Fetal Neuroimaging by Transvaginal 3D Ultrasound and MRI

Ritsuko K Pooh, KyongHon Pooh

ABSTRACT

Three-dimensional (3D) ultrasound is one of the most attractive modality in the field of fetal ultrasound imaging. In multiplanar imaging of the brain structure, it is possible to demonstrate not only the sagittal and coronal sections but also the axial section of the brain, which cannot be demonstrated from parietal direction by a conventional 2D transvaginal sonography. Parallel slicing provides a tomographic visualization of internal morphology similar to MRI imaging. Fetal neuroimaging with advanced 3D ultrasound technology is easy, noninvasive and reproducible methods. It produces not only comprehensible images but also objective imaging data. It has been controversial whether ultrasound or MRI is more practical and effective in prenatal assessment of fetal CNS abnormalities.

In the assessment of enlarged ventricles, no significant difference between dedicated neurosonography and MRI in detection of intracranial structure. However, MRI is superior to ultrasound in evaluation of the brainstem, posterior fossa and cortical development especially in the late pregnancy. Meanwhile, transvaginal high-frequency 3D ultrasound has superiority to MRI in detection of intracranial calcification, vascular anatomy, intratumorl vascularity, bony structure.

For CNS anomaly screening scan, ultrasound is no doubt the first modality, and once CNS abnormality is suspicious, after considering what to be detected and evaluated in each abnormal CNS case. Of course, those two technologies should be utilized as alternatives and complementaries as well. In terms of fetal neurological function analysis, four-dimensional ultrasound research on fetal behavior have been launched in multicenters, and it will be greatly expected to elucidate relations between antenatal behavior and postnatal neurological prognosis.

Keywords: Neuroimaging, Transvaginal ultrasound, Three-dimensional (3D), Magnetic resonance imaging (MRI).

INTRODUCTION

Imaging technologies have been remarkably improved and contributed to prenatal evaluation of fetal central nervous system (CNS) development, and assessment of CNS abnormalities in utero.

Conventional transabdominal ultrasonography, by which it is possible to observe fetuses through maternal abdominal wall, uterine wall and sometimes placenta, has been most widely utilized for antenatal imaging diagnosis. By transabdominal approach, whole central nervous system of fetuses can be well demonstrated, for instance, the brain in the axial section and the spine in the sagittal section. However, transabdominal approach to the fetal central nervous system, has several obstacles, such as maternal abdominal wall, placenta and fetal cranial bones, and it is difficult to obtain clear and detailed images of fetal CNS structure.

Introduction of high-frequency transvaginal transducer has contributed to establishing “sonoembryology” and recent general use of transvaginal sonography in early pregnancy enabled early diagnoses of major fetal anomalies. In the middle and late pregnancy, fetal CNS is generally evaluated through maternal abdominal wall. The brain, however, is three-dimensional structure, and should be assessed in basic three planes of sagittal, coronal and axial sections. Sonographic assessment of the fetal brain in the sagittal and coronal section, requires an approach from fetal parietal direction. Transvaginal sonography of the fetal brain opened a new field in medicine, “neurosonography”. Transvaginal approach to the normal fetal brain during the second and third trimester was introduced in the beginning of 1990s. It was the first practical application of three-dimensional central nervous system assessment by two-dimensional (2D) ultrasound. Transvaginal observation of the fetal brain offers sagittal and coronal views of the brain from fetal parietal direction through the fontanelles and/or the sagittal suture as ultrasound windows. Serial oblique sections via the same ultrasound window reveal the intracranial morphology in detail. This method has contributed to the prenatal assessment of congenital CNS anomalies and acquired brain damage in utero.

Basic Anatomical Knowledge of the Brain

As described above, the brain should be understood as a three-dimensional structure. It is generally believed that the brain anatomy is complicated and there must be lots of terms to remember. However, in order to demonstrate the brain structure
and evaluate fetal CNS disorders, it is not necessary to remember all the detailed structure. Here, essential anatomical structures are selected for neuroimaging and comprehension of fetal CNS diseases. Figure 1 shows the basic brain anatomy in the axial and sagittal sections, and Figure 2 shows the anterior coronal and posterior coronal sections.

**Transvaginal 3D Sonographic Assessment of Fetal CNS**

Three-dimensional (3D) ultrasound is one of the most attractive modality in the field of fetal ultrasound imaging. There are two scanning methods: free-hand scan and automatic scan. Automatic scan by dedicated 3D transducer produces motor driven automatic sweeping and is called as a fan scan. With this method, a shift and/or angle-change of the transducer is not required during scanning and scan duration needs only several seconds. After acquisition of the target organ, multiplanar and, tomographic imaging analyses are possible. Combination of both transvaginal sonography and 3D ultrasound may be a great diagnostic tool for evaluation of three-dimensional structure of fetal CNS. Recent advanced 3D ultrasound equipments have several useful functions as mentioned below:

- Surface anatomy imaging
- Bony structural imaging of the calvaria and vertebrae
- Multiplanar imaging of the intracranial structure
- Tomographic ultrasound imaging of fetal brain in any cutting section
- Thick-slice imaging of the intracranial structure
- Simultaneous volume contrast imaging of the same section or vertical section of fetal brain structure
- Volume calculation of target organs, such as intracranial cavity, ventricle, choroid plexus and intracranial lesions
- Three-dimensional sonoangiography of the brain circulation (3D power Doppler or 3D color Doppler).

It is well known that 3D ultrasound demonstrates the surface anatomy. In cases of CNS abnormalities, facial abnormalities and extremities abnormalities are often complicated. Therefore, surface reconstructed images are helpful. Bony structural imaging of the calvaria (Fig. 3) and vertebrae (Figs 4 and 5) are useful in cases of craniosynostosis and spina bifida. The vertebral level of spina bifida may provide important information to prospect postnatal neurological deficits. In multiplanar imaging of the brain structure, it is possible to demonstrate not only the sagittal and coronal sections but also the axial section of the brain, which cannot be demonstrated from parietal direction by a conventional 2D transvaginal sonography (Fig. 6). Transvaginal 3D ultrasound is the first modality during the first and early second trimesters. In the late second and third trimester, magnetic resonance imaging (MRI) is occasionally utilized as a prenatal diagnostic tool.

As shown in Figure 7, images obtained by tomographic ultrasound imaging (TUI) are quite similar to pictures of MRI. The superior point of TUI to MRI is that it is easily possible to change slice width, to magnify and rotate images in any direction. This function is extremely useful for detailed CNS assessment and also for consultation to neurosurgeons and neurologists. Thick-slice imaging of the intracranial structure (Fig. 8) and simultaneous volume contrast imaging (VCI) of the same plane or vertical plane of conventional 2D image are often convenient to observe the gyral formation and inside lateral ventricles. The premature brain image obtained by use of VCI clearly demonstrates anatomical CNS structure.

Volume extracted image and volume calculation of the fetal brain in early pregnancy were reported in 1990s. In our institute, Voluson 730 Expert (GE Medical Systems, Milwaukee, USA) with transvaginal 3D transducer and 3D or 4D view software (Kretztechnik AG, Zipf, Austria) has been used for volume extraction and volume estimation of the brain structure. On three orthogonal images, the target organ can be traced automatically or manually with rotation of volume imaging data. After tracing, volume extracted image and volume calculation data are shown (Fig. 9). Three-dimensional fetal brain volume measurements have a good intraobserver and interobserver reliability and could be used to determine estimated gestational age. Volume analysis by 3D ultrasound provides exceedingly informative imaging data. Volume analysis of the structure of interest provides an intelligible evaluation of the brain structure in total, and longitudinal and objective assessment of enlarged ventricles and intracranial occupying lesions (Fig. 10). Any intracranial organ can be chosen as a target for volumetry, no matter how distorted its shape and appearance may be. In new method of inversion mode,
Fig. 2: Basic anatomy of the fetal brain (coronal section)

Fig. 3: Fetal craniofacial skeletal structure at 11 and 14 weeks of gestation. Craniofacial bony structure rapidly develops in the first half of pregnancy. At 11 weeks, premature cranial bones (frontal and parietal bones) and facial bone (nasal bone, maxilla and mandible) are demonstrated. At 14 weeks, metopic suture and coronal sutures are well formed according to development of cranial bones.

Fig. 4: 3D image of normal vertebral structure at 16 weeks of gestation. 3D reconstructed image of the surface level (left), vertebral arch level (middle) and vertebral body level (right). Intervertebral disk spaces are well-demonstrated.

Fig. 5: Fetal vertebral development by 3D US from 9 to 22 weeks of gestation. Approaching stage of bilateral vertebral lamina according to neural tube closure is visible with advanced gestational weeks.

Fig. 6: 3D orthogonal view of normal brain at 18 weeks of gestation. Three orthogonal view is useful to obtain orientation of the brain structure. Coronal (left upper), sagittal (right upper) and axial (left lower) images can be visualized on a single screen. Any rotation of the brain image around any (x, y, z) axes is possible.
Fig. 7: Tomographic ultrasound imaging (TUI) of the fetal brain. Normal brain in the coronal cutting section at 31 weeks of gestation. Intracranial structure including gyral formation is clearly demonstrated.

Fig. 8: 3D thick slices of the brain (20 weeks of gestation). Axial thick slice (left) and coronal thick slice (right) of the premature brain. Observation by those 3D thick slices, anatomy of cortical structure and inside of ventricles become comprehensive.

Fig. 9: 3D volume extraction and volumetric analysis of lateral ventricle and choroid plexus. On three orthogonal sections, the target organ can be traced automatically or manually with rotation of volume imaging data. After tracing, volume extracted image (right) is demonstrated, and volume calculation data is shown. Middle graphs show normograms of ventricular size (upper) and choroid plexus size (lower) during pregnancy.

The cystic portions within the volume are displayed entirely as an echogenic area, while the grayscale portions of the image are rendered as transparent, and recently it has been applied in fetal diagnosis. Figure 11 shows inversion-mode images of enlarged ventricles seen at 19 weeks of gestation.

The brain circulation demonstrated by transvaginal 2D power Doppler was first reported in 1996. Thereafter, transvaginal 3D power Doppler assessment of fetal brain

Fig. 10: 3D volume extraction and volumetric analysis of lateral ventricle and intracranial cavity. Each volume of right (RV) and left ventricles (LV) and intracranial cavity volume can be calculated by 3D volumetry. Total ventricular volume/intracranial cavity (ICC) volume shows ventricles occupying rate, and it is useful for longitudinal assessment of ventriculomegaly cases.
vascularity was successful. Recently, by advanced technology of directional power Doppler, 3D angiostructural image has become furthermore sophisticated (Fig. 12). Recent high-frequent transvaginal neuroscan has been able to demonstrate the medullary veins from the cortex towards subependymal area (Fig. 13).

The three primary brain vesicles of forebrain (prosencephalon), midbrain (mesencephalon) and hindbrain (rhombencephalon) are formed in early embryonal period. At 7 and 8 weeks of gestation, these three primary brain vesicles are demonstrated on the midsagittal plane. The forebrain partly divides into two secondary brain vesicles of the telencephalon and diencephalons, and the hindbrain partly divides into the metencephalon and myelencephalon. The five secondary brain vesicles are consequently formed. The telencephalon forms derivatives of cerebral hemisphere and lateral ventricles. At 9 weeks of gestation, those secondary vesicles are detected by sonography. Thereafter, the premature brain vesicles rapidly develop during the first half of pregnancy. The choroid plexuses develop in the roof of the third ventricle, in the medial walls of the lateral ventricles and in the roof of the fourth ventricle. The choroid plexuses secrete ventricular fluid, which becomes cerebrospinal fluid (CSF). The choroid plexuses are high echogenic structure, detectable from 9th gestational week and conspicuous during the first trimester. From the beginning of the second trimester, the choroid plexuses of lateral ventricle gradually change its location backward. As the cerebral cortex develops, the commissures connect corresponding areas of the cerebral hemispheres with one another. The largest cerebral commissure is the corpus callosum, connecting neocortical areas. The corpus callosum initially lies in the lamina terminalis, but fibers are added to it as the cortex enlarges, as a result, it gradually extends beyond the lamina terminalis. The rest of the lamina terminalis lies between the corpus callosum and the fornix. It becomes stretched to form the thin septum pellucidum, a thin plate of brain tissue. The corpus callosum extends over
the roof of the diencephalon.27 The corpus callosum is detectable by ultrasound from around 16 weeks of gestation in some cases and at 18 weeks in most cases. Figure 14 shows normal 17-week brain. Neuroimaging in the third trimester, gyral formation is a main change of the brain development (Fig. 7). Initially, the surface of the hemispheres is smooth, however, as growth proceeds, sulci (grooves or furrows) and gyri (convolutions or elevations) develop. The sulci and gyri permit a considerable increase in the surface area of the cerebral cortex without requiring and extensive increase in cranial size. As each cerebral hemisphere grows, the cortex covering the external surface of the corpus striatum grows relatively slowly and is soon overgrown. This buried cortex, hidden from view in the depths of the lateral sulcus (fissure) of the cerebral hemisphere, is the insula.27

3D/4D Sonography and MRI: Alternatives or Complementaries

In multiplanar imaging of the brain structure, it is possible to demonstrate not only the sagittal and coronal sections but also the axial section of the brain, which cannot be demonstrated from parietal direction by a conventional 2D transvaginal sonography. Parallel slicing provides a tomographic visualization of internal morphology similar to MRI. Parallel slices used to be obtained on translating the cutting plane, however, recent advanced technology can produce tomographic ultrasound images and demonstrate a series of parallel cutting slices on a single screen as well as MRI does.14 As described above, images obtained by tomographic ultrasound imaging (TUI) are quite similar to those of MRI. The superior point of TUI to MRI is easy off-line analysis with changing slice width, magnifying images and rotating images in any directions. This function is extremely useful for detailed CNS assessment and also for consultation to neurosurgeons and neurologists. As shown in Figure 15 (hydrocephalus at 21 weeks of gestation, ultrasound and MRI) and Figure 16 (hydrocephalus ex vacuo, ultrasound and MRI), the transvaginal 3D tomographic ultrasound imaging demonstrates the detailed intracranial structures and seems not to require the further imaging modality.

Fetal neuroimaging with advanced 3D ultrasound technology is easy, noninvasive and reproducible method. It produces not only comprehensible images but also objective imaging data. Easy storage/extraction of raw volume data set enables easy off-line analysis and consultation to neurologists and neurosurgeons. Three-dimensional technology also provides us a longitudinal study of maldevelopment of CNS diseases by a serial neuroscan through a whole gestational period. Dedicated transvaginal 3D ultrasound is no doubt the first modality suitable for visualization and assessment of fetal CNS. Although, the first introduction of transvaginal fetal neurosonography, which has revolutionized the visualization of the fetal brain was almost 20 years ago, this approach has still not gained popularity in the world. Malinger et al28 described that this fact may be due to the relatively complex brain anatomy and pathology that is usually not familiar enough to most obstetricians and due to reluctance to use transvaginal sonography in many countries.

Fig. 15: Tomographic ultrasound imaging (TUI) and MRI of hydrocephalus at 21 weeks of gestation. (left) Sagittal, axial and coronal parallel cutting sections by sonography well-demonstrate ventriculomegaly. Partial agenesis of the corpus callosum is detected in the midsagittal section. (right) MRI images of the same case. No significant difference between sonography and MRI

Fig. 16: Tomographic ultrasound imaging (TUI) and MRI of hydrocephalus ex vacuo at 30 weeks of gestation. (upper) TUI coronal image of the brain. Note the conspicuous external subarachnoid/subdural space around hemispheres (lower). MR images of the same case. The cause of this phenomenon was unknown and this space spontaneously disappeared 3 weeks later. Array CGH of amnio cells was normal but postnatal neurological prognosis has been progressively deteriorated
Recent advances in fast MRI technology has remarkably improved the T2-weighted image resolution despite a short acquisition time, and minimized artifacts due to fetal movement and/or maternal respiratory motion. MRI is not influenced by physical factors, such as fetal location, fetal head position and ossification of fetal cranial bones, which sometimes obstruct transvaginal ultrasound approach. Magnetic resonance imaging is playing an increasingly prominent role in depicting brain maturation, especially cortical formation that follows a temporospatial pattern, and in detecting developmental abnormalities of the cortex and other brain sectors. MRI of fetal CNS possesses less abilities in detecting bony structure and angioarchitectonics and in volumetric assessment, compared with transvaginal 3D ultrasound imaging. However, in multiplanar imaging, MRI has much superiority in the assessment of a whole intracranial structure, including the brainstem (Figs 17 and 18), posterior fossa and gyral formation (Fig. 19) with better contrast between different tissue. In cases of microcephaly with difficulty of obtaining ultrasound windows of fontanelles and sutures, intracranial observation by MRI is much more helpful than transfontanelle ultrasound neuroscan.

It has been controversial whether ultrasound or MRI is more practical and effective in prenatal assessment of fetal CNS abnormalities. Several previous studies on MRI in diagnosis of fetal brain anomalies have reported that MRI added more valuable information than ultrasound. Kubic-Huch et al. published the statistical analysis study with the result finding no statistically significant difference between sonography and MRI for the detection of abnormality in any organ system. Malinger et al. criticized that the past reports describing superiority of MRI over ultrasound may have been biased because a comparison had been done with routine transabdominal ultrasound exams without insistence on additional confirmatory tertiary level ultrasound examination, especially by transvaginal sonography. Their opinion seems to be right to the point. In their other article, they described that dedicated neurosonography by transvaginal sonography is equal to MRI in the diagnosis of fetal brain anomalies, in most cases MRI confirmed the ultrasonographic diagnosis and in a minority of cases each modality provided additional/different information. They also concluded that the major role of MRI was in reassurance of the parents regarding the presence or absence of brain anomalies. This is an easily acceptable observation for sonographers with expertise.

In fact, as shown in Figures 15 and 16, there is no significant difference between dedicated neurosonography and MRI in...
Fig. 20: Features of 3D sonography and MRI in cases of myelomeningocele. In cases of myelomeningocele, 3D ultrasound can demonstrate the accurate vertebral level of spina bifida (upper left) and affected foot joint appearance (lower left). MRI can demonstrate the condition of chiari type II malformation (upper right, arrows) and spinal cord inside the spinal canal (lower right, arrows) in detail. In late pregnancy, cerebrospinal region and intravertebral structure cannot be depicted by sonography because of cranial/vertebral ossification, therefore, MRI is more reliable in demonstrating those structures.

Fig. 21: Comparison of MR and sonographic images in a case of cytomegalovirus infection. Cytomegalovirus infection often affects the brain development and representative features of the affected brain are ventriculomegaly, cortical maldevelopment and intracranial calcification. MR image at 34 weeks (left) well shows ventriculomegaly and cortical maldevelopment. Sonographic image at the same gestation (right) add the information of multiple intracranial calcification (inside circles), which is never demonstratable by MRI.

Fig. 22: Comparison of MR and sonographic images in a case of brain tumor at 26 weeks of gestation. (upper left and middle) Sonographic median and anterior-coronal images. (lower left and middle) MR median and anterior-coronal images. Note that the huge tumor below the oppressed bilateral hemispheres and oppressed brainstem. (upper right) Three orthogonal view and reconstructed image by 3D bidirectional power Doppler. (lower right) Intratumoral blood flow with low resistance is demonstrated. Intracranial morphology is more comprehensive by MRI than sonography due to MR feature of more contrast between different tissues, however, sonography is much more helpful in assessment of intratumoral vasculature and blood flow analysis.

Fig. 23: 3D sonographic feature of extra-CNS abnormality assessment. 3D sonographic surface anatomy can demonstrate extra-CNS abnormalities which are strongly associated or affected with brain anomalies, such as facial abnormalities and limb anomalies, (upper left) Facial anomaly with exophthalmos and prominent forehead in a case of Apert syndrome. (upper middle) Exophthalmos, nasal aplasia and cleft lip in a case of holoprosencephaly. (upper right and lower left) Syndactyly in a case of Apert syndrome. (lower right) Adducted thumb in a case of X-linked hydrocephalus.
Future Aspects

Regarding objectives of accurate prenatal diagnosis for proper management, any less-invasive modalities can be used. For CNS abnormaly screening scan, ultrasound is no doubt the first modality, and once CNS abnormality is suspicious, after considering each advantage and disadvantage of transvaginal 3D ultrasound and MR imaging, it is suggested to use those different technologies according to what to be detected and evaluated in each abnormal CNS case. Of course, those two technologies should be utilized as alternatives and complementsory as well.

Considering future in fetal neurology, it is no doubt that both technologies have great potential on further detailed morphological assessment. In terms of fetal neurological function analysis, four-dimensional ultrasound research on fetal behavior (KANET scoring system) have been launched in multicenters, and it will be greatly expected to elucidate relations between antenatal behavior and postnatal neurological prognosis.

REFERENCES


