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ABSTRACT

Owing to prenatal ultrasound technology, there has been an immense acceleration in understanding of early human development. Recent advanced three-dimensional (3D) technology has produced exciting new applications of high-definition live (HDlive) silhouette and HDliveFlow imaging.

By HDlive silhouette mode, an inner cystic structure with fluid collection can be depicted through the outer surface structure of the body and it can be appropriately named as 'see-through fashion'. Additionally, HDlive silhouette can depict hyperechoic structures, such as bones because skeletal system is demonstrated by ultrasound as conspicuously echogenic organs.

HDliveFlow imaging adds more spatial resolution to conventional 3D ultrasound angiogram. HDliveFlow imaging demonstrates fine peripheral blood vessels, such as vascularity of the lung, brain and eyeballs. HDliveFlow combined with silhouette mode demonstrates the accurate location of vascularity inside organs. Simultaneous visualization of both structure and vascularity is quite comprehensive and may add further clinical information of vascularization.

Thus, 'see-through fashion' imaging technology provides us comprehensive orientation and persuasive localization of inner morphological structure as well as of angiostructure inside the fetal organs. HDlive silhouette and flow imaging add further clinical significance to conventional three/four-dimensional (3D/4D) imaging in fields of sono-ophthalmology. Owing to novel applications with clinical significance, fetal ultrasound is at present noninvasive, direct-viewing of the embryo/fetus, and all-inclusive technology, and is definitely the first modality of prenatal diagnosis with infinite potential.

Keywords: Flow, Fetus, HDlive, Prenatal diagnosis, Seethrough fashion, Silhouette, Three-dimensional, Ultrasound.

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INTRODUCTION

Owing to prenatal ultrasound technology, there has been an immense acceleration in understanding of early human development. The anatomy and physiology of embryonic development is a field where medicine exerts greatest impact on early pregnancy at present, and it opens fascinating aspects of embryonic differentiation. Recent development of three-dimensional (3D)/fourdimensional (4D) sonography has revealed structural and functional early human development *in utero*.¹⁻⁴ Three-/ four-dimensional sonography moved prenatal diagnosis of fetal anomalies from the second to the first trimester of pregnancy.⁵ The 3D transducers take several hundreds or thousands of two-dimensional (2D) ultrasound images over a short (30-40°) arc. These images are then transferred to a computer that integrates them into a single image. The first generation of 3D ultrasound lacked the capability to reconstruct images rapidly and with high resolution. These limitations could explain why the method was not very popular initially.⁶ With current clinically available equipment, 3D sonographic reconstruction is fast, with high resolution, giving ultrasound the ability to image in real time. Also, 3D ultrasound allows volume data to be stored and manipulated long after the patient has left the examination room. Storage of a single volume of data is easy and quick, yet the stored volume permits interpretation of the scanned region in multiple planes.⁶ Three-/four-dimensional ultrasound has improved its functions with high-definition live (HDlive) technology and furthermore, great advances of ultrasound technology have produced new applications of HDlive silhouette and HDliveFlow.

This article demonstrates detailed and comprehensive fetal structural images and angiograms of normal and abnormal fetuses from the first trimester depicted by 3D HDlive silhouette and flows, which closely resemble those from anatomy atlases or scientific documentaries, and describes clinical significance and pitfalls of those novel applications.

HD Technique

Both 3D and 4D ultrasound have improved our knowledge regarding the development of the embryo and fetus and of a great number of fetal anomalies.⁶ The

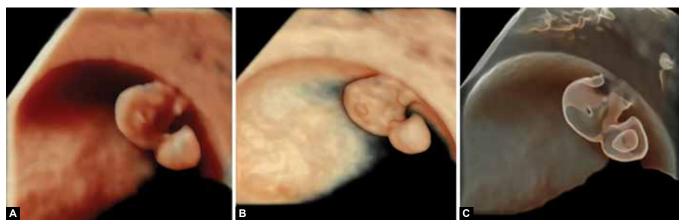


great achievement in the field of 3D/4D ultrasound is HDlive technology. This technology is a novel ultrasound technique that improves the 3D/4D images. HDlive ultrasound has resulted in remarkable progress in visualization of early embryos and fetuses and in the development of sonoembryology.⁷ With HDlive ultrasound, both structural and functional developments can be assessed from early pregnancy more objectively and reliably and indeed, those new technologies have moved embryology from post-mortem studies to the *in vivo* environment.⁶

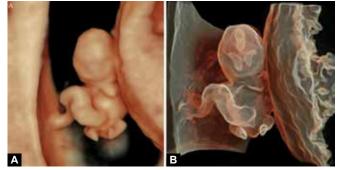
HDlive uses an adjustable light source and software that calculates the propagation of light through surface structures in relation to the light direction.⁸ The virtual light source produces selective illumination, and the respective shadows are created by the structures where the light is reflected. This combination of light and shadows increases depth perception and produces remarkable images that are more natural than those obtained with classic 3D ultrasound. The virtual light can be placed in the front, back, or lateral sides, where viewing is desired until the best image is achieved. A great advantage is that the soft can be applied to all images stored in the machine's memory.⁷ In obstetrical ultrasound, HDlive could be used during all three trimesters of pregnancy. There have been several reports on HDlive demonstration of fetal surface.^{7,9-11} Three-dimensional HDlive further 'humanizes' the fetus, enables detailed observation of the fetal face in the first trimester, and reveals that a small fetus is not more a fetus but a 'person' from the first trimester.¹¹

HDlive Silhouette and Flow Technique

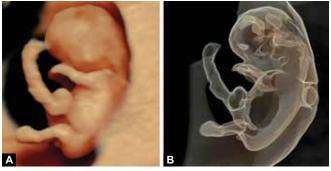
Recent advanced 3D technology has produced exciting new applications of HDlive silhouette and HDliveFlow, released at the end of 2014. The algorithm of HDlive silhouette creates a gradient at organ boundaries, fluid filled cavity and vessels walls, where an abrupt change of the acoustic impedance exists within tissues.^{12,13} By HDlive silhouette mode, an inner cystic structure with fluid collection can be depicted through the outer surface structure of the body and it can be appropriately named as 'see-through fashion'.¹² The examiner can adjust HDlive silhouette percentage with controlling threshold and gain simultaneously for visualizing target organs of interest. Figure 1 shows 6-week-embryo and yolk sac with different silhouette percentage.



Figs 1A to C: Six-week-embryo with HDlive silhouette: (A) Conventional HDlive image of embryo and yolk sac, (B) same image with silhouette demonstrated translucent embryo and yolk sac

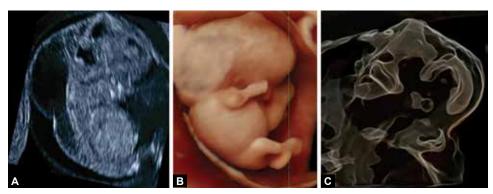


Figs 2A and B: Eight-week-embryo with HDlive silhouette: (A) Conventional HDlive image. Surface rendering with shadow demonstrates the outer surface of the embryo and umbilical cord and (B) same image with HDlive silhouette. Premature brain cavity is well-demonstrated within outer surface of embryo



Figs 3A and B: Ten-week-fetus with HDlive silhouette: (A) Conventional HDlive image. Surface rendering with shadow demonstrates the outer surface of the embryo, physiological umbilical hernia and umbilical cord and (B) same image with HDlive silhouette. Brain cavity is well-demonstrated within outer surface of fetus

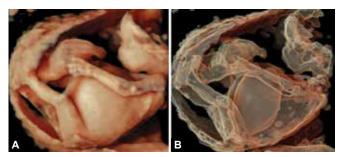
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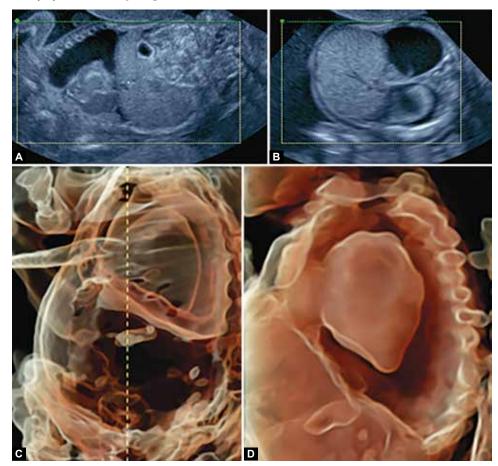
Figs 4A to C: Abnormal midbrain cavity at 10 weeks of gestation: (A) Two-dimensional image. Note the midbrain sharply sticking out of the head, (B) Three-dimensional HDlive image of the fetus. Note the prominent top of the fetal head due to abnormal midbrain and (C) HDlive silhouette image of the fetal head. Abnormal prominent midbrain is depicted between forebrain and hindbrain

HDlive Silhouette Imaging of Hypoechoic Structures

HDlive silhouette emphasizes the borderlines between organs with different echogenicity, therefore, both the target of interest floating within fluid correction and cystic area in echogenic organs are simultaneously demonstrated. The premature brain cavity inside fetal head is visualized with outer surface of fetal body from early pregnancy (Figs 2 and 3) and abnormal midbrain structure is clearly demonstrated as shown in Figure 4. Not only brain cavity in early pregnancy but huge bladder in a case of prune belly syndrome (Fig. 5), pleural effusion

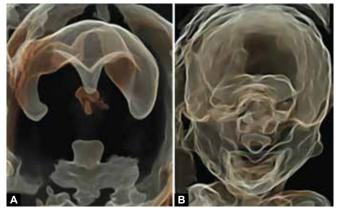


Figs 5A and B: Prune belly syndrome at 13 weeks of gestation: (A) Conventional HDlive image of the fetus. Prominent abdomen is visible and (B) same image with HDlive silhouette. Huge bladder is demonstrated inside outer surface of the fetus



Figs 6A to D: Fetal hydrothorax at 17 weeks of gestation: (A and B) Two-dimensional coronal and axial images of fetal thorax. Pleural effusion is more prominent in the left side, (C) HDlive silhouette image. Pleural effusion and lung floating in the fluid correction are well-demonstrated and (D) same image with different HDlive silhouette degree and gain. Lung is more emphasized than image C





Figs 7A and B: Brain ventricular shape of semilobar and alobar holoprosencephaly by HDlive silhouette imaging at 14 weeks of gestation: (A) Fused ventricle of semilobar holoprosencephaly demonstrated with HDlive silhouette and (B) single ventricle of alobar holoprosencephaly demonstrated with HDlive silhouette

(Fig. 6), the fused ventricle and the single ventricle in semilobar/alobar holoprosencephaly (Fig. 7) are well-visualized. Figure 8 demonstrates enlarged bilateral ventricles and third and fourth ventricles in a single volume dataset in a case of Dandy Walker malformation. Eyeball with outer surface of fetal face is depicted in Figure 9. Thus, any cystic area or hypoechoic part can be target of interest by HDlive silhouette imaging.

HDlive Silhouette Imaging of Hyperechoic Structures

Additionally, HDlive silhouettete can depict hyperechoic structures, such as bones because skeletal system is demonstrated by ultrasound as conspicuously echogenic organs. As shown in Figure 10, premature cranial structure including frontal, parietal and occipital bones at 13 weeks and anterior fontanel at 16 weeks are comprehensively depicted. Even bony structure of fingers and toes can be visualized from the first trimester by HDlive silhouette imaging (Figs 11 and 12). The vertebrae and ribs can be visualized from small fetus (Fig. 13) and interestingly extracted skeletal system is demonstrated in the early second trimester as shown in Figure 14. Thus, HDlive silhouette imaging of hyperechoic structure may possess a great potential of investigating skeletal dysplasia from early pregnancy.

HDliveFlow Imaging of Fetal Vascular Structures

HDliveFlow imaging adds more spatial resolution to conventional 3D ultrasound angiogram. Combination of HDliveFlow with silhouette imaging visualizes precise location of vascular structure inside organs. Figure 15 demonstrates vascularized area adjacent to embryo inside gestational sac at 6 weeks of gestation, which is going

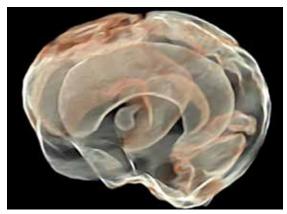
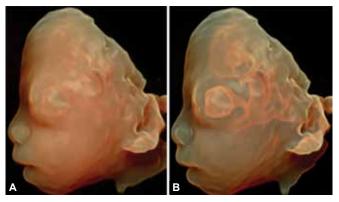
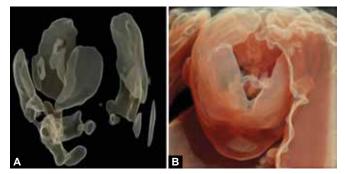


Fig. 8: Ventriculomegaly associated with Dandy Walker syndrome by HDlive silhouette imaging at 16 weeks of gestation. Enlargement of bilateral lateral ventricles, third ventricle and fourth ventricle is well-demonstrated inside the brain

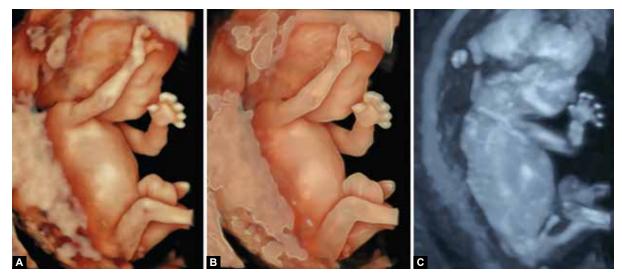


Figs 9A and B: Exophthalmos by HDlive silhouette imaging at 20 weeks of gestation: (A) Profile image with HDlive silhouette. Exophthalmos is demonstrated and (B) same image with different HDlive silhouette degree. Inner eyeball is well-depicted

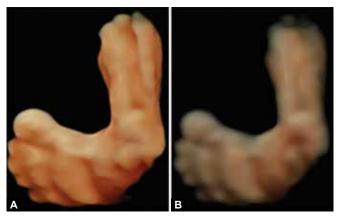


Figs 10A and B: Cranial bony structure by HDlive silhouette imaging at 13 and 16 weeks of gestation: (A) Premature cranial bones (frontal, parietal and occipital bones) are well-demonstrated and (B) anterior fontanelle at 16 weeks is clearly visible

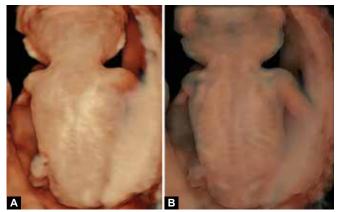
to be the placental area. Figure 16 shows intracorporeal vascularity of 8-week-embryo. Interestingly HDlive silhouette imaging depicts premature forebrain, midbrain and hindbrain and HDliveFlow shows premature vessels towards the center of brain. Figure 17 demonstrates fine pulmonary vessels at 20 weeks of gestation by HDliveFlow. Coiling of the umbilical cord



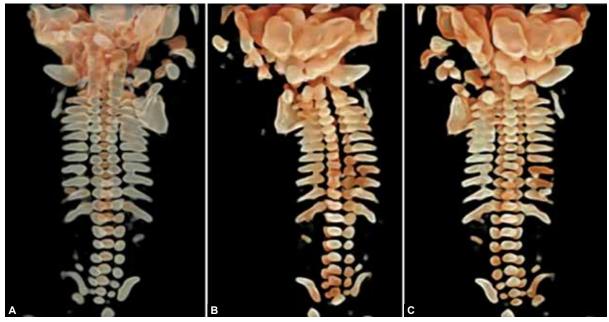
Figs 11A to C: Polydactyly of the fetus with trisomy 13 by HDlive silhouette and maximum mode imaging at 13 weeks of gestation: (A) Conventional HDlive image. Six fingers are well-demonstrated, (B) same image with HDlive silhouette image. Finger bones are demonstrated and (C) same image with maximum mode showing more emphasized finger bones



Figs 12A and B: Clubfoot by HDlive silhouette imaging at 18 weeks of gestation: (A) Conventional HDlive image and (B) same image with HDlive silhouette showing bony structure of the toe



Figs 13A and B: Vertebrae and ribs by HDlive silhouette imaging at 12 weeks of gestation: (A) Conventional HDlive image of fetal back and (B) same image with HDlive silhouette. Note the bony structure of vertebrae and bilateral ribs within outer surface of fetus



Figs 14A to C: Vertebrae, ribs and illia by HDlive silhouette imaging at 18 weeks of gestation: (A) Posterior-anterior view, (B) oblique-anterior view and (C) anterior-posterior view



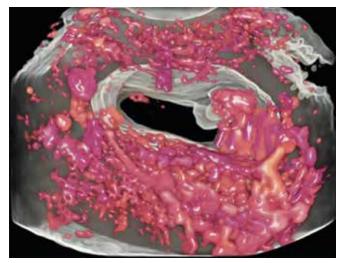


Fig. 15: Intrauterine vascularity by HDlive silhouette and flow imaging at 6 weeks of gestation. Inside of gestational sac, embryonal vascularity and rich vascularity area on the sac wall are well-demonstrated. This rich vascularized area will become the placenta

is clearly visualized from early pregnancy as shown in Figure 18 and aneurysmal malformation of the cord can be demonstrated (Fig. 19). Early cardiac imaging is one of the challenging fields in prenatal diagnostic imaging. HDliveFlow imaging demonstrates intracardiac dynamic flow from the first trimester as shown in Figure 20 and abnormal intracardiac flow due to congenital heart disease is clearly visualized (Fig. 21). Three-dimensional imaging of brain vascularity is expected because it is the most complicated angiostructure in fetus. HDliveFlow demonstrates precisely the cerebral angiogram as shown in Figure 22 and furthermore fine medullary vessels inside cerebrum can be visualized in Figure 23. HDliveFlow with silhouette imaging successfully visualizes vitreous humor, lens and hyaloid artery inside fetal eyeball at 19 weeks of gestation (Fig. 24). Thus, HDliveFlow combined with silhouette mode demonstrates the accurate location of vascularity inside organs. Simultaneous visualization of both structure and vascularity is quite comprehensive and may add further clinical information of vascularization.

Clinical Significance and Pitfalls of HDlive Silhouette and Flow Imaging

By using HDlive silhouette imaging, inner structure can be demonstrated with outer surface without cutting the image. Furthermore non-cystic structure as well as cystic structure can be demonstrated, such as bony structure. Skeletal image by HDlive silhouette may be similar to 3D-CT, therefore, investigation of skeletal system diseases by HDlive silhouette imaging with noninvasive technology will be one of our challenges in prenatal imaging diagnosis. HDliveFlow imaging demonstrated



Fig. 16: Intracorporeal vascularity of 8-week-embryo by HDlive silhouette and flow imaging. Premature brain cavities of forebrain, midbrain and hindbrain as well as fetal whole vascular structure are simultaneously demonstrated in the fetal body. Note the premature blood vessel of the central nervous system toward the brain cavity

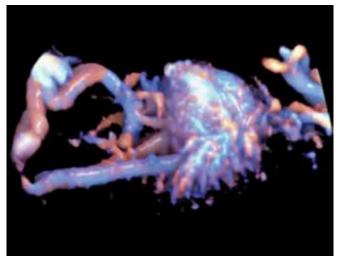
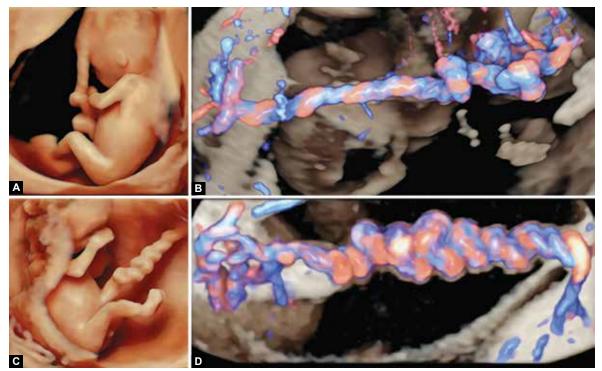
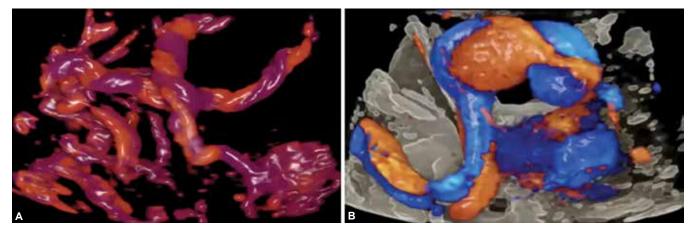


Fig. 17: Thoracoabdominal vascular structure by HDlive flow at 20 weeks of gestation. Plumonary vascular structure, descending aorta, umbilical artery, umbilical vein, ductus venosus and inferior vena cava are well-demonstrated. Note rich vascularity of the lung

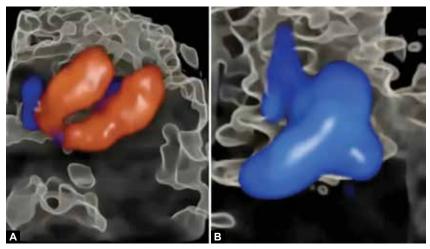
fine peripheral blood vessels, such as vascularity of the lung, brain and eyeballs. Moreover, HDliveFlow combined with silhouette mode demonstrates the precise location of vascularity inside fetal organs and may add further clinical information of vascularization. However, examiners should consider pitfalls of HDlive silhouette imaging. The degree of gain, threshold, and silhouette or combination of those, it is possible to create completely different images with different clinical information from a single volume dataset. This fact expands flexibility of imaging and demonstration, however, can create virtual reality. For obtaining accurate clinical information, examiners should consider that they might create false images and incorrect clinical information.



Figs 18A to D: Normal umbilical cord and excessive coiling cord by HDlive silhouette and flow imaging at 12 weeks of gestation: (A) HDlive fetal and umbilical cord image, (B) HDlive silhouette and flow image of the cord of fetus A, (C) HDlive fetal and excessive coiling cord image and (D) HDlive silhouette and flow image of the cord of fetus C. Note the high-pitch of coils seen in image D compared to image B



Figs 19A and B: Normal floating cord and umbilical arterial aneurysm by HDlive silhouette and flow imaging at 19 to 20 weeks of gestation: (A) Normal floating cord at 19 weeks and (B) umbilical arterial aneurysm at 20 weeks. Note the dilated umbilical artery with straight cord



Figs 20A and B: Normal heart structure by HDlive silhouette and flow imaging at 12 weeks of gestation: (A) Intracardiac flows of left and right heart and (B) great vessels flows of pulmonary artery and aorta



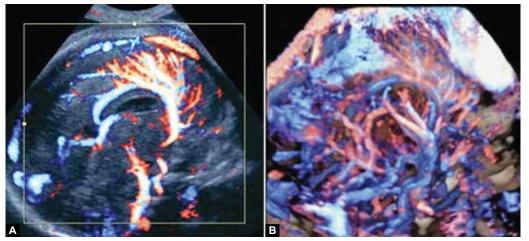


Fig. 21: Tetralogy of Fallot by HDlive silhouette and flow imaging at 15 weeks of gestation. Note the overriding aortic flow from both right and left ventricles

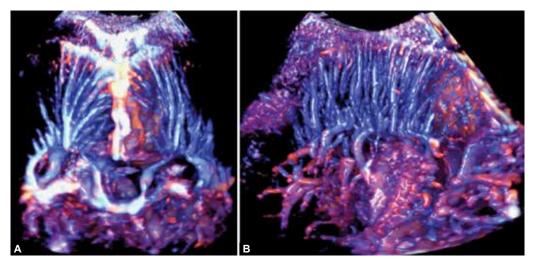
CONCLUSION

As described in this article, 'see-through fashion' imaging technology provides us comprehensive orientation and persuasive localization of inner morphological structure as well as of angiostructure inside the fetal organs. Conventional technology has detected morphological structure and angio-structure independently, however, simultaneous demonstration of both morphology and circulation can potentially provide more accurate clinical information for prenatal diagnoses and proper perinatal management.¹²

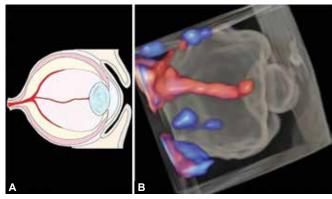
Prenatal ultrasound has established sonoembryology and neurosonology. HDlive silhouette and flow imaging add further clinical significance to conventional 3D/4D imaging in those fields and may open up a new field of sono-ophthalmology. Owing to novel applications with clinical significance, fetal ultrasound is at present noninvasive, direct-viewing of the embryo/ fetus, and all-inclusive technology, and is definitely the first modality of prenatal diagnosis with infinite potential.



Figs 22A and B: Normal brain vascular structure by HDlive silhouette and flow imaging at 20 weeks of gestation: (A) Two-dimensional sagittal image with bidirectional power Doppler imaging. Anterior cerebral artery and its branches are well-demonstrated and (B) Three-dimensional HDlive silhouette and flow image of the same fetal brain as image A. Three-dimensional brain vascular structure is clearly depicted



Figs 23A and B: Normal cerebral medullary veins by HDlive flow imaging at 29 weeks of gestation: (A) Coronal image and (B) sagittal image. Numerous fine medullary veins between cerebral surface and subependymal zone are well-demonstrated



Figs 24A and B: Vitreous humor, lens and hyaloid artery by HDlive silhouette and flow imaging at 19 weeks of gestation: (A) Schematic picture of the fetal eyeball. Hyaloid artery runs to the lens along with central canal inside vitreous humor and (B) HDlive silhouette and flow imaging of the eye at 19 weeks. Vitreous humor, lens and hyaloid artery are well-demonstrated

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