A New Approach to Fetal Echocardiography

Digital Casts of the Fetal Cardiac Chambers and Great Vessels for Detection of Congenital Heart Disease

Luís F. Gonçalves, MD, Jimmy Espinoza, MD, Wesley Lee, MD, Jyh Kae Nien, MD, Joon-Seok Hong, MD, Joaquin Santolaya-Forgas, MD, Moshe Mazor, MD, Roberto Romero, MD

Objective. The purpose of this study was to describe a method of 4-dimensional (4D) reconstruction of the cardiac chambers and outflow tracts using a combination of spatiotemporal image correlation, "inversion mode," and "B-flow" imaging. ***Methods.*** Spatiotemporal image correlation and the inversion mode were used in the examination of the volume data sets of 23 fetuses with congenital heart anomalies. A subset was also examined with B-flow imaging using the gradient light algorithm. Digital reconstructions from abnormal hearts were compared with a library obtained from fetuses without abnormalities. ***Results.*** Rendered images of the 4-chamber view using the inversion mode were characterized by: (1) echogenic chambers; (2) sharp delineation of chamber contours when compared with 2-dimensional (2D) images; and (3) distinct display of the myocardium, interventricular septum, interatrial septum, and mitral and tricuspid valves as anechoic structures. Ventricular septal defects, abnormal differential insertion of the atrioventricular valves, and valve atresia were well visualized with the inversion mode. The application of inversion mode or B-flow imaging to 4D rendering of the outflow tracts resulted in "digital casts" displaying the spatial relationships between the outflow tracts as well as the connections between the great arteries and ventricular chambers. The spatial relationships and communications among cardiac structures cannot be visualized with conventional 2D ultrasonography. ***Conclusions.*** The application of spatiotemporal image correlation, inversion mode, and B-flow imaging generates information about the anatomy and pathologic characteristics of the fetal heart (digital casts) that cannot be obtained with 2D fetal echocardiography. We propose that these modalities enhance the information provided by ultrasonographic interrogation of the fetal heart and will improve prenatal diagnosis. ***Key words:*** congenital heart disease; fetal echocardiography; 4-dimensional ultrasonography; spatiotemporal image correlation; 3-dimensional ultrasonography; 4D; 3D.

Abbreviations
4D, 4-dimensional; STIC, spatiotemporal image correlation; 2D, 2-dimensional; VSD, ventricular septal defect

Received November 15, 2004, from the Perinatology Research Branch, National Institute of Child Health and Human Development, National Institutes of Health, Department of Health and Human Services, Bethesda, Maryland USA (L.F.G., J.E., W.L., J.K.N., J.-S.H., J.S.-F., R.R.); Department of Obstetrics and Gynecology, Wayne State University/Hutzel Hospital, Detroit, Michigan USA (L.F.G., J.E., J.S.-F., R.R.); Division of Fetal Imaging, William Beaumont Hospital, Royal Oak, Michigan USA (W.L.); and Department of Obstetrics and Gynecology, Soroka Medical Center, Ben Gurion University of the Negev, Beer Sheva, Israel (M.M.). Revision requested December 8, 2004. Revised manuscript accepted for publication December 26, 2004.

We thank Mary Lou Schoen, RDMS, and Susan Stites, RDMS, for the quality of their ultrasonographic examinations and Patrick Schoff for multimedia assistance.

Address correspondence to Roberto Romero, MD, Perinatology Research Branch, National Institute of Child Health and Human Development, Wayne State University/Hutzel Women's Hospital, 3990 John R, Box 4, Detroit MI 48201 USA.
E-mail: warfiela@mail.nih.gov.

Video online at www.jultrasoundmed.org.

Four-dimensional (4D) fetal echocardiography with spatiotemporal image correlation (STIC) has been proposed as a valuable adjunctive technique to 2-dimensional (2D) examination of the fetal heart.[1–11] Acquired volume data sets can be conceptualized as "digital specimens" of the fetal heart that can be examined with multiplanar slicing and render-

ing techniques. The outflow tracts, for example, can be systematically visualized by multiplanar slicing of volume data sets acquired with a transverse sweep of the 4-chamber view using a reproducible 3-step approach to manipulate the volume data set.[3,10] Alternatively, 4D reconstruction of the outflow tracts can be accomplished with the use of color and power Doppler,[4,5,7] minimum mode,[8] and, more recently, "inversion mode"[9] and "B-flow" imaging.

The objective of this study was to report the anatomy of the fetal heart in cases of congenital cardiac anomalies displayed with a novel 4D-rendering method: the inversion mode. This modality allows 4D rendering of cardiovascular structures, with an end result similar to that obtained by postmortem pathologic casts.[12,13] In addition, we describe the use of B-flow imaging for 4D reconstruction of normal cardiac chambers and great vessels, which has an effect comparable with that of the inversion mode.

Materials and Methods

Study Population

Fetuses with suspected congenital anomalies underwent 4D ultrasonographic examinations between January 2003 and September 2004. Fetuses were included in the study if: (1) a cardiac anomaly was suspected by 2D ultrasonographic examination; (2) volume data sets of the fetal heart were acquired by STIC; and (3) the cardiac anomaly was confirmed either by an independent fetal cardiologist before delivery, or by neonatal echocardiography or autopsy after delivery. Cases of isolated small pericardial effusions and ventricular echogenic foci were not included. Selected volume data sets of 3 fetuses without abnormalities at 21, 25, and 26 weeks were included in the study to illustrate the normal cardiac anatomy by inversion mode and B-flow imaging. All patients underwent 4D ultrasonographic examinations exclusively for research purposes and gave written informed consent before participation. Research protocols were approved by the Institutional Review Boards of the National Institute of Child Health and Human Development (Bethesda, MD) and Wayne State University (Detroit, MI), as well as the Human Investigation Committee of William Beaumont Hospital (Royal Oak, MI).

Volume Acquisition

Volume data sets of the fetal heart were acquired by STIC with either a 2- to 5- or 4- to 8-MHz motorized curved array transducer (Voluson 730 Expert; GE Medical Systems, Kretztechnik, Zipf, Austria). The acquisition technique has been described previously.[3,4,8] Briefly, volume data sets were acquired by transverse sweeps through the fetal chest. The region of interest included the ventricular chambers, atrial chambers, and great vessels. The acquisition time lasted between 7.5 and 15 seconds and, whenever possible, was performed in the absence of fetal movement. Patients were also asked to momentarily suspend breathing during the procedure. B-mode imaging was used for volume acquisition throughout the study period, and B-flow imaging has been used since August 2004.

Volume Rendering

Volume data sets were examined offline on 4DView software (version 2.1, Luminary; GE Medical Systems, Kretztechnik). All volume data sets were first visualized with multiplanar slicing, after which 3D rendering was performed with gradient light or a mixture of gradient light plus surface smooth algorithms. The inversion mode was then applied to the volume data sets acquired with B-mode imaging. The inversion mode is a novel post processing tool that inverts the gray scale of the volume voxels.[9,14] Therefore, anechoic structures such as the heart chambers, vessel lumen, stomach, gallbladder, renal pelvis, and bladder appear echogenic in the rendered images, whereas structures that are normally echogenic before gray scale inversion (eg, bones) appear anechoic. Post processing adjustments were performed as necessary, including gamma curve correction to optimize tissue contrast resolution and gray scale threshold, and transparency to improve image quality. Volumes were rendered by adaptations of 2 previously reported techniques to obtain thick-slice views of the 4 chambers[8] and 4D reconstruction of the outflow tracts.[4]

Thick-Slice Imaging of the 4-Chamber View Using the Inversion Mode

Thick-slice rendered images of the 4-chamber view were obtained as follows[8]: (1) volume data sets were acquired by transverse sweeps through the fetal heart; (2) after acquisition, the volume data sets were displayed by multiplanar slicing;

(3) the original plane of acquisition containing the 4-chamber view are displayed in panel A (Figure 1); (4) whenever necessary, the volumes were manipulated until an apical 4-chamber view was displayed (with the use of this initial orientation, panel B represents the sagittal view of the heart, and panel C represents the coronal view); (5) a rendering box with the highest length and lowest possible width was adjusted on panel B; (6) the direction of view (green dotted line on the left of the rendering box) was set to display the 4-chamber view in the anteroposterior projection; (7) the rendering algorithm "gradient light" was selected, and the resulting image is displayed in panel D; and (8) the gray scale of the voxels was then inverted by selecting the inversion mode in the 4DView software, and the split-screen format was selected to display panel A on the left side of the screen and the corresponding rendered image on the right side (Figure 2 and Video 1).

Three- and 4-Dimensional Reconstruction of the Outflow Tracts

Three-dimensional reconstruction of the outflow tracts was performed as follows[4]: (1) once a volume data set of the 4-chamber view was acquired, the volume was rotated until the apical 4-chamber view was displayed in the original plane of acquisition (Figure 3, panel A); (2) the rendering box was adjusted in panel B to include the full extent of the heart; and (3) the direction of view was set from anterior to posterior. The resulting rendered image is displayed in panel D (Figure 3 and Video 2).

Descriptive Study of the Inversion Mode for Visualization of Normal and Abnormal Cardiac Anatomy

Thick-slice rendered images of the 4-chamber view in the inversion mode were compared with the corresponding 2D images. Potential advantages and limitations of the inversion mode are described. Reconstructed volume data sets of the outflow tracts in cases of congenital heart disease were compared with a representative example of a normal case. One case of transposition of the great arteries, 1 case of pulmonary atresia associated with tricuspid stenosis, and 1 case of a double-inlet right ventricle have been reported previously by our group, using different rendering techniques for 3D and 4D examination of the fetal heart.[3,4,7–9]

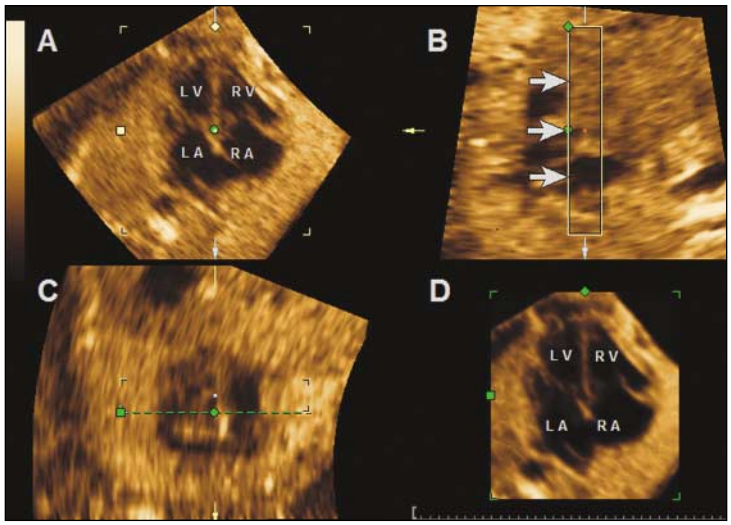
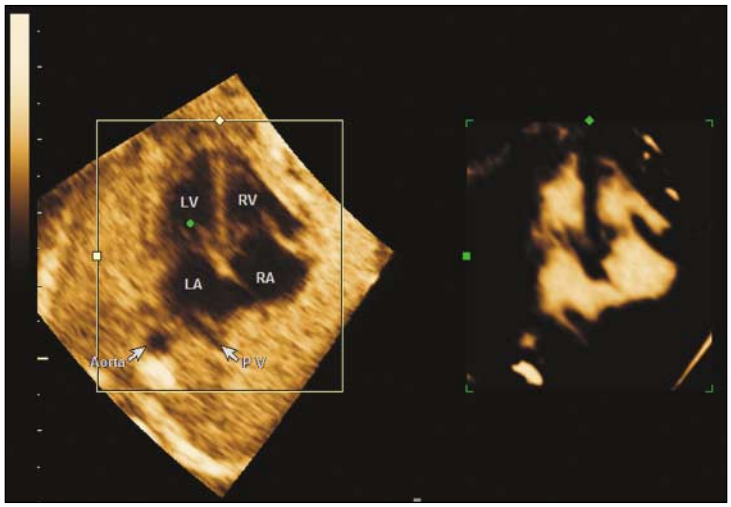


Figure 1. Normal heart at 25 weeks. The first step in obtaining a thick-slice rendered image of the 4-chamber view before application of the inversion mode is shown. The volume is manipulated in **A** until an apical 4-chamber view is displayed. The rendering box is adjusted in **B** with the highest length and lowest possible width. The direction of view (arrows) is set to display the 4-chamber view in the anteroposterior projection. A rendered image of the 4-chamber view using the gradient light mode is shown in **D**. **A**, Transverse plane; **B**, sagittal plane; **C**, coronal plane; **D**, rendered image. LA indicates left atrium; LV, left ventricle; RA, right atrium; and RV, right ventricle.

Results

Twenty-two fetuses with a confirmed diagnosis of congenital heart disease were included in the study (Table 1). The mean maternal age ± SD was 27.5 ± 7.5 years, and the mean gestational age at the time of ultrasonographic examination was 25.6 ± 5.1 weeks (mean ± SD).

Figure 2. Normal 4-chamber view at 25 weeks' gestation. A thick-slice rendered image of the 4 chambers is shown on the right. The corresponding 2D image is displayed on the left.



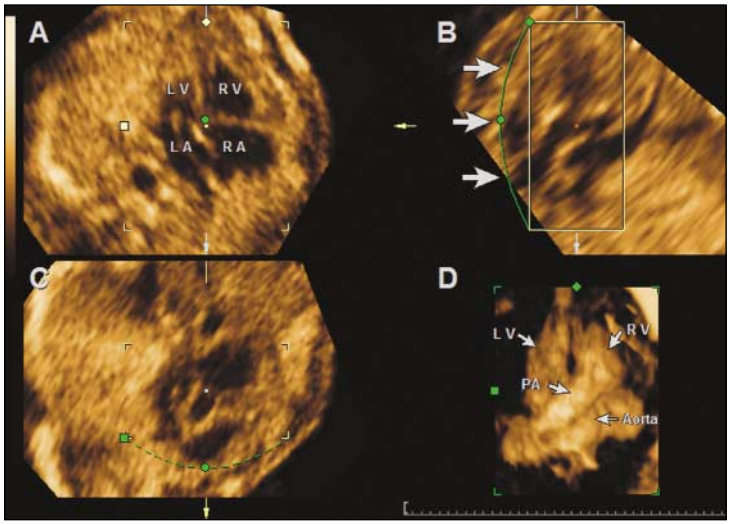


Figure 3. Normal heart at 21 weeks. The technique for obtaining a rendered image of the fetal heart and displaying crisscrossing of the outflow tracts using the inversion mode is shown. The 4-chamber view is shown in **A**. The volume is manipulated until an apical 4-chamber view is displayed. The rendering box is adjusted in **B** with enough width to include the whole heart within the region of interest. The direction of view (arrows) is set to display the heart in the anteroposterior projection. A rendered image of the great vessels crisscrossing as they exit the ventricles is obtained by selecting the gradient light algorithm and applying the inversion mode. Transparency and threshold settings are adjusted as necessary to clean unwanted background noise in the rendered image. **A**, Transverse plane; **B**, sagittal plane; **C**, coronal plane; **D**, rendered image. LA indicates left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; and RV, right ventricle.

Table 1. Cases of Congenital Cardiac Anomalies Included in the Study

Cardiac Anomaly	n
Tetralogy of Fallot	4
Pulmonary atresia	3
VSDs*	3
Atrioventricular septal defect†	2
Coarctation of the aorta‡	2
Double-inlet single ventricle§	2
Absent pulmonary valve syndrome	1
Aortic stenosis	1
Ebstein anomaly	1
Hypoplastic and double-outlet right ventricle	1
Situs inversus totalis	1
Transposition of the great arteries	1
Tricuspid atresia	1
Total	23

*One case associated with an interrupted inferior vena cava with azygous continuation.
†One case associated with an interrupted inferior vena cava with azygous continuation and a persistent left superior vena cava.
‡One case associated with a VSD.
§One case of a double-inlet left ventricle associated with transposition of the great arteries and coarctation of the aorta.

Thick-Slice Imaging of the 4 Chambers in the Inversion Mode

Thick-slice imaging of the 4-chamber view with the inversion mode was attempted in cases of ventricular septal defects (VSDs), Ebstein anomaly, hypoplastic right ventricle due to pulmonary atresia, double-inlet single ventricle, aortic stenosis, atrioventricular septal defects, and tricuspid atresia. The effect of inverting the gray scale on the rendered images can be summarized as follows (Figure 2): (1) the atrial and ventricular chambers were visualized as echogenic structures; (2) the contour of the chambers was sharply delineated when compared with the corresponding 2D images; and (3) the interventricular septum, interatrial septum, and mitral and tricuspid valves were distinctly displayed as anechoic structures.

Figure 4 shows a comparison between 2D imaging and thick-slice volume rendering of the 4-chamber view with the inversion mode in 3 cases of VSDs at 26, 29, and 25 weeks. The VSDs displayed in Figure 4, A and B, were detected in the prenatal period, whereas the VSD in Figure 5C was not diagnosed on the basis of either 2D or 4D multiplanar imaging at 25 weeks. In this case, an omphalocele and extreme deviation of the heart axis to the left were observed. However, the 4-chamber view and outflow tracts were difficult to image because of fetal position and maternal body habitus. A muscular VSD and coarctation of the aorta were detected after delivery by neonatal echocardiography. Retrospective review of the volume data set using the inversion mode revealed the VSD, which was still difficult to visualize in the corresponding 2D image.

Figure 5 shows thick-slice imaging with the inversion mode in cases of hypoplastic right ventricle. Sharper delineation of an atretic tricuspid valve and VSD in a case of tricuspid atresia (Figure 5A) and better visualization of a stenotic tricuspid valve in a case of a hypoplastic right ventricle secondary to pulmonary atresia (Figure 5B) were observed in the rendered images when compared with the corresponding 2D images.

Figure 6 shows thick-slice imaging with the inversion mode in cases of Ebstein anomaly (Figure 6A), double-inlet left ventricle (Figure 6B), and double-inlet right ventricle (Figure 6C). The rendered images were characterized by sharp delineation of the chamber contours, septa, and valves.

Four-Dimensional Reconstruction of the Outflow Tracts in the Inversion Mode

Rendered images of the outflow tracts in cases of coarctation of the aorta, pulmonary stenosis, pulmonary atresia, double-outlet right ventricle, and transposition of the great arteries were compared with a normal case. Representative images of each case are presented in Figure 7. Three-dimensional reconstruction of the outflow tracts allows the examiner to understand the spatial relationships between the outflow tracts as well as the connections between the arteries and the ventricular chambers. A comparison between reconstruction of the outflow tracts in the inversion mode or B-flow imaging is presented in Figure 8. Fewer speckle artifacts and clearer delineation of the great arteries were observed with B-flow imaging (Videos 2 and 3).

Discussion

Prenatal diagnosis of congenital heart disease represents a major challenge to obstetric sonographers because detection rates for congenital cardiac anomalies in population-based studies range from only 4% to 35%.[15–25] Detection rates are generally higher in specialized centers, and operator skill has been proposed to be an important contributor in determining the rate of accurate prenatal diagnosis.[26–28] Indeed, a recent study of 29,026 pregnancies demonstrated that 2 years of training are needed for a sonographer to become proficient in consistently imaging the 4-chamber view and the outflow tracts of the fetal heart.[28]

Improving the detection rates of congenital heart disease, especially transposition of the great arteries, hypoplastic left heart, and coarctation of the aorta, is a desirable goal of prenatal care.[29–31] Three- and 4-dimensional ultrasonography may play an important role in reducing the dependency on operator skills. Indeed, Viñals et al[2] reported visualization rates of greater than 90% for all cardiac structures using STIC. Our group has been interested in a series of techniques to image the outflow tracts systematically.[3,4,7–10] By using multiplanar slicing, we have shown that images of the left and right outflow tracts of good quality could be consistently obtained by different operators.[10] In addition, 3D and 4D reconstruction of the outflow tracts with demonstration of the spatial relationships between the aorta and the pulmonary artery in a

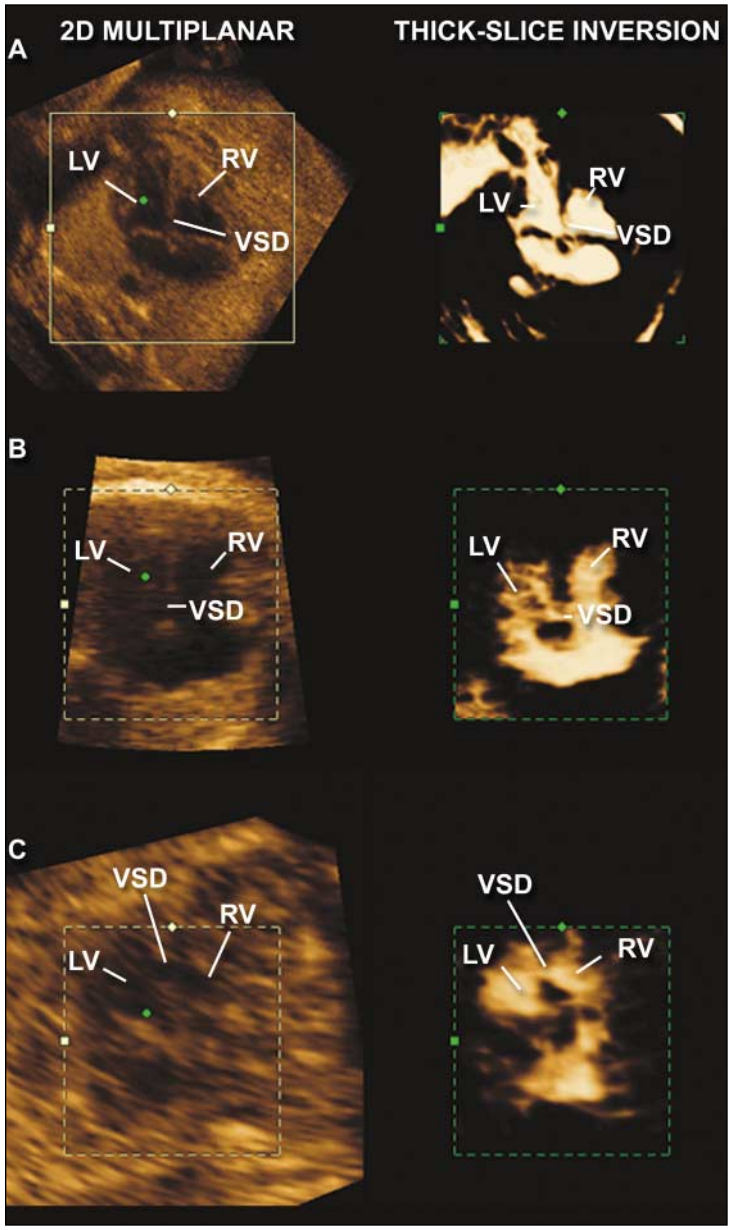


Figure 4. Thick-slice rendering of the 4-chamber view using the inversion mode in VSDs. **A**, Perimembranous VSD at 26$^{6}/_{7}$ weeks. **B**, Perimembranous VSD at 29$^{4}/_{7}$ weeks. **C**, Muscular VSD at 25 weeks. The increased imaging contrast provided by this technique facilitates visualization of VSDs. This is particularly evident in C; the VSD is evident in the rendered image (on the right) but difficult to visualize in the original 2D image. LV indicates left ventricle; and RV, right ventricle.

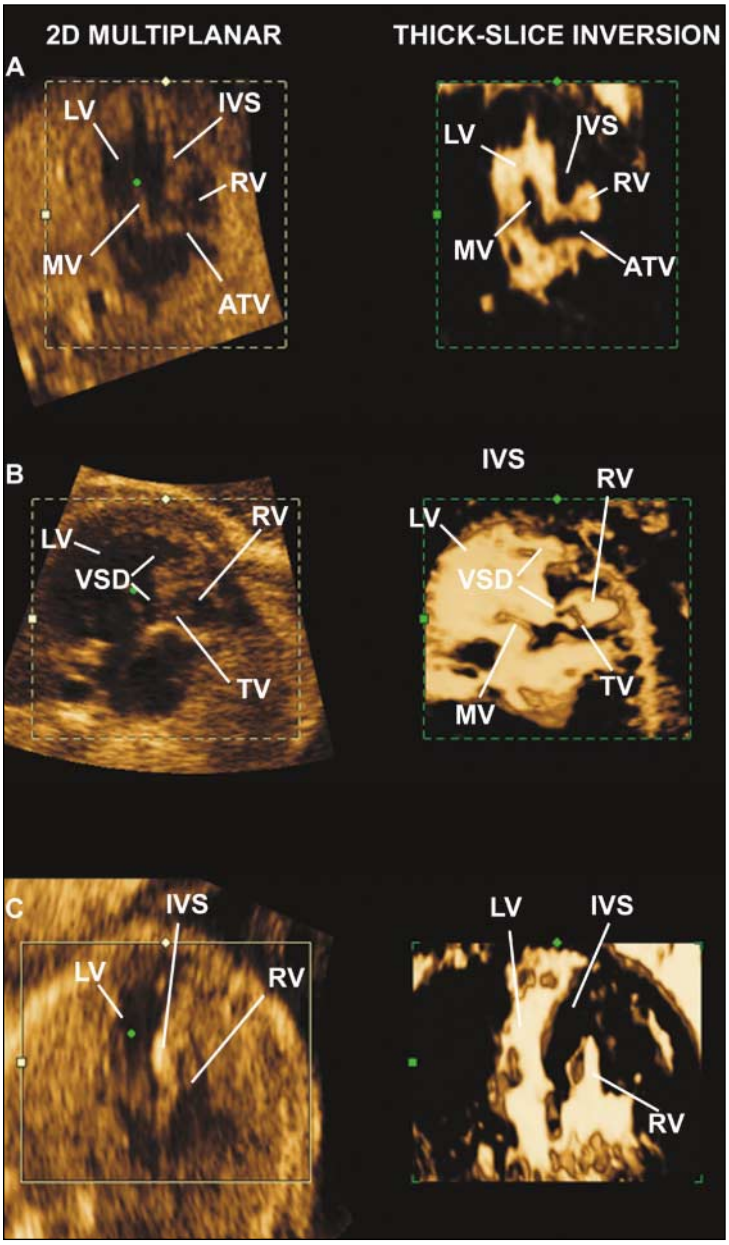


Figure 5. Thick-slice rendering of the 4-chamber view using the inversion mode in representative cases of hypoplastic right ventricle. **A**, Tricuspid atresia with a VSD at $20^{6}/_{7}$ weeks. The atretic tricuspid valve (ATV) appears as a thick and well-defined anechoic line in the rendered image. Compare with the opened mitral valve (MV) in the left ventricle (LV). A VSD communicating the left ventricle and right ventricle (RV) is visualized. **B**, Pulmonary atresia with a VSD and tricuspid stenosis at 35 weeks. The stenotic tricuspid valve (TV) is best visualized in the rendered image. **C**, Pulmonary atresia with an intact interventricular septum (IVS) at $24^{1}/_{7}$ weeks.

single image is possible with the use of color or power Doppler surface rendering[4,5] or the minimum projection mode.[8] Recently, DeVore et al[6] suggested using the "spin" technique in multiplanar images to examine the relationships of cardiac structures of interest with adjacent structures.

The inversion mode has been proposed as a technique capable of producing digital casts of the aortic and ductal arches.[9] In this study, we suggest incorporating this application of the inversion mode into prenatal diagnosis of congenital heart disease. Thick-slice rendering of the 4-chamber view with the inversion mode led to improved definition of the cardiac chambers and atrioventricular valves when compared with the corresponding 2D images. This feature may be useful in the detection of VSDs, especially in cases in which the original 2D images are of poor quality. For example, a muscular VSD that was not diagnosed prenatally by 2D and 4D multiplanar imaging at 25 weeks (Figure 4C) was easier to identify retrospectively with the use of the inversion mode. This specific case was associated with an omphalocele and extreme deviation of the fetal heart axis, and the heart was difficult to image because of the suboptimal fetal position and maternal body habitus. Despite these initial promising observations, the examiner is advised to exercise caution in the interpretation of VSDs using the inversion mode because it may not be possible to differentiate a true VSD from an echo dropout along the septum with this technique alone. When a VSD is suspected in the inversion mode, the examiner should consider the use of adjunctive imaging modalities, such as color Doppler ultrasonography, to confirm the diagnosis.

In this study, we showed that 4D reconstruction of the outflow tracts using either inversion mode or B-flow imaging produces images analogous to those obtained postmortem by injecting silicone rubber to create casts of the cardiovascular cavities.[12,13] It has been shown that postmortem casts aid in the interpretation of morphologic relationships, conceptualization of paths of flow, and evaluation of stenosis.[12] This technique has been used by pathologists to enhance the visualization of chamber morphologic characteristics, relative volumes, vascular constrictions, and distortions in cases of congenital heart disease.[12] Digital casts created with inversion mode or B-flow imaging allowed visualization of the relationships, size, and course of the outflow tracts in several cardiac

anomalies (coarctation of the aorta, pulmonary stenosis, pulmonary atresia, double-outlet right ventricle, and transposition of the great arteries). This modality may help the examiner to better understand the spatial relationships between the vessels in cases of congenital heart disease. In addition, the combination of inversion mode and B-flow imaging may facilitate the explanation of the cardiac anomalies to the parents, especially when these malformations are complex. Because the technology for reconstructing the outflow tracts of the fetal heart by 4D ultrasonography using either inversion mode or B-flow imaging is relatively new, some degree of training will be required before introducing these methods in clinical practice.

One of the limitations of this study was that the examiner had knowledge of the final diagnosis before reconstructing the volume data sets using inversion mode or B-flow imaging. Another limitation was that we did not have enough examples of cardiovascular anomalies with a confirmed postnatal outcome to compare 3D reconstructions produced by inversion mode or B-flow imaging. Although both techniques are capable of producing digital casts of cardiovascular cavities and blood vessels, B-flow imaging may be able to provide better border definition and fewer artifacts than the inversion mode. B-flow technology digitally enhances signals from weak blood reflectors from vessels and, at the same time, suppresses strong signals from surrounding tissues.[32,33] Because this technology does not rely on Doppler methods to display blood flow, it is angle independent and does not interfere with the frame rate.[32,34,35] This is potentially advantageous over color or power Doppler imaging when used in conjunction with STIC for 4D evaluation of the cardiovascular system. In our review of the literature, we found one study that reported the use of B-flow imaging for visualization of the umbilical cord in a fetus and the cerebral vasculature in a neonate.[36] B-flow imaging was able to distinguish the bilateral anterior cerebral arteries as 2 parallel vessels, a feature that had not been reported previously with the use of color or power Doppler imaging. Future studies of congenital cardiac anomalies involving the outflow tracts should compare the performance of these 2 methods in producing digital casts of the fetal heart for prenatal diagnosis of congenital heart disease.

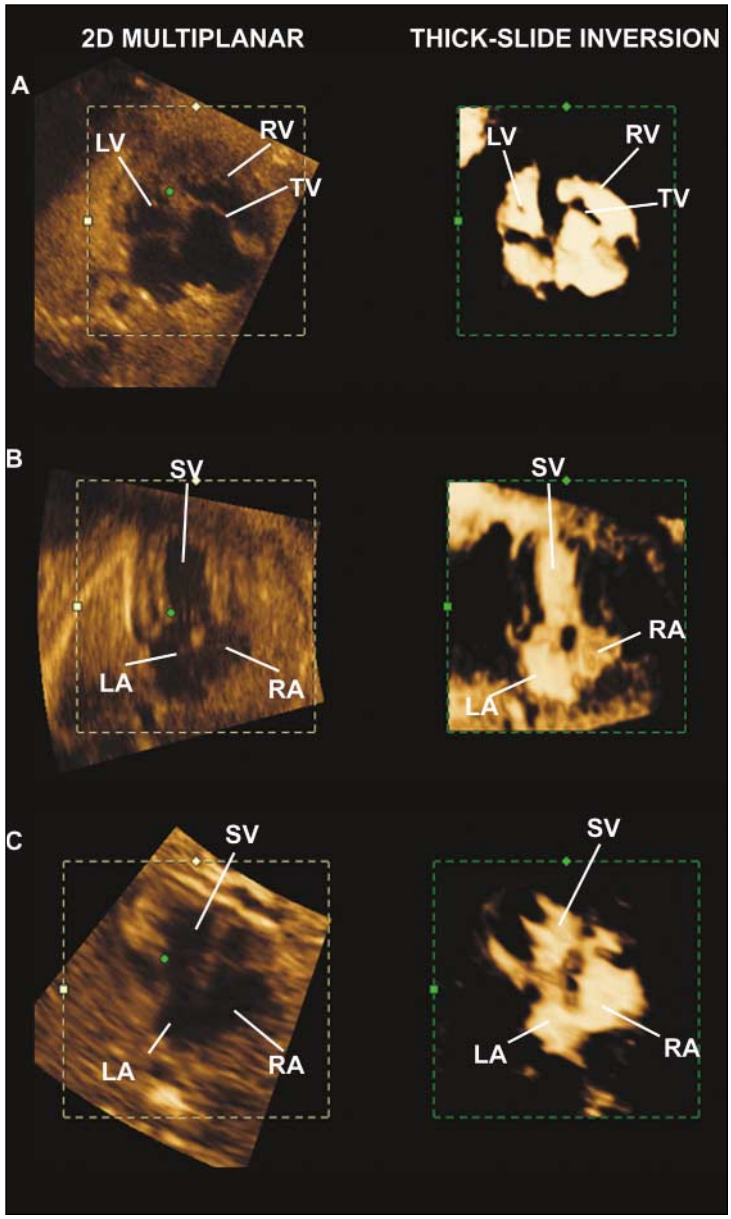


Figure 6. Thick-slice rendering of the 4-chamber view using the inversion mode in Ebstein anomaly at $34^{6}/_{7}$ weeks (**A**), a double-inlet left ventricle at $24^{1}/_{7}$ weeks (**B**), and a double-inlet right ventricle at $29^{1}/_{7}$ weeks (**C**). LA indicates left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; SV, single ventricle; and TV, tricuspid valve.

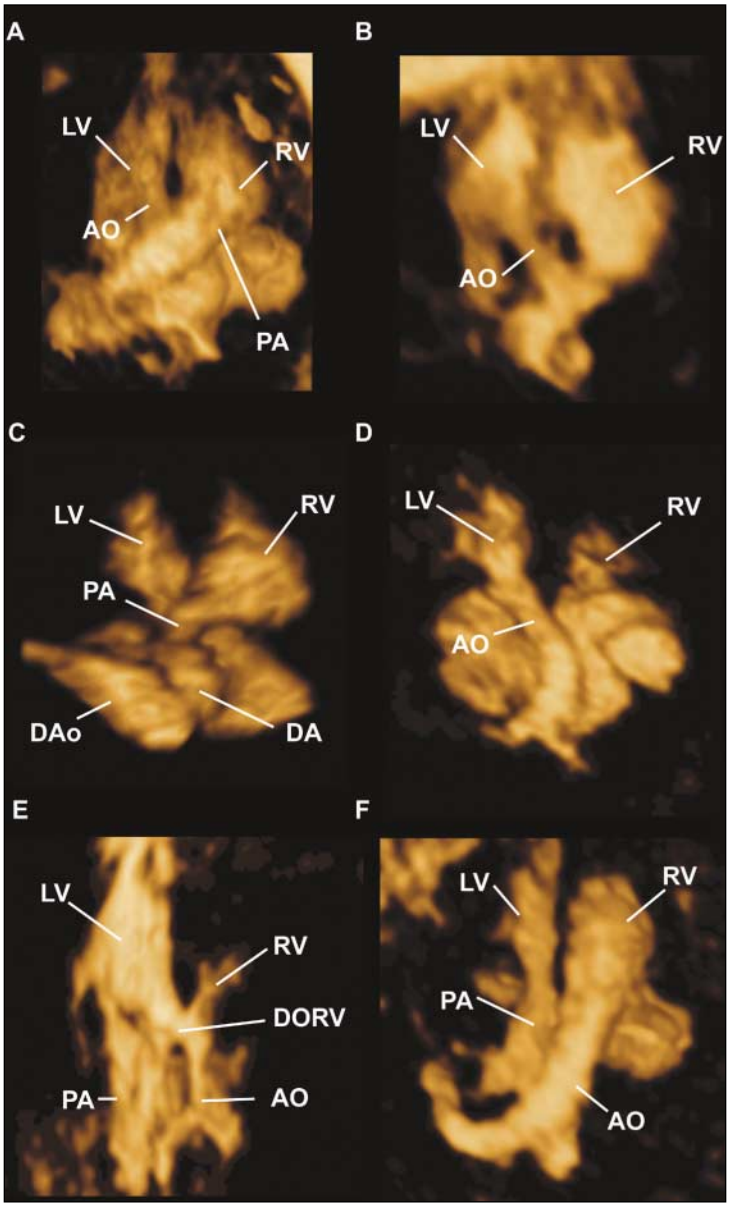


Figure 7. Three-dimensional reconstruction of the outflow tracts using the inversion mode. **A**, Normal outflow tracts at 21 weeks. The aorta (AO) leaves the left ventricle (LV), and the pulmonary artery (PA) leaves the right ventricle (RV); the pulmonary artery crosses in front of the aorta. **B**, Coarctation of the aorta at 25 weeks: the aorta is considerably narrower than the pulmonary artery. **C**, Pulmonary stenosis with a VSD at 23 weeks. The pulmonary artery is narrow, and the ductus arteriosus (DA) is tortuous before joining the descending aorta (DAo). **D**, Pulmonary atresia at 19 weeks: hypoplastic right ventricle. The pulmonary artery is not visualized; the aorta leaves the left ventricle normally. **E**, Hypoplastic and double-outlet right ventricle (DORV). The pulmonary artery and aorta connect preferentially to the right ventricle, with the pulmonary artery overriding the ventricular septum. **F**, Transposition of the great arteries at 20 weeks. The pulmonary artery connects to the left ventricle, and the aorta connects to the right ventricle; the vessels leave the ventricles parallel to each other.

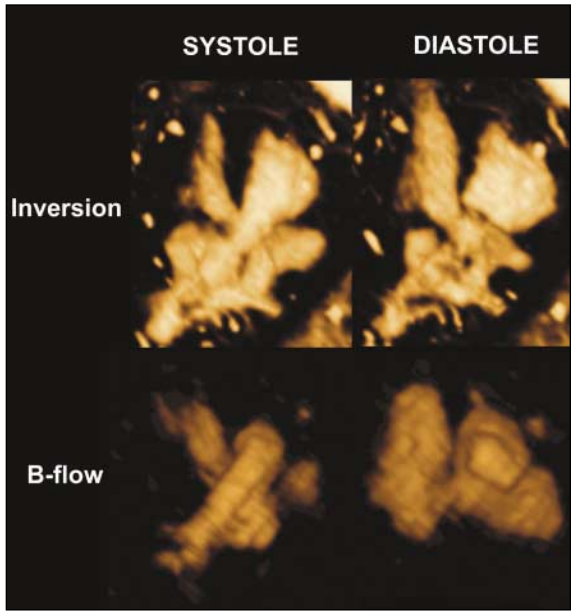


Figure 8. Comparison of digital casts of the outflow tracts in systole and diastole rendering using the inversion mode (top) and B-flow imaging (bottom) in a fetus without abnormalities at 26 weeks of gestation.

References

1. DeVore GR, Falkensammer P, Sklansky MS, Platt LD. Spatio-temporal image correlation (STIC): new technology for evaluation of the fetal heart. Ultrasound Obstet Gynecol 2003; 22:380–387.

2. Viñals F, Poblete P, Giuliano A. Spatio-temporal image correlation (STIC): a new tool for the prenatal screening of congenital heart defects. Ultrasound Obstet Gynecol 2003; 22:388–394.

3. Gonçalves LF, Lee W, Chaiworapongsa T, et al. Four-dimensional ultrasonography of the fetal heart with spatiotemporal image correlation. Am J Obstet Gynecol 2003; 189:1792–1802.

4. Gonçalves LF, Romero R, Espinoza J, et al. Four-dimensional ultrasonography of the fetal heart using color Doppler spatiotemporal image correlation. J Ultrasound Med 2004; 23:473–481.

5. Chaoui R, Hoffmann J, Heling KS. Three-dimensional (3D) and 4D color Doppler fetal echocardiography using spatio-temporal image correlation (STIC). Ultrasound Obstet Gynecol 2004; 23:535–545.

6. DeVore GR, Polanco B, Sklansky MS, Platt LD. The "spin" technique: a new method for examination of the fetal outflow tracts using three-dimensional ultrasound. Ultrasound Obstet Gynecol 2004; 24:72–82.

7. Gonçalves LF, Espinoza J, Romero R, et al. A systematic approach to prenatal diagnosis of transposition of the great arteries using four-dimensional ultrasound with spatiotemporal image correlation. J Ultrasound Med 2004; 23:1225–1231.

8. Espinoza J, Goncalves LF, Lee W, et al. The use of the minimum projection mode in four-dimensional examination of the fetal heart with spatiotemporal image correlation. J Ultrasound Med 2004; 23: 1337–1348.

9. Gonçalves LF, Espinoza J, Lee W, Mazor M, Romero R. Three- and four-dimensional reconstruction of the aortic arches using inversion mode: a new rendering algorithm for visualization of fluid-filled anatomical structures. Ultrasound Obstet Gynecol 2004; 24: 696–698.

10. Gonçalves LF, Lee W, Espinoza J, et al. Four-dimensional fetal echocardiography with spatio temporal image correlation (STIC): a systematic study of standard cardiac views assessed by different observers. Ultrasound Obstet Gynecol 2003; 22(suppl 1):50.

11. Abuhamad A. Automated multiplanar imaging: a novel approach to ultrasonography. J Ultrasound Med 2004; 23:573–576.

12. Kilner PJ, Ho SY, Anderson RH. Cardiovascular cavities cast in silicone rubber as an adjunct to postmortem examination of the heart. Int J Cardiol 1989; 22:99–107.

13. Cook AC, Fagg NL, Allan LD. Use of casts in the necropsy diagnosis of fetal congenital heart disease. Br Heart J 1992; 68:481–484.

14. Lee W, Gonçalves LF, Espinoza J, Romero R. Inversion mode: a new volume analysis tool for 3-dimensional ultrasonography. J Ultrasound Med 2005; 24: 201–207.

15. Buskens E, Grobbee DE, Frohn-Mulder IM, et al. Efficacy of routine fetal ultrasound screening for congenital heart disease in normal pregnancy. Circulation 1996; 94:67–72.

16. Crane JP, LeFevre ML, Winborn RC, et al. A randomized trial of prenatal ultrasonographic screening: impact on the detection, management, and outcome of anomalous fetuses. The RADIUS Study Group. Am J Obstet Gynecol 1994; 171:392–399.

17. Garne E, Stoll C, Clementi M. Evaluation of prenatal diagnosis of congenital heart diseases by ultrasound: experience from 20 European registries. Ultrasound Obstet Gynecol 2001; 17:386–391.

18. Jaeggi ET, Sholler GF, Jones OD, Cooper SG. Comparative analysis of pattern, management and outcome of pre- versus postnatally diagnosed major congenital heart disease: a population-based study. Ultrasound Obstet Gynecol 2001; 17:380–385.

19. Klein SK, Cans C, Robert E, Jouk PS. Efficacy of routine fetal ultrasound screening for congenital heart disease in Isere County, France. Prenat Diagn 1999; 19:318–322.

20. Rustico MA, Benettoni A, D'Ottavio G, et al. Fetal heart screening in low-risk pregnancies. Ultrasound Obstet Gynecol 1995; 6:313–319.

21. Stoll C, Alembik Y, Dott B, Roth PM, De Geeter B. Evaluation of prenatal diagnosis of congenital heart disease. Prenat Diagn 1993; 13:453–461.

22. Stoll C, Alembik Y, Dott B, et al. Evaluation of prenatal diagnosis of congenital heart disease. Prenat Diagn 1998; 18:801–807.

23. Todros T, Faggiano F, Chiappa E, Gaglioti P, Mitola B, Sciarrone A, Gruppo Piemontese for Prenatal Screening of Congenital Heart Disease. Accuracy of routine ultrasonography in screening heart disease prenatally. Prenat Diagn 1997; 17:901–906.

24. Grandjean H, Larroque D, Levi S. The performance of routine ultrasonographic screening of pregnancies in the Eurofetus study. Am J Obstet Gynecol 1999; 181:446–454.

25. Fernandez CO, Ramaciotti C, Martin LB, Twickler DM. The four-chamber view and its sensitivity in detecting congenital heart defects. Cardiology 1998; 90:202–206.

26. Carvalho JS, Mavrides E, Shinebourne EA, Campbell S, Thilaganathan B. Improving the effectiveness of routine prenatal screening for major congenital heart defects. Heart 2002; 88:387–391.

27. Campbell S, Allan L, Benacerraf B, et al. Isolated major congenital heart disease. Ultrasound Obstet Gynecol 2001; 17:370–379.

28. Tegnander E, Eik-Nes SH. The examiner's ultrasound experience has a significant impact on the detection rate of congenital heart defects at the second trimester fetal examination [abstract]. Ultrasound Obstet Gynecol 2004; 24(3):217.

29. Bonnet D, Coltri A, Butera G, et al. Detection of transposition of the great arteries in fetuses reduces neonatal morbidity and mortality. Circulation 1999; 99:916–918.

30. Franklin O, Burch M, Manning N, Sleeman K, Gould S, Archer N. Prenatal diagnosis of coarctation of the aorta improves survival and reduces morbidity. Heart 2002; 87:67–69.

31. Tworetzky W, McElhinney DB, Reddy VM, Brook MM, Hanley FL, Silverman NH. Improved surgical outcome after fetal diagnosis of hypoplastic left heart syndrome. Circulation 2001; 103:1269–1273.

32. Wachsberg RH. B-flow, a non-Doppler technology for flow mapping: early experience in the abdomen. Ultrasound Q. 2003; 19:114–122.

33. Deane C. Extended field-of-view and B-flow ultrasound: fashion or future? Ultrasound Obstet Gynecol 2000; 15:96–97.

34. Weskott HP. B-flow: a new method for detecting blood flow. Ultraschall Med 2000; 21:59–65.

35. Henri P, Tranquart F. B-flow ultrasonographic imaging of circulating blood. J Radiol 2000; 81:465–467.

36. Pooh RK. New application of B-flow sono-angiography in perinatology. Ultrasound Obstet Gynecol 2000; 15:163.