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Prenatal Imaging: Ultrasonography and Magnetic Resonance Imaging

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Abstract

The Eunice Kennedy Shriver National Institute of Child Health and Human Development held a workshop on September 18–19, 2006, to summarize the available evidence on the role and performance of current fetal imaging technology and to establish a research agenda. Ultrasonography is the imaging modality of choice for pregnancy evaluation due to its relatively low cost, real-time capability, safety, and operator comfort and experience. First-trimester ultrasonography extends the available window for fetal observation and raises the possibility of performing an early anatomic survey. Three-dimensional ultrasonography has the potential to expand the clinical application of ultrasonography by permitting local acquisition of volumes and remote review and interpretation at specialized centers. New advances allow performance of fetal magnetic resonance imaging (MRI) without maternal or fetal sedation, with improved characterization and prediction of prognosis of certain fetal central nervous system anomalies such as ventriculomegaly when compared with ultrasonography. Fewer data exist on the usefulness of fetal MRI for non-central nervous system anomalies.

Imaging technology for fetal diagnosis has rapidly evolved, but the clinical applicability of newer fetal imaging technology has not been defined. Two-dimensional ultrasonography, the modality most commonly used for pregnancy evaluation, provides cost-effective, real-time imaging, offers high resolution, and is considered safe for mother and fetus. Three-dimensional/four-dimensional ultrasonography is increasingly available and also has been successfully used for detection of fetal structural anomalies involving the central nervous system, face, limbs, thorax, and spine; however, few studies examine outcomes.

Magnetic resonance imaging (MRI) has revolutionized general diagnostic imaging. Dramatic reductions in image acquisition time have allowed more effective use of MRI for fetal evaluation. High-quality fetal images are now routinely achievable without fetal sedation. The National Institute of Child Health and Human Development held a workshop on September 18–19, 2006 to suggest future research directions and to address gaps in the clinical application of obstetric imaging to advance the diagnosis of pregnancy complications and fetal pathology.

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FETAL ULTRASONOGRAPHY

Ultrasonography is able to detect many fetal structural and functional abnormalities. Despite being widely assumed, the capacity of prenatal ultrasonography to improve pregnancy outcome has not been consistently demonstrated. This is crucial because the adoption of routine ultrasound screening in the United States may add considerably to the cost of care in pregnancy, with no improvement in perinatal outcome.

The National Institutes of Health held a Consensus Development Conference in 1984 on “Diagnostic Ultrasound Imaging in Pregnancy.”¹ The panel concluded that prenatal diagnostic ultrasonography improves patient management and pregnancy outcome when there is an accepted medical indication. Randomized trials were recommended to determine the efficacy of routine screening of all pregnancies.

The Routine Antenatal Diagnostic Imaging with Ultrasound (RADIUS) study² enrolled 15,151 low-risk pregnant women to determine whether ultrasound screening decreased the frequency of adverse perinatal outcomes. The women randomly assigned to the ultrasound-screening group underwent ultrasonographic examination at 15–22 and 31–35 weeks of gestation. The control group received ultrasonography only for medical indications. The screening ultrasonograms did not reduce perinatal morbidity or mortality when compared with the selective use of ultrasonography based on clinician judgment, and the detection of major anomalies by ultrasound examination did not alter outcomes.

The results of the RADIUS study differed from those of the Helsinki Ultrasound Trial, which showed a lower perinatal mortality rate in the ultrasound-screening group (4.6 compared with 9.0 per 1,000, $P < .05$) because of the higher detection rate of anomalies and the subsequent termination of the affected pregnancies.³ In the RADIUS trial, the anomaly detection rate of 35% in the ultrasound-screening group was higher than the 10% rate in the control group. However, the detection of anomalies by ultrasound screening did not reduce adverse perinatal outcome for several reasons, including late detection of anomalies and the infrequent election of pregnancy termination by mothers of affected fetuses.⁴

At the time of the consensus statement in 1984, only 15–40% of pregnant women received at least one ultrasonogram. Since then nearly 67% of women have at least one prenatal ultrasound.⁵ The role of ultrasonography includes screening for congenital abnormalities and the diagnosis and management of obstetric pathologies, such as erroneous dating, growth abnormalities, and placenta previa.

Although the American Institute of Ultrasound in Medicine, the American College of Radiology, and the American College of Obstetricians and Gynecologists have established standards for ultrasonograms, there are many unresolved issues. The optimal number and timing of ultrasounds is yet to be established. The addition of views to the standard examination should be preceded by research studies documenting their value. The inclusion of “soft markers” for Down syndrome screening, uterine artery screening, and the use of venous Doppler for the management of fetal growth restriction are examples that require demonstration of perinatal benefit before adoption.

First-Trimester Ultrasonography

First-trimester ultrasound biometry can be used to determine the estimated due date, assess chorionicity in multiple gestations, and assess risk for aneuploidy. At 11–14 weeks of gestation, the combination of nuchal translucency and serum markers (pregnancy-associated plasma protein A, and free or total β -hCG) has been demonstrated to be an effective screening test for Down syndrome.⁶ The First- and Second-Trimester Evaluation of Risk Research Consortium

trial,⁷ the largest prospective U.S. study of first-trimester risk assessment, found that first-trimester risk assessment provides efficient Down syndrome risk assessment with detection rates of 87%, 85%, and 82% at 11, 12, and 13 weeks, respectively, that is superior to the second-trimester quadruple screen at a fixed false-positive rate of 5% (ie, 5% of unaffected pregnancies will have a positive test result).

Ongoing improvements in ultrasound technology allow more detail of fetal anatomy to be visualized at earlier gestational ages. The advantages of an early anatomic scan include the fact that the entire fetus fits in the transducer's focal zone; the position of the fetus changes frequently, so the fetus can be evaluated from many directions, the position of the fetus can be changed using the vaginal probe and the abdominal hand, and some anomalies are seen better before 14 weeks because they regress subsequently (eg, some cystic hygromas) (Appendix 2; available online at www.greenjournal.org/cgi/content/full/112/1/145/DC2). Last, in the obese patient, this may be the only opportunity for a good structural evaluation. However, there are limitations of a first-trimester anomaly scan. Not all anomalies are seen well, eg, heart, skeletal, certain central nervous system anomalies, and diaphragmatic hernias. Most providers are unfamiliar with the technique, and higher-quality equipment is required. Early fetal anomaly scanning has been studied, with anomaly detection rates varying from 20% in low- to 80% in high-risk populations.^{8–10} In these studies, a subsequent second-trimester ultrasonogram has been performed to detect additional anomalies, thus doubling the number of ultrasonograms required. The essential role of training and the learning curve for performance of first-trimester ultrasound anatomic surveys has been demonstrated.¹¹

An early fetal anatomic survey potentially may be attached to the first-trimester nuchal translucency scan to achieve “one stop shopping” for early prenatal assessment. A study comparing the use of ultrasonography at 11 0/7 to 13 6/7 weeks of gestation (the time of nuchal translucency evaluation) with repeat ultrasonography at greater than 20 weeks of gestation compared with a single second-trimester ultrasonogram is needed to evaluate sensitivity for congenital anomaly detection, as well as efficacy.

Second-Trimester Ultrasonography

The sensitivity of ultrasound diagnosis of fetal anomalies requires additional study beyond the now 15-year-old RADIUS trial. In the Eurofetus study,¹² 56% of 4,615 malformations were detected, and 55% of the major abnormalities were detected at 24 or fewer weeks of gestation. A screening 18-week ultrasonogram has de facto become the expected standard of care among most obstetricians despite the RADIUS study, but a U.S study has yet to be done to support this clinical conclusion. Outcome data are needed to determine the accuracy and effect of prenatal diagnoses of fetal anomalies and to provide better opportunities for prenatal treatment. Most anomaly scans are done at 18–20 weeks of gestation. Some anomalies are missed or may develop later, such as microcephaly, renal anomalies, dysgenesis of the corpus callosum, hypoplastic left heart, and achondroplasia. Methods to standardize the ultrasound examination to make it less operator-dependent and more efficient, as well as increased accessibility of ultrasonography in remote communities, are areas that require evaluation.

Genetic Ultrasonogram

Although there are many well-established indications for second-trimester ultrasonography, such as dating, growth (size/date discrepancy), determination of fetal number, placental location, and assessment for fetal malformations, second-trimester ultrasonography for Down syndrome risk assessment has conflicting data. This application of ultrasonography is separate from its role to detect obstetric complications of pregnancy. The “genetic ultrasonogram” refers to a systematic algorithm combining multiple individual ultrasound markers of Down syndrome with structural anomaly detection during the mid trimester to improve Down

syndrome risk assessment. Markers associated with Down syndrome include shortened humerus or femur, an increased nuchal skin thickness, nasal bone hypoplasia, pyelectasis, echogenic intracardiac foci, hypoplastic fifth digit, sandal gap toe, echogenic bowel, and widened iliac angle. Risk is adjusted by multiplying the a priori risk by the product of the respective ultrasound markers' likelihood ratios. A scan in which none of the markers are detected is believed to reduce the Down syndrome risk by about 50% to 60%.¹³

This "screening" approach was developed and has been studied almost exclusively in high-risk referral populations. Hobbins et al¹⁴ performed an eight-center study that validated the concept that the genetic ultrasonogram can be used to adjust the Down syndrome risk for high-risk patients. Of the 176 cases of trisomy 21, 125 fetuses (71%) had an abnormal long bone length (femur and/or humerus), a major structural abnormality, or a Down syndrome marker. Center sensitivities varied (64–76%). The sensitivity of individual markers varied from 3% for sandal gap toe to 46.5% for increased nuchal skin fold thickness. A condensed regimen of nuchal skin fold thickness, femur length, and a standard anatomic survey detected 56.8% of fetuses with Down syndrome. Furthermore, there is a high incidence of cardiac anomalies among Down syndrome fetuses and evidence to support the conclusion that a greater focus on this aspect during screening can further increase detection rates.¹⁵

Because there are few data on the accuracy of "markers" in low-risk women, results for high-risk women have been extrapolated. Again, assessment for markers sought in the genetic ultrasonogram of high-risk women has de facto become "standard" in low-risk women, yet a meta-analysis of second-trimester Down syndrome markers concluded that ultrasonographic markers are not of practical value in the low-risk population.¹⁶ Therefore, further study is needed to assess the value of these markers in low-risk women.

Three-Dimensional Ultrasonography

Currently, a minority of imaging specialists routinely utilize three-dimensional ultrasound technology. Experienced ultrasonographers acquire two-dimensional slices in series and mentally build a three-dimensional image. Goncalves et al¹⁷ reviewed 525 articles on three-dimensional/four-dimensional ultrasonography and found that three-dimensional ultrasonography provides additional diagnostic information for the diagnosis of facial anomalies, especially facial clefts, neural tube defects, and skeletal malformations. However, overall studies comparing two-dimensional and three-dimensional ultrasonography for the diagnosis of congenital anomalies have not demonstrated a difference in detection rates. Prospective study of 99 fetuses demonstrated that the sensitivity and specificity of three-dimensional/four-dimensional ultrasonography and two-dimensional ultrasonography for congenital anomalies were not significantly different.¹⁸

The principle of three-dimensional acquisition, volume imaging, can provide both two-dimensional and three-dimensional reconstructed images and enable the examiner to obtain anatomic views that are not possible with direct two-dimensional scanning and simplifies visualization of the fetal face (Fig. 1) and spine (Appendix 3; available online at www.greenjournal.org/cgi/content/full/112/1/145/DC3). This allows less-skilled operators to acquire the data and create meaningful representations. Therefore, three-dimensional ultrasonography may decrease image acquisition time and allow local acquisition of volumes and remote review and interpretation at specialized centers.¹⁶ Last, three-dimensional imaging has the potential to offer significant advantages over two-dimensional in organ volume measurement and estimation of fetal weight.

Four-dimensional ultrasonography (real-time three-dimensional ultrasonography) for the fetal cardiac examination may improve visualization of cardiac anatomy and allow better assessment of valvular function.¹⁷ Other potential future applications of four-dimensional ultrasonography

include the ability to perform invasive fetal procedures and more detailed assessment of fetal well-being.

The research agenda for three-dimensional ultrasonography should include development of a standardized scanning protocol for image acquisition and determination of its role in improving the diagnosis of congenital anomalies and pregnancy complications. Automated methods of three-dimensional ultrasonography are needed to simplify image generation, image manipulation, and storage. The development of an optimal data set to represent fetal anatomy in three-dimensional ultrasonography and use of a central volume databank to store these images would be a great asset for the field.

FETAL GROWTH ABNORMALITIES

Fetal Growth Restriction

Fetal growth restriction is a leading contributor to perinatal mortality; 40% of stillbirths are associated with fetal growth restriction.¹⁹ Patterns of normal fetal growth and fetal growth restriction need uniform, consistent definitions.²⁰ Once diagnosed, the management of preterm fetal growth restriction is a major clinical challenge; it is difficult to balance the risks of a potential stillbirth against those of an indicated preterm delivery with attendant neonatal morbidity and mortality. Available studies suggest that Doppler velocimetry is useful in improving the management of pregnancies complicated by fetal growth restriction.²⁰ There is a natural progression of Doppler findings in studies of growth-restricted fetuses. Initially, umbilical artery Doppler changes reflect increased impedance to flow. Absence or reversal of end diastolic flow in the umbilical artery represents further deterioration. Concurrently, there may be blood flow redistribution resulting in “brain sparing,” reflected by decreasing resistance to middle cerebral artery flow. With further deterioration, cardiac dysfunction leads to abnormal venous flow manifested by umbilical vein pulsatility and abnormal ductus venosus waveforms. The final steps manifested include central nervous system damage, with abnormal antenatal testing (nonstress test or biophysical profile) and then fetal death. Ductus venosus Doppler identifies preterm fetal growth-restricted fetuses at highest risk for adverse outcome, so understanding its role in the timing of delivery is crucial.²¹

Macrosomia

Macrosomia is associated with increased risks of delivery complications, cesarean delivery, and metabolic abnormalities of the newborn, but ultrasound prediction of macrosomia, and especially of risk of delivery complications such as shoulder dystocia, have been disappointing. Fetal limb volume has been proposed as a novel way to assess fetal growth and nutrition.²² Use of fractional limb volume by measuring the humeral or femoral length and defining a cylindrical limb volume may better predict fetal weight during late pregnancy.¹⁷ Only small studies of this technique are currently available. Lee and colleagues²³ used fractional limb volume measurements to estimate fetal weight in 100 fetuses within 4 days of delivery; the estimates deviated from the true birth weight by $-0.025\% \pm 7.8\%$. Prospective testing of 30 additional fetuses confirmed the superior performance of fractional limb volume over traditional two-dimensional ultrasonography methods to estimate fetal weight. (Fig. 2) (See also Appendix 4 and Appendix 5, available online at www.greenjournal.org/cgi/content/full/112/1/145/DC4 and www.greenjournal.org/cgi/content/full/112/1/145/DC5).

Uterine Artery Doppler

During pregnancy, the spiral arteries undergo a series of vascular transformations to ensure adequate blood supply to the intervillous space. The trophoblast invades these blood vessels and replaces the endothelium and muscular layer, converting the spiral arteries from small-

diameter, high resistance vessels into larger-diameter vessels with low resistance and high compliance. Doppler ultrasonography allows noninvasive study of impedance to flow in the uterine arteries.

Preterm preeclampsia, fetal growth restriction, and stillbirth are associated with failure of trophoblastic invasion of the spiral arteries. Doppler studies have shown that impedance to flow in the uterine arteries is increased in women likely to develop these conditions.²⁴ However, the indications and optimal timing of uterine artery evaluation, performance coupled with serum markers to improve sensitivity of second-trimester Doppler, and appropriate subsequent interventions are all research questions that need answers for effective clinical application of uterine artery Doppler screening.

Fetal Anemia

Recent advances in Doppler technology have led to the noninvasive monitoring of alloimmunization in pregnant women. Moderate or severe anemia is predicted by fetal middle cerebral artery peak systolic velocities above 1.5 times the median for gestational age, with a sensitivity of 100% and a false-positive rate of 12%.²⁵

Future research questions include whether middle cerebral artery peak systolic velocity is reliable for the diagnosis of fetal anemia due to other causes such as parvovirus, Kell-sensitized pregnancies, fetomaternal hemorrhage, nonimmune hydrops, monochorionic twins after the death of the cotwin, and twin-to-twin transfusion syndrome after laser therapy. The role of middle cerebral artery peak systolic velocity Doppler to determine the optimal interval between fetal transfusions and optimal timing for delivery needs to be clarified. Last, the long-term outcome of fetuses transfused in utero requires further research.

Congenital Heart Disease

Congenital heart disease (CHD) affects 5 to 8 per 1,000 live births. Congenital heart disease is the most common major abnormality, contributing to greater than one third of congenital anomaly deaths in childhood.²⁶ Risk factors for CHD are listed in the Box, "High-Risk Groups for Congenital Heart Disease." (see Appendix 6, online at www.greenjournal.org/cgi/content/full/112/1/145/DC6).²⁷ However, the majority of infants with cardiac defects (50–90%) are born to mothers without risk factors. Prenatal diagnosis of CHD should prompt determination of fetal karyotype, search for associated anomalies, parental preparation and counseling, and planned delivery. Prenatal diagnosis permits planned delivery with an associated improvement in hemodynamic status, less preoperative acidosis, and potentially decreased mortality rates.^{28,29}

Research into optimizing CHD screening and diagnosis is necessary. The four-chamber view in conjunction with views of the great arteries remains the best approach to screening for CHD (Fig. 3) (see also Appendix 7, available online at www.greenjournal.org/cgi/content/full/112/1/145/DC7). Sensitivity is directly related to the operator's expertise and level of training. Technology needs to be developed to lessen operator dependency, standardize image display, and generate reproducible images. This might be achieved through automation software, eg, volume-assisted computer display. The development of methods of cardiac evaluation for the general ultrasonographer and standards for fetal echocardiography for fetuses at risk is required.

ULTRASOUND SAFETY

Ultrasound has a demonstrated record of safety for more than 50 years of clinical use. Although no independently replicated epidemiologic data exist to suggest harmful effects of ultrasonography in the fetus, ultrasonography is a form of energy with two main bioeffects in

tissue: heat, a direct effect, and oscillatory movements, secondary to the alternating positive and negative pressure waves. These effects are inherent in the physical properties of ultrasonography and have not been shown to be harmful in humans.³⁰ However, most safety data are epidemiologic, collected before the permissible output of scanners was increased by a factor of almost 8, around 1992.³¹ The U.S. Food and Drug Administration recommends against the use of medically unindicated or commercial prenatal ultrasonography.³²

Although there is no evidence of harm, ultrasound power levels have gone up, and there is increasing use of more powerful color and spectral Doppler in the first trimester, so safety cannot be presumed. Dose is a quantitative measure that combines intensity and exposure time. No standard dose quantity has been identified for ultrasonography. Variation in tissue properties between individuals and scanning conditions influence dose in unpredictable ways. For all practical purposes, fetal dose cannot be precisely quantified. Documentation of dwell time, type of machine, and transducer used would begin to address the problem of lack of a dose metric for ultrasonography.

The bioeffects of clinical ultrasound exams are approximated by the thermal index for heating and by the mechanical index for cavitation effects. Both are indices of exposure, but neither takes time into account. Thermal index predicts potential for temperature increase, not actual rise, and it remains unknown whether there is a threshold for temperature-related bioeffects. Mechanical index expresses potential to induce inertial cavitation. Mechanical effects are less likely in the fetus, because foci susceptible to cavitation (ie, containing gas) are not present.³⁰ Maternal body size is important because examinations may be prolonged in heavier women, whereas at the same time fetal exposure may be reduced per unit time due to attenuation of the acoustic beam at greater depths.

Evidence in animals shows that exposure to diagnostic ultrasonography can produce significant temperature increases in the fetal brain near bone. The critical questions include whether the extent of ultrasound-induced temperature rise is sufficient to create a hazard and whether there is a threshold for hyperthermia-induced birth defects. In addition, the determination of possible neurophysiologic effects or responses to clinically relevant exposures is needed. In a review of epidemiologic studies of human exposure to ultrasonography, there were no effects noted on childhood cancer, dyslexia, speech development, or congenital anomalies.³³ However, there is very limited evidence that the frequent exposure of the human fetus to ultrasound waves may be associated with a nonsignificant decrease in newborn body weight,³⁴ a reduction in the frequency of right-handedness,³⁵ and delayed speech.³⁶

Ang et al³⁷ examined the effect of ultrasound waves on neuronal position within the embryonic cerebral cortex in mice. When mice were exposed to ultrasound waves for a total of 30 minutes or longer during neuronal migration, a small but statistically significant number of neurons failed to acquire their proper position and remained scattered within inappropriate cortical layers and/or in the subjacent white matter. The magnitude of dispersion of labeled neurons systematically increased with duration of exposure to ultrasound waves. The relevance of these findings for cortical development in humans is unclear. The ultrasound beam characteristics used in this study were well within clinical norms for fetal exams. There are, however, significant differences in the number of neurons and the size of the cerebral cortex between mouse and human. The distance between the exposed cells and transducer in Ang's experiments was shorter than in humans. Furthermore, the duration of neuronal production and the migratory phase of cortical neurons last 18 times longer in the human fetus than in mice. Thus, an exposure of 30 minutes represents a much smaller proportion of the time dedicated to development of the cerebral cortex in humans than in mice, making human corticogenesis less vulnerable to ultrasound waves.³⁷ All these questions raise important future research issues.

Continuing research into bioeffects and safety of ultrasonography in pregnancy is warranted. It is essential to examine the possible effects of ultrasound waves on cortical development in nonhuman primates, where the duration of embryogenesis and the size and complexity of migratory pathways are similar to those in humans, as well as to perform comprehensive epidemiologic studies in humans.

ULTRASOUND TRAINING AND EDUCATION

Ultrasound training and education are of paramount importance because human factors drive both image quality and interpretation. The number of ultrasound examinations that should be performed to be considered competent and the definition of a quality scan have never been delineated. End users have very limited knowledge about the bioeffects and safety of ultrasonography. The general opinion was that studies should be designed to evaluate the minimal curriculum requirements for the performance of obstetric ultrasonography and to evaluate opportunities such as Web-based training to help trainees gain experience in a uniform, reproducible, and ultimately testable way. Systems for quality review of images need to be developed. Last, the development of simulators is crucial for teaching and ongoing quality monitoring.

FETAL MAGNETIC RESONANCE IMAGING

Ultrasonography has been the criterion standard for fetal imaging and will likely remain so. However, limitations include operator variability, fetal position, gestational age effects (poor visualization, skull ossification), and tissue definition. Early studies using MRI in the evaluation of fetal morphology were hindered by fetal motion. Current software and hardware for MRI now allow performance of MR examinations with high-quality images obtained in less than 1 second (Fig. 4), permitting fetal imaging without maternal or fetal sedation. Although fast MRI techniques are widely available, few practitioners have knowledge of fetal anatomy and pathology with this technique.

Central Nervous System Evaluation

Magnetic resonance imaging may aid in the diagnosis, patient counseling, and case management regarding fetuses suspected of having central nervous system (CNS) anomalies. Ultrasonographic evaluation of the fetal CNS is limited by: 1) the nonspecific appearance of some anomalies; 2) technical factors that limit resolution of the side of the brain near the transducer; 3) ossification, which can hamper visualization of posterior fossa structures; and 4) subtle parenchymal abnormalities that frequently cannot be visualized with ultrasonography. Magnetic resonance imaging allows direct multiplanar visualization of the brain parenchyma and thus allows detailed evaluation of CNS anatomy that may not be possible with ultrasonography due to fetal position or advanced gestational age and skull ossification.

Preliminary studies suggest that MRI may improve diagnostic accuracy and change counseling for many fetal CNS lesions (Fig. 5) (see also Appendix 8, available online at www.greenjournal.org/cgi/content/full/112/1/145/DC8).^{38,39} Further evaluation of the incremental benefit of MRI in understanding the prognosis of fetuses with ventriculomegaly and other lesions will result in better understanding of how MRI changes counseling and care.

Non-Central Nervous System Anomalies

Magnetic resonance imaging may contribute additional information in defining fetal abdominal, lung, and pelvic masses.³⁹ Magnetic resonance imaging is helpful in fetuses with congenital diaphragmatic hernias in assessing the amount of normal-appearing remaining lung, which may be poorly visualized with ultrasonography but better delineated with MRI.³⁹ Further

studies are needed to assess how additional information from MRI of abnormalities in the fetal chest and abdomen affect patient management and outcome.

We need to compare high-quality ultrasonography to MRI to determine the incremental benefit of MRI. In a study by Levine et al⁴⁰ in which confirmatory ultrasonograms were performed before MRI, of 74 fetuses with thoracic abnormalities, MRI provided additional information over ultrasonography in 38% of patients. However, MRI information regarding the thorax changed care in only 8% of fetuses. Prenatal thoracic MRI may affect care in the fetal surgery patient and in cases in which the diagnosis is unclear by ultrasonography.

The indications for MRI of the fetal abdomen and pelvis are less well established. In particular, MRI could be helpful in assessment of sacrococcygeal teratoma. Magnetic resonance imaging may provide better evaluation of intrapelvic and intraspinal extension than ultrasonography, which could affect surgical planning.³⁹

In Utero Surgical Evaluation

Magnetic resonance imaging is being used in the evaluation of fetuses that will undergo in utero surgery and in fetuses being assessed for a potential ex utero intrapartum treatment procedure for suspected airway obstruction. Maneuvers are undertaken in the ex utero intrapartum treatment procedure to secure the airway or put the fetus on extracorporeal membrane oxygenation before clamping the umbilical cord. Prenatal MRI has been used to assess potential airway obstruction from a tumor or lymphatic malformation (Fig. 6).³⁹ In patients undergoing in utero surgery for neural tube defects, MRI is helpful in characterizing the Chiari malformation, because the extent of cerebellar herniation is easily followed on serial MRI.³⁹

Magnetic Resonance Volumetry

Magnetic resonance volumetry is based on the assumption that fetal weight estimates computed from volume determinations will be more accurate than those obtained from two-dimensional ultrasonographic measurements. Although ultrasonographic estimates of fetal weight are accurate for the majority of the fetal population, at the extremes of weight, for the growth-restricted and macrosomic fetus, in which accuracy is most important, ultrasonographic weight predictions are frequently limited. Magnetic resonance imaging is less affected by patient body habitus, and instead of two-dimensional measurements being used for estimation of weight, a true fetal mass may be measureable.³⁹

A single MRI fetal liver volume measurement, performed several weeks before delivery can distinguish fetuses subsequently diagnosed as being growth-restricted with improved accuracy over ultrasonography.⁴¹ Magnetic resonance imaging may provide more reliable assessment of amniotic fluid volume and visualization of fetal anatomy compared with ultrasonography when oligohydramnios is present. Information regarding fetal fat, functional evaluation of the placenta, and placental volume assessments in combination with other data should be investigated to determine if we can improve our ability to distinguish between the constitutionally small but appropriately grown fetus and the fetus at risk due to placental insufficiency. Similarly, additional useful information for the evaluation of the macrosomic fetus may include pelvimetry, fetal shoulder width and fetal fat.³⁹ The incremental benefit of MRI beyond that of ultrasonography in the assessment of fetuses at the extremes of fetal growth remains to be determined in clinical practice.

Placenta Accreta

Placenta accreta occurs in about 1 of 2,500 deliveries.⁴² The incidence of placenta accreta is increasing primarily because of the rise in cesarean delivery rates. Small case series^{43–45} have

suggested that MRI may be helpful in diagnosing placenta accreta, but in one study, all six cases of anterior placenta accreta were diagnosed by ultrasonography.⁴⁶ Ultrasonographic findings of placenta accreta are loss of the retroplacental myometrial zone, thinning or disruption of the uterine serosa/bladder interface, focal exophytic masses, and lacunar flow in the placenta. Magnetic resonance imaging findings of placenta accreta are similar to those described ultrasonographically.³⁹ On both MRI and Doppler ultrasonography, when placenta percreta invades the bladder wall, vessels can be visualized extending from the placenta into the bladder. The largest study to date examined 300 cases of accreta diagnosed by ultrasonography prospectively and found that MRI accurately defined the area of invasion of placenta in the myometrium, guided surgical technique, led to a reduction in surgical morbidity, and increased the frequency of conservative surgery.⁴⁷ The diagnostic indices of MRI compared with ultrasonography for abnormalities of placental implantation need to be understood before the more expensive technology of MRI becomes clinically adopted for this indication.

Functional Magnetic Resonance Imaging

Magnetic resonance spectroscopy is being developed for clinical use in the fetus. Functional MRI shows changes in composition of fetal tissues and fluids, potentially allowing assessment of third-trimester brain ischemia or hypoxia, or study of fetal metabolism by liver assessment. Magnetic resonance imaging can measure uterine artery blood flow, spiral artery blood movement, and movement of blood in the placenta. Placental oxygen transport and placental perfusion can be studied. There are challenges for performing functional MRI, including acquisition strategies, dealing with motion, and task design.³⁸

Fetal Magnetic Resonance Imaging Safety

The safety of fetal MRI has not been fully evaluated. Fetal MRI using 1.5-T magnets may be performed in any trimester.⁴⁸ However, because of limited data, MRI in the first trimester is currently avoided whenever feasible. Even less is known about the safety of MRI with newer 3-T magnets, and even higher strength MRI systems are becoming available.³⁹

When the fetus is imaged by MRI, it is exposed to a combination of three electromagnetic fields of varying strengths and frequencies: static magnetic fields, radiofrequency fields, and fast switching gradient fields. Overall, there is no indication that the use of clinical MR procedures during pregnancy produces adverse effects, but the safety of such procedures during pregnancy has not been proven.

Relatively little work has been done to date on fetal development after exposure to static fields, and among those few studies, the results are inconclusive. Static magnetic field experiments on animals have identified malformations and crown-rump length reduction (mice), increased fetal loss (rat), and developmental effects (chick embryo).^{49,50} A 2005 review stated that no adverse effects on reproduction and development have been consistently demonstrated from static magnetic field, but further studies with exposure to fields in excess of 1 T are still needed.⁵⁰

Exposure to radiofrequency (RF) fields causes tissue heating. The amount of RF allowed is controlled by measuring and limiting the specific absorption rate, the rate at which RF energy is deposited in tissue. According to the Health Protection Agency (UK), the fetus is particularly sensitive to RF-induced heating because normal pathways for heat loss in mammals are not available to the fetus.⁵¹ Temperature loss requires a heat gradient that is not available to the fetus, because the mother's body temperature is 37°C. With MRI it is difficult to ascertain the degree of direct fetal heating; it is dependent on whether the fetus is in the scanning zone. In 2004 the International Commission on Non-Ionizing Radiation stated that there is a need to

“define more precisely the spatial deposition of RF energy during an MR procedure and the corresponding temperature fields in the human body including modeling of the pregnant woman and fetus.”⁵²

Last, with regard to gradient fields in fetal imaging, fast sequences are used to overcome image quality artifacts caused by fetal motion. This can lead to use of high specification magnetic field gradients. The main concerns are induced currents and acoustic noise. With acoustic noise, the concern is damage to the developing auditory pathways.⁵²

Research is needed to develop better models of the pregnant woman to more accurately investigate exposure to static and radiofrequency fields and acoustic noise effects. There is a further need for good computer and animal exposure models. Improved acquisition times and increased signal-to-noise ratio for functional MRI of fetuses are required.

The Box, “Potential Applications of Fetal Magnetic Resonance Imaging” lists conditions for which prenatal MRI may potentially provide useful information in addition to ultrasonography in defining anomalies and stratification of fetal prognosis (see Appendix 9 online at www.greenjournal.org/cgi/content/full/112/1/145/DC9). The fetal MRI research agenda should focus on anatomic information provided by MRI, effect on counseling, ascertaining postnatal and long-term outcomes, cost-effectiveness, and technology development. Last, a national registry of normal fetal MRI images in pregnancy would be a valuable resource.

FUTURE IMAGING DEVELOPMENTS

The development of an imaging phantom that replicates the properties of living tissues and sets standards for imaging would significantly advance the field. New imaging technologies such as medical reflectance photonic imaging and the ability to directly assess fetal neurologic assessment are additional important research areas. Whereas biophysical profile testing only allows for assessment of brainstem functioning, SQUID Array for Reproductive Assessment provides direct cortical assessment using magnetoencephalography, which noninvasively records magnetic signals generated from the brain. Fetal neurologic assessment by SQUID Array for Reproductive Assessment involves detection of fetal auditory evoked responses, visual evoked responses and spontaneous brain activity.⁵³ Persistent electrographic background abnormalities are associated with adverse neurodevelopmental outcome.⁵⁴ Spontaneous cortical activity is likely important in the fetus because reproducible patterns are seen in the healthy early preterm infant. Fetal magnetoencephalography may add functional information when cerebral abnormalities are detected and permit classification of the severity of fetal neurologic diseases.

CONCLUSION

Ultrasonography continues to be the imaging modality of choice for pregnancy evaluation due to its relatively low cost, real-time capability, and operator comfort and experience. First-trimester ultrasonography is extending pregnancy evaluation earlier and three-dimensional ultrasonography has the potential to improve the clinical application of ultrasonography. Fetal MRI seems to have a role in improved characterization and prediction of prognosis of certain anomalies such as ventriculomegaly. However, limitations of fetal MRI include the lack of availability of equipment and radiology expertise, higher cost, and longer time to perform an examination.

Overall, there was consensus that every fetus deserves to have a “physical examination,” ie, all fetuses should have a screening ultrasonogram for the detection of fetal anomalies and pregnancy complications. Collaborative studies involving maternal–fetal medicine specialists,

radiologists, neonatologists, and developmental pediatricians to assess the effect of fetal imaging on improving short- and long-term pregnancy outcomes are needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.
Three-dimensional ultrasonography of fetal face, 31-week profile. Courtesy of Philips Medical Systems.
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Fig. 2.

Qualitative differences are visually evident between two different term infants. **A.** Decreased soft tissue of a neonatal thigh for an infant with intrauterine growth restriction at 2,845 g and 39.7 menstrual weeks; **B.** increased soft tissue of a neonatal thigh in an infant with macrosomia at 4,368 g and 38.4 menstrual weeks. Corresponding differences in the fetal thigh can be quantified using three-dimensional ultrasonography. Reprinted from Lee W, Deter RL, McNie B, Gonçalves LF, Espinoza J, Chaiworapongsa T, et al. Individualized growth assessment of fetal soft tissue using fractional thigh volume. *Ultrasound Obstet Gynecol* 2004;24:766–74. Reddy. *Prenatal Imaging*. Obstet Gynecol 2008.

Fig. 3. Fetal heart. A four-chamber view of a fetal heart shows normal cardiac axis, normal chamber size, and normal mediastinal position and pulmonary veins; the atrial and ventricular septae and the atrioventricular valves “divide” the four chambers. Courtesy of Dr. Roy Filly. Reddy. Prenatal Imaging. Obstet Gynecol 2008.

Fig. 4.

A. Fetal magnetic resonance imaging. Reproduced with permission from Dr. Deborah Levine from Web site bidmc.harvard.edu/fetalatlas/. **B.** Fetal magnetic resonance imaging. Reddy. Prenatal Imaging. Obstet Gynecol 2008.

Fig. 5. Fetal magnetic resonance imaging with ventriculomegaly showing **A.** kinked brainstem (*arrow*) and **B.** polymicrogyria (*arrow*). Courtesy of Dr. Roy Filly. Reddy. Prenatal Imaging. Obstet Gynecol 2008.

Fig. 6.
Fetal magnetic resonance imaging with thyroid teratoma. Courtesy of Dr. Deborah Levine.
Reddy. Prenatal Imaging, Obstet Gynecol 2008.