Three-dimensional ultrasonographic depiction of fetal brain blood vessels

Eran Danon¹, Boaz Weisz¹, Reuven Achiron¹, Dolores H. Pretorius², Alina Weissmann-Brenner^{1*} and Liat Gindes¹

¹Department of Obstetrics and Gynecology, Chaim Sheba Medical Center (Affiliated to the Sackler School of Medicine, Tel-Aviv University), Ramat Gan, Israel ²Department of Radiology, University of California, San Diego, Thornton Hospital, San Diego, CA, USA

*Correspondence to: Alina Weissmann-Brenner. E-mail: alinabrenner@yahoo.com

ABSTRACT

Objective The objective of this study is to evaluate the fetal cerebral vasculature by three-dimensional (3D) ultrasonography and Doppler technologies in normal fetuses and to describe a systematic method for analysis of volume data sets.

Methods 3D volumes of the fetal brain were acquired prospectively in 25 patients between 12.3 and 36.3 weeks' gestation. Volumes were acquired with high-definition Doppler flow. The feasibility of identifying the fetal cerebral blood vessels and venous sinuses was analyzed.

Results A step-by-step systematic approach to identify the cerebral vasculature from ultrasonographic volume data sets was developed. The volumes were rotated into a standard anatomic orientation in the multiplanar display, and then, by systematic navigation, the vessels were demonstrated. Arteries of the circle of Willis, basilar artery, pericallosal artery, and internal carotid arteries were demonstrated in more than half of the fetuses. Tiny vessels such as those that supply the cerebellum and those that branch from the pericallosal artery were demonstrated in less than 50% of the volumes.

Conclusions The essential fetal cerebral vessels can be visualized by 3D volume analysis. Systematic analysis enables identification of the fetal brain arteries, veins, and sinuses and provides knowledge about anatomical variations and the diversity of human anatomy. © 2016 John Wiley & Sons, Ltd.

Funding sources: None.

Conflicts of interest: This work was performed in partial fulfillment of the M.D. thesis requirements of the Sackler Faculty of Medicine, Tel Aviv University.

INTRODUCTION

The anatomical structure of the early fetal cerebral circulation is of great importance for identifying normal development as well as fetal brain anomalies. Fetal cerebral vasculature is rarely studied during routine fetal ultrasonographic examinations except for MCA (middle cerebral artery) interrogation to assess for fetal anemia¹ and visualization of the pericallosal arteries to assess for absence of the corpus callosum.² Despite many years of fetal vasculature imaging by Doppler technology,³ the data regarding the prenatal sonographic appearance of fetal cerebral blood vessels are very limited.^{4,5}

Cerebral vessel malformations such as cerebral arteriovenous malformation, cavernous malformation, and aneurysms are often associated with hemorrhagic and ischemic pediatric stroke,⁶ with cerebral malformations⁷ (e. g. synophthalmicholoprosencephaly), and with cerebral and systemic consequences (e.g. congestive heart failure), that can be manifested in the first year of life.⁸ Allagile syndrome and posterior fossa malformations–hemangiomas–arterial anomalies–cardiac defects–eye abnormalities–sternal cleft and supraumbilical raphe (PHACE) syndrome are two genetic syndromes that are associated with cerebral vessel malformations.^{9–13}

The recent advent of three-dimensional ultrasonography (3DUS) enables 3D interrogation of the fetal brain. This new technology permits, for the first time, visualization of the fetal brain vasculature *in vivo*, using various color Doppler, power Doppler, high-definition (HD) flow, and B-flow imaging modes.¹⁴ Transvaginal 3D ultrasound enables early investigation of the fetal brain circulation, even during the first trimester of pregnancy.

Sonographic vasculature imaging is a well-established method. Previous studies of the fetal abdominal vasculature¹⁵ and fetal liver vasculature¹⁶ demonstrated the use of this method as a virtual angiogram of the fetal vasculature. The ability to demonstrate the whole fetal brain in one volume and perform systematic analysis of the cerebral vasculature in online and offline modes is the main advantage of the three-dimensional ultrasonography. Expanding the knowledge of

the normal fetal brain vasculature may play an important role in advancing our understanding of cerebral vessel malformations. Indeed, the possibility of precise and reproducible investigations of the fetal cerebral circulation provided by 3DUS will undoubtedly contribute to better understanding of the physiology and pathophysiology of the brain.

The objective of this study was to develop a systematic and simple method of identifying the normal fetal cerebral blood vessels using HD Doppler with 3D ultrasound volume data sets.

MATERIALS AND METHODS

Study design and patients

This was a prospective study conducted at the Sheba Medical Center. The study group included healthy pregnant women referred to the ultrasound unit at the obstetrics and gynecology department because of varied indications for routine fetal ultrasonographic examination between 12.3 and 36.3 weeks' gestation. Gestational age was confirmed by first trimester ultrasound. Inclusion criteria were singleton pregnancy, adequate for gestational age fetuses, normal complete anatomical scan, and normal clinical postnatal evaluations performed within 6 h after birth and within 48 h after birth by a specialized pediatrician. Exclusion criteria were maternal hypertension, diabetes, fetal growth restriction (<10th percentile), and suspected structural malformation on diagnostic ultrasonography. All women signed informed consent prior to performance of ultrasonographic examinations after oral and written clarification of the study's objectives. The study protocol was approved by the Institutional Review Board.

Ultrasonographic examination

The 3D volumes were taken during conventional scanning while examining the fetal headwith Voluson E8, 730 Expert, and Pro ultrasound machines (GE Healthcare, Kretz Ultrasound, Zipf, Austria) using volumetric abdominal RAB 4–8 and volumetric transvaginal RIC 5–9 transducers. The transvaginal approach was used in the earlier gestational ages and later when the fetal head was the presenting part. Low pulse repetition frequency of 0.6 kHz was used. Pulse Doppler was performed to confirm the type of vessel. The brain volumes were acquired in the sagittal and axial planes, at the thalamus level using high-definition color Doppler (HDD). The volume acquisition took approximately 15 and 22 s. Static 3D volumes were stored in the device storage memory, enabling processing of the volumes later.

Volume analysis

Offline analysis and a post processing evaluation were performed using GE Healthcare '4D View' software. Initially, a systematic method was developed to compare the anatomy described in anatomy atlases to the fetal sonographic findings. Each vessel that was noted on the axial ultrasound image at the level of the circle of Willis was correlated to the appropriate image on the anatomical atlas. Navigation cephalic and caudal to this plane and repeat the process of identify of the vessels. Next step was study the sagittal planes, starting at the median sagittal with the pericallosal artery. The same process was made at the coronal planes. The coronal plane is less familiar, and we used the knowledge from the other planes to verify the vessels by standing on known vessel at axial or sagittal plane and look at its course on the coronal plane. The first seven volumes were analyzed in a long and not systematic process, to learn the anatomy. Afterwards a systematic method to identify the vessels was developed. This method was used independently by two investigators - an experienced sonographer (L.G.) and a medical student trained to use 4D View software (E.D.). The reading process according to the newly produced method was made 2 months later.

Three-dimensional ultrasound images were displayed by several methods. The basic method used was multiplanar display showing that three perpendicular gray scale images displayed simultaneously. The three planes intersected at one point (Figure 1). Evaluation of the volumes using the cursor dot to tract a particular vessel enabled vessel identification in all three dimensions, tracking of each vessel course and characterization of the adjacent brain anatomy. The Doppler information and ultrasound information (B mode) were displayed in two layers simultaneously in the same image, allowing demonstration of vessels course and adjacent brain anatomy (Figure 1).

Distinguishing between arteries and veins was made by the anatomical course of the vessels and by the directionality of blood flow in the brain compared with the directionality demonstrated by Doppler. Many of the brain vessels are bilateral and symmetrical; thus, it was noted if the vessel was demonstrated unilaterally or bilaterally. In cases where vessels were not demonstrated, the cause was identified (e.g. known artifacts of ultrasound technology such as acoustic shadowing or reverberations).

Anatomical landmarks of brain vascularity, as seen in the fetus by 3D ultrasound, are shown in Table 1. Instructions for systematic visualization of the fetal brain blood vessels, according to the approach used by the authors, are given in Table 2.

Statistical analysis was performed comparing the two investigators evaluation of each blood vessel, including the optimal acquisition plane. Fetal arteries investigated included the internal carotid, basilar artery, anterior cerebelar artery (ACA), polar frontal artery, callosomarginal artery, pericallosal artery, precuneal artery, MCA, posterior cerebral artery (PCA), posterior communicating artery (PCom), superior cerebellar artery (SCA), anterior inferior cerebellar artery (AICA), and the posterior inferior cerebellar artery (PICA). Veins investigated included the superior sagital sinus, inferior sagital sinus, straight sinus, transverse sinus, internal veins, basal veins, and the great cerebral vein (vein of Galen).

RESULTS

Between August 2007 and March 2011, 3D volumes, combined with HDD were acquired prospectively in 25 patients at 12 weeks and 3 days to 36 and 3 days' gestation (mean, 21 weeks 6 days; median, 22 weeks 6 days). Indications for



Figure 1 The median view (midline sagittal). (A and B) 3D volume of the head in a fetus at 25 weeks' gestation. (A) The volume rotated to optimal viewing of vascular anatomy of the median plane. Box A, median plane, the anterior part (frontal) at the left and posterior (occcipital) part at the right, the superior part at the top. This box is showing the median vessels. Box B. coronal plane, the superior part is at the top of the image, the right side of the head at the left side of the image. Box C, axial plane, the right is at the top of the image and the left is at the bottom of the image. (B) Magnified image of the median plane (same as box A in the preceding texts) showing the median vascular anatomy. The polar frontal artery and the inferior sagittal sinus are not demonstrated at the ultrasonic image (left) and illustrated in pale color in its anatomic position on the right image. (C) Multiplanar and rendered image. It demonstrates the orientation of the region of interest in a fetus at 36 weeks' gestation. The volume was rotated to optimal viewing of vascular anatomy at the median plane. The rendered image in box D (bottom right) is obtained by having the viewing direction (green line) to the left in box B and to the bottom in box C (top right and bottom left). Notice that in box A (top left) it has no green line and is in the same orientation as Box D. The vessel numbers are as in Tables 1–3. The cursor dot is emphasized by an arrow

409

Table 1	Anatomical	landmarks	. as seen	in the	fetus b	v 3DUS

Vessel no.	Vessel	Anatomic landmarks (30)
1	Int. carotid a.	Arises from the common carotid at C4 level, enters the skull through the carotid canal, and ends in the circle of Willis where it splits to the MCA, ACA, and Pcom.
2	ACA	Splits from the internal carotid at the circle of Willis, travels anteriorly, connects to the parallel ACA through the Acom, and curves backward over the corpus callosum.
3	Pericallosal a.	Distal to the origin of the callosomarginal artery; passes above the corpus callosum.
4	Polar frontal a.	Arises perpendicularly from the ascending part of the ACA and supplies the anterior part of the frontal lobe.
5	Callosomarginal a.	Arises perpendicularly from the transverse part of the ACA and supplies the frontal and temporal lobes.
6	Precuneal a.	A terminal branch of the pericallosal artery arises above the posterior part of the corpus callosum.
7	MCA	Begins at the bifurcation of the internal carotid artery and takes an indirect course through the lateral sulcus, along the surface of the insular cortex.
8	PCA	Originating where the basilar artery bifurcates, courses around the lateral margin of the midbrain. It supplies the occipital lobe and portions of the medial and inferior temporal lobes.
9	PCom	Connecting between the PCA to the int. carotid artery and the MCA bifurcation.
10	Basilar a.	Originating from the fusion of the two vertebral arteries, lies unpaired along the midline, frontal to the pons and bifurcates to the PCA and the Pcom at the level of the circle of Willis.
11	Vertebral a.	Arises from the subclavian artery on each side of the body, enters deep to the transverse process at C6 level, and joins to form the basilar a. at the level of the inferior part of the pons.
12	AICA	Arises from the lower part of the basilar a., at the level of the lower part of the pons, and supplies the dorsolateral portion of the caudal pons.
13	PICA	Arises from the vertebral artery and winds posteriorly to supply the inferior part of the cerebellum and the upper part of the medulla oblongata.
14	SCA	Arises from the superior part of the basilar artery, at the level of the superior part of the pons and winds posteriorly to supply the superior part of the cerebellum and the superior part of the pons.
15	Straight sinus	Drains from the inferior sagittal sinus and the great cerebral vein to the transverse sinus.
16	Sup. Sagittal sinus	Drains from the upper median part of the skull, between the two cerebral hemispheres, to the transverse sinus.
17	Inf. Sagittal sinus	Located at the lower part of the falx cerebri, drains from the superior part of the corpus callosum between the two cerebral hemispheres
18	Great cerebral v. (of Galen)	Forms by the fusion of the internal veins and the basal veins and ends where it fused with the inferior sagittal sinus to form the straight sinus.
19	Basal v. (of Rosenthal)	Originates on the medial surface of the temporal lobe and runs posteriorly and medially into the vein of Galen.
20	Int. cerebral v.	Forms behind the column of the fornix and travels back parallel to one another and to the tela choroidea beneath the splenium of the corpus callosum where they unite to form the great cerebral vein.
21	Transverse sinus	Originates from the confluence of sinuses and runs anteriorly and laterally to become the sigmoid sinus that exits the skull through the jugular foramen and becomes continuous with the internal jugular vein.

ACA, anterior cerebral artery; MCA, middle cerebral artery; PCA, posterior cerebral artery; SCA, superior cerebellar artery; AICA, anterior inferior cerebellar artery; AICA, anterior inferior cerebellar artery; PCA, posterior communicating artery; PCA, posterior communicating artery.

the sonographic examinations included routine nuchal translucency (2 patients), routine anatomical scan (16 patients), and routine estimation of fetal weight (7 patients).

The step-by-step method for obtaining optimal visualization of the fetal cerebral blood vessels is described in Table 2 and Figures 1–5. With this method the fetal head is positioned in the sagittal plane in box A, the coronal plane in box B, and in the axial plane in box C (Figure 1). On boxes A and C the anterior aspect of the fetus (the face) is on the left side of the screen, which was found to be the most intuitive position for the fetus in manipulating the volumes. In box B the right side of the fetus is on the right side of the screen, as if we are looking at it from

Table 2 Instructions for showing the fetal head vasculature step-by-step with 3D sectional planes

Step	Instructions
1	Make the sagittal plane in box A with posterior part towards box B. The coronal plane in box B and the axial plane in box C. In fetuses after 20 weeks: To straighten the volume, put the cursor dot on the middle part of the corpus callosum and make sure that it straight in all planes. In younger fetuses, straight the volume at the level of the circle of Willis and the orbits.
2	Magnify the image and optimize the image settings of both gray scale and color.
3	The first image: the median view (Figure 1). The ACA is demonstrated in box A as one vessel, and this is the most anterior vessel. It courses upward to create the pericallosal artery that curve above the corpus callosum and gives off a variable number of branches: polar frontal artery, callosomarginal artery, and precuneal artery. The superior sagittal sinus is also demonstrated in box A, between the most superior part of the brain and the skull. The two internal cerebral veins situated mildly lateral to the midline and below the corpus callosum and the precuneal artery, fuse to become the great cerebral vein which fuses with the inferior sagittal sinus to form the straight sinus which should be demonstrated on this plane. The basilar artery is in the inferior midline part, near the base of the skull (anterior to the brain stem) in box A. Place the cursor dot on the internal veins.
4	The second image: the coronal view of the deep veins of the brain (Figure 2). The internal and basal veins drain into the great cerebral vein. Move the cursor dot of in box A to the internal veins posteriorly, the basal veins will appear in box B (coronal plane), fusing in a lateral-medial position to create the great cerebral vein.
5	The third image: the low axial plane at the pontine level (Figure 3). Place the dot of interest on the basilar artery in box A (median plane) at the level of the cerebellum. The basilar artery will appear in box C (axial plane) and anterior to it the internal carotid arteries will appear, making a triangular shape. Place the cursor dot on one of the internal carotid arteries in box C; box A will become a lateral sagittal plane, at the internal carotid level. In box B (coronal plane) the internal carotid arteries will be demonstrated.
6	Move the cursor dot back to the basilar artery in box C. The upper part of the vermis near the circle of Willis will appear in box C
7	The forth image: axial plane of the circle of Willis (Figure 4). Circle of Willis contains the following vessels: ACA, MCA, PCA, and the PCom artery. Place the cursor dot in box C at the center of the circle of Willis, between the MCAs. The internal carotid and the coronal course of the MCA will appear in box B.
8	Move the cursor dot in box C to the posterior part of the circle of Willis to the point of the PCA split from the basilar artery. The upper part of the basilar artery will appear in box A.
9	The fifth image: tomographic ultrasound imaging, or multislice imaging, of the vertebrobasilar in the axial planes (Figure 5). Place the cursor dot in box A at the level of the circle of Willis and identify the PCA – the transverse sinus can be seen on the posterior pole of the skull. Move the cursor dot down along the basilar artery in box A and try to identify the cerebellar arteries emerging from the basilar and vertebral arteries in box C. The SCA emerge below the origin of the PCA. The AICA emerges from the inferior part of the basilar artery, just above the vertebral arteries fusion point that creates the basilar artery. The PICA emerges from the vertebral arteries, inferior to the AICA and superior to the foramen magnum.

ACA, anterior cerebral artery; MCA, middle cerebral artery; PCA, posterior cerebral artery; SCA, superior cerebellar artery; AICA, anterior inferior cerebellar artery; PICA, posterior inferior cerebellar artery; ACom, anterior communicating artery; PCom, posterior communicating artery.

behind. In box C the right side of the fetus is superior. It took approximately 5 min to evaluate each of the volumes.

The axial plane was found to be optimal as an analysis plane for identifying vessels that took a horizontal course including arteries (e.g. circle of Willis, SCA, AICA, and PICA) and veins (e.g. transverse sinus and internal cerebral veins). Analysis at the mid-sagittal plane demonstrated the vessels in the midline and slightly lateral to the midline: the arteries (ACA, basilar artery, polar-frontal artery, callosomarginal artery, pericallosal artery, and precuneal artery) and veins (superior sagital sinus, inferior sagital sinus, straight sinus, great cerebral vein, and internal cerebral veins). The coronal plane was found useful as the analysis plane for identifying vessels that have a lateral course (e.g. MCA, transverse sinuses, and basal veins) and vertical course (e.g. internal carotid artery).

Unilateral and bilateral visualization rate of the brain blood vessels is presented in Table 3. Arteries of the circle of Willis, basilar artery, pericallosal artery, and internal carotid arteries were demonstrated in more than half of the fetuses. Tiny vessels such as those that supply the cerebellum and those that branch from the pericallosal artery were demonstrated in less than 50% of the volumes. The anterior communicating artery was the small vessel between the two anterior cerebral arteries and could not be demonstrated separately.

The straight sinus was demonstrated in 68% of the volumes, and the great cerebral vein of Galen was demonstrated in 56%. Other sinuses and veins were demonstrated in less than 50% of the volumes, and the inferior sagittal sinus was demonstrated on only three volumes.

Paired vessels were mainly demonstrated on both sides in volumes acquired on sagittal plane as well as on axial planes. The transverse sinus was demonstrated mainly on one side. Both transverse sinuses were demonstrated in only five patients.

The rate of detection of all vessels was not statistically significant between the two authors. The intra-rater agreement for all vessels was moderate with Kappa 0.494 (95% CI 0.42-0.57).

DISCUSSION

Knowledge of the normal fetal cerebrovascular anatomy can assist in identification of brain birth defects and brain developmental abnormalities. Identification of vascular abnormalities might raise the suspicion of an abnormality at



Figure 2 Coronal view of the deep veins of the brain. 3D volume of the head in a fetus at 33 weeks' gestation at the level of the basal veins and the internal veins fusing point to become the great cerebral vein. (A) Box A, median plane. Box B, coronal plane. Box C, axial plane. The cursor dot is located on the internal veins (demonstrated here as one fused elliptic vessel) at the level of the fusion point with the basal veins to become the great cerebral vein. (B) Magnified image of the coronal plane (same as box B in the preceding texts) showing the coronal view of the internal veins and the basal veins just before they merge to become the great cerebral vein. The vessel numbers are as in Tables 1–3. The cursor dot is emphasized by the arrow

an earlier stage of pregnancy. This study shows that fetal brain vascularization can be demonstrated by 3D ultrasound with Doppler, to identify their normal course and to demonstrate extremely small vessels. In the literature, data regarding fetal cerebral circulation anatomy and physiology *in vivo* are very limited. The morphology of the brain vascularity as seen by ultrasound was described 20 years ago¹⁷ and used mainly for prenatal diagnosis of vein of Galen malformation.^{18–22}

The ability to demonstrate the spatial relations between the blood vessels is a major advantage of 3D ultrasound. A systematic approach of detection of the abdominal vasculature was developed, utilizing this quality.^{15,16} The spaces between the bones forming the skull become narrower as the fetus advances in gestation, making visualization of blood vessels easier at early stages of pregnancy. Doppler usage was limited to 12 weeks and on, because of the warming effect that may harm the embryo's development.²³ Although visualization of the vascular network has been described as early as 7 and 9 weeks of gestation,⁵ we chose to avoid examinations in such young fetuses.

The major arteries were demonstrated in the majority of the study population. These vessels included the circle of Willis (ACA, MCA, and PCom) and the vertebro-basilar circulation arteries (basilar artery, vertebral artery, SCA, AICA, and PICA). Small vessels such as the pericallosal artery and its branches could be demonstrated from 15 weeks onward. Limited resolution of current ultrasound machines restricted the visualization of many small vessels even though the most advanced machines available commercially were utilized in this study, and the transvaginal route was used in the early cases. For example, the pericallosal artery was recorded in 56% of the fetuses overall, and in 77% of fetuses greater than 23 weeks of gestation.

The volume acquisition plane determines the ability to visualize the blood vessels. The ideal acquisition plane to demonstrate the midline vessels is the sagittal plane, and the ideal acquisition plane to demonstrate the circle of Willis is the axial plane. In our study, the visualization rate of the pericallosal artery was 100% when the volumes were acquired



Figure 3 Low axial plane at the pontine level. 3D volume of the head in a fetus at 24 weeks' gestation. (A) Box A, median plane. Box B, coronal plane. Box C, low axial plane. (B) Magnified image of the axial plane (same as Box C in the preceding texts) the cursor dot is on the basilar artery (No. 10) and anterior to it (on the left in the image) the internal carotid arteries, making a triangle shape. (C) Same volume as in Figure 3a and b, at the level of the internal carotid artery. Box A, lateral sagittal plane. Box B, coronal plane. Box C, low axial plane. The cursor dot is on the left internal carotid artery, demonstrating both internal carotid arteries on boxes B and C and the left carotid artery in box A. The vessel numbers are as in Tables 1–3. The cursor dot is emphasized by the arrow



Figure 4 Axial plane of the circle of Willis. 3D volume of the head in a fetus at 24 weeks' gestation. (A) Box A, median plane. The volume was acquired from lateral (axial) aspect; thus, median vessels are not seen because of perpendicular acquisition plane. Box B, coronal plane. The cursor dot is located between the internal carotid arteries, enabling to demonstrate the MCA at this plane. Box C, axial plane. It demonstrates the circle of Willis. (B) Magnified image of the circle of Willis as seen in the axial plane (same as box C in image 4A). (C) 3D volume of the head in a fetus at 16 weeks' gestation. Box A, median plane. The volume was acquired from lateral (axial) aspect; thus, most of the median aspect vessels are not seen because of perpendicular acquisition plane. Box B, coronal plane. The cursor dot is located on the end of the basilar artery, at the splitting point to the PCA. Box C, axial plane. It demonstrates the circle of Willis. (D) Magnified image of the basilar artery and the PCA as seen in the coronal plane (same as box B in image Figure 4C). The vessel numbers are as in Tables 1–3. The cursor dot is emphasized by the arrow



Figure 5 Tomographic ultrasound imaging, or multislice imaging, of cerebral and cerebellar vessels in the axial plane in a fetus at 15 weeks' gestation. The top left image is a reference image in the lateral sagittal plane showing where the other seven images are from the volume. The images are displayed at 2.0-mm intervals. The vessel numbers are as in Tables 1–3

Table 3 Unilateral and bilateral visualization rate of the brain blood vessels

Vessel no.	Vessel	Total identified	Both identified	Only one side identified	None identified
1	Int. carotid	86% (43/50)	21	1	3
2	ACA	70% (35/50)	13	9	3
3	Pericallosal A.	56% (14/25)	-	14	11
4	Polarfrontal A.	20% (5/25)	_	5	20
5	Callosomarginal A.	48% (12/25)	_	12	13
6	Precuneal A.	40% (10/25)	_	10	15
7	MCA	90% (45/50)	21	3	1
8	PCA	78% (39/50)	18	3	4
9	PCom.	66% (33/50)	16	1	8
10	Basilar A.	88% (22/25)		22	3
11	Vertebral A.	10% (5/50)	2	1	22
12	AICA	12% (6/50)	3	0	22
13	PICA	8% (4/50)	2	0	23
14	SCA	42% (21/50)	9	3	13
15	Straight sinus	68% (17/25)	_	17	8
16	Supp. Sagittal sinus	44% (11/25)	_	11	14
17	Inf. Sagittal sinus	12% (3/25)	_	3	22
18	Great cerebral V.	56% (14/25)	_	14	11
19	Transverse sinus	36% (18/50)	5	8	12
20	Basal V.	32% (16/50)	7	2	16
21	Internal cerebral V.	26% (13/50)	5	3	17

ACA, anterior cerebral artery; MCA, middle cerebral artery; PCA, posterior cerebral artery; SCA, superior cerebellar artery; AICA, anterior inferior cerebellar artery; PICA, posterior inferior cerebellar artery; ACom, anterior communicating artery; PCom, posterior communicating artery.

in the sagittal plane (six volumes) and could not be visualized in volumes acquired in the axial plane (seven volumes). The pericallosal artery identification rate described in the literature reaches 95% when the volume is acquired in the sagittal plane.² Therefore, in order to increase the identification of vessels, every examination should include two or more volumes acquired in perpendicular acquisition planes.

Most of the arteries in the brain are symmetrical, but because of artifacts such as reverberation and acoustic shadowing, both arteries were demonstrated bilaterally in only two thirds of the cases in this study. The ACA, PCA, and MCA were demonstrated symmetrically in 54%, 72%, and 84% respectively. Pooh *et al.* managed to demonstrate both arteries of bilateral arteries in half of the cases and concluded that fetal head movements during volume acquisition were the main reason for inability to demonstrate the vessels.⁴ We found that even with movement artifacts, vascular mapping was possible. Acoustic shadowing was the most common cause of limited visualization of vessels in our study.

The midline paired vessels, situated between the two hemispheres (the ACA, pericallosal, polar frontal, callosomarginal, and precuneal arteries), course adjacent to the parallel symmetric vessel. Because of the anatomic proximity and technical resolution limitation, these vessels were demonstrated as a single wide fused vessel.²⁴

Anatomic variability is very common in the anterior part of the circle of Willis. The morphologic diversity of the ACA and the pericallosal artery has been described in adults.^{25,26} The branches originating from the pericallosal artery may vary in number and in their courses. The polar frontal artery (Figure 1B) was demonstrated in only three volumes, and we attributed this finding to its course and small diameter. Another example is the ACA, which originates from an embryonic vascular net across the midline. During fetal development the net coalesces to form two parallel ACAs. During this process, common variability (up to 40–82%) can evolve to create different anatomical configurations, such as accessory arteries parallel to the ACA or a single ACA that supplies both hemispheres.

The major venous system vessels (superior sagittal and transverse sinuses) could be identified as early as 15 weeks of gestational age. Identification rates improved with advancing gestational age and smaller venous vessel identification

REFERENCES

- 1. Mari G, Adrignolo A, Abuhamad AZ, *et al.* Diagnosis of fetal anemia with Doppler ultrasound in the pregnancy complicated by maternal blood group immunization. Ultrasound Obstet Gynecol 1995; 5(6):400–5.
- Bornstein E, Monteagudo A, Santos R, *et al.* A systematic technique using 3-dimensional ultrasound provides a simple and reproducible mode to evaluate the corpus callosum. Am J Obstet Gynecol 2010;202 (2):201.e1–5.
- Wladimiroff JW, Tonge HM, Stewart PA. Doppler ultrasound assessment of cerebral blood flow in the human fetus. Br J ObstetGynaecol 1986;93:471–5.
- Pooh RK, Pooh KH. The assement of fetal brain morphology and circulation by transvaginal 3D sonography and power Doppler. J Periant Med 2002;30:48–56.

became possible. The superior sagittal sinus and the straight sinus could be identified in 40% and 50% of the volumes, respectively. The cerebral venous system has been identified by two-dimensional color Doppler at 20 to 42 weeks of gestation by multiple investigators.^{17,27-29} One explanation of such low identification rate can be the fact that the Doppler flow rate is limited to 8 cm/s, preventing identification of vessels with slower flow rate.^{27,29} The inferior sagittal sinus could be identified in only three volumes, most probably because of its small size and slow blood flow in it.

The inter observer variability was moderate (0.49), as the expert physician had a higher rate of identification of the blood vessels. We conclude that the ability to identify fetal blood vessels is acquirable, but requires expertise.

Limitations of this study include the following. The study was limited to a normal population. All variations in vascular anatomy could not be demonstrated in the small group of fetuses studied in this cohort, and one should be careful when different anatomy is demonstrated. Most of the volumes in our study had movement artifacts that could cause difficulty in identifying vessels. Further research is required to identify vascular abnormalities and related brain developmental defects.

In conclusion, the major fetal cerebral blood vessels can be detected by a 3D volume sweep with HD flow. A systematic step-by-step review of the volume may be helpful in the detection of fetal cerebral and cerebellar blood vessels. Because brain vasculature visualization demands specific expertise, we do not recommend conducting it in normal population screening. The benefit of the examining the vascular system in diagnosing brain abnormalities should be investigated further.

WHAT'S ALREADY KNOWN ABOUT THIS TOPIC?

 Fetal cerebral vasculature is rarely studied during routine fetal ultrasonographic examinations except for middle cerebral artery interrogation to assess for fetal anemia and visualization of the pericallosal artery to assess for absence of the corpus callosum.

WHAT DOES THIS STUDY ADD?

- The present study developed a step-by-step systematic approach to identify the cerebral vasculature and demonstrated that the essential fetal cerebral vessels can be visualized by 3D volume analysis.
- Pooh RK. Neurosonoembryology by three-dimensional ultrasound. Semin Fetal Neonatal Med 2012;17(5):261–8.
- Beslow LA, Jordan LC. Pediatric stroke: the importance of cerebral arteriopathy and vascular malformations. Childs Nerv Syst 2010;26 (10):1263–73.
- Arnold WH, Sperber GH, Machin GA. Anatomy of the circle of Willis in three cases of human fetal synophthalmicholoprosencephaly. Ann Anat 1996;178:553–8.
- Zuccaro G, Argañaraz R, Villasante F, Ceciliano A. Neurosurgical vascular malformations in children under 1 year of age. Childs Nerv Syst 2010;26(10):1381–94.
- Guclu B, Ozturk AK, Pricola KL, *et al.* Cerebral venous malformations have distinct genetic origin from cerebral cavernous malformations. Stroke 2005;36(11):2479–80.

- Young WL, Yang GY. Are there genetic influences on sporadic brain arteriovenous malformations? Stroke 2004;35:2740–5.
- Riant F, Bergametti F, Ayrignac X, *et al.* Recent insights into cerebral cavernous malformations: the molecular genetics of CCM. FEBS J 2010;277(5):1070–5.
- Kamath BM, Spinner NB, Emerick KM, *et al.* Vascular anomalies in Alagille syndrome: a significant cause of morbidity and mortality. Circulation 2004;109:1354–8.
- 13. Heyer GL, Dowling MM, Licht DJ, *et al.* The cerebral vasculopathy of PHACES syndrome. Stroke 2008;39:308–16.
- Sciaky-Tamir Y, Cohen SM, Hochner-Celnikier D, et al. Three-dimensinal power Doppler (3DPD) ultrasound in the diagnosis and follow-up of fetal vascular anomalies. Am J ObstetGynecol 2006;194:274–81.
- Gindes L, Pretorius DH, Romine LE, et al. Three-dimensional ultrasonographic depiction of fetal abdominal blood vessels. J Ultrasound Med 2009;28:977–88.
- Kivilevitch Z, Gindes L, Deutsch H, Achiron R. In-utero evaluation of the fetal umbilical-portal venous system: two- and three-dimensional ultrasonic study. Ultrasound Obstet Gynecol 2009;34(6):634–42.
- Pooh RK, Aono T. Transvaginal power Doppler angiography of the fetal brain. Ultrasound Obstet Gynecol 1996;8(6):417–21.
- Yuval Y, Lerner A, Lipitz S, *et al.* Prenatal diagnosis of vein of Galen aneurysmal malformation: report of two cases with proposal for prognostic indices. PrenatDiagn 1997;17(10):972–7.
- Heling KS, Chaoui R, Bollmann R. Prenatal diagnosis of an aneurysm of the vein of Galen with three-dimensional color power angiography. Ultrasound Obstet Gynecol 2000;15(4):333–6.

- 20. Lee TH, Shih JC, Peng SS, *et al.* Prenatal depiction of angioarchitecture of an aneurysm of the vein of Galen with three-dimensional color power angiography. Ultrasound Obstet Gynecol 2000;15(4):337–40.
- Ruano R, Benachi A, Aubry MC, *et al.* Perinatal three dimensional color power Doppler ultrasonography of vein of Galen aneurysms. J Ultrasound Med 2003 Dec; 22(12):1357–62.
- Degani S. Evaluation of fetal cerebrovascular circulation and brain development: the role of ultrasound and Doppler. SeminPerinatol 2009;33(4):259–69.
- Abramowicz JS. Fetal Doppler: how to keep it safe? ClinObstet Gynecol 2010;53(4):842–50.
- 24. Gray H. Gray's Anatomy: The Anatomical Basis of Clinical Practice, 40th ed. Churchil&Livingstone: New York, NY; 2008. p 247.
- Stefani MA, Schneider FL, Marrone AC, et al. Anatomic variations of anterior cerebral artery cortical branches. Clin Anat 2000;13(4):231–6.
- 26. Okahara M, Kiyosue H, Mori H, *et al.* Anatomic variations of the cerebral arteries and their embryology: a pictorial view. EurRadiol 2002;12(10):2548–61.
- 27. Pooh RK, Pooh KH, Nakagawa Y, *et al.* Transvaginal Doppler assessment of fetal intracranial venous flow. Obstet Gynecol 1999;93:697–701.
- Laurichesse-Delmas H, Grimaud O, Moscoso G, Ville Y. Color Doppler study of the venous circulation in the fetal brain and hemodynamic study of the cerebral transverse sinus. Ultrasound Obstet Gynecol 1999;13(1):34–42.
- 29. Degani S. Fetal cerebrovascular circulation: a review of prenatal ultrasound assessment. GynecolObstet Invest 2008;66(3):184–96.