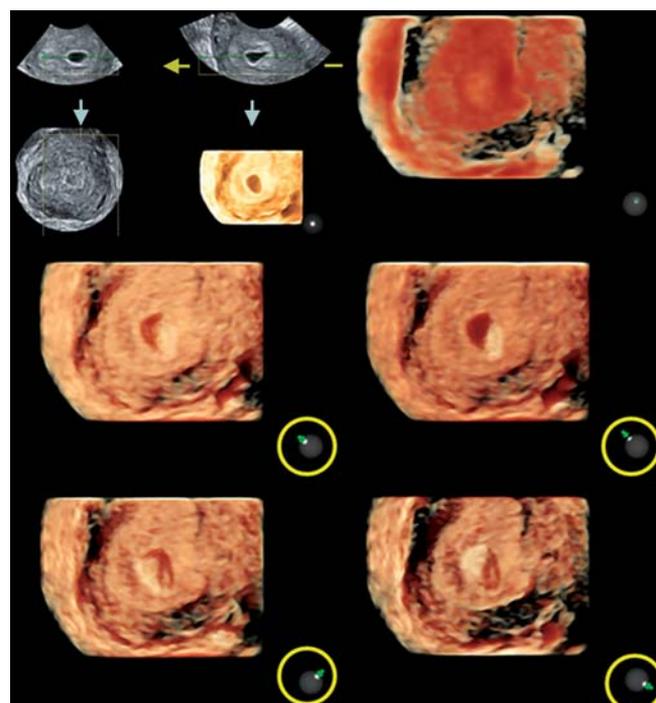
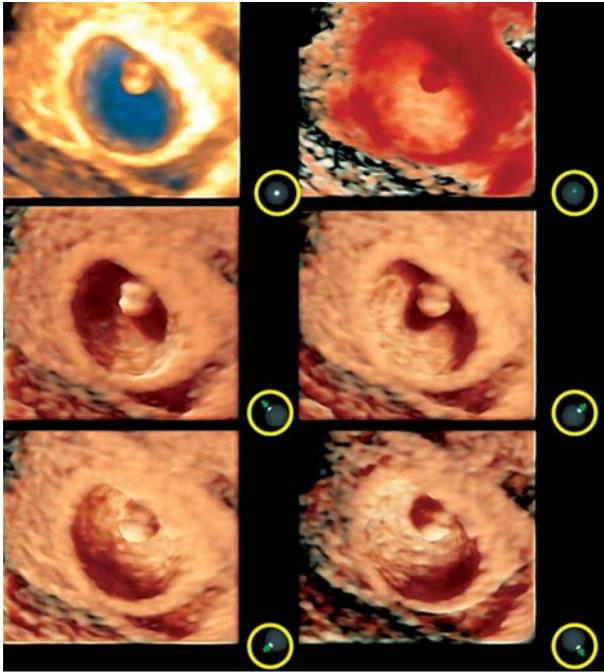


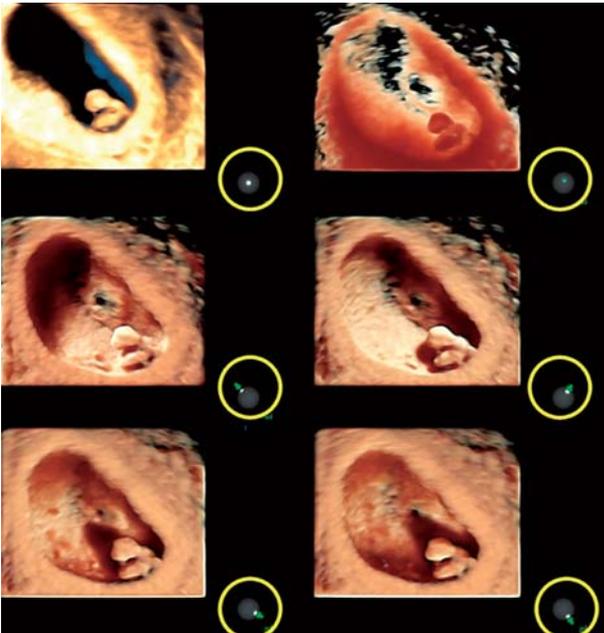
Fig. 2: HDLive US image of a 4th week pregnancy clearly showing the yolk sac and the chorion frondosum. Upper left: Orthogonal planes and 3D surface mode. Upper right: The light source enters the region of interest from behind. The other images show the yolk sac and the light source entering from different points (highlighted in yellow circles)

images that are much more natural than those obtained with 3D.

The source can be used on 3D images (Figs 3, 4, 6 and 8), either with orthogonal planes (Figs 2 and 7) or with 2D/3D Doppler AVC or VOCAL modes (Figs 9, 13 and 15),



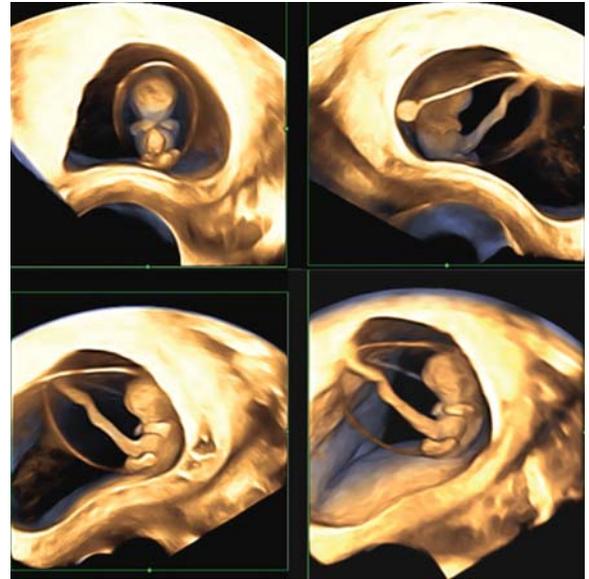
**Fig. 3:** Fifth week pregnancy, notice the gestational sac and the yolk sac close to the embryo in the inner part. Notice the 'shadows' along the inner part of the gestational sac which appear as the light source moves around the region of interest (yellow circles). The embryo and the yolk sac are visualized and showed in a 'photo-like' image



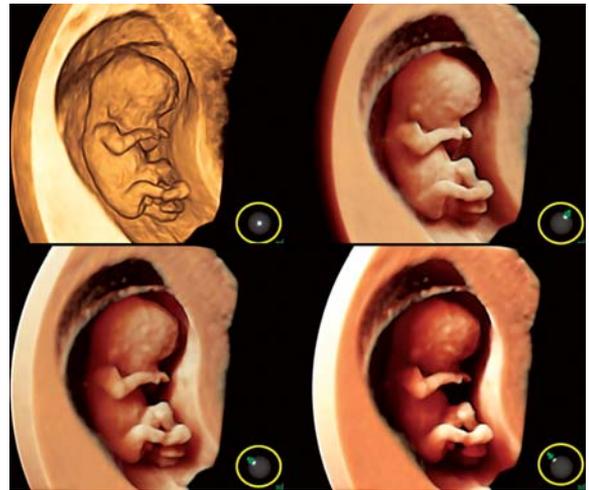
**Fig. 4:** The image shows the yolk sac and the omphalomesenteric duct. Upper images were made using 3D US and maximum transparency tool, while the others were performed using HDLive US, note the 'shadows' than enhance image quality offering a 'real view' of embryonic structures

including 'magic cut' (Figs 9 and 17). In summary, this light source can be freely positioned to illuminate the desired area of interest.

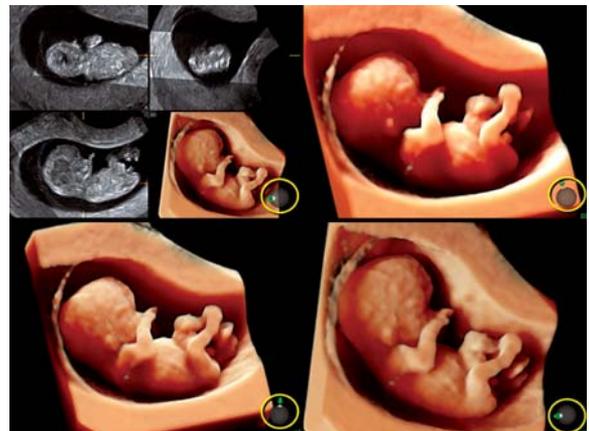
Sonographers can 'play' with the light source so that by using more light intensity they can produce more intensive



**Fig. 5:** HDLive US of the amniotic sac, a long thick umbilical cord and the yolk sac. Also the face, limbs and umbilical herniation are clearly seen from different 'light angles'



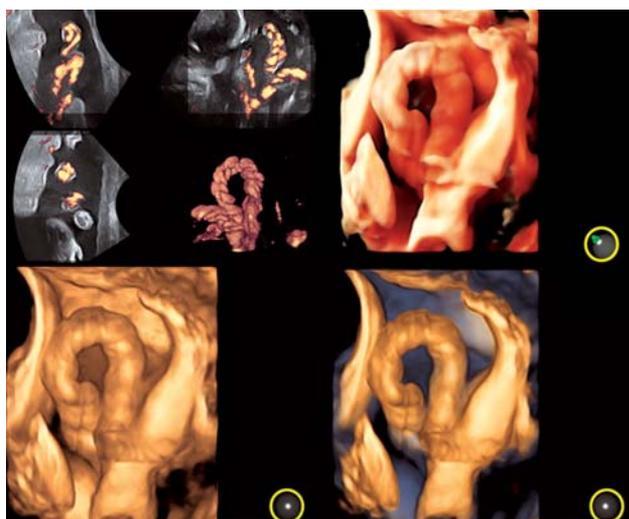
**Fig. 6:** Sagittal view of the fetus using surface 3D mode (upper left) showing the 'typical' yellow color. The other images show HDLive US of the same region of interest, clearly showing the enhancement of the image quality, allowing a better view of fetal structures



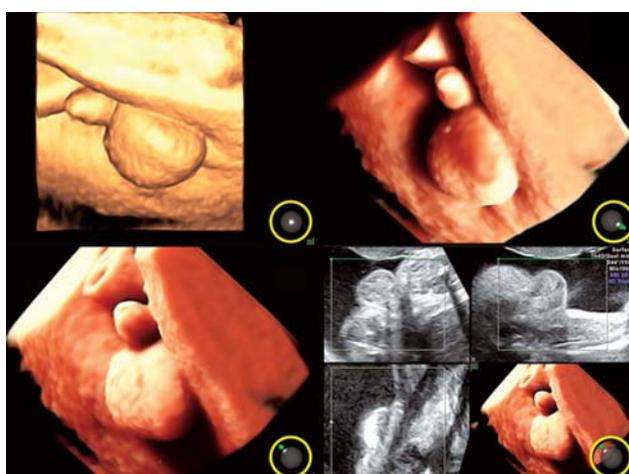
**Fig. 7:** The previous case in orthogonal planes (upper left); the frontal view of the fetus (of just 14 weeks) is 'spectacular'. Note the fetal structures, especially the limbs with the 'shadows' created as the light source moves around the region of interest



**Fig. 8:** The image of a fetal face using conventional 3D US surface mode (upper left) and HDLive technology



**Fig. 9:** Umbilical cord with normal flows (upper left); HDLive image (upper right) and conventional 3D US (bottom). Magic cut (upper left) has been used to observed the umbilical cord isolated



**Fig. 10:** Male genitalia observed with conventional 3D US (upper left) and HDLive US. Note the difference in image quality

shadows, which allow generation of better pictures and enhancement of image quality. They can also 'play' with the 'global' image by rotating it on a desired orthogonal plane or by using the sonographic cutoff system. By seeing what is looked for with better lighting and with a sense of depth, a better image is obtained.

The virtual light source can illuminate globally from the front, from the back, from the sides, placing it on the side where viewing is desired.

When the light source is positioned behind the region of interest, splendid effects of translucency can be obtained<sup>2</sup> giving the operator the opportunity to create lightening and shadowing effects increasing depth perception and improving 3D image quality.

It thus allows a more natural and better image quality, a better sensation of 'depth' and an easier visualization of inner tumor structures (papillae, wall thickness, endophytic growths, etc).<sup>3</sup>

Images can be generated *a posteriori* from material stored in the computer, which facilitates teaching. They can be used in daily clinical practice and showing the HDLive images to the patients can help to improve physician-patient communication, and also may facilitate a more complete understanding of ultrasound results, especially when pathologic findings are diagnosed.

In obstetric patients, HDLive provides embryo and fetal images of stunning quality, which allows couples the possibility of understanding findings,<sup>4-8</sup> and especially of understanding malformations.<sup>9-11</sup> Also this mode has been used in assisted reproduction<sup>2</sup> and gynecological oncology with success<sup>7,8</sup> showing a better image definition quality.

## OBSTETRIC APPLICATIONS

It is well accepted that 3D ultrasound allows an early observation of embryonic and fetal structures; moreover, 3D combined with 2D ecography results in a perfect combination to diagnose malformations early in pregnancy, but also in specific fetal organs.<sup>9</sup>

The next figures show normal pregnancies to notice quality image improvement obtained with HDLive technology.

### 4th Week + 5 Days Pregnancy

Here, we can visualize the yolk sac with the chorion frondosum (Fig. 2).

### 5th Week + 4 Days Pregnancy

The main ultrasound features are the yolk sac and the embryo (Fig. 3).

## 6th Week Pregnancy

The embryo is growing in the longitudinal axis, the cranial and caudal pole are shown, the yolk sac separates from the embryo and the omphalomesenteric duct is clearly seen (Fig. 4).

## 9th Week Pregnancy

In this period we can observe well-delimited small structures corresponding to superior and inferior extremities; we can also see the amnion surrounding the embryo, a long omphalomesenteric duct and the yolk sac located outside the gestational sac (Fig. 5).

## 14th Week Pregnancy

Figures 6 and 7 show comparative views of orthogonal planes (Fig. 7) and surface 3D mode (Fig. 6) in a 14th week normal gestation. Observe how many details can be seen when using this new technology, in comparison with conventional 3D.

## 34th Week Pregnancy

This last image of normal gestations shows the fetal face of an advanced pregnancy using conventional 3D US and HDLive technology, both technologies result in images of great quality, but once again HDLive images adds increased sensation of 'natural' shapes, volume and deepness that mimics a 'photo-like' picture of a newborn.

## MISCELLANEOUS

### Umbilical Cord

We have selected (Fig. 15) some umbilical cord images to show that HDlive software could be use for the study of specific organs and areas of interest. This novel technology shows a great potential for the diagnosis of fetal malformations, as recently proposed.<sup>3,10,11</sup>

### GENDERS

In clinical practice, the physician is frequently asked for the fetus' gender. HDLive images improve physician-patient communication with the aid of life-like images (Fig.10).

## INTERESTING APPLICATIONS IN PATHOLOGIC SITUATIONS

### Nuchal Translucency and Hygroma Colli

#### Nuchal Translucency

Determination of nuchal translucency (NT) thickness has become the standard technique for establishing prenatal risk for chromosomal abnormalities. The risk increases with maternal age, thickness of NT and gestational age.<sup>12,13</sup>

As an ultrasound marker of chromosomal anomalies, NT exceeds 3 mm in 80% of fetal trisomías. Under physiological conditions NT develops because an excess of lymphatic drainage into the still immature internal jugular vein.<sup>12</sup>

It continues until the complete development of the veins and neural components of the posterior fosse and the foramen magnum and closure of the vertebral column. An increase in pressure would result from the lymphatic excess.

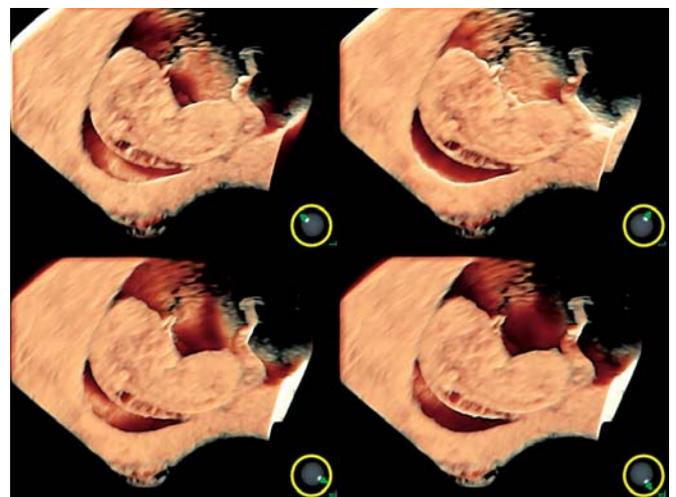
The incomplete development of the intervillous space, added to the lack of closure of the axis and atlas, act as a defensive window of decompression that prevents a potentially pathological increase in pressure.

This transitory window of decompression protects the CNS of hyper perfusion. This is a vascular phenomenon that results from increasing blood flow secondary to the rapid growth of the intervillous space after 9 weeks of gestation. The increase of blood flow creates an overload mechanism in the right chambers of the heart, resulting in a transitory cardiac insufficiency.

For this reason it is easily manifested in fetuses with congenital cardiopathies as in the case of aneuploidias which show structural and functional failure of the canalicular, lymphatic and cardiac system.

Measurement of the NT is well and internationally established.<sup>13</sup> Nevertheless, we have insisted in the importance of the use of the 3D for the morphological evaluation of the NT, showing that the presence of walls, septae, bullae and papillae might worsen the prognosis and are frequently related to cromosomopatias.<sup>12</sup>

Figure 11 shows outstanding findings of HDLive, like the clear visualization of septae in the inner part of the NT which means a worse prognosis.



**Fig. 11:** HDLive US view of a NT in an 11 weeks pregnancy. Note in yellow circles that is the light source entering from different points. Observe the 'membranes' and septums in the inner part of the NT

### Hygroma Colli

In these cases NT may increase owing to a failure of communication between the lymphatic sacs and the jugular veins (monosomies, trisomies, etc.) or owing to general edema and anasarca.<sup>12</sup>

Hygroma colli curses with cysts, bullae and septations almost always associated with Turner syndrome and trisomies (Fig. 12).

### TWIN PREGNANCY AND THE VANISHING TWIN SYNDROME

The following picture shows a twin gestation with one normal gestational sac and embryo; however, the other sac is considerably smaller and without evidence of the embryo (Fig. 13).

### TIPLETS AFTER ICSI

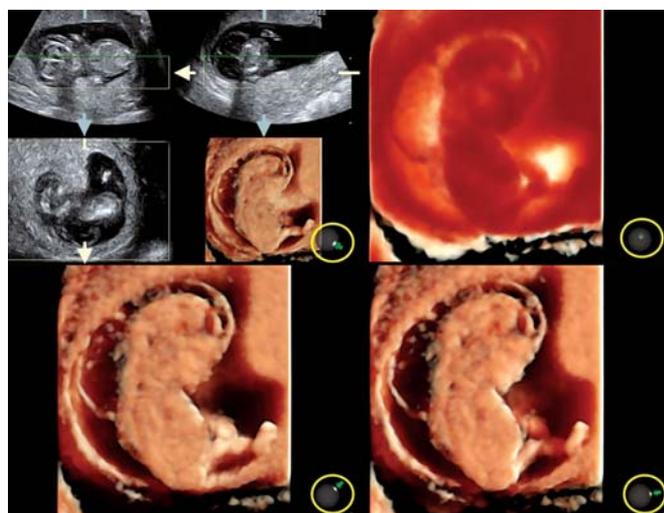
Herein we show a pregnancy obtained after assisted reproduction technique (ICSI) due to severe male factor. Interestingly, only two embryos were transferred under ultrasound guidance; however, the result was a triple gestation (two monozygotic twins and one single gestation) (Fig. 14).

### UMBILICAL CORD CYSTS

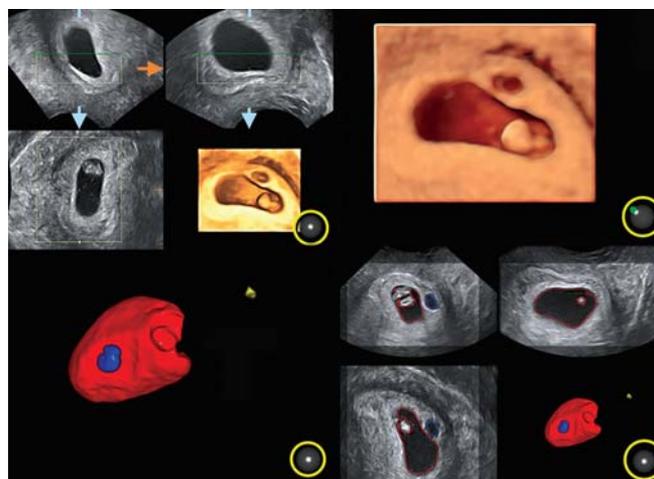
Are rare findings and are classified as:<sup>14,15</sup>

Celomic epithelium cysts, or amniotic epithelium-inclusion cysts, develop in a small area in any part of the cord where a portion of the amniotic membrane is trapped.

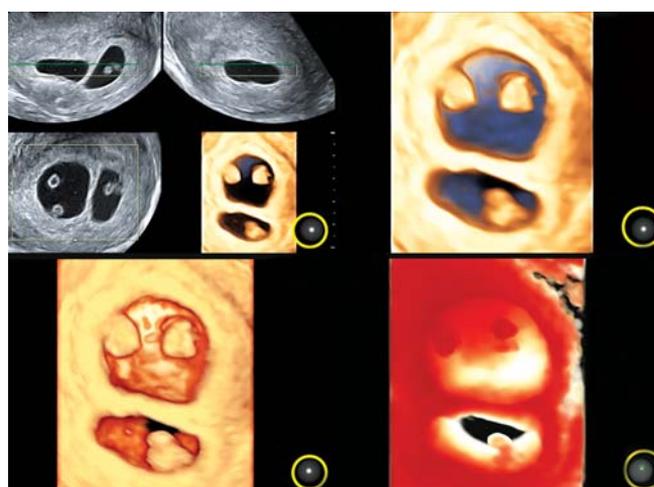
Pseudocysts do not have epithelium. They develop in areas of edema and/or necrosis in Wharton's jelly.



**Fig. 12:** Enormous hygroma colli observed with maximal luminescence and HDLive. Bullae and septations are clearly observed



**Fig. 13:** Vanishing twin syndrome. The images show a twin pregnancy in which one of the gestational sacs is considerably small and underdeveloped. Upper left: 3D US orthogonal planes and image rendering. Upper right: HDLive clearly showing the difference between the two sacs. Bottom: Automatic volume calculation of the gestational sacs, the vanishing sac is depicted in blue



**Fig. 14:** Upper: Orthogonal planes using conventional 3D in surface mode. Bottom left: View in detail of the monozygotic pregnancy (top) and the single one (down). Bottom right: HDLive view using transparency mode, note the clear visualization of the sacs and embryos in 'photo-like' anatomic image

True cysts develop from the following embryonic remnants:

- The allantois, which has a simple cuboidal epithelium
- The omphalomesenteric duct, which has a secretory columnar epithelium
- The amnion
- Cysts that originate in blood vessels.

True cysts have been associated with chromosomal and pseudocysts with congenital anomalies, although the magnitude of the association, especially with trisomy 21, is not known. The likelihood of an association with a chromosomal disorder or with a congenital anomaly seems to depend on origin, time of appearance, the size, the number and the location of the cyst.

**Table 1:** Association of umbilical cord cysts with chromosomopatias and malformations

Feature	Low-risk	High-risk
Size	<5 mm	>5 mm
Gestational age at detection	Before 12 weeks' gestation	After 12 weeks' gestation
Resolution	Before 12 weeks' gestation	Persistent
Appearance	First trimester	Second and third trimester
Walls	Smooth, regular borders	Irregular borders
Location	Centrally located	Close to fetal abdomen or placenta
Number (also for pseudocysts)	Single	Multiple
Risks	None	Omphalocele/urinary/vertebral/patent urachus defects, Meckel's diverticulum, Polyhydramnios
Chromosomopathy risk	Pseudocyst	Cyst
Structural defect risk	Cyst	Pseudocyst
Overall risk	1 to 2%	13% for trisomy 13 or 18. Also risk for trisomy 21

Table 1 shows the differences between low-risk and high-risk umbilical cord cysts.

Pseudocysts occur with greater frequency and have a lower association with chromosomal anomalies, but are associated with structural defects, especially if observed late in gestation.

Are usually small, well defined, appear as oval or round structures, have a smooth and regular contour, and their walls are homogeneous and hypoechoic. They lack internal echoes, and are eccentrically situated in relation to the longitudinal axis of the umbilical cord.

3D sonography allowed much more clarity than 2D imaging in visualizing malformations (Figs 15 and 16).

**Acrania, Exencephaly Anencephaly**

These severe malformations are thought to evolve around three phases that start from a single process and as a

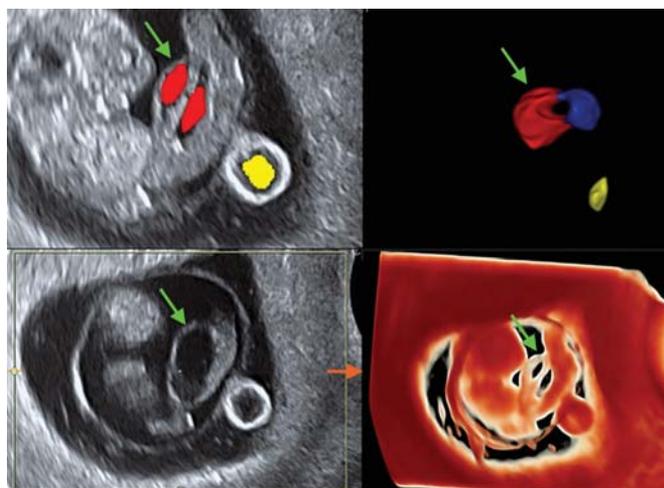
consequence of an early closure defect of the anterior neuropore, which normally occurs in the 4th week.<sup>16,17</sup>

Anencephalic fetuses have the absence of the cranial vault and partial or total absence of cerebral hemispheres. Fetuses with exencephaly and acrania on the other hand, show partial or total absence of the calvarium, but have complete or partially preserved cerebral masses.

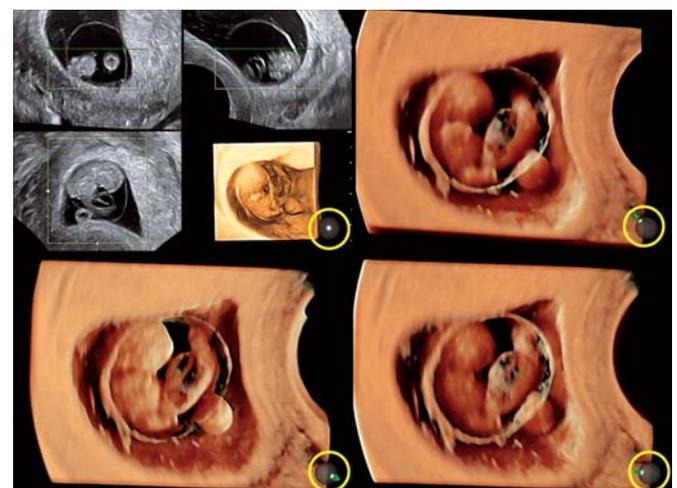
It starts in early pregnancy as an acranium fetus (absent skull bones). It progresses with gestational age to exencephaly (presence of brain tissue, with or without meninges, exposed in the amniotic fluid). The last stage of the sequence is the anencephalic fetus, which is the most common variety of the sequence observed in newborn babies (Fig. 17).

**Omphalocele or Exomphalos**

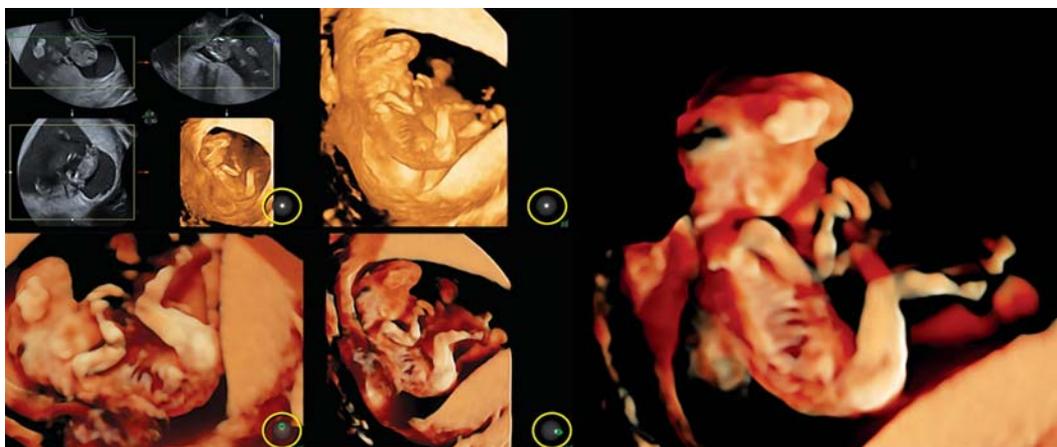
Is a fetal ventral wall defect characterized by herniation of some of the gut into the base of the umbilical insertion



**Fig. 15:** Umbilical cord cyst observed with AVC and VOCAL (above), 2D and maximal luminescence (below). 2D and maximal luminescence show more clearly that the cyst is located in the central part of the umbilical cord, is double, irregular and has the form of a number eight



**Fig. 16:** Orthogonal planes, 3D and HDLive of the same cyst. This last technique allow a better resolution and quality

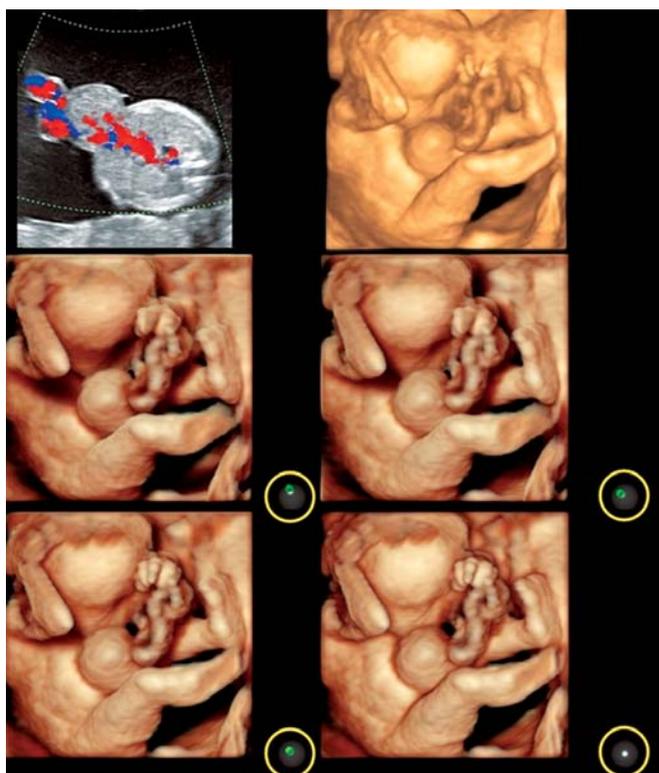


**Fig. 17:** We compare a case of inencephaly studied using orthogonal planes, 3D and HDLive. HDLive allows a much better perspective of the whole malformation

(Fig. 18). The whole herniation is coated by a fine limiting membrane, nearly transparent and very similar to the amnion or peritoneum, through which the herniated abdominal structures can be seen in the newborn.<sup>18,19</sup>

The umbilical cord is always inserted, and fully conserved, in the herniated sac apex, where the vessels arrive, which can be clearly studied with color Doppler (Fig. 18).

The most common herniated organs are the gut loops, the stomach, and depending on the sac size the liver, and in exceptional cases the heart (i.e. pentalogy of Cantrell).



**Fig. 18:** *In vitro* fertilization twin pregnancy with a normal fetus and the second showing an omphalocele with abnormal hands configuration

The diagnosis can be established in the first trimester of pregnancy after week 12 to avoid the confusion with the physiological herniation.

The omphalocele is usually associated with chromosomal abnormalities (35-60%). Most of them are trisomy 18 (70-80%) and less trisomy 13, triploidies and Klinefelter's syndrome.

Chromosomal anomalies are very usual when the herniation contains only gut loops (65%), and are very rare when the liver is the herniated organ. Nevertheless, this second eventuality is usually associated with other structural malformations.

Among the most frequent other associated organ malformations in omphalocele with aneuploidies (50%) are: Facial, renal, neural or limb defects.

When there is no a chromosomal disorder, omphalocele is also frequently found associated with other structural anomalies, such as cardiac (50%), kidney, gastrointestinal, facial, neural, limb anomalies or growth restriction.

## COMMENTS

Although its capability needs to be further explored, HDLive technique represents, in our opinion, an innovative tool and a step toward an even more realistic anatomical visualization of embryo and fetal surfaces.

The full potential of this new technology is still to be revealed<sup>1-8,10-12</sup> and, we believe, that its clinical use may go beyond the gynecological field. The volume ultrasound technology software HDLive represents, in our opinion, an innovative tool, a step toward an even more realistic anatomical visualization of fetuses and gynecological organs.

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