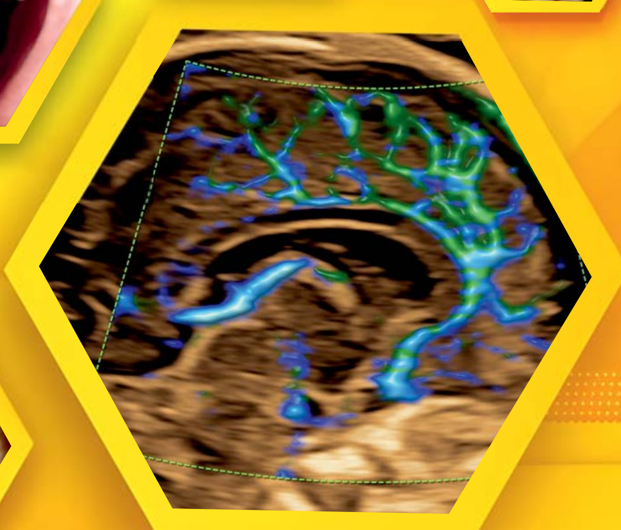
SOCIETY OF
FETAL MEDICINE

SFM FetalNeurocon 2024

International Fetal Neurology Congress

FETAL BRAIN

BIOMETRY & PUBLISHED PROTOCOLS



SOCIETY OF FETAL MEDICINE

FETAL BRAIN

BIOMETRY & PUBLISHED PROTOCOLS

EDITOR-IN-CHIEF

Ashok Khurana
Mentor Emeritus SFM
Chairman and Consultant in Reproductive Ultrasound
The Ultrasound Lab,
Defence Colony, New Delhi

EXECUTIVE EDITOR

Alok Varshney
Senior Consultant Radiologist,
Central Diagnostics,
Dwarka, New Delhi

CONTRIBUTORS

Chanchal
Lead Consultant, Department of Fetal Medicine
Madhukar Rainbow Children's Hospital,
& BirthRight by Rainbow Hospitals,
Malviya Nagar, New Delhi

Varun Ashok Thakur
Consultant Radiologist
Shri Mauli Diagnostic Services LLP,
Moshi, Pune, Maharashtra

Vrunda Appannagari
Consultant, Department of Fetal Medicine
Madhukar Rainbow Children's Hospital,
& BirthRight by Rainbow Hospitals,
Malviya Nagar, New Delhi

Shreya Goel
Fellow, Department of Fetal Medicine
Madhukar Rainbow Children's Hospital,
& BirthRight by Rainbow Hospitals,
Malviya Nagar, New Delhi

Muralidhar G. Kamalapur
Assistant Professor, Department of Radiology
Consultant, Department of Fetal Medicine,
Father Muller Medical College & Hospital,
Mangalore, Karnataka

Seema S. Yadagiri
Director & Consultant Radiologist
Janani Scanning Centre, Kalaburgi,
Karnataka

Mohit N
Consultant, Department of Fetal Medicine
Madhukar Rainbow Children's Hospital,
& BirthRight by Rainbow Hospitals,
Malviya Nagar, New Delhi

Meenu Batra
Consultant Radiologist
and Fetal Medicine Specialist,
CIMAR - The Women's Hospital,
Kochi, Kerala

COVER PAGE

Faisal Khan
Editorial Administrator, Journal of Fetal Medicine

ILLUSTRATIONS

Alok Varshney

SOCIETY OF FETAL MEDICINE

NATIONAL EXECUTIVE COMMITTEE 2024-2026

Mentor Emeritus
Ashok Khurana (Delhi)

President
Mohit V Shah (Maharashtra)

Immediate Past President
Bimal Sahni (Maharashtra)

President Elect
Sunil Mehta (Rajasthan)

Vice President
Krishna Gopal (Delhi)

Executive Secretary
Reema Kumar Bhatt (Delhi)

Treasurer
K Aparna Sharma (Delhi)

Joint Secretary
Meenu Batra (Kerala)

Executive Members

Girish Somabhai Patel (Gujarat)
Ritu Khanna (Uttar Pradesh)
Chanchal (Delhi)
Aniruddha Kulkarni (Maharashtra)
Alok Varshney (Delhi)
Prasanna Roy (Bengal)
Sweta Singh (Odisha)

Chinmayee Ratha (Telangana)
Prakash P (Karnataka)
Renu Makwana (Rajasthan)
Santosh Sabnis (Maharashtra)
Kanchan Mukherjee (Bengal)
Naveen Pereira (Punjab)

CONTENT

CONTENT

MESSAGE FROM THE PRESIDENT

Central nervous system (CNS) structural malformations are the most common abnormalities detected on antenatal ultrasound, often leading to long-term neurodevelopmental and structural defects. As our knowledge and understanding have evolved, many disorders once considered undiagnosable on prenatal ultrasound are now being detected. Consequently, the systematic evaluation of the fetal brain has developed into a discipline beyond fetal biometry and evaluation in three axial planes.

This booklet on fetal neurosonography is a valuable tool for accurately depicting and interpreting fetal CNS abnormalities. It offers pictorial depictions of the fetal brain, providing an essential resource for learning neuroanatomy. Additionally, it serves as a quick reference guide for acquiring the correct plane for biometry, understanding the trimester-wise normal appearance of structures, identifying key findings, and using standardized nomograms for interpretation. This will help you master the skill of obtaining the perfect imaging plane, crucial for detecting normal and abnormal appearances. The booklet also includes ISUOG practice guidelines with extensive teaching materials and an article on a state-of-the-art review of first-trimester fetal neurosonography.

On behalf of the Society of Fetal Medicine, I express sincere gratitude to the team of SFM members led by Dr. Alok Varshney for compiling this booklet. The schematics and images are a testament to their hard work and meticulous planning. I envision this booklet as an indispensable resource in your ultrasound practice, serving as a comprehensive guide to keep in mind while performing a neurosonogram.

Wish you happy learning.

Mohit V. Shah
National President
Society of Fetal Medicine

INTRODUCTION

Fetal brain is a fascinating mystery to explore through prenatal ultrasound. Its rapidly evolving anatomical landmarks hold the potential for a lifetime of cognitive and functional abilities, making precise assessment crucial for understanding its growth and maturation. Achieving this understanding requires a solid grasp of imaging protocols, neuroanatomy, and fetal brain biometry. Unfortunately, these essential components are often scattered across various sources and textbooks.

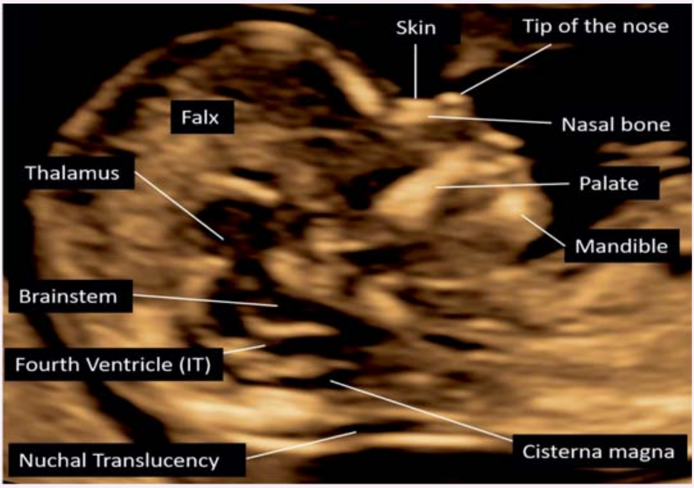
Therefore, I am pleased to introduce a new academic resource published by the Society of Fetal Medicine, **Fetal Brain : Biometry and Published Protocols.** This comprehensive volume is designed for clinicians and students interested in fetal brain examination. It covers basic imaging neuroanatomy, technical aspects of fetal brain measurements, their clinical significance, and useful nomograms. This compilation serves as a handy reference for every screening examination and neurosonogram, aiding in the diagnosis of neurodevelopmental disorders. I congratulate the team of dedicated SFM members who sifted through vast amounts of information to create a clear and concise guide filled with valuable insights.

As we work to enhance prenatal care, we must remember that every measurement and observation carries the potential for understanding, intervention, and, ultimately, the well-being of future generations we are dedicated to safeguarding.

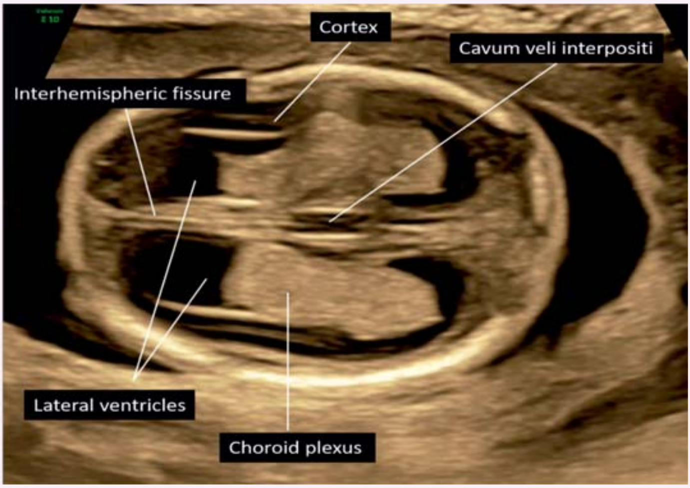
Ashok Khurana
Mentor Emeritus
Society of Fetal Medicine

FETAL CNS SONOANATOMY

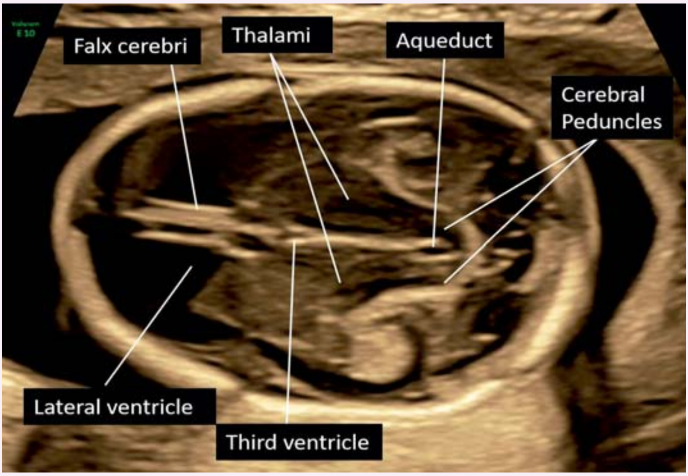
FIRST TRIMESTER



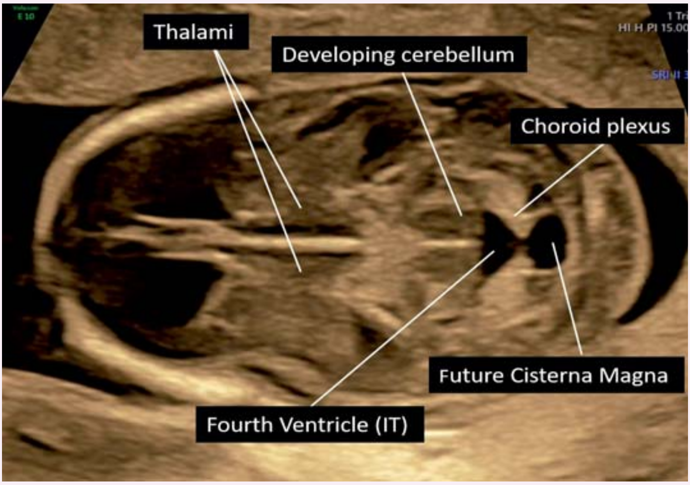
MIDSAGITTAL PLANE OF THE FETAL HEAD



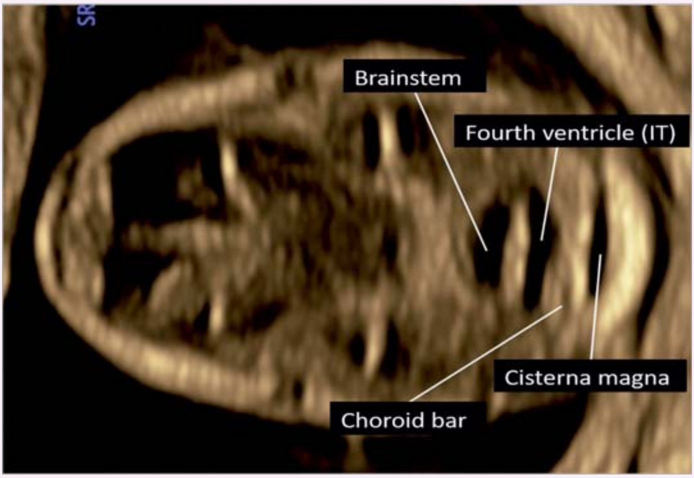
AXIAL TRANSVENTRICULAR PLANE



AXIAL TRANSTHALAMIC PLANE

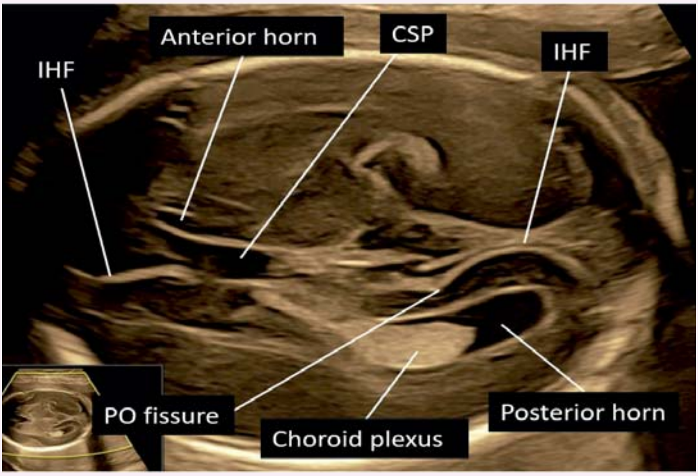


AXIAL TRANSCEREBELLAR PLANE

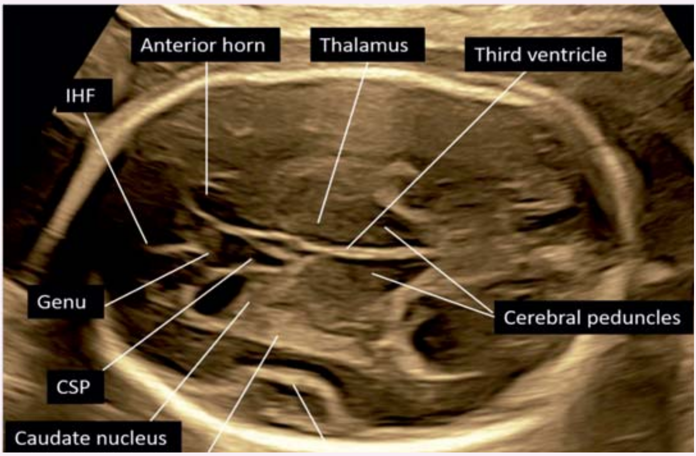


TILTED AXIAL PLANE

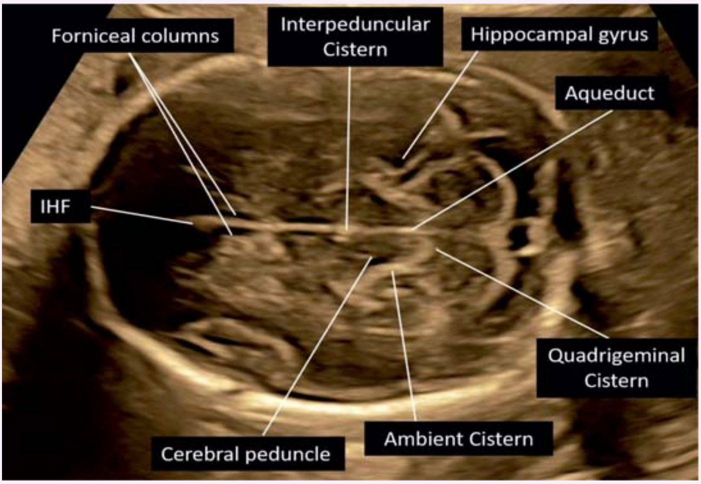
SECOND TRIMESTER



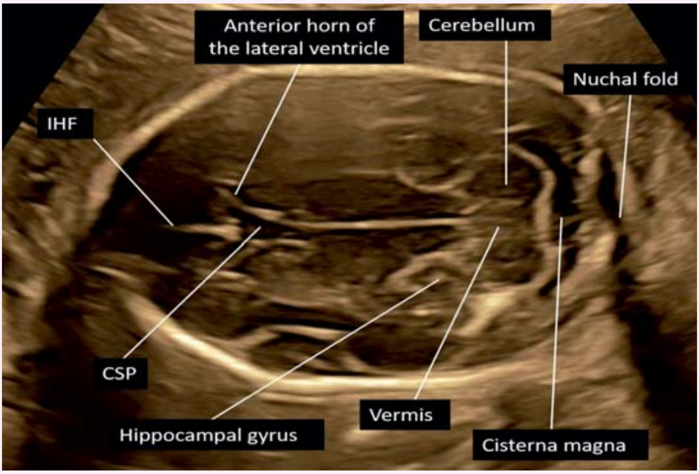
AXIAL TRANSVENTRICULAR PLANE



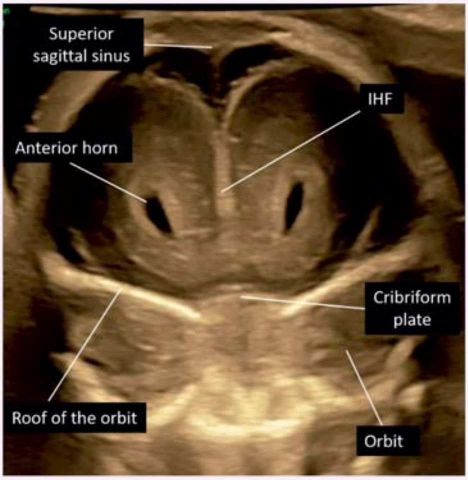
AXIAL TRANSTHALAMIC PLANE



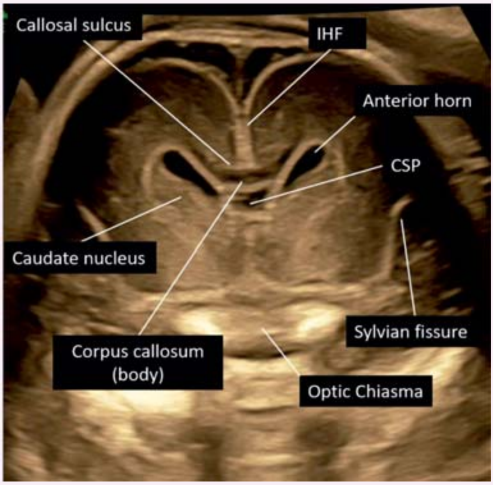
AXIAL INFRATHALAMIC PLANE



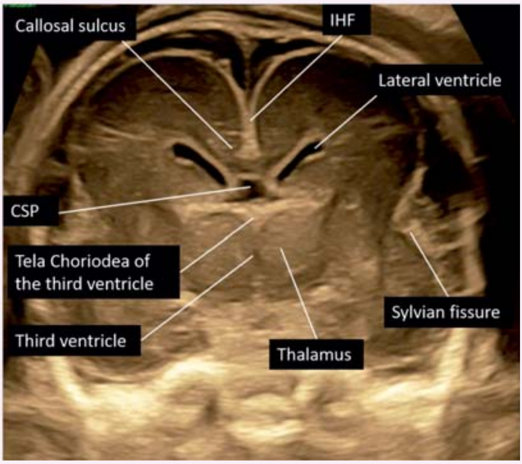
AXIAL TRANSCEREBELLAR PLANE



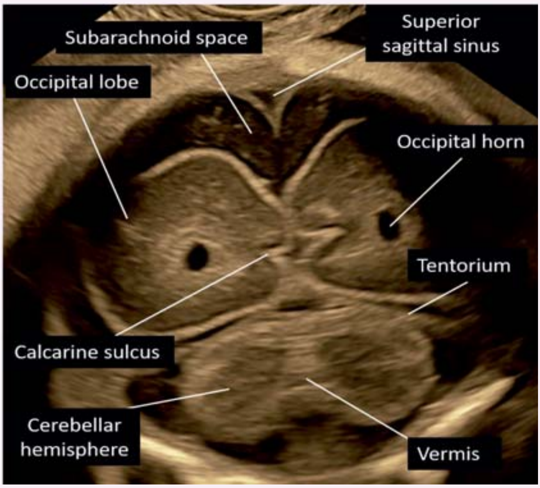
CORONAL TRANSFRONTAL PLANE



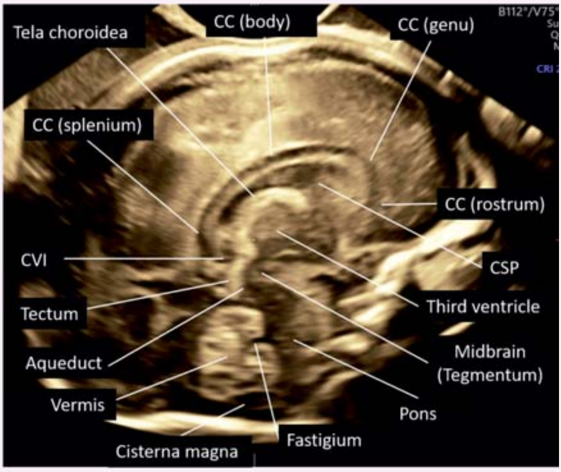
CORONAL TRANSCAUDATE PLANE



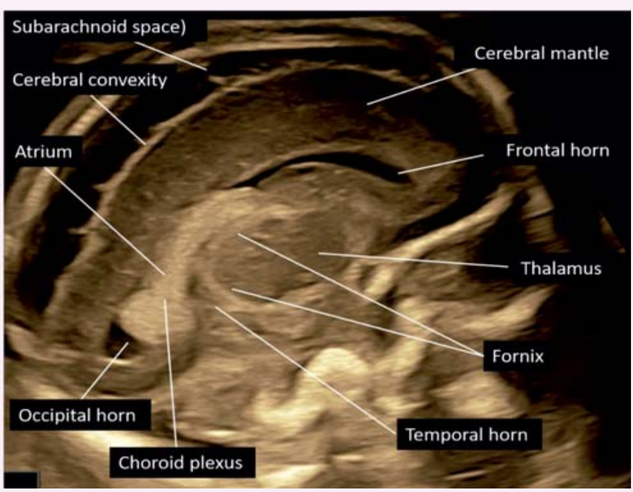
CORONAL TRANSTHALAMIC PLANE



CORONAL TRANSCEREBELLAR PLANE

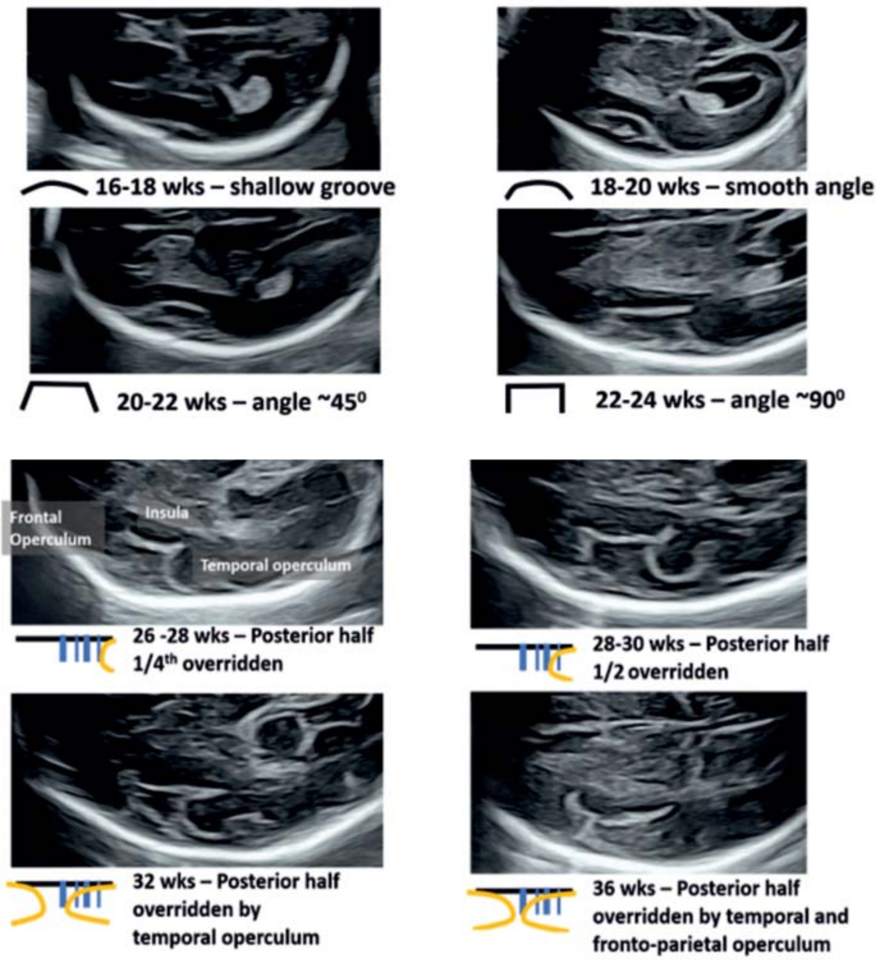


MIDSAGITTAL PLANE



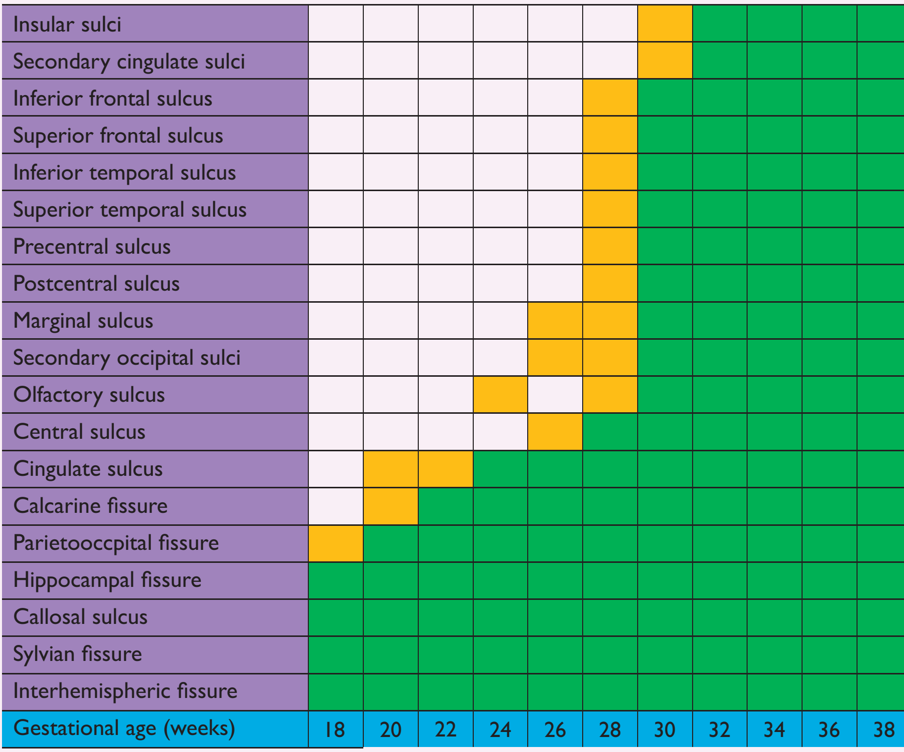
PARASAGITTAL PLANE

SYLVIAN FISSURE



Adapted from: Quarello, E., Stirnemann, J., Ville, Y. and Guibaud, L. (2008), Assessment of fetal Sylvian fissure operculization between 22 and 32 weeks: a subjective approach. Ultrasound Obstet Gynecol, 32: 44-49. https://doi.org/10.1002/uog.5353

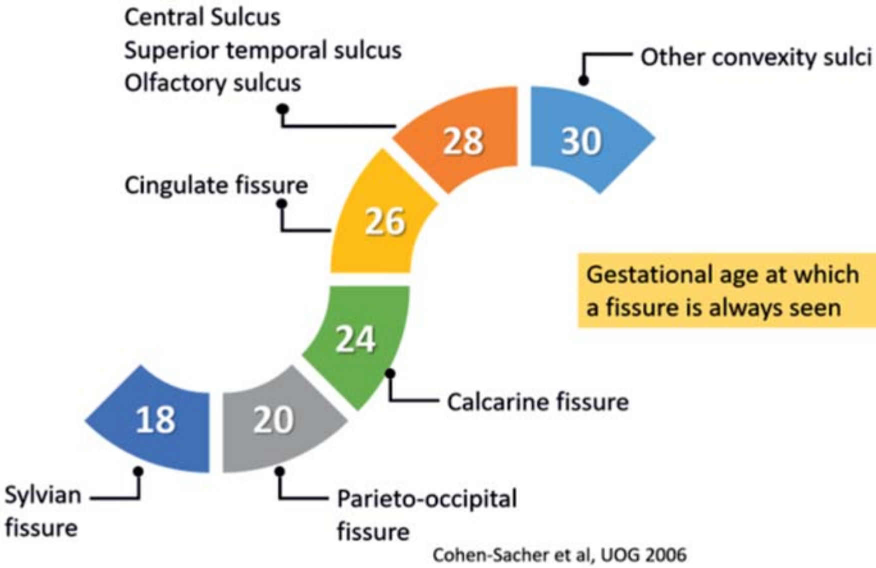
DETECTABILITY OF SULCI AND GYRI ACCORDING TO GESTATIONAL AGE



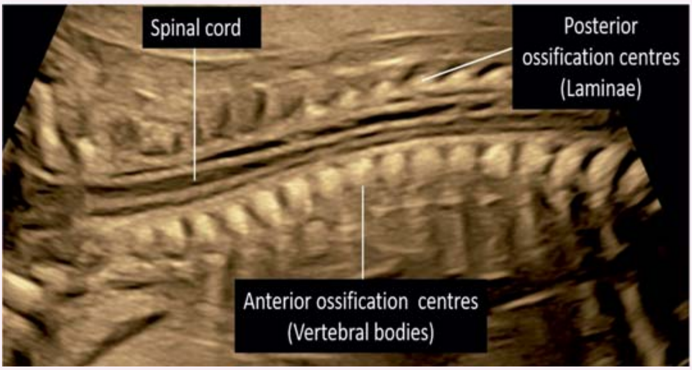
Comment

- The authors considered a particular structure to be present when it was seen in more than 75% of the fetuses (green boxes), detectable if it was observed in 25–75% of the examinations (yellow boxes) and absent when it was not observed in at least 25% of the examinations (white

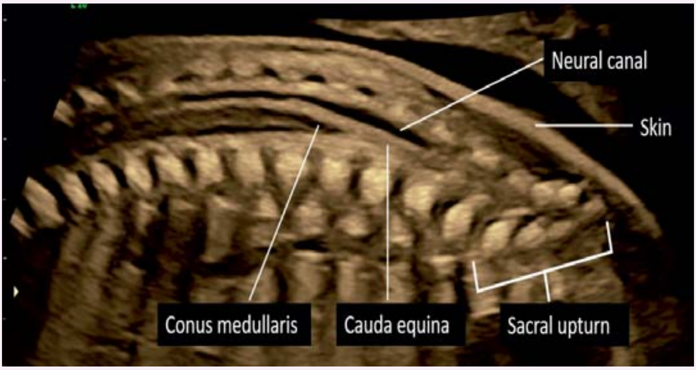
Reference: Cohen-Sacher B, Lerman-Sagie T, Lev D, Malinger G. Sonographic developmental milestones of the fetal cerebral cortex: a longitudinal study. Ultrasound in Obstetrics and Gynecology. 2006;27(5):494-502. doi:10.1002/uog.2757


Central Sulcus
Superior temporal sulcus
Olfactory sulcus
Other convexity sulci
28
30
Cingulate fissure
26
Gestational age at which a fissure is always seen
24
Calcarine fissure
18
20
Sylvian fissure
Parieto-occipital fissure
Cohen-Sacher et al, UOG 2006

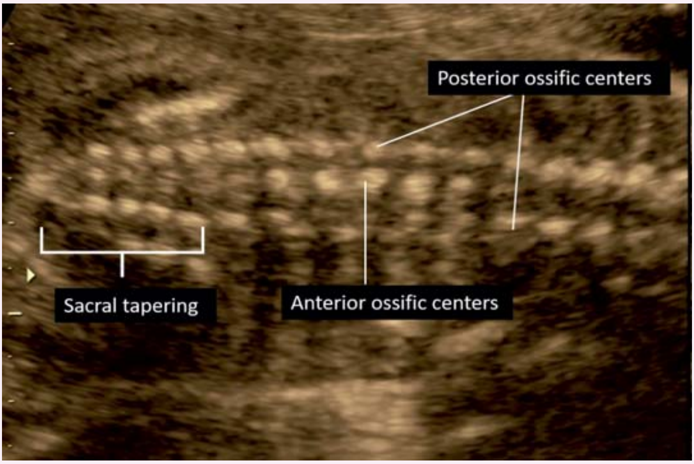
SPINE



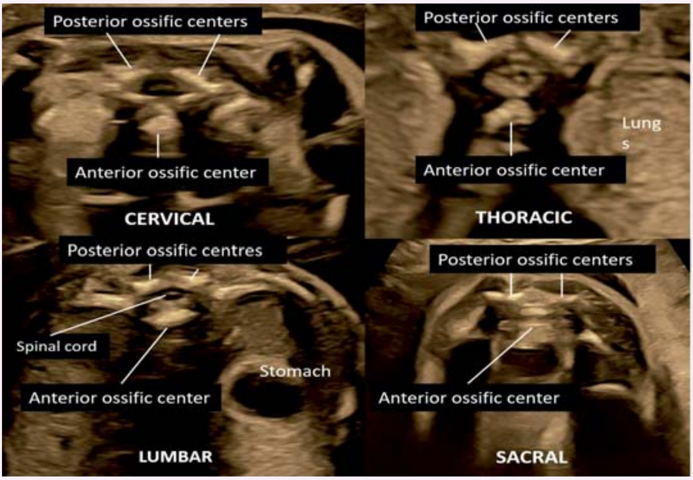
SAGITTAL PLANE CERVICO-THORACIC SPINE



SAGITTAL PLANE LUMBO-SACRAL SPINE



CORONAL PLANE

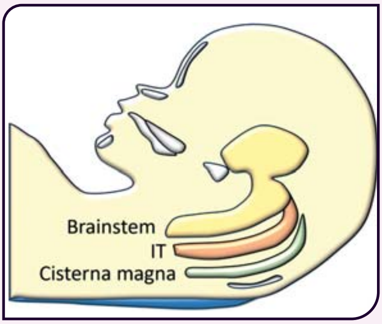


AXIAL PLANES

BIOMETRY OF THE BRAIN

FIRST TRIMESTER

INTRACRANIAL TRANSLUCENCY



Definition

- Intracranial translucency (IT) refers to the ultrasound visualization of the fourth ventricle in the mid-sagittal plane during an 11-14 weeks scan.

How To Measure

- Obtain a mid-sagittal plane of the fetal head, neck, and upper chest, which is the same plane used for measuring nuchal translucency and the nasal bone.
- Identify the brainstem, fourth ventricle, and cisterna magna as three hypoechoic spaces. These are separated by two echogenic lines: the posterior border of the brainstem and the choroid plexus of the fourth ventricle.
- The anteroposterior diameter of the fourth ventricle is measured between two echogenic lines formed by the posterior border of the brainstem anteriorly, and the choroid plexus of the fourth ventricle posteriorly (inner-to-inner measurement).

Comments

- Reduced IT serves as a marker for open neural tube defects, with its absence often indicating open spina bifida.
- Enlarged IT is associated with chromosomal abnormalities and posterior fossa malformations, such as Blake's pouch cyst, Dandy-Walker malformation and Joubert syndrome.

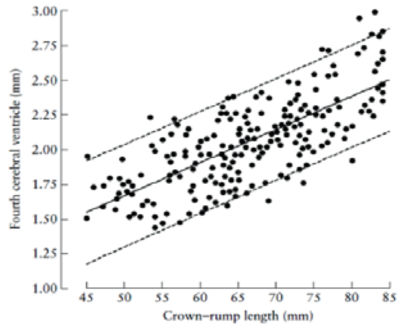


Figure 2 Reference range (mean, 5th and 95th centiles) of fourth ventricle anteroposterior diameter according to crown–rump length.

From: Chaoui et al, UOG, 2009

Table: The values of IT according to CRL ranges

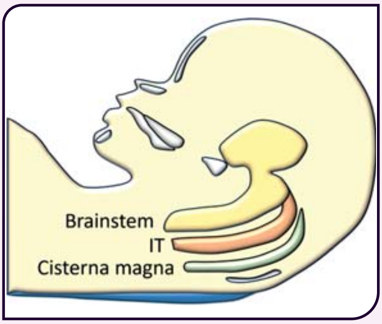
CRL Ranges	Mean	Std. Deviation	Median
45–54 mm	1.46	0.22	1.40
55–64 mm	1.65	0.19	1.70
65–74 mm	1.84	0.24	1.85
75–84 mm	2.03	0.25	2.00

From: Ergin et al, J Turk Ger Gynecol assooc. 2012

References :

1. Chaoui R, Benoit B, Mitkowska-Wozniak H, Heling KS, Nicolaides KH. Assessment of intracranial translucency (IT) in the detection of spina bifida at the 11-13-week scan. Ultrasound Obstet Gynecol. 2009 Sep;34(3):249-52. doi: 10.1002/uog.7329.
2. Ergin RN, Yayla M. The nomogram of intracranial translucency in the first trimester in singletons. J Turk Ger Gynecol Assoc. 2012 Sep 1;13(3):153-6. doi: 10.5152/jtgga.2012.19.

BRAINSTEM DIAMETER



Definition

- Brain stem diameter (BS) refers to the ultrasound visualization of the brainstem in the mid-sagittal plane during an 11-13^{+6} weeks scan.

How To Measure

- Obtain a mid-sagittal plane of the fetal head, neck, and upper chest, which is the same plane used for measuring nuchal translucency and the nasal bone.
- Identify the brainstem, fourth ventricle, and cisterna magna as three hypoechoic spaces. These are separated by two echogenic lines: the posterior border of the brainstem and the choroid plexus of the fourth ventricle. Additionally, the sphenoid bone can be identified as an echogenic structure anterior to the brainstem in line with the hard palate.
- The anteroposterior diameter of the brainstem is measured at the level of the sphenoid bone.

Comments

- BS diameter serves as a marker for open neural tube defects, with its thickening often indicating open spina bifida.

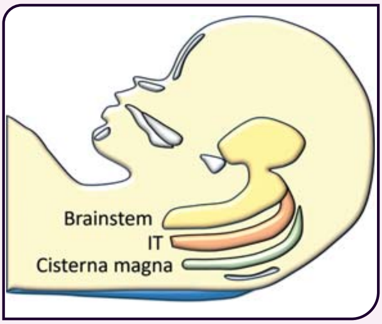
TABLE

PERCENTILE VALUES OF BRAINSTEM DIAMETER (mm) BY GESTATIONAL AGE

GA (weeks)	5th	25th	50th	75th	95th
10+6	1.7	1.7	1.9	2.2	2.3
11+0	1.4	1.9	2.0	2.3	2.6
11+1	1.7	2.0	2.1	2.3	2.9
11+2	1.8	2.0	2.2	2.4	2.8
11+3	1.7	2.0	2.3	2.5	2.9
11+4	2.0	2.3	2.5	2.7	3.0
11+5	2.1	2.3	2.5	2.6	3.1
11+6	2.0	2.4	2.5	2.8	3.2
12+0	2.1	2.4	2.6	2.9	3.2
12+1	2.3	2.6	2.8	3.0	3.5
12+2	2.4	2.6	2.9	3.2	3.6
12+3	2.5	2.7	3.0	3.2	3.8
12+4	2.4	2.8	3.0	3.3	3.9
12+5	2.5	2.9	3.1	3.4	3.9
12+6	2.5	3.0	3.2	3.5	4.1
13+0	2.8	3.1	3.4	3.6	4.1
13+1	2.8	3.2	3.4	3.7	4.4
13+2	2.9	3.2	3.5	3.8	4.2
13+3	2.9	3.3	3.5	3.8	4.2
13+4	3.1	3.3	3.7	3.9	4.4
13+5	3.1	3.3	3.8	4.1	4.3
13+6	3.0	3.5	3.8	4.0	4.3

Reference: Yang SH, An HS, Lee JS, Kim C. Normal intracranial BS/BSOB ratio values in the first trimester of single gestations with live fetuses in a Korean population. Medical Ultrasonography. 2017;19(2):190. doi:10.11152/mu-829

BRAINSTEM TO OCCIPITAL BONE DISTANCE



Definition

- Brain stem to occipital bone distance (BSOB) refers to the distance of the brainstem in the mid-sagittal plane from the occipital bone during an 11-13^{+6} weeks scan.

How To Measure

- Obtain a mid-sagittal plane of the fetal head, neck, and upper chest, which is the same plane used for measuring nuchal translucency and the nasal bone.
- Identify the brainstem, fourth ventricle, and cisterna magna as three hypoechoic spaces. These are separated by two echogenic lines: the posterior border of the brainstem and the choroid plexus of the fourth ventricle. Additionally, the sphenoid bone can be identified as an echogenic structure anterior to the brainstem in line with the hard palate. The occipital bone is visualized as a brightly echogenic structure in the fetal head posteriorly.
- The BSOB is measured as a vertical distance from the posterior border of the brain stem to the anterior margin of the occipital bone at the level of the sphenoid bone.

Comments

- Reduced BSOB serves as a sensitive marker for open spina bifida in the first trimester.

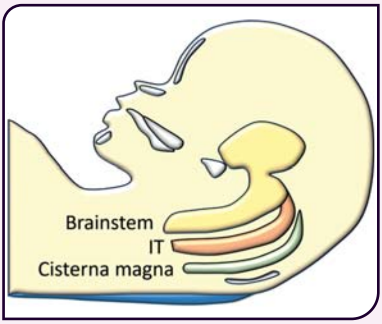
TABLE

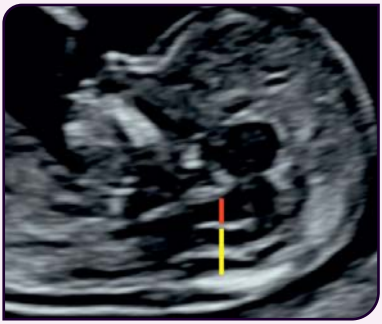
PERCENTILE VALUES OF BRAINSTEM TO OCCIPITAL BONE DISTANCE (mm) BY GESTATIONAL AGE

GA (weeks)	5th	25th	50th	75th	95th
10+6	3.2	3.5	3.7	4.0	4.3
11+0	3.2	3.6	3.8	4.0	4.4
11+1	3.1	3.5	3.8	4.0	4.4
11+2	3.5	3.8	4.0	4.3	4.7
11+3	3.3	3.7	4.1	4.5	4.9
11+4	3.5	4.0	4.3	4.5	4.9
11+5	3.7	4.0	4.3	4.6	5.1
11+6	3.8	4.2	4.5	4.8	5.3
12+0	3.8	4.3	4.6	4.9	5.4
12+1	4.1	4.5	4.8	5.1	5.6
12+2	4.3	4.7	5.0	5.4	5.7
12+3	4.4	4.8	5.1	5.4	6.0
12+4	4.5	5.0	5.3	5.6	6.1
12+5	4.7	5.1	5.4	5.8	6.3
12+6	4.7	5.3	5.7	6.0	6.5
13+0	4.9	5.5	5.9	6.4	6.8
13+1	5.1	5.6	6.0	6.5	7.0
13+2	5.3	6.1	6.5	6.8	7.1
13+3	5.6	5.9	6.5	6.9	7.7
13+4	5.7	6.1	6.6	7.0	7.7
13+5	5.4	6.1	6.5	7.0	7.7
13+6	5.3	6.6	7.1	7.5	8.3

Reference: Yang SH, An HS, Lee JS, Kim C. Normal intracranial BS/BSOB ratio values in the first trimester of single gestations with live fetuses in a Korean population. Medical Ultrasonography. 2017;19(2):190. doi:10.11152/mu-829

BRAINSTEM TO BRAINSTEM-OCCIPITAL BONE DISTANCE RATIO





Definition

- Brain stem to Brain-stem occipital bone distance ratio (BS-BSOB ratio) is the ratio calculated between the brainstem (BS) diameter and the distance between the brainstem to the occipital bone (BSOB) in the mid-sagittal plane during an 11-13+6 weeks scan.
- In a normal fetus, BS diameter is lower compared to BSOB distance. Hence, BS-BSOB ratio is < 1. In fetuses with open spina bifida, BS diameter is higher than BSOB distance. Hence, BS-BSOB ratio is > 1.

How To Measure

- The BS diameter and the BSOB distance are measured as described previously.
- The BS diameter is divided by the BSOB distance to calculate the ratio.

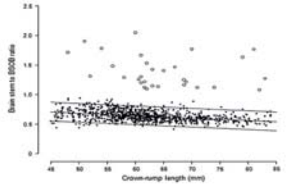
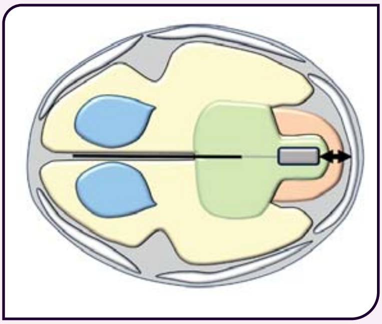


Figure 4—Individual measurements of the ratio between the brain stem diameter and BSOB diameter in fetuses with OSB (open circles) and normal controls (closed circles) plotted on the reference range for CRL (median, 5th and 95th percentiles)

Reference: Lachmann R, Chaoui R, Moratalla J, Picciarelli G, Nicolaides KH. Posterior brain in fetuses with open spina bifida at 11 to 13 weeks. Prenatal Diagnosis. 2010;31(1):103-106. doi:10.1002/pd.2632

AQUEDUCT TO OCCIPITAL BONE DISTANCE



Definition

- The distance between the aqueduct of Sylvius (AoS) and the occiput.
- This distance is reduced in the fetuses with open spina bifida.

How To Measure

- Measured in an axial plane slightly caudal to the transthalamic plane at 11 to 14 weeks, showing the midbrain.
- The aqueduct of Sylvius is identified as a prominent lucent 'box' in the center of the midbrain.
- Avoid an oblique superoinferior plane by keeping the choroid plexuses in the lateral ventricles out of view and ensuring that the aqueduct of Sylvius appears 'square' rather than elongated.
- Avoid a lateral oblique plane by ensuring symmetry of the right and left halves of the brain.
- The calipers are placed on the posterior border of the aqueduct of Sylvius and the anterior border of the occipital bones.

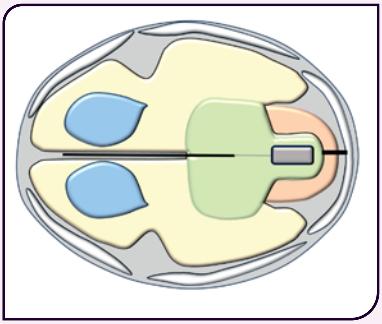
TABLE

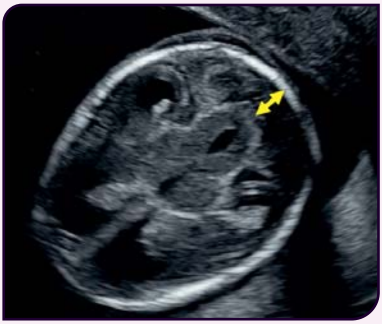
AQUEDUCT OF SYLVIUS (AOS)-TO-OCCIPUT DISTANCE ACCORDING TO CROWN–RUMP LENGTH (CRL)

	AOS-TO-OCCIPUT DISTANCE (mm)		
CRL (mm)	Mean – 2 SD	Mean	Mean + 2 SD
45–49	1.7	2.3	2.6
50–54	2.0	2.8	3.6
55–59	2.1	3.5	4.9
60–64	2.5	3.9	5.3
65–69	2.6	4.1	5.8
70–74	3.1	4.7	6.3
75–79	3.6	5.2	6.8
80–84	3.7	5.7	7.7

Reference: Finn M, Sutton D, Atkinson S, et al. The aqueduct of Sylvius: a sonographic landmark for neural tube defects in the first trimester. Ultrasound in Obstetrics & Gynecology. 2011;38(6):640-645. doi:10.1002/uog.10088

MIDBRAIN TO OCCIPITAL BONE DISTANCE





Definition

- The distance between the midbrain (mesencephalon) and the occiput.
- This distance is reduced in the fetuses with open spina bifida.

How To Measure

- Measured in an axial plane slightly caudal to the transthalamic plane at 11 to 14 weeks, showing the midbrain.
- The midbrain is visualized as a semicircular structure in the posterior brain and appears as a continuation of the thalami.
- The aqueduct of Sylvius is identified as a prominent lucent 'box' in the center of the midbrain.
- Avoid superoinferior oblique plane of insonation by ensuring that the choroid plexuses in the lateral ventricles are not visible.
- Avoid a lateral oblique plane by ensuring symmetry of the right and left halves of the brain.
- The calipers are placed on the posterior border of the midbrain and the anterior border of the occipital bones.

TABLE

MIDBRAIN-TO-OCCIPUT DISTANCE ACCORDING TO CROWN–RUMP LENGTH (CRL)

	MIDBRAIN-TO-OCCIPUT DISTANCE (mm)				
	Percentile				
CRL (mm)	1st	5th	50th	95th	99th
45–49	1.31	1.36	1.70	2.30	3.22
50–54	1.43	1.45	1.89	2.53	3.45
55–59	1.51	1.61	2.11	2.79	3.70
60–64	1.6	1.79	2.34	3.08	3.96
65–69	1.69	1.98	2.61	3.39	4.25
70–74	1.78	2.20	2.90	3.74	4.55
75–79	1.88	2.43	3.23	4.12	4.88
80–84	1.99	2.70	3.59	4.54	5.22

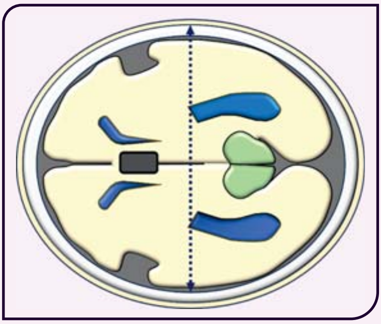
Reference: Nemescu D, Adam A, Tanasa I, et al. Reference ranges for the fetal mesencephalon to occiput measurement at 11 to 13+6 weeks of gestation. Experimental and Therapeutic Medicine. Published online May 28, 2020. doi:10.3892/etm.2020.8803

BIOMETRY OF THE BRAIN

SECOND AND THIRD TRIMESTER

SUPRATENTORIAL COMPARTMENT

BIPARIETAL DIAMETER



Definition

- The biparietal diameter (BPD) represents the widest transverse dimension of the fetal head.

How To Measure

- The fetal head is imaged in the axial plane.
- Symmetrical cerebral hemispheres
- Structures seen (from anterior to posterior): Anterior falx cerebri, cavum septi pellucidi (CSP), thalami, cerebral peduncles and posterior falx cerebri.
- Cerebellum should not be visible
- Measure perpendicular to the midline.
- Measure from the outer surface of the parietal bone near the transducer to the inner margin of the parietal bone on the opposite side.
- Exclude scalp.

Comment

- The BPD is a reliable predictor of menstrual age in the first half of pregnancy, being the most accurate between 12 and 18 (± 1.2) weeks.
- As pregnancy progresses, the accuracy of the BPD in predicting gestational age decreases.
- BPD may be misleading if the fetal head shape is abnormal, i.e., brachycephalic or dolichocephalic.

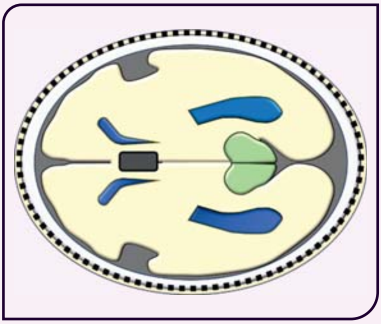
TABLE

PREDICTED FETAL BIPARIETAL DIAMETER AT SPECIFIC GESTATIONAL AGES

Gestational Age (weeks)	Biparietal Diameter (cm)	Gestational Age (weeks)	Biparietal Diameter (cm)
12.0	1.7	26.0	6.5
12.5	1.9	26.5	6.7
13.0	2.1	27.0	6.8
13.5	2.3	27.5	6.9
14.0	2.5	28.0	7.1
14.5	2.7	28.5	7.2
15.0	2.9	29.0	7.3
		29.5	7.5
15.5	3.1	30.0	7.6
16.0	3.2	30.5	7.7
16.5	3.4	31.0	7.8
17.0	3.6	31.5	7.9
17.5	3.8	32.0	8.1
18.0	3.9	32.5	8.2
18.5	4.1	33.0	8.3
19.0	4.3	33.5	8.4
19.5	4.5	34.0	8.5
20.0	4.6	34.5	8.6
20.5	4.8	35.0	8.7
21.0	5.0	35.5	8.8
21.5	5.1	36.0	8.9
22.0	5.3	36.5	8.9
22.5	5.5	37.0	9.0
23.0	5.6	37.5	9.1
23.5	5.8	38.0	9.2
24.0	5.9	38.5	9.2
24.5	6.1	39.0	9.3
25.0	6.2	39.5	9.4
25.5	6.4	40.0	9.4

Reference: Hadlock FP, Deter RL, Harrist RB, et al. Estimating fetal age: Computer assisted analysis of multiple fetal growth parameters. Radiology. 1984;152(2):497–501.

HEAD CIRCUMFERENCE



Definition

- The head circumference (HC) refers to the measurement of the outer perimeter of the fetal skull at the level of the BPD (transthalamic plane).

How To Measure

- The fetal head is imaged in the axial plane.
- Symmetrical cerebral hemispheres
- Structures seen (from anterior to posterior): Anterior falx cerebri, cavum septi pellucidi (CSP), thalami, cerebral peduncles and posterior falx cerebri.
- Cerebellum should not be visible
- Place cursors (ellipse/ manual trace) along the outer margin of the skull bones.
- Exclude scalp

Comment

- HC is a better predictor of fetal age than BPD as it is independent of the shape of the head.
- HC equations, especially Hadlock's, are not designed for diagnosing microcephaly, as their 2 standard deviation range is narrow.

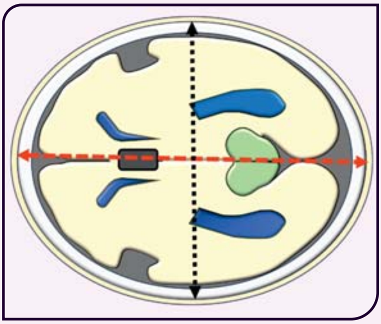
TABLE

PREDICTED FETAL HEAD CIRCUMFERENCE AT SPECIFIC GESTATIONAL AGES

Gestational Age (weeks)	Head Circumference (cm)	Gestational Age (weeks)	Head Circumference (cm)
12.0	6.8	26.5	25.1
12.5	7.5	27.0	25.6
13.0	8.2	27.5	26.1
13.5	8.9	28.0	26.6
14.0	9.7	28.5	27.1
14.5	10.4	29.0	27.5
15.0	11.0	29.5	28.0
15.5	11.7	30.0	28.4
16.0	12.4	30.5	28.8
16.5	13.1	31.0	29.3
17.0	13.8	31.5	29.7
17.5	14.4	32.0	30.1
18.0	15.1	32.5	30.4
18.5	15.8	33.0	30.8
19.0	16.4	33.5	31.2
19.5	17.0	34.0	31.5
20.0	17.7	34.5	31.8
20.5	18.3	35.0	32.2
21.0	18.9	35.5	32.5
21.5	19.5	36.0	32.8
22.0	20.1	36.5	33.0
22.5	20.7	37.0	33.3
23.0	21.3	37.5	33.5
23.5	21.9	38.0	33.8
24.0	22.4	38.5	34.0
24.5	23.0	39.0	34.2
25.0	23.5	39.5	34.4
25.5	24.1	40.0	34.6
26.0	24.6		

Reference: Hadlock FP, Deter RL, Harrist RB, et al. Estimating fetal age: Computer assisted analysis of multiple fetal growth parameters. Radiology. 1984;152(2):497–501.

CEPHALIC INDEX



Definition

- Cephalic index (CI) is the relationship between the short and long axes of the fetal skull, measured at the level of the BPD (transthalamic plane).

How To Measure

- The widest transverse and longitudinal (occipitofrontal diameter [OFD]) dimensions of the fetal skull at the level of the BPD are measured from outer margin to outer margin.
- The CI can then be calculated using the following simple equation:
  CI = short axis (transverse)/long axis (OFD) × 100

Comment

- Using the CI, the variations in the shape of the fetal skull, such as dolichocephaly (CI below 74) and brachycephaly (CI above 84), can be identified. In these conditions fetal age estimation based on the BPD is misleading.

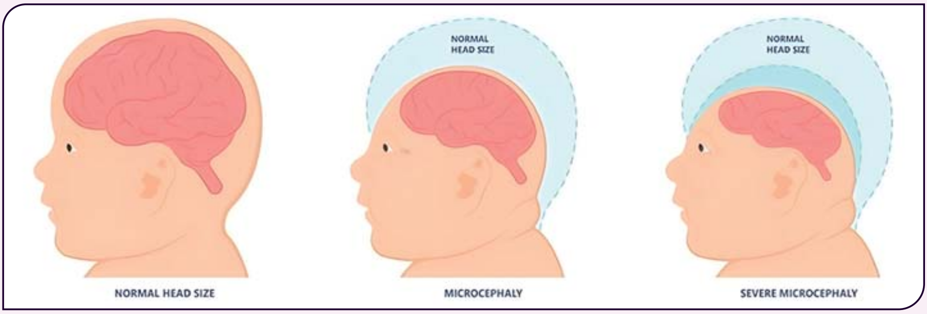
TABLE

CEPHALIC INDEX: MEAN AND NORMAL RANGE

Week	Mean Cephalic Index	–1 SD	+1 SD
14	81.5	77.8	85.3
15	81.0	77.3	84.8
16	80.5	76.8	84.3
17	80.1	76.4	83.9
18	79.7	76.0	83.5
19	79.4	75.7	83.2
20	79.1	75.4	82.9
21	78.8	75.1	82.6
22	78.6	74.9	82.4
23	78.4	74.7	82.2
24	78.3	74.6	82.0
25	78.1	74.4	81.9
26	78.0	74.3	81.8
27	78.0	74.3	81.8
28	78.0	74.3	81.8
29	78.0	74.3	81.8
30	78.1	74.4	81.9
31	78.2	74.5	82.0
32	78.3	74.6	82.1
33	78.5	74.8	82.3
34	78.7	75.0	82.5
35	78.9	75.2	82.7
36	79.2	75.5	83.0
37	79.5	75.8	83.3
38	79.9	76.2	83.7
39	80.3	76.6	84.1
40	80.7	77.0	84.5

Reference: Gray DL, Songster GS, Parvin CA, et al: Cephalic index: a gestational age-dependent biometric parameter, Obstet Gynecol. 1989 Oct;74(4):600–603.

MICROCEPHALY



Definition

- Microcephaly is an abnormally small fetal head. This is defined as having a head circumference (HC) that is 3 standard deviations (SD) or more below the mean for the gestational age.

How To Measure

- Fetal head circumference is measured.

Comment

- This condition is typically caused by fetal developmental disorders that result in reduced brain size and volume.
- The diagnosis of microcephaly should be suspected when the HC is 3 SD below the mean for a given gestational age. However, the antenatal accuracy for the diagnosis of microcephaly using this definition is low.
- The presence of a sloping forehead should raise the suspicion for microcephaly.
- A detailed neurosonographic examination should be performed on fetuses with HC more than 2 standard deviations below the mean to check for intracranial abnormalities. It is recommended to conduct a follow-up ultrasound in 3 to 4 weeks for these cases.

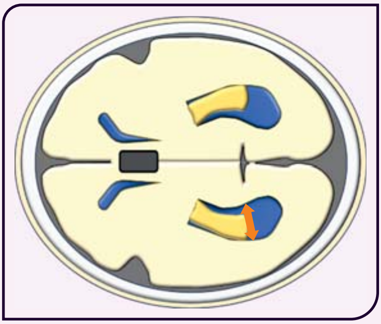
TABLE

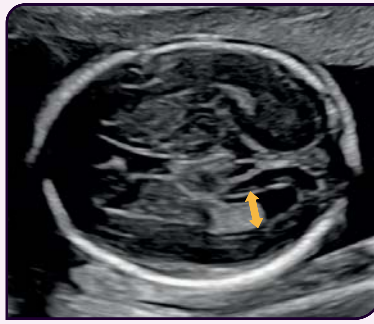
HEAD CIRCUMFERENCE (mm) AS A FUNCTION OF GESTATIONAL AGE - MEANS AND STANDARD DEVIATIONS

Week	+5SD	+4SD	+3SD	+2SD	+1SD	Mean	–1SD	–2SD	–3SD	–4SD	–5SD
12	148	133	119	104	90	75	60	46	31	17	2
13	161	146	132	117	103	88	73	59	44	30	15
14	174	159	145	130	116	101	86	72	57	43	28
15	186	171	157	142	128	113	98	84	69	55	40
16	199	184	170	155	141	126	111	97	82	68	53
17	211	196	182	167	153	138	123	109	94	80	65
18	224	209	195	180	166	151	136	122	107	93	78
19	236	221	207	192	178	163	148	134	119	105	90
20	248	233	219	204	190	175	160	146	131	117	102
21	260	245	231	216	202	187	172	158	143	129	114
22	271	256	242	227	213	198	183	169	154	140	125
23	283	268	254	239	225	210	195	181	166	152	137
24	294	279	265	250	236	221	206	192	177	163	148
25	305	290	276	261	247	232	217	203	188	174	159
26	315	300	286	271	257	242	227	213	198	184	169
27	325	310	296	281	267	252	237	223	208	194	179
28	335	320	306	291	277	262	247	233	218	204	189
29	344	329	315	300	286	271	256	242	227	213	198
30	354	339	325	310	296	281	266	252	237	223	208
31	362	347	333	318	304	289	274	260	245	231	216
32	370	355	341	326	312	297	282	268	253	239	224
33	378	363	349	334	320	305	290	276	261	247	232
34	385	370	356	341	327	312	297	283	268	254	239
35	392	377	363	348	334	319	304	290	275	261	246
36	398	383	369	354	340	325	310	296	281	267	252
37	403	388	374	359	345	330	315	301	286	272	257
38	408	393	379	364	350	335	320	306	291	277	262
39	412	397	383	368	354	339	324	310	295	281	266
40	416	401	387	372	358	343	328	314	299	285	270

Reference: Chervenak FA, Jeanty P, Cantraine F, et al: The diagnosis of fetal microcephaly. Am J Obstet Gynecol. 1984;149(5):512–517.

DIAMETER OF THE ATRIUM OF THE LATERAL VENTRICLE





Definition

- The atrium (trigone) is the triangular portion of the lateral ventricle that is connected anteriorly to the body, posteriorly to the occipital horn, and inferiorly to the temporal horn.

How To Measure

- The atrium is measured in the axial transventricular plane of the fetal head.
- It is measured at the level of the glomus of the choroid plexus. Alternatively, it can be measured at the level of the parieto-occipital sulcus, which becomes visible after 20 weeks of gestation.
- Calipers are placed on the medial and the lateral walls of the atrium.
- Measure perpendicular to the long axis of the ventricle.
- Inner to inner measurement.

Comment

- The atrial diameter (AD) is a reliable indicator of the ventricular system's state, independent of gestational age.
- The mean diameter is 7.6 mm ($\pm$ 0.6 mm) throughout gestation.
- The upper limit for normal atrial width is 10 mm.
- Fetal ventriculomegaly is defined as the atrial width of more than 10mm.

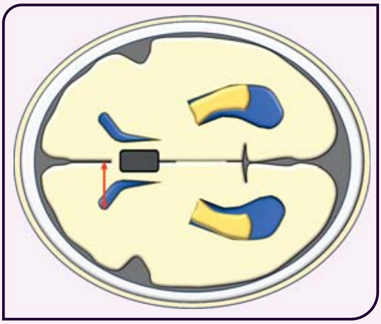
TABLE

DIAMETER OF THE ATRIUM OF THE LATERAL VENTRICLE AT SPECIFIC GESTATIONAL AGES

DIAMETER OF THE ATRIUM (mm)						
GA (weeks)	Sample size (n)	Centiles				
		3rd	5th	50th	95th	99th
15 + 0	18	4.71	4.99	6.94	8.88	9.16
16 + 0	19	4.49	4.77	6.78	8.78	9.07
17 + 0	18	4.28	4.58	6.64	8.70	9.00
18 + 0	19	4.10	4.40	6.52	8.64	8.94
19 + 0	19	3.92	4.23	6.41	8.58	8.89
20 + 0	22	3.76	4.08	6.31	8.54	8.86
21 + 0	16	3.61	3.94	6.22	8.51	8.84
22 + 0	18	3.46	3.80	6.14	8.49	8.82
23 + 0	21	3.33	3.67	6.07	8.47	8.81
24 + 0	18	3.20	3.55	6.00	8.46	8.81
25 + 0	20	3.07	3.43	5.94	8.46	8.82
26 + 0	19	2.95	3.32	5.89	8.46	8.83
27 + 0	19	2.84	3.22	5.84	8.46	8.84
28 + 0	19	2.73	3.11	5.79	8.48	8.86
29 + 0	22	2.62	3.01	5.75	8.49	8.88
30 + 0	21	2.52	2.92	5.71	8.51	8.91
31 + 0	20	2.42	2.83	5.68	8.53	8.94
32 + 0	17	2.32	2.74	5.65	8.55	8.97
33 + 0	22	2.23	2.65	5.62	8.58	9.00
34 + 0	22	2.14	2.57	5.59	8.61	9.04
35 + 0	19	2.05	2.49	5.56	8.64	9.08
36 + 0	14	1.96	2.41	5.54	8.67	9.12
Total measurements				422		

Reference: Napolitano R, Molloholli M, Donadono V, et al. International standards for fetal brain structures based on serial ultrasound measurements from Fetal Growth Longitudinal Study of INTERGROWTH-21st Project. Ultrasound Obstet Gynecol. 2020;56:359-370.

ANTERIOR HORN OF THE LATERAL VENTRICLE



Definition

- The anterior or frontal horn corresponds to the portion of the lateral ventricles anterior to the interventricular foramen of Monro.

How To Measure

- The anterior horns are measured in the axial transventricular plane of the fetal brain, which is slightly cranial to the plane in which BPD is taken (the transthalamic plane).
- In this section one should be able to recognize, anteriorly-to-posteriorly, the anterior horns, the CSP, and the atria of the lateral ventricles.
- For the nomogram provided, the anterior horn diameter was measured from the lateral wall of the anterior horn to the midline (known as the cerebrofrontal horn distance).

Comment

- The two anterior or frontal horns of the lateral ventricles are separated by cavum septi pellucidi (CSP) during most of the second and the third trimester, and by the septum pellucidum during the rest of the gestation.
- The relative size of the AH decreases with advancing gestational age.

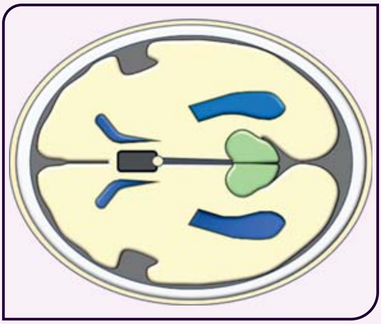
TABLE

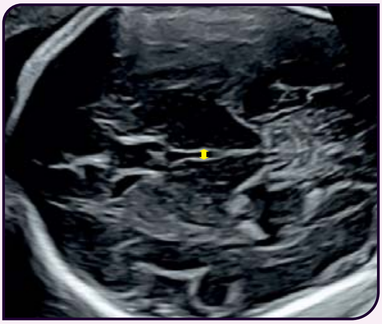
DIAMETER OF THE ANTERIOR HORN OF THE LATERAL VENTRICLE AT SPECIFIC GESTATIONAL AGES

DIAMETER OF THE ANTERIOR HORN (mm)						
		Centiles				
Gestational age (weeks)	3rd	10th	50th	90th	95th	99th
15+0	17	4.34	4.62	6.61	8.59	8.87
16+0	15	4.39	4.67	6.65	8.63	8.91
17+0	17	4.44	4.72	6.70	8.68	8.97
18+0	18	4.49	4.78	6.76	8.74	9.02
19+0	19	4.56	4.84	6.82	8.8	9.09
20+0	20	4.63	4.91	6.89	8.87	9.16
21+0	15	4.71	4.99	6.97	8.95	9.24
22+0	18	4.79	5.08	7.06	9.04	9.32
23+0	21	4.89	5.17	7.15	9.13	9.42
24+0	15	4.99	5.27	7.25	9.24	9.52
25+0	19	5.10	5.38	7.37	9.35	9.63
26+0	18	5.22	5.51	7.49	9.47	9.75
27+0	17	5.35	5.64	7.62	9.60	9.88
28+0	19	5.49	5.78	7.76	9.74	10.02
29+0	22	5.65	5.93	7.91	9.89	10.17
30+0	19	5.81	6.09	8.07	10.05	10.34
31+0	17	5.98	6.26	8.24	10.23	10.51
32+0	13	6.17	6.45	8.43	10.41	10.69
33+0	18	6.36	6.65	8.63	10.61	10.89
34+0	17	6.57	6.85	8.84	10.82	11.10
35+0	15	6.79	7.08	9.06	11.04	11.32
36+0	9	7.03	7.31	9.29	11.27	11.56
Total	378					

Reference: Napolitano R, Molloholli M, Donadono V, et al. International standards for fetal brain structures based on serial ultrasound measurements from Fetal Growth Longitudinal Study of INTERGROWTH-21st Project. Ultrasound Obstet Gynecol. 2020;56:359-370.

THIRD VENTRICLE





Definition

- The third ventricle is a narrow, midline cavity that connects to the lateral ventricles via the foramen of Monro and to the fourth ventricle through the cerebral aqueduct.
- It is seen as a linear slit-like structure, located between the two thalami.

How To Measure

- The third ventricle is identified between the two thalami in the axial transthalamic plane on transabdominal ultrasound.
- Maximum transverse diameter is measured.

Comment

- The third ventricle shows a single-line configuration early in the second trimester. However, later in pregnancy, the third ventricle walls can be discerned as parallel or divergent lines outlining a fluid-filled lumen.
- A third ventricle greater than 3.5 mm in width at any gestational age should be viewed with concern for abnormality.

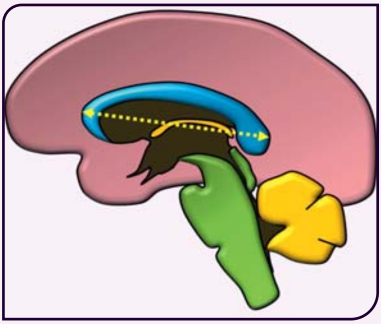
TABLE

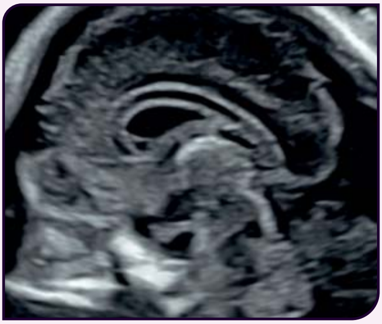
THIRD VENTRICLE DIAMETER ACCORDING TO GESTATIONAL AGES

THIRD VENTRICLE DIAMETER (mm)					
Gestational age (weeks)	Percentile				
	3rd	10th	50th	90th	97th
12	1.0	1.0	1.0	1.0	1.0
13	1.0	1.0	1.0	1.1	1.1
14	1.0	1.0	1.1	1.2	1.2
15	1.0	1.0	1.1	1.2	1.2
16	1.0	1.0	12	1.3	1.3
17	1.0	1.1	12	1.3	1.4
18	1.2	1.2	1.3	1.4	1.5
19	1.2	1.3	1.4	1.5	1.6
20	1.2	12	1.4	1.5	1.6
21	1.3	1.3	1.4	1.5	1.6
22	1.3	1.3	1.5	1.6	1.7
23	1.3	1.3	1.5	1.7	IJ
24	1.3	1.3	1.5	1.6	1.7
25	1.4	1.4	1.5	1.8	1.9
26	1.4	1.4	1.5	1.8	2.0
27	1.5	1.5	1.7	1.9	20
28	1.4	1.5	1.6	2.0	2.1
29	1.6	1.0	1.8	2.2	2.3
30	1.7	1.7	1.9	2.2	2.3
31	1.8	1.8	2.0	2.4	2.5
32	2.0	2.0	2.0	2.5	2.5
33	2.0	2.0	2.5	2.5	2.6
34	2.3	2.3	2.5	2.7	2.7
35	2.4	2 4	2.5	2.6	2.7
36	2.5	2.5	2.6	2.7	2.7
37	2.5	2.5	2.7	2.8	2.8
38	2.9	2.9	3.0	3.2	3.2
39	3.0	3.0	32	3.4	3.5
40	3.0	3.1	3.4	3.6	3.6

Reference: Sari A, Ahmetoglu A, Dinc H, Saglam A, Kurtoglu U, Kandemir S, Gümele HR. Fetal biometry: size and configuration of the third ventricle. Acta Radiol. 2005 Oct;46(6):631-5.

CORPUS CALLOSUM ANTEROPOSTERIOR LENGTH





Definition

- The corpus callosum (CC) is the largest commissure of the brain, composed of tightly packed axons connecting the cerebral hemispheres with each other.
- It is seen as a hypoechoic structure in the midsagittal plane of the brain, bound superiorly by the Callosal sulcus and inferiorly by the Cavum Septi Pellucidi and the Cavum Vergae.
- It consists of four parts-Rostrum, Genu, Body and Splenium.

How To Measure

- The CC is imaged in the mid-sagittal plane.
- Measure from the most anterior aspect of the genu to the most posterior aspect of the splenium along a straight line.

Comment

- The normal range of the measurements of the length of corpus callosum is wide. Hence, the nomograms provided by various authors may show variations.
- A dysgenetic corpus callosum may appear much shorter than the expected length for the gestational age. However, it is important to consider not only the length but also the morphology of the corpus callosum.

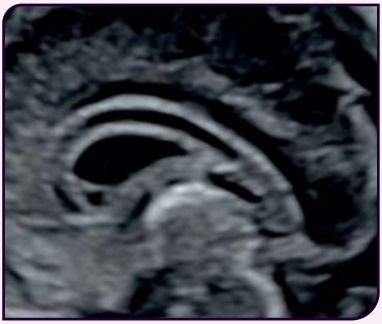
TABLE

CORPUS CALLOSUM ANTEROPOSTERIOR LENGTH AT SPECIFIC GESTATIONAL AGES

CORPUS CALLOSUM LENGTH (mm)				
Gestational age (weeks)	5th Centile	Mean	95th Centile	SD
19	17.45	18.78	20.10	1.33
20	19.59	21.02	22.46	1.43
21	21.66	23.20	24.74	1.54
22	23.65	25.30	26.94	1.65
23	25.56	27.31	29.07	1.76
24	27.38	29.24	31.10	1.86
25	29.10	31.07	33.04	1.97
26	30.73	32.81	34.89	2.08
27	32.26	34.45	36.63	2.18
28	33.68	35.97	38.26	2.29
29	34.98	37.38	39.78	2.40
30	36.17	38.68	41.18	2.51
31	37.23	39.85	42.46	2.61
32	38.17	40.89	43.61	2.72
33	39.97	41.80	44.62	2.83
34	39.63.	42.56	45.50	2.94
35	40.14	43.19	46.23	3.04
36	40.51	43.66	46.81	3.15
37	40.72	43.98	47.24	3.26

Reference: Cignini P, Padula F, Giorlandino M, Brutti P, Alfò M, Giannarelli D, Mastrandrea ML, D'Emidio L, Vacca L, Aloisi A, Giorlandino C. Reference charts for fetal corpus callosum length: a prospective cross-sectional study of 2950 fetuses. J Ultrasound Med. 2014 Jun;33(6):1065-78.

CORPUS CALLOSUM THICKNESS



How To Measure

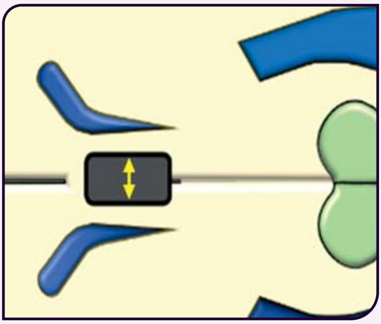
- The corpus callosum (CC) is imaged in the mid-sagittal plane.
- Measure the maximum thickness of the Genu, the Body or the Splenium.
- Exclude the bright lines of the callosal sulcus superiorly and the cavum inferiorly.

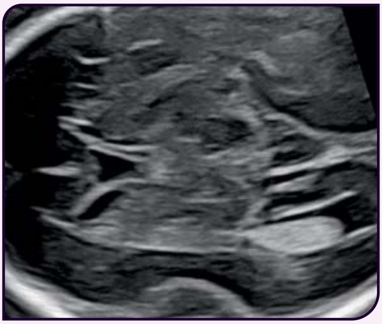
BIOMETRY OF THE CORPUS CALLOSUM ON TRANSVAGINAL SONOGRAPHY (mm ± 1 SD)

Gestational Age (weeks)	Length	Genu	Body	Splenium
18–19	16.9 ± 2.4	2.2 ± 0.5	1.3 ± 0.1	2.1 ± 0.1
20–21	20.6 ± 4.4	2.3 ± 0.6	1.6 ± 0.1	2.1 ± 0.1
22–23	23.3 ± 3.0	2.7 ± 0.6	1.7 ± 0.2	3.1 ± 0.2
24–25	29.8 ± 2.3	3.0 ± 0.6	1.9 ± 0.3	3.0 ± 0.3
26–27	33.7 ± 2.4	3.5 ± 0.6	2.0 ± 0.2	3.3 ± 0.6
28–29	35.8 ± 2.8	4.0 ± 0.7	2.0 ± 0.4	4.0 ± 0.8
30–31	36.8 ± 1.4	4.2 ± 0.5	2.1 ± 0.4	4.1 ± 0.7
32–33	39.1 ± 4.3	4.5 ± 1.2	2.5 ± 0.6	4.2 ± 0.8
34–35	40.6 ± 6.4	4.6 ± 0.5	2.5 ± 0.5	4.4 ± 0.8
36–37	41.9 ± 3.5	5.0 ± 0.4	2.5 ± 0.4	4.4 ± 1.3
38–39	43.0 ± 4.2	4.8 ± 0.7	2.6 ± 0.5	4.4 ± 0.6
40–42	44.0 ± 3.8	4.8 ± 0.4	2.6 ± 0.5	4.4 ± 0.7

Reference: Malinger G, Zakut H. The corpus callosum: normal fetal development as shown by transvaginal sonography, AJR Am J Roentgenol. 1993;161(5):1041–1043.

TRANSVERSE DIAMETER OF THE CAVUM SEPTI PELLUCIDI





Definition

- The Cavum Septi Pellucidi (CSP) is a fluid filled cavity situated between the membranes which form the septum pellucidum.
- The CSP is consistently visible in fetuses between 18 and 37 weeks of gestation.

How To Measure

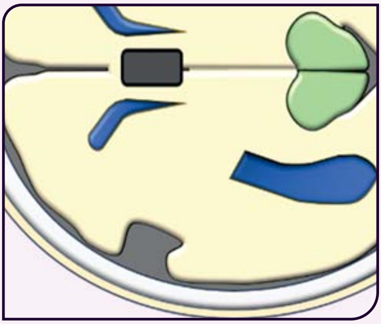
- The CSP is identified on an axial transventricular plane.
- Measure maximal width by placing the calipers on the inner borders of the CSP (inner-to-inner).

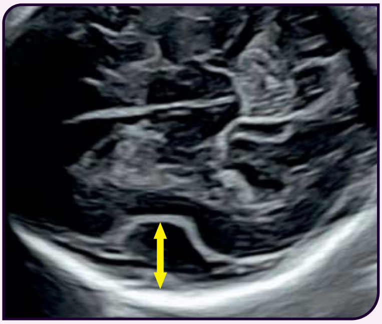
CAVUM SEPTI PELLUCIDI WIDTH (mm) AT SPECIFIC GESTATIONAL AGES

Gestational age (weeks)	- 2 SD	Mean	+ 2 SD	Gestational age (weeks)	- 2 SD	Mean	+ 2 SD
15	1.8	2.8	3.7	**29**	4.3	6.4	8.5
16	2.1	3.2	4.2	**30**	4.3	6.5	8.7
17	2.4	3.5	4.6	**31**	4.4	6.6	8.8
18	2.7	3.9	5.0	**32**	4.3	6.7	9.0
19	2.9	4.2	5.5	**33**	4.3	6.7	9.1
20	3.2	4.5	5.8	**34**	4.3	6.7	9.2
21	3.4	4.8	6.2	**35**	4.2	6.7	9.3
22	3.6	5.1	6.6	**36**	4.1	6.7	9.4
23	3.7	5.3	6.9	**37**	4.0	6.7	9.4
24	3.9	5.5	7.2	**38**	3.8	6.6	9.4
25	4.0	5.8	7.5	**39**	3.7	6.6	9.5
26	4.1	5.9	7.8	**40**	3.5	6.5	9.4
27	4.2	6.1	8.0	**41**	3.3	6.4	9.4
28	4.3	6.3	8.3				

Reference: Falco P, Gabrielli S, Visentin A, Perolo A, Pilu G, Bovicelli L. Transabdominal sonography of the cavum septum pellucidum in normal fetuses in the second and third trimesters of pregnancy. Ultrasound Obstet Gynecol. 2000 Nov;16 (6): 549-53.

DEPTH OF THE SYLVIAN FISSURE





Definition

- The Sylvian fissure (SF), also known as the lateral sulcus, is a deep groove on the lateral surface of each hemisphere that separates the frontal and parietal lobes from the temporal lobe.
- The Sylvian fissure forms due to the relative overgrowth of the fronto-parietal (anterior operculum) and the temporal lobes (posterior operculum) over the insula.

How To Measure

- Axial transthalamic plane is acquired.
- The SF is measured in the cerebral hemisphere far from the ultrasound probe.
- The SF is measured from the lateral edge of the roof of the fissure to the medial edge of the skull at its widest point, parallel to the biparietal diameter ('inner to inner').

Comment

- A shallow Sylvian fissure for the gestational age may indicate a malformation of cortical development, such as lissencephaly.
- In addition to assessing the depth of the Sylvian fissure, its morphology should also be evaluated in both the axial and coronal planes.

TABLE

SYLVIAN FISSURE DEPTH

SYLVIAN FISSURE DEPTH (mm)						
GA (weeks)	Sample size (n)	Percentile				
		3rd	5th	50th	95th	97th
15 + 0	18	0.4	0.57	1.77	2.98	3.15
16 + 0	15	0.91	1.13	2.65	4.17	4.38
17 + 0	18	1.46	1.72	3.49	5.27	5.52
18 + 0	18	2.03	2.31	4.31	6.3	6.59
19 + 0	17	2.60	2.91	5.09	7.27	7.58
20 + 0	20	3.18	3.51	5.85	8.18	8.51
21 + 0	15	3.75	4.10	6.57	9.04	9.40
22 + 0	18	4.32	4.69	7.27	9.86	10.23
23 + 0	20	4.87	5.26	7.95	10.64	11.02
24 + 0	17	5.42	5.82	8.60	11.38	11.78
25 + 0	20	5.96	6.37	9.23	12.09	12.50
26 + 0	18	6.49	6.91	9.84	12.77	13.19
27 + 0	16	7.01	7.44	10.43	13.42	13.85
28 + 0	19	7.52	7.95	11	14.05	14.48
29 + 0	22	8.01	8.45	11.55	14.65	15.09
30 + 0	20	8.49	8.94	12.09	15.23	15.68
31 + 0	20	8.97	9.42	12.61	15.79	16.25
32 + 0	17	9.43	9.89	13.11	16.33	16.79
33 + 0	22	9.88	10.34	13.60	16.86	17.32
34 + 0	22	10.32	10.79	14.07	17.36	17.83
35 + 0	18	10.75	11.22	14.54	17.85	18.33
36 + 0	14	11.17	11.64	14.99	18.33	18.80
Total measurements 404						

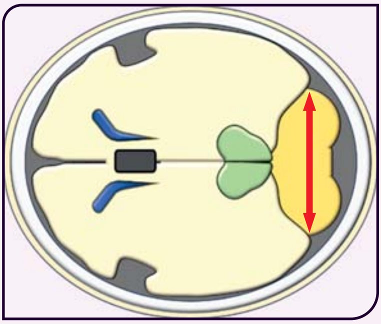
Reference: Napolitano R, Molloholli M, Donadono V, et al. International standards for fetal brain structures based on serial ultrasound measurements from Fetal Growth Longitudinal Study of INTERGROWTH-21st Project. Ultrasound Obstet Gynecol. 2020;56:359-370.

BIOMETRY OF THE BRAIN

SECOND AND THIRD TRIMESTER

INFRATENTORIAL COMPARTMENT

TRANSVERSE CEREBELLAR DIAMETER



Definition

- The transverse cerebellar diameter (TCD) represents the widest transverse dimension of the fetal cerebellum.

How To Measure

- An axial transcerebellar plane is obtained slightly lower than the transthalamic plane, with a slight posterior tilt.
- For best resolution and to avoid shadowing artifacts from the calvaria, the cerebellum should be insonated at an angle of 45° through the lambdoid suture or the mastoid fontanelle.
- The view should show the characteristic butterfly-like appearance cerebellar lobes and the vermis. Interhemispheric fissure and the cavum septi pellucidi should be visible in the anterior brain in midline.
- Measure the widest diameter of the cerebellum in an outer-to-outer fashion.

Comment

- During the second trimester, the cerebellum's size increases in a linear relationship with gestational age. Hence, its measurement in millimeters roughly corresponds to the number of weeks of gestation. In contrast, during the third trimester, cerebellum growth slows down, and its size no longer aligns as closely with gestational age.
- TCD is more effective in predicting gestational age in cases where the fetal head shape varies, such as in dolichocephaly or brachycephaly, and in fetuses with growth restriction.
- A TCD measurement below the fifth percentile can signal associated anomalies during routine ultrasound examinations in the second or third trimester. This finding is linked to a higher incidence of fetal malformations, chromosomal abnormalities, and genetic disorders.

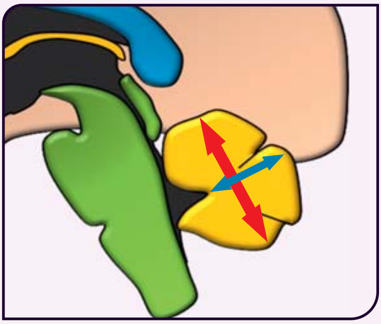
TABLE

TRANSCEREBELLAR DIAMETER AT SPECIFIC GESTATIONAL AGES

CENTILES OF TCD VALUES (cm)					
Gestational Age (weeks)	5th	10th	50th	90th	95th
15	1.42	1.45	1.58	1.71	1.74
16	1.46	1.50	1.65	1.79	1.86
17	1.52	1.56	1.73	1.89	1.96
18	1.59	1.64	1.82	1.99	2.05
19	1.68	1.73	1.92	2.11	2.17
20	1.77	1.83	2.04	2.24	2.30
21	1.88	1.94	2.16	2.38	2.45
22	1.99	2.05	2.30	2.59	2.60
23	2.12	2.18	2.44	2.68	2.76
24	2.25	2.32	2.50	2.85	2.93
25	2.39	2.46	2.74	3.02	3.10
26	2.53	2.60	2.91	3.19	3.28
27	2.67	2.76	3.07	3.38	3.47
28	2.82	2.91	3.24	3.56	3.66
29	2.98	3.07	3.42	3.75	3.86
30	3.19	3.22	3.59	3.95	4.06
31	3.28	3.38	3.77	4.15	4.26
32	3.44	3.54	3.95	4.34	4.47
33	3.59	3.70	4.13	4.54	4.67
34	3.78	3.85	4.31	4.74	4.88
35	3.88	4.00	4.48	4.95	5.09
36	4.01	4.14	4.65	5.14	5.30
37	4.14	4.28	4.82	5.34	5.50
38	4.27	4.41	4.99	5.54	5.71

Reference: Chavez MR, Ananth CV, Smulian JC, Lashley S, Kontopoulos EV, Vintzileos AM. Fetal transcerebellar diameter nomogram in singleton gestations with special emphasis in the third trimester: a comparison with previously published nomograms. Am J Obstet Gynecol. 2003 Oct;189(4):1021-5.

BIOMETRY OF THE CEREBELLAR VERMIS



Definition

- The vermis is the median portion of the cerebellum that connects the two hemispheres.
- It is seen as an echogenic structure in the midsagittal plane of the posterior fossa, limited anteriorly by the 4th ventricle and posteriorly by the cisterna magna.

How To Measure

- Obtain a midsagittal plane of the posterior fossa. A precise mid-sagittal plane should clearly show the corpus callosum anteriorly.
- The vermis craniocaudal diameter (CC) is the maximum distance between the most cranial portion of the Vermis (culmen) and the most caudal portion (uvula). This is generally parallel of the axis of the brainstem.
- The anteroposterior (AP) diameter is measured from the peak of the fourth ventricle (fastigium), to the most posterior part of the vermis.
- Circumference or perimeter is measured by tracing a line that follows the vermian outer margins.
- Surface area is calculated by drawing the same peripheral line.

Comment

- To assess the posterior fossa structures more accurately, it is best to use a posterior approach by directing the ultrasound beam through the posterior fontanelle.
- Abnormal vermian biometry and morphology is an important clue to many midbrain-hindbrain anomalies, including Dandy-Walker malformation and vermian hypoplasia.
- The rotation of the vermis can be assessed by measuring the brainstem-vermian angle.

TABLE

FETAL CEREBELLAR VERMIS CRANIOCAUDAL DIAMETER (HEIGHT) ACCORDING TO GESTATIONAL AGE

GA (weeks)	Number of fetuses	Mean (mm)	SD (mm)	95% Confidence Interval
20+0–20+6	636	11.27	0.58	10.69–11.85
21+0–21+6	4549	11.96	0.67	11.29–12.63
22+0–22+6	4160	12.71	0.76	11.95–13.47
23+0–23+6	692	13.50	0.85	12.65–14.35
24+0–24+6	89	14.32	0.94	13.38–15.26
25+0–25+6	66	15.16	1.03	14.13–16.19
26+0–26+6	56	16.01	1.12	14.89–17.13
27+0–27+6	52	16.85	1.21	15.64–18.06
28+0–28+6	36	17.67	1.30	16.37–18.97
29+0–29+6	47	18.47	1.39	17.08–19.86
30+0–30+6	51	19.22	1.48	17.74–20.70
31+0–31+6	77	19.91	1.57	18.34–21.48
32+0–32+6	53	20.54	1.66	18.88–22.20
33+0–33+6	26	21.09	1.75	19.34–22.84
34+0–34+6	6	21.54	1.84	19.70–23.38
35+0–35+6	9	21.90	1.93	19.97–23.82

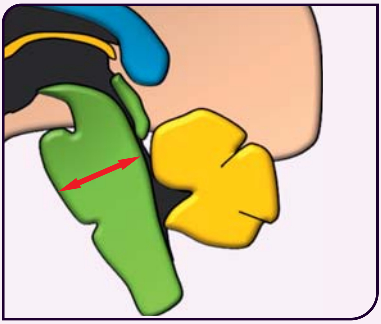
Reference : Cignini P, Giorlandino M, Brutti P, et al: Reference Charts for Fetal Cerebellar Vermis Height: A Prospective Cross-Sectional Study of 10605 Fetuses. PLoS One. 2016;11(1):e0147528.

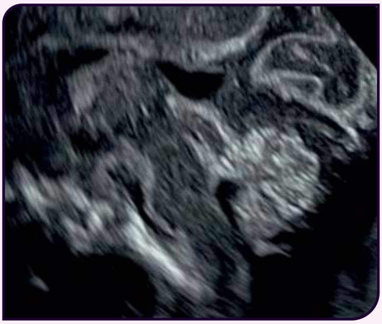
VERMIAN BIOMETRY

Gestational age (weeks	Sagittal AP (mm)	Sagittal CC (mm)	Circumference (mm)	Surface area (cm2)
21–22	10.6±1.4	11.1±1.1	43.8±3.3	0.9±0.2
23–24	12.9±1.1	12.3±1.4	47.5±5.5	1.2±0.2
25–26	13.5±2.1	13.6±0.9	50.9±4.4	1.4±0.2
27–28	16.3±2.7	16.0±1.6	58.9±6.8	2.0±0.5
29–30	17.5±2.2	17.7±2.1	64.7±6.5	2.3±0.4
31–32	19.0±1.9	19.2±1.1	70.7±6.9	2.8±0.4
33–34	19.2±1.9	21.2±2.3	72.7±8.3	3.0±0.8
35–36	21.4±1.5	19.8±1.0	77.6±5.1	3.4±0.3
37–38	22.1±3.8	23.0±4.6	80.7±9.9	3.9±1.4
39–40	25.7±2.3	25.0±2.6	86.7±7.0	4.9±0.7

Reference: Malinger G, Ginath S, Lerman-Sagie T, et al: The fetal cerebellar vermis: normal development as shown by transvaginal ultrasound. Prenat Diagn. 2001;21(8):687–692.

ANTEROPOSTERIOR DIAMETER OF THE PONS





Definition

- The pons is a major part of the brainstem between the midbrain above and the medulla oblongata below.

How To Measure

- A midsagittal plane of the fetal brain is taken.
- The midsagittal plane should clearly show the corpus callosum, the brainstem-vermis and the fourth ventricle.
- The anteroposterior diameter is taken at its widest part of the pons, perpendicular to its long axis.
- The anterior edge of pons can be delineated, when needed, by the course of the basilar artery over the clivus of the occipital and sphenoid bones. The posterior border is represented by the margin of the fourth ventricle.

Comment

- For a more accurate assessment of the posterior fossa structures, it is recommended to use a posterior approach by directing the ultrasound beam through the posterior fontanelle, ideally with a transvaginal scan.
- Pons may show abnormalities in some midbrain-hindbrain anomalies, e.g., pontocerebellar hypoplasia and Walker-Warburg syndrome etc.

TABLE

ANTEROPOSTERIOR DIAMETER OF THE FETAL PONS ACCORDING TO GESTATIONAL AGE

AP DIAMETER (mm)						
GA (weeks)	N	Percentile				
		5th	25th	50th	75th	95th
19–20	18	4.2	6.3	6.8	7.0	7.5
21–22	114	6.8	7.2	7.5	8.0	8.3
23–24	82	7.2	7.7	8.2	8.5	9.1
25–26	20	8.4	9.3	9.6	10.2	11.0
27–28	15	9.3	10.0	10.3	10.9	11.5
29–30	11	9.9	10.7	11.4	11.7	12.0
31–32	13	10.9	11.7	12.3	12.8	14.0
33–34	14	12	12.4	12.8	13.5	15.7

Reference: Achiron R, Kivilevitch Z, Lipitz S, Gamzu R, Almog B, Zalel Y. Development of the human fetal pons: in utero ultrasonographic study. Ultrasound in Obstetrics & Gynecology. 2004;24(5):506-510. doi:10.1002/uog.1731

TECTAL LENGTH

Definition

- The tectum (roof) is the region of the midbrain posterior to the aqueduct of Sylvius.
- It contains the nuclei of the superior and inferior colliculi. These are involved in preliminary processing of the visual (superior colliculi) or auditory stimuli (inferior colliculi) before they reach their corresponding primary processing centers.

How To Measure

- A midsagittal plane of the fetal brain is acquired.
- The tectal plate is located in the midbrain, where it overlays the aqueduct. Its superior margin lies beneath the splenium of the corpus callosum, while its inferior margin abuts the cerebellar vermis.
- The tectal length is measured as the distance between the superior and inferior edges of the tectal plate.

Comment

- For a more accurate assessment of the posterior fossa structures, it is recommended to use a posterior approach by directing the ultrasound beam through the posterior fontanelle, ideally with a transvaginal scan.
- Abnormalities of the tectum may be seen in midbrain-hindbrain anomalies.

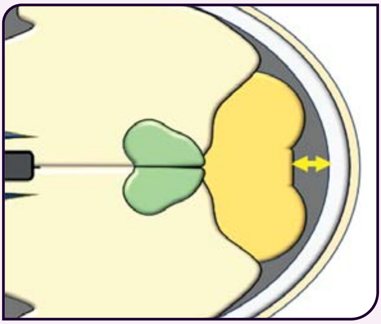
TABLE

TECTAL LENGTH ACCORDING TO GESTATIONAL AGES

Gestational Week	Number of Fetuses	Mean (cm)	Mean -2 SD (cm)	Mean +2 SD (cm)
15w+1d – 16w+0d	13	0.66	0.58	0.73
16w+1d – 18w+0d	10	0.71	0.52	0.89
18w+1d – 20w+0d	11	0.77	0.62	0.92
20w+1d – 22w+0d	10	0.84	0.70	0.97
22w+1d – 23w+0d	21	0.85	0.71	1.00
23w+1d – 24w+0d	70	0.89	0.75	1.03
24w+1d – 25w+0d	27	0.92	0.79	1.05
25w+1d – 27w+0d	17	0.96	0.81	1.11
27w+1d – 29w+0d	13	0.96	0.83	1.10
29w+1d – 31w+0d	20	1.00	0.77	1.23
31w+1d – 33w+0d	43	1.04	0.84	1.23
33w+1d – 35w+0d	21	1.07	0.91	1.22

Reference: Leibovitz Z, Shkolnik C, Haratz KK, et al: Assessment of fetal midbrain and hindbrain in mid-sagittal cranial plane by three-dimensional multiplanar sonography. Part 1: comparison of new and established nomograms. Ultrasound Obstet Gynecol. 2014;44(5):575–580.

CISTERNA MAGNA DIAMETER



Definition

- The cisterna magna is a cerebrospinal fluid filled space located in the posterior fossa dorsal to the medulla and caudal to the cerebellum.
- It is typically visualized in transcerebellar plane as an anechoic space located behind the cerebellum.

How To Measure

- An axial transcerebellar plane is obtained, preferably through a posterior insonation.
- The view should show the cerebellar lobes and the vermis, interhemispheric fissure, and the occipital horns of the lateral ventricles. Cavum septi pellucidi should be visible in the anterior brain in midline.
- Measure the anteroposterior diameter of the cisterna magna from the posterior surface of the vermis to the inner table of the calvarium in the midline.

Comments

- Cisterna magna frequently shows thin septa posterior to the vermis. These are considered as Blake's pouch remnant.
- Mega cisterna magna refers to an enlarged cisterna magna > 10 mm in transcerebellar plane, absence of hydrocephalus, and an intact cerebellar vermis.
- Differential diagnosis of mega cisterna magna includes Dandy-Walker malformation, Blake's pouch cyst, cerebellar hypoplasia, etc.
- In the absence of other findings to suggest a posterior fossa lesion, a prominent cisterna magna is unlikely to be clinically significant.

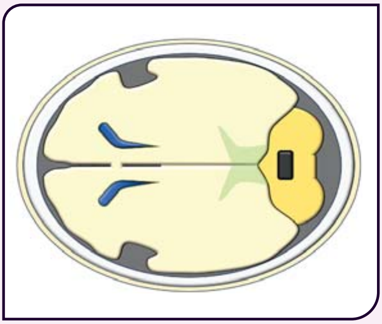
TABLE

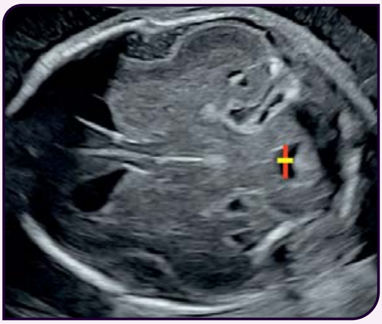
CISTERNA MAGNA DIAMETER AT SPECIFIC GESTATIONAL AGES

DIAMETER OF CISTERNA MAGNA (mm)						
		Percentile				
GA (weeks)	Sample size (n)	3rd	5th	50th	95th	97th
15+0	19	1.71	1.82	2.82	4.36	4.64
16+0	17	1.96	2.08	3.2	4.92	5.24
17+0	17	2.19	2.33	3.56	5.44	5.79
18+0	18	2.41	2.56	3.89	5.92	6.29
19+0	19	2.61	2.77	4.20	6.36	6.75
20+0	21	2.80	2.97	4.48	6.76	7.17
21+0	15	2.97	3.15	4.73	7.12	7.55
22+0	18	3.12	3.31	4.97	7.45	7.90
23+0	21	3.26	3.46	5.18	7.75	8.21
24+0	16	3.39	3.60	5.37	8.02	8.50
25+0	17	3.51	3.72	5.55	8.27	8.76
26+0	19	3.62	3.83	5.71	8.50	8.99
27+0	15	3.72	3.94	5.85	8.70	9.21
28+0	16	3.81	4.03	5.99	8.89	9.41
29+0	20	3.90	4.12	6.11	9.06	9.59
30+0	16	3.97	4.20	6.22	9.22	9.75
31+0	13	4.04	4.27	6.33	9.36	9.90
32+0	14	4.11	4.34	6.42	9.49	10.04
33+0	12	4.17	4.40	6.51	9.62	10.17
34+0	13	4.22	4.46	6.59	9.73	10.28
35+0	11	4.27	4.51	6.66	9.83	10.39
36+0	5	4.32	4.56	6.73	9.92	10.49
Total measurements	352					

Reference: Napolitano R, Molloholli M, Donadono V, et al. International standards for fetal brain structures based on serial ultrasound measurements from Fetal Growth Longitudinal Study of INTERGROWTH-21st Project. Ultrasound Obstet Gynecol. 2020; 56:359-370.

FOURTH VENTRICLE





Definition

- The fourth ventricle is the most inferiorly located ventricle, located in the midline of the posterior fossa.
- It is surrounded anteriorly by the pons and medulla and posteriorly by the cerebellum. Superiorly, it connects to the third ventricle through aqueduct of Sylvius, and inferiorly by the spinal canal and spinal cord.

How To Measure

- The fourth ventricle is identified in the axial plane of the brain acquired slightly caudal to the level of the transcerebellar plane. Its anteroposterior (AP) diameter and width (transverse diameter) are measured.[1]
- The anteroposterior diameter may also be measured in the mid sagittal plane from the fastigial peak to the anterior wall of the fourth ventricle.[2]

AXIAL PLANE ANTEROPOSTERIOR (AP) DIAMETER AND WIDTH OF THE FOURTH VENTRICLE ACCORDING TO GESTATIONAL AGES[1]

Gestational age (wks)	n	AP diameter (mm)					Width (mm)				
		10th	50th	90th	Mean	SD	10th	50th	90th	Mean	SD
13–13.9	15	4.7	5.8	7.1	5.9	0.8	2.1	2.5	3	2.5	0.3
14	82	5.0	5.9	7.2	6.0	0.8	2.0	2.4	3.1	2.5	0.3
15	68	5.0	5.9	7.5	6.0	0.8	2.0	2.5	3.1	2.6	0.4
16	21	5.2	5.8	7.5	5.9	0.8	2.0	2.6	3.2	2.7	0.4
17–18	12	4.9	6.0	8.4	6.2	1.2	2.2	2.8	3.4	2.8	0.4
19–21	11	4.1	6.0	7.5	5.7	1.2	2.2	3.0	5.6	3.2	1.1
22–24	11	6.0	7.1	8.4	7.1	0.8	3.1	4.4	6.0	4.6	1.1
25–27	24	5.4	7.0	8.9	7.2	1.1	4.0	5.0	7.0	5.3	1.2
28–30	23	6.0	8.0	11.8	8.3	2.0	4.2	6.0	8.2	6.1	1.3
31–33	15	6.4	8.0	10.4	8.3	1.5	4.4	6.0	8.0	6.1	1.3
34–40	17	7.0	9.0	12.2	9.2	1.9	6.0	7.0	9.3	7.3	1.3

TABLE

MID SAGITTAL PLANE ANTEROPOSTERIOR DIAMETER OF THE FOURTH VENTRICLE ACCORDING TO GESTATIONAL AGE[2]

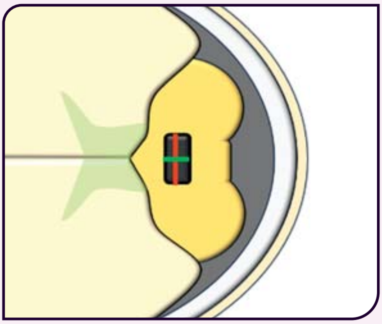
Gestational Week	Number of Fetuses	Mean (cm)	Mean -2 SD (cm)	Mean + 2 SD (cm)
15w+1d – 16w+0d	13	0.19	0.14	0.25
16w+1d – 18w+0d	10	0.21	0.13	0.28
18w+1d – 20w+0d	11	0.24	0.08	0.40
20w+1d – 22w+0d	9	0.21	0.10	0.31
22w+1d – 23w+0d	14	0.27	0.16	0.39
23w+1d – 24w+0d	56	0.30	0.15	0.44
24w+1d – 25w+0d	19	0.34	0.18	0.49
25w+1d – 27w+0d	11	0.32	0.20	0.44
27w+1d – 29w+0d	12	0.34	0.18	0.51
29w+1d – 31w+0d	16	0.42	0.26	0.59
31w+1d – 33w+0d	33	0.47	0.27	0.67

References:

1.Goldstein I, Makhoul IR, Tamir A, Rajamim BS, Nisman D. Ultrasonographic Nomograms of the Fetal Fourth Ventricle. Journal of Ultrasound in Medicine. 2002;21(8):849-856. doi:10.7863/jum.2002.21.8.849

2. Leibovitz Z, Shkolnik C, Haratz KK, et al: Assessment of fetal midbrain and hindbrain in mid-sagittal cranial plane by three-dimensional multiplanar sonography. Part 1: comparison of new and established nomograms. Ultrasound Obstet Gynecol. 2014;44(5):575–580.

FOURTH VENTRICLE INDEX



Definition

- Fourth ventricle index (4VI) is the ratio of the lateral diameter of the fourth ventricle and the anteroposterior diameter.

How To Measure

- The fourth ventricle is identified in the axial plane of the brain acquired slightly caudal to the level of the transcerebellar plane.
- For best resolution and to avoid shadowing artifacts from the calvaria, the cerebellum should be insonated at an angle of 45° through the lambdoid suture or the mastoid fontanelle.
- The anteroposterior (AP) diameter and width (laterolateral diameter) are measured (inner to inner).
- The 4VI is calculated using the following simple equation:
  4VI = Laterolateral diameter / AP diameter

Comments

- The 4th ventricular index (4VI) serves as a sonographic indicator for severe fetal vermian dysgenesis or agenesis when an open fourth ventricle is not present. This finding can be associated with midbrain-hindbrain anomalies, including Joubert syndrome, Rhomboencephalosynapsis, ponto-cerebellar hypoplasia, and Cobblestone malformation.
- The 4VI in the normal fetuses is always >1.
- In affected fetuses, it is always below mean-2 SD and <1.
- 4VI<1 indicates a need for dedicated fetal neuroimaging for diagnosis and prenatal counseling.

TABLE

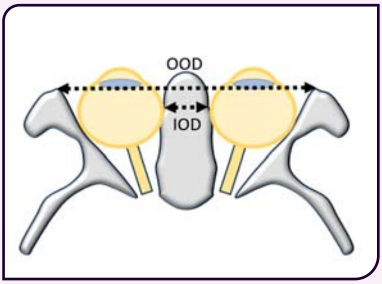
REFERENCE RANGES (MEAN ± 2SD) FOR FOURTH VENTRICULAR ANTEROPOSTERIOR (APD), LATEROLATERAL (LLD) DIAMETERS AND INDEX (4VI) THROUGHOUT GESTATION

		APD (mm)			LLD (mm)			4VI		
Number of Fetuses	N	Mean	Mean –2SD	Mean +2SD	Mean	Mean –2SD	Mean +2SD	Mean	Mean –2SD	Mean +2SD
14	16	2.1	1.2	3	4.4	3.02	5.78	2.1	1.4	2.8
15	16	2.1	1.16	3.04	4.7	3.8	5.6	2.4	1.36	3.44
16	15	2.3	1.34	3.26	5	3.6	6.4	2.1	1.52	2.68
17	17	2	1.42	2.58	4.7	4.1	5.3	2.1	1.64	2.56
18	15	2.2	1.82	2.58	5	4.2	5.8	2.38	2.16	2.6
19	17	2.4	1.92	2.88	4.7	3.82	5.58	1.99	1.47	2.51
20	15	2.2	1.64	2.76	4.4	3.3	5.5	1.99	1.45	2.53
21	17	2.7	1.86	3.54	4.7	3.34	6.06	1.78	1.02	2.54
22	28	2.7	1.8	3.6	4.8	3.36	6.24	1.77	1.07	2.47
23	17	2.6	1.9	3.3	4.4	3.2	5.6	1.75	1.19	2.31
24	15	2.8	2.1	3.5	5.5	4.32	6.68	2.01	1.43	2.59
25	15	2.6	1.82	3.38	4.8	3.8	5.8	1.99	1.19	2.79
26	15	2.6	1.7	3.5	5.5	3.9	7.1	2.15	1.05	3.25
27	15	2.9	1.88	3.92	5.7	3.9	7.5	1.99	0.99	2.99
28	15	2.7	2.04	3.36	6	5.4	6.6	2.23	1.67	2.79
29	15	3.2	1.98	4.42	6.2	5.02	7.38	1.94	1.34	2.54
30	15	3.2	1.78	4.62	6.4	4.8	8	2.08	1.2	2.96
31	15	3.4	1.42	5.38	6.3	4.5	8.1	1.93	1.01	2.85
32	29	3.6	2.04	4.96	6.7	5.02	8.38	1.91	1.19	2.63
33	17	4	2.04	5.96	7.1	5.1	9.1	1.85	1.13	2.57
34	15	3.3	1.52	5.08	7.2	5.7	8.7	2.26	1.42	3.1
35	15	3.7	1.94	5.46	7.5	5.58	9.42	2.15	1.07	3.23
36	15	3.9	2.66	5.14	7.7	6.38	9.02	2.04	0.92	3.16

Reference: Haratz KK, Shulevitz SL, Leibovitz Z, et al. Fourth ventricle index: sonographic marker for severe fetal vermian dysgenesis/agenesis. Ultrasound in Obstetrics & Gynecology. 2019;53(3):390-395. doi:10.1002/uog.19034

THE ORBITS AND THE OPTIC CHIASMA

THE ORBITS



Definition

- Outer orbital diameter (OOD) / biorbital diameter (BOD) - the distance between the lateral borders of the two orbits.
- Inner orbital/ interorbital diameter (IOD) - the distance between the medial borders of the two orbits.

How To Measure

- Measured in an axial plane slightly caudal to the transthalamic plane.
- The axial section should be symmetrical, with both eyeballs visible and of equal diameter, and should show the largest possible diameter of the eyes.

Comment

- The study of the orbital diameters should help in the diagnosis of hypotelorism, hypertelorism, and microphthalmia.
- In cases of hypotelorism, both the IOD and the OOD fall below 2 SD of the mean.
- In cases of hypertelorism, the IOD falls above the 95th percentile, whereas the OOD measurement falls within normal limits but near the 95th percentile.
- Microphthalmia is suspected when the orbital diameter falls below the 5th percentile for gestational age. In such cases, a careful examination of the intraorbital anatomy is warranted.

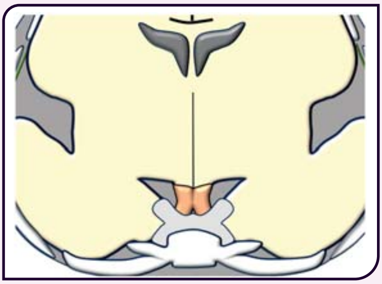
TABLE

INNER AND OUTER ORBITAL DIAMETERS IN THE FETUS VERSUS GESTATIONAL AGE

Gestational Age (weeks	Inner Orbital Diameter (mm)			Outer Orbital Diameter (mm)		
	5th Percentile	50th Percentile	95th Percentile	5th Percentile	50th Percentile	95th Percentile
13	4	7	10	12	16	20
14	5	8	11	14	18	22
15	5	8	11	17	21	25
16	6	9	12	19	23	27
17	7	10	13	21	25	29
18	8	11	14	24	27	31
19	8	11	14	26	30	34
20	9	12	15	28	32	36
21	10	13	16	30	34	38
22	10	13	16	32	36	40
23	11	14	17	33	37	41
24	12	14	17	35	39	43
25	12	15	18	37	41	45
26	13	16	19	39	43	47
27	13	16	19	40	44	48
28	14	17	20	42	46	50
29	14	17	20	43	47	51
30	15	18	21	45	49	52
31	15	18	21	46	50	54
32	16	19	22	47	51	55
33	17	20	23	48	52	56
34	17	20	23	49	53	57
35	18	21	24	50	54	58

Reference: Trout T, Budorick NE, Pretorius DH, et al. Significance of orbital measurements in the fetus. J Ultrasound Med. 1994;Dec 1;13(12):937–943.

OPTIC CHIASMA DIAMETER



Definition

- The optic chiasma (OC) is an X-shaped structure, which represents a commissure formed by converging optic nerves anteriorly and diverging optic tracts posteriorly.
- It is located in the suprasellar cistern, just above the pituitary gland and below the hypothalamus.

How To Measure

- Obtain a coronal frontal view of the fetal brain, focusing on the suprasellar cistern.
- Identify the OC in the suprasellar cistern as a horizontal, dumbbell-shaped structure of moderate echogenicity situated in the midline.
- Measure the diameter of the optic chiasm from one side to the other, typically from the inner borders of the structure. Ensure that the measurement is taken perpendicularly to the long axis of the chiasm for accuracy.

Comment

- Measurement of the OC is helpful in prenatal evaluation of septo-optic dysplasia (SOD), a condition with heterogeneous phenotype. It is defined by the variable association of hypoplasia of the visual connecting pathways, agenesis of the septum pellucidum and/or pituitary endocrine impairment.
- A hypoplastic OC associated with absence of the SP can be indicative of SOD.
- However, a normal-sized OC does not rule out SOD.

TABLE

REFERENCE RANGE FOR FETAL OPTIC CHIASMA (OC) WIDTH BETWEEN 21 AND 29 WEEKS OF GESTATION

GA (weeks)	n	3rd centile	5th centile	50th centile	95th centile	97th centile
21	4	5.6	5.6	6.0	6.3	6.3
22	15	5.6	5.6	6.0	7.5	7.5
23	27	5.4	5.48	6.4	7.74	7.92
24	23	5.7	5.74	6.5	7.96	8.02
25	25	5.5	5.56	6.8	9.0	10.0
26	7	5.7	5.7	7.0	8.1	8.1
27	3	6.8	6.8	7.0	8.1	8.1
28	2	7.1	7.1	7.85	8.6	8.6
29	3	6.9	6.9	8.2	8.7	8.7

Reference: Viñals F, Ruiz P, Correa F, Pereira PG. Two – dimensional visualization and measurement of the fetal optic chiasm: improving counseling for antenatal diagnosis of agenesis of the septum pellucidum. Ultrasound in Obstetrics & Gynecology. 2016;48(6):733-738. doi:10.1002/uog.15862

FETAL CNS
PUBLISHED PROTOCOLS

Ultrasound Obstet Gynecol 2021; 57: 204–214
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.23149

State-of-the-Art Review

First-trimester fetal neurosonography: technique and diagnostic potential

N. VOLPE, A. DALL'ASTA, E. DI PASQUO, T. FRUSCA and T. GHI*

Department of Medicine and Surgery, Unit of Surgical Sciences, Obstetrics and Gynecology, University of Parma, Parma, Italy
**Correspondence. (e-mail: tullioghi@yahoo.com)*

ABSTRACT

Most brain abnormalities are present in the first trimester, but only a few are detected so early in gestation. According to current recommendations for first-trimester ultrasound, the fetal head structures that should be visualized are limited to the cranial bones, the midline falx and the choroid-plexus-filled ventricles. Using this basic approach, almost all cases of acrania, alobar holoprosencephaly and cephalocele are detected. However, the majority of other fetal brain abnormalities remain undiagnosed until the midtrimester. Such anomalies would be potentially detectable if the sonographic study were to be extended to include additional anatomic details not currently included in existing guidelines. The aim of this review article is to describe how best to assess the normal fetal brain by first-trimester expert multiplanar neurosonography and to demonstrate the early sonographic findings that characterize some major fetal brain abnormalities. © 2020 International Society of Ultrasound in Obstetrics and Gynecology.

INTRODUCTION

Fetal brain abnormalities are among the most common congenital malformations, with a reported prevalence in Europe of about 1 per 1000 births[1]. According to the area of the brain involved and the type of abnormality, the prognosis is mostly poor, with a substantial impact on both neurodevelopmental and cognitive outcome. The sensitivity of prenatal ultrasound for detection of central nervous system (CNS) congenital malformations ranges between 68% and 92%[2,3], but a comprehensive evaluation and diagnosis of the defect is usually difficult on standard examination. While fetal CNS defects are usually suspected at the screening ultrasound evaluation, an expert multiplanar examination is required for an accurate diagnosis and classification of each brain anomaly. The multiplanar fetal neurosonogram is usually performed at around 20 weeks' gestation or later, and its methodology has been described by the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG)[4].

Most brain abnormalities are in fact present in the first trimester, but only a few are detected so early in gestation[5–14]. According to the current ISUOG recommendations for the first-trimester scan[15], the fetal head structures that should be visualized are limited to the cranial bones, the midline falx and the choroid-plexus-filled ventricles. Using this basic approach, almost all cases of acrania, alobar holoprosencephaly and cephalocele are detected[6–8,10,13], while the majority of other brain abnormalities remain undiagnosed until the midtrimester. The low detection rates of brain abnormalities in the first trimester could be related to the small size of the fetal brain structures as well as to the fact that some develop only later in pregnancy. Moreover, in the first trimester, some brain abnormalities do not affect the sonographic appearance of the basic intracranial structures whose examination is suggested at this stage. Most of these anomalies are potentially detectable, but only if the sonographic study is extended to include anatomic details which are not currently specified in first-trimester guidelines. Indeed, only a detailed knowledge of the normal sonographic appearance of the fetal brain in the first trimester allows recognition of the early anatomic modifications which herald the typical appearance of major cerebral abnormalities in the second trimester, when their sonographic findings are more widely recognized. For some brain malformations, such as severe ventriculomegaly, callosal agenesis, cranial posterior fossa (CPF) anomalies and Chiari-II anomaly, the sonographic appearance is considerably different at 12 weeks compared with that in the second trimester and they are suspected in the first trimester only if particular ultrasonographic landmarks are assessed by an expert eye.

In recent years, high-resolution ultrasound machines have provided the opportunity to evaluate the subtle details of fetal anatomy earlier in gestation and to improve our understanding of the normal and abnormal sonoembryological development of the fetal brain. Studies on the development of the fetal brain during the first weeks of pregnancy have characterized the developing brain structures using H-thymidine labeling[16] of anatomic specimens. Thanks to these studies, good correlation between high-resolution sonographic images and anatomic findings may be achieved.

The aims of this review article are two-fold: to describe how best to assess the normal fetal brain by first-trimester expert multiplanar neurosonography and to demonstrate the early sonographic findings that characterize some major fetal brain abnormalities.

NORMAL FIRST-TRIMESTER FETAL BRAIN ANATOMY

Axial views

Approaching the 11 + 0 to 13 + 6-week fetal brain using axial views, it is possible to evaluate its sonographic appearance in two different anatomical planes: a plane just above the third ventricle and thalami (Figure 1: suprathalamic section) and a plane at the level of the thalami (Figure 2: transthalamic section). These two planes are obtained when the ultrasound beam is oriented perpendicular to the midline echo.

The suprathalamic view represents the most common scanning plane obtained in the first trimester, and allows evaluation of the interhemispheric fissure (midline echo), the lateral ventricles, containing their choroid plexuses, the rudimentary cortex and the surrounding calvarium (Figure 1). At this early stage, the calvarium shape, integrity and calcification can be assessed; the absence of intact cranial bones surrounding the brain can be a sign of acrania or other neural tube defects[17,18]. The midline echo should be seen as a straight, uninterrupted hyperechoic line, dividing the brain into two equal symmetric parts. Any interruption of the midline echo should be noted, as this could be suggestive of alobar holoprosencephaly. On both sides of the cerebral midline are seen the two lateral ventricles, each occupied almost entirely by its choroid plexus. The two choroid plexuses are expected to be similar in size and symmetric in terms of shape and position, giving an overall appearance that resembles a butterfly[19]. The rudimentary surrounding cortex seems not to show any fissure or gyri at this stage, with the exception of the mild lateral recess, which represents the future Sylvian fissure.

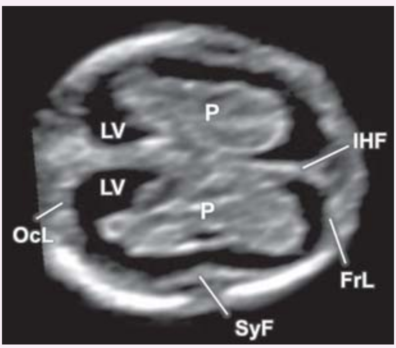


Figure 1 Axial view (suprathalamic section) on two-dimensional ultrasound imaging in normal 11–13-week fetus. FrL, frontal lobe cortex; IHF, interhemispheric fissure; LV, lateral ventricle; OcL, occipital lobe cortex; P, choroid plexus; SyF, future Sylvian fissure.

Sweeping the transducer more caudally, the transthalamic view (Figure 2) is obtained as a slightly oblique head section, with the third ventricle, then the thalami and finally the aqueduct of Sylvius being visualized (Figure 2). In this view, only the anterior third of the midline echo is visible, being interrupted posteriorly by the third ventricle. The latter structure appears as a thin, anechoic space, between the two thalami. On prenatal ultrasound, the thalami appear as two separate, symmetrical, anechoic ovoid structures and, posterior to them, on the midline, it is possible to visualize the aqueduct of Sylvius as an anechoic rectangle-shaped cavity, lined by the anechoic tectum on either side.

Sagittal views

Since the initial publications, more than 25 years ago[20,21], on the clinical usefulness of nuchal translucency (NT) measurement on first-trimester screening for fetal chromosomal abnormalities, the acquisition of the midsagittal

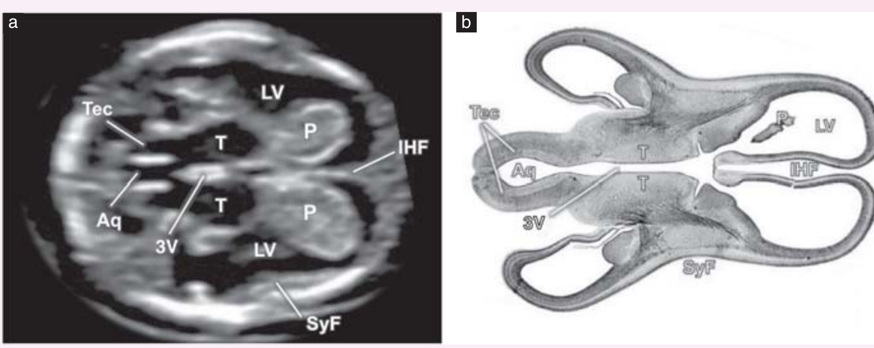


Figure 2 Axial view (transthalamic section) on two-dimensional ultrasound imaging in normal 11–13-week fetus (a) and corresponding anatomic specimen (b). 3V, third ventricle; Aq, aqueduct of Sylvius; IHF, interhemispheric fissure; LV, lateral ventricle; P, choroid plexus; SyF, future Sylvian fissure; T, thalamus; Tec, tectum. Anatomic specimen reproduced from Bayer and Altman[16] with permission.

view of the fetal head in the first trimester has become widely used. This is the only scanning plane in which the NT thickness can be measured properly, following strict methodological criteria that ensure high accuracy, reproducibility and repeatability of the measurement. In order to obtain the midsagittal view of the fetal head at 11–13 weeks, the ultrasound beam should be aligned with the midsagittal suture from the direction of the anterior fontanel[15,22]. In this scanning plane, in addition to NT measurement, a thorough sonographic assessment of the midline cerebral structures can be performed. The diencephalon is visible as a hypoechoic, round structure. Caudal to this is the brainstem (BS), which includes the mesencephalon, the pons and the medulla (Figure 3). The BS has a typical 'S' shape due to the mesencephalic and pontine flexures. Behind the BS, within the CPF, it is possible to visualize the fourth ventricle (4V, also referred to as the 'intracranial translucency') and the

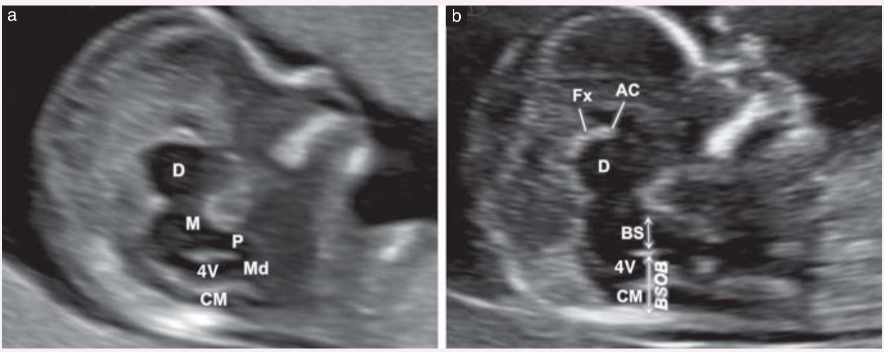


Figure 3 Midsagittal view (frontal approach) of normal fetal brain on two-dimensional ultrasound imaging at 11–13 weeks, showing: (a) detailed anatomy of cranial posterior fossa and (b) measurements of posterior fossa structures and detailed anatomy of visible midline structures. 4V, fourth ventricle; AC, anterior commissure; BS, brainstem; BSOB, brainstem-to-occipital bone distance; CM, cisterna magna; D, diencephalon; Fx, fornix; M, mesencephalon; Md, medulla; P, pons.

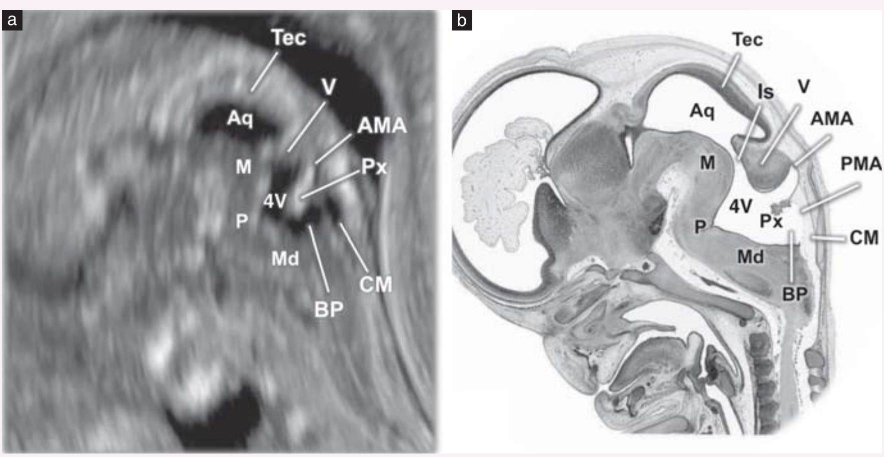


Figure 4 Midsagittal view (posterior approach) of normal fetal brain, showing: (a) detailed anatomy of cranial posterior fossa and aqueduct of Sylvius (Aq) on two-dimensional ultrasound imaging at 11–13 weeks and (b) corresponding anatomic specimen. 4V, fourth ventricle; AMA, anterior membranous area; BP, Blake's pouch; CM, cisterna magna; Is, isthmus; M, mesencephalon; Md, medulla; P, pons; PMA, posterior membranous area; Px, plexus of fourth ventricle; Tec, tectum; V, cerebellar vermis. Anatomic specimen reproduced from Bayer and Altman[16] with permission.

cisterna magna (CM), these three structures (BS, 4V and CM) forming three parallel anechoic spaces between the sphenoid bone and the occipital bone[23]. Under normal circumstances, the ratio between the BS thickness and its distance to the occipital bone is 0.5–1.0[24,25]. Above the diencephalon, it is possible to distinguish the fornix, as a thin, hyperechoic line, whose cranial extremity is slightly thickened and forms the anterior commissure (Figure 3).

When approaching the fetal head in the midsagittal plane posteriorly, through the posterior fontanel, a comprehensive view of the posterior cerebral structures can be obtained. In this view, the subtle anatomic details of the developing BS and CPF can be demonstrated[16,26–28]. The aqueduct of Sylvius and the 4V can be visualized as anechoic spaces behind the BS, separated by the isthmus at the level of the mesencephalic flexure (Figure 4). At the end of the first trimester, the aqueduct is larger than it is in the second trimester, with a size similar to that of the 4V and an elongated shape, and is roofed by the tectum. The 4V sits behind the BS, mainly within its pontine flexure. The roof of the 4V is a medullary velum divided into two parts by the choroid plexus of the ventricle, which protrudes into the middle. Above the plexus, the velum is defined as the anterior membranous area, which is in continuity with the cerebellar vermis at its upper extremity. Below the choroid plexus, the velum is defined as the posterior membranous area, protruding into the CM as a finger-shaped structure, Blake's pouch. Sonographic demonstration of some of these structures, along with their development and measurement, has been reported recently[28,29].

Coronal views

Aligning the ultrasound beam perpendicularly to the sagittal suture, a parallel sweep of the probe, from the forehead to the occiput, obtains, in sequence, the coronal planes of the fetal brain: the frontal, transcaudate, transthalamic and occipital planes (Figure 5).

The frontal view, passing through the frontal horns of the developing lateral ventricles, displays the anterior part of the corresponding choroid plexuses on either side of the interhemispheric fissure (Figure 6). Just below the

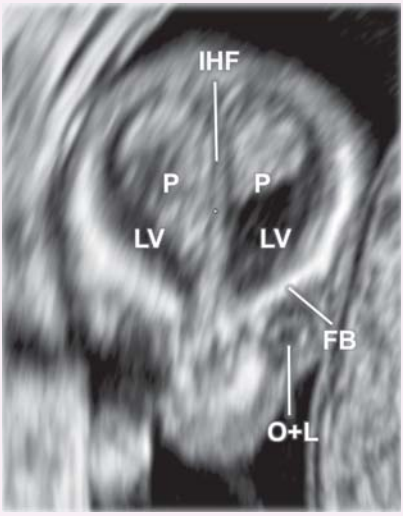


Figure 6 Frontal coronal view of normal fetal brain on two-dimensional ultrasound imaging at 11–13 weeks. FB, frontal bone; IHF, interhemispheric fissure; LV, lateral ventricle; O+L, eye orbit and lens; P, choroid plexus.

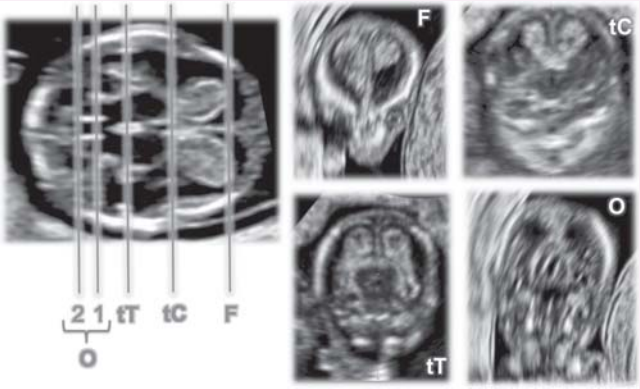


Figure 5 Coronal views of normal fetal brain on two-dimensional ultrasound imaging at 11–13 weeks: frontal (F), transcaudate (tC), transthalamic (tT) and occipital (O) planes.

brain, in this plane, it is possible to visualize the fetal orbits with the lenses.

In the transcaudate view, the lateral ventricles with their choroid plexuses on either side of the interhemispheric fissure, the ganglionic eminences at the bases of the lateral ventricles and the basal ganglia (including the caudate) below them can be seen. Between the basal ganglia it is possible to visualize the third ventricle (Figure 7).

In the transthalamic view, the thalami are seen, appearing as round symmetric structures with low echogenicity. The two lateral ventricles are also visible in this plane. Between the thalami, it is possible to visualize the caudal portion of the third ventricle (Figure 8).

Finally, in the occipital view, the posterior horns of the lateral ventricles are depicted, together with the aqueduct just below them, on the midline, and the two rudimentary cerebellar hemispheres on either side of the midline. The upper portion of the aqueduct is surrounded by the tectum, and its lower portion by the isthmus. It is possible to distinguish two occipital coronal planes, a

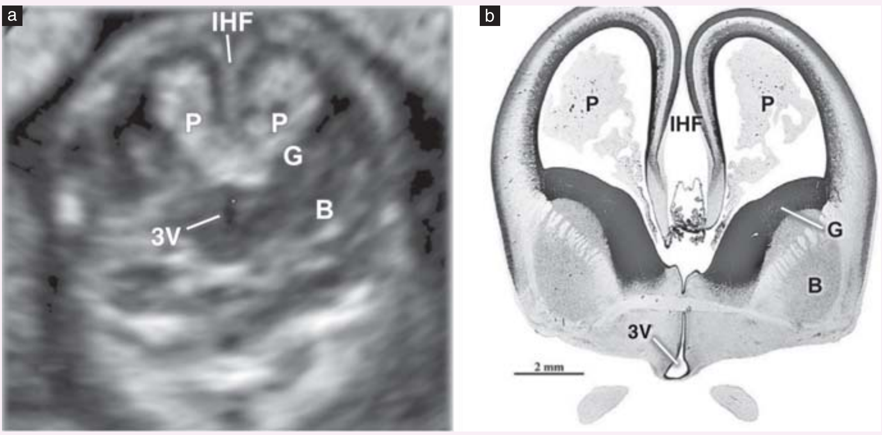


Figure 7 Transcaudate coronal view of normal fetal brain, showing: (a) detailed anatomy on two-dimensional ultrasound imaging at 11–13 weeks and (b) corresponding anatomic specimen. 3V, third ventricle; B, basal ganglion; G, ganglionic eminence; IHF, interhemispheric fissure; P, choroid plexus of lateral ventricle. Anatomic specimen reproduced from Bayer and Altman[16] with permission.

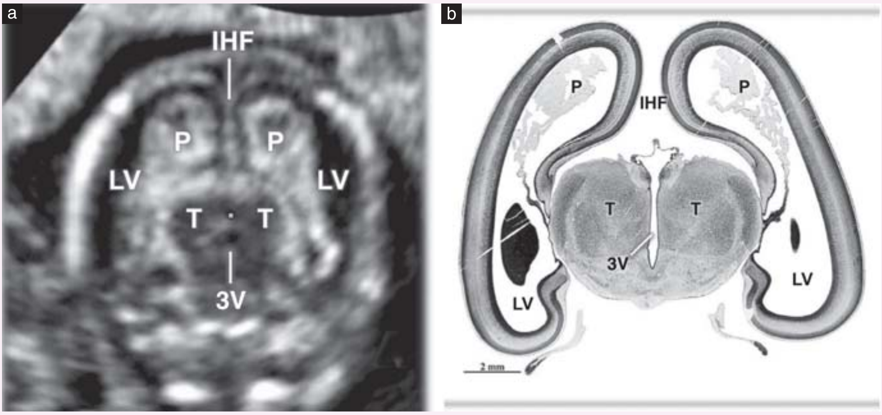


Figure 8 Transthalamic coronal view of normal fetal brain, showing: (a) detailed anatomy on two-dimensional ultrasound imaging at 11–13 weeks and (b) corresponding anatomic specimen. 3V, third ventricle; IHF, interhemispheric fissure; LV, lateral ventricle; P, choroid plexus; T, thalamus. Anatomic specimen reproduced from Bayer and Altman[16] with permission.

more anterior one, passing through the pons and medulla (Figure 9), and a more posterior one, including the 4V and the medulla below it (Figure 10).

Vascular anatomy at 11–13 weeks

Thanks to the use of new, highly sensitive Doppler technology, visualization of the main fetal cerebral vessels is also feasible at 11–13 weeks[30,31]. In the sagittal views (Figure 11), it is possible to display the pericallosal arteries with their branches, and the internal carotid artery below them. A few venous structures are also visible, such as the superior sagittal sinus underneath the calvarium, the straight sinus at the level of the cerebellar tentorium, continuing into the vein of Galen anteriorly, and joining the straight sinus into the torcular herophili, posteriorly. In the axial views, Doppler imaging allows visualization of the circle of Willis, including anterior, middle and posterior cerebral arteries (Figure 12).

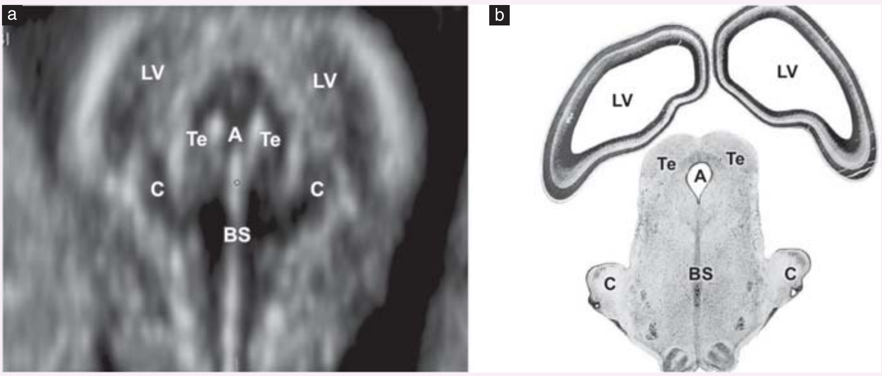


Figure 9 Occipital coronal view of normal fetal brain, anterior to fourth ventricle, showing: (a) detailed anatomy on two-dimensional ultrasound imaging at 11–13 weeks and (b) corresponding anatomic specimen. A, aqueduct of Sylvius; BS, brainstem (pons and medulla); C, future cerebellar hemisphere; LV, lateral ventricle; Te, tectum. Anatomic specimen reproduced from Bayer and Altman[16] with permission.

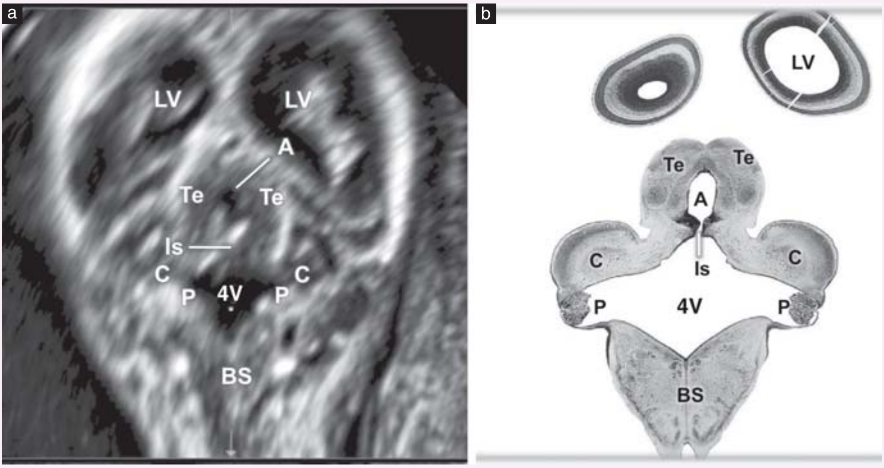


Figure 10 Occipital coronal view of normal fetal brain, at level of fourth ventricle, showing: (a) detailed anatomy on two-dimensional ultrasound imaging at 11–13 weeks and (b) corresponding anatomic specimen. 4V, fourth ventricle; A, aqueduct of Sylvius; BS, brainstem (pons and medulla); C, future cerebellar hemisphere; Is, isthmus; LV, lateral ventricle; P, rhombencephalic (fourth ventricle) choroid plexus; Te, tectum. Anatomic specimen reproduced from Bayer and Altman[16] with permission.

ANOMALIES POTENTIALLY DETECTABLE BY FIRST-TRIMESTER EXPERT NEUROSONOGRAPHY

CNS abnormalities involving the structures included in a basic ultrasound examination are often identified early in gestation. High detection rates of acrania, encephalocele and alobar holoprosencephaly have been reported for the basic ultrasound examination[6,7,12,17–19]. However, an expert evaluation may allow early recognition of other major CNS anomalies, such as ventriculomegaly, open spina bifida (OSB), Dandy–Walker malformation and agenesis of the corpus callosum.

Figure 11 Sagittal view of normal fetal brain using highly sensitive Doppler imaging (MV flow) at 11–13 weeks. B, basilar artery; C, internal carotid artery; G, vein of Galen; P, pericallosal artery; St, straight sinus; Su, superior sagittal sinus; TH, torcular herophili; V, vertebral artery.

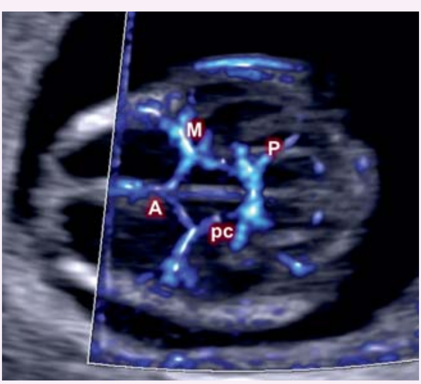


Figure 12 Axial view of normal fetal brain showing circle of Willis using highly sensitive Doppler imaging (MV flow) at 11–13 weeks. A, anterior cerebral artery; M, middle cerebral artery; P, posterior cerebral artery; pc, posterior communicating artery.

Ventriculomegaly

While the conventional definition of ventriculomegaly in the second trimester is an atrial diameter ≥ 10 mm, the diagnosis of this condition in the first trimester is not based on ventricular width. At the end of the first trimester, if the fluid content of a lateral ventricle is increased, it is a relative reduction of choroid plexus size, rather than an enlargement of the ventricle, that is noted[32,33] (Figure 13). It has been shown that a reduced ratio between the choroid plexus and ventricular areas may herald the diagnosis of ventriculomegaly according to its traditional definition on second-trimester ultrasound[32,33]. Specifically, at 11–13 weeks, ratios $< 5^{th}$ percentile between the areas

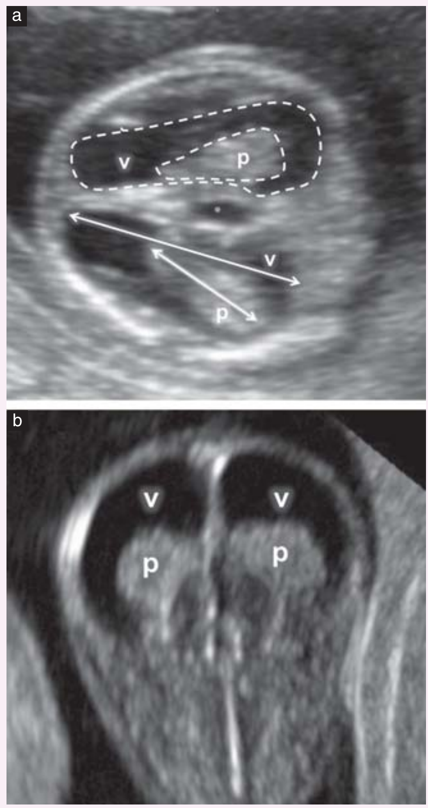


Figure 13 Ventriculomegaly in first trimester. (a) In axial suprathalamic plane, ratios between lengths (arrows) and areas (dotted lines) of choroid plexus (p) and lateral ventricle (v) are reduced. (b) In coronal transthalamic view, neither choroid plexus reaches roof of corresponding lateral ventricle.

(5^{th} percentile, 0.48–0.36), the lengths (5^{th} percentile, 0.66–0.56) and the widths (5^{th} percentile, 0.60–0.54) of these two structures have been reported to predict the diagnosis of ventriculomegaly in the mid trimester in 94%, 94% and 82% of cases, respectively[32]. It is therefore possible to establish a tentative diagnosis of cerebral ventriculomegaly in the first trimester, based on these ratios, although the available evidence is still limited. According to some, regardless of any quantitative measurement, the qualitative observation of hypoplastic choroid plexuses, i.e. being too small to reach the roof of the ventricles, should raise suspicion of early-onset ventriculomegaly[34] (Figure 13).

Open spina bifida (OSB)

An abnormal appearance of the CPF in the mid-trimester has been shown to be associated with OSB in the majority of cases[23,24,35,36]. Recent studies have demonstrated that early indirect cranial findings of OSB can be noted in the midsagittal view in the first trimester, when direct visualization of the spinal defect may be challenging. Among fetuses affected by Chiari-II malformation, a reduced width of the CM can be demonstrated. In the frontal midsagittal view, instead of the three parallel anechoic spaces described above (BS, 4V/intracranial translucency and CM, Figure 3), the dominance of the BS, combined with a thinning of the 4V and CM and/or an absence of separation between them, have been described as fair predictors of OSB[23,24,35,36]. It has been determined that, due to the caudal displacement of the BS and 4V, the CM is collapsed and therefore not visible sonographically in the majority of these cases (Figure 14).

Some recent studies have proposed quantifying the anteroposterior diameter ratios between the three CPF structures visible in the midsagittal view, in order to demonstrate objectively Chiari-II malformation and to predict the presence of OSB. It has been proven that an increased ratio between BS thickness and its distance from the occipital bone (BS-to-occipital bone distance (BSOB), Figure 3) is a reliable and reproducible sonographic marker of OSB. Specifically, a BS/BSOB ratio $> 95^{th}$ percentile between 11 + 0 and 13 + 6 weeks has been found to predict almost all cases of OSB[24,25,37], performing better than does qualitative assessment or measurement individually of every structure of the CPF, including the BS, BSOB and intracranial translucency.

In axial views also, the presence of abnormal brain findings in fetuses with OSB has been reported at 11–13 weeks of gestation. Due to leakage of fluid through the foramen magnum, in the case of Chiari-II anomaly, the amount of fluid in the ventricular system is reduced; the sonographic appearance of this has been described as ‘dry brain’[38,39] (Figure 15), with the third ventricle and the aqueduct of Sylvius barely visible. Moreover, the sonographic appearance as a result of the displacement backwards of the midbrain and aqueduct, which are pushed closer to the occipital bone, known as ‘crash sign’ (Figure 15), has been found to herald the presence of OSB in the majority of cases and seems to reflect the early changes in shape of the BS in fetuses with Chiari-II anomaly[40,41]. Some authors have proposed quantifying in the axial plane the proximity of the aqueduct to the occipital bone, reporting a significant shortening of the distance between these two structures in cases of OSB[42].

Recently, a multicenter case series compared the accuracy of all sonographic markers of OSB in both midsagittal and axial views of the fetal brain in the first trimester[25]. This study found the most accurate predictor of OSB to be the BS/BSOB ratio, with an area under the receiver-operating-characteristics curve of 0.997 and no cases of intact spine having a ratio > 1.

Since the CPF structures can be visualized exactly in the same scanning plane as that in which the NT is measured,

Figure 14 Appearance of Chiari-II malformation in midsagittal view in first trimester. Brainstem (BS) is thicker than usual and displaced posteriorly, compressing fourth ventricle (4V), with consequent collapse of cisterna magna.

Figure 15 Appearance of Chiari-II malformation in axial transthalamic view in first trimester. Third ventricle and aqueduct of Sylvius (arrow) are barely visible (‘dry brain’) and midbrain is displaced backwards, with aqueduct pushed close to occipital bone (‘crash sign’).

routine evaluation of the CPF seems feasible without much additional effort when performing routine screening for chromosomal abnormalities in the first trimester. This extended examination has been demonstrated to improve the early detection of OSB[6,24,25,37]. In a recent study, including a large population, it was shown that the detection rate of OSB improved from 15% to about 60% after implementing routine evaluation of the CPF structures in the anatomic protocol for the first-trimester ultrasound examination[6].

Dandy–Walker malformation (DWM)

Historically, sonographic diagnosis of cystic CPF anomalies and accurate differentiation between the classic DWM and the more common and benign Blake's pouch cyst (BPC) have been considered feasible only after 20 gestational weeks. In the last decade, first-trimester detection of CPF malformations by expert fetal brain scanning has been reported independently by several research groups[27,29,36,43–48]. In the frontal midsagittal plane, in fetuses with DWM or BPC, an increased amount of fluid in the 4V and CM, with fusion of these two structures, has been reported at 11–13 weeks[36,43,47,48]. Due to the wide communication between the 4V and CM, others have suggested that, in fetuses with cystic anomalies of the CPF, only two, rather than three, parallel anechoic spaces are visible in the midsagittal plane[36,44,49]. A reduced BS/BSOB ratio has been proposed as an early objective marker of cystic CPF anomaly; BS/BSOB < 5^{th} percentile in the first trimester has been shown to predict the sonographic appearance of DWM or BPC at mid-gestation in a large proportion of cases, and to suggest a cystic CPF anomaly rather than OSB when only two parallel anechoic spaces are visible in the midsagittal plane[36,43,49] (Figure 16).

Upward displacement of the tentorium cerebelli with respect to its normal insertion on the occipital clivus is among the major criteria that differentiate DWM from BPC in fetuses with abnormal communication between the 4V and the CM. Although antenatal visualization of the position of the tentorium cerebelli is technically challenging, especially in the first trimester, the torcular herophili, which lies at the intersection between the tentorium and the falx cerebri, may be depicted sonographically by means of highly sensitive Doppler imaging (Figure 11). On this basis, antenatal demonstration of the torcular herophili on Doppler imaging has been proposed as a proxy for the insertion of the tentorium on the fetal skull. Some recent studies have suggested that, thanks to visualization of the torcular herophili on first-trimester fetal neurosonography, the differential diagnosis between DWM and BPC may be feasible[31]. Volpe *et al.*[31] have shown that, in the frontal midsagittal view of the brain in fetuses with abnormal communication between the 4V and the CM, a very small angle between the BS and the tentorium (with the straight sinus appearing almost parallel to the BS) may predict the occurrence of DWM even in the first trimester[31]. Research by our group has shown that sonographic demonstration of the torcular herophili in the second trimester is feasible and may assist in the differential diagnosis between BPC and DWM[50].

In fetuses with suspected CPF anomalies, a detailed sonographic study of the developing cerebellar vermis is feasible in the midsagittal plane only via the posterior fontanel. In this scanning plane, the vermis can be visualized and measured[46]. Moreover, additional quantitative and qualitative parameters have been proposed recently, such as the angle formed by the vermis and the pons (pontovermian angle) and the appearance of the aqueduct of Sylvius. It has been suggested, that among fetuses with CPF anomalies, the pontovermian angle is > 100°, being increased considerably in DWM and to a lesser extent in BPC[29]. Furthermore, in the first trimester, the aqueduct of Sylvius might appear smaller or larger than normal in case of DWM or BPC, respectively[29].

Agenesis of the corpus callosum

In the midsagittal plane of the fetal head, the corpus callosum becomes detectable sonographically after

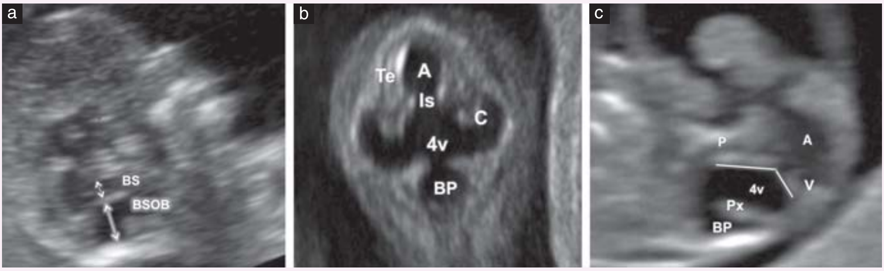


Figure 16 Appearance of cystic anomaly of posterior fossa in first trimester. In midsagittal view (a), ratio between brainstem (BS) thickness and BS-to-occipital bone distance (BSOB) is reduced and only two rather than three parallel anechoic spaces are seen. In occipital coronal view (b), fourth ventricle (4v) appears enlarged, with prominence of aqueduct of Sylvius (A) and Blake's pouch (BP). (c) In midsagittal view, pontovermian angle is increased. C, future cerebellar hemisphere; Is, isthmus; P, pons; Px, plexus of fourth ventricle; Te, tectum; V, vermis.

Figure 17 Agenesis of corpus callosum in midsagittal view in first trimester, showing increased ratio between diencephalon (D) and falx (F) diameters.

16–18 weeks[51,52]. In the first trimester it is therefore not possible to suspect callosal agenesis based on the lack of its direct visualization on grayscale ultrasound imaging. However, some authors have proposed seeking indirect signs of callosal absence at 11–13 weeks. In 80% of fetuses that had agenesis of the corpus callosum diagnosed later in gestation, Lachmann *et al.*[53] demonstrated an increased ratio between the diencephalon diameter (from midbrain to falx, including third ventricle and thalami) and the falx diameter (Figure 17). This sonographic marker seems to reflect early in gestation the upward displacement and dilatation of the third ventricle, which is commonly noted in the midtrimester in fetuses with absent corpus callosum.

Several groups, independently, have used 2D and 3D power Doppler ultrasound to evaluate the presence and course of the pericallosal arteries in the first trimester. It was demonstrated that visualization of a normal artery was associated with the later appearance of a normal corpus callosum in all cases, whereas callosal agenesis was diagnosed in the midtrimester when the artery was not demonstrated in the first trimester[30,54,55]. In accordance with this finding, sonographic visualization of the pericallosal artery was suggested as an indirect but reliable sign to rule out callosal agenesis on first-trimester neurosonography.

CONCLUSION

In conclusion, in the axial planes, a 'basic' examination of the fetal brain may be performed in accordance with current ISUOG guidelines for first-trimester ultrasound examination. However, using this approach, only the most severe or lethal brain abnormalities can be picked up sonographically at 11–13 weeks. With inclusion of non-axial planes, multiplanar neurosonography may be carried out at the end of the first trimester, following the methodology recommended for dedicated fetal brain scanning in the midtrimester. Expert neurosonography with two- and three-dimensional imaging in the first trimester, combined with detailed knowledge of fetal anatomy and sonoembryology, allows detection of early signs of several brain abnormalities which are commonly diagnosed only later in gestation and whose early diagnosis can be clinically advantageous. This detailed examination of the CNS can be offered to parents at high risk for fetal anomalies based on the family history or on the presence of abnormal findings during the basic ultrasound examination. A standardized protocol for first-trimester neurosonography at 11–13 weeks, including systematic evaluation of specific markers for structural abnormalities (such as the BS/BSOB ratio), is expected to detect or predict the development of most severe brain anomalies.

ACKNOWLEDGMENT

We acknowledge the contribution of Dr Paolo Volpe, whose commitment and research activity on expert assessment of the fetal anatomy in the first trimester inspired the design of this work.

REFERENCES

1. Morris JK, Wellesley DG, Barisic I, Addor MC, Bergman JEH, Braz P, Cavero-Carbonell C, Draper ES, Gatt M, Haeusler M, Klungsoyr K, Kurinczuk JJ, Lelong N, Luyt K, Lynch C, O'Mahony MT, Mokoroa O, Nelen V, Neville AJ, Pierini A, Randrianaivo H, Rankin J, Rissmann A, Rouget F, Schaub B, Tucker DF, Verellen-Dumoulin C, Wiesel A, Zymak-Zakutnia N, Lanzoni M, Garne E. Epidemiology of congenital cerebral anomalies in Europe: A multicentre, population-based EUROCAT study. *Arch Dis Child* 2019; **104**: 1181–1187.
2. Anderson N, Boswell O, Duff G. Prenatal sonography for the detection of fetal anomalies: Results of a prospective study and comparison with prior series. *Am J Roentgenol* 1995; **165**: 943–950.
3. Bernaschek G, Stuempflen I, Deutinger J. The value of sonographic diagnosis of fetal malformations: Different results between indication-based and screening-based investigations. *Prenat Diagn* 1994; **14**: 807–812.
4. International Society of Ultrasound in Obstetrics & Gynecology Education Committee. Sonographic examination of the fetal central nervous system: guidelines for performing the 'basic examination' and the 'fetal neurosonogram'. *Ultrasound Obstet Gynecol* 2007; **29**: 109–116.
5. Syngelaki A, Chelemen T, Dagklis T, Allan L, Nicolaides KH. Challenges in the diagnosis of fetal non-chromosomal abnormalities at 11-13 weeks. *Prenat Diagn* 2011; **31**: 90–102.
6. Syngelaki A, Hammami A, Bower S, Zidere V, Akolekar R, Nicolaides KH. Diagnosis of fetal non-chromosomal abnormalities on routine ultrasound examination at 11–13 weeks' gestation. *Ultrasound Obstet Gynecol* 2019; **54**: 468–476.
7. Rossi AC, Prefumo F. Accuracy of ultrasonography at 11-14 weeks of gestation for detection of fetal structural anomalies: A systematic review. *Obstet Gynecol* 2013; **122**: 1160–1167.
8. Rayburn WF, Jolley JA, Simpson LL. Advances in ultrasound imaging for congenital malformations during early gestation. *Birth Defects Res A Clin Mol Teratol* 2015; **103**: 260–268.
9. Iliescu D, Tudorache S, Comanescu A, Antsaklis P, Cotarcea S, Novac L, Cernea N, Antsaklis A. Improved detection rate of structural abnormalities in the first trimester using an extended examination protocol. *Ultrasound Obstet Gynecol* 2013; **42**: 300–309.
10. Grande M, Arigita M, Borobio V, Jimenez JM, Fernandez S, Borrell A. First-trimester detection of structural abnormalities and the role of aneuploidy markers. *Ultrasound Obstet Gynecol* 2012; **39**: 157–163.
11. Bardi F, Smith E, Kuilman M, Snijders RJM, Bilardo CM. Early Detection of Structural Anomalies in a Primary Care Setting in the Netherlands. *Fetal Diagn Ther* 2019; **46**: 12–19.
12. Karim JN, Roberts NW, Salomon LJ, Papageorghiou AT. Systematic review of first-trimester ultrasound screening for detection of fetal structural anomalies and factors that affect screening performance. *Ultrasound Obstet Gynecol* 2017; **50**: 429–441.
13. Vayna AM, Veduta A, Duta S, Panaitescu AM, Stoica S, Buinoiu N, Nedelea F, Peltecu G. Diagnosis of fetal structural anomalies at 11 to 14 weeks. *J Ultrasound Med* 2018; **37**: 2063–2073.
14. Kenkhuis MJA, Bakker M, Bardi F, Fontanella F, Bakker MK, Fleurke-Rozema JH, Bilardo CM. Effectiveness of 12–13-week scan for early diagnosis of fetal

congenital anomalies in the cell-free DNA era. *Ultrasound Obstet Gynecol* 2018; **51**: 463–469.
15. Salomon LJ, Alfirevic Z, Bilardo CM, Chalouhi GE, Ghi T, Kagan KO, Lau TK, Papageorghiou AT, Raine-Fenning NJ, Stirnemann J, Suresh S, Tabor A, Timor-Tritsch IE, Toi A, Yeo G. ISUOG Practice Guidelines: performance of first-trimester fetal ultrasound scan. *Ultrasound Obstet Gynecol* 2013; **41**: 102–113.
16. Bayer S, Altman J. *The Human Brain During The Late First Trimester. Atlas of Human Central Nervous System Development*, *Volume 4*. CRC Press: Boca Raton, 2006.
17. Sepulveda W, Wong AE, Andreeva E, Odegova N, Martinez-Ten P, Meagher S. Sonographic spectrum of first-trimester fetal cephalocele: Review of 35 cases. *Ultrasound Obstet Gynecol* 2015; **46**: 29–33.
18. Cheng CC, Lee FK, Lin HW, Shih JC, Tsai MS. Diagnosis of fetal acrania during the first trimester nuchal translucency screening for Down syndrome. *Int J Gynecol Obstet* 2003; **80**: 139–144.
19. Sepulveda W, Wong AE. First trimester screening for holoprosencephaly with choroid plexus morphology (‘‘butterfly’’ sign) and biparietal diameter. *Prenat Diagn* 2013; **33**: 1233–1237.
20. Nicolaides KH, Azar G, Byrne D, Mansur C, Marks K. Fetal nuchal translucency: Ultrasound screening for chromosomal defects in first trimester of pregnancy. *Br Med J* 1992; **304**: 867–869.
21. Nicolaides KH, Brizot ML, Snijders RJM. Fetal nuchal translucency: ultrasound screening for fetal trisomy in the first trimester of pregnancy. *ACOG Curr J Rev* 1995; **8**: 42.
22. Nicolaides KH, Heath V, Cicero S. Increased fetal nuchal translucency at 11-14 weeks. *Prenat Diagn* 2002; **22**: 308–315.
23. Chaoui R, Benoit B, Mitkowska-Wozniak H, Heling KS, Nicolaides KH. Assessment of intracranial translucency (IT) in the detection of spina bifida at the 11–13-week scan. *Ultrasound Obstet Gynecol* 2009; **34**: 249–252.
24. Lachmann R, Chaoui R, Moratalla J, Picciarelli G, Nicolaides KH. Posterior brain in fetuses with open spina bifida at 11 to 13 weeks. *Prenat Diagn* 2011; **31**: 103–106.
25. Wertaschnigg D, Ramkrishna J, Ganesan S, Tse C, Scheier M, Volpe N, Ghi T, Meagher S, Rolnik DL. Cranial sonographic markers of fetal open spina bifida at 11 to 13 weeks of gestation. *Prenat Diagn* 2020; **40**: 365–372.
26. Robinson AJ. Inferior vermian hypoplasia - Preconception, misconception. *Ultrasound Obstet Gynecol* 2014; **43**: 123–136.
27. Robinson AJ, Goldstein R. The cisterna magna septa: Vestigial remnants of Blake’s pouch and a potential new marker for normal development of the rhombencephalon. *J Ultrasound Med* 2007; **26**: 83–95.
28. Altmann R, Scharnreitner I, Scheier T, Mayer R, Arzt W, Scheier M. Sonoembryology of the fetal posterior fossa at 11 + 3 to 13 + 6 gestational weeks on three-dimensional transvaginal ultrasound. *Prenat Diagn* 2016; **36**: 731–737.
29. Paladini D, Donarini G, Parodi S, Chaoui R. Differentiating features of posterior fossa at 12–13 weeks’ gestation in fetuses with Dandy–Walker malformation and Blake’s pouch cyst. *Ultrasound Obstet Gynecol* 2019; **53**: 850–852.
30. Conturso R, Contro E, Bellussi F, Youssef A, Pacella G, Martelli F, Rizzo N, Pilu G, Ghi T. Demonstration of the pericallosal artery at 11–13 weeks of gestation using 3D ultrasound. *Fetal Diagn Ther* 2015; **37**: 305–309.
31. Volpe P, Persico N, Fanelli T, De Robertis V, D’Alessandro J, Boito S, Pilu G, Votino C. Prospective detection and differential diagnosis of cystic posterior fossa anomalies by assessing posterior brain at 11–14 weeks. *Am J Obstet Gynecol MFM* [Internet]. 2019; **1**: 173–181. https://doi.org/10.1016/j.ajogmf.2019.06.004.
32. Manegold-Brauer G, Oseledchyk A, Floeck A, Berg C, Gembruch U, Geipel A. Approach to the sonographic evaluation of fetal ventriculomegaly at 11 to 14 weeks gestation. *BMC Pregnancy Childbirth* [Internet]. 2016; **16**: 1–8. http://dx.doi.org/10.1186/s12884-016-0797-z.
33. Loureiro T, Ushakov F, Maiz N, Montenegro N, Nicolaides KH. Lateral ventricles in fetuses with aneuploidies at 11–13 weeks’ gestation. *Ultrasound Obstet Gynecol* 2012; **40**: 282–287.
34. Ushakov F, Chitty LS. P30.03: Ventriculomegaly at 11–14 weeks: diagnostic criteria and outcome. *Ultrasound Obstet Gynecol* 2016; **48** (Suppl): 267.
35. Chaoui R, Nicolaides KH. From nuchal translucency to intracranial translucency: Towards the early detection of spina bifida. *Ultrasound Obstet Gynecol* 2010; **35**: 133–138.
36. Martinez-Ten P, Illescas T, Adiego B, Estevez M, Bermejo C, Wong AE, Sepulveda W. Non-visualization of choroid plexus of fourth ventricle as first-trimester predictor of posterior fossa anomalies and chromosomal defects. *Ultrasound Obstet Gynecol* 2018; **51**: 199–207.
37. Chaoui R, Benoit B, Heling KS, Kagan KO, Pietzsch V, Sarut Lopez A, Tekesin I, Karl K. Prospective detection of open spina bifida at 11–13 weeks by assessing intracranial translucency and posterior brain. *Ultrasound Obstet Gynecol* 2011; **38**: 722–726.
38. Loureiro T, Ushakov F, Montenegro N, Gielchinsky Y, Nicolaides KH. Cerebral ventricular system in fetuses with open spina bifida at 11–13 weeks’ gestation. *Ultrasound Obstet Gynecol* 2012; **39**: 620–624.
39. Chaoui R, Benoit B, Entezami M, Frenzel W, Heling KS, Ladendorf B, Pietzsch V, Sarut Lopez A, Karl K. Ratio of fetal choroid plexus to head size: simple sonographic marker of open spina bifida at 11–13 weeks’ gestation. *Ultrasound Obstet Gynecol* 2020; **55**: 81–86.
40. Ushakov F, Sacco A, Andreeva E, Tudorache S, Everett T, David AL, Pandya PP. Crash sign: new first-trimester sonographic marker of spina bifida. *Ultrasound Obstet Gynecol* 2019; **54**: 740–745.
41. Chaoui R, Nicolaides KH. Detecting open spina bifida at the 11–13-week scan by assessing intracranial translucency and the posterior brain region: mid-sagittal or axial plane? *Ultrasound Obstet Gynecol* 2011; **38**: 609–612.
42. Finn M, Sutton D, Atkinson S, Ransome K, Sujenthiran P, Ditcham V, Wakefield P, Meagher S. The aqueduct of Sylvius: A sonographic landmark for neural tube defects in the first trimester. *Ultrasound Obstet Gynecol* 2011; **38**: 640–645.
43. Lachmann R, Sinkovskaya E, Abuhamad A. Posterior brain in fetuses with Dandy-Walker malformation with complete agenesis of the cerebellar vermis at 11-13weeks: A pilot study. *Prenat Diagn* 2012; **32**: 765–769.
44. Volpe P, Contro E, Fanelli T, Muto B, Pilu G, Gentile M. Appearance of fetal posterior fossa at 11-14 weeks in fetuses with Dandy-Walker malformation or chromosomal anomalies. *Ultrasound Obstet Gynecol* 2016; **47**: 720–725.
45. Iuculano A, Zoppi MA, Ibba RM, Monni G. A Case of Enlarged Intracranial Translucency in a Fetus with Blake’s Pouch Cyst. *Case Rep Obstet Gynecol* 2014; 2014: **968089**.
46. Altmann R, Schertler C, Scharnreitner I, Arzt W, Dertinger S, Scheier M. Diagnosis of Fetal Posterior Fossa Malformations in High-Risk Pregnancies at 12-14 Gestational Weeks by Transvaginal Ultrasound Examination. *Fetal Diagn Ther* 2020; **47**: 182–187.
47. Lafouge A, Gorincour G, Desbriere R, Quarello E. Prenatal diagnosis of Blake’s pouch cyst following first-trimester observation of enlarged intracranial translucency. *Ultrasound Obstet Gynecol* 2012; **40**: 479–480.
48. Garcia-Posada R, Eixarch E, Sanz M, Puerto B, Figueras F, Borrell A. Cisterna magna width at 11-13 weeks in the detection of posterior fossa anomalies. *Ultrasound Obstet Gynecol* 2013; **41**: 515–520.
49. Volpe P, Muto B, Passamonti U, Rembouskos G, De Robertis V, Campobasso G, Tempesta A, Volpe G, Fanelli T. Abnormal sonographic appearance of posterior brain at 11-14weeks and fetal outcome. *Prenat Diagn* 2015; **35**: 717–723.
50. Dall’Asta A, Grisolia G, Volpe N, Schera GBL, Sorrentino F, Frusca T. Prenatal visualization of the torcular herophili by means of a Doppler technology highly sensitive for low velocity flow in the expert assessment of the posterior fossa: a prospective study. *BJOG* 2020. DOI:10.1111/1471-0528.16392.
51. Malinger G, Zakut H. The corpus callosum: normal fetal development as shown by transvaginal sonography. *Am J Roentgenol* 1993; **161**: 1041–1043.
52. Achiron R, Achiron A. Development of the human fetal corpus callosum: a high-resolution, cross-sectional sonographic study. *Ultrasound Obstet Gynecol* 2001; **18**: 343–347.
53. Lachmann R, Sodre D, Barmpas M, Akolekar R, Nicolaides KH. Midbrain and falx in fetuses with absent corpus callosum at 11-13 weeks. *Fetal Diagn Ther* 2013; **33**: 41–46.
54. Pati M, Cani C, Bertucci E, Re C, Latella S, D’Amico R, Mazza V. Early visualization and measurement of the pericallosal artery: An indirect sign of corpus callosum development. *J Ultrasound Med* 2012; **31**: 231–237.
55. Díaz-Guerrero L, Giugni-Chalbaud G, Sosa-Olavarría A. Assessment of pericallosal arteries by color Doppler ultrasonography at 11-14 weeks: An early marker of fetal corpus callosum development in normal fetuses and agenesis in cases with chromosomal anomalies. *Fetal Diagn Ther* 2013; **34**: 85–89.

Ultrasound Obstet Gynecol 2020; **56**: 476–484
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.22145

isuog.org GUIDELINES

ISUOG Practice Guidelines (updated): sonographic examination of the fetal central nervous system. Part 1: performance of screening examination and indications for targeted neurosonography

Clinical Standards Committee

The International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) is a scientific organization that encourages sound clinical practice, and high-quality teaching and research related to diagnostic imaging in women's healthcare. The ISUOG Clinical Standards Committee (CSC) has a remit to develop Practice Guidelines and Consensus Statements as educational recommendations that provide healthcare practitioners with a consensus-based approach, from experts, for diagnostic imaging. They are intended to reflect what is considered by ISUOG to be the best practice at the time at which they are issued. Although ISUOG has made every effort to ensure that Guidelines are accurate when issued, neither the Society nor any of its employees or members accepts any liability for the consequences of any inaccurate or misleading data, opinions or statements issued by the CSC. The ISUOG CSC documents are not intended to establish a legal standard of care, because interpretation of the evidence that underpins the Guidelines may be influenced by individual circumstances, local protocol and available resources. Approved Guidelines can be distributed freely with the permission of ISUOG (info@isuog.org).

INTRODUCTION

Central nervous system (CNS) malformations are some of the most common congenital abnormalities. Neural tube defects are the most frequent CNS malformations and amount to about one to two cases per 1000 births. The incidence of intracranial abnormalities with an intact neural tube is uncertain, as most of these abnormalities probably go undetected at birth and manifest only in later life. However, long-term follow-up studies suggest that the incidence may be as high as one in 100 births[1].

Ultrasound has been used for nearly 30 years as the main modality to help diagnose fetal CNS anomalies. The aim of these Guidelines is to review, describe and update the technical aspects of the screening evaluation of the fetal brain to be performed as part of the midtrimester anomaly scan, which is referred to in this document as a 'screening examination'. This Guideline also presents the indications for the detailed evaluation of the fetal CNS, which constitutes 'targeted fetal neurosonography', a dedicated examination of the fetal brain and spine that requires specific expertise and sophisticated ultrasound equipment. This examination is described in Part 2 of this Guideline, in which we also discuss the indications for fetal brain magnetic resonance imaging (MRI). Details of the grades of recommendation and levels of evidence used in this Guideline are given in Appendix 1.

GENERAL CONSIDERATIONS

Gestational age

Recommendation

- Examiners involved in screening for CNS abnormalities should be familiar with normal CNS appearance at different gestational ages (**GOOD PRACTICE POINT**).

The appearance of the brain and the spine changes throughout gestation. To avoid diagnostic errors, it is important to be familiar with normal CNS appearance at different gestational ages (Figure 1), although most efforts to diagnose CNS anomalies are focused around midgestation[2]. Hence, it is recommended that this Guideline is applied during the midtrimester anomaly scan.

However, during the last decade, it has become evident that an increasing number of CNS and neural tube abnormalities, mainly dorsal and rhombencephalic induction defects, may be visible from the end of the first trimester[3–9]. Although these are in the minority, they are usually severe and therefore deserve special consideration. While early examination of the CNS requires certain skills, it is always worthwhile paying particular attention to the fetal head and brain at early gestational ages. The advantage of early fetal neurosonography at 12–15 weeks is that the bones are thin and the brain may be evaluated

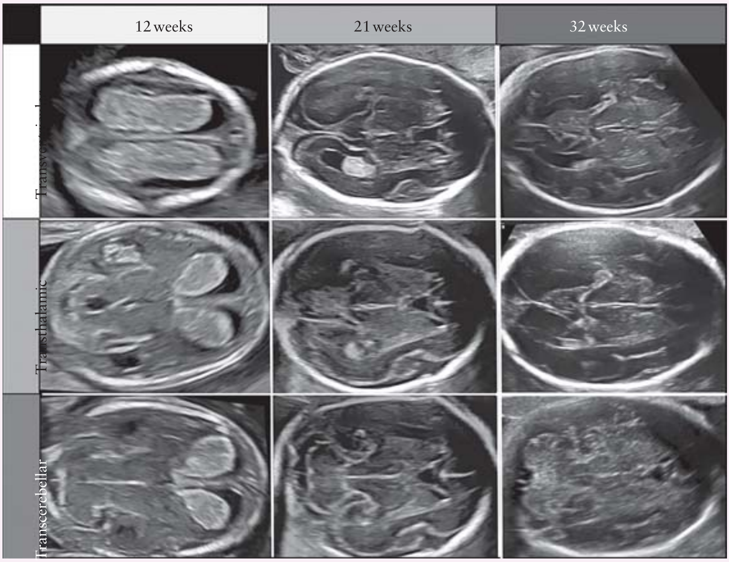


Figure 1 Normal morphological changes of fetal brain throughout gestation, as visualized on sonographic examination in axial planes: views in transventricular, transthalamic and transcerebellar planes at 12, 21 and 32 gestational weeks. Note significant structural change of lateral ventricles and choroid plexus from late first trimester to midgestation, along with appearance of cavum septi pellucidi only from early second trimester onwards. Nevertheless, ventricular atrial width remains relatively stable during second and third trimesters.

from almost all angles, especially with a high-frequency transvaginal transducer.

Generally, a satisfactory evaluation of the fetal CNS can be performed from the end of the first trimester. As pregnancy advances, visualization of the intracranial structures becomes more difficult due to advanced ossification of the calvarium.

Technical factors

Ultrasound transducers

High-frequency ultrasound transducers increase spatial resolution but decrease the penetration of the sound beam. The choice of optimal transducer and operating frequency is influenced by a number of factors, including maternal habitus, fetal position, gestational age and the approach used. Most screening examinations are performed satisfactorily with a 3–5-MHz transabdominal transducer, although recent wideband transducers can also be employed advantageously.

Imaging parameters

The examination is performed with grayscale two-dimensional ultrasound. Harmonic and crossbeam imaging, as well as speckle-reduction filters, may enhance visualization of subtle anatomic details and in patients who scan poorly, for example those with increased body mass index or abdominal scarring.

SCREENING EXAMINATION OF FETAL BRAIN AFTER 18 WEEKS

Qualitative evaluation

Recommendation

- Transabdominal sonography is the technique of choice for the screening examination of the fetal CNS during the midtrimester scan in low-risk pregnancies. This examination should include evaluation of the fetal head and spine (**GOOD PRACTICE POINT**).

The fetal CNS screening examination during the midtrimester scan in low-risk pregnancies should include evaluation of the fetal head and spine, using transabdominal sonography. Evaluation of two axial planes allows visualization of the relevant cerebral structures to assess the anatomic integrity of the fetal brain[10]. These planes are commonly referred to as the transventricular (Figure 2a) and transcerebellar (Figure 2b) planes. A third plane, the

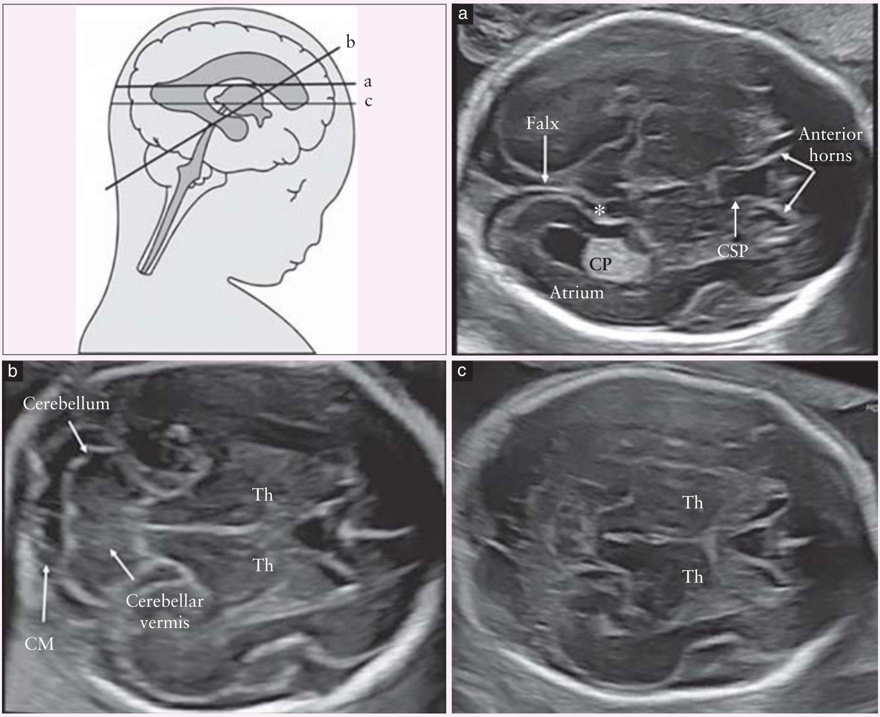


Figure 2 Fetal central nervous system screening examination (normal 21-week fetus) in three axial planes. (a) Transventricular plane, showing anterior and posterior portions of lateral ventricles. Comma-shaped anterior horns are separated centrally by cavum septi pellucidi (CSP). Atrium and posterior horn of ventricle distal to transducer are also demonstrated, along with choroid plexus (CP), as anatomic reference for measurement of atrial width, and parieto-occipital fissure (*). (b) For transcerebellar plane, transducer is tilted posteriorly in order to depict middle and posterior fossa structures: thalami (Th), cerebellar hemispheres and cerebellar vermis, demonstrated as butterfly shape, and retrocerebellar anechoic space corresponding to cisterna magna (CM). (c) Transthalamic plane is frequently used for biometry of fetal head (biparietal diameter, occipitofrontal distance and head circumference) and is inferior and parallel to transventricular plane. In this plane, falx, anterior horns of lateral ventricles and CSP are also observed, as well as thalami (Th) and hippocampal gyri bilaterally. Line diagram (top left) illustrates positions of axial planes.

Table 1 Structures usually noted on screening ultrasound examination of fetal central nervous system

- Head shape
- Lateral ventricles
- Cavum septi pellucidi
- Thalami
- Cerebellum
- Cisterna magna
- Spine

so-called transthalamic plane (Figure 2c), is frequently added, mostly for the purpose of biometry. Structures that should be noted in the routine examination include the lateral ventricles, the cerebellum and cisterna magna, and the cavum septi pellucidi (CSP). Head shape and brain texture should also be noted on these views (Table 1).

Transventricular plane (Figure 2a)

Recommendation

- In the transventricular plane, the aspect of the atrium distal to the transducer and the presence of the CSP should be assessed and documented (**GOOD PRACTICE POINT**).

The transventricular plane demonstrates the anterior and posterior portions of the lateral ventricles. The anterior portion (frontal or anterior horns) appears as two comma-shaped, fluid-filled structures. They have a well-defined lateral wall and are separated medially by the CSP. The CSP is a fluid-filled cavity between two thin membranes. In late gestation or the early neonatal period, these membranes usually fuse to become the septum pellucidum. The CSP becomes visible between 17 and 20 weeks and disappears near term. Using transabdominal ultrasound, it should always be demonstrable between 17–20 and 37 weeks, or at a biparietal diameter (BPD) of 44–88 mm[11]. Failure to demonstrate the CSP prior to 16 weeks or later than 37 weeks is a normal finding; rarely, absence of fluid in the CSP is seen in completely normal fetuses[12]. The importance of visualizing the CSP between 17 and 37 gestational weeks is due to the fact that its non-visualization or an abnormal appearance is associated with commissural anomalies, which may be an indirect sign of corpus callosal agenesis on screening views (usually in conjunction with a tear-shaped appearance of the lateral ventricles, known as colpocephaly[13]). Failure to visualize the membranes of the septum pellucidum is highly suspicious for the presence of a number of severe cerebral malformations, such as holoprosencephaly, severe hydrocephaly and septo-optic dysplasia[14]. Recently, an abnormal shape of the CSP has been described as a relatively reliable marker of partial agenesis of the corpus callosum[15,16].

From about 16 weeks, the posterior portion of the lateral ventricles (also referred to as occipital horns) is, in reality, a complex formed by the atrium that continues posteriorly into the occipital horn. The atrium is characterized by the presence of the glomus of the choroid plexus, which is highly echogenic, while the occipital horn is filled with cerebrospinal fluid. Particularly in the second trimester of gestation, both medial and lateral walls of the ventricle are parallel to the midline and are therefore well-depicted sonographically as well-demarcated echogenic lines. Under normal conditions, the glomus of the choroid plexus completely fills the cavity of the ventricle at the level of the atrium, being in close contact with the medial and lateral walls, although in some normal cases a small amount of fluid may be present between the medial wall and the choroid plexus[17–20].

It should be noted that, due to artifacts in the near field of the image, caused by shadowing from the proximal parietal bone, in the standard transventricular plane, only the hemisphere and the lateral ventricle on the far side of the transducer are usually visualized clearly. However, most severe cerebral lesions are bilateral or associated with a significant deviation or distortion of the midline echo, and it has been suggested that, in screening examinations, symmetry of the brain can be assumed.

Transcerebellar plane (Figure 2b)

Recommendation

- In the transcerebellar plane, the presence and shape of the cerebellum, as well as the presence of cerebrospinal fluid in the cisterna magna, should be assessed and documented (**GOOD PRACTICE POINT**).

The transcerebellar plane is slightly caudal to the transventricular one, and it is usually obtained with slight posterior tilting of the transducer. It is used to visualize the thalami, cerebellum and cisterna magna. The cerebellum appears as a butterfly-shaped structure formed by the round cerebellar hemispheres joined in the middle by the slightly more echogenic cerebellar vermis. The cisterna magna, or cisterna cerebellomedullaris, is a fluid-filled space posterior to the cerebellum. It normally contains thin septations, which are not usually demonstrated in the presence of pathology[21]. In the second half of gestation, the anteroposterior diameter of the cisterna magna remains stable and should not exceed 10 mm[10]. Before 19–20 gestational weeks, the cerebellar vermis has not yet completely covered the fourth ventricle, and this unusual appearance may give the false impression of a defect of the vermis. As a rule of thumb, by 19 gestational weeks, there should be no midline fluid-filled space between the two cerebellar hemispheres; should this finding, referred to as 'keyhole sign', be detected, it may be associated with an anomaly of the cerebellar vermis and the fetus should be referred for neurosonography[22]. Care should be taken to avoid 'over-tilting' of the probe, since this will increase the likelihood of false-positive diagnosis of a vermian anomaly.

Transthalamic plane (Figure 2c)

Commonly referred to as the transthalamic or BPD plane, a third scanning plane, obtained parallel but caudal to the transventricular plane, is also frequently used in the sonographic assessment of the fetal head. The anatomic landmarks include, from anterior to posterior, the frontal horns of the lateral ventricles, the CSP, the thalami and the hippocampal gyri[23]. This plane is used for biometry of the fetal head. It is easier to identify in late gestation and allows more reproducible measurements than does the transventricular plane[24].

Fetal spine

Recommendation

- When technically feasible, a longitudinal section of the fetal spine should be obtained, in order to screen for open and closed spinal dysraphism (**GOOD PRACTICE POINT**).

Technical advice

- Up to 97% of cases of open spina bifida present with the so-called 'banana sign', which is due to Chiari-II malformation[25] (**GRADE OF RECOMMENDATION: C**).

Detailed examination of the fetal spine requires expertise and meticulous scanning, and the results are heavily dependent on the fetal position. Therefore, a full and detailed evaluation of the fetal spine in every plane is not part of the screening examination. One of the most frequent severe spinal abnormalities, open spina bifida, is usually associated with abnormal intracranial anatomy: up to 97% of cases present with the so-called 'banana sign', which is due to Chiari-II malformation[25]. However, a longitudinal section of the fetal spine should be sought[4] if technically feasible, because it may reveal, at least in some cases, other spinal malformations, including vertebral abnormalities and sacral agenesis, although the latter diagnosis may be challenging even for experts, due to the physiological non-ossification of the caudal spine in the mid trimester[26]. Under normal conditions, a sagittal section of the spine at 18–24 gestational weeks demonstrates the three ossification centers of the vertebrae (one inside the body and one on each side at the junction between the lamina and pedicle) that surround the neural canal, and that appear as either two or three parallel lines, depending on the orientation of the ultrasound beam (Figure 3). The three ossification nuclei are best visualized on an axial view of individual vertebrae (Figure 4). In addition, an attempt should be made to demonstrate the intactness of the skin overlying the spine, on either a transverse or a longitudinal view.

Quantitative evaluation

Recommendation

- The following measurements represent an integral part of sonographic screening for CNS malformations: atrial width and transverse cerebellar diameter. Additional measurements usually performed for general biometry purposes (BPD and head circumference (HC)) are also part of the examination, since they may, in some cases, reveal proliferation abnormalities (e.g. microcephaly or macrocephaly) (**GOOD PRACTICE POINT**).

Technical advice

- The atrial width should be measured inner-to-inner and should be <10 mm throughout pregnancy (**GRADE OF RECOMMENDATION: C**).

Biometry is an essential part of sonographic examination of the fetal head. In the second-trimester anomaly scan, a standard examination includes measurement of the BPD, HC, internal diameter of the atrium and transverse cerebellar diameter. The cisterna magna depth should be measured if this structure is visually thinner or wider than normal on qualitative assessment of the posterior fossa.

BPD and HC are commonly used for assessing fetal age and growth and may also be useful to identify some cerebral anomalies. They may be measured either in the transventricular plane or in the transthalamic plane. There are various techniques for measuring BPD. Most frequently, the calipers are positioned outside the fetal calvarium (so-called 'outer-to-outer' measurement)[24]. However, some commonly used charts were produced using an outer-to-inner technique, to avoid artifacts generated by the distal echo of the calvarium, an issue that is less relevant now, with modern transducers, than it was several years ago[23]. These two approaches to measurement result in a difference of a few millimeters, which may be clinically relevant in early gestation. It is important, therefore, to know the technique that was used to construct the reference charts that one uses. HC can be measured directly, with the ellipse method, by placing the ellipse around the outer outline of the calvarium echoes. Alternatively, it can be calculated after measuring the BPD and occipitofrontal diameter (OFD), using the equation: $HC = 1.62 \times (BPD + OFD)$. The BPD/OFD ratio is usually 70–85%. However, molding of the fetal head, particularly in early gestation, is frequent, and fetuses in breech presentation may show some degree of dolicocephaly. It is not appropriate to use HC nomograms intended for

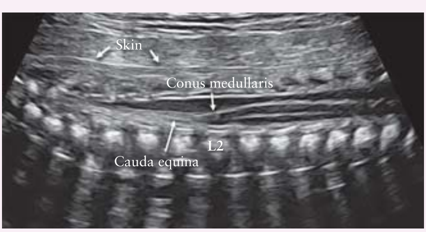


Figure 3 Sagittal view of lower thoracic and sacral fetal spine. Using unossified spinous process of vertebrae as acoustic window, contents of neural canal are demonstrated. Conus medullaris is clearly demonstrated and is normally located at level of L2 in midgestation. Its sharp end should point anteriorly, to vertebral body, with fluid filling neural canal posteriorly. Note intact skin observed as hyperechogenic line along fetal back.

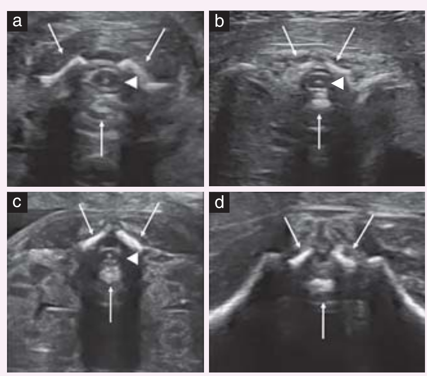


Figure 4 Axial views of fetal spine at different levels: (a) cervical, (b) thoracic, (c) lumbar and (d) sacral. Arrows indicate three ossification centers of vertebrae, and arrowheads indicate spinal cord, which is observed at cervical, thoracic and lumbar levels. Hyperechogenic dot corresponds to central canal of medulla. At sacral level (d), only fibers of cauda equina are observed. Note thin strip of fluid behind cord at all levels and intact skin overlying spine.

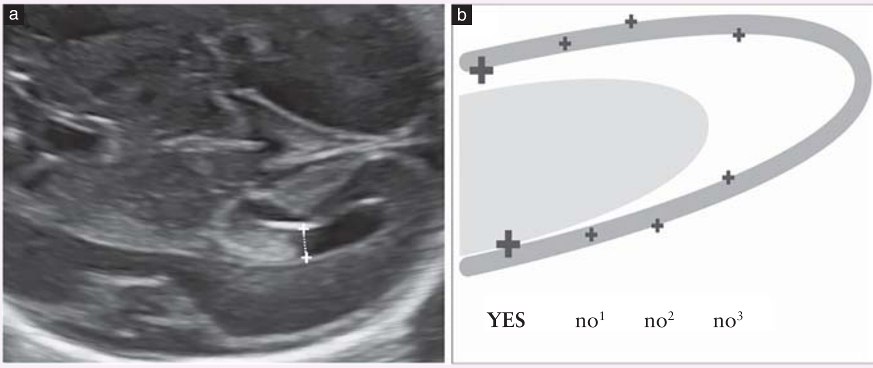


Figure 5 (a) Measurement of atrial width of lateral ventricles. Calipers are positioned at level of glomus of choroid plexus, inside echoes generated by ventricular walls. (b) Diagram illustrating correct caliper placement for ventricular measurement. Calipers are placed correctly when touching inner edge of ventricular wall at its widest part and aligned perpendicular to long axis of ventricle (YES). Incorrect placements include middle–middle (no[1]), outer–outer (no[2]) and placement that is too posterior in narrower part of ventricle or not perpendicular to ventricular axis (no[3]).

fetal weight estimation if the endpoint of the measurement is to exclude microcephaly.

Measurement of the atrium is recommended because several studies suggest that this is the most effective approach for assessing the integrity of the ventricular system[18], and ventriculomegaly is a frequent marker of abnormal cerebral development. Measurement is performed at the level of the glomus of the choroid plexus, perpendicular to the ventricular cavity, positioning the calipers inside the echoes generated by the lateral walls (Figure 5). This measurement remains stable in the second and early third trimesters, with a mean diameter between 6 and 8 mm[18,27]; it is considered normal when $<$10 mm[27–31]. Although this cut-off was determined several years ago, it remains valid even with more modern equipment, particularly at midgestation. Therefore, an atrial width $\geq$ 10 mm should be considered suspicious. It is useful to emphasize here that: (1) the atrial width may change during gestation, either increasing or decreasing, and (2) moderate asymmetry in atrial width between the two sides should be considered normal, if both atria measure $<$10 mm[32,33].

The transverse cerebellar diameter increases by about 1 mm per week of pregnancy between 14 and 21 gestational weeks. This measurement, along with the HC and BPD, is helpful to assess fetal growth. In cases in which the anteroposterior diameter of the cisterna magna should be measured (because it is subjectively considered abnormal), the calipers should be positioned in a correct transcerebellar plane, between the outer edge of the most dorsal point of the cerebellar vermis and the internal side of the occipital bone. A normal measurement is 2–10 mm[34]. With dolicocephaly, measurements slightly larger than 10 mm may be encountered.

In a low-risk midtrimester pregnancy, if the transventricular and transcerebellar planes are obtained satisfactorily, the head measurements (HC in particular) are within normal limits for gestational age, the atrial width is $<$10 mm and the cisterna magna width is between 2 and 10 mm, many cerebral malformations are excluded, the risk of a CNS anomaly that can be diagnosed at this gestational age is exceedingly low and further examinations are not indicated[10].

SCREENING EXAMINATION OF FETAL BRAIN BEFORE 18 WEEKS

Recommendation

- If a screening ultrasound examination is carried out before 18 gestational weeks, efforts should be made to visualize and document the transventricular and transcerebellar planes (**GOOD PRACTICE POINT**).

Fetal ultrasound examinations are being performed increasingly during the last few weeks of the first trimester and the early second trimester[4,8]. These examinations include evaluation of the brain, but, until now, there have been no clinical guidelines for its examination. In our opinion, every fetal brain examination should include, at the very least, visualization of the transventricular and transcerebellar planes (Figure 6). Due to the rapid and dynamic developmental changes of the brain that occur both during pregnancy and after delivery, the patient should be informed not only of the technical limitations of these examinations but also of those related to temporal issues.

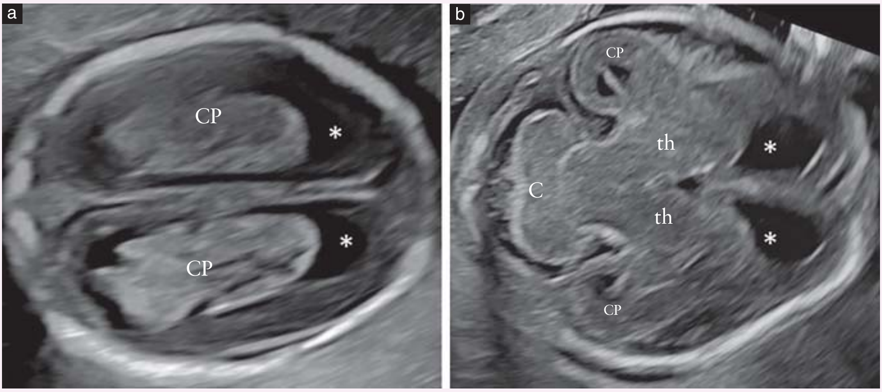


Figure 6 Transventricular (a) and transcerebellar (b) planes of fetal brain at 16 weeks. (a) In transventricular plane, lateral ventricles are large in relation to surrounding thin brain parenchyma. Frontal horns (∗) are round and filled with cerebrospinal fluid. Choroid plexuses (CP) fill body, atria, occipital and temporal horns of lateral ventricles and may present irregular external boundaries. (b) In transcerebellar plane, in early second trimester, cerebellum (C) has dumbbell shape and superior vermis is present and isoechogenic relative to hemispheres (whereas it becomes weakly hyperechogenic later in gestation). Anterior horns (∗), thalami (th), part of occipital horns of lateral ventricles and choroid plexuses (CP) are observed.

INDICATIONS FOR TARGETED FETAL NEUROSONOGRAPHY

Recommendation

- If suspicion of a brain or spinal abnormality is raised during the obstetric ultrasound screening examination, the woman should undergo targeted fetal neurosonography as a diagnostic examination (**GOOD PRACTICE POINT**).

Targeted fetal neurosonography is a dedicated, multiplanar, diagnostic examination for fetuses at high risk or with suspicion of CNS or spinal malformations. Indications for referral are shown in Table 2. Analogous to fetal echocardiography in the context of congenital heart disease, neurosonography has a much greater diagnostic potential than does the screening transabdominal ultrasound examination, and it is particularly helpful in the evaluation of complex malformations. Of note, this examination requires a high level of expertise in both transabdominal and transvaginal approaches as well as in three-dimensional ultrasound, which is still not available in many settings worldwide. In addition to the planes used in the screening examination, it requires coronal and sagittal views. All details regarding the technical and practical aspects of targeted fetal neurosonography are addressed in Part 2 of this Guideline.

Table 2 Indications for targeted fetal neurosonography

• Suspicion of CNS or spinal malformation at routine screening ultrasound
• Suspicion of CNS or spinal malformation at nuchal translucency scan
• Family history of inheritable CNS or spinal malformations
• Previous pregnancy complicated by fetal brain or spinal malformation
• Fetus with congenital heart disease
• Monochorionic twins
• Suspected congenital intrauterine infection
• Exposure to teratogens known to affect neurogenesis
• Chromosomal microarray findings of unknown significance

CNS, central nervous system.

INDICATIONS FOR FETAL BRAIN MRI

Recommendation

- Fetal brain MRI should be indicated by the findings of the expert performing the targeted neurosonographic examination. It is not appropriate to request MRI based only on suspicion of brain abnormality raised at screening ultrasound (**GOOD PRACTICE POINT**).

The introduction of MRI for evaluation of the fetal brain has provided a new and important diagnostic tool and has boosted research into and education on the complexities of the developing brain[35,36]. ISUOG Guidelines for the performance and reporting of fetal MRI have been published recently and provide important information on this technique[37]. However, stricter adherence to standard referral protocols is mandatory in order to avoid requests for fetal brain MRI directly from the operator performing a screening examination or a scan that is marginally more advanced than screening[38,39]. Inappropriate referrals have resulted in both a falsely high rate of clinically relevant malformations being detected only by MRI (and published as such) and an exponential rise in fetal brain MRI requests for questionable sonographic findings. In fact, when the results of these publications are analyzed carefully, the clinical usefulness of MRI in fetuses with suspicion of a CNS anomaly is much lower[40,41]. Furthermore, the issue of high rates of false-positive MRI findings has been raised recently[42]. It is therefore important that fetal brain MRI is performed only after, and to complement, a neurosonographic examination, and only if indicated by an expert.

GUIDELINE AUTHORS

This Guideline was produced on behalf of the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) by the following authors, and peer reviewed by the Clinical Standards Committee.

G. Malinger, Division of Ultrasound in Obstetrics and Gynecology, Lis Maternity Hospital, Tel Aviv Sourasky Medical Center, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

D. Paladini, Fetal Medicine and Surgery Unit, Istituto G. Gaslini, Genoa, Italy

K. K. Haratz, Division of Ultrasound in Obstetrics and Gynecology, Lis Maternity Hospital, Tel Aviv Sourasky Medical Center, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

A. Monteagudo, Carnegie Imaging for Women, Obstetrics, Gynecology and Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, NY, USA

G. Pilu, Obstetric Unit, Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy

I. E. Timor-Tritsch, Division of Obstetrical and Gynecological Ultrasound, NYU School of Medicine, New York, NY, USA

CITATION

This Guideline should be cited as: 'Malinger G, Paladini D, Haratz KK, Monteagudo A, Pilu G, 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; **56**: 476–484.

REFERENCES

1. Myrianthopoulos NC. Epidemiology of central nervous system malformations. In *Handbook of Clinical Neurology*,Vinken PJ, Bruyn GW (eds). Elsevier: Amsterdam, 1977; 139–171.
2. Salomon LJ, Alfirevic Z, Berghella V, Bilardo C, Hernandez-Andrade E, Johnsen SL, Kalache K, Leung KY, Malinger G, Munoz H, Prefumo F, Toi A, Lee W, Committee ICS. Practice guidelines for performance of the routine mid-trimester fetal ultrasound scan. *Ultrasound Obstet Gynecol* 2011; **37**: 116–126.
3. Timor-Tritsch IE, Rottem S. *Transvaginal Sonography*. Elsevier: New York, 1988.
4. Rottem S, Bronshtein M, Thaler I, Brandes JM. First trimester transvaginal sonographic diagnosis of fetal anomalies. *Lancet* 1989; **1**: 444–445.
5. Johnson SP, Sebire NJ, Snijders RJ, Tunkel S, Nicolaides KH. Ultrasound screening for anencephaly at 10–14 weeks of gestation. *Ultrasound Obstet Gynecol* 1997; **9**: 14–16.
6. Ghi T, Pilu G, Savelli L, Segata M, Bovicelli L. Sonographic diagnosis of congenital anomalies during the first trimester. *Placenta* 2003; **24** (Suppl B): S84–87.
7. Monteagudo A, Timor-Tritsch IE. Normal sonographic development of the central nervous system from the second trimester onwards using 2D, 3D and transvaginal sonography. *Prenat Diagn* 2009; **29**: 326–339.
8. Chaoui R, Nicolaides KH. Detecting open spina bifida at the 11–13-week scan by assessing intracranial translucency and the posterior brain region: mid-sagittal or axial plane? *Ultrasound Obstet Gynecol* 2011; **38**: 609–612.
9. D'Antonio F, Familiari A, Thilaganathan B, Papageorghiou AT, Manzoli L, Khalil A, Bhide A. Sensitivity of first-trimester ultrasound in the detection of congenital anomalies in twin pregnancies: population study and systematic review. *Acta Obstet Gynecol Scand* 2016; **95**: 1359–1367.
10. Filly RA, Cardoza JD, Goldstein RB, Barkovich AJ. Detection of fetal central nervous system anomalies: a practical level of effort for a routine sonogram. *Radiology* 1989; **172**: 403–408.
11. Falco P, Gabrielli S, Visentin A, Perolo A, Pilu G, Bovicelli L. Transabdominal sonography of the cavum septum pellucidum in normal fetuses in the second and third trimesters of pregnancy. *Ultrasound Obstet Gynecol* 2000; **16**: 549–553.
12. Malinger G, Lev D, Oren M, Lerman-Sagie T. Non-visualization of the cavum septi pellucidi is not synonymous with agenesis of the corpus callosum. *Ultrasound Obstet Gynecol* 2012; **40**: 165–170.
13. Paladini D, Pastore G, Cavallaro A, Massaro M, Nappi C. Agenesis of the fetal corpus callosum: sonographic signs change with advancing gestational age. *Ultrasound Obstet Gynecol* 2013; **42**: 687–690.
14. Malinger G, Lev D, Kidron D, Heredia F, Hershkovitz R, Lerman-Sagie T. Differential diagnosis in fetuses with absent septum pellucidum. *Ultrasound Obstet Gynecol* 2005; **25**: 42–49.
15. Shen O, Gelot AB, Moutard ML, Jouannic JM, Sela HY, Garel C. Abnormal shape of the cavum septi pellucidi: an indirect sign of partial agenesis of the corpus callosum. *Ultrasound Obstet Gynecol* 2015; **46**: 595–599.
16. Karl K, Esser T, Heling KS, Chaoui R. Cavum septi pellucidi (CSP) ratio: a marker for partial agenesis of the fetal corpus callosum. *Ultrasound Obstet Gynecol* 2017; **50**: 336–341.
17. Cardoza JD, Filly RA, Podrasky AE. The dangling choroid plexus: a sonographic observation of value in excluding ventriculomegaly. *AJR Am J Roentgenol* 1988; **151**: 767–770.
18. Cardoza JD, Goldstein RB, Filly RA. Exclusion of fetal ventriculomegaly with a single measurement: the width of the lateral ventricular atrium. *Radiology* 1988; **169**: 711–714.
19. Mahony BS, Nyberg DA, Hirsch JH, Petty CN, Hendricks SK, Mack LA. Mild idiopathic lateral cerebral ventricular dilatation in utero: sonographic evaluation. *Radiology* 1988; **169**: 715–721.
20. Pilu G, Reece EA, Goldstein I, Hobbins JC, Bovicelli L. Sonographic evaluation of the normal developmental anatomy of the fetal cerebral ventricles: II. The atria. *Obstet Gynecol* 1989; **73**: 250–256.
21. Pretorius DH, Kallman CE, Grafe MR, Budorick NE, Stamm ER. Linear echoes in the fetal cisterna magna. *J Ultrasound Med* 1992; **11**: 125–128.
22. Bromley B, Nadel AS, Pauker S, Estroff JA, Benacerraf BR. Closure of the cerebellar vermis: evaluation with second trimester US. *Radiology* 1994; **193**: 761–763.
23. Shepard M, Filly RA. A standardized plane for biparietal diameter measurement. *J Ultrasound Med* 1982; **1**: 145–150.
24. Snijders RJ, Nicolaides KH. Fetal biometry at 14–40 weeks' gestation. *Ultrasound Obstet Gynecol* 1994; **4**: 34–48.
25. Bahlmann F, Reinhard I, Schramm T, Geipel A, Gembruch U, von Kaisenberg CS, Schmitz R, Stupin J, Chaoui R, Karl K, Kalache K, Faschingbauer F, Ponnath M, Rempen A, Kozlowski P. Cranial and cerebral signs in the diagnosis of spina bifida between 18 and 22 weeks of gestation: a German multicentre study. *Prenat Diagn* 2015; **35**: 228–235.
26. Jian N, Lin N, Tian MM, Zhang S, Li G, Zhao H, Xiao LX, Liang WJ, Lin XT. Normal development of costal element ossification centers of sacral vertebrae in the fetal spine: a postmortem magnetic resonance imaging study. *Neuroradiology* 2019; **61**: 183–193.
27. Pilu G, Falco P, Gabrielli S, Perolo A, Sandri F, Bovicelli L. The clinical significance of fetal isolated cerebral borderline ventriculomegaly: report of 31 cases and review of the literature. *Ultrasound Obstet Gynecol* 1999; **14**: 320–326.
28. Gaglioti P, Danelon D, Bontempo S, Mombro M, Cardaropoli S, Todros T. Fetal cerebral ventriculomegaly: outcome in 176 cases. *Ultrasound Obstet Gynecol* 2005; **25**: 372–377.
29. Pagani G, Thilaganathan B, Prefumo F. Neurodevelopmental outcome in isolated mild fetal ventriculomegaly: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2014; **44**: 254–260.
30. Mehlhorn AJ, Morin CE, Wong-You-Cheong JJ, Contag SA. Mild fetal cerebral ventriculomegaly: prevalence, characteristics, and utility of ancillary testing in cases presenting to a tertiary referral center. *Prenat Diagn* 2017; **37**: 647–657.
31. Scelsa B, Rustico M, Righini A, Parazzini C, Balestriero MA, Introvini P, Spaccini L, Mastrangelo M, Lista G, Zuccotti GV, Veggiotti P. Mild ventriculomegaly from fetal consultation to neurodevelopmental assessment: A single center experience and review of the literature. *Eur J Paediatr Neurol* 2018; **22**: 919–928.
32. Atad-Rapoport M, Schweiger A, Lev D, Sadan-Strul S, Malinger G, Lerman-Sagie T. Neuropsychological follow-up at school age of children with asymmetric ventricles or unilateral ventriculomegaly identified in utero. *BJOG* 2015; **122**: 932–938.
33. Sadan S, Malinger G, Schweiger A, Lev D, Lerman-Sagie T. Neuropsychological outcome of children with asymmetric ventricles or unilateral mild ventriculomegaly identified in utero. *BJOG* 2007; **114**: 596–602.
34. Mahony BS, Callen PW, Filly RA, Hoddick WK. The fetal cisterna magna. *Radiology* 1984; **153**: 773–776.
35. Wimberger-Prayer D. *Fetal MRI*. Springer-Verlag: Berlin, Heidelberg, 2011.
36. Garel C. *MRI of the Fetal Brain. Normal Development and Cerebral Pathologies*. Springer-Verlag: Berlin, Heidelberg, 2004.
37. Prayer D, Malinger G, Brugger PC, Cassady C, De Catte L, De Keersmaecker B, Fernandes GL, Glanc P, Goncalves LF, Gruber GM, Laifer-Narin S, Lee W, Millischer

AE, Molho M, Neelavalli J, Platt L, Pugash D, Ramaekers P, Salomon LJ, Sanz M, Timor-Tritsch IE, Tutschek B, Twickler D, Weber M, Ximenes R, Raine-Fenning N. ISUOG Practice Guidelines: performance of fetal magnetic resonance imaging. *Ultrasound Obstet Gynecol* 2017; **49**: 671–680.

38. Levine D, Barnes PD, Robertson RR, Wong G, Mehta TS. Fast MR imaging of fetal central nervous system abnormalities. *Radiology* 2003; **229**: 51–61.
39. Griffiths PD, Bradburn M, Campbell MJ, Cooper CL, Graham R, Jarvis D, Kilby MD, Mason G, Mooney C, Robson SC, Wailoo A, on behalf of the MERIDIAN collaborative group. Use of MRI in the diagnosis of fetal brain abnormalities in utero (MERIDIAN): a multicentre, prospective cohort study. *Lancet* 2017; **389**: 538–546.
40. Malinger G, Paladini D, Pilu G, Timor-Tritsch IE. Fetal cerebral magnetic resonance imaging, neurosonography and the brave new world of fetal medicine. *Ultrasound Obstet Gynecol* 2017; **50**: 679–680.
41. Paladini D, Donarini G, Rossi A. Indications for MRI in fetal isolated mild ventriculomegaly . . . '*And then, there were none*'. *Ultrasound Obstet Gynecol* 2019; **54**: 151–155.
42. Birnbaum R, Ben-Sira L, Lerman-Sagie T, Malinger G. The use of fetal neurosonography and brain MRI in cases of cytomegalovirus infection during pregnancy: A retrospective analysis with outcome correlation. *Prenat Diagn* 2017; **37**: 1335–1342.

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

Ultrasound Obstet Gynecol 2021; **57**: 661–671
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.23616

isuog.org GUIDELINES

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

Clinical Standards Committee

The International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) is a scientific organization that encourages sound clinical practice, and high-quality teaching and research related to diagnostic imaging in women's healthcare. The ISUOG Clinical Standards Committee (CSC) has a remit to develop Practice Guidelines and Consensus Statements as educational recommendations that provide healthcare practitioners with a consensus-based approach, from experts, for diagnostic imaging. They are intended to reflect what is considered by ISUOG to be the best practice at the time at which they are issued. Although ISUOG has made every effort to ensure that Guidelines are accurate when issued, neither the Society nor any of its employees or members accepts any liability for the consequences of any inaccurate or misleading data, opinions or statements issued by the CSC. The ISUOG CSC documents are not intended to establish a legal standard of care, because interpretation of the evidence that underpins the Guidelines may be influenced by individual circumstances, local protocol and available resources. Approved Guidelines can be distributed freely with the permission of ISUOG (info@isuog.org). Details of the grades of recommendation and levels of evidence used in ISUOG Guidelines are given in Appendix 1.

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**).

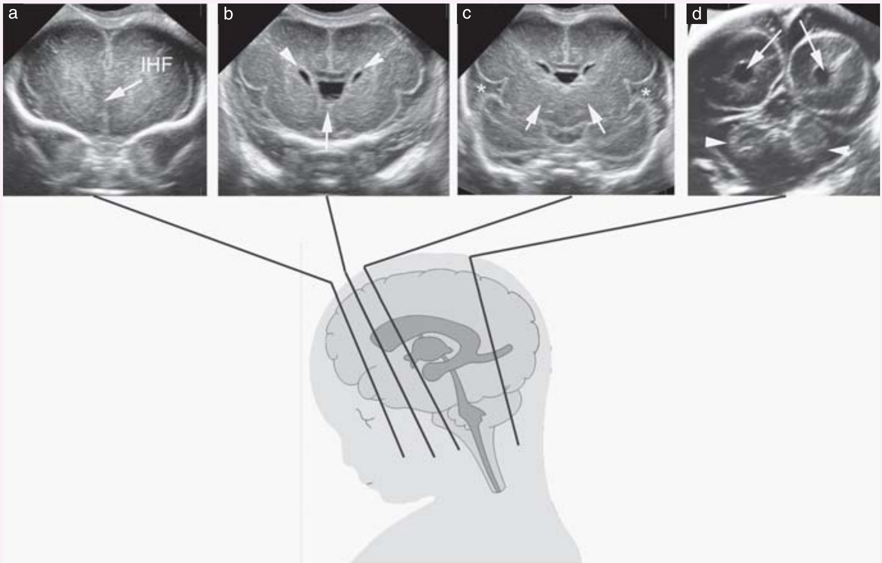


Figure 1 Coronal views of fetal head. (a) Transfrontal plane. Interhemispheric fissure (IHF) is visible between the two frontal lobes. Sphenoid bone forming roof of orbits as well as orbits themselves are also visible. (b) Transcaudate plane. The two frontal horns (arrowheads) are displayed, on either 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.

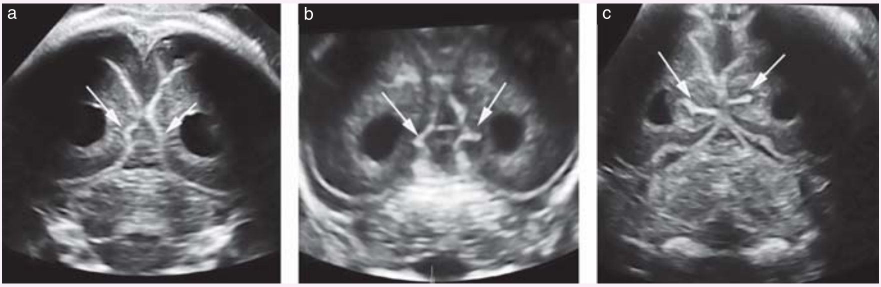


Figure 3 On transcerebellar view of fetal head, progressive development of calcarine sulci (arrows) can be seen: (a) 21 gestational weeks; (b) 26 gestational weeks; (c) 31 gestational weeks.

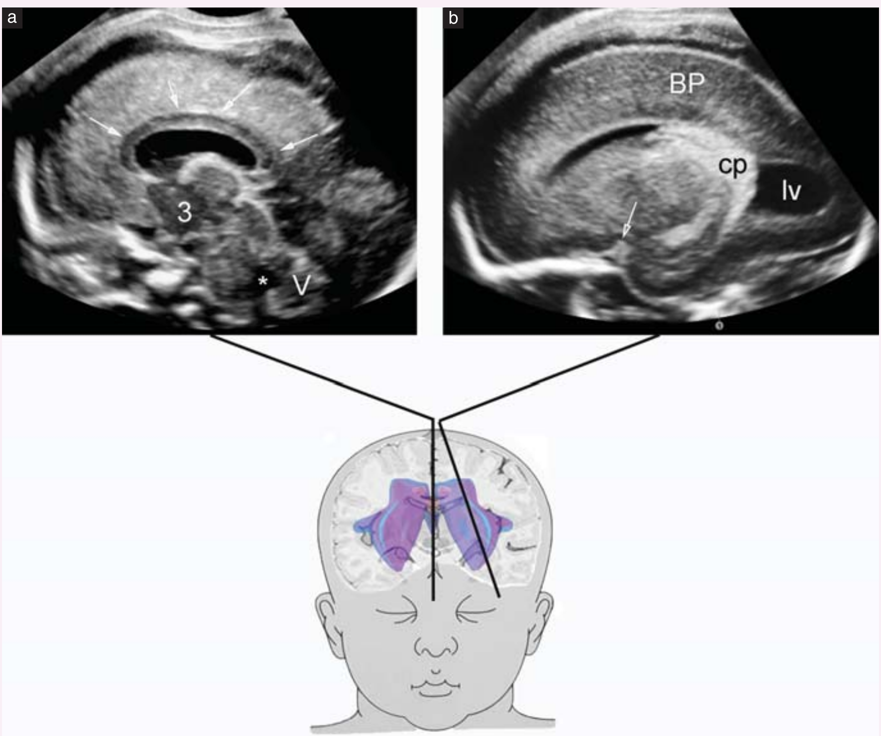


Figure 4 Sagittal planes of fetal head. (a) Midsagittal anterior plane. Anatomical landmarks that can be identified in this plane: median section of corpus callosum (arrows); below it, cavum septi pellucidi with cavum vergae (when present); third ventricle (3); fourth ventricle (⋆); cerebellar vermis (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.

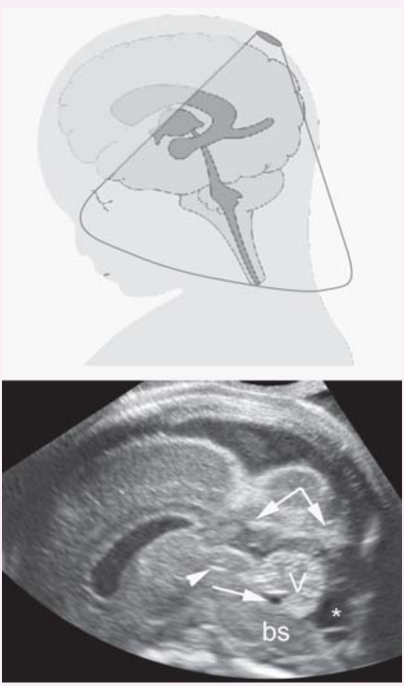


Figure 5 Midsagittal or median posterior plane is obtained by indenting posterior fontanelle and is best for assessing posterior fossa. Anatomical landmarks seen in this plane: cerebellar vermis (V), with fastigium and fourth ventricle (arrow); cisterna magna (*); tentorium (double arrow); brainstem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

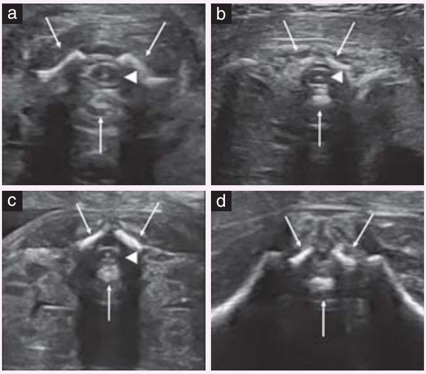


Figure 6 Axial views of fetal spine at different levels: (a) cervical; (b) thoracic; (c) lumbar; (d) sacral. Arrows indicate the three ossification centers of a vertebra. Note intact skin overlying spine. In (a–c), spinal cord is visible as hypoechoic ovoid with central white dot (arrowhead).

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,

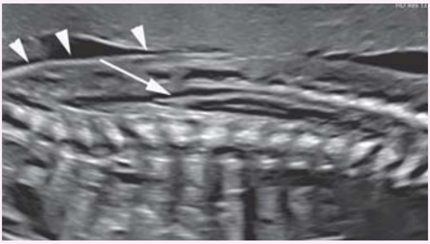


Figure 7 Sagittal view of fetal spine. Using unossified spinous process of vertebrae as acoustic window, contents of neural canal are demonstrated. After 20 weeks, conus medullaris (arrow) is normally positioned at level of second/third lumbar vertebrae (L2–L3), leaving, dorsally, triangular zone filled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

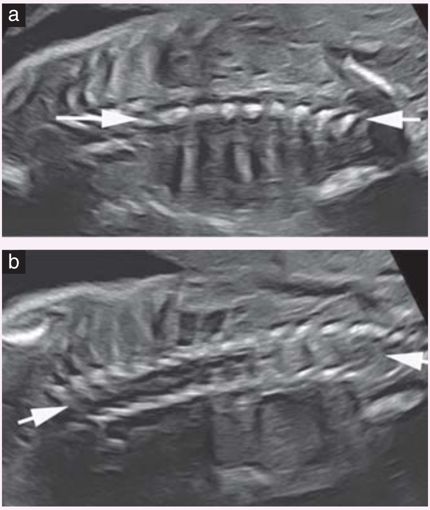


Figure 8 Coronal view of fetal spine (arrows). This plane is useful to rule out hemivertebrae and diastematomyelia. It can be obtained at level of vertebral bodies (a) or, more posteriorly, at level of arches (b). Objective is to rule out abnormal angling of spine.

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

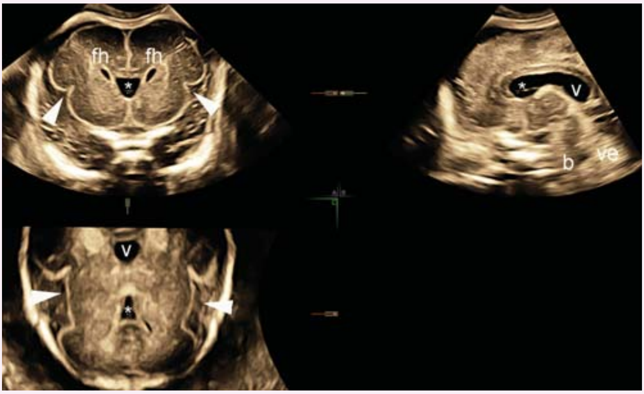


Figure 9 Three-dimensional multiplanar image correlation helps significantly in assessment of fetal brain. In this image of 26-week fetus, perfect orthogonal alignment allows visualization of all major cerebral structures in three planes. Coronal transcaudate plane (Plane A) shows frontal horns (fh) 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).

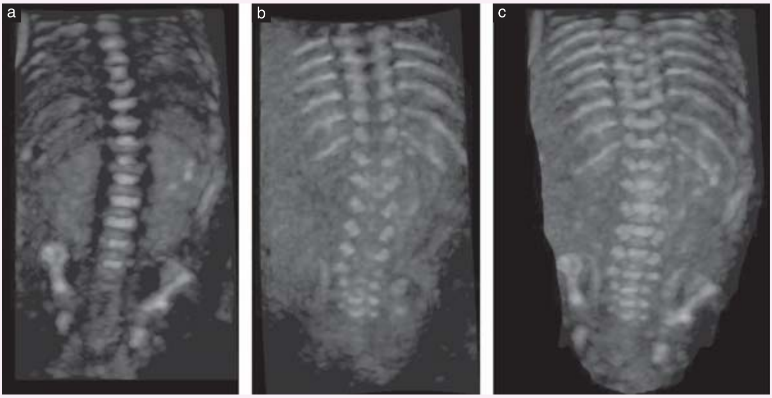


Figure 10 Three-dimensional (3D) surface-rendering of fetal spine at 22 gestational weeks: coronal views. These images were obtained with 3D ultrasound from same sonographic volume, using different angulations and thicknesses of ultrasound beam: (a) thin beam oriented through bodies of vertebrae; (b) 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

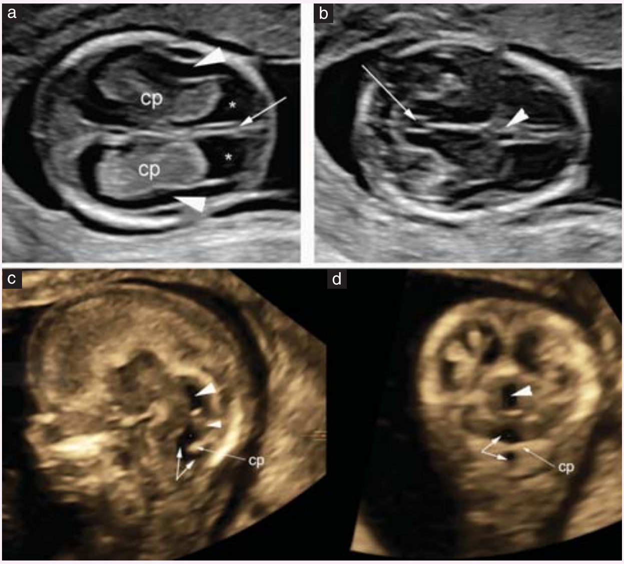


Figure 11 Neurosonography at 13 gestational weeks. (a) Transventricular axial plane, showing falx in midline (arrow) and 'butterfly sign' formed by prominent choroid plexuses (cp), with cerebrospinal fluid evident (*). Also, thin rim of developing brain parenchyma is visible as virtually anechoic strip 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

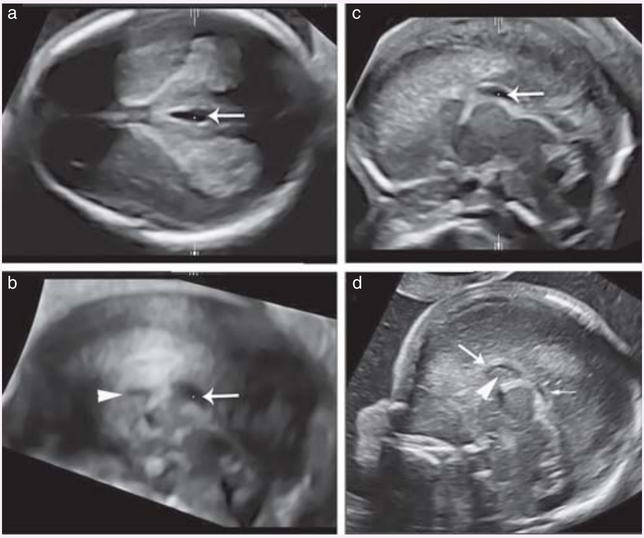


Figure 12 (a–c) Neurosonography at 15 gestational weeks. (a) In axial transventricular plane, oval anechogenic structure (arrow) is evident along midline. (b) Corresponding midsagittal plane reconstructed from (a), demonstrating that, due to its position, this structure is cavum veli interpositi (CVI) (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].

GUIDELINE AUTHORS

This Guideline was produced on behalf of the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) by the following authors, and peer reviewed by the Clinical Standards Committee.

D. Paladini, Fetal Medicine and Surgery Unit, Istituto G. Gaslini, Genoa, Italy

G. Malinger, Division of Ultrasound in Obstetrics and Gynecology, Lis Maternity Hospital, Tel Aviv Sourasky Medical Centre, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

R. Birnbaum, Division of Ultrasound in Obstetrics and Gynecology, Lis Maternity Hospital, Tel Aviv Sourasky Medical Centre, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

A. Monteagudo, Carnegie Imaging for Women, Obstetrics, Gynecology and Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, NY, USA

G. Pilu, Obstetric Unit, Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy

L. J. Salomon, Hôpital Necker Enfants Malades, AP-HP, and LUMIERE platform, EA 7328 Université de Paris, Paris, France

I. E. Timor-Tritsch, Division of Obstetrical and Gynecological Ultrasound, NYU School of Medicine, New York, NY, USA

CITATION

This Guideline should be cited as: '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. https://doi.org/10.1002/uog.23616.

REFERENCES

1. Tagliabue G, Tessandori R, Caramaschi F, Fabiano S, Maghini A, Tittarelli A, Vergani D, Bellotti M, Pisani S, Gambino ML, Frassoldi E, Costa E, Gada D, Crosignani P, Contiero P. Descriptive epidemiology of selected birth defects, areas of Lombardy, Italy, 1999. *Popul Health Metr* 2007; **5**: 4.
2. Atta CA, Fiest KM, Frolkis AD, Jette N, Pringsheim T, St Germaine-Smith C, Rajapakse T, Kaplan GG, Metcalfe A. Global Birth Prevalence of Spina Bifida by Folic Acid Fortification Status: A Systematic Review and Meta-Analysis. *Am J Public Health* 2016; **106**: e24–34.
3. Myrianthopoulos NC. Epidemiology of central nervous system malformations. In *Handbook of Clinical Neurology*. Vinken PJ, Bruyn GW (eds). Elsevier: Amsterdam, 1977; 139–171.
4. Salomon LJ, Alfirevic Z, Berghella V, Bilardo C, Hernandez-Andrade E, Johnsen SL, Kalache K, Leung KY, Malinger G, Munoz H, Prefumo F, Toi A, Lee W, Committee ICS. Practice guidelines for performance of the routine mid-trimester fetal ultrasound scan. *Ultrasound Obstet Gynecol* 2011; **37**: 116–126.
5. 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; **56**: 476–484.
6. Malinger G, Birnbam R, Haratz KK. Dedicated neurosonography for recognition of pathology associated with mild-to-moderate ventriculomegaly. *Ultrasound Obstet Gynecol* 2020; **56**: 319–323.
7. Monteagudo A, Timor-Tritsch IE, Mayberry P. Three-dimensional transvaginal neurosonography of the fetal brain: 'navigating' in the volume scan. *Ultrasound Obstet Gynecol* 2000; **16**: 307–313.
8. Malinger G, Katz A, Zakut H. Transvaginal fetal neurosonography. Supratentorial structures. *Isr J Obstet Gynecol* 1993; **4**: 1–5.
9. Timor-Tritsch IE, Monteagudo A. Transvaginal fetal neurosonography: standardization of the planes and sections by anatomic landmarks. *Ultrasound Obstet Gynecol* 1996; **8**: 42–47.
10. Timor-Tritsch IE, Monteagudo A, Pilu G, Malinger G. *Ultrasonography of the fetal brain*. McGraw-Hill: New York, 2012.
11. Paladini D, Donarini G, Rossi A. Indications for MRI in fetal isolated mild ventriculomegaly… 'And then, there were none'. *Ultrasound Obstet Gynecol* 2019; **54**: 151–155.
12. Napolitano R, Molloholli M, Donadono V, Ohuma EO, Wanyonyi SZ, Kemp B, Yaqub MK, Ash S, Barros FC, Carvalho M, Jaffer YA, Noble JA, Oberto M, Purwar M, Pang R, Cheikh Ismail L, Lambert A, Gravett MG, Salomon LJ, Bhutta ZA, Kennedy SH, Villar J, Papageorghiou AT, International F, Newborn Growth Consortium for the 21st C. International standards for fetal brain structures based on serial ultrasound measurements from Fetal Growth Longitudinal Study of INTERGROWTH-21st Project. *Ultrasound Obstet Gynecol* 2020; **56**: 359–370.
13. Droulle P, Gaillet J, Schweitzer M. [Maturation of the fetal brain. Echoanatomy: normal development, limits and value of pathology]. *J Gynecol Obstet Biol Reprod* 1984; **13**: 228–236.
14. Monteagudo A, Timor-Tritsch IE. Development of fetal gyri, sulci and fissures: a transvaginal sonographic study. *Ultrasound Obstet Gynecol* 1997; **9**: 222–228.
15. Cohen-Sacher B, Lerman-Sagie T, Lev D, Malinger G. Developmental milestones of the fetal cerebral cortex. A longitudinal sonographic study. *Ultrasound Obstet Gynecol* 2006; **27**: 494–502.
16. Toi A, Chitayat D, Blaser S. Abnormalities of the foetal cerebral cortex. *Prenat Diagn* 2009; **29**: 355–371.

17. Poon LC, Sahota DS, Chaemsaithong P, Nakamura T, Machida M, Naruse K, Wah YM, Leung TY, Pooh RK. Transvaginal three-dimensional ultrasound assessment of Sylvian fissures at 18–30 weeks' gestation. *Ultrasound Obstet Gynecol* 2019; **54**: 190–198.
18. Acanfora MM, Stirnemann J, Marchitelli G, Salomon LJ, Ville Y. Ultrasound evaluation of development of olfactory sulci in normal fetuses: a possible role in diagnosis of CHARGE syndrome. *Ultrasound Obstet Gynecol* 2016; **48**: 181–184.
19. Perlitz Y, Izhaki I, Ben-Ami M. Sonographic evaluation of the fetal conus medullaris at 20 to 24 weeks' gestation. *Prenat Diagn* 2010; **30**: 862–864.
20. Mottet N, Saada J, Jani J, Martin A, Riethmuller D, Zerah M, Benachi A. Sonographic Evaluation of Fetal Conus Medullaris and Filum Terminale. *Fetal Diagn Ther* 2016; **40**: 224–230.
21. Rodriguez MA, Prats P, Rodriguez I, Comas C. Prenatal Evaluation of the Fetal Conus Medullaris on a Routine Scan. *Fetal Diagn Ther* 2016; **39**: 113–116.
22. Fratelli N, Taddei F, Prefumo F, Franceschetti L, Farina G, Frusca T. Interobserver reproducibility of transabdominal 3-dimensional sonography of the fetal brain. *J Ultrasound Med* 2009; **28**: 1009–1013.
23. Maiz N, Alonso I, Belar M, Burgos J, Irasarri A, Molina FS, de Paco C, Pijoan JI, Plasencia W, Rodo C, Rodriguez MA, Tajada M, Tubau A. Three dimensional ultrasonography for advanced neurosonography (Neurosofe-3d). Analysis of acquisition-related factors influencing the quality of the brain volumes. *Prenat Diagn* 2016; **36**: 1054–1060.
24. Buyukkurt S, Binokay F, Seydaoglu G, Gulec UK, Ozgunen FT, Evruke C, Demir C. Prenatal determination of the upper lesion level of spina bifida with three-dimensional ultrasound. *Fetal Diagn Ther* 2013; **33**: 36–40.
25. Bronshtein M, Blumenfeld Z. Transvaginal sonography-detection of findings suggestive of fetal chromosomal anomalies in the first and early second trimesters. *Prenat Diagn* 1992; **12**: 587–593.
26. Pooh RK. Neurosonoembryology by three-dimensional ultrasound. *Semin Fetal Neonatal Med* 2012; **17**: 261–268.
27. Rottem S, Bronshtein M, Thaler I, Brandes JM. First trimester transvaginal sonographic diagnosis of fetal anomalies. *Lancet* 1989; **1**: 444–445.
28. Votino C, Kacem Y, Dobrescu O, Dessy H, Cos T, Foulon W, Jani J. Use of a high-frequency linear transducer and MTI filtered color flow mapping in the assessment of fetal heart anatomy at the routine 11 to 13 + 6-week scan: a randomized trial. *Ultrasound Obstet Gynecol* 2012; **39**: 145–151.
29. Chaoui R, Nicolaides KH. From nuchal translucency to intracranial translucency: towards the early detection of spina bifida. *Ultrasound Obstet Gynecol* 2010; **35**: 133–138.
30. Salomon LJ, Alfirevic Z, Bilardo CM, Chalouhi GE, Ghi T, Kagan KO, Lau TK, Papageorghiou AT, Raine-Fenning NJ, Stirnemann J, Suresh S, Tabor A, Timor-Tritsch IE, Toi A, Yeo G. ISUOG practice guidelines: performance of first-trimester fetal ultrasound scan. *Ultrasound Obstet Gynecol* 2013; **41**: 102–113.
31. Paladini D, Donarini G, Parodi S, Chaoui R. Differentiating features of posterior fossa at 12-13 weeks' gestation in fetuses with Dandy-Walker malformation and Blake's pouch cyst. *Ultrasound Obstet Gynecol* 2019; **53**: 850–852.
32. Chen FC, Gerhardt J, Entezami M, Chaoui R, Henrich W. Detection of Spina Bifida by First Trimester Screening - Results of the Prospective Multicenter Berlin IT-Study. *Ultraschall Med* 2017; **38**: 151–157.
33. Meller C, Aiello H, Otano L. Sonographic detection of open spina bifida in the first trimester: review of the literature. *Childs Nerv Syst* 2017; **33**: 1101–1106.
34. Chaoui R, Benoit B, Entezami M, Frenzel W, Heling KS, Ladendorf B, Pietzsch V, Sarut Lopez A, Karl K. Ratio of fetal choroid plexus to head size: simple sonographic marker of open spina bifida at 11–13 weeks' gestation. *Ultrasound Obstet Gynecol* 2020; **55**: 81–86.
35. Ushakov F, Sacco A, Andreeva E, Tudorache S, Everett T, David AL, Pandya PP. Crash sign: new first-trimester sonographic marker of spina bifida. *Ultrasound Obstet Gynecol* 2019; **54**: 740–745.
36. Volpe P, Persico N, Fanelli T, De Robertis V, D'Alessandro J, Boito S, Pilu G, Votino C. Prospective detection and differential diagnosis of cystic posterior fossa anomalies by assessing posterior brain at 11–14 weeks. *Am J Obstet Gynecol MFM* 2019; **1**: 171–183.
37. Malinger G, Lev D, Lerman-Sagie T. The fetal cerebellum. Pitfalls in diagnosis and management. *Prenat Diagn* 2009; **29**: 372–380.
38. Birnbaum R, Barzilay R, Brusilov M, Wolman I, Malinger G. The normal cavum veli interpositi at 14-17 weeks: three-dimensional and Doppler transvaginal neurosonographic study. *Ultrasound Obstet Gynecol* 2020. DOI: 10.1002/uog.22176.
39. Birnbaum R, Barzilay R, Brusilov M, Wolman I, Malinger G. The early pattern of human corpus callosum development: A transvaginal 3D neurosonographic study. *Prenat Diagn* 2020; **40**: 1239–1245.
40. Babcook CJ, Chong BW, Salamat MS, Ellis WG, Goldstein RB. Sonographic anatomy of the developing cerebellum: normal embryology can resemble pathology. *AJR Am J Roentgenol* 1996; **166**: 427–433.
41. Contro E, Volpe P, De Musso F, Muto B, Ghi T, De Robertis V, Pilu G. Open fourth ventricle prior to 20 weeks' gestation: a benign finding? *Ultrasound Obstet Gynecol* 2014; **43**: 154–158.
42. Prayer D, Malinger G, Brugger PC, Cassady C, De Catte L, De Keersmaecker B, Fernandes GL, Glanc P, Goncalves LF, Gruber GM, Laifer-Narin S, Lee W, Millischer AE, Molho M, Neelavalli J, Platt L, Pugash D, Ramaekers P, Salomon LJ, Sanz M, Timor-Tritsch IE, Tutschek B, Twickler D, Weber M, Ximenes R, Raine-Fenning N. ISUOG Practice Guidelines: performance of fetal magnetic resonance imaging. *Ultrasound Obstet Gynecol* 2017; **49**: 671–680.
43. Malinger G, Ben-Sira L, Lev D, Ben-Aroya Z, Kidron D, Lerman-Sagie T. Fetal brain imaging: a comparison between magnetic resonance imaging and dedicated neurosonography. *Ultrasound Obstet Gynecol* 2004; **23**: 333–340.
44. Paladini D, Quarantelli M, Sglavo G, Pastore G, Cavallaro A, D'Armiento MR, Salvatore M, Nappi C. Accuracy of neurosonography and MRI in clinical management of fetuses referred with central nervous system abnormalities. *Ultrasound Obstet Gynecol* 2014; **44**: 188–196.
45. Malinger G, Paladini D, Pilu G, Timor-Tritsch IE. Fetal cerebral magnetic resonance imaging, neurosonography and the brave new world of fetal medicine. *Ultrasound Obstet Gynecol* 2017; **50**: 679–680.
46. Di Mascio D, Sileo FG, Khalil A, Rizzo G, Persico N, Brunelli R, Giancotti A, Panici PB, Acharya G, D'Antonio F. Role of magnetic resonance imaging in fetuses with mild or moderate ventriculomegaly in the era of fetal neurosonography: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2019; **54**: 164–171.

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

DE GRUYTER J. Perinat. Med. 2021; 49(9): 1033–1041

WAPM Recommendations

Valentina De Robertis*, Cihat Sen, Ilan Timor-Tritsch, Rabih Chaoui, Paolo Volpe, Alberto Galindo, Reuven Achiron, Ritsuko Pooh, Asma Khalil, Nicola Volpe, Francesco D'Antonio and Roee Birnbaum

WAPM-World Association of Perinatal Medicine Practice Guidelines: Fetal central nervous system examination

https://doi.org/10.1515/jpm-2021-0183
Received April 16, 2021; accepted April 24, 2021;
published online June 4, 2021

Abstract: These practice guidelines follow the mission of the World Association of Perinatal Medicine in collaboration with the Perinatal Medicine Foundation, bringing together groups and individuals throughout the world, with the goal of improving the ultrasound assessment of the fetal Central Nervous System (CNS) anatomy. In fact, this document provides further guidance for healthcare practitioners for the evaluation of the fetal CNS during the mid-trimester ultrasound scan with the aim to increase the ability in evaluating normal fetal anatomy. Therefore, it is not intended to establish a legal standard of care. This document is based on consensus among perinatal experts throughout the world, and serves as a guideline for use in clinical practice.

Keywords: anatomy scan; central nervous system; fetal brain; fetal spine; guidelines; second trimester; WAPM.

***Corresponding author: Valentina De Robertis**, Fetal Medicine Unit, Di Venere and Sarcone Hospitals, ASL BA, Via Ospedale Di Venere, Bari, Italy, Phone: +390805015007, E-mail: derobertis_v@libero.it
Cihat Sen, Perinatal Medicine Foundation, Istanbul, Turkey
Ilan Timor-Tritsch, Division of Obstetrical and Gynecological Ultrasound, NYU School of Medicine, New York, NY, USA
Rabih Chaoui, Center for Prenatal Diagnosis and Human Genetics, Berlin, Germany
Paolo Volpe, Fetal Medicine Unit, Di Venere and Sarcone Hospitals, ASL BA, Bari, Italy
Alberto Galindo, Department of Obstetrics and Gynaecology, Fetal Medicine Unit, Maternal and Child Health and Development Network, University Hospital 12 de Octubre, Complutense University of Madrid, Madrid, Spain
Reuven Achiron, Department of Obstetrics and Gynecology, Fetal Medicine Unit, The Chaim Sheba Medical Center Tel-Hashomer, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel
Ritsuko Pooh, Fetal Diagnostic Center, CRIFM Clinical Research Institute of Fetal Medicine, Osaka, Japan
Asma Khalil, Fetal Medicine Unit, St George University Hospital NHS Foundation Trust, London, UK
Nicola Volpe, Department of Medicine and Surgery, Unit of Surgical Sciences, Obstetrics and Gynecology, University of Parma, Parma, Italy
Francesco D'Antonio, Department of Obstetrics and Gynecology, Center for Fetal Care and High-Risk Pregnancy, University of Chieti, Chieti, Italy
Roee Birnbaum, OB-GYN Ultrasound Unit, Lis Maternity Hospital, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

Introduction

Rationale of this recommendation

Fetal central nervous system (CNS) abnormalities are fairly common, with an incidence of about 0.1–0.2% in live births and an even higher occurrence of about 3–6% in stillbirths. Such anomalies have clinical importance as they are associated with high rates of morbidity and mortality, influencing the neurocognitive and motor development of the survivors, who may have lifelong sequelae. Therefore, it is extremely important to evaluate the fetal CNS anatomy throughout the pregnancy in order to assess its normal and abnormal development.

Prenatal ultrasound (US) has been shown to be an effective primary imaging modality for depiction of normal development of CNS anatomic structures and it offers a relatively accurate, safe, and cost-effective screening in pregnancy [1, 2].

Although some abnormalities may be suspected and diagnosed in the first trimester of pregnancy [3–5], most efforts to detect CNS malformations occur during the second trimester, in the examination of fetal morphology conducted at 22 (18–24) weeks of gestation. The majority of national and international guidelines recommend at this gestational age an US examination to delineate fetal anatomy as a part of standard obstetric care.

As a matter of fact, at this gestational age, the major intracranial structures have formed from their embryologic origins and can be well visualized by US.

The aim of the mid-trimester scan in low-risk pregnancies is fundamentally to establish the normal anatomy of the fetal brain and spine. For anatomical evaluation of CNS in routine practice, axial planes have been proposed as the standard planes. However, the major disadvantages of the use of these axial planes are the poor visualization of the hemisphere proximal to the transducer and the difficult depiction of midline brain structures, mainly the corpus callosum and the cerebellar vermis due to its anatomical location and orientation. Therefore, additional planes such as median/midsagittal view should be taken into consideration [6].

If the ultrasonographic finding of CNS structures differs from normal anatomy, a further evaluation by a competent/expert operator is required in order to make a conclusive diagnosis or reassure the patient when structural anomalies are ruled out. Therefore, all the suspected abnormal cases at the anatomy scan should be referred for a "fetal neurosonography", a dedicated examination of the fetal brain and spine that requires specific expertise and sophisticated ultrasound equipment.

The prenatal detection of CNS anomalies allows, not only a specific prenatal management and counseling, but also facilitate appropriate prognostic definition with the support of supplementary diagnostic tests as MRI [7–9] and genetic tests [10]. However, it is important to emphasize that a normal CNS assessment in the second-trimester morphology scan does not rule out the emergence of fetal anomalies later in pregnancy. In fact, some of the CNS anomalies can be diagnosed only during late second and third trimesters of pregnancy. Consequently, in patients who have a third trimester scan for any reason, assessment of the fetal CNS should be considered [11, 12].

The scope of this document is to reach a consensus about an optimized approach to the evaluation of the CNS anatomy in routine obstetric care in low-risk pregnancies at 22 (18–24) weeks of gestation in order to improve the prenatal detection of these severe anomalies.

Technical issues

Ultrasound transducers

High-frequency ultrasound transducers increase spatial resolution but decrease the penetration of the sound beam. The selection of the optimal transducer and frequency depends on gestational age, maternal habitus, position of the fetus, and the scanning approach used. Transabdominal transducers with 3–5 MHz, are mostly used, however while they "penetrate" deeper, their resolution is lower than high frequency probe such as 4–8 MHz and those of the transvaginal probe, which operate at higher frequencies increasing resolution [6].

The examination is usually performed with grayscale 2D ultrasound. It may be important to mention that harmonic and speckle-reduction filters, may enhance image quality mainly in patients with increased body mass index or abdominal scars.

The use of transvaginal probes should be always entertained if the fetus is in cephalic presentation. At times, if relevant, a gentle external version of a breech to vertex presentation can be helpful [12].

Methods

With the scope of reaching a consensus among experts, a survey was conducted among members of the group.

All possible anatomical structures of the fetal brain and spine were listed and group members were asked to answer the following questions:

- Should the following anatomical structures be evaluated always, possibly or never at the time of second trimester anatomy scan?
- Do you suggest one or more planes?
- Which would be the need for transvaginal approach to visualize the listed anatomical structures on each plane?

Agreement among members was evaluated for each anatomical structure and scanning plane.

The evaluation of anatomical structures and scanning planes that should always be evaluated with an agreement among members exceeding 75%, are referred in this document as "recommended" as part of the mid-trimester anatomy scan. The evaluation of anatomical structures and scanning planes that should be possibly evaluated with an agreement among members exceeding 75%, are referred in this document as "suggested" as part of the mid-trimester anatomy scan. The evaluation of anatomical structures and scanning planes that should never be evaluated with an agreement among members exceeding 75%, are considered in this document as not being part of the mid-trimester anatomy scan.

The same method was applied for the quantitative assessment.

All possible anatomical structures of the fetal brain reported in the literature as measurable were listed and group members were asked to answer the following questions:

- Should the following anatomical structures be measured always, possibly or never?
- Do you suggest one or more planes?

The measurements of anatomical structures and scanning planes that should always be evaluated with an agreement among members exceeding 75%, are referred in this document as "recommended" as part of the mid-trimester anatomy scan. The measurement of anatomical structures and scanning planes that should be possibly evaluated with an agreement among members exceeding 75%, are referred in this document as "suggested" as part of the mid-trimester anatomy scan. The measurement of anatomical structures and scanning planes that should never be evaluated with an agreement among members exceeding 75%, are considered in this document as not being part of the mid-trimester anatomy scan.

CNS examination in routine practice

1) Skull ossification

Under normal condition the skull has a regular oval shape with no bony defects (distortion or disruption) (Figure 1A). An hypoechoic rim is identifiable only at the level of the sutures, in particular the coronal one between the frontal and the parietal bones.

Recommendations

- The normal shape of the fetal head/skull and the cranial bone ossification should be assessed at the anatomy scan by axial scans (trans-thalamic or trans-ventricular planes).
- It is suggested to look specifically for bone ossification also in sagittal plane. The frontal area should be examined and to rule out frontal bossing and the occipital area for posterior encephalocele.

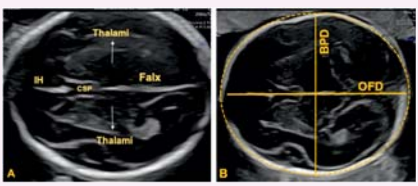


Figure 1: Trans-thalamic plane.
(A) The cavum septi pellucidi (CSP), the interhemispheric fissure (IH), the falx, the thalami and the symmetry of the cerebral hemispheres can be assessed. (B) Biometric measurements of the fetal head: biparietal diameter (BPD), occipito-frontal diameter (OFD) and head circumference (dotted line).

- The measurement of biparietal diameter (BPD) and circumference of the head (HC) should be performed at the anatomy scan by axial scan (trans-thalamic plane).

Technical issues

- BPD should be measured with the caliper either on the external edges of the parietal bones (out-out), or with just one caliper on the outer and the other on the inner edge of these bones, according to the methodology described for the chosen growth charts. The HC could either be measured adjusting the ellipse tool of the ultrasound machine on the calvarium, or it can be calculated by the ellipsoid formula after combining the BPD and the occipito-frontal diameter (OFD) (Figure 1B).

2) Symmetry of hemispheres

Under normal condition the hemispheres appear symmetrical (Figure 1A) (Supplementary Material Video 1).

Recommendation

- Symmetry of hemispheres should be assessed at the anatomy scan by axial scans (trans-thalamic or trans-ventricular planes).

3) Falx (interhemispheric fissure)

Under normal condition the hemispheres appear separated by a clearly visible interhemispheric fissure and falx (Figures 1A and 2A) (Supplementary Material Video 1).

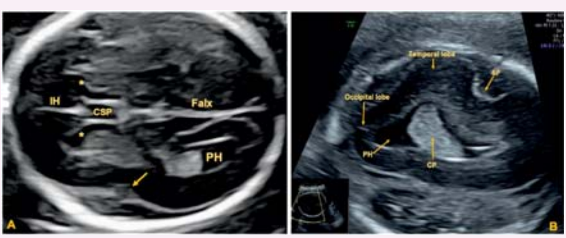


Figure 2: Qualitative evaluation of the occipital horns of the lateral ventricle.
(A) Trans-ventricular plane: The transventricular plane provides an adequate visualization of the hemisphere distal to the transducer. In this plane the interhemispheric fissure (IH), cavum septi pellucidi (CSP), two frontal horns (*), falx and insula (arrow) can also be assessed. (B) Angling the transducer from the axial transthalamic view cranially by up to 45°, the ultrasound access to the proximal hemisphere is feasible (PH, posterior horn; CP, choroid plexus; SF, sylvian fissure).

Recommendation

- The presence of a central interhemispheric fissure and a falx dividing equally the hemispheres should be assessed at the anatomy scan by axial scans (trans-thalamic or trans-ventricular planes).

4) Lateral ventricles: occipital horns (atrium)

Under normal condition the occipital horns of lateral ventricles appear as sonolucent structures with the echoic choroid plexuses filling the ventricular bodies and atria. Atria are characterized by the presence of the glomus of the choroid plexus, which is highly echogenic and fills the cavity of the ventricle at the level of the atrium, while the occipital horn is filled with cerebrospinal fluid (Figure 2A) (Supplementary Material Video 1).

Recommendations

- The occipital horn of the lateral ventricle distal to the transducer should be assessed at the anatomy scan by axial scans (trans-ventricular plane).
- Efforts should be made to evaluate both occipital horns of the lateral ventricles.
- The atrial width of the lateral ventricle distal to the transducer should be measured at the anatomy scan by axial scan (trans-ventricular plane).

Technical issues

- The transventricular plane provides an adequate visualization of the hemisphere distal to the transducer. However, one of the major disadvantages of the use of this axial plane is the poor visualization of the hemisphere proximal to the transducer. In order to reduce near-field reverberation to the bony calvarium, the suggestion is to angle the transducer from the axial transthalamic view cranially by up to 45° (Figure 2B). This technique showed to allow the ultrasound access to the proximal hemisphere [12, 13].
- For evaluating the atrial width of the lateral ventricle distal to the transducer the line should be traced perpendicular to the axis of the posterior horn, at the level of the glomus. Some authors suggest to use the parieto-occipital fissure as landmark, in order to improve the reproducibility of this measurement (Figure 3A) [14]. Calipers should be placed “in to in” as shown in Figure 3B. The axial width of the atrium has a normal range <10 mm, independently from gestational age.
- There is no a standardized technique for the measurement of the atrial width of the lateral ventricle proximal to the transducer. To detect unilateral ventriculomegaly affected the proximal ventricle, a qualitative assessment should be performed to obtain a valuable information on the global symmetry of the ventricles. In the case of ventricular asymmetry with the proximal ventricle significantly larger than the distal ventricle, the suggestion is to wait until fetal position changes and the suspected abnormal ventricle becomes distal to the transducer or the patient should be referred for expert evaluation [14].

5) Lateral ventricles: frontal horns

Under normal condition the anterior portion of the lateral ventricles (frontal or anterior horns) appears as two comma-shaped, fluid-filled structures medially separated by the cavum septi pellucidi (CSP) (Figures 2A and 4A) (Supplementary Material Video 1).

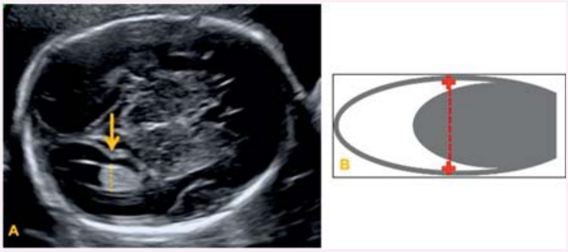


Figure 3: Quantitative assessment of the atrial width.
(A) Trans-ventricular plane for evaluating the atrial width of the lateral ventricle distal to the transducer: the line should be traced perpendicular to the axis of the posterior horn, at the level of the glomus using the parieto-occipital fissure (arrow) as landmark. (B) Calipers should be placed “in to in”.

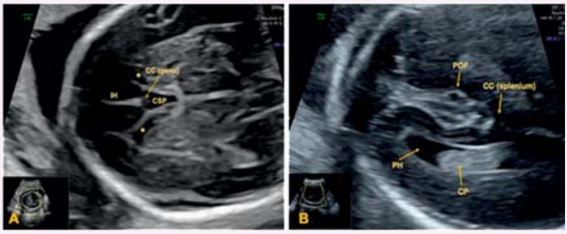


Figure 4: Anterior and posterior complex. (A) The anterior complex visible in the routine transventricular plane, shows the interhemispheric fissure (IH), two frontal horns (*) medially separated by the cavum septi pellucidi (CSP) and a cross section through the genu of the CC. (B) The posterior complex shows a cross section through the splenium of the CC (PH, posterior horn; CP, choroid plexus; POF, parieto-occipital fissure).

Recommendation

– The presence and orientation of two frontal horns of the lateral ventricles medially separated by CSP should be assessed at the anatomy scan by axial scans (trans-thalamic or trans-ventricular planes).

6) Cavum septi pellucidi

Under normal condition the CSP is detected as a fluid-filled cavity between two thin membranes located between the frontal horns of the lateral ventricles (Supplementary Material Video 1). The CSP becomes visible at about 16–18 weeks. It remains visible until about 37 weeks, when the fluid disappears and the cavity is closed by the fusion of the two layers of the septum pellucidum. It is best visible on anterior coronal views transecting the genu and the anterior portion of the body of the corpus callosum (CC) as well as the transventricular view of the brain [15] (Figures 2A and 4A). Failure to visualize the CSP or its abnormal appearance [16] is predictive of commissural anomalies. However, the normal appearance of CSP does not exclude all CC abnormalities.

Recommendation

– The presence of the CSP should be assessed at the anatomy scan by axial scans (trans-thalamic or trans-ventricular planes).

7) Corpus callosum

The CC represents the major commissure between the two cerebral hemispheres; it extends from the frontal lobe anteriorly to above the quadrigeminal plate and into the quadrigeminal cistern posteriorly. Under normal condition the corpus callosum is present with all its components, going front to back: rostrum, genu, body and splenium. The leaves of the septum pellucidum enclose the space of the cavum septi pellucidi, which is located under the CC.

The CC appears as hypoechoic midline structure at US. Recently the possibility to visualize some portions of CC in axial planes has been described [15]. The anterior complex, a group of anatomical structures visible on the routine transventricular imaging plane, allows to visualize a cross section through the genu of the CC (Figure 4A). Although technically more difficult, slicing cranially from the trans-ventricular plane, the posterior complex may be depicted showing a cross section through the splenium of the CC (Figure 4B).

However, the ultimate proof of the presence of the CC has been proven only by median/mid-sagittal plane of the fetal brain. Although some indirect signs of the absence of the CC could be identifiable in axial scans, the direct evaluation of CC in all its components requires a median/midsagittal plane (Figure 5) (Supplementary Material Videos 2 and 3) [17]. In addition, it is worth mentioning that the depiction of an apparently normal corpus callosum is not necessarily a guarantee that it will remain normal, since this does not exclude the possibility of subtle callosal developmental congenital anomalies or callosal pathologies that may develop later in pregnancy or even after delivery due to brain insults such as ischemia or infection [18].

Recommendation

– The median/midsagittal view should be performed to directly demonstrate the CC in terms of presence/absence (complete-partial).

Technical issues

– The median/midsagittal plane is obtained aligning the transducer with the large midline acoustic window,

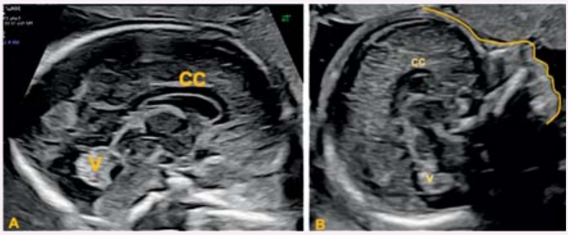


Figure 5: Median/midsagittal plane. (A) The plane obtained through the anterior fontanelle showing simultaneously the corpus callosum (CC) and the cerebellar vermis (v). (B) Transfrontal view: The median/midsagittal plane obtained through the frontal or metopic suture showing simultaneously the facial profile, the corpus callosum (CC) and the cerebellar vermis (v).

formed from anterior to posterior by the frontal or metopic suture, the bregmatic fontanel, the sagittal suture and posterior fontanel. During mid pregnancy, the large anterior fontanelle provides the optimal acoustic window for the midsagittal visualization of the entire CC, enabling a shadow free and perpendicular insonation approach (Figure 5A) (Supplementary Material Video 2). When technically limited, a more frontal midsagittal view obtained through the metopic suture, showing simultaneously the facial profile, may be optional (Figure 5B) (Supplementary Material Video 3) [2, 6, 19]. This approach is often feasible transabdominally, subjected to maternal habitus and fetal position. Obtain a standard mid-sagittal view of the fetal profile, angulate the transducer in order to use the acoustic window of the frontal suture and the anterior fontanel, thus demonstrating the CC, fine side-to-side movements may be needed in order to achieve an ideal image of the CC (Figure 5B) (Supplementary Material Video 3). The transfrontal view allows clear visualization of the midline structures of the fetal brain comparable with that obtained through the anterior or bregmatic fontanelle [19].
- Adequate demonstration of the CC in the second trimester can often be achieved by standard transabdominal ultrasonography. However, in cephalic fetal presentation, a transvaginal scan provides better resolution. In breech presentation, a transfundal approach is the only possibility [18].
- It is important to know that the position of the fetal head is dynamic and may be gently manipulated during sonography by the transducer or the physician's free hand [18].
- If the fetal position is not adequate to obtain a median view of the fetal brain, please repeat the evaluation in 15–30 min until the fetus changes position. If after a reasonable time the fetal position could not be appropriately obtained to assess this anatomical target, a note on the report should be written in order to reevaluate it in a week.

8) Thalami

Under normal condition two thalami separated from each other in the midline are detectable (Figure 1A).

Recommendation

- The presence of two thalami separated from each other in the midline should be assessed at the anatomy scan by axial scans (trans-thalamic plane).

9) Insula

The Sylvian fissure (SF) is among the most well-studied anatomical structures of the fetal cortex and demonstrate a typical pattern of development through gestation. In the early second trimester, the SF appears on the US axial view as a smooth-margined, shallow notch on the lateral side of the cerebral hemisphere (Supplementary Material Video 1). Over the course of the subsequent weeks of pregnancy, the morphology of this structure changes, showing a more prominent indentation with distinct angularity (Figure 2A) [20].

Recommendation

- The presence of a normal developed SF could be assessed for its shape at the mid-trimester anatomy scan by axial scans (trans-ventricular plane as well as transthalamic plane). That doesn't mean that we can rule out every abnormality.

10) Cerebellum

Under normal condition in the axial plane the cerebellum appears as a butterfly shaped structure (Figure 6A) (Supplementary Material Video 4) formed by the round

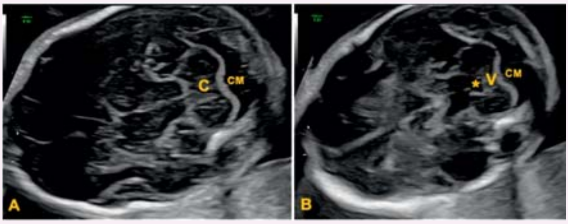


Figure 6: Transcerebellar planes.
(A) The plane includes the cerebellum (C) and behind the cerebellum, the cisterna magna (CM). (B) Moving slightly downwards the fourth ventricle (*) becomes visible, with the vermis (V) and the cisterna magna (CM) behind it.

cerebellar hemispheres joined in the middle by the slightly more echogenic cerebellar vermis.

Recommendations

- The presence of normal cerebellar hemispheres joined in the middle by the cerebellar vermis should be assessed at the anatomy scan by axial scan (trans-cerebellar plane).
- The measurement of the transverse cerebellar diameter should be performed at the anatomy scan by axial scan (trans-cerebellar plane).

11) Cerebellar vermis

Under normal condition the cerebellar vermis appears as a slightly more echogenic structure located between the cerebellar hemispheres in an axial scan. At the time of mid-trimester scan the cerebellar vermis completely covers the fourth ventricle resulting in a narrow passage between the cisterna magna and the fourth ventricle (foramen Magendie).

While the normal appearance of the cerebellar hemispheres, fourth ventricle and cisterna magna is expected to be seen by axial scan (trans-cerebellar plane), on this plane only a narrow segment of the vermis is seen. Serial axial planes with slight angulations between them performs better than a single axial plane to demonstrate the portions of the cerebellar vermis (Figure 6B) (Supplementary Material Video 4). Therefore, the direct evaluation of the cerebellar vermis in all its components in a single plane requires the median/mid-sagittal plane [21].

Recommendation

- The midsagittal/median view should be performed to directly demonstrate the cerebellar vermis in terms of presence or absence (or extreme hypoplasia).

Technical issues

- The median/midsagittal plane is obtained aligning the transducer with the large midline acoustic window, formed from anterior to posterior by the frontal or metopic suture, the bregmatic fontanel, the sagittal suture and the posterior fontanel. Even if all these approaches are possible, more details of the cerebellar vermis could be obtained by posterior insonation through the sagittal suture and the posterior fontanel (Figure 7). However, considering that the frontal or metopic suture is patent at the time of the anatomy scan, it is possible to use it as an acoustic window, showing simultaneously the facial profile and the midline structures of the brain including cerebellar vermis (Figure 5B) (Supplementary Material Video 3) [2, 6, 19]. This approach is usually feasible transabdominally.
- Adequate demonstration of the cerebellar vermis in the second trimester can often be achieved by standard

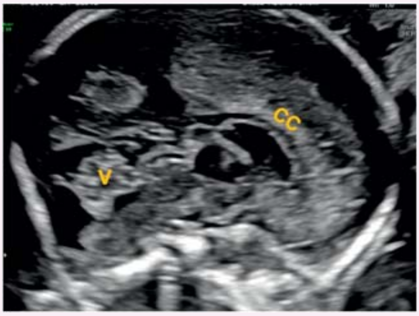


Figure 7: Posterior median/midsagittal plane through the sagittal suture.
With this approach both corpus callosum (CC) and cerebellar vermis (V) may be visualized, but more details of the cerebellar vermis could be obtained.

transabdominal ultrasonography. However, in vertex fetal presentation, a transvaginal scan provides better resolution. In breech presentation, a transfundal approach is the only possibility.
- It is important to know that the position of the fetal head is dynamic and may be gently manipulated during sonography by the transducer or the physician's free hand.
- If the fetal position is not adequate to obtain a median view of the fetal brain, please repeat the evaluation in 15–30 min until the fetus changes the position. If after a reasonable time the fetal position could not be appropriately obtained to assess this anatomical target, a note on the report should be written in order to reevaluate it in a week.

12) Cisterna magna

Under normal condition the cisterna magna or cisterna cerebello-medullaris is a fluid filled space posterior to the cerebellum (Figure 6) (Supplementary Material Video 4). It contains thin septations, that are normal structures. An abnormal cisterna magna, enlargement or obliteration, has been associated with CNS anomalies.

Recommendation

- The presence of a normal cisterna magna should be assessed at the anatomy scan by axial scan (transcerebellar plane).
- The measurement of the cisterna magna should be performed at the anatomy scan by axial scan (transcerebellar plane).

Technical issues

- The use of an angled semi-coronal plane may cause the false appearance of an enlarged cisterna magna.
- While at the time of the second trimester anatomy scan the normal developmental remnant of the Blake's pouch already disappears, at times a thin walled, anechoic fluid filled outpouching in the shape of a small "balloon" is seen in the cisterna magna. This is normal and should not be confused with any malformation of the posterior fossa [22].
- The antero-posterior diameter of the cisterna magna is the distance between the vermis and the inner border of the occipital bone, and it should not exceed 10 mm.

Figure 8: Midsagittal view of the fetal spine, showing a normal S-shaped line without any abnormal curvatures and the skin above the spine appears continuous without interruption.

- In case of an apparently large cisterna magna, it is important to proceed to a median/midsagittal plane of the posterior fossa to evaluate the normal anatomy and position of the cerebellar vermis.

13) Spine

Under a normal condition the spine appears as an S-shaped line without any abnormal curvatures and the skin above the spine appears continuous without interruption (Figure 8).

Recommendation

- The presence and regularity of the whole spine (including the sacrum) and integrity of the skin should be assessed at the anatomy scan by a sagittal scan.

Technical issues

- In most of open spina bifida there are abnormal cerebellar and cisterna magna findings, therefore if a pathology of the spine is seen a renewed evaluation of the posterior fossa is a prudent practical move to do.

Research funding: None declared.
Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.
Competing interests: Authors state no conflict of interest.
Informed consent: Not applicable.
Ethical approval: Not applicable.

References

1. Gonçalves LF, Lee W, Mody S, Shetty A, Sangi-Haghpeykar H, Romero R. Diagnostic accuracy of ultrasonography and magnetic resonance imaging for the detection of fetal anomalies: a blinded case-control study. Ultrasound Obstet Gynecol 2016;48:185–92.
2. Monteagudo A, Timor-Tritsch IE. Normal sonographic development of the central nervous system from the second trimester onwards using 2D, 3D and transvaginal sonography. Prenat Diagn 2009;29:326–39.
3. Chaoui R, Benoit B, Mitkowska-Wozniak H, Heling KS, Nicolaides KH. Assessment of intracranial translucency (IT) in the detection of spina bifida at the 11–13-week scan. Ultrasound Obstet Gynecol 2009;34:249–52.
4. Volpe P, Persico N, Fanelli T, De Robertis V, D'Alessandro J, Boito S, et al. Prospective detection and differential diagnosis of cystic posterior fossa anomalies by assessing posterior brain at 11–14 weeks. Am J Obstet Gynecol MFM 2019;1:173–81.
5. Volpe N, Dall'Asta A, Di Pasquo E, Frusca T, Ghi T. First-trimester fetal neurosonography: technique and diagnostic potential. Ultrasound Obstet Gynecol 2021;57:204–14.
6. Timor-Tritsch IE, Monteagudo A. Transvaginal fetal neurosonography: standardization of the planes and sections by anatomic landmarks. Ultrasound Obstet Gynecol 1996;8:142–7.
7. Hart AR, Embleton ND, Bradburn M, Cannolly DJA, Mandefield L, Mooney C, et al. Accuracy of in-utero MRI to detect fetal brain abnormalities and prognosticate developmental outcome: postnatal follow-up of the MERIDIAN cohort. Lancet Child Adolesc Health 2020;4:131–40.
8. Di Mascio D, Sileo FG, Khalil A, Rizzo G, Persico N, Brunelli R, et al. Role of magnetic resonance imaging in fetuses with mild or moderate ventriculomegaly in the era of fetal neurosonography: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2019;54:164–71.
9. Wataganara T, Ebrashy A, Dayyabu Aliyu L, Moreira de Sa RA, Pooh R, Kurjak A, et al. Recommendation and guidelines for perinatal practice. Fetal magnetic resonance imaging and ultrasound. J Perinat Med 2016;44:533–42.
10. Reches A, Hiersch L, Simchoni S, Barel D, Greenberg R, Sira LB, et al. Whole-exome sequencing in fetuses with central nervous system abnormalities. J Perinatol 2018;38:1301–8.
11. Yinon Y, Katorza E, Nassie DI, Ben-Meir E, Gindes L, Hoffmann C, et al. Late diagnosis of fetal central nervous system anomalies following a normal second trimester anatomy scan. Prenat Diagn 2013;33:929–34.
12. Malinger G, Birnbam R, Harats KK. Dedicated neurosonography for recognition of pathology associated with mild-to-moderate ventriculomegaly. Ultrasound Obstet Gynecol 2020;56:319–23.
13. Hormazabal L, Correa F, Escribano D, Quiroz G, Saint-Jean C, Espinel A, et al. Feasibility and agreement of including anterior-posterior complexes and landmarks of the proximal hemisphere into basic examination of the fetal brain: a prospective study. Prenat Diagn 2020;40:596–604.
14. Guibaud L. Fetal cerebral ventricular measurement and ventriculomegaly: time for procedure standardization. Ultrasound Obstet Gynecol 2009;34:127–30.
15. Vinals F, Correa F, Goncalves-Pereira PM. Anterior and posterior complexes: a step towards improving neurosonographic screening of midline and cortical anomalies. Ultrasound Obstet Gynecol 2015;46:585–94.
16. Karl K, Esser T, Heling KS, Chaoui R. Cavum septi pellucidi (CSP) ratio: a marker for partial agenesis of the fetal corpus callosum. Ultrasound Obstet Gynecol 2017;50:336–41.
17. Achiron R, Achiron A. Development of the human fetal corpus callosum:a high-resolution, cross-sectional sonographic study. Ultrasound Obstet Gynecol 2001;18:343–7.
18. Malinger G, Lev D, Lerman-Sagie T. The fetal corpus callosum. 'The truth is out there'. Ultrasound Obstet Gynecol 2007;30:140–1.
19. Youssef A, Ghi T, Pilu G. How to image the fetal corpus callosum. Ultrasound Obstet Gynecol 2013;42:718–20.
20. Pooh RK, Machida M, Nakamura T, Uenishi K, Chiyo H, Itoh K, et al. Increased Sylvian fissure angle as early sonographic sign of malformation of cortical development. Ultrasound Obstet Gynecol 2019;54:199–206.
21. Volpe P, Contro E, De Musso F, Ghi T, Farina A, Tempesta A, et al. Brainstem-vermis and brainstem-tento-rium angles allow accurate categorization of fetal upward rotation of cere-bellar vermis. Ultrasound Obstet Gynecol 2012;39:632–5.
22. Paladini D, Quarantelli M, Pastore G, Sorrentino M, Sglavo G, Nappi C. Abnormal or delayed development of the posterior membranous area of the brain: anatomy, ultrasound diagnosis, natural history and outcome of Blake's pouch cyst in the fetus. Ultrasound Obstet Gynecol 2012;39:279–87.

Supplementary Material: The online version of this article offers supplementary material (https://doi.org/10.1515/jpm-2021-0183).

SOCIETY OF FETAL MEDICINE

…….offering every fetus an optimal outcome

The Society of Fetal Medicine (SFM) is dedicated to advancing fetal care through education, research, and collaboration. We envision a world where every fetus receives the highest standard of care for optimal health outcomes. As a global forum with Indian origins, we drive innovation and foster a multidisciplinary approach to fetal medicine. Our mission includes:

- Promoting education and research through comprehensive programs and cutting-edge initiatives.
- Translating research into practice to enhance clinical outcomes.
- Encouraging interdisciplinary collaboration among experts in various fields related to fetal care.
- Organizing ongoing educational programs for healthcare professionals.
- Raising awareness and advocating for high standards of practice in fetal health.
- Upholding professional ethics to ensure integrity and quality in fetal medicine.

Through these efforts, we aim to improve fetal health worldwide, supporting families and communities in achieving better health outcomes.

SOCIETY OF
FETAL MEDICINE