REVIEW ARTICLE

Ultrasound Frontiers: 3D Doppler, Automatic Fetal Biometry, Handheld Ultrasound

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Abstract

Ultrasound frontiers are infinitive and some recent developments are discussed in this review. The author aims to provide the reader with the definition of 3D Doppler and its potential clinical applications. It also describes automatic fetal biometry and discusses clinical potentials of handheld ultrasound. The rapid development of these new sonographic techniques will continue to enlarge the scope of ultrasound applications in obstetrics and gynecology. 3D Doppler is a unique technique that enables assessment of vascular signals within the whole investigated area. Homodynamic changes included in the process of placentation are one of the most exciting topics in the investigation of early human development. The measurement errors produced by automated fetal biometry translate into very small errors regarding gestational age of the fetus. The automation of ultrasound measurements has great potentials in improving productivity and patient throughput, enhancing accuracy and consistency of measurements and reducing the risk of repetitive stress injuries users. Handheld ultrasound exam is reliable in making initial diagnosis required by the limited ultrasound exam in obstetrics and gynecology.

Objectives
- Define 3D Doppler and its potential clinical applications
- Describe automatic fetal biometry
- Discuss clinical potentials of handheld ultrasound

Keywords: 3D Doppler, automatic fetal biometry, handheld ultrasound.

3D DOPPLER

Doppler ultrasound waveform analysis of the maternal-fetal circulation has emerged to add useful information in the determination of fetal well-being. The uterine and placental vascularizations are important for normal pregnancy development.[1] Abnormal vascularization can produce increased resistance to flow through the uterine circulation, and the resulting placental insufficiency can significantly reduce the delivery of oxygen to the fetus. Abnormal placental development is associated with fetal and neonatal morbidity, growth impairment, incidence of major congenital anomalies, increased incidence of preterm birth, fetal non-reassuring status in labor, neonatal intensive care admissions, and overall mortality. Early studies suggested that Doppler ultrasound held great promise as a noninvasive, repeatable, and simple method of predicting hypertension in pregnancy and identifying those pregnancies at high-risk for maternal and fetal complications.[2,3] Subsequent studies have emphasized the complexity of factors that may influence the pulsed Doppler waveform analysis.[4]

During normal pregnancy, the spiral arteries are transformed into distended low-resistance channels capable of increasing the blood supply to the fetal-placental unit until the third trimester to 10 times that of the nonpregnant uterus. This uteroplacental vascular adaptation is dependent on invasion of the spiral arteries by trophoblast which becomes incorporated into the vessel wall. This invasion occurs in a stepwise fashion starting with plugging of the distal ends of the arteries followed by migration into the decidual segments and, after several weeks' delay, into the myometrial segments. The first phase of this process starts from at least 8 weeks of gestation and continues to the 10th week, and the second phase is at 14 to 24 weeks. Establishment of the uteroplacental circulation in the second trimester is not a random phenomenon, but rather a consequence of events in the first trimester. Figures 1 to 5 are showing different forms of placental and spiral arteries 3D power Doppler evaluations. The virtual organ computer-aided anaLysis (VOCAL) imaging program can be used to calculate vascularization index (VI), flow index (FI) and

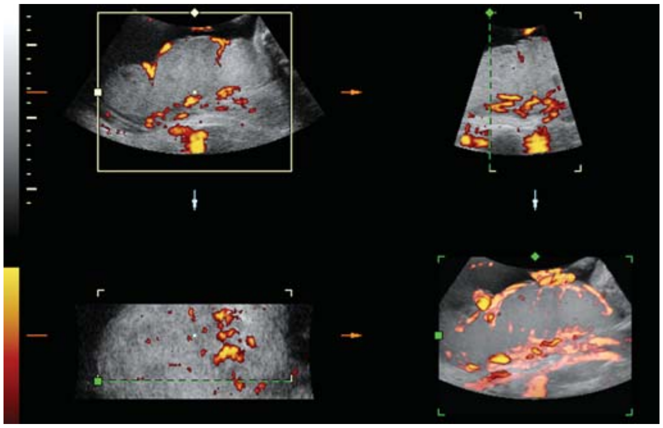

Figure 1: Three orthogonal planes with 3D power Doppler of placental and spiral arteries blood flow. Three-dimensional reconstruction of the placenta was shown in the lower right corner

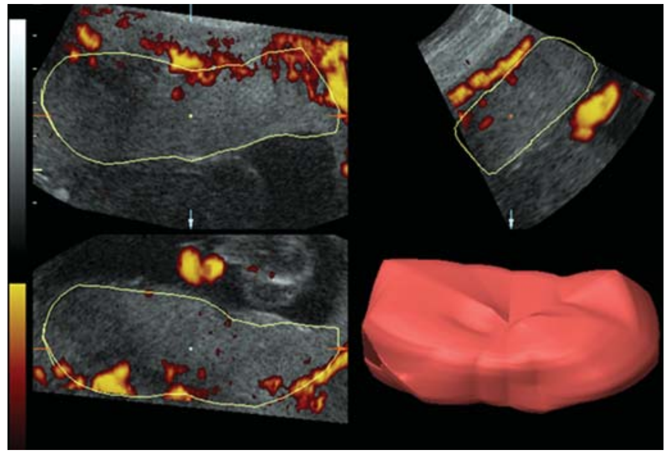

Figure 4: 3D placental volume calculations (lower right corner)

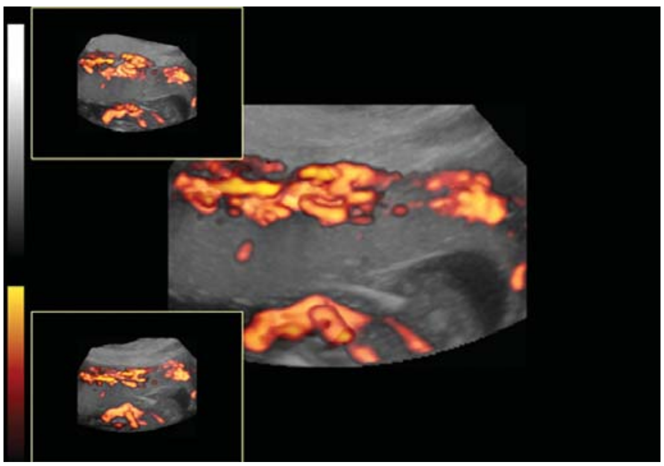

Figure 2: Another 3D power Doppler reconstruction of the placental (mid), spiral arteries (upper) and umbilical cord (lower) blood flow

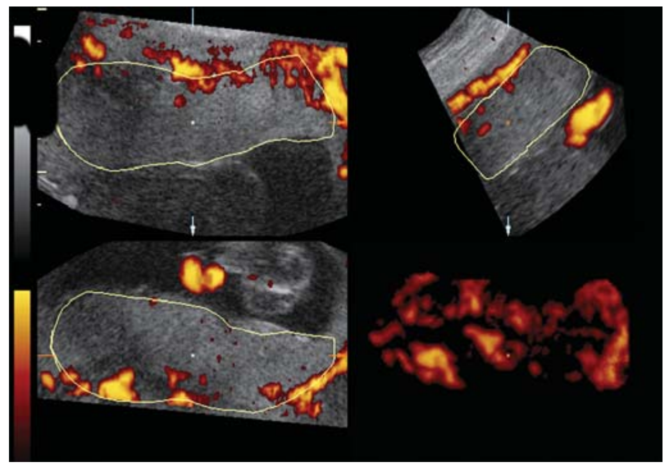

Figure 5: Placental "angiogram" as presented by 3D power Doppler

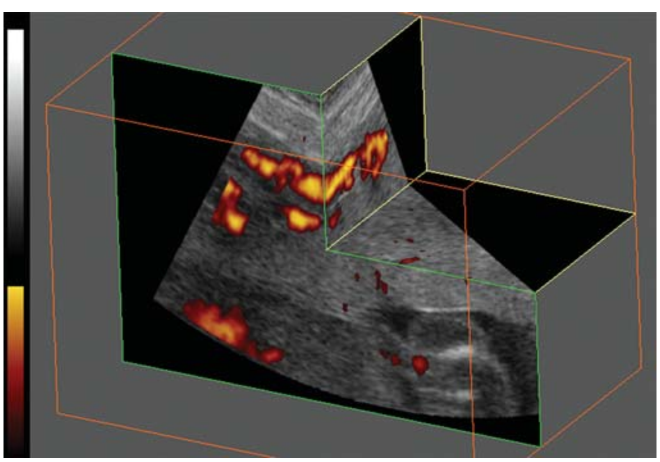

Figure 3: Placental blood flow shown in Niche mode

vascularization flow index (VFI). Vascularization index gives information in percentages about the amount of color values in the placenta and spiral arteries. Flow index is a dimensionless index (0 to 100) with information about the intensity of blood flow. It is calculated as a ratio of weighted color values (amplitudes) to the number of color values. Vascularization flow index is the combined information of vascularization and mean blood flow intensity. It is also a dimensionless index (1 to 100) calculated by dividing weighted color values (amplitudes) by the total voxels minus background voxels. 3D Doppler is aimed to minimize operator influence on obtained results and allows assessment of the blood flow in real volume and remotely. It is the hope that future investigation protocols would prove this scientifically true and clinically useful.

Our recent study was aimed to define normal placental and spiral arteries blood flow as assessed by 3D Doppler in the second trimester of pregnancy.[5] This trimester is the critical time for placental development and possible early prediction of pre-eclampsia and intrauterine growth restriction (IUGR) and therefore we limited our study to this time frame. We also believe that in this trimester we can still visualize most of the placenta in the single view. This study presented the normative data of the spiral arteries and placental blood flow that could serve as a basis for study of abnormal vascular development, particularly in pre-eclampsia and IUGR. We studied uncomplicated singleton pregnancies with normal pregnancy outcomes. Placental vascular indices slowly increased indicating progressive development of vascular network and increase in the volume blood flow. These changes were not rapid in nature but rather slow progressing. The same was true for spiral arteries blood flow. Our study reported nomograms for spiral arteries and placental blood flow in normal pregnancies between 14 to 25 weeks as assessed by 3D power Doppler analysis. These findings could serve as a basis for future studies of abnormal vascular development as known in pre-eclampsia and intrauterine growth restriction. It can be postulated that changes in 3D Doppler indices could reflect early changes in the hemodynamics of placenta and especially spiral arteries in patients with pre-eclampsia and/or IUGR. Further investigations are needed to address the exact extent of these vascular changes that could be detected *in vivo* by 3D Doppler ultrasound modalities.

The study done by Yu et al. was aimed to test the hypothesis that the placental fractional moving blood volume was different with advancing gestational age.[6] The study was performed using 3D power Doppler ultrasound on 100 healthy pregnant patients with gestational age between 20 to 40 weeks. Their results showed that fractional moving blood volume of the placenta was positively correlated with the increment of gestational age and the fetal growth indices. Merce et al. described the evolution of placental vascularization during a normal pregnancy obtained by "placental vascular biopsy".[7] In this study all 3D Doppler indices had a significant relationship with gestational age. The most significant relationship was observed for FI, and the least significant for VI. The FI increased linearly with gestation, whereas the VI showed a dispersion of values with a plateau from the 30th week onwards and a decrease from 37th week to the end of pregnancy. The VFI behaved as a combination of both VI and FI indices from which it was derived. All 3D Doppler indices were significantly related to fetal biometric parameters, except VI and fetal weight. The authors concluded that 3D power Doppler technique of "placental vascular biopsy" is an appropriate tool for evaluation of the human placental vascular tree during gestation. 3D Doppler indices changed as pregnancy progresses and were significantly related with fetal biometry and umbilical artery Doppler waveform analysis.

Doppler studies are not new in obstetrics. In addition to anatomical information, Doppler measurements give us the opportunity to study hemodynamics of the uterus, placenta and fetus *in vivo*. Steady and sometimes abrupt changes in the uterine artery, umbilical artery or middle cerebral artery can be observed by pulsed Doppler waveform analysis but this can be seen usually toward the end of pathological events making early diagnosis unreliable. Thorough knowledge of Doppler physics and understanding of instrumentation is essential. Several studies showed that the reproducibility of 3D Doppler ultrasound technique is very high. We would like to mention a prospective study on normal singleton pregnancies from 14 to 40 weeks.[8] Placental volume and mean gray presented an intra-class correlation coefficient of 0.98 and 0.94 respectively, with differences approaching zero. All 3D power Doppler vascular indices (VI, FI and VFI) showed a correlation greater than 0.85, with a better intraobserver agreement for the flow indices (FI and VFI). Their results provide the validation of the technique demonstrating a good reproducibility of the 3D power Doppler parameters when applied to the study of the placental vascular tree in normal pregnancies. Jarvela et al in their study also confirmed excellent 3D Doppler reproducibility.[9] Their results suggested that measurement of gray-scale and color Doppler flow indices were reproducible thus allowing them to be used in clinical practice and research. We have similar experience.

Three-dimensional power Doppler sonography has the potential to study the process of placentation and evaluate the development of the embryonic and fetal cardiovascular system.[10,11] Rapid technological development will allow real-time 3D ultrasound to provide improved and expanded patient care on one side, and increased knowledge of developmental anatomy on another. Three-dimensional power Doppler ultrasound is a unique instrument that enables assessment of vascular signals within the whole investigated area. Homodynamic changes included in the process of placentation are one of the most exciting topics in the investigation of early human development.

AUTOMATIC FETAL BIOMETRY

Fetal biometry is essential part of each comprehensive ultrasound exam and determines gestational age and fetal growth rate. All standard biometry measurements are routinely done by a sonographer or a physician. This procedure requires knowledge, experience and manual skills. Standard ultrasound images are obtained and then linear or ellipsoid measurements are done on the screen as required by the American Institute for Ultrasound in Medicine (AIUM) guidelines.[12] Based on these manual measurements gestational age is calculated and fetal weight estimated automatically. The manual measurements could be time consuming and prone to inter-observer and intra-observer error affecting clinical value of obtained results.[13,14] The studies showed that multiple keystrokes required to accomplish the task could also contribute to operator's repetitive stress injury.[15,16] Expectations are that with current rapid development of ultrasound technology, these problems could be solved eliminating inter-observer errors, reducing or eliminating risks for repetitive stress injury and making obtained results more accurate and clinically relevant.

Precise assessment of gestational age and fetal weight are among the most important clinical information that practicing obstetrician faces when managing pregnancy at risk. The clinicians relay on these measurements to manage normal and even more so at risk pregnancy. Ultrasound measurements require considerable training. As an examiner gains experience than inter-observer and intra-observer error will decrease. Ultrasound measurements need to be accurate in order to be clinically useful. Fetal biometry requires time to perform measurements. Multiple key strokes are needed to accomplish the task and this could contribute to the repetitive stress injuries.[15,16] The whole exam could be lengthily and there is unavoidable operator variability. With multiple sonographers at the single ultrasound center, this variability increases.

The concept of automatic fetal biometry consists of automatically generated biometric measurements like BPD, HC, FL and AC on B-mode ultrasound images (Figures 6 to 8). Automatic fetal biometry is aimed to automate core biometric measurements by the pattern recognition. This approach could reduce keystrokes and therefore reduce repetitive stress injuries. It could also improve everyday workflow to increase patient throughput and productivity. A sonographer or physician could dedicate more time for anatomical survey and communication with the patient. Not to underestimate is also potential of automatic biometry to decrease examiners variability (intra-observer and inter-observer error) and improve accuracy and consistency of obtained measurements.

Our just published study showed that Auto OB measurements are comparable with measurements obtained

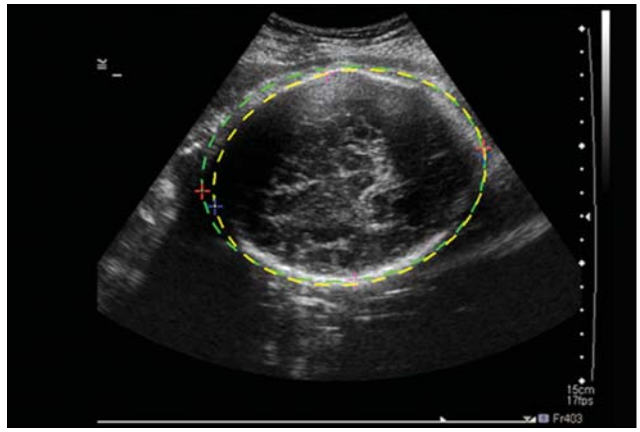

Figure 6: Automatic fetal biometry showing HC measurements by experienced sonographer (green) and by pattern recognition computer analysis (yellow). Pattern recognition software based automatic fetal biometry (Auto OB, Siemens, Mountain View, CA)

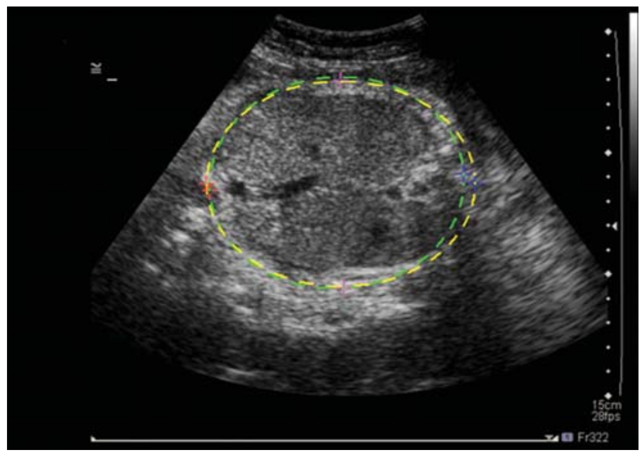

Figure 7: Automatic fetal biometry showing AC measurements by experienced sonographer (green) and by pattern recognition computer analysis (yellow). Pattern recognition software based automatic fetal biometry (Auto OB, Siemens, Mountain View, CA)

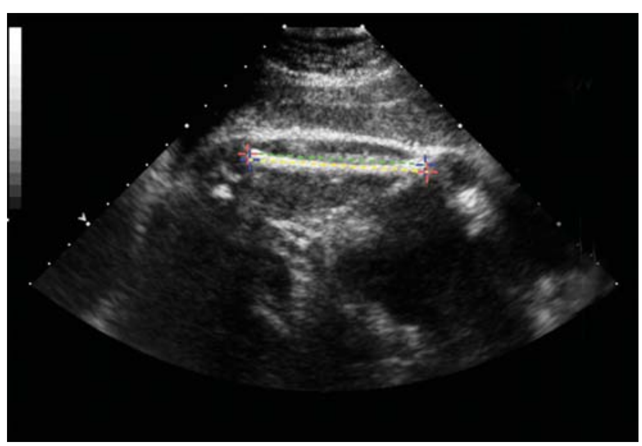

Figure 8: Automatic fetal biometry showing FL measurements by experienced sonographer (green) and by pattern recognition computer analysis (yellow). Pattern recognition software based automatic fetal biometry (Auto OB, Siemens, Mountain View, CA)

by very experienced sonographers and maternal fetal medicine physician.[17] Obviously less time is needed for these measurements when done by the computer. Auto OB does not replace knowledgeable sonographer since the examiner needs to be experienced. The pattern recognition program requires good standardized images to be obtained during ultrasound exam. We showed that Auto OB produces an average error of 1.89% in 80% of the cases for the four fetal biometry measurements mentioned. The Pearson correlation coefficient was r = 0.998. The automatic measurements produced by Auto OB have a mean error of 1.80%, while the examiners have a mean error of 1%. The Pearson correlation coefficient was lowest for BPD (r = 0.996) and highest for AC (r = 0.999). The range of sonographers error was 0.01 to 6.36% and the range of Auto OB errors was 0.07 to 3%. As expected, Auto OB measurements were more consistent with narrower range of measurements errors.

The concept of automatic fetal biometry is not new but just recently it gained clinical interest. One of the first attempts to evaluate automatic fetal biometry was the study done by Thomas JG and coauthors in 1991.[18] They investigated whether it would be possible for a computer to measure long bones of the fetus. In this study, the images were scanned and analyzed off-line using morphological operators. They concluded that the procedure described allowed the authors to measure the long bones and has a very high coefficient of correlation with measurements obtained by humans. They predicted that the whole procedure could be part of the computer instructions that are built into the machine. However, until now there was not direct implication of this idea into clinical practice.

Chalana V et al. designed an image processing technique to automatically measure BPD and HC from fetal ultrasound images.[19] They evaluated the performance of the algorithm by comparing the resulting measurements with those made by experienced sonographers. The BPD and HC were automatically computed by detecting the inner and outer boundaries of the fetal skull using the computer vision technique known as the "active contour model." Six experienced sonographers also measured the BPD and HC on these images. The mean absolute difference between the automated measurements and the average of the six observers was 1.4% for BPD and 2.9% for HC. The correlations were 0.999 for the BPD and 0.994 for the HC. The computer's measurements were no different from the six observers' measurements than the observers' measurements were from one another. Our result were concordant but our study was more comprehensive including AC and FL measurements.

Similar results were obtained by Pathak and others.[20] They developed a tool to automatically detect inner and outer skull boundaries of a fetal head in ultrasound images. These boundaries were used to measure BPD and HC. This study showed reduction in the overall execution time from 32 s to 248 ms. In recent study, Lu et al. described an image-processing and object-detection method that was developed to automate the measurements of BPD and HC in ultrasound fetal images.[21] The heads in 214 of 217 images were detected by aniterative randomized Hough transform. A head was assumed to have an elliptical shape with parameters progressively estimated by the iterative randomized Hough transform. No user input or size range of the head was required. The detection and measurement took 1.6 s on a personal computer. The interrun variations of the algorithm were small at 0.84% for BPD and 2.08% for HC. The differences between the automatic measurements and sonographers' manual measurements were 0.12% for BPD and –0.52% for HC. The 95% limits of agreement were –3.34%, 3.58% for BPD and –5.50%, 4.45% for HC. The results demonstrated that the automatic measurements were consistent and accurate. The other studies confirmed feasibility of automatic fetal biometry.[22,23] However, our study was first to include all most commonly used parameters (BPD, HC, AC and FL) to assess gestational age and fetal growth by automatic fetal biometry measurements. Results of our evaluations have direct clinical value and ultrasound industry already started to implement research results into practical clinical applications.

The measurement errors produced by Auto OB translated into very small errors regarding GA of the fetus. In general, an error of 1.8% represents a deviation of less than two days for 20 weeks of GA, less than four days for 30 weeks of GA, and, usually less than seven days for 40 weeks of GA. The automation of these ultrasound measures has great potential of improving productivity and patient throughput, enhancing accuracy and consistency of measurements, and reducing the risk of repetitive stress injuries to users. Future studies are needed to address these issues.

HANDHELD ULTRASOUND

Ultrasound exam is an integral part of contemporary Obs/Gyn practice. It allows noninvasive and safe evaluation of female pelvic organs and pregnancy. Traditionally, ultrasound exam is done at the highly specialized tertiary care centers utilizing very expensive and large ultrasound machines. More basic ultrasound exam utilizing mobile ultrasound units is done in labor and delivery room, emergency room, resident clinic and some physician's offices. In these situations portable laptop style ultrasound machine is utilized. Handheld ultrasound is a miniature ultrasound device that fits in physician hand/pocket and can be utilized for a very basic ultrasound evaluation during routine Obs or Gyn practice. This type of ultrasound machine provides a simple ultrasound evaluation in variety clinical situations without dependence of limited availability of large ultrasound machine in the practitioner's office or in the hospital. Such ultrasound machine can be available to the physician all the time like for instance a stethoscope is.

Until recently, ultrasound was used primarily for diagnosis. Handheld ultrasound offers potential for screening applications. System is designed to enhance the physical exam by providing visual information to support clinicians in early care decisions. There is an obvious need for earlier, faster and more accurate triage, more information from the physical exam and immediate access (seconds, not minutes). The vision of handheld ultrasound is to have a dedicated screening device, handheld, personal imaging tool (not a laptop on a cart) and a "visual stethoscope". This approach is changing the paradigm of the physical exam in Obs/Gyn practice.

Research using the handheld ultrasound machine is currently limited mostly to the military, ER, adult cardiology and neonatal applications.[24-32] Handheld ultrasound exams are considered safe, simple and valuable for evaluation of pregnancy and Obs/Gyn patients. Our research is one of the first applications of handheld ultrasound exam in routine Obs/Gyn practice.[33] We hypothesized that handheld ultrasound can help the clinicians in basic evaluation of Obs/Gyn patients, replacing a limited availability of standard larger ultrasound machines. Two hundred patients were recruited from the pool of patients referred for standard Obs/Gyn ultrasound exams. Handheld ultrasound device (P-10, Siemens, Mountain View, CA) with 3 to 5 MHz transabdominal probe was used in this study (Figures 9 to 12). Clinical utility of this small device was evaluated in variety of clinical scenarios like amniotic fluid measurement, determination of fetal presentation, position of the placenta, detection of fetal heart activity and fetal movements, evaluation of the uterus and adnexal. We observed clinical utility of the handheld ultrasound exams in the following clinical situations:

- Determination if patient is pregnant
- Determination of number of fetuses

Figure 9: Handheld ultrasound (P-10, Siemens, Mountain View, CA)

Figure 10: Complete system: Handheld ultrasound (P-10, Siemens, Mountain View, CA)

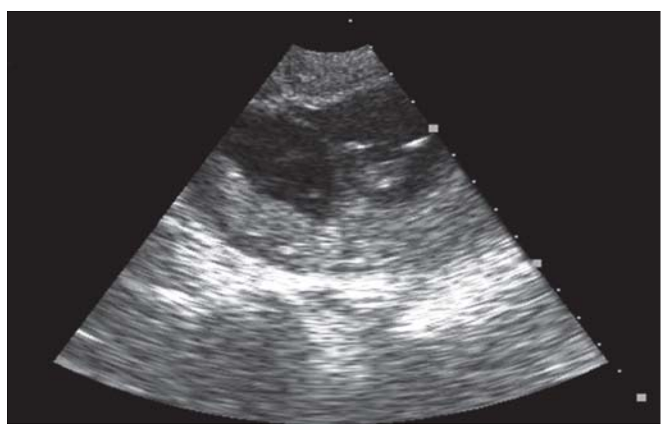

Figure 11: Early twin gestation as seen on handheld ultrasound

- Determination if fetus is alive
- Determination of fetal movements
- Measurements of amniotic fluid index
- Determination of fetal presentation (cephalic, transverse or breech)
- Determination of placenta and its position

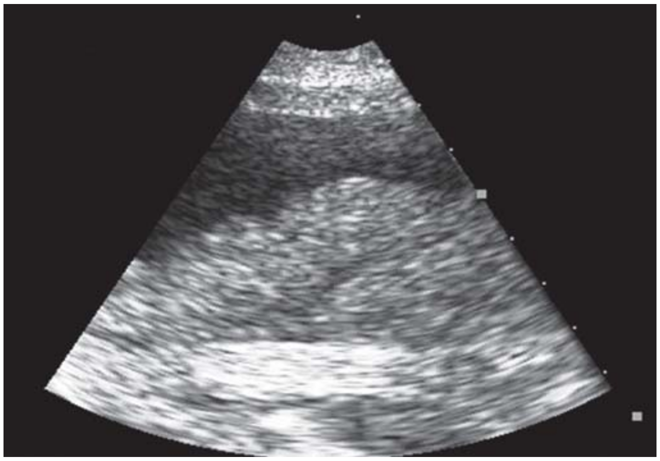

Figure 12: Placenta as seen on handheld ultrasound

- Measurement of uterine size
- Measurements of adnexal mass
- Determination of free fluid in cul-de-sac

Findings on the handheld ultrasound exam were compared with the formal ultrasound exams. Our aim was to determine if the handheld ultrasound exam can replace a very basic formal ultrasound exam done on the standard larger ultrasound machines. Handheld ultrasound exam took 5 minutes or less. Our study showed that the handheld ultrasound exam was reliable in making initial diagnosis required by the limited ultrasound exam in obstetrics and gynecology. The results showed that the caution should be taken when examining patients with placenta previa and IUGR.

ULTRASOUND FRONTIERS

Ultrasound is proven to be the imaging modality that has profoundly advanced and is constantly advancing clinical practice in obstetrics and gynecology. 3D Doppler applications have potential clinical role in early detection of pre-eclampsia, IUGR, aneuploidy, preterm labor, chorioamnionitis and twin-to-twin transfusion syndrome. And if 3D ultrasound is not the advancement enough by itself, 4D ultrasound is opening complete new era in evaluation of fetal neurodevelopment and study of intrauterine behavior. The fetal face represents a “diagnostic window” for fetal diseases and syndromes.[34,35] By adding the temporal component to the examination, 4D ultrasound allows visualization of facial expressions that might be useful in the study of fetal behavior and this could potentially enable better understanding of intrauterine environment that could lead to detrimental tragedy called cerebral palsy.

CONCLUSIONS

- 3D Doppler is a unique technique that enables assessment of vascular signals within the whole investigated area.
- Homodynamic changes included in the process of placentation are one of the most exciting topics in the investigation of early human development.
- The measurement errors produced by automated fetal biometry translated into very small errors regarding gestational age of the fetus.
- The automation of ultrasound measurements has great potentials in improving productivity and patient throughput, enhancing accuracy and consistency of measurements and reducing the risk of repetitive stress injuries users.
- Handheld ultrasound exam is reliable in making initial diagnosis required by the limited ultrasound exam in obstetrics and gynecology.

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