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isuog.org GUIDELINES

ISUOG Practice Guidelines (updated): sonographic examination of the fetal central nervous system. Part 2: performance of targeted neurosonography

Clinical Standards Committee

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INTRODUCTION

Central nervous system (CNS) malformations are some of the most common congenital abnormalities, with an incidence at birth of 14/10 000[1]. Neural tube defects are the most frequent CNS malformation, with a prevalence in pregnancy of 52/100 000[2]. The incidence of intracranial abnormalities with an intact neural tube is uncertain, as most of these abnormalities are likely to escape detection at birth and manifest only in later life. Long-term follow-up studies suggest, however, that the incidence may be as high as one in 100 births[3]. During pregnancy, ultrasound screening for CNS malformations is carried out mainly at the time of the mid-trimester anomaly scan[4] and relies on visualization of three axial planes, namely, the transventricular, transthalamic and transcerebellar planes; basic evaluation of the fetal spine is also part of this screening procedure, and has been described in Part 1 of these guidelines[5]. However, of note is that some malformations may be detectable as early as the first-trimester scan.

The focus of this Guideline is to describe the protocol for the diagnostic ultrasound examination that should be performed in any case in which there is an increased risk of CNS malformation. A detailed list of indications for this targeted fetal neurosonography was published in Part 1 of these guidelines[5]. It is commonly accepted that targeted fetal neurosonography has a much greater diagnostic potential than does the basic screening examination, and is particularly helpful in the evaluation of complex malformations[6,7]. However, this targeted examination of the fetal CNS requires a high level of expertise that is not always available in many ultrasound facilities, since the method has not yet been implemented universally.

GENERAL CONSIDERATIONS

Recommendations

- The transvaginal approach is the preferred method to perform an adequate high-resolution targeted neurosonographic examination. When this is not technically feasible (e.g. breech presentation; twin pregnancy), the examination is performed transabdominally (**GOOD PRACTICE POINT**).
- When a transvaginal approach is not technically feasible, the use of high-resolution linear or microconvex transducers (i.e. multiband emission frequency reaching 8–9 MHz) is encouraged, because these provide higher resolution than do conventional convex probes (**GOOD PRACTICE POINT**).

The basis of the neurosonographic examination of the fetal brain is the multiplanar approach, which is obtained by aligning the transducer with the sutures and fontanelles of the fetal head[8–10]. When the fetus is in vertex presentation, a transvaginal approach should always be used, because it provides significant advantages over the transabdominal one. In particular, this approach allows both higher resolution, due to the higher emission frequency, and an unobstructed display of sagittal and coronal planes, as the acoustic shadowing produced by the calvarium is circumvented. In fetuses in breech presentation, a transfundal approach is used, positioning the probe on the uterine fundus, parallel instead of perpendicular to the abdomen. However, gentle external version, performed in conjunction with ultrasound examination, is often possible until the early third trimester and should be attempted when technically feasible[11].

Evaluation of the spine is also part of the neurosonographic examination, and this is performed using a combination of axial, coronal and sagittal planes, as described in Part 1 of these guidelines[5]. During the neurosonographic examination of the spine, the position of the conus medullaris is assessed in the sagittal plane.

The neurosonographic examination should include the same measurements as those commonly obtained during a basic examination: biparietal diameter, head circumference, atrial width of the lateral ventricles and the transverse cerebellar diameter. The anteroposterior diameter of the cisterna magna is not measured routinely; it should be measured only if there is suspicion of megacisterna magna. Many nomograms of different brain structures are available and can be used when needed[10,12]. The specific measurements obtained may vary depending upon the gestational age and the clinical setting.

NEUROSONOGRAPHIC TECHNIQUE

Fetal brain

Whether the examination is performed transvaginally or transabdominally, proper alignment of the probe along the correct section planes usually requires gentle manipulation of the fetus. A variety of scanning planes can be used, depending upon the position of the fetus[10]. A systematic evaluation of the brain usually includes visualization of four coronal and three sagittal planes. We present herein a description of the different structures that can be imaged in the second and third trimesters. Apart from the anatomic structures, fetal neurosonography should also include evaluation of the convolutions of the fetal brain, which change throughout gestation[13–17].

Recommendation

- Targeted anatomic assessment of the fetal brain relies on a continuum of sagittal and coronal planes. The key planes are described below, but the trained operator should be able to choose and document those most suited to demonstrating normal/abnormal anatomy (**GOOD PRACTICE POINT**).

Coronal planes (Figure 1)

Transfrontal plane (Figure 1a). Visualization of the transfrontal plane is through the anterior fontanelle. It depicts the midline interhemispheric fissure and the frontal lobes of the brain. The plane is anterior to the corpus callosum and therefore demonstrates an uninterrupted interhemispheric fissure. Other structures that appear on the image are the sphenoid bone and, sometimes, the orbits. Late in gestation, the olfactory sulci are also visible[15,18] (Figure 2).

Transcaudate plane (Figure 1b). The transcaudate plane is obtained through a more posterior approach, tilting and/or sliding the transducer towards the posterior edge of the anterior fontanelle. It is one of the most important views in fetal neurosonography. It shows: the frontal horns of the lateral ventricles; the cavum septi pellucidi (a triangular/trapezoid structure below the corpus callosum and between the two frontal horns); the cross-section of the anterior part of the body of the corpus callosum, appearing as a mildly hypoechoic band on top of the cavum septi pellucidi and between the frontal horns; the cerebral falx; the ganglionic eminence; and the caudate nuclei.

Transthalamic plane (Figure 1c). The transthalamic plane is relatively close to the transcaudate plane. It is obtained sometimes through the anterior fontanelle, by angulation of the probe, and sometimes through the open sagittal suture. Both thalami are found in close apposition. The third ventricle may be observed in the midline with the interventricular foramina of Monro; in a slightly more posterior plane, the atrium of the lateral ventricle with choroid plexus appears on each side. Close to the cranial base and in the midline, the basal cistern contains the blood vessels of the circle of Willis and the optic chiasm. This plane also provides a full view of the Sylvian fissures. Evaluation of this latter anatomic landmark is of crucial importance; to image it, it is useful to indent, gently but firmly, the anterior fontanelle, otherwise the lateral shadowing from the parietal bones will impair visualization of the insula and the Sylvian regions.

Transcerebellar plane (Figure 1d). The transcerebellar plane is the only coronal plane that is obtained through the posterior fontanelle. It enables visualization of the occipital horns of the lateral ventricles and the interhemispheric fissure. Depending upon gestational age, the calcarine fissure (Figure 3) and, more deeply, the parieto-occipital fissure, can also be seen. Both cerebellar hemispheres and the vermis are also seen in this plane, in cross-section. The vermis is more echogenic than are the cerebellar hemispheres.

Sagittal planes (Figure 4)

Recommendations

- The midsagittal or median plane is the reference plane for assessing all major midline organs and their anomalies. In order to ensure adequate evaluation of supra- and infratentorial anatomy, this plane should be sought through the anterior or posterior fontanelle, or even the sagittal non-ossified suture, depending on the particular structure of interest. This is achieved by gentle manipulation of the fetal head into the desired position using the free hand (**GOOD PRACTICE POINT**).

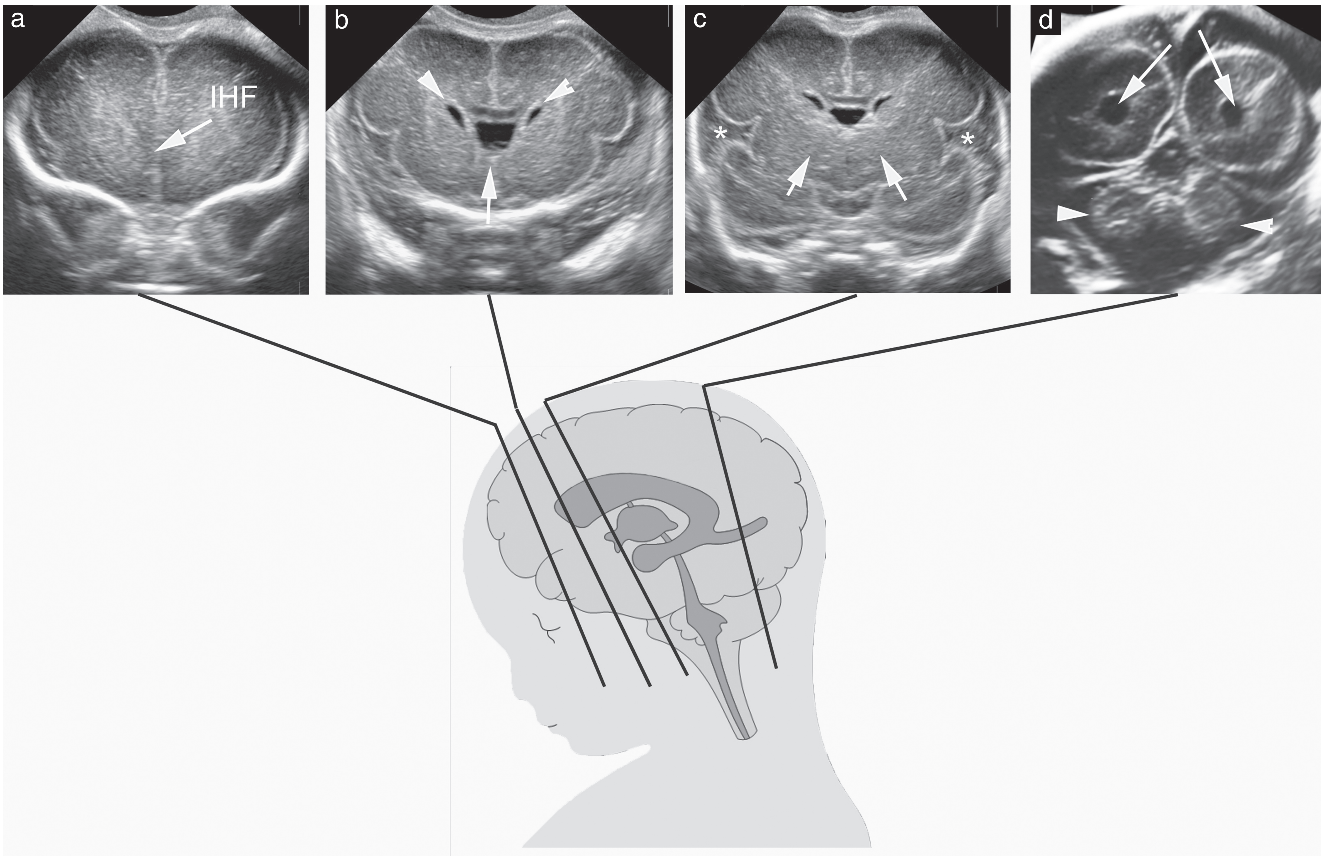

Figure 1 Coronal views of fetal head. (a) Transfrontal plane. Interhemispheric fissure (IHF) is visible between the two frontal lobes. Sphenoid bone forming roof of orbits as well as orbits themselves are also visible. (b) Transcaudate plane. The two frontal horns (arrowheads) are displayed, on either side of cavum septi pellucidi (arrow). Cross-section of anterior part of body of corpus callosum is also evident as mildly hypoechoic band on top of cavum septi pellucidi and between frontal horns. Ganglionic eminences are visible inferolateral to frontal horns. (c) Transthalamic plane. Thalami (arrows) and insulae (*) are indicated. (d) Transcerebellar plane. Occipital horns of lateral ventricles (arrows) and cerebellum (arrowheads) are indicated.

- Care should be taken in using corpus callosal biometry to diagnose hypoplasia of the corpus callosum, since a short, thin or thick corpus callosum is not necessarily synonymous with abnormality of this anatomical structure. For this reason, a qualitative assessment is much more important than a quantitative one, i.e. check that all four components of the corpus callosum are visible and sonographically normal (**GOOD PRACTICE POINT**).

Median or midsagittal anterior plane (Figure 4a). The midsagittal anterior plane is obtained through the anterior fontanelle and enables good visualization of the cerebral midline. When examining the infratentorial structures, an approach through the posterior fontanelle is preferred (see below). This median view shows the corpus callosum with all its components. In particular, the four parts of the corpus callosum – rostrum, genu, body and splenium – and their strict relationship with the cavum septi pellucidi and the cavum vergae, when present, should be visualized. Below the cavum septi pellucidi, the third ventricle can be identified as a hypoechoic structure, but its cranial portion is hyperechogenic due to the presence

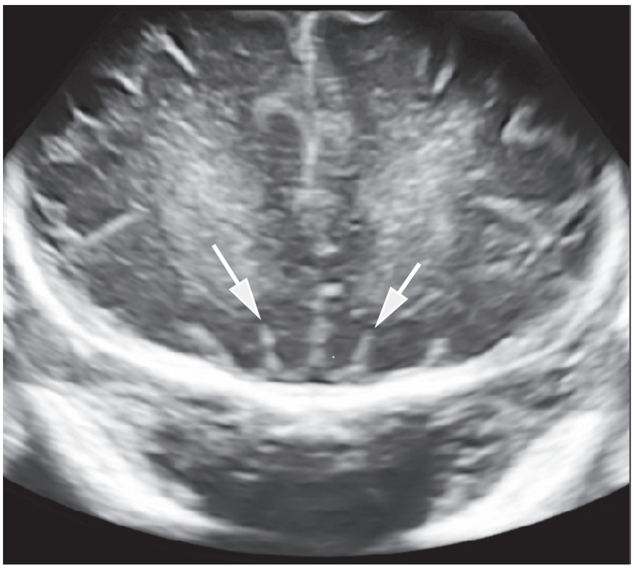

Figure 2 Transfrontal plane of fetal head. After 26 gestational weeks, olfactory sulci (arrows) can be visualized just above sphenoid bone.

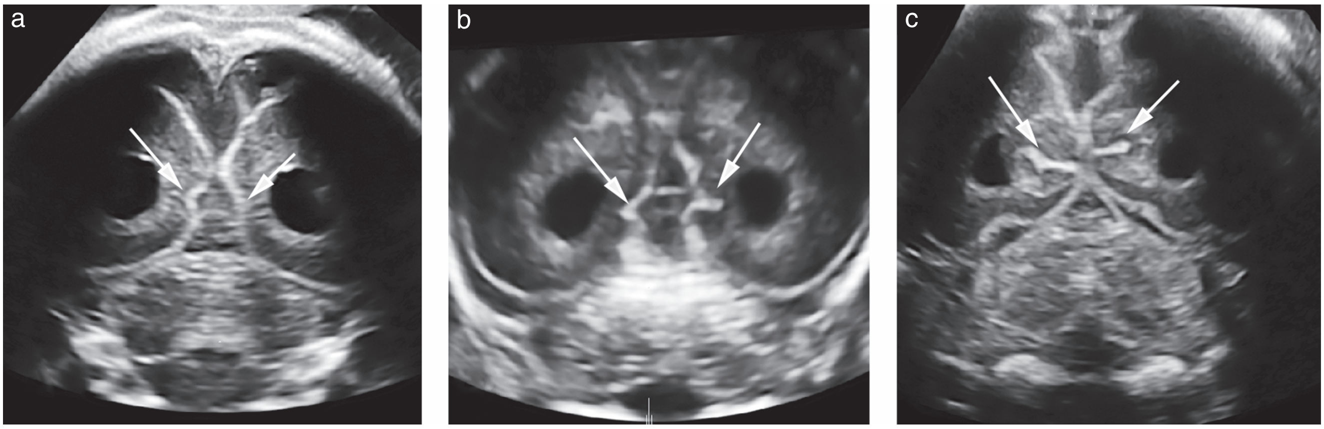

Figure 3 On transcerebellar view of fetal head, progressive development of calcarine sulci (arrows) can be seen: (a) 21 gestational weeks; (b) 26 gestational weeks; (c) 31 gestational weeks.

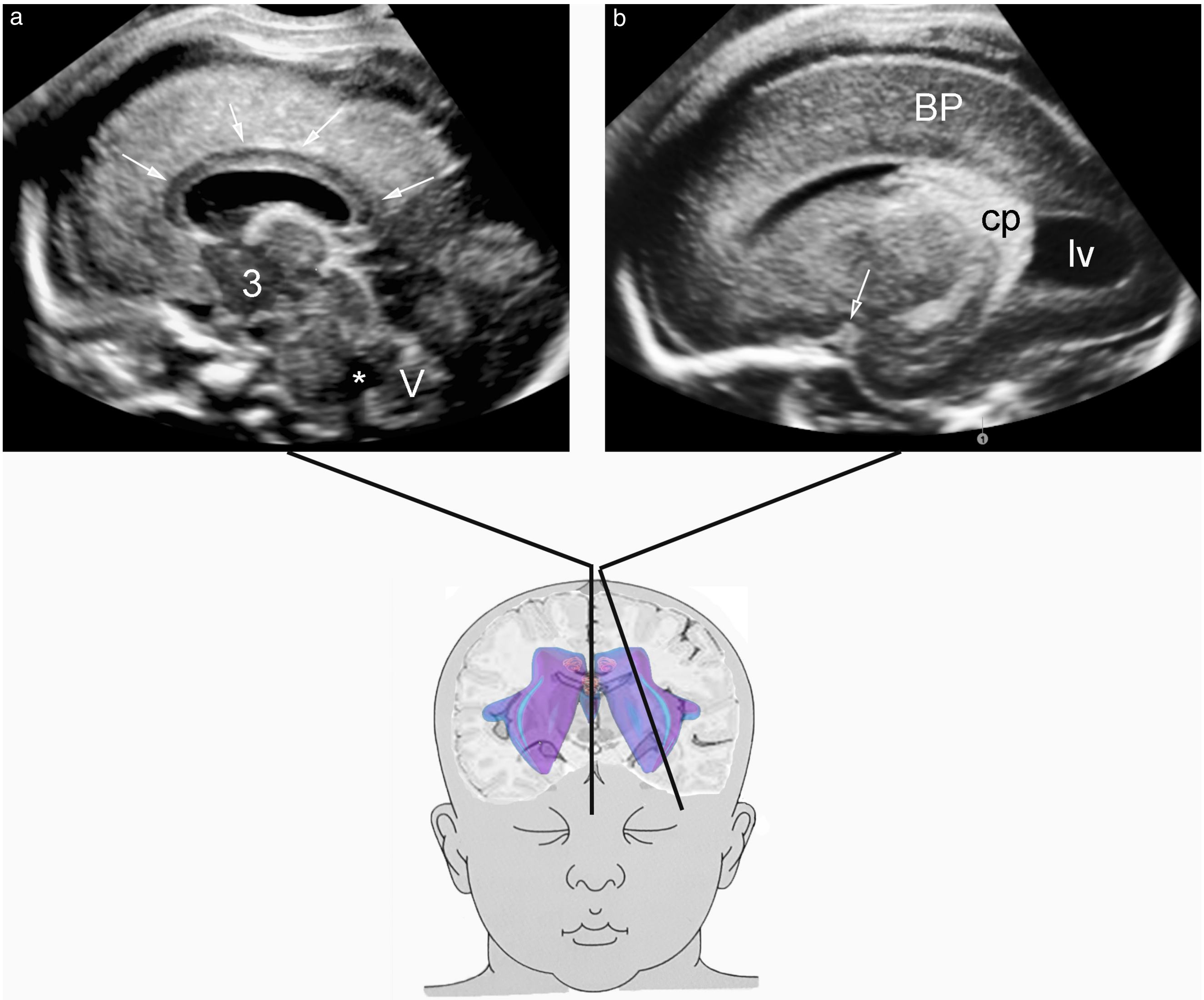

Figure 4 Sagittal planes of fetal head. (a) Midsagittal anterior plane. Anatomical landmarks that can be identified in this plane: median section of corpus callosum (arrows); below it, cavum septi pellucidi with cavum vergae (when present); third ventricle (3); fourth ventricle (*); cerebellar vermis (V). Sylvian aqueduct may also be visualized. (b) Parasagittal plane. Anatomical landmarks seen in this plane: brain parenchyma (BP); lateral ventricle (lv) with its choroid plexus (cp); temporal horn; depending on gestational age and degree of lateral angling, small part of Sylvian fissure (arrow).

of the tela choroidea. The infratentorial anatomy is also visible in this plane, particularly the vermis and the fourth ventricle. However, to display adequately and assess these structures, it is recommended to use a posterior approach (median or midsagittal posterior plane; see below). Using color Doppler, the anterior cerebral artery, pericallosal arteries with their branches and the vein of Galen may be seen, but its role is marginal in the assessment of the corpus callosum.

Median or midsagittal posterior plane (Figure 5). The midsagittal posterior plane is obtained through the sagittal suture or, better, the posterior fontanelle. Care should be taken to avoid shadowing from the occipital bone onto the posterior fossa and the cisterna magna, which may limit, or make impossible, clinical interpretation of the image. With this posterior approach, the cerebellar vermis is insonated from above and the ultrasound beam is at approximately 90° relative to the brainstem, creating the best conditions for visualizing this part of the brain which may be challenging to display on ultrasound. All the anatomical midline landmarks of the vermis and the posterior fossa can be studied thoroughly using this approach. These include: the median plane of the entire vermis, with the fastigium, the primary fissure (and also the secondary fissure, late in pregnancy) and the vermian lobules; the triangular fourth ventricle; the cisterna magna; the brainstem with the midbrain, pons and medulla oblongata. The upper boundary of the posterior fossa, represented by the tentorium, can also be identified. On this median view, it is often possible to visualize fluid in the Sylvian aqueduct, particularly during the second trimester.

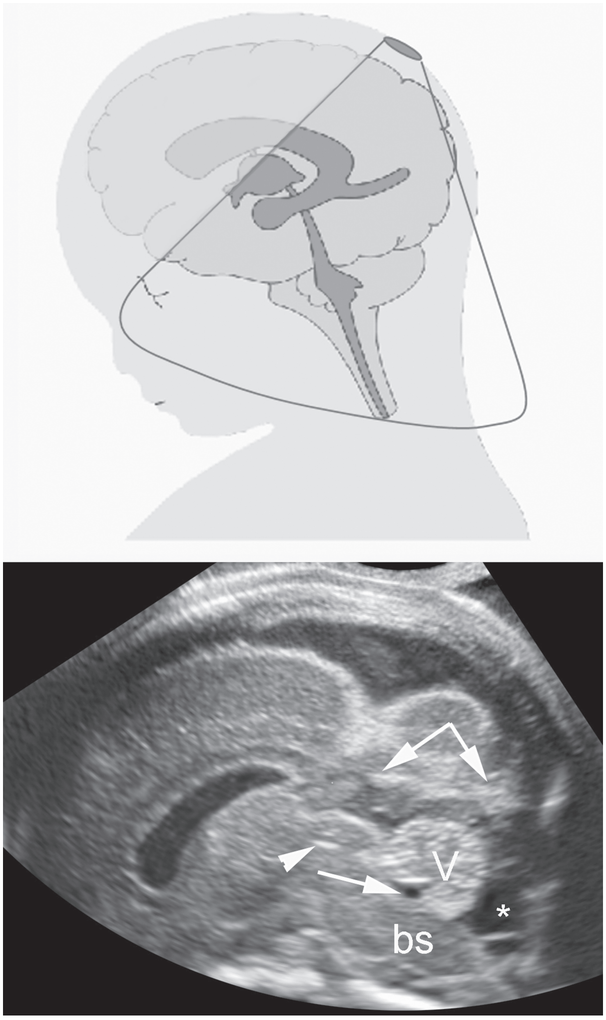

Figure 5 Midsagittal or median posterior plane is obtained by indenting posterior fontanelle and is best for assessing posterior fossa. Anatomical landmarks seen in this plane: cerebellar vermis (V), with fastigium and fourth ventricle (arrow); cisterna magna (*); tentorium (double arrow); brainstem (bs) with pons. Sylvian aqueduct (arrowhead) may also be demonstrated.

Parasagittal planes (Figure 4b). The parasagittal planes are obtained by moving or tilting the transducer slightly laterally from the midsagittal plane, to either side. They depict the lateral ventricles, choroid plexuses, periventricular brain parenchyma and, mainly in the third trimester, the gyri of the cortex, on the convex surface of the brain, as well as a variable portion of the insulae/Sylvian fissures. A more lateral view will enable visualization of the temporal horns of the ventricles and the insulae.

Additional planes. The planes described above represent the key planes to be obtained and evaluated every time a targeted fetal neurosonographic examination is performed. However, according to the focus of the examination, other intermediate sagittal and coronal planes can be displayed and are sometimes very useful. In particular, for example, for a thorough examination of the posterior fossa, additional coronal planes focused on the cross-section of the vermis may be required.

Fetal spine

Recommendation

- The ability to visualize the conus medullaris lying on the ventral border of the spinal canal, close to the vertebral bodies, is a good hint to determine the normality of the lumbosacral spine (**GOOD PRACTICE POINT**).

Three scanning planes can be used to evaluate the integrity of the spine. The choice depends upon the fetal position. Usually, only two of these scanning planes are possible in any given case, but manipulation of the fetus or three-dimensional (3D) ultrasound can be used to obtain the third plane when needed.

Transverse or axial planes. In transverse or axial planes, the examination of the spine is a dynamic process, performed by sweeping the transducer along the entire length of the spine, while remaining within the axial plane of the level being examined (Figure 6). The vertebrae have different anatomic configurations at different levels: fetal thoracic and lumbar vertebrae have a triangular shape, with the ossification centers surrounding the neural canal; the cervical vertebrae are quadrangular in shape; and sacral vertebrae are flat.

Sagittal planes. In sagittal planes, the ossification centers of the vertebral body and posterior arches form two parallel lines that converge in the sacrum. When the fetus is prone, a true sagittal section can also be obtained,

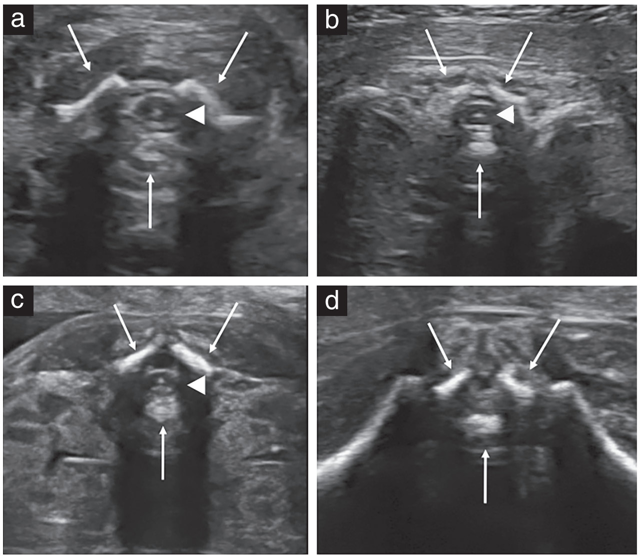

Figure 6 Axial views of fetal spine at different levels: (a) cervical; (b) thoracic; (c) lumbar; (d) sacral. Arrows indicate the three ossification centers of a vertebra. Note intact skin overlying spine. In (a–c), spinal cord is visible as hypoechoic ovoid with central white dot (arrowhead).

by directing the ultrasound beam across the non-ossified spinous process. This allows imaging of the spinal canal and of the spinal cord within it (Figure 7). In the late second and third trimesters, the conus medullaris is usually found at the level of the second/third lumbar vertebrae (L2–L3)[19–21]. Integrity of the neural canal is also inferred from the regular disposition of the ossification centers of the spine and the presence of soft tissue covering the spine. If a true sagittal section can be obtained, visualizing the conus medullaris in its normal location further strengthens the diagnosis of normality (Figure 7).

Recommendation

- The use of high-frequency transabdominal linear/microconvex transducers enhances the assessment of the spinal cord and conus medullaris in the midsagittal view of the spine (**GOOD PRACTICE POINT**).

Coronal planes. In coronal planes of the spine, one, two or three parallel lines are seen, depending upon the orientation of the ultrasound beam. These correspond to cutting planes, in a ventral–dorsal direction, across the vertebral bodies (one line), the vertebral bodies and posterior arches (three lines) or the posterior arches (two lines) (Figure 8). These planes are more easily demonstrated with 3D imaging, as discussed below.

Three-dimensional ultrasound

Recommendation

- The use of a 3D ultrasound approach is recommended in targeted neurosonography, particularly when a good two-dimensional image is difficult to obtain, in order to benefit from both the enhanced resolution and the possibility of performing multiplanar imaging correlation (**GOOD PRACTICE POINT**).

While there are some useful landmarks ensuring adequacy of a midsagittal/median plane of the fetal brain (e.g. corpus callosum and vermis), it is not uncommon for minor deviation from the perfect midsagittal view to go unnoticed by the operator. This, in turn, may affect not only measurements but also qualitative assessment of the brain and brainstem. The employment of 3D ultrasound for targeted neurosonography may, therefore,

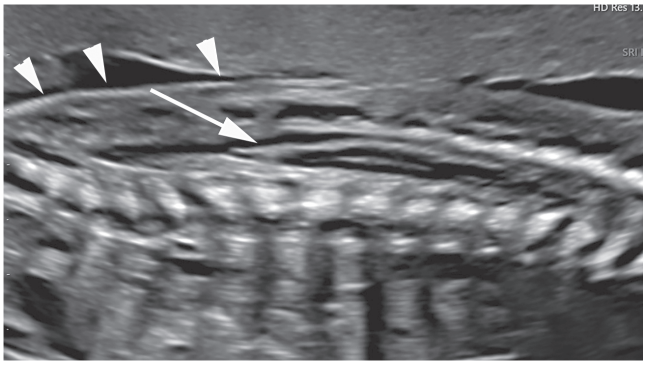

Figure 7 Sagittal view of fetal spine. Using unossified spinous process of vertebrae as acoustic window, contents of neural canal are demonstrated. After 20 weeks, conus medullaris (arrow) is normally positioned at level of second/third lumbar vertebrae (L2–L3), leaving, dorsally, triangular zone filled with cerebrospinal fluid. Note continuity of skin (arrowheads).

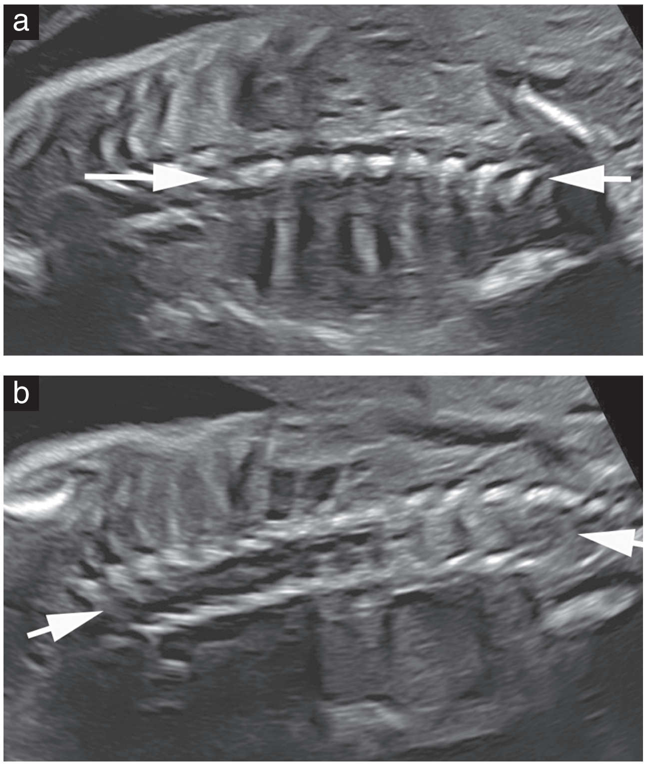

Figure 8 Coronal view of fetal spine (arrows). This plane is useful to rule out hemivertebrae and diastematomyelia. It can be obtained at level of vertebral bodies (a) or, more posteriorly, at level of arches (b). Objective is to rule out abnormal angling of spine.

be particularly useful, contributing in two main ways. First, by using multiplanar image correlation, it is possible to obtain perfectly aligned views on the three orthogonal planes (Figure 9); second, the possibility of displaying thicker 'slices' of the brain increases the signal-to-background noise ratio on all three planes, with significant enhancement of image quality. These advantages support our recommendation to use a 3D approach to neurosonography[7,22,23].

In addition, assessment of the fetal spine benefits from 3D rendering and reconstruction of the coronal planes at the level of the vertebral bodies and/or posterior arches[24] (Figure 10).

Neurosonography at 13–17 gestational weeks

Introduction into clinical practice of high-frequency transducers[25–28] and the increasing trend to perform

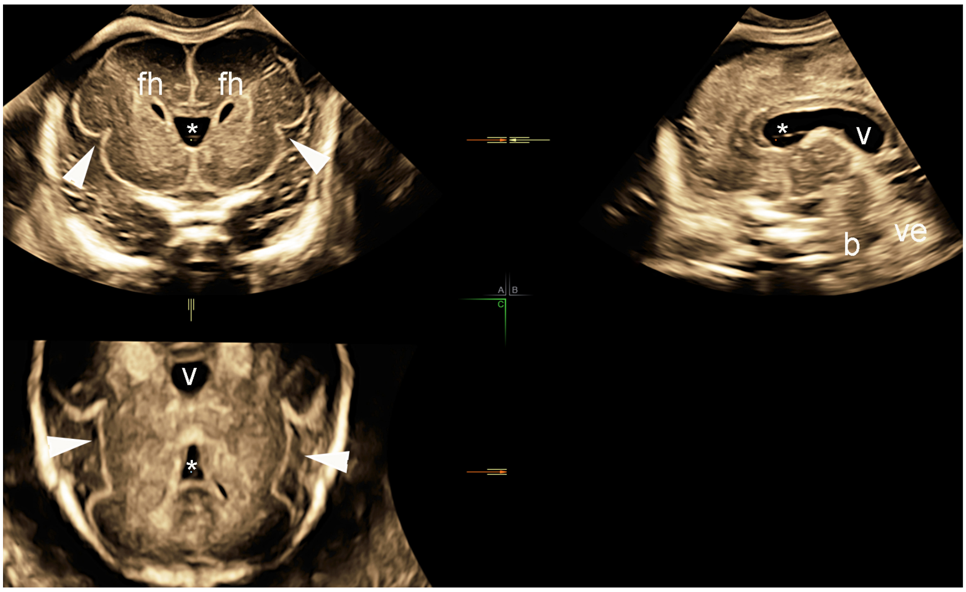

Figure 9 Three-dimensional multiplanar image correlation helps significantly in assessment of fetal brain. In this image of 26-week fetus, perfect orthogonal alignment allows visualization of all major cerebral structures in three planes. Coronal transcaudate plane (Plane A) shows frontal horns (fh) of lateral ventricles, on either side of cavum septi pellucidi (⋆), and anterior parts of insulae (arrowheads). In midsagittal plane (Plane B), corpus callosum, cavum septi pellucidi (⋆) and cavum vergae (V) are visible, together with vermis (ve) and, to lesser extent (due to insonation angle), brainstem (b). On reconstructed axial plane (Plane C), insulae are seen clearly (arrowheads), together with cavum septi pellucidi (⋆) and cavum vergae (V).

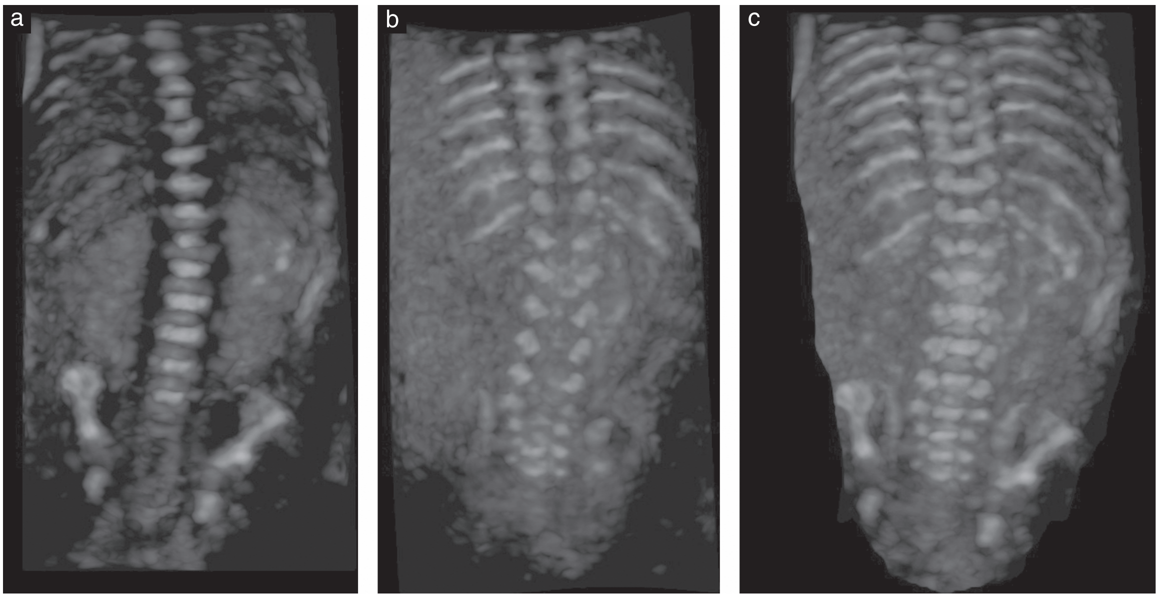

Figure 10 Three-dimensional (3D) surface-rendering of fetal spine at 22 gestational weeks: coronal views. These images were obtained with 3D ultrasound from same sonographic volume, using different angulations and thicknesses of ultrasound beam: (a) thin beam oriented through bodies of vertebrae; (b) same beam oriented more posteriorly to demonstrate posterior arches of vertebrae; (c) thick ultrasound beam used to demonstrate simultaneously all three ossification centers.

an anatomic evaluation earlier in gestation, also recommended by ISUOG, amongst others[29–31], have led to early referrals for suspicion of brain or spinal malformations. However, the advanced assessment of the fetal brain at 13–14 gestational weeks differs somewhat from that at 15–17 weeks, owing to the rapid changes that the fetal CNS undergoes around these gestational ages.

The recommended approach is to use transvaginal ultrasound. Although the newer high-frequency transabdominal transducers allow an adequate early neurosonographic examination, especially if the maternal body mass index is $\leq 25\,kg/m^2$ and the focus of the examination is not the posterior fossa, use of higher-frequency transvaginal transducers (6–12 MHz) leads to significant enhancement in the display of early fetal cerebral anatomy and allows more thorough assessment of this anatomic region. The approach of choice at 13–14 weeks of gestation includes assessment of the axial transventricular (Figure 11a) and transthalamic (Figure 11b) planes, in association with the midsagittal plane (Figure 11c) reconstructed from 3D volume datasets that are acquired, unlike in later gestation, from an axial view of the fetal head. This is possible due to the significantly lower degree of ossification of the fetal skull at this early gestational age. This, combined with the use of multiplanar imaging, leads to perfect midsagittal and coronal images of the ventricular system and the whole brain, although attention at this gestational age is often focused mainly on the diencephalon and posterior fossa (Figure 11c,d)[31]. The need to assess the axial planes is related to the mounting body of evidence supporting the early diagnosis of open spina bifida[32,33]. All sonographic signs described are due to the leakage of cerebrospinal fluid through the open dysraphism. The key views to detect these signs are the transventricular plane[34,35] (Figure 11a) and the posterior midsagittal one[29,32] (Figure 11c). The latter is also the reference plane for the early assessment of cystic vermian abnormalities[31,36]; such an assessment has to be undertaken with great caution, particularly when these abnormalities are apparently isolated, due to

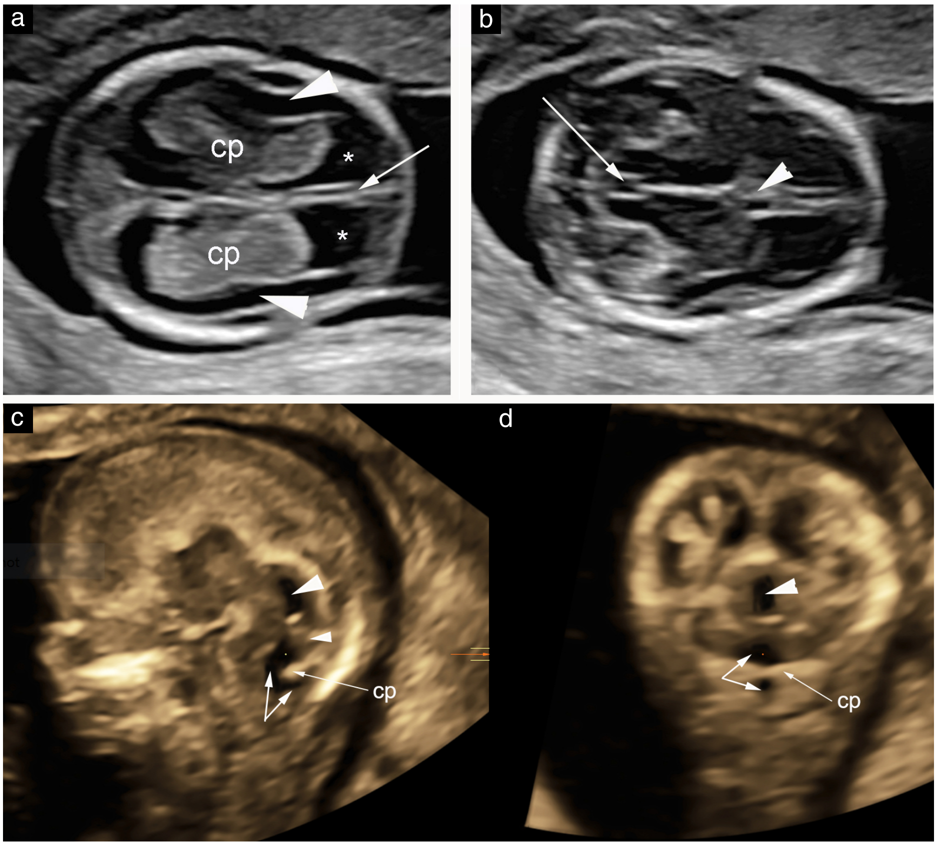

Figure 11 Neurosonography at 13 gestational weeks. (a) Transventricular axial plane, showing falx in midline (arrow) and 'butterfly sign' formed by prominent choroid plexuses (cp), with cerebrospinal fluid evident (*). Also, thin rim of developing brain parenchyma is visible as virtually anechoic strip of tissue (arrowheads), outlined by hyperechoic meninges on outer surface and by similarly hyperechoic ependymal lining medially. (b) Transthalamic axial plane. Plane cuts across diencephalon and prominent aqueduct (arrow). Falx is also evident anteriorly, as is very first hint of cavum septi pellucidi (CSP), appearing as irregularity of falx (arrowhead). It should be underlined that CSP is only evident in some cases, with high-frequency transducers. (c,d) Midsagittal and posterior coronal planes are better visualized if reconstructed from three-dimensional volume acquired transvaginally, due to obvious need for multiplanar image correlation. (c) Structures that can be recognized in reconstructed midsagittal plane: prominent aqueduct of Sylvius (large arrowhead), typical of this gestational age; hypoechoic diencephalon, in front of aqueduct; posterior fossa, with continuity between fourth ventricle and physiologic Blake's pouch (double arrow). Hyperechoic choroid plexus (cp) of fourth ventricle is visible between fourth ventricle and Blake's pouch, with vermis (small arrowhead) above. (d) On reconstructed posterior coronal plane, at level of aqueduct of Sylvius, aqueduct is seen clearly (arrowhead). Below, fourth ventricle and Blake's pouch (double arrow) are separated by choroid plexus of fourth ventricle (cp).

the high risk of false-positive diagnoses[37]. Should there be any suspicion of open spina bifida, direct evidence of the malformation should then be obtained with a high-resolution transvaginal assessment of the fetal spine.

At 15–17 gestational weeks, the recommendation to use the transvaginal approach remains, enabling evaluation of structures not seen at earlier ages[10,38,39]. Preferred acquisition planes are coronal and sagittal ones, due to the position of the head facilitating a transfontanellar/sagittal suture approach (Figure 12). The axial planes are obtained either using the transabdominal approach, using the transvaginal approach with manipulation of the fetal head, or using 3D reconstructions.

Transventricular plane. At 13–14 gestational weeks, the transventricular plane allows assessment of the amount of cerebrospinal fluid around the choroid plexuses, the midline and the thin layer of developing brain parenchyma around the lateral ventricle (Figure 11a). At 15–17 gestational weeks, more information can be gathered about the brain parenchyma and the ventricular system. It should also be underlined that an oval anechogenic structure is often evident at this gestational age, along the midline (Figure 12a). It was demonstrated recently that this structure, formerly thought to represent the third ventricle, is in fact the cavum veli interpositi (Figure 12), and that it is rather common, being visible in almost half of fetuses at 13–17 gestational weeks[38].

Midsagittal/median view. At 13–14 gestational weeks, the reconstructed midsagittal/median plane allows complete assessment of the ventricular system, since the aqueduct is much more prominent than it is later in gestation (Figure 11c). In addition, this is the best approach to assess the infratentorial anatomy in cases in which a 'cystic posterior fossa' (mostly a normal finding related to the development of these structures) is detected at nuchal translucency screening[31]. In some cases, starting from 14–17 gestational weeks, the first evidence of the cavum septi pellucidi[38] and the anterior portions of the corpus callosum can be visualized[39] (Figure 12d). In the posterior fossa, the anatomy of the developing cerebellar vermis and the brainstem can be studied. The operator should be aware of the fact that, at this gestational age, the appearance of the cerebellum is completely different from that which we are used to seeing during the 18–23-week examination. An example is the fourth ventricle, which is continuous, initially, with the Blake's pouch, and, when the Blake's pouch ruptures to create the Magendie foramen, with the cisterna magna (Figures 11 and 12)[40,41].

Even though the potential of the early anatomical assessment has increased considerably, for most CNS abnormalities, a follow-up neurosonographic

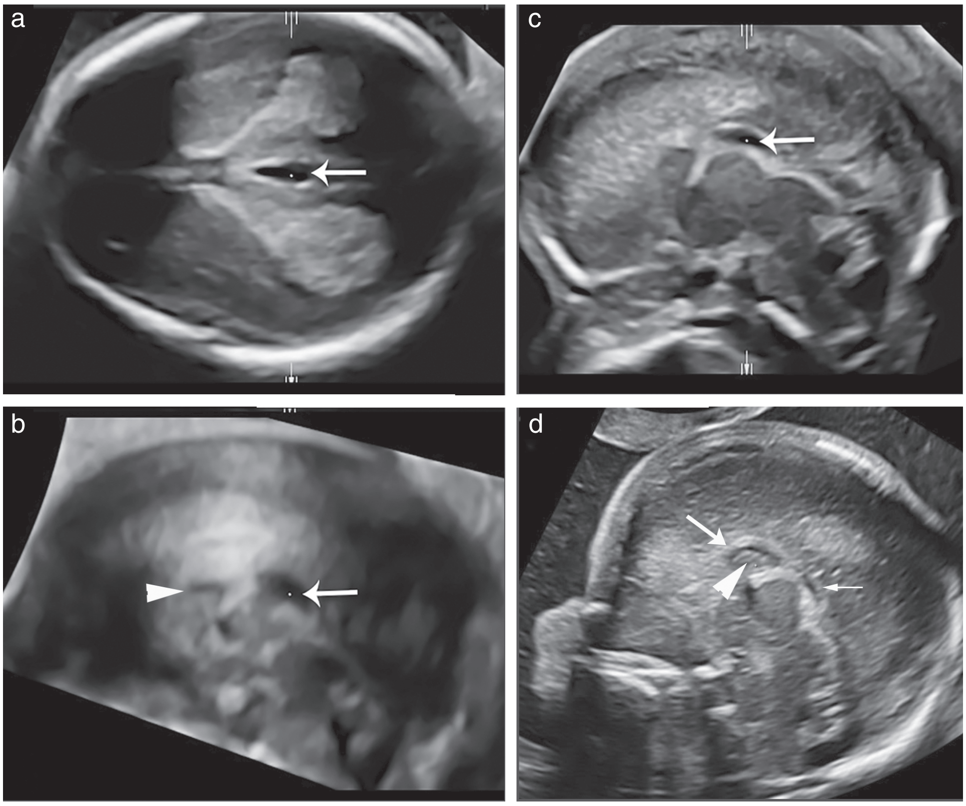

Figure 12 (a–c) Neurosonography at 15 gestational weeks. (a) In axial transventricular plane, oval anechogenic structure (arrow) is evident along midline. (b) Corresponding midsagittal plane reconstructed from (a), demonstrating that, due to its position, this structure is cavum veli interpositi (CVI) (arrow). Initial bud of corpus callosum is also evident in this plane (arrowhead). (c) Two-dimensional image in midsagittal view of same fetus, showing same findings as in (b), but with higher resolution. (d) At 16 gestational weeks, initial bud of corpus callosum (large arrow) and small cavum septi pellucidi (arrowhead) can be demonstrated on high-frequency transvaginal ultrasound. Regression of CVI can also be seen (small arrow).

examination after 20 weeks of gestation is warranted. Significant exceptions, with straightforward diagnosis and no need for a follow-up scan, are the lethal or near-lethal anomalies, such as exencephaly-anencephaly, gross cephalocele and holoprosencephaly.

FETAL BRAIN MRI

Recommendation

- Fetal brain magnetic resonance imaging (MRI) is considered complementary to neurosonography; it can add significant clinical information when requested to answer specific questions posed by the neurosonologist that the targeted fetal CNS evaluation could not answer. When neurosonographic evaluation is unavailable or the level of performance inadequate, it can replace neurosonography as the second-line evaluation, as long as the operator has sufficient training in fetal brain MRI (**GOOD PRACTICE POINT**).

ISUOG guidelines for the performance and reporting of fetal MRI are available and provide useful information on this technique[42]. It should be underlined that, when the indication for this complementary imaging modality is appropriate, and the diagnostic query specified clearly, MRI may contribute significantly to the final diagnosis. However, MRI should be performed only after, and to complement, a neurosonographic examination, if this is considered to be indicated by the trained operator in order to address a relevant diagnostic or clinical query. Published evidence indicates that, when an adequate neurosonographic examination is carried out by an experienced operator, according to the criteria specified in this Guideline, a MRI examination is required in only 7–15% of cases[43–45]. It is important, both for the sake of the patient and to avoid inappropriate referral, not to rush from suspicion of CNS malformation on screening ultrasound, or on suboptimal neurosonography not meeting the technical criteria described herein, to MRI[42,46].

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APPENDIX 1 Grades of recommendation and levels of evidence used in ISUOG Guidelines

Classification of evidence levels

1++	High-quality meta-analyses, systematic reviews of randomized controlled trials or randomized controlled trials with very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of randomized controlled trials or randomized controlled trials with low risk of bias
1−	Meta-analyses, systematic reviews of randomized controlled trials or randomized controlled trials with high risk of bias
2++	High-quality systematic reviews of case–control or cohort studies or high-quality case–control or cohort studies with very low risk of confounding, bias or chance and high probability that the relationship is causal
2+	Well-conducted case–control or cohort studies with low risk of confounding, bias or chance and moderate probability that the relationship is causal
2−	Case–control or cohort studies with high risk of confounding, bias or chance and significant risk that the relationship is not causal
3	Non-analytical studies, e.g. case reports, case series
4	Expert opinion

Grades of recommendation

A	At least one meta-analysis, systematic review or randomized controlled trial rated as 1++ and applicable directly to the target population; or a systematic review of randomized controlled trials or a body of evidence consisting principally of studies rated as 1+ applicable directly to the target population and demonstrating overall consistency of results
B	Body of evidence including studies rated as 2++ applicable directly to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+
C	Body of evidence including studies rated as 2+ applicable directly to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or evidence extrapolated from studies rated as 2+
Good practice point	Recommended best practice based on the clinical experience of the guideline development group