3D AND 4D SONOGRAPHIC ASSESSMENT OF MULTIPLES

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INTRODUCTION

Three-dimensional sonography (3D US) provides completely new modalities of sonographic scanning including coronar section imaging, three-dimensional reconstruction, volumetric calculations and angio-mode. Improved visualization rate, depiction of spatial relationship, "sculpture like" plastic imaging and volume measurement are the main benefits of new technology. Acceleration in scanning and rendering capabilities of the last generation of three-dimensional machines provided three-dimensional imaging almost in real-time. Stated another way/ surface rendered and multi-planar images can be observed in near real-time. This imaging technique is characterized as four-dimensional sonography (4D US). If one performs 4D US, accomplishing of three-dimensional image reconstruction is less time consuming because simultaneous with probe movement adequate image is displayed. Therefore, 4D US is more suitable and acceptable for routine prenatal care than 3D US.

3-D MULTIPLANAR IMAGING

Multiplanar imaging offers an option of synchronous scanning in three orthogonal sections, including even coronal section. Computer data processing provides numerous sections unobtainable by 2D US. Multiplanar view will result in simultaneous depiction of three sections orthogonal one to the others. Two of them (transverse and longitudinal) are dependent on angle of insonation, whereas the third one (coronal) is not. This section is orthogonal to the insonation beam.

Because of limitations regarding probe manipulations due to the anatomy of female reproductive tract and contemporary probe design some sections are unobtainable by 2D US. Using this method, the examiner should be aware that sometimes all gestational sacs are impossible to visualize in sections referent for counting of the gestational sac, measurement of the gestational sac diameter and confirmation of the presence of embryo within each gestational sac. Furthermore, poor visualization rate of desired sections for evaluation of anatomy of each fetus and placental junction are the main limitations of two-dimensional sonography in the second trimester. Because significant amount of referent sections are unachievable in multiple gestation by two-dimensional sonography, this method is not completely suitable.

The ideal visualization rate of a desired structure regardless of its anatomical limitations is the major advance of 3D US. This advantage can be used when the finding of 2D sonography is incomplete in terms of either number and quality of gestational sac in the first trimester, fetal anatomy or placentation in the second trimester, due to inconvenient anatomical relations (Table 1).

Pregnancy number before the 6th week is determined by counting the number of gestational sacs (Figure 1.).

Using this method, the examiner must be aware of what has been characterized as the late-appearing twin phenomenon "undercounting". The late appearance of twins is recognized on the basis of the discrepancy between two sonograms, in which comparison of an initial sonogram, usually obtained at 5.0-5.9 weeks, and a subsequent sonogram 6 or more weeks demonstrates more embryos or fetuses than the previously counted gestational sacs.

Table 1. *Advantages of multi-planar imaging in management of multiple pregnancy.*

First trimester:
1. ELIMINATION OF UNDERCOUNTING PHENOMENON
2. IMPROVED PREDICTION OF SPONTANEOUS ABORTION
Second trimester:
3. IMPROVED DIAGNOSIS OF VANISHING PHENOMENON
4. EARLY DETECTION OF FETAL ANOMALIES
5. IMPROVED EVALUATION OF FETAL MALFORMATION
6. IMPROVED DETERMINATION OF PLACENTATION

Figure 1. *Transvaginal ultrasound of triplets at 6 weeks of gestation: There is a high probability for triplets as each gestational sac contains a single yolk sac. However, quadruplets can not be excluded from this static sonogram.*

Three-dimensional volume acquisition provides the possibility of simultaneous depiction of three orthogonal planes of examinations. Moreover, it is possible to perform systematic examinations of acquired volumes with three different directions of scanning. For example, frontal (coronal) plane enables examination of the uterine cavity in sections which are unobtainable with conventional 2D sonography (Figure 2).

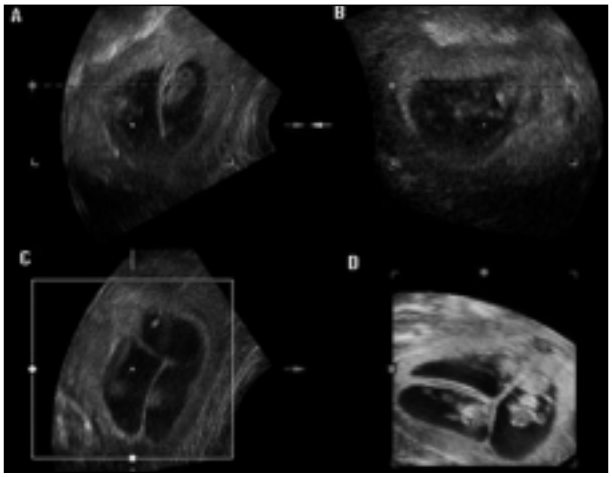

Figure 2. *Three-dimensional multiplanar view in determination of accurate number of gestational sac. Transvaginal multiplanar view of triplet pregnancy at 12 weeks. An example to illustrate possible pitfall regarding undercounting of the gestational sacs. The advantages of coronal section are presented (Figure 2C). In transverse section only two gestational sacs are present (Figure 2A), whereas on a sagittal section (Figure 2B) only single gestational sac is seen. On a coronal section, three gestational sacs with Y-sign are seen (Figure 2C). The most informative mode of three-dimensional sonography is its surface rendering mode (Figure 2D). Using this mode, in addition to the correct number of embryos, separation phenomenon can be seen which was unobtainable with conventional sonography. Using conventional 2D sonography, sagittal (Figure 2A) and transverse sections (Figure 2 B) of the uterus are seen. First two images (Figures 2A,2B) represent the limits of 2D in which twin pregnancy is diagnosed. However, on the third section-coronal plane (Figure 2C) three gestational sacs are clearly seen. This is finally confirmed by 3D reconstruction (Figure 2D).*

Further, 3D sonography enables the appropriate counting of gestational sacs without risk of undercounting even for less experienced ultrasonographers. Therefore, inter-observer variability in detecting the number of gestational sacs is significantly lower. Even quadruplets and quintuplets are recognizable without much difficulties. This advantage strongly suggests that 3D US should become the new standard in the early management of high order multiple pregnancies (Figure 3).. Before introduction of 3D ultrasound, 11% of bichorionic twins were initially undercounted as singletons, and 16% of high order multiple gestation were also undercounted.[1]

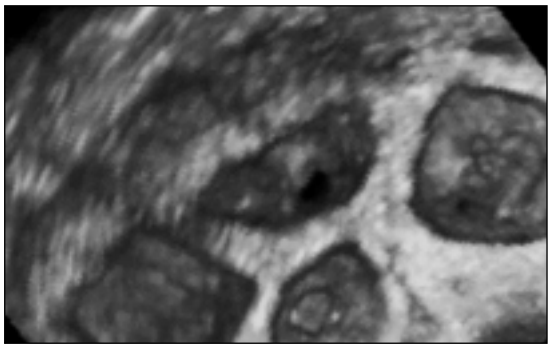

Figure 3. *Three-dimensional diagnosis of an accurate number of gestational sac. Final diagnosis of quadruplets with 3D surface rendering mode. In contrast to 2D manual slicing, an analysis of 3D volugrams reveals the accurate number of gestational sacs.*

The quality of gestational sac is an important parameter for management of multiple gestation and includes: gestational sac diameter, the ratio of mean sac to crown-rump length, presence or absence of embryo within the gestational sac.

First-trimester spontaneous abortions can be predicted from alterations in the gestational sac size. For this purpose nomograms relating the ratio of mean sac diameter to crown-rump length (S/CR) to the gestational age (last menstrual period [LMP]) were constructed.[2] Using this method a sensitivity of 78.3%, a specificity of 97.8% and a false-positive rate of 2.2% can be achieved. Therefore, S/CR measurement in early pregnancy is a simple and reliable method of predicting first-trimester abortions.

Embryo is recognizable sonographically at 7th weeks of gestation (Figure 4). Therefore, reliable confirmation of the presence or absence embryo or embryos within each gestational sac should be then performed. An empty gestational sac in high-order pregnancy should be recognized as vanishing phenomenon (Figure 5). The viability of each embryo can be confirmed using color Doppler imaging of circulation (Figure 6).

Figure 4. *Transvaginal ultrasound of triplets at 8 weeks of gestation: 3 embryos in three gestational sac (TCTA-trichorionic-triamniotic triplets)*

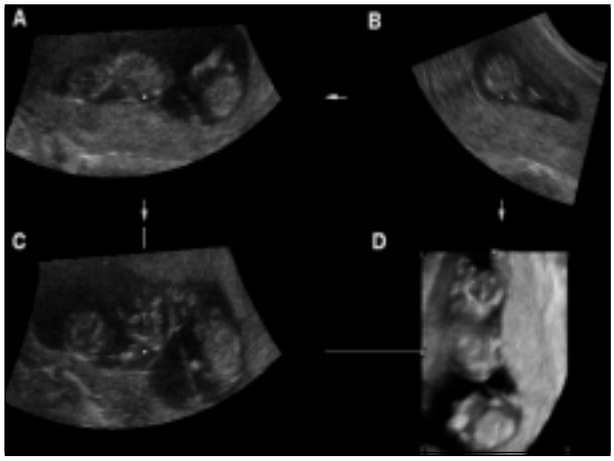

Figure 5. *Transvaginal multiplanar view of missed triplet pregnancy at 12 weeks of gestation. An example to illustrate possible pitfall regarding missed triplet. The superiority of surface rendering mode over multiplanar view is presented (Figure 5 C). In transverse section two fetuses within gestational sac are present, whre as the third gestational has triangular shape and seems empty (Figure 5 A). On sagittal section only single fetus within gestational sac (Figure 5 B) is seen. On coronal section, three gestational sacs with Y-sign are seen. According to images in transverse and coronal sections there is suspicion for missed triplet. The surface rendering mode confirmed definitively that the gestational sac is empty and the diagnosis of missed triplet.*

Figure 6. *Diagnosis of the viability of each triplet: color Doppler reveals three viable embryos*

A recent meta-analysis showed that more than 50% pregnancies with 3 or more gestational sacs have spontaneous reduction before 12 weeks. The surviving fetuses weigh less and are born earlier than unreduced pregnancies with the same initial number of fetuses.[3]

When spontaneous reduction is suspected in high-order multiple pregnancy on conventional sonographic exam, the additional use of surface rendering mode is recommended. If one uses surface rendering mode, distinguishing between the spontaneous reduction and normal pregnancy in high-order pregnancy can be easily done (Figure 5).

Genetic defects in multiples

Congenital defects are classified into two main groups:

1. Those unique to twinning such as twin to twin transfusion syndrome, conjoined twins, acardia and fetus in fetu.
2. Those not unique to twinning but more common in twins, such as anencephalus, hydrocephalus and congenital heart disease

The knowledge of sonoembryology enables diagnosis of fetal anomalies in the first trimester.
Three-dimensional sonography is useful to recognize the surface morphology of embryos and early fetuses[4] (Figure 7).

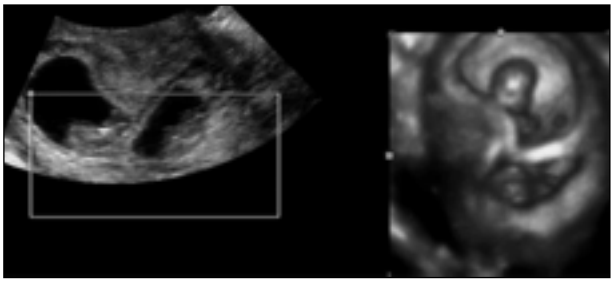

Figure 7. *Comparison between 2D (left) and 3D sonography (right). Both modalities provides an examiner with essential information concerning the management of twin pregnancy including number of fetuses and chorionic status. The advantages of spatial visualization in early pregnancy include improved visualization of both fetuses and their gestational sacs. The relationship between the size of fetus and gestational sacs can be assessed on single.*

Maggio and colleagues reported in 1985 about the first-trimester ultrasonic diagnosis of conjoined twins.[5] Since then several cases confirmed the use of proposed diagnostic criteria.[6,7,8] The great progress concerning the time of diagnosis-embryonic and early fetal period is achieved, however it seems that delineating of organ sharing can not be properly done before the second trimester. Moreover, examiner must be aware that following criteria proposed by Maggio is sometimes problematic because two cases false positive diagnosis of conjoined twins are reported.[9,10]

Unfortunately, two-dimensional transvaginal sonography limits the number of examination planes to sagittal and transverse. Because the uterus can only be examined in these two planes, it is possible that examiner fails to visualize the coronar section through fetus. Stated another way, a conjoined twin are overlooked.

This problem can be solved using both modalities of the three-dimensional sonography, multiplanar view and surface rendering view. Using the multiplanar imaging the visualization rate of coronar section through fetus is 100%, due to unlimited number of section which can be generated by data manipulation.

Maymon and colleagues reported that in a case of conjoined twins at 10 weeks of pregnancy, the exact area could be successfully identified by transvaginal three-dimensional ultrasound.[11] We diagnosed this anomaly at 11 weeks of amenorrhea in a fetus of 27 mm in maximum length, showing two separated heads with twins joined at level of the thorax (Figure 8). The fetal orientation remained unchanged despite manipulation with transvaginal probe and prolonged scanning by sonographers.

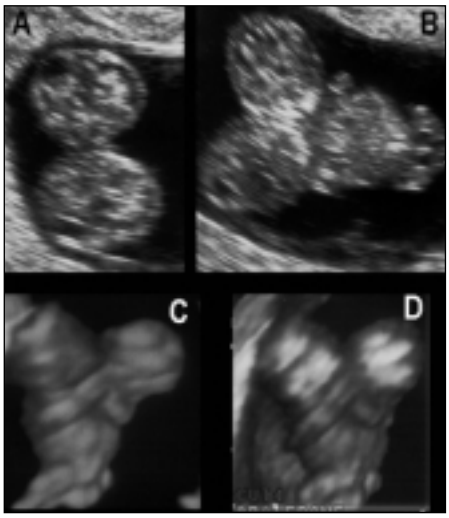

Figure 8. *Conjoined twins at 12 weeks of gestation by 2D and 3D transvaginal sonography. Figure 8A and 8B shows transverse sections through fetal heads which reveals two normal heads adjacent each other. Figure 8C and 8D shows surface rendered reconstruction of conjoined twins is useful for classification of malformation-thoracophagus.*

The morphological anomalies of acrania and anencephalia could be confirmed even before 10 weeks of pregnancy. Bonilla-Musoles and colleagues reported two-dimensional diagnosis of two cases of anencephaly at 10 weeks of gestation.[12]

In a singleton pregnancy, the empiric risk for major fetal malformations is approximately 3%. In trichorionic triplets the empiric risk for major fetal malformations within each fetus is independent of the others, so that probability of having at least one malformed fetus is approximately 9% (59). According to the Eurofetus study sensitivity of a routine 2D sonography for detecting malformation is 61.4%.[13] The sensitivity is lower in multiple pregnancy as a consequence of overcrowding. As 3D US offers an ideal visualization rate of the desired structure, achieved by the manipulation within the volugram data, it is reasonable to expect that usage of this technology will increase sensitivity of the detection of malformations in multifetal pregnancies.

There are variety of anomalies involving the multifetal pregnancy. They can be divided in those unique to twins, especially monochorionic twins, such as conjoined twins or acardiac twins, and those not unique to twins such as neural tube defects, teratomas and congenital heart defects.

Three-dimensional sonography improves the diagnostic capability by offering more diagnostic information in evaluating fetal malformation, particularly in displaying the fetal malformations of the cranium, face, spine and extremities and body surface.[14]

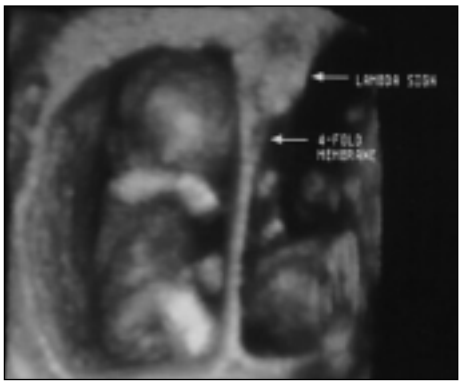

Figure 9. *Three-dimensional lambda sign and intertwin membrane. Spatial reconstruction of membrane take-off site provides easier differentiation between di-chorionic and mono-chorionic placentation.*

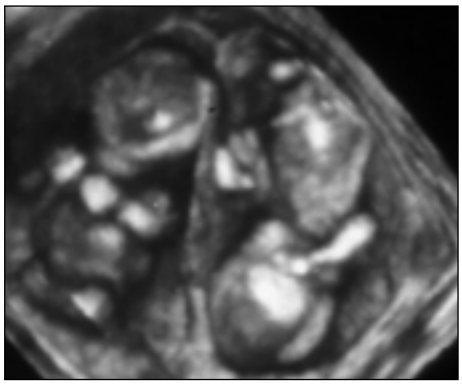

Figure 11. *3D scan of bichorionic-biamniotic twins in the second trimester of gestation. Figure 11 shows that on single image chorionicity and external frontal anatomy can be evaluated.*

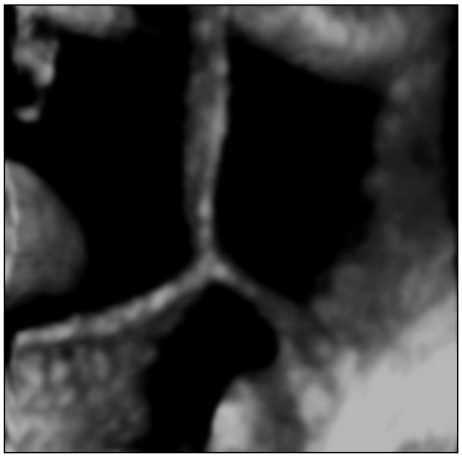

Figure 10. *3D ultrasound determination of the chorionicity in the late second trimester. "Mercedes" sign represents the junction of fetal membranes.*

Using 2D ultrasound, membranes can be evaluated, counted and measured only when they are at 90°. In other words, the orientation of the membranes studied should be positioned parallel with the transducer cristal array. Clearly, 3D ultrasound enables us to achieve a "perfectly" oriented picture. The rate of appropriate chorionicity determinations should be ideal (100%) in the second and third trimester (Figure 9 and 10). The most revealing area in which to study the chorionicity and amnionicity of the multifetal pregnancy is the location within the uterine cavity in which the membranes change the orientation of their surfaces from covering the placenta(s) or the uterine wall to meet each other and to form the inter-fetal or inter-twin membrane. Using 2D ultrasound this area should be studied by placing the scanning plane at 90° to the plane of the inter-twin membrane. This fact explains the potential role of 3D ultrasound in the examination of the origin of the inter-twin membranes. The most important step in management of the triplet pregnancy is determination of the number of placentas. When placentas are separate, this is not a problem. Unfortunately, the placentas are usually fused (Figure 11).

3D SPATIAL RECONSTRUCTION

Integration of data obtained by volume scanning can be used to depict 3D plastic sculpture-like) reconstruction of the region of interest (ROI). Three-dimensional reconstruction can be presented in surface mode. In the surface mode, only the signals from the surface of ROI are extracted and displayed in plastic appearance. Surface rendering provides an examiner with additional information confirming the normal anatomy either evaluation of the extent of lesion (Figure 8). Surface rendering provides spatial reconstruction of inter-twin area, which may be useful in distinguishing between conjoined twins from monoamniotic twins positioned next to each other. At present, it is the safest means to accomplish this distinction.

With 3D ultrasound conjoined twins can be demonstrated in three perpendicular two-dimensional planes (i.e. sagittal, coronal and transverse) which are simultaneously displayed on the monitor, allowing access to an almost infinite array of sections in any desired plane. On the other hand, surface rendering enables assessment of their topographic orientation to each other. From these acquired 3D volumes, the exact area of conjunction can be analyzed to assist in planning the postnatal management (Figure 8).

VOLUMETRIC CALCULATIONS

Three-dimensional measurement of the organ volume (volumetry) is obtainable using sequential slice-stepping measurements of areas through the volugram of the targeted organ. The volume assessment by 2D sonography includes the approximation of volume based on assumption that fetal organs have an ideal geometric shape, however it could be erroneous.

Two-dimensional volumetry of gestational sac volume (GSV) is performed using the ellipsoid formula, whereas the 3D volumetry is carried out in all three planes using the contour mode and the volume from the measured circumferences and the distances between them were computed by a software. 3D volumetry of first trimester GSV is superior to 2D volumetry in its estimation, but seems to be without a prognostic significance for gestational outcome in singleton pregnancy.[15] However our group consider that the comparison between volume of each gestational sac in multiple pregnancy could be an important parameter for confirmation of early concordant growth.

The prognostic meaning of early discordant growth in multiple pregnancy is still matter of scientific controversy. Some authors report about association of early discordant growth with major anomalies and poor pregnancy outcome.[16,17] In contrast, early discordant growth with normal pregnancy outcomes was reported.[18] All cases were after IVF ET was performed.

Gassner et al. proposed the role of sonographic placental volumetry as a mean of early detection of chromosomal anomaly in multiple pregnancy.[19] They described a bichorionic twin pregnancy discordant in growth with distinctly small placental volume of a growth restricted fetus at 12 weeks of gestation. These two markers were present before a severe heart defect and bilateral cleft lip and palate were sonographically recognizable. Placental volume should be recommended criterion for distinguishing between pregnancy at risk and without risk for major anomalies and poor outcome in multiple pregnancy.[19] Small placental volume in addition to growth restriction of one fetus early in the course of a twin pregnancy could be an important early marker influencing the decision for chorionic villous sampling at 12 weeks instead of amniocentesis at 16 weeks and it could lead to an earlier selective pregnancy termination of a triploid twin.

Placental volumetry is easy to perform when the placentas are separated. Unfortunately, in multichorionic pregnancies fusion of different placentas occurs during the second trimester. Therefore, volumetry should be performed at the end of the first trimester or at the beginning of the second trimester.

3-D ANGIO MODE

Three-dimensional angio-mode operates on technological basis of high-energy powered Doppler. Its greater sensitivity is related to direction independent scanning and better detection of smaller vessels. This mode provides optimal visualization and selective 3D reconstruction even of tortuous parts of vessels and blood flow arborization. More recently, 3D reconstruction of the vascular channels has been accomplished utilizing the Doppler amplitude mode.[20,21] The implementation of 3D power Doppler imaging permits the physician to investigate the anatomy and topography of hemodynamics within the particular organ or ROI.

The diagnosis of cord entanglement with 2D real-time sonography usually requires long examination period. Due to limitations of sectional imaging, examination is informative only to the quality and number of loops and final diagnosis is postponed. The main problem is distinguishing between adjacent and entangled cord. Cords positioned close to each other without torsion around one over the other umbilical cord is defined as adjacent umbilical cords, whereas, cords torquired one over other is called cord entanglement.

Much more information about umbilical cord can be obtained by 3D sonography. Three-dimensional power Doppler permits imaging of curvatures of the umbilical cord and the number of involved loops in entanglement can be easily determined. Counting the number of the loops involved in entanglement is useful method for longitudinal evaluation of entanglement.

There are two types of the umbilical cord knots: true and false. A focal redundancy of the vessels, which sonographically appear as a vascular protuberance that does not persist in all scanning planes is called false umbilical cord knot.[22] This condition should be differentiated between true umbilical cord knot which is a life threatening condition (Figure 12).

Figure 12. *3D power Doppler reconstruction of umbilical cord*

FOUR DIMENSIONAL SONOGRAPHY IN MULTIPLE PREGNANCY

Real-time 2D sonography enabled visualization of the spontaneous motor activity in singleton pregnancy. Reinold was one of the first to describe fetal activity using ultrasound, and he stressed the spontaneous character of early prenatal movements.[23] There are two types of motor activity in multiple gestation: spontaneous and stimulated. Spontaneous motoric activity is defined as each embryonic or fetal activity which not evoked by internal or external stimuli. On the other hand, activity evoked by inter-twin contacts is called stimulated activity. Spontaneous motoric precedes to the stimulated motoric. The effect of prenatal reactions evoked by internal stimuli in twinning phenomenon due to inter-twin contacts on the neurologic maturation was in the focus of interest of the systematic research initiated by the group Arabin et al.[24] They used real-time 2D sonography for detection and evaluation of the inter-twin contacts. Due to sectional imaging simultaneous visualization of both fetuses and assessment of their motor activity was impossible.

Therefore, motor activity of a single fetus was possible to assess and unfortunately only to a limited extent. Similarly the inter-twin area is tomogramically visualized and some of inter-twin contacts are overlooked.

Therefore, using this method distinguishing between spontaneous and stimulated motor activity is very difficult and sometimes impossible. If one performs 3D sonography, complete anatomy of more fetuses and embryos can be visualized simultaneously. In spite of achieved progress, this technology is not suitable for behavioral research because the images are static. Moreover, fetal movements which are in the focus of interest for behavioral studies cause significant artifacts in visualization.

Four-dimensional sonography (4D US) provides spatial visualization of the fetal anatomy and movements almost simultaneous with their appearance. Simultaneous visualization of the entire anatomy (head, body and extremities) of two or more fetuses with their movements can be achieved by 4D US. Therefore, the type of movements, isolated movement of each twin or high order multiple, inter-twin contacts and interactions can be recognized without difficulties (Figure 13-16). We found that movement activity of each fetus in twin or multiple pregnancy can be easily determined by 4D US in the first and early second trimester.[25] For the first time we can see that one twin is active whereas co-twin or co-triplets are active or not. Simultaneous visualization of motoric activity of each fetus enables study of their isolated motoric activity (Figure 13).

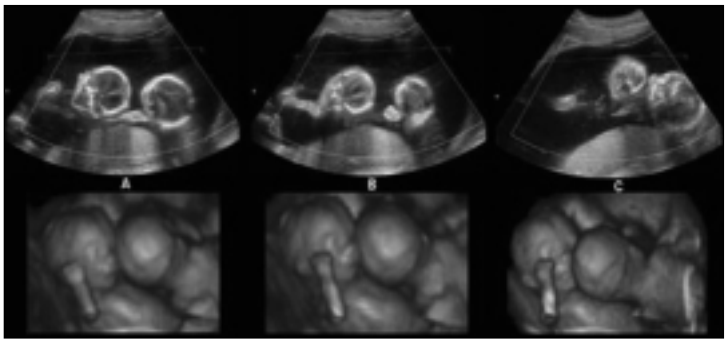

Figure 13. *Comparison between two techniques for evaluation of fetal behavior. Using 2D real-time sonography (upper) hand to head contact together with head inter-twin contact can be recognized. 3D image sequence (below) shows advantages of spatial visualization. Hand to head movement can be differentiated to the hand to ear contact with following the movement of the right hand forward.*

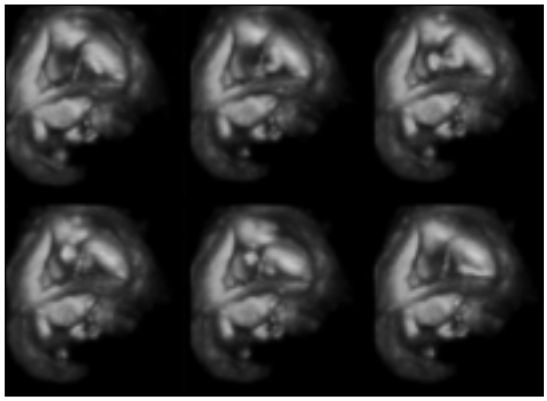

Figure 14. *4D image sequence illustrates reconstruction of fetal motoric activity in twins at 13 weeks of pregnancy.*

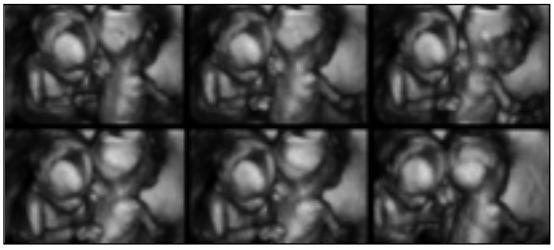

Figure 15. *4D sequence demonstrated intertwin contact. Note lateral head rotation from the second twin (right) when the first twin seems try to touch the second twin's back*

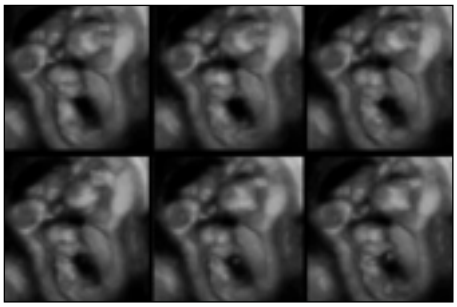

Figure 16. *4D sequence demonstrated separated evaluation of fetal activity of each twin in triplet pregnancy*

Arabin et al. defined for the first time inter-twin contacts.[20] Among them complex interactions can be recognized but complete definition of this phenomenon could not be achieved due to limitations of real-time 2D sonography. According to this group those movement patterns are consisted of initiations and reactions of both twins which are sometimes difficult to distinguish and last longer than a few seconds. Using 4D US complex parts of these interactions could be analyzed for the first time. Furthermore, 4D US could be useful in evaluation of the altered motoric development such as in pathologic pregnancy.[14] The delay in activity pattern is described in twins with triploidy XXX, and some activities such as yawning and stretching are even not present.[14] This is particularly important in dyzigotic twinning. Sadovsky stated " The possibility that movements of one twin stimulate the other to move was rejected by the fact that in no instant did one fetus move immediately after the second started to move".[26] Ferrari et al. also came to different conclusion. According to their observations inter-twin contacts have been supposed to cause increased rates of simultaneous twin activities in early pregnancy.[27] Finally, Arabin et al. used video documentation for continuous observation of inter-twin activity.[20] The first inter-human contacts were determined (action and reaction within a second of interaction). Using the speed of initiations this group found slow initiations followed by slow or fast reactions and fast initiations followed by slow or fast reactions.[20] 4D US could be used for further analyzis of the quality of inter-human contacts. The initiation and reaction movements are visualized in three dimensions allowing more detailed study of this subject.

CONCLUSION

Despite the great progress achieved in management of multiple pregnancy, due to limitations of two-dimensional sonography an additional three-dimensional scan is recommended, because it provides more reliable or additional information important for management of multiple pregnancy. Four-dimensional sonography has several advantages over three-dimensional sonography which include more economic concerning time consuming, elimination of movement artifacts and visualization of fetal movement in three dimension. Degradation in image quality of surface rendered or multi-planar view is compensated with mentioned advantages. Four-dimensional sonography is undoubtedly new powerful imaging tool whose total scientific and clinic potential should be established in the coming decade.

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