Chapter

1

Sonoembryology, Machine Settings and Imaging Techniques

INTRODUCTION

Scanning the fetal brain is a mandatory part of the anomaly scan, also called targeted imaging for fetal anomalies (TIFFA). However, this evaluation is limited to the documentation of relatively few structures in three axial (transverse) planes: the transventricular, transthalamic, and transcerebellar planes.

Similar to echocardiography for the fetal heart, neurosonography goes a step further in studying the fetal brain in multiple axes and planes to evaluate structures that are not adequately visualized in the screening planes. Transitioning from TIFFA to neurosonography is more challenging than transitioning to echocardiography because the fetal brain is structurally complex and undergoes continuous developmental changes during gestation.

DEVELOPMENT OF THE FETAL BRAIN

Fetal brain development begins with the formation of three primary vesicles from the neural tube **(Fig. 1.1 and 1.2)**. The three primary vesicles further develop into five secondary vesicles, each giving rise to specific brain structures **(Fig. 1.3 and Table 1.1)**.

Formation of the Neural Tube

The early human embryo consists of three layers: the outer layer, called the ectoderm; the middle layer, called the mesoderm; and the inner layer, called the endoderm. The entire nervous system (other than its vascular and skeletal support) is formed from the ectoderm.

By the third embryonic week, a group of cells in the ectoderm, called the neuroectoderm, becomes organized to form a flat structure known as the neural plate. The neural plate starts folding inwards to form the neural groove, which deepens and separates from the overlying ectoderm to form a tube known as the neural tube.

The newly formed neural tube has openings at both ends, called rostral (superior) and caudal (inferior)

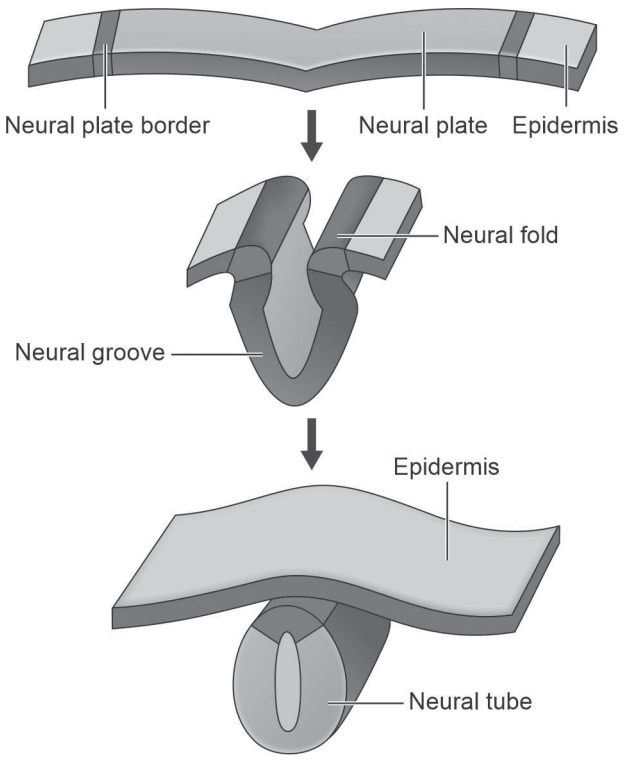

Fig. 1.1: Formation of the neural tube.

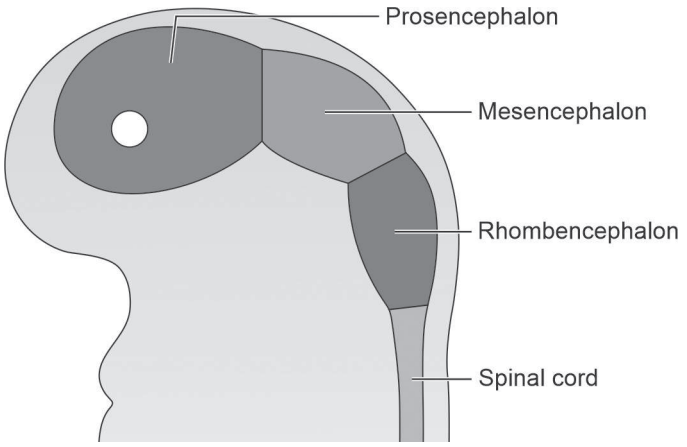

Fig. 1.2: Three primary vesicles of the developing brain.

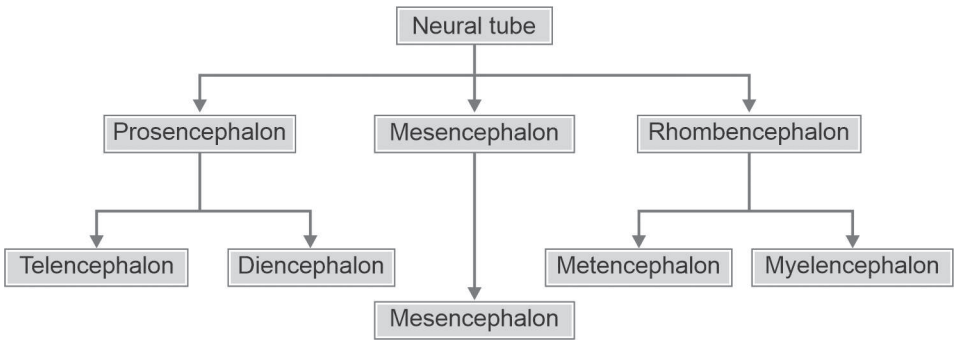

Fig. 1.3: Five major subdivisions of the developing brain.

Table 1.1: Structures arising from each subdivision and their corresponding CSF-containing cavities

Subdivision	*Structures formed*	*Related CSF cavity*
Telencephalon	• Cerebral cortex • Basal ganglia	Lateral ventricles
Diencephalon	• Thalamus • Hypothalamus • Retina	Third ventricle
Mesencephalon	Midbrain	Aqueduct of Sylvius
Metencephalon	• Cerebellum • Pons	Fourth ventricle
Myelencephalon	Medulla	Fourth ventricle

neuropores. The closure of the neural tube is completed by the 5th week of embryonic development. Failure of closure of the rostral neuropore results in anencephaly, whereas failure at the caudal end results in open spina bifida.

Division of the Primitive Brain

The brain develops from the rostral region of the neural tube. The neural tube develops distinct folds that divide it into three parts or primary vesicles: the forebrain (prosencephalon), midbrain (mesencephalon), and hindbrain (rhombencephalon) **(Fig. 1.2)**. The prosencephalon further differentiates into the telencephalon (paired cerebral hemispheres) and diencephalon (central forebrain structures). The rhombencephalon forms the metencephalon and myelencephalon.

Development of the Ventricular System

The ventricular system develops from the inner walls of the neural tube. The walls of the early developing brain are thin; therefore, the ventricular system is relatively large. As the embryo develops, the ratio of ventricular to brain volume reduces considerably. This is most noticeable in the midbrain, where the cavity is converted into a narrow tube, called the aqueduct of Sylvius. The lateral ventricles drain into the 3rd ventricle through the foramina of Monro. The aqueduct of Sylvius connects the 3rd and 4th ventricles. The median aperture draining the 4th ventricle (foramen of Magendie) develops early in the embryonic period, whereas lateral apertures (foramina of Luschka) are not present until the second trimester. These apertures cannot be demonstrated on prenatal ultrasound.

Other Structures

The development of specific structures pertaining to neurosonography, such as the corpus callosum, vermis, gyri, and sulci, is discussed in the relevant chapters.

INDICATIONS FOR TARGETED NEUROSONOGRAPHY

Targeted neurosonography requires expertise and dedicated examination time. Just as targeted fetal echocardiography is restricted to fetuses presumed to be at risk for cardiac anomalies, neurosonography should be performed in fetuses at high risk for CNS anomalies. The indications are as follows:

1. Abnormal size of the head
2. Suspected CNS abnormality on a screening ultrasound (e.g. non-visualized CSP)
3. Anomalies in other systems (suspected to be part of a syndrome)
4. CNS abnormality in a previous child or fetus
5. Family history of heritable CNS abnormality
6. Fetal infection—suspected or confirmed
7. Complicated monochorionic twins
8. Maternal exposure to teratogens
9. Abnormal microarray or exome sequencing result known to be associated with a CNS abnormality.

ACOUSTIC WINDOWS IN THE FETAL SKULL

Ultrasound evaluation of the fetal brain is influenced by the attenuating properties of the calvarial bones. As ossification progresses during gestation, ultrasound beams are partially reflected and absorbed by the skull, resulting in acoustic shadowing and reduced visualization of intracranial structures, particularly those located in the near field of the ultrasound beam.

However, various sutures and fontanelles, where the bones have not yet fused, allow for improved transmission of ultrasound waves and function as acoustic windows of the skull. The most important

acoustic windows used in fetal neurosonography are the anterior fontanelle, metopic suture, sagittal suture, posterior fontanelle, and squamosal suture **(Fig. 1.4)**. Each of these windows permits imaging of different brain structures, depending on the orientation of the ultrasound beam **(Table 1.2)**.

The three orthogonal planes

- *The axial plane* is obtained when the ultrasound beam passes perpendicular to the long axis of the fetal body, producing a horizontal cross-section of the fetal head.
- *The sagittal plane* divides the brain into the right and left hemispheres.
- *The coronal plane* divides the brain into anterior and posterior portions.

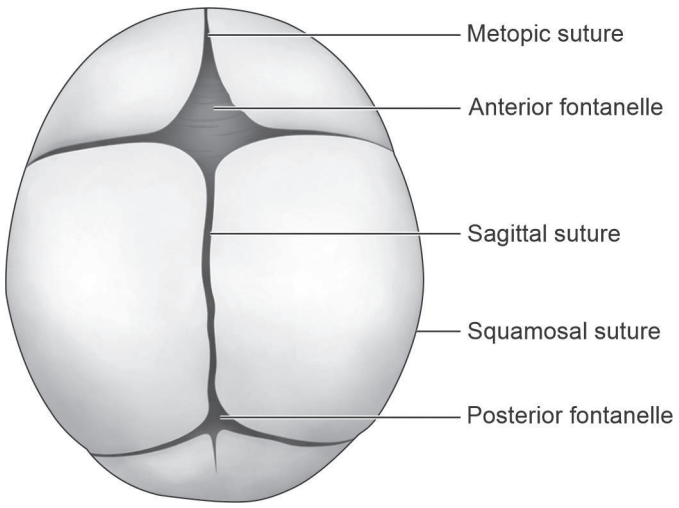

Fig. 1.4: Acoustic windows used in neurosonography.

EQUIPMENT AND MACHINE SETTINGS

Correct equipment and optimization of machine settings are crucial to obtain maximum information from the fetal brain and to detect subtle abnormalities that may be otherwise missed. In this section, we discuss the probes, imaging routes, and image optimization. Once the machine is set up, it is recommended to save the settings as a 'neurosonography' preset, which can be used for every subsequent patient.

Transabdominal (TAS) versus Transvaginal (TVS) Approach

In most patients with a BMI <25 kg/m², satisfactory examination of the fetal brain (other than the posterior fossa) can be achieved using a combination of low-frequency and high-frequency curvilinear transabdominal transducers.

Table 1.2: Importance of acoustic windows in the fetal skull

Acoustic window	*Importance*	*Key structures imaged*
Metopic suture	Useful window for imaging anterior cerebral structures, particularly when performing sagittal or oblique sagittal imaging.	• Frontal lobes • Frontal horns • CSP • Anterior corpus callosum
Anterior (bregmatic) fontanelle	Provides excellent access for transvaginal neurosonography, particularly for obtaining coronal and sagittal planes.	• Lateral ventricles • CSP • Corpus callosum • Third ventricle • Cerebral hemispheres
Sagittal suture	Imaging of midline structures in the midsagittal plane. Particularly useful during TVS, to obtain a true midsagittal section.	• Corpus callosum • CSP • Thalamus • Brainstem • Cerebellar vermis
Squamosal suture (between the temporal and parietal bones)	Imaging in the axial planes and acquisition of axial volumes for three-dimensional ultrasound.	• Lateral ventricles • Third ventricle • Thalami • Cerebral hemispheres • Midline falx • Cerebellum
Posterior fontanelle	Provides optimal access for imaging posterior fossa structures in coronal and posterior midsagittal planes.	• Cerebellum • Cerebellar vermis • Fourth ventricle • Cisterna magna • Occipital lobes • Posterior horns of the lateral ventricles

Formal neurosonography ideally includes transvaginal sonography (TVS), whenever feasible. Image quality and detail are much greater with transvaginal transducers due to their higher frequency and short probe-to-brain distance when the fetus is in a cephalic presentation **(Fig. 1.5)**. Additionally, transabdominal imaging of the hemisphere close to the probe is usually suboptimal because of the shadowing effect of the overlying bone.

Transvaginal neurosonography is easy to perform in the first trimester (when the entire fetus is in the pelvis) and third trimester when the fetus is in cephalic presentation (when the fetal head lies in the maternal pelvis). In the second trimester, the operator often faces the challenge of maneuvering the fetal head into the pelvis, which is not an easy task. This may be facilitated by gentle external manipulation of the fetal head with the left hand while pushing the TVS probe up with the right hand and using either a foot pedal or an assistant to capture images.

External cephalic version of breech fetuses has also been suggested to permit TVS examination, but it can cause significant discomfort in pregnant women. In most cases, we prefer to complete the examination using the transabdominal approach alone, or in obese women, to reschedule the scan for the next day when the fetus is likely to be in a favorable position.

Another drawback of TVS is that the high frequency of the probe results in poor penetration of the sound waves through the skull bone. To overcome this, the ultrasound beam must be directed through the sagittal suture or one of the fontanelles. Hence, obtaining all axial sections using real-time 2D TVS is difficult because of limitations in probe movement.

Table 1.3 summarizes the differences between the two approaches.

Choice of Transducers

Transabdominal convex transducers are of two types: low-frequency (e.g. 1–5 MHz) or high-frequency (e.g. 2–9 MHz). A low-frequency transducer offers a lower resolution but better penetration, whereas the opposite is true for high-frequency transducers. Low-frequency

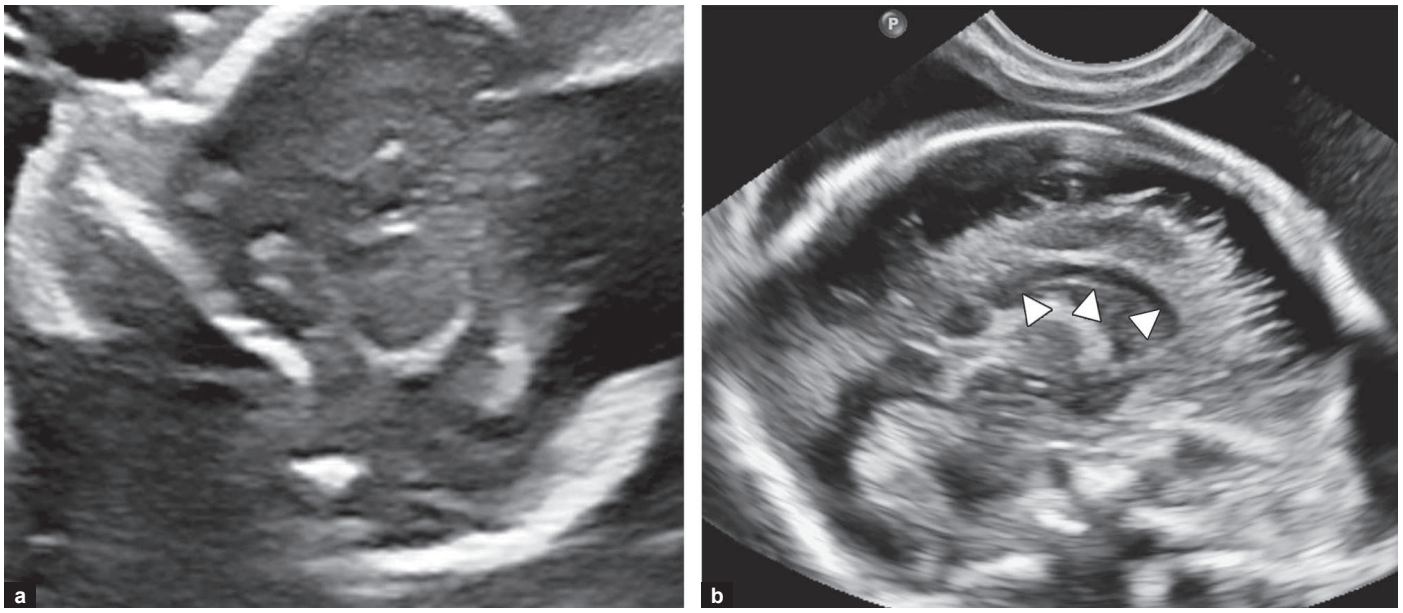

Fig. 1.5: Midsagittal sections of a 24-week fetus with a non-visualized CSP. (a) TAS image—the corpus callosum cannot be seen; (b) TVS image—a partially formed corpus callosum is clearly demonstrated (arrowheads)

Table 1.3: TAS versus TVS approach to neurosonography

Parameter	*Transabdominal (TAS)*	*Transvaginal (TVS)*
Primary indication	Routine evaluation; axial planes; low-BMI patients	Detailed evaluation; coronal and sagittal planes; high-BMI patients
Advantages	Real-time axial sections; wider field of view	Significantly higher resolution; reduced probe-to-brain distance
Limitations	Near-field bone shadowing; maternal obesity	Limited penetration through calvarium; unfavorable fetal position; limited probe movement
Role in 3D imaging	Volume acquisition in axial plane	Volume acquisition in coronal and sagittal planes

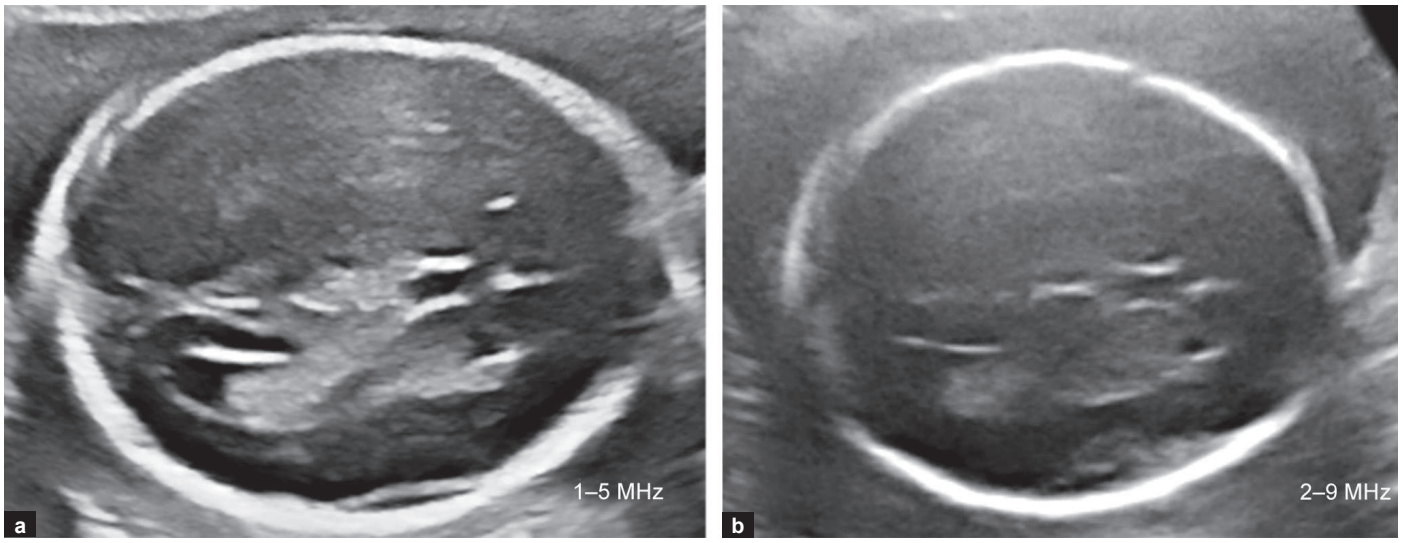

Fig. 1.6: Axial section through the skull bone in a high-BMI patient. A low-frequency transducer (a) captures more details than a high-frequency transducer (b).

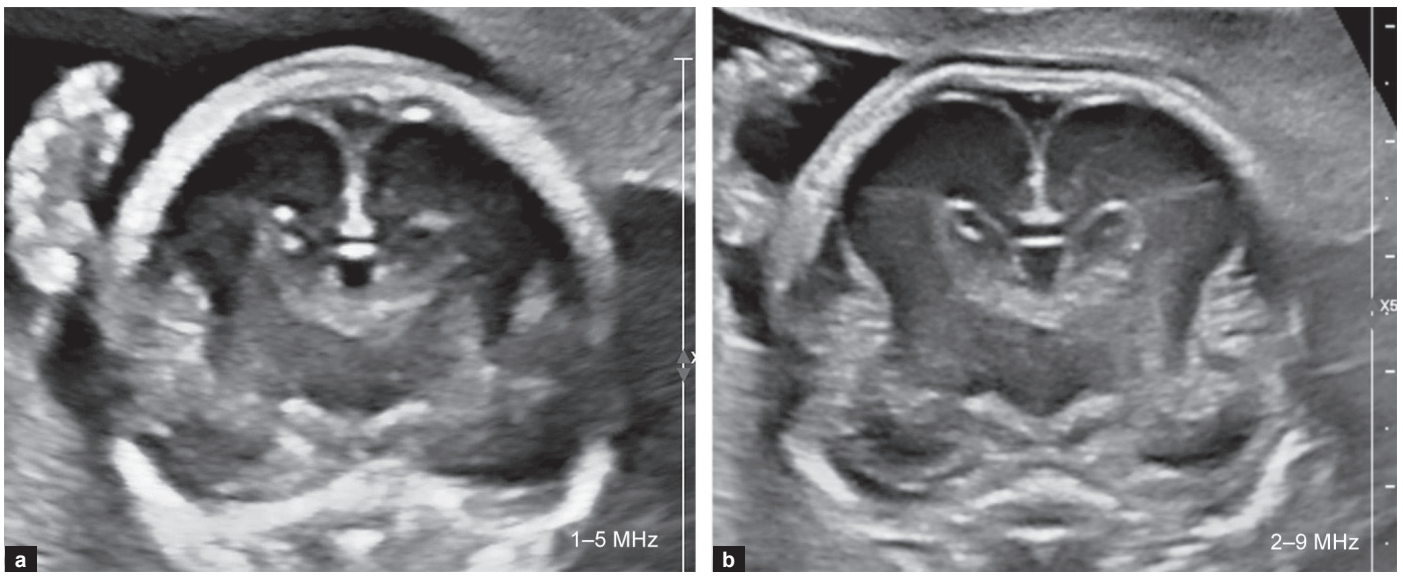

Fig. 1.7: For coronal plane imaging through the anterior fontanelle, a high-frequency transducer (b) provides a significantly more detailed image than a low-frequency transducer (a).

transducers are preferred when imaging through the skull bone, particularly in obese women **(Fig. 1.6)**.

High-frequency transducers provide better resolution when imaging through the fontanelles or sutures **(Fig. 1.7)**, and in women with a low BMI. Ultimately, the operator should utilize both to obtain the maximum possible information. Transvaginal transducers have significantly higher frequencies than transabdominal transducers.

Machine Settings

Transmission power defines the energy transferred per unit time. High power improves the image resolution to some extent but increases the thermal index (TI) and mechanical index (MI).

REMEMBER

Ultrasound exposure should follow the ALARA (As Low As Reasonably Achievable) principle. During B-mode imaging, the Thermal Index (TI) and Mechanical Index (MI) should be maintained below 1.0. Prolonged Doppler exposure, particularly with spectral Doppler, should be avoided when imaging the fetal brain. The output power should be minimized once an adequate image quality is achieved, and the examination time should be limited.

Depth and sector width should be reduced until the fetal skull occupies most of the screen area. This improves the frame rate and lateral resolution by enhancing the signal-to-noise ratio.

Read zoom and write (box) zoom should be used if one needs to study small structures of interest.

Focal zone should be adjusted at the level of the structure of interest.

Monochrome grayscale is typically used for neurosonography.

Dynamic range should be adjusted to moderate levels. A higher dynamic range displays more shades of gray for a smoother, softer image, whereas a lower range creates a 'contrasty' black-and-white image. Unlike echocardiography, where a high contrast is preferred to delineate the cardiac chamber walls, the brain has subtle structures with varying degrees of echogenicity, which are masked if the dynamic range is low, i.e. image contrast is too high **(Fig. 1.8)**.

Harmonic imaging is a technique in which reverberating frequencies from tissue interfaces are selectively displayed, resulting in reduced artifacts and improved contrast resolution.

Compound imaging steers the ultrasound beams in different directions to insonate the same structure at various angles. This results in a reduction in the background noise in the image while increasing its detail.

Speckle reduction uses advanced image-processing algorithms to remove artifacts caused by the interference of multiple ultrasound echoes. The combination of harmonic, compound, and speckle-reduction imaging is ideal for fetal brain imaging.

Storage of images should be in DICOM format. The storage of 3D volumes is strongly recommended when any abnormality is suspected, as it permits the subsequent evaluation of a large number of sections.

ROLE OF THREE-DIMENSIONAL IMAGING

Three-dimensional ultrasonography (3D US) involves acquiring a volume that can be used to render images in any plane of interest.

Neurosonography can be performed using a transfundal approach in fetuses in the breech position. The quality of images obtained by direct imaging is generally superior to that of images generated from 3D volumes. In fetuses with cephalic presentation, 3D ultrasound helps obtain coronal and sagittal planes, which are otherwise difficult to image because the fetal head is usually in a transverse position. In transvaginal (TVS) neurosonography, the range in which the probe can be moved is usually limited, and 3D volume acquisition is useful in this regard. Finally, the 3D volume can be archived for subsequent expert reviews.

REMEMBER

Although many ultrasound systems offer three-dimensional (3D) imaging, only high-end machines can produce orthogonally reconstructed planes with sufficient resolution for detailed fetal neurosonography. In lower- and mid-tier systems, the rendered planes often lack adequate anatomical details and have limited practical value.

Therefore, operators should primarily focus on developing expertise in direct real-time two-dimensional (2D) imaging.

Consideration Prior to Acquiring the 3D Dataset

The following points must be considered before volume acquisition:

Fetal position and movement: The ultrasound operator, patient, and fetus should be still when the 3D volume is acquired, as movement produces artifacts in the

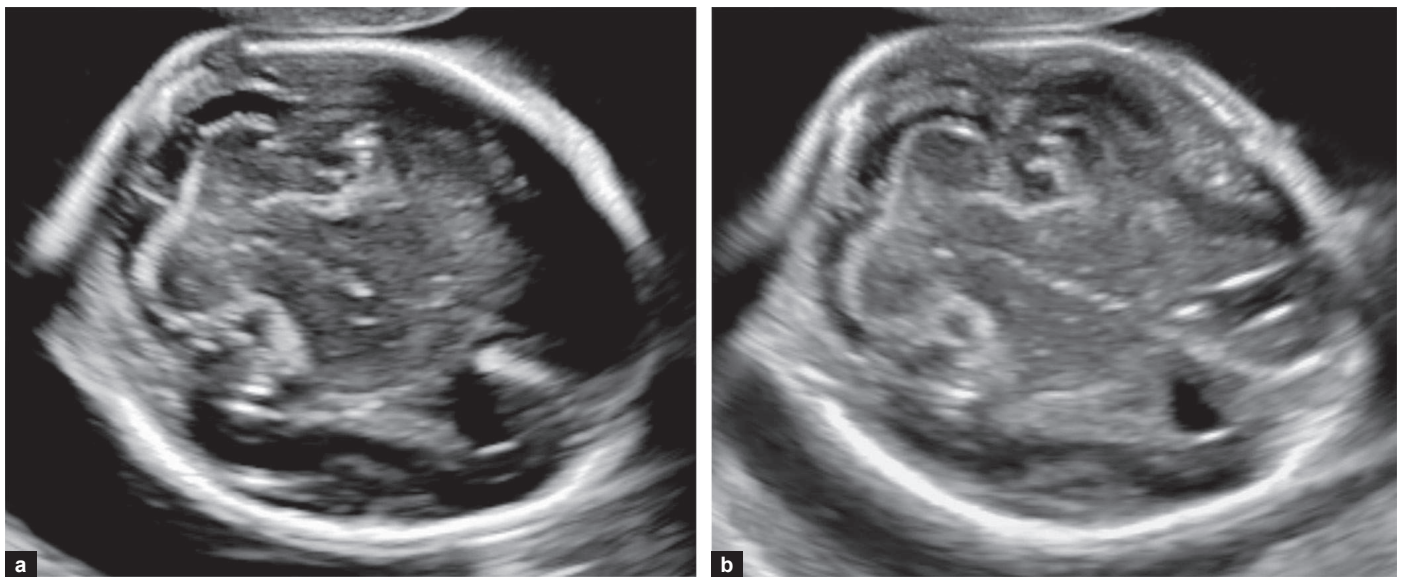

Fig. 1.8: Effect of dynamic range. (a) A low dynamic range of 45 results in a significant loss of tissue detail; (b) Increasing the dynamic range to 65 recovers the lost details.

rendered planes. Volumes should be obtained during fetal quiescence, and the patient may be asked to briefly hold her breath to reduce motion artifacts. If the fetus is moving, a faster acquisition time can be selected to reduce artifacts; however, this is at the cost of reduced resolution.

Grayscale 2D imaging: The quality of the images obtained by slicing a 3D volume directly depends on the 2D image quality during volume acquisition. Therefore, the grayscale settings (including contrast, depth, and zoom) should be appropriately adjusted to ensure excellent pre-acquisition 2D image quality.

Visibility of structures of interest: Acoustic shadowing present during acquisition cannot be overcome by post-processing or rotating the 3D volume. If the fetal head is in a transverse position, the structures in the near-field hemisphere are obscured in the 3D volume and in any planes derived from it **(Fig. 1.9)**.

In the transabdominal (TAS) approach, the squamosal suture provides a window for acquiring volume in the axial plane, whereas the metopic suture provides a window for sagittal acquisition.

In transvaginal (TVS) imaging, the bregmatic fontanelle and sagittal suture offer similar imaging windows. The fetal head can be gently maneuvered transabdominally to bring it into an optimal position before acquiring the TVS 3D volume.

Sweep angle: The wider the angle of rotation (sweep), the larger the number of structures captured in the volume. However, selecting a large sweep angle significantly increases the acquisition time, resulting in artifacts in the reconstructed images. Such volumes also require increased storage space. A sweep angle of 60–80° for sagittal or coronal acquisition and 40–60° for axial acquisition is adequate.

Basic Protocol

1. The initial mode for 3D evaluation of the brain is the multiplanar mode. In this mode, the image in the left upper corner (A or 1) corresponds to

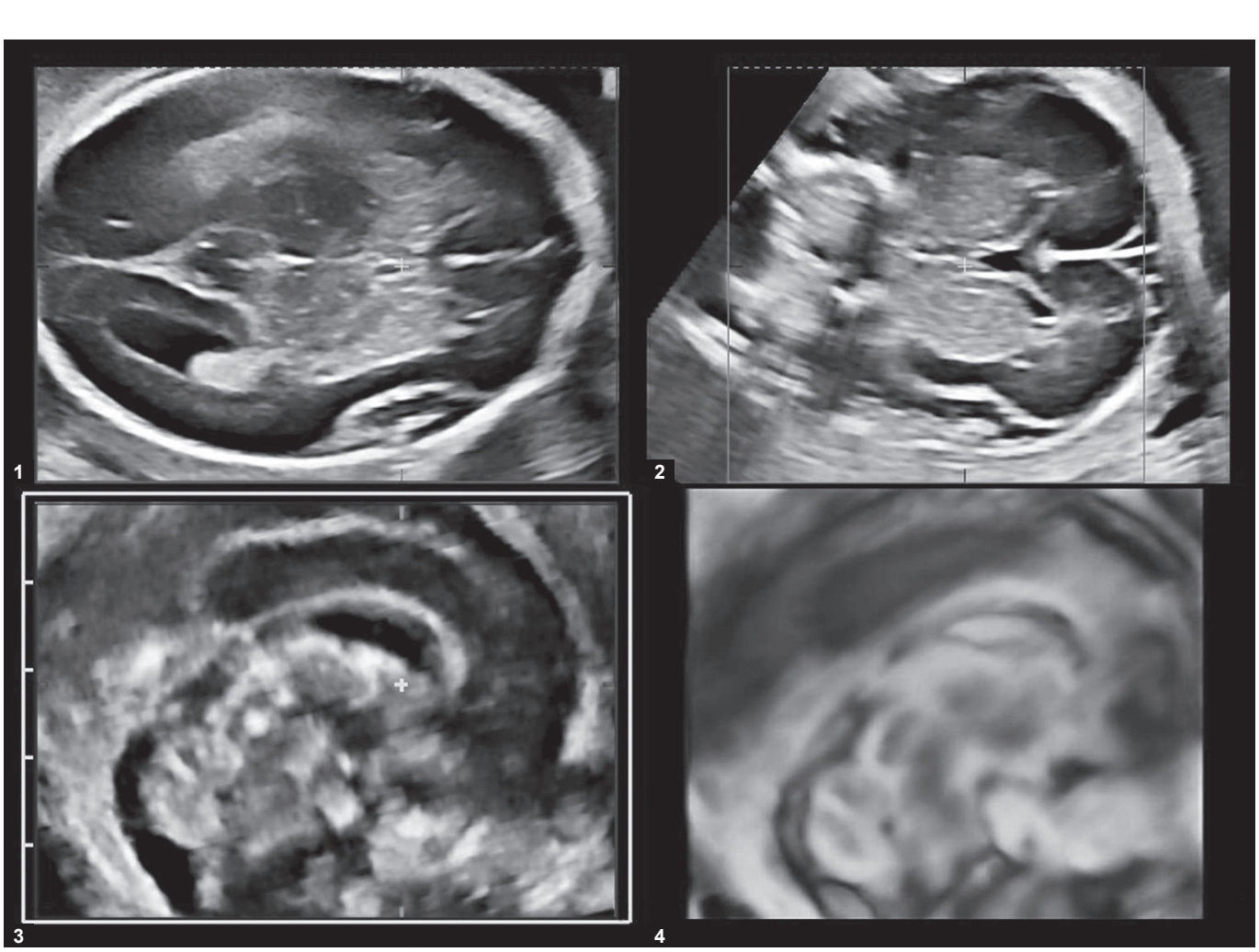

Fig. 1.9: Three-dimensional (3D) ultrasound in the multiplanar mode. Plane 1 shows the volume acquired in the axial plane. The rendered coronal and sagittal sections are obtained in planes 2 and 3, respectively. The marker dot (yellow cross) is placed on the columns of the fornix. Note the loss of detail caused by near-field shadowing in plane 2. For color version, *see* Plate 1.

the starting 2D plane, which is also known as the plane of acquisition. The plane perpendicular to the starting image but parallel to the ultrasound beam is rendered in the upper-right corner (B or 2). The third rendered plane appears in the lower right corner (C or 3) and is perpendicular to the other planes.

2. If the volume is obtained in the axial section, the same section appears in plane 1, with the coronal and sagittal sections rendered in plane 2 and 3, respectively **(Fig. 1.9)**.
3. An important tool available in the multiplanar mode is the marker dot, which denotes the same structure in all three planes. By placing the marker dot on a structure of interest in any one plane, the same structure can be located in the other two planes **(Fig. 1.9)**.
4. Each plane can be selected and freely rotated in the X, Y, or Z axis or 'sliced' as required to obtain the corresponding images in other planes. The combination of the 3-axis rotation and slicing provides unlimited planes for evaluating the structures of interest.
5. In addition to the multiplanar mode, the midsagittal plane can be obtained using the OmniView/FlexVue mode (*See* Chapter 4).
6. If 3D US is performed to visualize a posterior fossa structure, such as the vermis, the probe should be placed closer to the posterior fossa and angled approximately 45° to the midline, such that the cerebellum is clearly imaged in the original 2D plane of acquisition.
7. The complete evaluation of the lateral ventricles is difficult in axial plane volume acquisition. The parasagittal view, which shows the anterior, posterior, and inferior horns, is best obtained by TVS transfontanelle 3D imaging.
8. The tomographic ultrasound imaging (TUI) mode shows multiple successive and sequential planes obtained from a volume, similar to those generated by CT or MR imaging. The number of planes and the distance between two consecutive planes can be adjusted.
9. The inversion mode can be used to display an anechoic, fluid-filled structure as a 3D echogenic object. This is particularly useful for demonstrating the lateral ventricles in 3D and comparing the shape and size of the right and left lateral ventricles **(Fig. 1.10)**.
10. Finally, the maximum or skeletal mode can demonstrate the cranial bones and sutures through surface rendering **(Fig. 1.11)**.

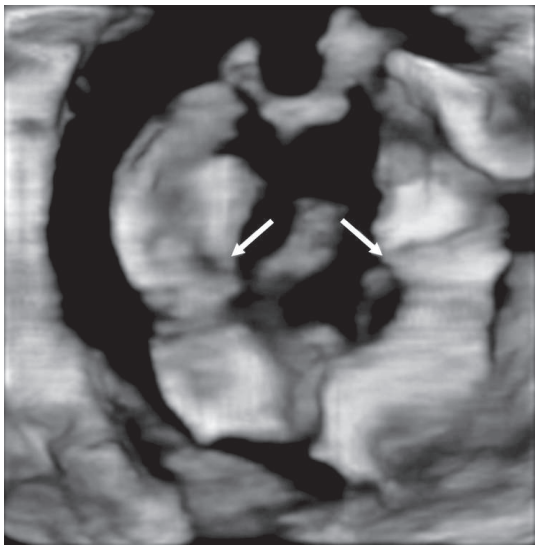

Fig. 1.10: Lateral ventricles (arrows) visualized in the inversion mode. For color version, *see* Plate 2.

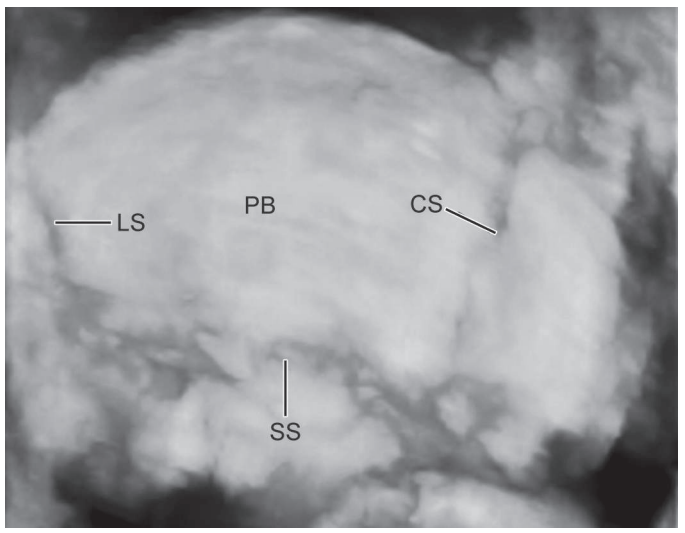

Fig. 1.11: Demonstration of cranial bones and sutures using the maximum/skeletal mode. The parietal bone (PB), coronal suture (CS), lambdoid suture (LS), and squamosal suture (SS) are noted. For color version, *see* Plate 2.

ROLE OF FETAL MRI

Magnetic resonance imaging (MRI) is increasingly used as a diagnostic tool for fetal imaging. Although the contrast resolution provided by MRI is significantly higher than that of ultrasound, it does not provide significant additional diagnostic benefits over a well-performed neurosonography examination in most fetuses. Overall, MRI may be required in approximately 10% of fetuses to reach a diagnosis that cannot be achieved using neurosonography alone.

REMEMBER

Fetal movement is the main limiting factor in MR imaging, overshadowing many of its benefits over ultrasound.

Advantages of MRI over Neurosonography

MRI provides superior soft-tissue contrast resolution, which is particularly valuable for identifying subtle

Table 1.4: Comparison between neurosonography and fetal MRI

Feature	*Neurosonography*	*Fetal MRI*
Spatial resolution	Adequate with high-frequency probes	Superior soft-tissue contrast resolution
Optimal timing	20–24 weeks primary evaluation	26–32 weeks (optimal diagnostic window)
Plane acquisition	Real-time multiplanar capability	Primarily acquisition-plane dependent; other planes reconstructed
Accessibility	Widely available, inexpensive	Limited availability; expensive
Main limitations	Bone shadowing, maternal habitus	Fetal movements during acquisition
Primary role	First-line diagnostic modality	Adjunct for complex or inconclusive cases; Subtle malformations of midline structures, cerebral cortex, and the posterior fossa.

CNS abnormalities when an initial finding is detected on ultrasound. Unlike ultrasound, MRI is not affected by calvarial bone shadowing, resulting in clear visualization of the structures adjacent to the skull. Additionally, the image quality in MRI is not compromised by the maternal body habitus or variations in the amniotic fluid volume.

Limitations of MRI

Fetal movement: This is the main concern with fetal brain MRI. As fetal paralysis is not used, rapid fetal movement makes image acquisition and accurate 3D reconstruction difficult and prone to errors. To some extent, this can be addressed by using ultrafast T2-weighted MR sequences or single-shot fast spin echo sequences (SSFSE) for the rapid acquisition of several frames. This results in motion blur being restricted to only specific frames when fetal movement occurs. However, fetal movement still makes the alignment between individual slices difficult (which is required for 3D reconstruction and obtaining planes other than the acquisition plane).

Lack of trained specialists: The fetal brain differs from the adult brain in several ways. Fetal brain structure and appearance vary widely across gestation as the brain undergoes rapid development. Unless the operator evaluating the MRI is specifically trained in fetal MR imaging, the accuracy is far lower than that of neurosonography.

Gestational age limitations: MRI is less accurate in fetuses less than 22 weeks of gestational age because of increased fetal movements, smaller brain size, and lower spatial resolution at earlier gestations. It is most useful between 26 and 32 weeks of gestation.

Indications for Fetal Brain MRI

Fetal MRI for the diagnosis of brain abnormalities should be considered only after expert neurosonography has been performed, the diagnosis is still unclear, and the MRI results are expected to change the outcome or management. Typical indications include.

1. Characterizing a subtle or complex anomaly detected on neurosonography and searching for associated findings (corpus callosum dysgenesis, malformations of cortical development, etc.).
2. Targeted neurosonography is not feasible (maternal obesity, abdominal scarring, oligohydramnios, and lack of experienced operators).
3. Familial conditions affecting the CNS (e.g. Joubert syndrome).
4. Suspected cases of cerebral ischemia or hemorrhage (fetal infections, following co-twin demise, or LASER photocoagulation in monochorionic twins).

REMEMBER

MRI can provide answers—but fetal neurosonography tells us the questions that need to be asked.

Neurosonography versus Fetal MRI

The following comparison highlights the key differences between the two modalities across important practical and diagnostic parameters **(Table 1.4)**.

SUGGESTED READING

1. Malinger G, Paladini D, Haratz KK, Monteagudo A, Pilu GL, Timor-Tritsch IE. ISUOG Practice Guidelines (updated): sonographic examination of the fetal central nervous system. Part 1: performance of screening examination and indications for targeted neurosonography. Ultrasound Obstet Gynecol. 2020 Sep;56(3):476–84.
2. Paladini D, Malinger G, Birnbaum R, Monteagudo A, Pilu G, Salomon LJ, Timor-Tritsch IE. ISUOG Practice Guidelines (updated): sonographic examination of the fetal central nervous system. Part 2: performance of targeted neurosonography. Ultrasound Obstet Gynecol. 2021 Apr;57(4):661–71.