

A Prospective Study of the Use of Fetal Intelligent Navigation Echocardiography (FINE) to Obtain Standard Fetal Echocardiography Views

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Key Words

4D ultrasound · Cardiac screening · Fetal heart · Prenatal diagnosis · Spatiotemporal image correlation · STIC · STICLoop™ · Ultrasound · Virtual Intelligent Sonographer Assistance · VIS-Assistance®

Abstract

Objective: To evaluate the performance of Fetal Intelligent Navigation Echocardiography (FINE) applied to spatiotemporal image correlation (STIC) volume datasets of the normal fetal heart in generating standard fetal echocardiography views. **Methods:** In this prospective cohort study of patients with normal fetal hearts (19–30 gestational weeks), one or more STIC volume datasets were obtained of the apical four-chamber view. Each STIC volume successfully obtained was evaluated by STICLoop™ to determine its appropriateness before applying the FINE method. Visualization rates for standard fetal echocardiography views using diagnostic planes and/or Virtual Intelligent Sonographer Assistance (VIS-Assistance®) were calculated. **Results:** One or more STIC

volumes (total n = 463) were obtained from 246 patients. A single STIC volume per patient was analyzed using the FINE method. In normal cases, FINE was able to generate nine fetal echocardiography views using: (1) diagnostic planes in 76–100% of the cases, (2) VIS-Assistance® in 96–100% of the cases, and (3) a combination of diagnostic planes and/or VIS-Assistance® in 96–100% of the cases. **Conclusion:** FINE applied to STIC volumes can successfully generate nine standard fetal echocardiography views in 96–100% of cases in the 2nd and 3rd trimesters. This suggests that the technology can be used as a method of screening for congenital heart disease.

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Introduction

Congenital heart disease (CHD) is the leading cause of infant morbidity and mortality among those born with birth defects [1], and represents the most prevalent organ-specific birth defect [2]. However, the prenatal diag-

nosis of CHD remains suboptimal, with sensitivities ranging from 22.5 to 52.8% [3–6]. Since most cases of CHD occur in pregnancies without risk factors [7], midtrimester screening for CHD is the most rational approach for the detection of cardiac anomalies [8–11]. Professional organizations have recommended guidelines for sonographic examination of the fetal heart [12, 13], which reflect current knowledge about the prenatal detection of CHD. For example, the addition of outflow tract views to the four-chamber view in cardiac screening is an important step forward to improve such detection [12, 13].

Volumetric sonography – specifically, four-dimensional (4D) ultrasound with spatiotemporal image correlation (STIC) [14–17] – facilitates examination of the fetal heart [14, 15, 18–41], and has been proposed in both cardiac screening and prenatal diagnosis of CHD [16, 25, 42–55], because it improves the ability to identify complex intracardiac relationships and can shorten the examination time [14, 22]. However, the optimal method of interrogating STIC volume datasets remains a challenge, and several algorithms have therefore been proposed for this purpose [15, 18, 21, 24, 28, 31, 33].

Fetal Intelligent Navigation Echocardiography (FINE) has recently emerged as a novel approach to examine the fetal heart after a STIC volume has been acquired [56–58]. Such a method allows the automatic generation and display of nine standard fetal echocardiography views in normal hearts, including those universally recommended by professional organizations such as the American Institute of Ultrasound in Medicine (AIUM) and the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) [59, 60]. Through the use of Virtual Intelligent Sonographer Assistance (VIS-Assistance[®]), which is a feature of FINE, operator-independent sonographic navigation and exploration of surrounding structures in each of the nine cardiac diagnostic planes is also possible [56–58], and this has been proposed to be of value in reducing the false positive rate and improving the quality of the examination.

In the first report on the FINE method, there was successful generation of nine fetal echocardiography views in 98–100% of normal cases, using a combination of diagnostic planes and/or VIS-Assistance[®] [56]. The authors concluded that this method can simplify examination of the fetal heart and reduce the operator dependency associated with manipulation and analysis of STIC volume datasets. Recently, Garcia et al. [58] reported that in the 2nd and 3rd trimesters, one or more STIC volumes could be prospectively obtained in 72.5% of women attending

a prenatal clinic, and that 96.2% of such volumes were appropriate for analysis using FINE.

While these findings are encouraging, since they suggest that nearly three fourths of patients can be examined using the FINE method, further prospective studies are required to determine the frequency with which fetal echocardiography views can be obtained using FINE in different populations. Therefore, the objective of the current study was to prospectively evaluate the performance of the FINE method in successfully generating nine standard fetal echocardiography views when applied to STIC volume datasets.

Subjects and Methods

Subjects

In this prospective cohort study, women having singleton fetuses with normal fetal hearts between 19 and 30 gestational weeks underwent 4D sonography with STIC volume acquisition. The study was conducted at the Unit of Maternal Fetal Medicine, Department of Women's and Children's Health, Azienda Ospedaliera di Padova (AOP), Padua, Italy. All patients were enrolled according to a research protocol approved by the local ethics committee, and provided written informed consent for the use of ultrasound images for research purposes. The hospital has a Federalwide Assurance (FWA) negotiated with the Office for Human Research Protections (OHRP), US Department of Health and Human Services. The research protocol was considered to convey less than minimal risk, as it only required sonographic examination.

STIC Volume Acquisition

Using STIC technology (Voluson E8 Expert; GE Healthcare, Zipf, Austria), 4D volume datasets of the fetal heart (1–5 per patient) were obtained from an apical four-chamber view using a curved array transducer (4–8 MHz) by means of transverse sweeps through the fetal chest. The ultrasound examination was conducted using settings for fetal echocardiography, with adjustments to obtain clear 2D images. The frame rate was maximized by decreasing the depth, narrowing the sector width, and placing a single focal zone at or below the level of the fetal heart. The acquisition time was set to 10 s, and the angle of acquisition ranged between 20 and 45°, depending upon the gestational age. The goal was to set an acquisition angle at least 5° greater than the value of the gestational age in weeks. Mothers were asked to temporarily suspend breathing movements during STIC volume acquisition. Volumes were obtained in the absence of fetal breathing or gross movements as well as hiccups. Attempts were made to acquire STIC volume datasets when the fetal spine was located between the 5 and 7 o'clock positions, to reduce the likelihood of acoustic shadowing derived from the spine. Optimally, STIC volumes were obtained when there was a clearly visible transverse aortic arch [56].

Volumes were saved onto the hard drive of the ultrasound machine when examination of the multiplanar display demonstrated the following: (1) normal fetal heart rate; (2) fetal upper mediastinum and stomach present and visualized within the STIC volume;

(3) minimal or no motion artifacts observed in the sagittal plane, and (4) minimal or absent acoustic shadowing so as not to hinder visualization of the cardiac structures [56].

STICLoop™ Evaluation

All saved STIC volume datasets were then imported into a software system for analysis (SONOCUBIC FINE™ Classic Blue Series version 2013.04.05; Medge Platforms, Inc., New York, N.Y., USA), which was installed on a Sony Vaio PCG 71211M desktop computer (Sony Corp., Minato, Tokyo, Japan), using the Operative System Microsoft Windows 7 PRO 64-bit Service pack (Microsoft Corp., Redmond, Wash., USA). Once a STIC volume is loaded into this software system, it is immediately converted into a 2D cine loop that automatically scrolls in a continuous fashion (i.e. STICLoop™) [56]. This tool allows the sonologist to determine the appropriateness of STIC volume datasets before applying the FINE method [52]. With STICLoop™, the image on the screen begins with the initial frame that was obtained by the mechanical probe, and automatic scrolling through all the frames occurs until the last frame acquired in the sweep is reached [56]. We used a cine rate of 8–12 loops/min to evaluate all the STIC volumes.

Using STICLoop™, the criteria for defining appropriate STIC volumes were the following: (1) fetal spine located between the 5 and 7 o'clock positions (reducing the possibility of shadowing from the ribs or spine); (2) minimal or absent shadowing [including the three-vessels and trachea view (3VT)]; (3) adequate image quality; (4) upper mediastinum and stomach included within the volume; (5) minimal or no motion artifacts observed in the loop (i.e. smooth sweep without evidence of abrupt jumps or discontinuous movements); (6) chest circumference contained within the region of interest; (7) sequential axial planes parallel to each other, similar to a sliced loaf of bread (i.e. no 'drifting spine' from the four-chamber view down to the stomach); (8) no observed azimuthal issues or tilted planes (i.e. atria/ventricles do not appear foreshortened in the four-chamber view), and (9) minimal or no motion artifacts (observed in the sagittal plane) [56].

The sonologist determined whether STIC volumes were appropriate by: (1) observing the scrolling frames on the screen and evaluating them according to criteria 1 through 8 and (2) clicking on the cross section of the fetal aorta, so that the displayed sagittal plane of the heart can be evaluated for motion artifacts (criterion 9) (see online suppl. video clip S1; for all online suppl. material, see www.karger.com/doi/10.1159/000446982). From all the STIC volumes determined to be appropriate using STICLoop™, only a single volume per patient was chosen for analysis using the FINE method.

Testing of the FINE Method

After marking seven anatomical structures of the fetal heart using the Anatomic Box® feature, nine standard fetal echocardiography views are automatically generated and displayed by FINE (as diagnostic planes and/or VIS-Assistance®) [56]. In sequential order, the seven structures are: (1) cross section of the aorta at the level of the stomach; (2) cross section of the aorta at the level of the four-chamber view; (3) crux; (4) right atrial wall; (5) pulmonary valve; (6) cross section of the superior vena cava, and (7) transverse aortic arch. It is noteworthy that FINE helps sonologists to correctly identify and mark such anatomical structures in the following manner [56, 57]: (a) a menu and reference image is displayed for each anatomical structure to be marked, and the order of marking is also specified; (b) the software system automatically scrolls

through the STIC volume to the level of the most likely location of the anatomical structure to be marked, and (c) the software system recognizes the cardiac phase, which facilitates marking of anatomical structures (e.g. automatically closes the pulmonary valve).

The nine fetal echocardiography views generated are: (1) four chamber; (2) five chamber; (3) left ventricular outflow tract; (4) short-axis view of the great vessels/right ventricular outflow tract; (5) 3VT; (6) abdomen/stomach; (7) ductal arch; (8) aortic arch, and (9) superior and inferior venae cavae. If an operator is not familiar with the cardiac structures for marking and marks them incorrectly, FINE may not be successful in generating fetal echocardiography views [56]. Yet, in this situation the method can still be successful, depending upon which structure(s) is (are) being marked, the degree of 'incorrectness' in marking structures (e.g. being slightly off vs. marking the wrong structure completely), and the echocardiography view being generated (e.g. abdomen/stomach). The nine fetal echocardiography views are displayed simultaneously in a single template (as nine diagnostic planes) approximately 3 s after the marking process is completed (fig. 1; online suppl. video clip S2). For each diagnostic plane, VIS-Assistance® may also be activated. This 'virtual' sonographer tool scans the STIC volume in a targeted approach (as a video clip) to allow the complexity of the fetal heart to be studied in greater detail [56, 57]. In other words, VIS-Assistance® allows operator-independent sonographic navigation and exploration of surrounding structures in each of the nine cardiac diagnostic planes (e.g. left ventricular outflow tract) [56, 57]. VIS-Assistance® also improves the success of obtaining the fetal echocardiography view of interest (fig. 2; online suppl. video clip S3).

Using the FINE method, we determined the frequency of generating nine fetal echocardiography views using diagnostic planes and/or VIS-Assistance®. For four cardiac VIS-Assistance® views (3VT, left ventricular outflow tract, short-axis view of the great vessels/right ventricular outflow tract, and abdomen/stomach), VIS-Assistance® was considered successful in depicting the echocardiography view if certain anatomical structures were also visualized: (a) 3VT: three-vessel view, pulmonary valve, and transverse aortic arch view; (b) left ventricular outflow tract: mitral valve, aortic valve, and ventricular septum; (c) short-axis view of the great vessels/right ventricular outflow tract: pulmonary valve and tricuspid valve, and (d) abdomen/stomach: stomach and four-chamber view (to determine situs) [56].

For each STIC volume dataset, we also determined the following: (1) the maximum number of fetal echocardiography views successfully obtained through diagnostic planes or VIS-Assistance® and (2) the success rate of obtaining four fetal echocardiography views (four chamber, left ventricular outflow tract, short-axis view of the great vessels/right ventricular outflow tract, and abdomen/stomach) through diagnostic planes or VIS-Assistance®.

Intelligent and Marking Alerts

Since the original report on FINE [56], its inventors subsequently developed 'intelligent alerts' as part of this method to notify the sonologist about potential issues with the STIC volume dataset. Alerts are composed of captions and/or a movie which automatically appear: (a) during the process of marking anatomical structures of the fetal heart and (b) in specific situations. There are three types of intelligent alerts:

1 Breech alert: notifies the user that the fetus appears to be in a breech presentation. The system asks if the STIC volume can

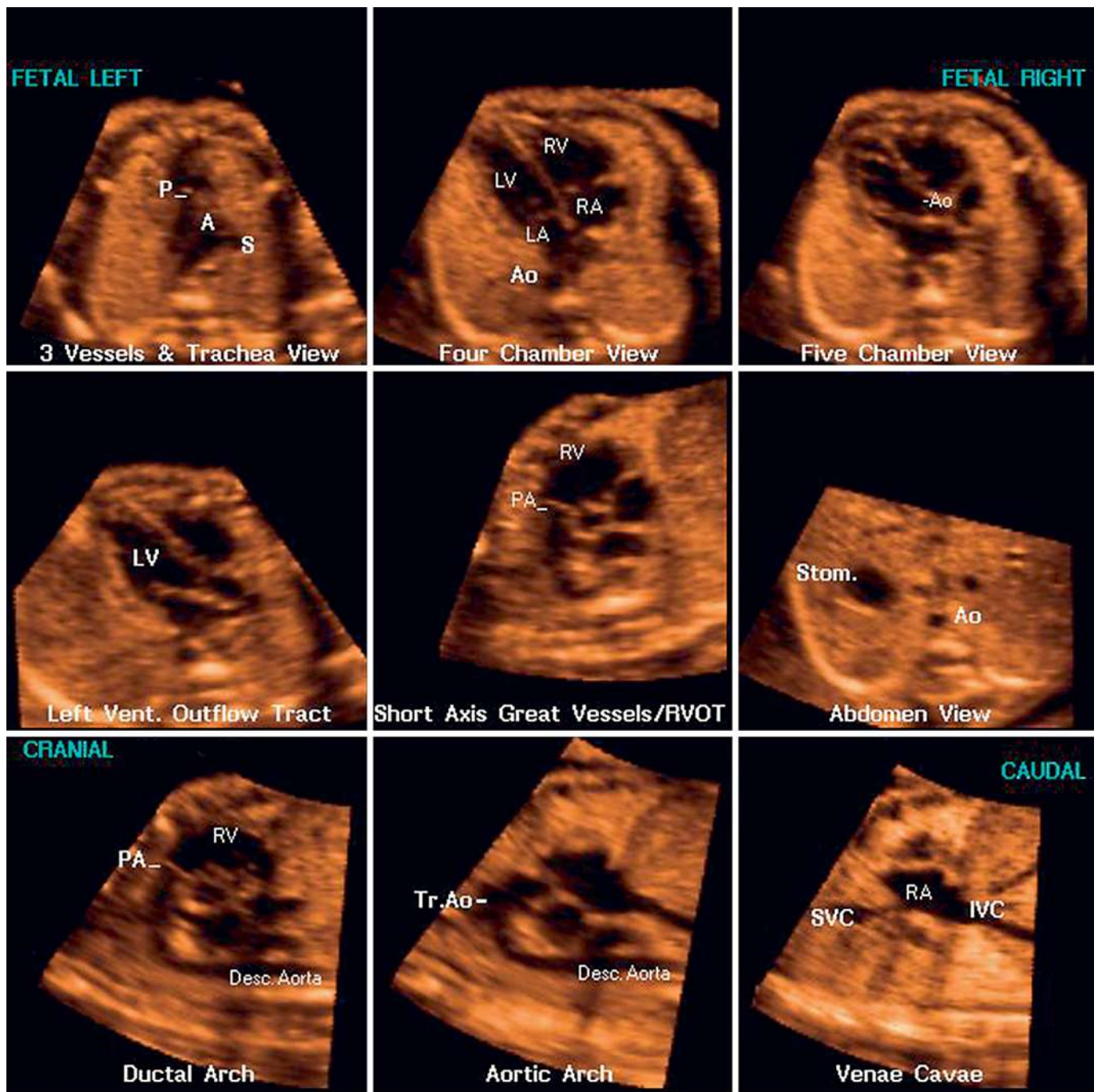
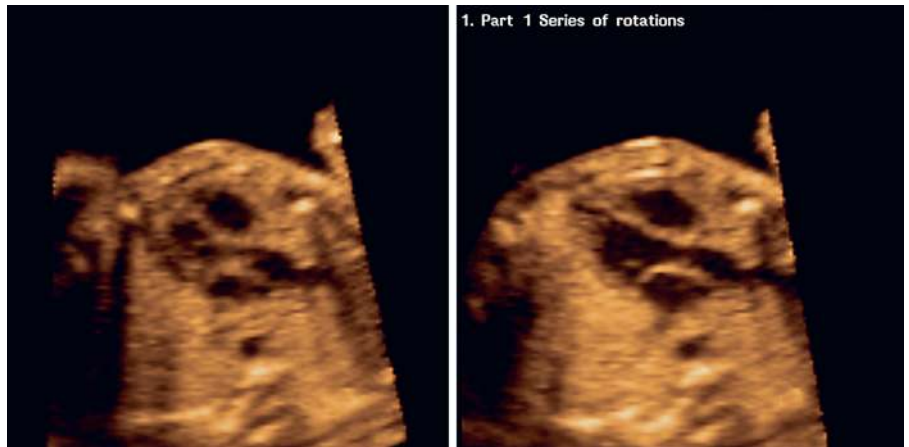


Fig. 1. STIC volume dataset of a fetal heart showing nine cardiac diagnostic planes displayed automatically in a single template through FINE. There is automatic labeling (through intelligent navigation) of each echocardiography view (i.e. diagnostic plane), anatomical structures, fetal left and right sides, and cranial and caudal ends (also see online suppl. video clip S2). A = Transverse

aortic arch; Ao = aorta; Desc. = descending; IVC = inferior vena cava; LA = left atrium; LV = left ventricle; P or PA = pulmonary artery; RA = right atrium; RV = right ventricle; RVOT = right ventricular outflow tract; S = superior vena cava; Stom. = stomach; SVC = superior vena cava; Tr. = transverse; Vent. = ventricular.

Fig. 2. STIC volume dataset of a fetal heart showing the left ventricular outflow tract view through the FINE method. The left ventricular outflow tract was not successfully obtained using the diagnostic plane (left image). However, after VIS-Assistance[®] was activated, the automatic navigational movements allowed the left ventricular outflow tract to be successfully obtained (right image). Also see online supplementary video clip S3.



- be reoriented as if the fetus is in a ‘vertex’ presentation. If the user clicks ‘Yes’, the system automatically realigns the volume dataset, and reorients and standardizes the anatomical position so that the fetus is ‘converted’ to a vertex presentation
- 2 Possible drifting spine alert: notifies the user that there may be a ‘drifting’ fetal spine in the STIC volume dataset (i.e. when the spine location migrates on the screen). The caption also states that marking of anatomical structures may be difficult and successful visualization of echocardiography views may be affected
 - 3 Spine location alert: notifies the user that the fetal spine appears to be located at a position (e.g. 8 o’clock) that is different from what is recommended (i.e. between 5 and 7 o’clock). The caption also states that this STIC volume is not recommended and the spine location may lead to shadowing and a suboptimal image quality. It is noteworthy that once a spine location alert has appeared, three ‘marking alerts’ will next appear in sequence (‘pulmonary valve alert’, ‘superior vena cava alert’, and ‘transverse aortic arch alert’). Such marking alerts are composed of captions/movies which notify the user that fetal anatomical structures for marking (e.g. pulmonary valve) may be in a different location than what is expected

Based upon how the alerts were designed, if appropriate STIC volume datasets have been obtained by a sonologist, the prevalence of alerts is expected to be low (one exception is the breech alert). It has been the inventors’ observation that for most sonologists, the appearance of alerts tends to be disconcerting and leads to an improvement in the STIC volume acquisition technique to avoid such alerts from appearing in the future. For the current study, we recorded both the number and type of alerts which automatically appeared while marking anatomical structures of the fetal heart.

Results

STIC Volumes and Alerts

One or more STIC volumes ($n = 463$) were acquired in 246 pregnancies with a normal fetal heart, as determined by 2D sonographic examination. The gestational age dis-

tribution of the patients from whom STIC volumes were acquired was: (1) 19–22 weeks ($n = 167$); (2) 23–26 weeks ($n = 60$), and (3) 27–30 weeks ($n = 19$). The median (interquartile range) gestational age was 21 (20–23) weeks. From the STIC volumes determined to be appropriate using STICLoop[™], only a single volume per patient was selected for analysis using the FINE method. When there were multiple appropriate STIC volumes available per fetus, we chose the dataset that was considered to be of the highest quality.

During the process of marking anatomical structures of the fetal heart in the STIC volume dataset, an intelligent alert appeared in 39.4% (97/246) of the cases: (1) a breech alert in 30.1% ($n = 74$); (2) a spine location alert in 8.5% ($n = 21$), and (3) a possible drifting spine alert in 0.8% ($n = 2$). Therefore, 30.1% of the fetuses were in an original breech presentation so that the cardiac apex was originally pointing to the right side of the monitor’s screen. Yet, the breech alert allowed reorientation of the STIC volume so that the fetus would be in a ‘vertex’ presentation. This is done so that (1) marking anatomical structures is easier, since each structure is expected to be in the same location on the screen, and (2) the structures and fetal anatomy would be more easily recognizable by users [56].

The spine location alert appeared in only 8.5% ($n = 21$) of cases, and the alert was automatically activated during the marking process because the fetal spine in the STIC volume was located in a position other than between 5 and 7 o’clock: (1) 7 to 8 o’clock in 47.6% ($n = 10$); (2) 8 o’clock in 28.6% ($n = 6$); (3) 4 to 5 o’clock in 14.3% ($n = 3$), and (4) 4 o’clock in 9.5% ($n = 2$) of the cases. Therefore, when evaluating STIC volumes via STICLoop[™], we had correctly identified that in 91.5% (225/246) of the volumes, the fetal spine was located between the 5 and 7 o’clock posi-

Table 1. Success rates of obtaining nine fetal echocardiography views after applying the FINE method to 246 normal STIC volume datasets using diagnostic planes and/or VIS-Assistance®

Fetal echocardiography view	Diagnostic planes (n = 246)		VIS-Assistance® (n = 246)		Diagnostic planes and/or VIS-Assistance® (n = 246)	
	n (%)	95% CI ¹	n (%)	95% CI ¹	n (%)	95% CI ¹
1. Four-chamber	229 (93)	89 to 96	246 (100)	98 to 100	246 (100)	98 to 100
2. Five-chamber	231 (94)	90 to 96	245 (99.6)	98 to >99.9	245 (99.6)	98 to >99.9
3. LVOT	225 (91)	87 to 94	243 (99)	96 to 99.7	243 (99)	96 to 99.7
4. Short-axis view of the great vessels/RVOT	216 (88)	83 to 91	245 (99.6)	98 to >99.9	245 (99.6)	98 to >99.9
5. 3VT	226 (92)	88 to 95	245 (99.6)	98 to >99.9	245 (99.6)	98 to >99.9
6. Abdomen/stomach	246 (100) ²	98 to 100	246 (100) ³	98 to 100	246 (100)	98 to 100
7. Ductal arch	205 (83)	78 to 88	239 (97)	94 to 99	239 (97)	94 to 99
8. Aortic arch	214 (87)	82 to 91	238 (97)	94 to 98	238 (97)	94 to 98
9. SVC/IVC	187 (76)	70 to 81	236 (96)	93 to 98	236 (96)	93 to 98
SVC	230 (93)	90 to 96	-	-	-	-
IVC	200 (81)	76 to 86	-	-	-	-

IVC = Inferior vena cava; LVOT = left ventricular outflow tract; RVOT = right ventricular outflow tract; SVC = superior vena cava. ¹ The Wald method was used to calculate two-sided CIs for proportions expressed in the table; as the true proportion cannot exceed 100%, the upper confidence limits are truncated at 100%. ² Defined as visualization of the stomach in the diagnostic plane. ³ Defined as visualization of both the stomach and four-chamber view in VIS-Assistance® (to determine situs).

tions. For each spine location alert that was automatically activated, three marking alerts (pulmonary valve, superior vena cava, and transverse aortic arch alerts) also appeared next in sequence. Such alerts noted that fetal anatomical structures for marking (e.g. transverse aortic arch) could be in a different location than expected, since the fetal spine was not located between the 5 and 7 o'clock positions.

Performance of the FINE Method in Generating Fetal Echocardiography Views

To evaluate the performance of the FINE method, we evaluated a total of 4,428 images: 2,214 diagnostic planes (246 STIC volumes × 9) and 2,214 VIS-Assistance® video clips (246 STIC volumes × 9). The FINE method was able to generate nine fetal echocardiography views using: (a) diagnostic planes in 76–100% of the cases; (b) VIS-Assistance® in 96–100% of the cases, and (c) a combination of diagnostic planes and/or VIS-Assistance® in 96–100% of the cases (table 1). Figure 1 shows an example of the nine cardiac diagnostic planes in a single template with the additional feature of automatic labeling through intelligent navigation [56]. This unique feature allows labeling to occur for the nine fetal echocardiography views (i.e. diagnostic planes), the left and right side of the fetus, the cranial and caudal ends, as well as the atrial and ventric-

ular chambers, great vessels (aorta and pulmonary artery), superior and inferior vena cavae, and stomach [56]. Automatic labeling is an optional feature, and is activated by pressing a single button. Online supplementary video clip S2 demonstrates the same nine cardiac diagnostic planes both before and after activation of automatic labeling.

The maximum number of fetal echocardiography views successfully obtained through diagnostic planes or VIS-Assistance® for each normal STIC volume dataset (n = 246) is displayed in table 2. Using diagnostic planes, 77% (n = 189) of the STIC volumes demonstrated either eight (33%; n = 81) or all nine (44%; n = 108) echocardiography views, while 13% (n = 31) demonstrated seven views. Using VIS-Assistance®, 97% (n = 240) of the STIC volumes demonstrated either eight (7%; n = 18) or all nine (90%; n = 222) echocardiography views, while the remaining 3% (n = 6) demonstrated seven views.

For each normal STIC volume dataset (n = 246), the success rate of obtaining the four-chamber view, left ventricular outflow tract view, short-axis view of the great vessels/right ventricular outflow tract, and abdomen/stomach view was 80% (n = 198) using diagnostic planes and 99% (n = 243) using VIS-Assistance®.

Table 2. Number of fetal echocardiography views obtained successfully through diagnostic planes or VIS-Assistance[®] for each normal STIC volume dataset (n = 246)

Number of views obtained (max. = 9)	Diagnostic planes (n = 246)	VIS-Assistance [®] (n = 246)
5	8 (3%)	–
6	17 (7%)	–
7	31 (13%)	6 (3%)
8	81 (33%)	18 (7%)
All 9 views obtained	108 (44%)	222 (90%)
Total	246 (100%)	246 (100%)

Discussion

Principal Findings of the Study

The principal findings are: (1) nine fetal echocardiography views were generated by the FINE method using a combination of diagnostic planes and/or VIS-Assistance[®] in 96–100% of the cases; (2) for each STIC volume dataset, 77% of the volumes demonstrated either eight or all nine echocardiography views via diagnostic planes, while 97% of volumes demonstrated either eight or all nine echocardiography views via VIS-Assistance[®]; (3) for each STIC volume dataset, the success rate of obtaining four views (four chamber, left ventricular outflow tract, short-axis view of the great vessels/right ventricular outflow tract, and abdomen/stomach) was 80 and 99% using diagnostic planes and VIS-Assistance[®], respectively, and (4) during the process of marking structures of the fetal heart in STIC volumes, an intelligent alert appeared in 39.4% (97/246) of the cases; the majority of the intelligent alerts were of the breech alert type (76.3%; 74/97). Collectively, these findings indicate that FINE is a reliable method of obtaining the cardiac views required for detailed examination of the fetal heart and, hence, may be used in prenatal screening for CHD.

The Study in Context

The invention of FINE involved two phases (i.e. development and testing) [56]. During the first phase, the inventors used 51 STIC volume datasets from fetuses with a normal heart to determine a parsimonious set of anatomical landmarks that would produce a geometrical model of the fetal heart and yield nine fetal echocardiography views. In this developmental phase, the FINE method was able to generate nine cardiac views using a combination of diag-

nostic planes and/or VIS-Assistance[®] in 98–100% of cases [56]. For the second phase, the inventors then tested the FINE method on a new set of 50 STIC volume datasets of normal hearts from an independent set of patients to determine the validity of the method. This was necessary to evaluate whether the relationships among anatomical structures determined from the first 51 fetuses were maintained in a different fetal population. In this testing phase, the FINE method generated nine fetal echocardiography views using a combination of diagnostic planes and/or VIS-Assistance[®] in 98–100% of the cases [56].

Since this original publication, Garcia et al. [58] reported that STIC volumes appropriate for analysis using the FINE method could be obtained prospectively in the 2nd and 3rd trimesters in 72.5% of women attending a prenatal clinic. The same authors also reported the success rate of obtaining nine standard fetal echocardiography views (98–100%) using diagnostic planes and/or VIS-Assistance[®] in this population. Thus far, work published on the FINE method has been generated in the same unit in Detroit, Michigan, USA.

The study herein represents the first independent test of the performance of FINE in a different ultrasound unit, in which data were obtained prospectively by different sonologists. It is noteworthy that our study includes nearly 5 times the number of patients (i.e. 246) that were studied for the testing phase of FINE in the original report [56]. Prior to initiation of the current study, the team in Padua, Italy, was trained by the same investigators who invented the FINE method. Such training included: (1) attending theoretical lectures on FINE; (2) marking anatomical structures of the fetal heart in previously acquired STIC volume datasets; (3) acquisition of STIC volumes from normal fetal hearts under direct supervision; (4) review of such volumes using FINE, and (5) review of STIC volumes of CHD cases using FINE. After training was completed, the investigators in Padua conducted the study herein presented.

Clinical Implications of the Study

The challenges of prenatal screening for CHD using ultrasound are well known [5], with studies reporting low sensitivities (22.5–52.8%) for the detection of CHD even when more than 90% of the population undergo sonographic examination [3–6]. Unfortunately, over the last two decades, prenatal detection of CHD has not improved substantially, despite improved imaging techniques and equipment as well as intense training of sonologists [61]. STIC technology allows acquisition of a volume dataset of the fetal heart, displaying a cine loop

of a complete, single cardiac cycle in motion. Therefore, this technology has made it feasible to theoretically capture all the information (i.e. fetal cardiac anatomy) incorporated within the transducer sweep. Sonologists can then interrogate the volume dataset to examine anatomical areas of interest in planes of section other than the original acquisition plane [17]. However, ‘manual navigation’ (e.g. operating the x, y, z controls, scaling, and parallel shifting) [57] to retrieve and display all the relevant cardiac views is difficult, time-consuming, and operator dependent and requires an in-depth knowledge about anatomy. As a result, algorithms based upon STIC have been developed over the years [15, 18, 21, 24, 28, 31, 33] to simplify and systematically extract information as well as display cardiac planes with the objective of reducing operator dependency.

The FINE method represents a substantial advance compared to other techniques for obtaining fetal cardiac views, since manual standardization or manipulation of the STIC volume dataset and reference planes is not required (e.g. manual rotation or alignment) [56]. Moreover, this automatic method: (a) allows the successful display of cardiac diagnostic planes, despite different gestational ages and also in the presence of anatomical variability (e.g. cardiac axis and geometry); (b) is predictable (diagnostic planes are generated in a consistent manner) and adaptive (‘fits’ the anatomy of each particular fetus under examination); (c) includes the novel feature VIS-Assistance[®] (fig. 2; online suppl. video clip S3); (d) allows automatic labeling of anatomical structures (fig. 1; online suppl. video clip S2); (e) incorporates cardiac phase recognition technology, and (f) can be applied over a broad range of gestational ages [56]. Additional features of FINE developed recently include intelligent alerts (notifying the sonologist about potential issues with the STIC volume dataset) and marking alerts (notifying the user that fetal anatomical structures for marking may be in a different location than what is expected). As predicted, the prevalence of two of the types of intelligent alerts (i.e. spine location and possible drifting spine) was low (9.3%) in the current study. This can be explained by the criteria for STIC volume acquisition, as well as the STICLoop[™] criteria that were employed.

Our view is that FINE can complement and add to a sonologist’s training and education, as well as increase the knowledge base of those performing fetal cardiac examinations. Indeed, we have received feedback from users that FINE is valuable as a teaching and training tool. For example, the marking process facilitates the learning of cardiac anatomy. Moreover, in cases of CHD, FINE al-

lows multiple echocardiography views and anatomical abnormalities to be studied in detail [56].

Prior to implementing the FINE method in prenatal screening programs for CHD, a key question is whether the findings initially reported by the unit that developed FINE could be replicated by different sonologists located elsewhere. The current observation that nine standard fetal echocardiography views can be generated successfully using a combination of diagnostic planes and/or VIS-Assistance[®] in 96–100% of cases in the 2nd and 3rd trimesters provides evidence that this is the case.

Implications for Future Research

The next steps to be undertaken for application of the FINE method include an evaluation of its diagnostic performance in cases of CHD (i.e. sensitivity and specificity). We believe that such studies are justified, based upon the data generated thus far [56, 58]. There is already evidence that in cases of proven CHD, FINE is able to demonstrate abnormal cardiac anatomy in multiple echocardiography views displayed at the same time [56]. Moreover, for some CHD cases, VIS-Assistance[®] provides additional information that is not evident in the diagnostic planes [56].

Adequate education and training of sonologists is an essential step to assure that: (1) STIC volumes are appropriately acquired in the clinical setting and are of high quality [17, 58, 62]; (2) determination of the appropriateness of such volumes occurs (i.e. STICLoop[™]), and (3) there is maximal utilization of the features of the FINE method (e.g. VIS-Assistance[®]). We believe that a certification process of the FINE method, similar to that already implemented for sonographic examination of less complex anatomical structures (e.g. nuchal translucency, uterine cervix), should be considered, given the complex anatomy of the fetal heart, the challenges in the diagnosis of CHD, and the importance of prenatal diagnosis of CHD for short- and long-term outcomes [63–71].

Conclusion

FINE applied to STIC volumes can successfully generate nine standard fetal echocardiography views in 96–100% of cases in the 2nd and 3rd trimesters. Therefore, this technology is ready for evaluation as a method of screening for CHD.

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Disclosure Statement

An application for a patent ('Apparatus and Method for Fetal Intelligent Navigation Echocardiography') has been filed with the US Patent and Trademark Office, and the patent is pending. L.Y. and R.R. are co-inventors, along with Mr. Gustavo Abella and Mr. Ricardo Gayoso. The rights of L.Y. and R.R. have been assigned to Wayne State University and the NICHD/NIH, respectively. None of the authors has a financial relationship with either GE Healthcare (Milwaukee, Wis.) or Medge Platforms, Inc. (New York, N.Y.). R.R. has contributed to this work as part of his official duties as employee of the US Federal Government.

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