New Insights and Observations in Three-Dimensional Echocardiographic Visualization of Ventricular Septal Defects: Experimental and Clinical Studies

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**Background**—The positions, sizes, and shapes of ventricular septal defects (VSDs) can be difficult to assess by 2-dimensional echocardiography (2DE). Volume-rendered 3-dimensional echocardiography (3DE) can provide unique views of VSDs from the left ventricular (LV) side, allowing complete assessment of their circumference and spatial orientations to other anatomic structures.

**Methods and Results**—Seventeen experimentally created defects of various locations, sizes, and shapes were imaged and reconstructed in 9 explanted porcine hearts. From an en face projection, major and minor axis diameters of the defects were measured, and these data were compared with direct anatomic measurements. Optimal reconstructions of the VSDs were obtained in all heart specimens, accurately depicting their positions and shapes. The correlations between 3DE and anatomy for the VSD major and minor axis diameters were $y = 1.0x + 0.3$ ($r = 0.88, P < 0.001$) and $y = 1.0x - 1.4$ ($r = 0.89, P < 0.001$), respectively. Good agreement between the 2 methods was demonstrated for all measurements. Our experience from the in vitro model was then applied to patient studies. Optimal LV en face reconstructions were obtained in 45 of 51 patients, permitting detailed assessment of the positions, sizes, and shapes of the VSDs. In the 25 patients with comparative surgical measurements, the correlations between 3DE and surgery for the VSD major and minor axis diameters were $y = 0.81x + 2.1$ ($r = 0.92, P < 0.001$) and $y = 0.73x + 2.0$ ($r = 0.91, P < 0.001$), respectively. Good agreement was demonstrated between measurements made by 3DE and those obtained at surgery.

**Conclusions**—3DE provides excellent visualization of various types of VSDs. From an LV en face projection, the positions, sizes, and shapes of VSDs can be accurately determined. Such precise imaging will be beneficial for surgical and catheter-based closure of difficult perimembranous and singular or multiple muscular VSDs. (Circulation. 1998;98:1307-1314.)

**Key Words:** echocardiography • heart septal defects • pediatrics

Two-dimensional echocardiography (2DE) is a well-established method for the diagnosis and management of ventricular septal defects (VSDs). Currently, however, 2DE requires mental integration of composite orthogonal views to conceptualize the position of the defect within the interventricular septum and its relationship with other anatomic structures. Accurate assessment of the size and shape of a VSD is also difficult, because complete visualization of the borders of a defect cannot be achieved in a single 2D view. More precise delineation of certain VSDs might be advantageous for surgical and transcatheter device closure.

Recent studies have successfully used 3-dimensional echocardiography (3DE) to evaluate atrial septal defects. The 3D en face reconstructions of the interatrial septum provide unique views that allow accurate assessment of the sizes, shapes, and spatial orientations of these defects. Preliminary experience has demonstrated that 3DE can provide important information pertaining to the morphological and spatial features of various types of VSDs. Similar to a surgeon’s perspective, direct visualization of certain membranous and muscular VSDs from the right ventricular (RV) en face view is frequently obscured by overlying tissue or cardiac structures. The 3D rendering from the smooth-walled left ventricular (LV) surface might provide unique, unobstructed views of the interventricular septum, hence obviating many of the problems encountered from the RV side. From an LV en face view, the entire circumference of the VSD might be seen, allowing accurate size and shape determination.

The objectives of this study were (1) to assess the accuracy of 3DE in demonstrating the positions, sizes, and shapes of VSDs in an in vitro model and to determine the optimal operator settings of threshold and opacification to most
 operators-dependent image-processing factors of threshold and opacification were independently altered to determine the effects on 3DE measurements. The 3D reconstructions were again rendered after the threshold was first increased and then decreased by 10 U, and the opacity was increased by 10 and then 20 U. After each change, the major and minor axis diameters were measured with on-line electronic calipers. These measurements were then compared with the actual measurements of the pathological specimens.

Clinical Study

Subjects

Fifty-one patients, with a median age 3.8 months (range, 1 day to 16 years) and known to have a VSD by clinical examination and 2DE, were studied prospectively. In 4 patients, 2DE images were obtained by a transesophageal approach after probe placement for intraoperative monitoring. In all others, a transthoracic approach was used, with the probe placed in a subcostal position. These studies were performed in conjunction with the patient’s standard 2D Doppler echocardiographic examination. When clinically indicated, infants and young children received either chloral hydrate or versed sedation. Diagnoses included perimembranous VSD in 35 patients, muscular VSDs in 9 patients, both perimembranous and muscular VSDs in 3 patients, and doubly committed subarterial VSDs in 4 patients. Associated lesions included coarctation of the aorta (5 patients), pulmonary valve stenosis (5 patients), and transposition of the great arteries (3 patients). Patients with AV septal defects and large malalignment conotruncal defects were excluded from the study. Twenty-nine patients underwent surgical closure of their VSDs; in 25 of these patients, the major and minor axis diameters were determined by direct measurement for comparison with 3DE data. In nearly all cases, surgical repair was performed through a right atriotomy with the patient on cardiopulmonary bypass, and VSD measurements were made after complete exposure of the defect.

Instrumentation and Data Acquisition

The 2D image acquisition for 3D reconstruction was performed with a commercially available echocardiographic system (Vingmed CFM 800, Acuson 128 XP/10, and Hewlett-Packard Sonos 2500) coupled to a dedicated 3D image-processing unit (Echo-scan, TomTec). Transthoracic studies were done with rotational scanning from a subcostal position with a 5-MHz probe mounted on a prototype rotational device. A stepper motor driven by a steering logic within the computer allowed rotation of the probe in 2° increments around a 180° arc, thereby acquiring 90 sequential cross-sectional slices of the heart over an entire scan. ECG and respiratory gating were used to optimize spatial and temporal resolution. Transosophageal acquisitions (Vingmed CFM 800) were obtained in a similar rotational manner with a 5-MHz, 64-element multiplane probe with its control knob connected by a mechanical linkage to the stepper motor. During acquisitions, careful attention was paid to ensure that the resulting conical data set included the entire interventricular septum and surrounding structures. Acquisition times were typically 60 to 90 seconds, and 2 to 3 acquisitions were usually performed on each patient.

Image Processing and Display

Storage of the digital images in a volume matrix required ~5 minutes. Manipulation of the data set was performed off-line as previously described. From the postprocessed data, a cut plane was placed through the LV from base to apex (Figure 2A), parallel to the ventricular septum, and an en face view of the LV septal surface was rendered (Figure 2B). Optimal threshold and opacity values were determined by placing a cut plane in a longitudinal direction through the ventricular septum and to separate cardiac structures from the blood pool and background. An opacity value was then selected that best distinguished the solid surface of the interventricular septum from the transparent area of the septal defect.

Image Analysis

The positions and shapes of the VSDs by 3DE were compared with the anatomic data. With the use of on-line electronic calipers, the major and minor axis diameters were measured directly on the 3DE image. Interobserver variability was compared in all hearts. Operator-dependent image-processing factors of threshold and opacification were independently altered to determine the effects on 3DE measurements. The 3D reconstructions were again rendered after the threshold was first increased and then decreased by 10 U, and the opacity was increased by 10 and then 20 U. After each change, the major and minor axis diameters were measured with on-line electronic calipers. These measurements were then compared with the actual measurements of the pathological specimens.

Methods

In Vitro Study

Experimental Preparation

In 9 explanted porcine hearts, portions of the ventricular septum were directly incised to create 17 VSDs of various locations, shapes, and sizes (Figure 1). The hearts were then fixed in formaldehyde for 2 weeks. With the hearts suspended in a water bath, 3DE was performed by use of parallel scanning. Immediately after 3DE data acquisition, the RV free wall was removed, and the defect borders were traced on a transparency placed directly on the defect. Major and minor orthogonal diameters of the VSDs were then measured for later comparison with 3DE data.

Instrumentation and Data Acquisition

The 3DE data acquisition was performed on the same day that the measurements on the anatomic specimens were obtained. The hearts were suspended in a water bath, and 2D images were acquired with a commercially available 5-MHz probe located 4 to 5 cm from the heart and situated within a motor housing unit for parallel scanning. The probe and ultrasound imaging system (Interspec) were inter- faced with a dedicated 3D image-processing unit (Echo-scan, TomTec). As the transducer moved longitudinally from the apex of the heart to the outflow tracts, a total of 216 image slices were acquired over a length of 60 mm.

Image Processing and Display

Data processing was performed off-line by the TomTec system. A cut plane placed in a longitudinal direction through the ventricular free wall parallel to the ventricular septum was used to derive an en face view of the VSD (Figure 1). Once the appropriate cut plane was chosen, an optimal threshold value was selected to best identify the borders of the VSD and to separate cardiac structures from the blood pool and background. An opacity value was then selected that best

Figure 1. A, Anatomic specimen with RV free wall removed to display large muscular inlet VSD (left) and corresponding volume-rendered 3D reconstruction depicting en face view of the VSD (right). B, Anatomic specimen with RV free wall removed to display outlet VSD (left) and corresponding 3D reconstruction (right).
Selected to identify the borders of the VSD. Ultimate reconstruction time varied considerably, depending on the complexity of the VSD, and ranged from 10 minutes for many perimembranous VSDs to 60 minutes for more complex defects.

**Image Analysis**

All echocardiograms were analyzed by 3 experienced observers. Two observers were blinded to the 2DE findings and any cardiac catheterization or surgical details. Assessment of the position, size, and shape of the VSD and observations relating to surrounding structures were made independently by the blinded observers. From the volume-rendered display, orthogonal major and minor axis measurements of the VSD were made with electronic calipers. Interobserver variability was assessed by comparing measurements made by 2 observers in 10 patients. In the same 10 patients, the intraobserver variability was determined by reconstructing the VSD at a later time and repeating the major and minor diameter measurements.

**Statistical Analysis**

Results are expressed as mean±SD. The relations between diameters calculated with 3DE and pathological or surgical measurements were analyzed by linear regression analysis. The agreement between the 2 methods was evaluated according to the method of Bland and Altman. Variability was expressed as a percentage error of each measurement and determined as the difference between the 2 measurements divided by the mean value of the 2 measurements. Statistical significance was defined as P<0.05.

**Results**

**In Vitro Study**

Optimal reconstructions were obtained in all heart specimens, accurately depicting the positions and shapes of the VSDs (Figure 1). The mean major axis VSD diameter measurement in the anatomic specimens was 10.0±3.8 mm (range, 4.0 to 16.0 mm), and the mean 3DE measurement was 10.4±4.3 mm (range, 5.0 to 19.0 mm). The mean difference between the 2 measurements was 0.4±2.0 mm (P=0.05); the 95% CI was −0.6 to 1.5 mm; and the 95% limits of agreement for the differences were −3.5 and 4.4 mm (r=0.88; y=1.0x+0.3; SEE=0.14; P<0.001) (Figure 3A and 3B). In the same 17 anatomic specimens, the mean minor axis VSD diameter measurement was 8.9±3.1 mm (range, 4.0 to 15.0 mm), and the mean 3DE measurement was 7.9±3.6 mm (range, 3.0 to 15.0 mm). The mean difference between the 2 measurements was −1.0±1.6 mm (P=0.020); the 95% CI was −1.9 to −0.2 mm; and the 95% limits of agreement for the difference were −4.3 and 2.2 mm (r=0.89; y=1.0x−1.4; SEE=0.07; P<0.001) (Figure 3C and 3D). The statistically significant mean difference reveals a bias of the 3DE measurements toward an underestimation of the anatomic measurements. Interobserver variability was 9.8% for the major axis diameter and 7.1% for the minor axis diameter.

An increase in threshold by 10 U led to overestimation of major VSD diameter size by 6±18% and overestimation of the minor diameter by 6±5%. A decrease in threshold by 10 U resulted in underestimation of major VSD diameter size by 8±13% and underestimation of the minor diameter by 6±4%. An increase in the opacity by 10 or 20 U led to no significant change in the major diameter size. However, an increase in opacity by 10 and 20 U led to overestimation of VSD minor diameter measurement by 11±29% and 17±23%, respectively.

**Clinical Study**

Optimal 3D LV en face reconstructions permitting assessment of the position, size, and shape of the defect(s) could be obtained in all 4 of the transesophageal and 41 of the 47 transthoracic studies. Excessive patient or transducer motion or both prevented adequate reconstruction in 4 infants. In 2 patients, the subcostal 2D images were suboptimal, and the rendered data sets were unsuitable for 3D reconstruction. In all 45 optimal reconstructions, the position of the VSD was identified. Twenty-nine of these patients subsequently underwent surgical closure, at which time the 3DE diagnosis of the type and position of the VSD was confirmed.

The 3D en face projection depicted a defect immediately beneath the aortic valve in the perimembranous region of the interventricular septum in 35 patients (Figure 2B). The entire circumference of the defect could be easily identified in relationship to the smooth-walled LV septal surface. The ratio between major and minor axis diameter was >1.3 in 20 of the defects, depicting the defect as oval. In 5 patients, a short ridge of tissue separated the superior margin of the defect from the aortic valve (Figure 2C). Certain large defects could
be seen extending into the inlet or outlet regions. In 19 patients, separate echo-dense projections could be imaged through the defect into the RV, presumably representing either the septal leaflet of the tricuspid valve or remnants of the membranous septum (Figure 2D). These characteristic findings were subsequently confirmed at surgery in 23 patients.

A VSD was identified entirely within the muscular portion of the ventricular septum in 10 patients (Figure 4). The relationship of the VSD to the anterior or posterior muscular septum and toward the base or apex of the LV could be appreciated by use of this unique en face view. Various VSD shapes were delineated, including circular, oval, triangular, and crescentic (Figure 4A through 4C). Multiple muscular VSDs were identified in 3 patients. The individual defects could be delineated by 3DE but were not apparent by conventional 2DE (Figure 4D). Both muscular and perimembranous defects could be appreciated by 3DE reconstruction in 3 patients. In 5 of the patients with muscular VSDs, the positions of the defects were subsequently confirmed at surgery.

In 3 patients, a doubly committed subarterial VSD was visualized. From an LV en face view, the VSD appeared subaortic in position (Figure 5A). Further delineation of the precise position of the defect was achieved with an RV en face projection. This projection revealed an unobstructed view of the defect immediately below the pulmonic valve in the supracristal region of the right-sided interventricular septum (Figure 5B). Two of these patients had prolapse of the right aortic cusp identified by 3DE before surgery.

In all 45 patients (52 VSDs), major and minor axis measurements could be made. The mean 3DE major axis measurement was 7.5 ± 2.4 mm (range, 3.5 to 12.0 mm), and the mean minor axis measurement was 5.3 ± 1.7 mm (range, 2.8 to 9.6 mm). In the 25 patients with surgical measurements, the mean major diameter measured at surgery was 8.6 ± 2.2 mm (range, 4.0 to 12.0 mm), and the mean 3DE measurement was 9.0 ± 2.0 mm (range, 5.0 to 12.0 mm). The mean difference between the 2 measurements was 0.4 ± 0.09 mm (P = 0.030); the 95% CI was 0.0 to 0.8 mm; and the 95% limits of agreement for the difference were –1.3 and

Figure 3. Regression analysis comparing anatomic and 3DE measurements of VSD major diameter (A) and minor diameter (B) from experimental model. Agreement is shown between anatomy and 3DE measurements of VSD major diameter (C) and minor diameter (D).
2.1 mm ($r=0.92; y=0.81x+2.06; P<0.001$) (Figure 6A and 6B). The mean minor axis diameter measured at surgery was 5.8 ± 1.8 mm (range, 3.0 to 11.0 mm), and the mean 3DE measurement was 6.3 ± 1.5 mm (range, 4.0 to 9.6 mm). The mean difference between the 2 measurements was 0.5 ± 0.8 mm ($P=0.007$); the 95% CI was 0.1 to 0.8 mm; and the 95% limits of agreement for the difference were −1.1 and 2.0 mm ($r=0.91; y=0.73x+2.0; P<0.001$) (Figure 6C and 6D). The statistically significant mean difference for both the major and minor axis diameters reveals a small but observable bias of the 3DE measurements toward overestimation of the surgical measurements.

Intraobserver variability was 4.7% for the major axis diameter and 5.9% for the minor axis diameter. The absolute mean difference between observations was 0.1 mm for both the major and minor axis diameters. Assuming that the true population mean difference is 0, then 95% of all absolute individual intraobserver differences should be <1.3 mm for the major diameter and <1.0 mm for the minor diameter. Interobserver variability was 2.7% for the major axis diameter and 4.1% for the minor axis diameter. The absolute mean difference between observations was 0.1 mm for the major axis diameter and 0.2 mm for the minor axis diameter. Again assuming that the true population mean difference is 0, 95% of all individual absolute interobserver major diameter differences should be <0.8 mm, and 95% of all individual absolute interobserver minor diameter differences should be <0.7 mm.

**Discussion**

This study demonstrates that 3DE accurately depicts the positions, sizes, and shapes of various types of VSDs. The methodology was substantiated in an experimental model, and then the basic principles were extended to a clinical study. Specific cut planes were developed, and unique images from the LV side were rendered to serve as a future reference for subsequent studies.

In the in vitro model, the 3DE images closely resembled the shapes and positions of anatomic specimens. Moreover, good agreement was found between major diameter measurements obtained by 3DE and those made directly on the anatomic specimens. Although 3DE tended to underestimate the minor diameter measurements, the difference was very small. From the in vitro model, we found that an increase in either the threshold or opacity above an “optimum” level led to overestimation of the VSD minor diameter measurement. This may, in part, explain the small but consistent overestimation by 3DE in the in vitro model. In clinical practice, we have learned not to apply large changes in opacity, even though the appearance of the reconstruction is slightly smoother.

Enhanced 3D reconstructions were obtained in the explanted hearts, because neither heart rate nor respiratory cycle gating was required. No movement artifact was encountered, and the echocardiographic signal was not attenuated by the chest wall or other anatomic structures, as would be experienced with typical clinical studies. Additionally, the acquisition for 3DE reconstruction was done with parallel scanning. Theoretically, no divergence of digital information in the far field would be encountered with parallel scanning, as would be experienced with the rotational or fanlike scanning. Although we realize that higher-quality 3D reconstructions were obtained, the in vitro model provided a firm foundation for the clinical studies.
From the 3DE clinical study, we recognized specific features to differentiate the anatomy of the various defects. However, we encountered difficulties in applying standard nomenclature for the VSDs, in part related to the different terminology used in the literature. To date, nomenclature established in pathologic specimens has been adapted to correspond to 2D imaging. However, because 3D imaging can provide a better depiction of the true spatial relationships of the VSDs, future classification may rely on such imaging.

Initially, we chose an RV cutting plane to visualize and measure the VSDs. We had developed considerable experience in the utility of the right-sided en face views in previous studies on atrial septal defects. Additionally, in designing this study, we wanted comparative surgical measurements. In most cases, the surgeon makes comparative measurements from the right side, and we wanted to simulate that methodology. However, we realized that, as in a surgeon’s view, VSDs were often hidden or difficult to visualize from the RV cutting plane. In particular, perimembranous VSDs were obscured by either tricuspid valve tissue or remnants of the membranous septum. Muscular defects were often hidden by either heavy, course RV trabeculations or tricuspid valve apparatus. The LV en face projections provided unobstructed evaluation of the defects, their borders, and surrounding structures. In juxtaposition to the smooth-walled LV surface, the perimeters of the muscular defects could be more clearly defined.

Importantly, from this study, we developed standardized cutting planes to best evaluate the various VSDs. For example, perimembranous VSDs were best seen from a 3-chamber view, which included the left atrium, left ventricle, and aorta. Muscular VSDs were more difficult to render. Similar to the perimembranous VSDs, the cut plane was initially oriented parallel to the LV septal surface. However, the cut plane was then rotated in various directions to better visualize the muscular defects, dependent on their location within the ventricular septum. For example, the cut plane was rotated to include the aorta to best visualize high muscular defects. A 2-chamber view, including only the left atrium and left ventricle, was used to best depict more posterior and/or...
inferior defects. Standardization of imaging planes should reduce the subsequent reconstruction time.

We discovered specific anatomic characteristics on the basis of 3D imaging to aid in future recognition. All perimembranous VSDs were either circular or oval and could consistently be seen immediately below the aortic valve. However, in ≈15% of patients, a small, thin rim of tissue, <2 mm in length, was interposed between the aortic valve and superior rim of the defect. Additionally, echo-dense projections could often be imaged through the defect on the RV side. We assume that this represents either tricuspid valve tissue or remnants of the membranous septum. From the LV cut plane, certain large perimembranous defects could be seen extending posteriorly to the AV septum or inferiorly to the muscular septum.

Unbeknown to the investigators, en face LV cutting planes showed the muscular defects to be of complex shapes. In particular, triangular and crescentic VSDs were identified by 3DE and then subsequently confirmed at the surgery. This left-sided cut plane could also depict the positions and sizes of multiple muscular VSDs, including anterior and apical defects. The curvilinear relationship of the ventricular septum makes the latter muscular defects difficult to appreciate by 2D imaging. Vogel et al. maintain that a volume-based data set allows easier recognition of muscular VSDs that might otherwise be missed by 2DE. Furthermore, a volumetric data set allows cut planes to be placed and rotated in a multitude of directions, allowing en face views of complex muscular defects.

The LV en face projection showed doubly committed VSDs to be directly subaortic, albeit slightly more anterior than the typical perimembranous defect. The RV en face projection portrayed the defects directly subpulmonic, away from the membranous septum and adjacent tricuspid valve. Two patients had marked prolapse of the right aortic cusp through the defect, resulting in significant aortic insufficiency. The 3D echocardiography not only allowed accurate assessment of the VSD size and degree of valve prolapse but also provided enhanced spatial appreciation of the commitment of the defect to both great arteries.

In a blinded, controlled manner, the 3DE measurements compared well with those obtained at surgery. Because the en face projection allows delineation of the entire perimeter, determination and measurement of the major and corresponding minor diameters could be made directly in noncircular defects. This advantage of 3D imaging was even more apparent when measurements were made for the crescentic and triangular muscular defects. A very good comparison was apparent when measurements were made for the crescentic defect. Additionally, echo-dense projections could often be imaged through the defect on the RV side. We assume that this represents either tricuspid valve tissue or remnants of the membranous septum. From the LV cut plane, certain large perimembranous defects could be seen extending posteriorly to the AV septum or inferiorly to the muscular septum.

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Several problems were encountered in the clinical protocol. Because all studies were predicated on rendering the 3D displays from 2DE data sets, the general positions and types of the defects were known to one of the investigators during both the acquisition and rendering phases. Nonetheless, actual measurements were done in a blinded manner. Additionally, the intraobserver variability was done on completely different rendered images, not just different measurements on the same image.

Twelve percent of studies were not suitable for 3D rendering because of a combination of difficulties, including movement artifact, poor gating, and suboptimal 2D imaging. Our clinical study also lacked a true gold standard to provide accurate VSD size and shape determinations. Surgical measurements were done on an empty flaccid heart after the institution of low-flow bypass. This may account for the small but consistent overestimation by 3DE compared with surgical measurements. Furthermore, as already mentioned, our 3DE measurements were made from the LV side, whereas those made at surgery were from the RV side. We do realize that the size of the defect measured from the LV side may not relate to the hemodynamic importance. For example, flow through a perimembranous defect may be restricted by membranous septum or tricuspid valve tissue on the RV side. Furthermore, what may appear as a singular, large muscular VSD from the LV septum may present as multiple, smaller muscular VSDs from the RV side. Flow streams may be divided and restricted by RV trabecular tissue. In the future, 3D analysis of flow reconstructions may help to further define multiple muscular defects.

The 3D display of VSDs could have important applications for planning optimal surgical approaches for defect repair. Residual VSDs are well recognized as a cause of significant postoperative hemodynamic compromise. Difficulties in visualization of apical and anterior muscular VSDs have prompted surgeons to perform left ventriculotomies. The 3D echocardiographic left ventricular en face views may provide the same information without potential complications from an LV incision.

These unique left-sided en face views may be distinctly applicable for device closure in the cardiac catheterization laboratory. Precise delineation of the size, shape, and position of the VSD will help in appropriate preselection of patients. Accurate measurement will aid in the selection of the appropriately sized device to better anchor on the LV side. Knowledge of the precise relationship to other anatomic landmarks will help to avoid complications from device closure such as damage to the aortic or tricuspid valves. The very complex variety of VSD shapes may culminate in customized production of occluding devices.

The 3D reconstruction of VSDs may provide an excellent tool for educational purposes, for standardizing imaging, and for establishing a more universal nomenclature. Van Praagh et al. in a letter to the editor, used a schematic of an LV en face view to better demonstrate their concept of VSD anatomy. Visualizing VSDs in a dynamic mode from multiple projections should contribute to the medical and surgical treatments of this common congenital heart defect.

References


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