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The role of 3D and 4D ultrasound diagnosis and screening in first trimester

Diploma thesis

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Written Declaration

I declare that I completed the submitted work individually and only used the mentioned sources and literature. Concurrently, I give my permission for this diploma/bachelor thesis to be used for study purposes.

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Abstract

Early spontaneous abortions occur in 6-20% of all pregnancies; however, the exact mechanisms involved in these losses remain unclear.[12] In this context, several 2D ultrasonographic parameters have been tested as predictors of early gestational losses including the shape and diameter of the yolk sac, and embryonic heart rate. The mean gestational sac diameter has also been correlated with gestational age and fetal growth.

There have been first trimester studies on the volumetric examination of the gestational sac, amniotic fluid, placenta and yolk sac.

This dissertation will focus on early pregnancy loss and the investigation of its etiology. Conventional ultrasonographic methods will be reviewed and compared with novel, more sophisticated methods in order to evaluate if scientific research has come closer to the etiology and early diagnosis of miscarriage. Special focus will be put on the predictive value of gestational sac shape and volume.

Introduction

Since the first obstetrical application of ultrasound imaging by Donald and co-workers (1958), this technique has become indispensable for evaluation of the fetus.[5]

Ultrasound imaging is used on a daily basis to identify pathology and confirm normality. 3DUS has added major new capabilities to the assessment of anatomical structures.

Gonçalves et al. [9] have given a summary of 3D ultrasound advantages:

- Actual 3D visualization rather than mental reconstruction.
- Many planes can be used
- Review of volume data possible after the patient has left the examination room
- Different kinds of volume rendering available
- Rotation and examining anatomical structures from different perspectives
- Improved accuracy for volume measurements including volume of irregular objects
- Possibility to standardize ultrasound examinations
- Ability to transmit data over networks for consultation in tertiary care centers
- Potential use of offline software programs as an interactive education tool
- 4D incorporates motion information into 3D volume datasets and fetal heart can now be examined using either spatiotemporal image correlation (STIC) or 2D matrix array technology

3D/ 4D is now used as a target scan, after an initial diagnosis has been established on 2D scans.

Early pregnancy loss

Definition. Abortion, or miscarriage is defined as expulsion of a fetus <500g, occurring before week 20[14]. An abortion is termed early, if it occurs before week 12. The majority of these pregnancy losses are due to fetal chromosomal abnormalities[14].

Epidemiology. Spontaneous abortions occur in 15- 25% of all pregnancies[14]. Miscarriages in week four to six are often not noticed or confused with late menses, hence an even higher incidence is suspected[14].

Pathology. Hemorrhage into the basal part of the decidua causes tissue necrosis[5]. In early abortions, the ovum detaches and stimulates uterine contractions leading to expulsion of the products of conception[5].

Etiology. 80% occur by week 12[5]. In more than 50% of these cases, a chromosomal abnormality can be found[5]. Relative risks seem to increase with increasing number of parities, advanced maternal, as well as paternal age[5]. Another underestimated risk factor is conception within three month post partum[5]. Abortions preceding the third month of gestation are commonly characterized by preceding fetal death, whereas later cases show expulsion to be the initiating event with fetal demise occurring secondarily[5].

50% of all miscarriages are idiopathic, raising interest among obstetricians to determine possible causes[14].

Diagnosis. A patient suffering from early abortion clinically often presents with vaginal bleeding, cramping, abdominal pain and possibly with decreased symptoms of pregnancy[14].

It is possible, however, for the patient to be asymptomatic.

Royal College of Obstetricians and Gynecologists (RCOG) guidelines for diagnosis of fetal demise are[3]:

- CRL >6mm without fetal heart rate
- Chorionic cavity diameter >20mm without embryo or yolk sac

Therapy. Hemostasis has to be established, followed by POC (products of conception) assessment[14]. If this shows incomplete abortion, further steps have to be taken to prevent adverse outcomes, namely hemorrhage, infection and trophoblastic disease.

One can await spontaneous completion or interfere with expectant management, such as dilation and curettage or administration of the prostaglandin misoprostol[14].

Fetal factors	
Abnormal development of:	zygote, embryo, fetus
Aneuploidy:	Trisomy, monosomy, tri- and tetraploidy, chromosomal structural abnormalities
Euploidy:	Usually aborts later than aneuploidy
Maternal factors	
Infections:	Mycoplasma, Ureaplasma, Lues, CMV, HSV, Listeria, Chlamydia, GBS, possibly Toxoplasma
Chronic debilitating disease:	Carcinomatosis, TBC, coeliac
Endocrine abnormalities:	DM, progesterone deficiency, hypothyroidism; polycystic ovarian syndrome
Drugs and environmental factors:	Tobacco, alcohol, caffeine, radiation, contraceptives, environmental toxins (lead, benzene, arsenic, formaldehyde, ethylene oxide)
Immunologic:	Anti-phospholipid syndrome, inherited thrombophilia, SLE
Uterine defects:	Leiomyomas, Asherman syndrome, developmental defects, incompetent cervix (conization, obstetric trauma, curettage, cauterization, amputation, in utero DES exposure)

Table reproduced from Williams Obstetrics 22nd edition (p.134-7) and Clinical Obstetrics and Gynecology 1st edition (p. 165-7)

Routine ultrasound scans in 1st trimester

Ultrasound is a very popular tool in obstetric diagnostics and treatment. As it is non-invasive and safe, the average pregnant woman is advised to attend three routine scans throughout her pregnancy. A short overview is listed below.

First screening. The first routine evaluation normally takes place in week 6-12. or 11-14[17]

Its main concerns are[7],[17]:

- diagnosing a viable pregnancy
- exact determination of gestational age
- crown- rump length (CRL)
- biparietal diameter (BPD)
- transverse abdominal diameter (TAD)
- nuchal translucency (NT)
- femoral length
- choroid plexus, planum frontooccipitale, cerebellum
- vertebral column
- presence of all four extremities
- heart
- urinary bladder

The aims of early pregnancy scanning are to determine viability, gestational age and fetal number[13].

The gestational age can either be calculated from the last menstrual period (LMP), or can be measured by CRL[13]. As a rule of the thumb, 10mm refers to a mean gestational age of seven weeks, 30mm to about nine weeks and 5days, and 60mm to about 12 weeks and three days.[13]

The earliest sign of a viable intrauterine pregnancy is possible to be visualized at 4,5 weeks (day 31 mostly) via TVA and about one week later via TAA. At this time the chorionic cavity measures about 2-4 mm.[13]

The chorionic cavity contains the amniotic cavity, the fetus and the yolk sac[3]. An intrauterine gestational sac can be identified, containing a fetal pole and a fetal heart[13]. A visible cardiac pulsation confirms viability. The yolk sac appears in week five, but has no predictive value other than confirming an intrauterine pregnancy[13].

A non-viable pregnancy is diagnosed, if no fetal heart rate can be found[13]. Such a pregnancy will result in miscarriage. If there is no visible embryo and no fetal heart rate, this is termed anembryonic[13]. Evaluation has to be done carefully, as an empty gestational sac can be a sign of an early viable pregnancy or an ectopic pregnancy as well[13]. Therefore, if the mean sac diameter is less than 20mm or the CRL is less than 6mm, a repeated scan should be undertaken after at least seven days[13].

Once viability is confirmed, the gestational age can be investigated. Other than LMP, ultrasonographic parameters such as CRL, BPD, FL, volume and diameter of the chorionic cavity can be matched with population and race specific computerized growth charts to determine the gestational age[16]. The earlier this is done, the more exact the due date will be. TVA ultrasound is best in week 1-9[3].

Nuchal translucency, another hallmark of early ultrasound scans is one of the most commonly used predictors of numeric chromosomal aberrations[15]. It is measured in week 11-14[15]. Exact measurements need visualization of a lateral profile of the fetal head, visible nasal bones and amniotic fluid at the posterior aspect of the neck[15].

Second screening[7]. In week 18-22, ultrasonographic documentation includes:

- biometry
- amniotic fluid volume
- exclude intrauterine growth retardation (IUGR)
- evaluate and determine umbilical blood vessels
- determine location of placenta

Biometry[17]. Biometry scans are done from head, abdomen and extremities. They assess normal fetal groth and development. On the head, the examiner checks BPD, frontooccipital diameter, head circumference and transverse diameter of the cerebellum. Important measurements of the abdomen are transverse diameter of the abdomen, abdominal sagittal diameter and abdominal circumference. Limb measurements include femoral and tibial length as well as dimensions of fibula and humerus, radius and ulna.

Sonoanatomy[17]. Sonoanatomical documentation is required to exclude morphological abnormalities. The cranium is investigated for contour, lateral ventricles, choroids plexus cysts, cerebellar abnormalities. Facial abnormalities,

such as cleft lip and cleft palate is ruled out by frontal visualization of nose and mouth, along with median sagittal plane- the lateral profile of the fetus. The neck contour can be evaluated as well for cystic hygroma and NT. Neural tube defects manifest as closure defects in the thoracolumbal spine and the overlying skin. Therefore sagittal longitudinal planes and skin contour over the vertebral comlumn are documented. Fetal heart frequency and rhythm are measured. In the thorax, lung structure is noted.

Third screening. week 28-32[7]:

- biometry
- exclude IUGR and macrosomia
- Doppler US evaluation
- Fetal position
- Exclude cervical insufficiency

The third trimester scan has similar targets as the second trimester scan. Previously noted defects are followed up and evaluated in more detail. Routine evaluation of the heart consists of its size, shape, position, 4-chamber-view as well as RV- and LV- outflow tract[17]. Contour and topography of liver, stomach and diaphragm along with intestinal echogenicity are investigated. Kidney, urinary bladder and extremities are checked[17].

These are routine scans, every normal pregnancy is subject to. If any risk factors are present, or developmental abnormalities have been found, more sophisticated and advanced techniques can be used. High risk groups can be provided with fetal echo, amniocentesis, chorionic villi sampling, periumbilical fetal blood sampling or fetoscopy[17].

Examples of detectable anomalies on ultrasound are: nuchal translucency (autosomal trisomies), choroids plexus cysts (trisomy 18), cystic hygroma, omphalocele, megacystis[17]. The most common findings are however cardiac defects[17]. An echogenic intracardiac focus 'white spot' can be a sign of Down's syndrome[17].

Second trimester ultrasound examinations are helped by integrating the values of the maternal serum values of the triple test (estriol, MSAFP, βhCG, ± PAPP-A).[14]

Special ultrasound scans

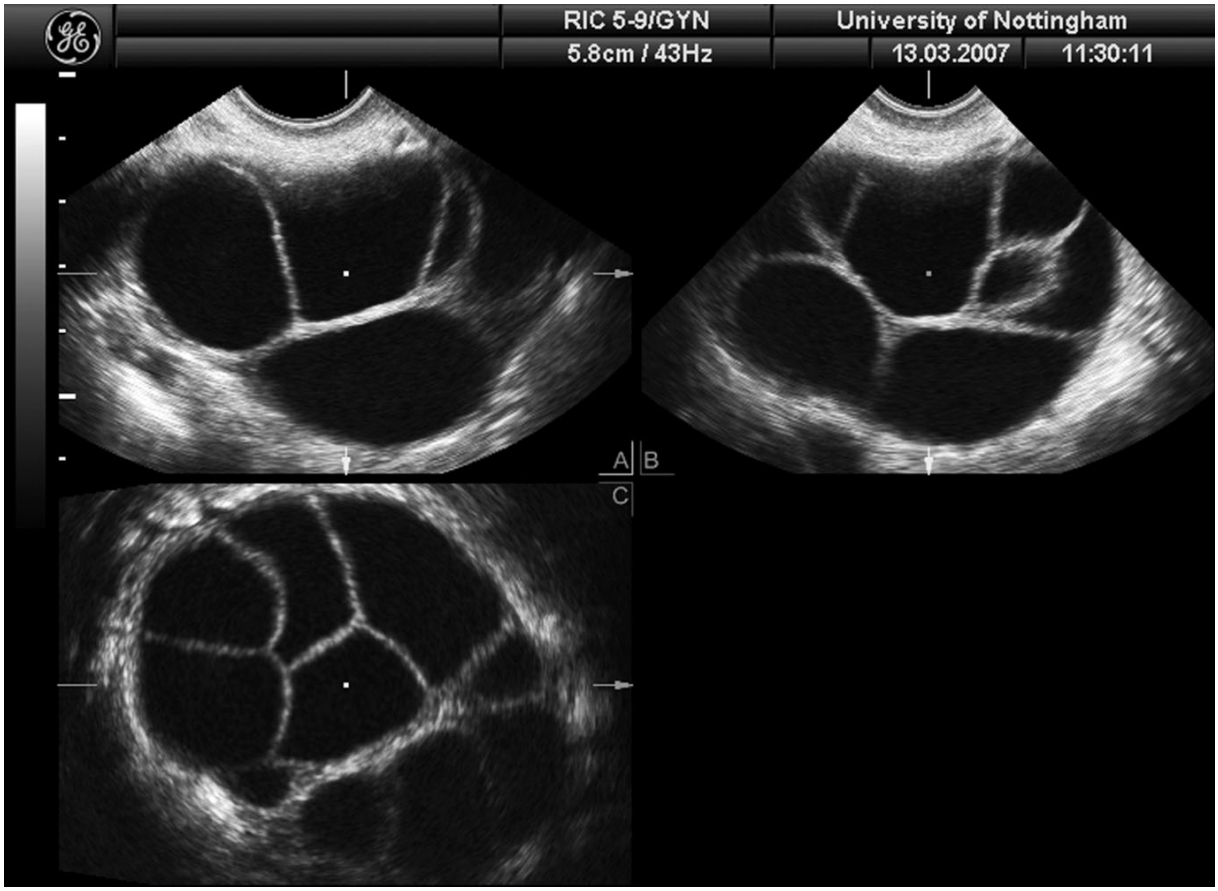
SonoAVC

SonoAVC (Automatic Volume Calculation) is a new software designed to assess volume of fluid- filled areas on three- dimensional ultrasound measurements. It was first clinically tested by Raine- Fenning[11] et al. in 2008. Fenning and

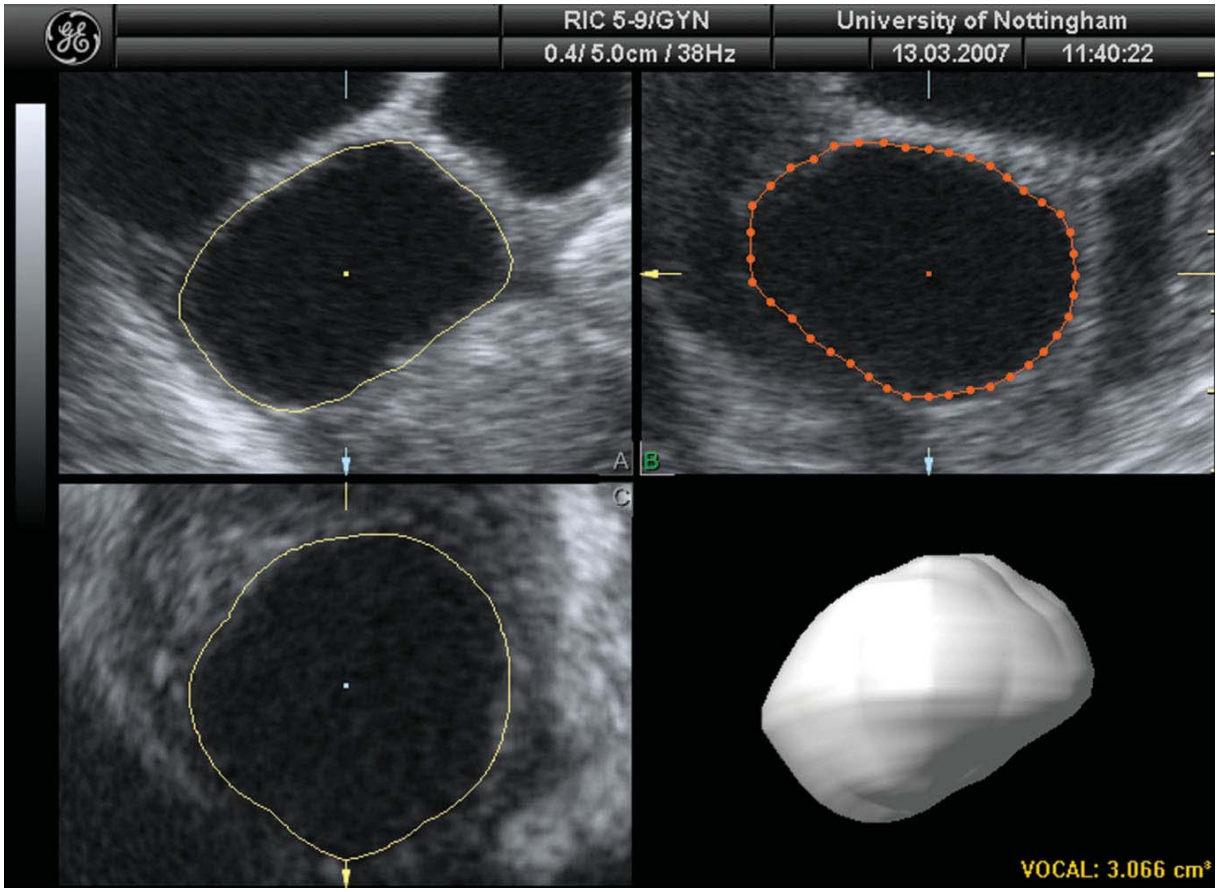
colleagues constructed a clinical trial – not for gestational sac size- but for follicular volume measurement in IVF treatment after ovarian stimulation.
The aim of the study was to compare actual follicular volume, with volume data aquired by VOCAL, SonoAVC, and mathematical estimation using the sphere formula based on 2D diameters.
The actual volume was determined by manual measurement of the follicular aspirate.[11]

Results. SonoAVC provided highly accurate automatic follicular measurements.[11] Mathematical estimations, applying the sphere formula to three perpendicular diameters, didn't prove to be valid in all cases.[11] VOCAL measurements were highly valid, but less accurate than SonoAVC due to the fact that VOCAL requires manual tracing.[11]
The least accurate data was derived from purely manual data acquisition.[11]
One could observe a trend towards decreased accuracy with increasing follicular volume.
It was concluded, that SonoAVC has proven to achieve high degrees of accuracy and validity, making its results superior to the ones aquired by VOCAL and conventional methods.[11] The possibility to identify and give quantitative information about hypoechogenic regions, their absolute dimensions, mean diameter and volume, makes SonoAVC a candidate for a future standard technique.[11]

SonoAVC provides valid and reliable results and its automatic direct data analysis eliminates any observer bias[11]. Another advantage is its low time consumption.



Multiplanar view demonstrating the three orthogonal views of a stimulated ovary, with the follicle of interest highlighted by a centrally placed marker.[11]



Virtual Organ Computer-aided AnaLysis (VOCAL) was used to manually define the contour of the follicle.[11]

Quantitative and morphological assessment by VOCAL

In 1969, the gestational sac diameter was first introduced[10]. Over the last three decades, GSV became a measure of gestational age and fetal growth, it also correlates with maternal serum human chorionic gonadotropin (hCG) levels.

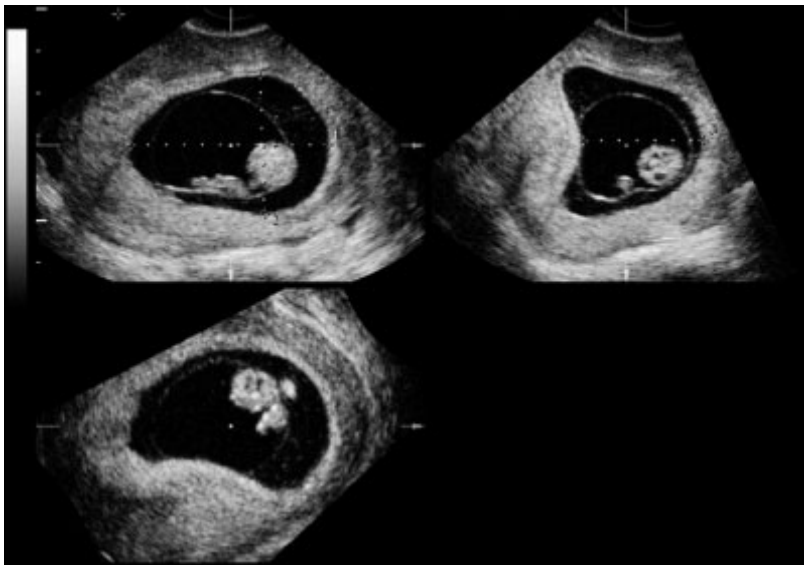
The Idea of Lee et al.[10], was to investigate whether or not three- dimensional ultrasound and Virtual Organ Computer- aided AnaLysis (VOCAL) are useful in

gestational sac volume and shape determination. VOCAL is an upcoming computer-aided technique, which allows semi-automated volume evaluation. Evaluation is done offline from 3D ultrasonographic recordings by manual contouring.

Their study in 2006 focused on normal first-trimester pregnancies. Participants underwent transabdominal (TAS) and transvaginal (TVS) sonography every two weeks. VOCAL- aided surface models were generated and classified into gestational sac shapes.

Six 30° rotations were done and electronic markers were placed on the outlines of the gestational sac.

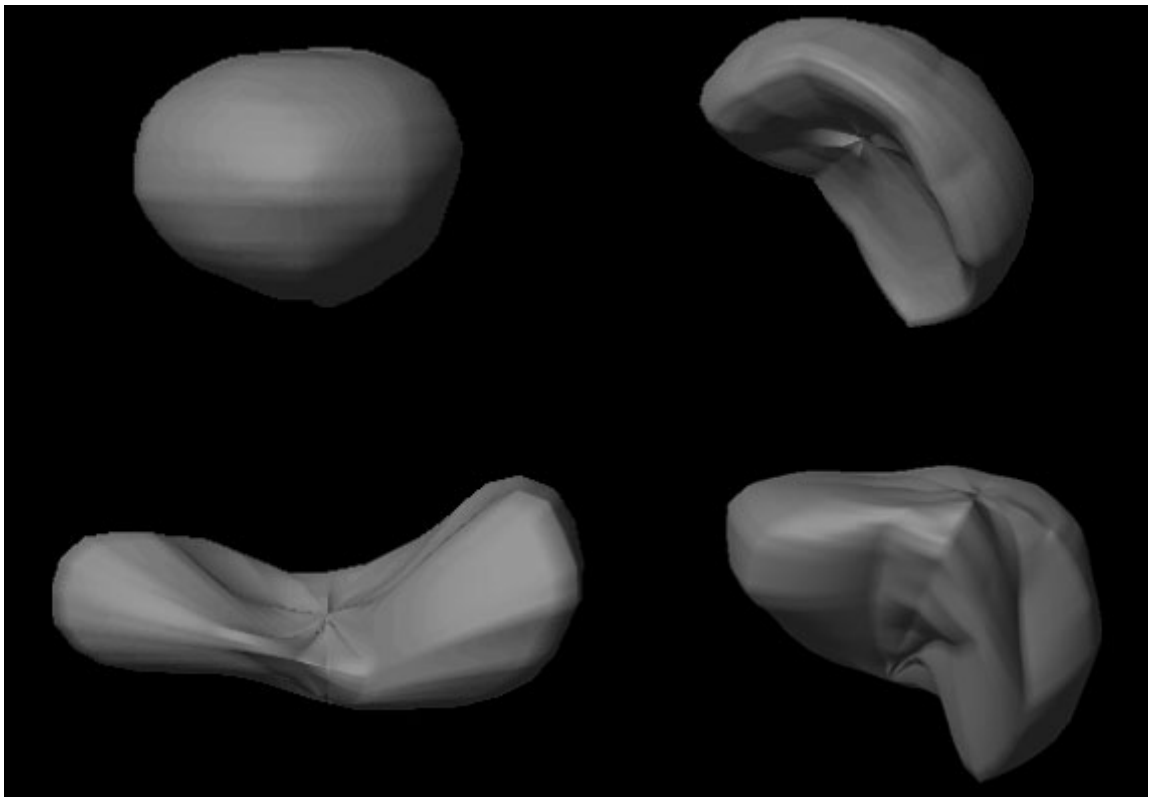
Thereafter, results were compared with results from 2D imaging and differences were evaluated. An estimation was calculated used the ellipsoid formula and data from maximal sac diameters[10]. Only normal pregnancy outcomes were included in order to develop a classification on normal shapes[10].



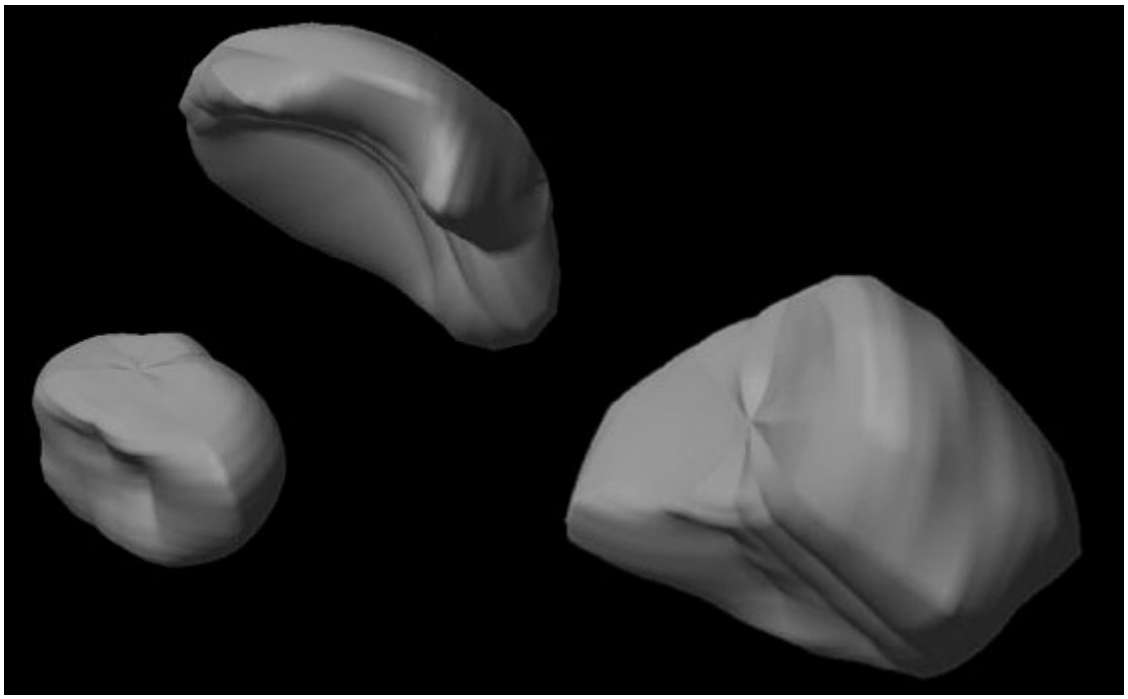
Gestational sac volume measurement using multiplanar ultrasonography. Dotted lines between calipers show the maximal gestational sac diameters.[10]

Results. Each patient had three scans, at mean gestational ages 7.9 ± 0.6, 9.9 ± 0.6 and 11.9 ± 0.6 weeks respectively. Studied patients were of mixed ethnicities. Significant increases in GSV were observed over time. A mean GSV from originally 22 ± 11ml advanced to 57 ± 21 ml on the second scan, to 116 ± 35 ml on the third scan[10].

Different shapes were classified into following: ellipsoid, discoid, concave, irregular and smooth[10]. 19% of measured gestational sacs were found to have more than one shape component[10].



Variable surface-rendered gestational sac shapes using Virtual Organ Computer-aided AnaLysis. (a) Ellipsoid; (b) disk–concave; (c) ellipsoid–concave; (d) ellipsoid–irregular.[10]



Serial gestational sac shape changes using Virtual Organ Computer-aided AnaLysis at three different time points in one pregnancy: (a) 9.4 weeks; (b) 10.1 weeks; (c) 12.0 weeks.[10]

The VOCAL technique provided insignificantly higher GSV[10]. TAS yielded minimally smaller volumes than TVS[10].

Conclusion. Data aquired by VOCAL provides reproducible values by both vaginal and abdominal approaches[10]. The main shape subtypes of the gestational sac is mostly discoid or ellipsoid, showing a concave indentation at the site of the placenta[10]. Ellipsoid volumes are prone to be underestimated[10].

Gestational sac volume:

comparison between SonoAVC and VOCAL week 11-13

In 2009, Borenstein et al.[2], performed a study to compare first trimester results delivered by VOCAL (Virtual Organ Computer-aided AnaLysis) and SonoAVC (Sonography-based automated volume count).
The aim was to calculate gestational sac volume in weeks 11+0 and 13+6 weeks of gestation, to compare the two methods and to assess reproducibility of SonoAVC calculations.

VOCAL measurements used 12-step 15° rotations to determine GSV[2]. SonoAVC tests were done in three different settings. The sweep angle was set to 85° and the data was stored for offline analysis with 4D View software[2]. Following contour tracing, the gestational sac volumes (excluding fetus and placenta) were obtained. SonoAVC calculation was done as follows: SonoAVC mode and screen adjustments were done to visualize the target appropriately, then threshold modification, medium growth and medium separation were chosen[2]. Subsequent volume calculation results could be edited according to the sac outline.
The results were compared to those aquired by high and low growth settings. The medium separation setting was maintained for all measurements.

Results. SonoAVC delivered reproducible results in 95% of cases[2]. The volume measurements provided equal results with VOCAL applications, when SonoAVC

settings for high and medium growth were used[2]. SonoAVC was not able to achieve results in 15%, due to poor quality of the stored image and software problems[2]. The mean GSV increased from 50.4 ml at 77 days' gestation to 78.9 ml at 97 days gestation[2]. SonoAVC values agreed with these results in medium and high growth settings or medium and low growth settings[2]. However it was found that there is a slight deviation between low and high growth setting measurements. In general, the correlation between the two methods was found to be good[2].

Conclusion. SonoAVC measurements are realistic and comparable to VOCAL measurements in most cases[2]. SonoAVC relies on a good quality of the 2D image, making it dependent on optimal maternal tissue composition[2] (e.g. posterior placental location, non-obese female, etc.).

Further interfering factors are proximity of anechoic and echoic structures (maternal bladder, irregularly shaped fetus), which VOCAL on the other hand isn't subject to, since data acquisition occurs from multiple planes[2].

With low growth setting measurements, the discrimination between fluid-filled and surrounding structures is reduced, which requires more post- process steps and therefore reduces the quality of the results[2]. High and medium growth settings deliver more accurate results, but larger studies are necessary for its standardization[2]. Thus, SonoAVC is a relieable method, if the correct settings are chosen and calculation is based on a clear 2D image[2].

If above mentioned conditions are present, SonoAVC provides a more advanced approach without time-consuming manual processing[2].

Gestational sac volume and chromosomal defects

As previously mentioned, chromosomal defects are the most common cause of early pregnancy loss. To evaluate the role of gestational sac dimensions in predicting such diagnoses, Falcon et Al[8]. designed a study in 2005 that measured GSV (gestational sac volume) simultaneously with chorionic villus sampling. Gestational week 11-13 ultrasonographic results (VOCAL) were compared with karyotypes from CVS.

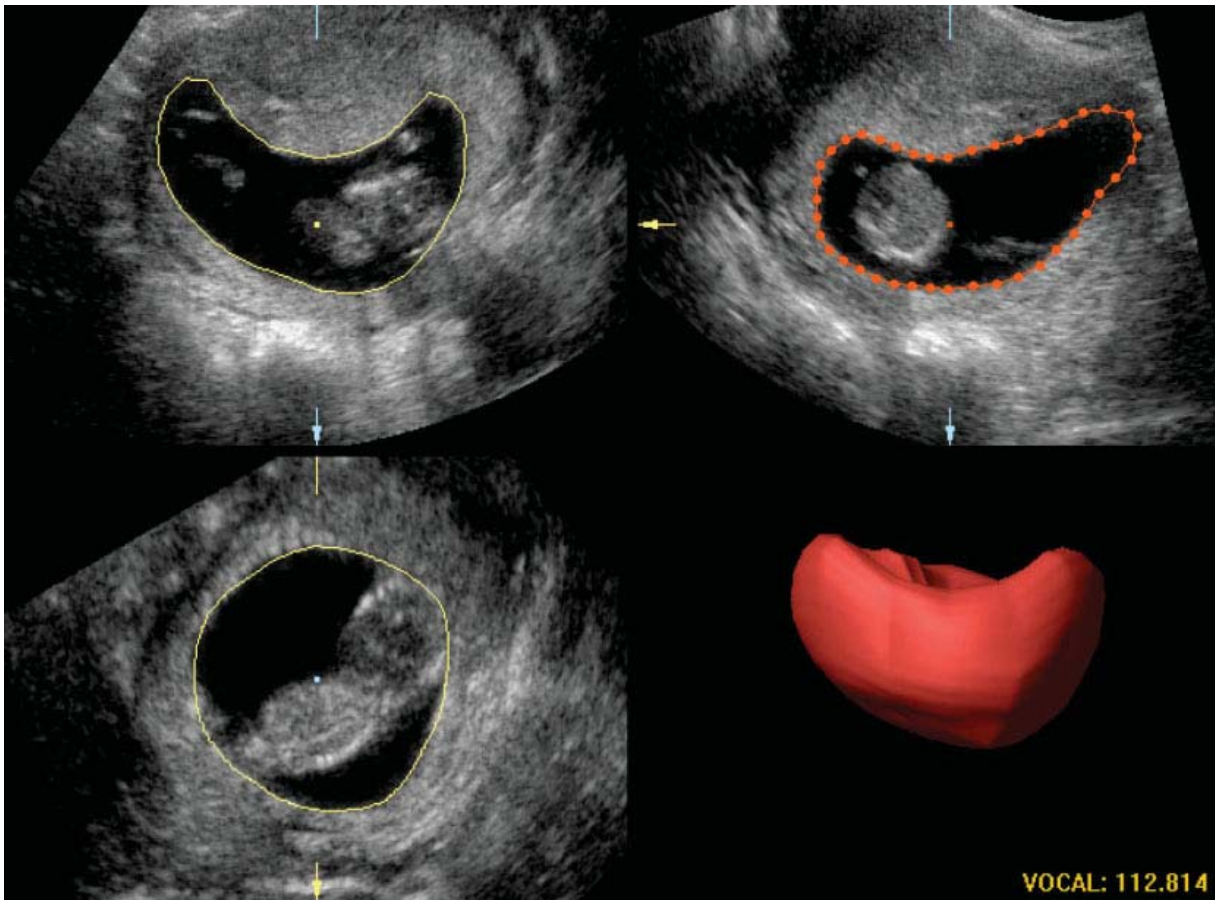
Results. Depending on karyotype, the gestational sac volumes varied. Trisomy 21, Turner and trisomy 18 syndrome didn't show any diversions from normal volume[8]. Trisomy 13 and triploidy, however, were smaller[8].

The mean GSV compared to CRL was larger in trisomy 18, smaller in triploidy and trisomy 13, and normal in trisomy 21 and Turner syndrome[8].

The mean CRL for gestational age was decreased in trisomy 18, trisomy 13 and triploidy[8].

Conclusion. In normal pregnancies, the GSV increases with gestational age. An alteration of GSV can, but doesn't have to suggest a chromosomal abnormality[8]. At the same time, a normal GSV cannot guarantee euploidy[8]. Trisomy 21 and Turner often present with normal GSV[8]. Trisomy 13 and triploidy are associated with significantly decreased sac volumes[8]. GSV values have to be supplemented with the results of maternal serum screening and nuchal translucency to be of any value, since the majority of measurements doesn't show any abnormalities[8].

First trimester GSV assessment is inaccurate concerning reliable diagnosis of chromosomal abnormalities[8]. Intrauterine growth retardation and reduced amniotic fluid volume associated with trisomy 13 and triploidy can cause reduced GSV[8]. Trisomy 18 might present with increased GSV due to fetal swallowing problems[8].



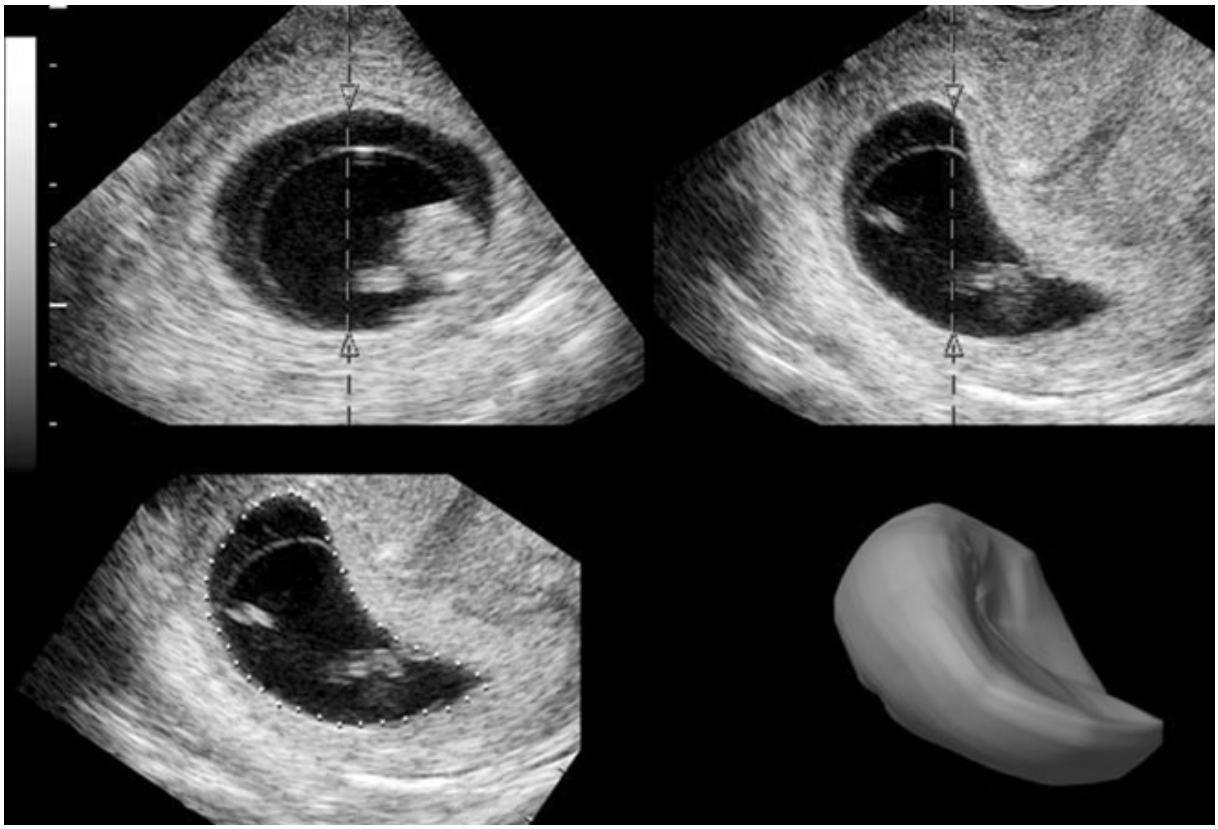
Three-dimensional volume of the gestational sac obtained using the Virtual Organ Computer-aided AnaLysis (VOCAL) technique.[8]

GSSS - The gestational sac shape score

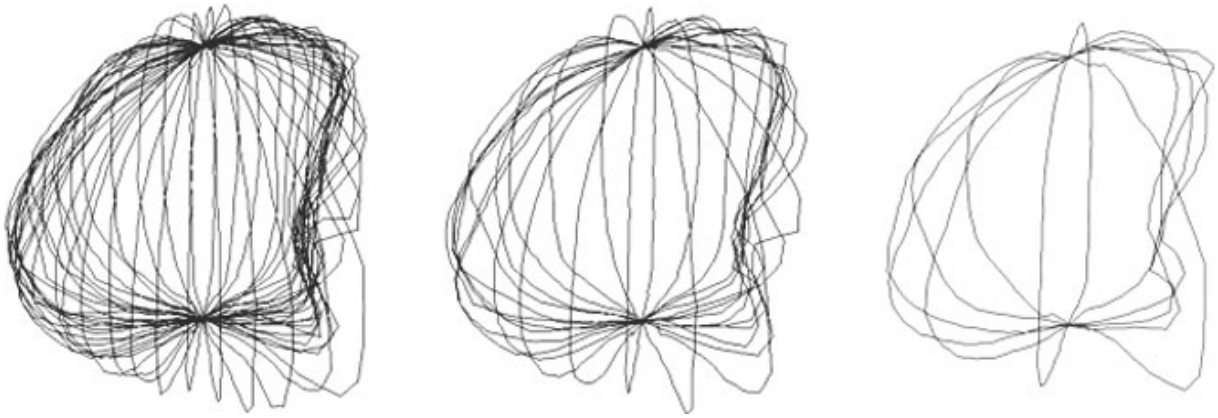
Aim. A novel scientific approach to describe a method for reliable quantitative assessment of the gestational sac shape, appliable for all normal pregnancies in first trimester. This approach is intended to help define a normal gestational sac shape in a manner suitable for standard evaluations. Thus helping to distinguish normal from abnormal tissue outlines in order to provide information about favourable vs. non- favourable pregnancy outcomes in future, as atypical gestational sac shape might be an indicator of abnormal fetal development.
The gestational sac shape score (GSSS) – a single number- describes the gestational sac quantitatively, derived from surface point coordinates of standardized gestational sacs.[6]

Data acquisition. A group of pregnant women underwent three- dimensional transabdominal ultrasonography studies in their first trimester. All of these pregnancies had normal outcomes, pregnancies with risk factors (advanced maternal age, ultrasonographic abnormalities, absent fetal cardiac activity) were excluded.[6] The mean gestational age was 9.3 ± 0.9 weeks. 3D coordinates and surface point sets were obtained from the recording via 4D viewing software and manual tracing.[6] The study compared data aquired from three different approaches: 30-, 15- and six-slice sampling, each completing a 180° sweep.[6] Each gestational sac was sampled in the above mentioned manner, using cubic spline interpolation to supplement non-measured values in the six- and 15- slice

samples and results were compared. 3660 surface points were named standard for each slice. The degree of accuracy of shape estimation correlates with the number of chosen surface points.[6]



Gestational sac contouring, illustrating the steps used to obtain sac contours. (a) The sac-sectioning axis is chosen (arrowheads). (b) A section made at right angle to the sectioning axis in (a). (c) The small white dots outline the sac contour of the sac surface. (d) The data obtained by contouring are in the form of a three-dimensional image of the sac or the *x*, *y* and *z* coordinates of surface points[6]



6-degree interval 12-degree interval 30-degree interval

Gestational sac slice sampling, depicting the three slice samples used in this investigation. Slices of each gestational sac are generated at 6-degree intervals using VOCAL and their contours determined manually (30-slice set). To obtain a 15-slice set, every other contour is selected (slices at 12-degree intervals). If every fifth slice is selected (six-slice set), the slice interval is 30 degrees.[6]

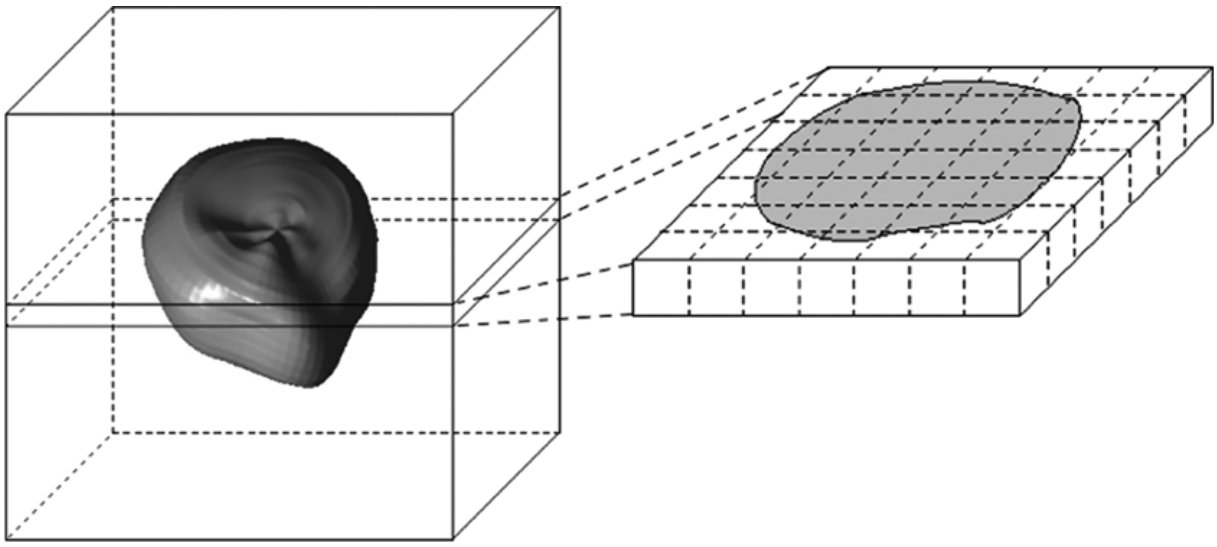
Data processing. The surface points contained information about shape, as well as location, orientation and volume. Definition of shape can be done simply by means of Cartesian coordinates.

To reduce the information to shape only, following steps were taken: (1) center of gravity was moved to the origin, (2) inertial axes were matched with coordinate axes, (3) sac volume was converted to 1ml.[6]

Thereafter, a volume shape descriptor was calculated: standard voxels inside the sac were assigned 1 and those outside 0.[6] The voxels are part of a 3 x 3 x 3 cm cube of 27mL volume, placed around the target. The volume is determined by adding of all voxels with the value 1 and dividing it by the total numer of voxels (all 1 and 0 voxels) in the box.[6] After being converted into a vector, including

only shape information, principal components analysis yielded principal component scores.[6]

Based on these results, the gestational sac shape score (GSSS) was defined: GSSS-6, GSSS-15 and GSSS-30 (the number referring to the total amount of slices).[6]



Volume shape descriptor, illustrating the box (left side) into which each standardized gestational sac is placed, their centers of gravity coinciding. The box is subdivided into cubes, some completely inside or outside the sac and some partially inside/outside the sac (right side). The locations of the cubes with respect to the sac are determined only by sac shape[6]

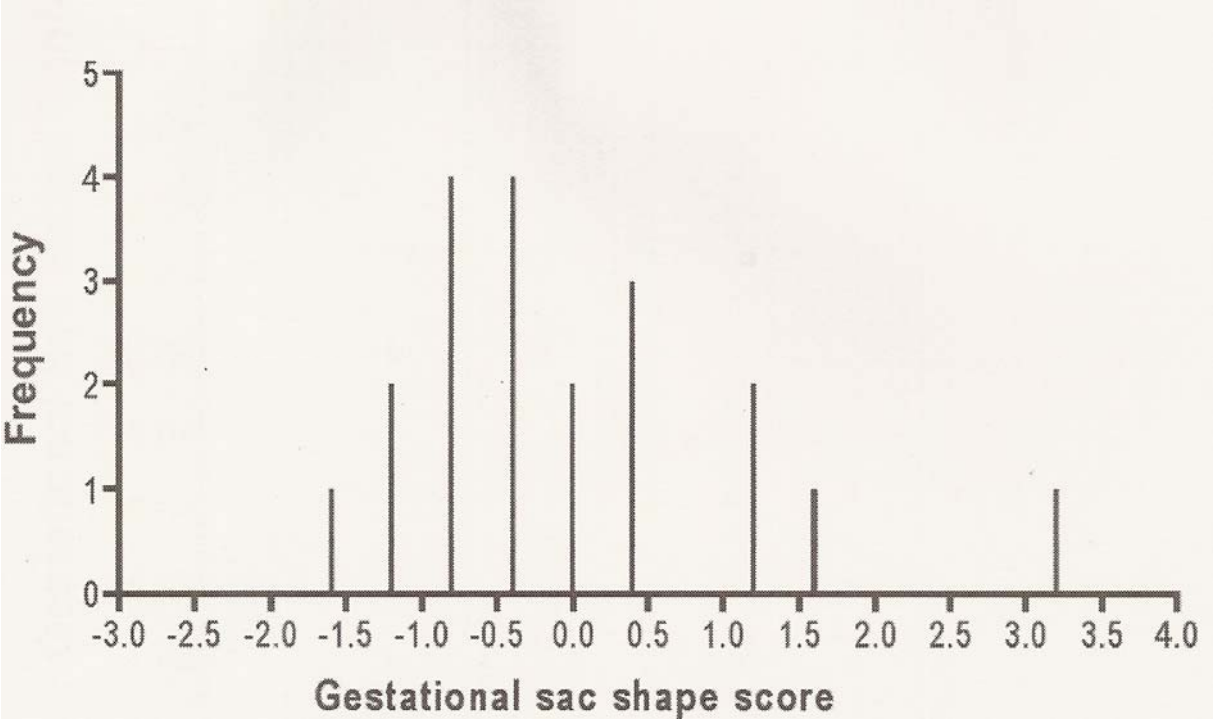
Results. A comparison of these individual GSSS values for the same gestational sacs showed no significant differences.[6] It was concluded that these facts prove a low sample size as in GSSS-6 does not present significant loss of shape information and is therefore more convenient as its manual tracing is less time consuming.[6]

Voxel assignment permits the use of the shape descriptor for complex shapes, with guaranteed precise shape assessment, even in the presence of concavities.[6] If box size adjustment has to be made, one should rather change the number of cubes than cube size to retain good resolution.[6]

As all new approaches, this study has to be repeated with a large number of participants to make the GSSS definition more accurate.[6]

Once a standard is defined, abnormal gestational sacs can be measured and rated against the standard values. This will be one step closer to resolve the question whether chorionic sac shape can be an indicator for developmental challenges.

Another idea for the future is a serial follow-up of a gestational sac, with repeated measurements throughout pregnancy. This could help define ‘shape trajectories’ and give information about time-dependent functions of the aquired GSSS sets.[6] In this manner one could find the exact time interval in which pathologic changes started to take place, which is not possible with single measurements alone, since they can only be normal or abnormal, while giving no information about the timing of the pathologic insult.[6]



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supplementary material of Ultrasound in Obstetrics and Gynecology vol. 29 issue 5

Conclusion

To summarize, the causes of early pregnancy loss are still unknown in about 50% of cases. Ultrasound, however, is an indispensable tool of daily obstetric diagnosis and follow-up. 3DUS has proven superior to conventional ultrasound in volume analysis of irregular objects.

SonoAVC has proven to provide highly accurate automatic volume measurements. It is capable of identifying and assessing volume of hypoechogenic regions, their absolute dimensions and diameters; attributes that make it a candidate for future standard evaluations.

GSV has showed to increase over time. Its shapes can be put into five main classifications (discoid, ellipsoid, concave, irregular and smooth). A gestational sac often has more than one of these characteristics.

The VOCAL technique is highly valid, but needs manual tracing, which makes it more time- consuming than SonoAVC and slightly less accurate. VOCAL, however, is relatively independent from maternal tissue composition and picture quality, as it can measure in multiple planes. The latter is the weak point of SonoAVC: it depends on a clear image for its direct volume evaluation. Shadows on a 2D image make it impossible to generate volume estimations. Consequently, SonoAVC is more advanced, if good data quality is present, whereas VOCAL is more independent, but requires more time.

The relative significance of qualitative sac shape appearance versus sac volumetry is at present unclear. Therefore, more sophisticated methods are required to optimally classify sac features that best predict pregnancy outcome. Future research should apply these observations to a broader range of normal and abnormal pregnancies in order to provide important baseline parameters for identifying patients at risk of pregnancy failure.

References

1. Asim Kurjak, David Jackson: An Atlas of three- and four- dimensional sonography in obstetrics and gynecology
   2004 Taylor & Francis, ISBN 1- 84214-238-0

2. Borenstein M, Perez GA, Garcia FM, Romero M, Anderica JR: Gestational sac volume: comparison between SonoAVC and VOCAL measurements at 11 + 0 to 13 + 6 weeks of gestation, Ultrasound Obstet Gynecol 2009; 34: 510-514

3. Chudleigh, Trish: Ultraschalldiagnostik in der Geburtshilfe, 1st ed, 2007, chapter 3, Urban & Fischer Verlag**,** Elsevier publishing,
   ISBN-10: 3437242903, ISBN-13: 978-3437242908

4. Christof Sohn, Wolfgang Holzgreve: Ultraschall in Gynäkologie und Geburtshilfe, Thieme Verlag, Stuttgart (1995), ISBN-10: 3131019719, ISBN-13: 978-3131019714

5. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Gilstrap LC III, Wenstrom KD, Williams Obstetrics 22nd edition 2005, p.134-7

6. Deter RL, Li J, Lee W, Liu S, Romero R:
   Quantitative assessment of gestational sac shape: the gestational sac shape score, Ultrasound Obstet Gynecol 2007; 29: 574-582

7. Eberhard Merz: Sonographische Diagnostik in Gynäkologie und Geburtshilfe Band 2, Thieme Verlag Auflage: 2., neubearb. u. erw. Aufl. (7. Mai 1997), ISBN-10: 3137012023, ISBN-13: 978-3137012023

8. Falcon O, Wegrzyn P, Faro C, Peralta CFA, Nicolaides KH:
   Gestational sac volume measured by three-dimensional ultrasound at 11 to 13 + 6 weeks of gestation: relation to chromosomal defects,
   Ultrasound Obstet Gynecol 2005; 25: 546-550

9. Gonçalves LF, Nien JK, Espinoza J, Kusanovic, Lee W, Swope B, Soto E, Treadwell MC, Romero R: What does two-dimensional add to three-dimensional obstetric ultrasound?, J Ultrasound Med. 2006, 25: 691-699

10. Lee W, Deters RL, McNie B, Powell M, Balasubramaniam M, Gonçalves LF, Espinoza J, Romero R: Quantitative and morphological assessment of early gestational sacs using three-dimensional ultrasonography
Ultrasound Obstet Gynecol 2006; 28: 255- 260

11. Raine-Fenning N, Jayaprakasan K, Clewes J, Joergner I, Bonaki SD, Chamberlain S, Devlin L, Priddle H, Johnson I: SonoAVC: a novel method of automatic volume calculation, Ultrasound Obstet Gynecol 2008; 31: 691- 696

12. Rolo LC, Nardozza LMM, Araujo E Jr., Nowak PM, Moron AF:
Gestational sac volume by 3D- sonography at 7-10 weeks of pregnancy using the VOCAL method, Arch Gynecol Obstet (2009) 279: 821 -827

13. Smith NC, Smith PM: Obstetric ultrasound made easy
Churchill Livingstone 2003

14. Tamara L. Callahan, Aaron B. Caughey
Blueprints of obstetrics & gynecology 4th edition, p.15ff.
2007 Lippincott Williams & Wilkins
ISBN 1- 4051- 0489-9

15. www.fetalmedicine.com : the week 11-13 scan

16. www.praenatal.com

17. www.praenatal-medizin.de