Beating Atrial Septal Defect Closure Monitored by Epicardial Real-Time Three-Dimensional Echocardiography Without Cardiopulmonary Bypass

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Background—We assessed the feasibility of beating atrial septal defect (ASD) closure monitored by real-time 3D echocardiography (RT3DE).

Methods and Results—RT3DE was developed with prototype ultrasound equipment consisting of a high-speed 3D rendering unit with a frame rate of 5 to 10 frames/s. We also developed a prototype semiautomatic suture device and suture cutting system. In the experiment, 12 mongrel dogs were anesthetized, and after median sternotomy, the echo probe was applied directly to the surface of the right atrium. Three surgical maneuvers (balloon atrial septectomy, enlargement of the ASD, and ASD closure) were performed through the atrial port inserted into the right atrial appendage. The heart was then excised, and the area of the ASD measured by RT3DE was compared with its area measured directly. The ASD was successfully closed in all experimental animals except the first 2. Examination of the excised heart showed that none of the sutures were loose. The mean area of the ASD was $82.5 \pm 38.6 \text{ mm}^2$ when measured by RT3DE and $81.6 \pm 38.2 \text{ mm}^2$ when measured directly, and there was a significant correlation between the areas measured by RT3DE and those measured directly ($r = 1.007 \times \text{direct measurements} + 0.337; P < 0.0001$). A Bland-Altman analysis revealed close agreement between the results obtained by the 2 methods ($7.807 \text{ mm}^2$ upper and $-6.024 \text{ mm}^2$ lower limit of agreement).

Conclusions—Introduction of RT3DE, a semiautomatic suture device, and a suture cutting system made beating ASD closure without cardiopulmonary bypass possible. (Circulation. 2003;107:785-790.)

Key Words: cardiopulmonary bypass ■ echocardiography ■ heart septal defects

The first successful clinical case of cardiac surgery in which cardiopulmonary bypass was used was reported in 1953 and was performed to correct an atrial septal defect (ASD).1 Although subsequent technological advances in cardiopulmonary bypass have made cardiac surgery safe and reliable, cardiopulmonary bypass is still widely recognized as having a number of adverse effects.2 Nevertheless, there has never been an acceptable approach to off-pump intracardiac surgery until now.

3D echocardiography has been developed recently and offers clinicians and surgeons a new means of visualizing the heart. This new methodology makes it possible to obtain both qualitative and quantitative information on cardiac disorders.3–6 Schmidt et al7 demonstrated that 3D echocardiography allows rapid and accurate measurement of left ventricular volume and mass. Nevertheless, because it takes a long time to display the 3D images, 3D ultrasonography can generally only be used as a diagnostic method and not to assist treatment, except according to a few reports.8,9 Faster and more highly automated image processing was needed, and to meet this need, we developed real-time 3D echocardiography (RT3DE) and applied it to monitoring heart operations, especially ASD closure, as a means of assisting treatment. We assessed the feasibility of off-pump ASD closure during monitoring by RT3DE in an animal experiment and evaluated the reliability of the images obtained by RT3DE.

Methods

Echographic Equipment
RT3DE has been achieved with a high-speed 3D rendering unit installed in ultrasound equipment SSD-5500 (Aloka Co, Ltd) and a special probe for acquisition of 3D echocardiographic data. The 3D probe consists of a microconvex array transducer with a 6-MHz center frequency and a motor that mechanically moves the array transducer in order to transmit ultrasound and receive echocardiographic data from 3D space. An ultrasound beam transmitted from the transducer is scanned both electrically and mechanically within a $45^\circ \times 45^\circ$ area. The frame rate of the 3D images rendered by RT3DE changes from 5 to 10 frames/s depending on the size of the area and the image resolution required.

The 3D rendering unit contains our original technology, referred to as “volume mode imaging” (VMI).10–12 VMI is based on a...
volume-rendering algorithm widely used for volume visualization in the computer graphics field.\textsuperscript{13,14} VMI is characterized by the ray for rendering coinciding with an ultrasonic beam and the viewpoint invariably being fixed on the ultrasonic transducer (Figure 1). This feature allows the rendering process to start as soon as the first echo is received, without the data-reconstruction process generally used in computer graphics. After all echo data have been obtained from an ultrasonic beam, the volume-rendering values obtained are plotted on a screen as pixel brightness. Scanning of ultrasonic beams electrically yields column elements of a 3D image, and mechanical scanning with the transducer gradually produces a 3D image on the screen. At an imaging rate of 10 frames/s, each 3D image is displayed on the monitor with a maximum delay of 130 ms after the first echo is received. A 3D image of ASD is obtained by the user’s manipulation of a region of interest.

Surgical Devices
In addition to developing the original RT3DE system, to make the surgical procedure easier, we compensated for the shortcomings of conventional surgical devices by developing a prototype semiautomatic suture device (Figure 2A) suitable for off-pump intracardiac surgery. A thread (4-0 Prolene) is attached to one end of a needle that has a conical point at the top end. The bottom end of the needle is fixed in a niche at the tip of the proximal jaw of the semiautomatic suture device by pulling down on the thread with one hand. The jaws close, and the needle is passed through the tissue to be sutured. When the jaw is slowly opened again, the tip of the needle is automatically grasped by the distal jaw, which has a resilient slit. When the device is gently lifted off the tissue, the thread should penetrate the tissue properly. After the device is extracted from the cardiac cavity with the needle, the same action is repeated. The device is 5 mm in diameter so that it can be inserted into the cardiac cavity through a 5-mm trocar.

We used a commercially available knot pusher (Olympus Co) for minimally invasive cardiac surgery to tie the thread and a suture-cutting device (Figure 2B), which we designed to make it easy to cut the thread. The suture-cutting device consists of a shaft with a cutting edge and a handle. The shaft in turn consists of an inner tube and an outer tube, and the outer diameter of the outer tube is 2.5 mm. The inner tube has a cutting edge. The handle is joined to the end of the shaft to turn the inner tube. Thread can be cut by inserting it between the inner and outer tubes.

Animal Study
The study protocol was approved by a review committee at the University of Tokyo. All animals received humane care in compliance with the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health (NIH publication 85-23, 1985) and with the approval of the University of Tokyo Institutional Animal Care and Use Committee.

Twelve mongrel dogs (weight 10.5 to 24.3 kg) were anesthetized with Nembutal (30 mg/kg IV), and anesthesia was maintained with 2% isoflurane. Respiration was maintained with a volume-control respirator. The ECG was monitored continuously throughout the procedure. Arterial blood gases were determined every 30 minutes, and bicarbonate was added as needed to maintain a physiological pH between 7.35 and 7.45. Aortic blood pressure was monitored with a 5F micromanometer-tipped catheter (Millar Instruments) introduced through the left femoral artery.

A median sternotomy was performed. The right atrium was suspended upward with a few stay sutures, and the echo probe was applied directly to the surface of the right atrium. A purse-string suture of 4-0 polypropylene was placed around the right atrial appendage. Three surgical maneuvers were performed through a dilating tip trocar (Ethicon Inc) inserted through the purse-string suture after intravenous administration of heparin 100 U/kg (Figure 3). When the devices were inserted, blood was slowly drawn through the side hole of the trocar to prevent introduction of air into the cardiac cavity. The surgeon performed all of the surgical maneuvers while monitoring them by RT3DE. First, a balloon catheter was inserted, and after the balloon was used to perform atrial septectomy within the fossa ovalis, the atrial communication was enlarged with a Kerrison bone punch\textsuperscript{15} and the area of the ASD on the real-time 3D images was calculated. Next, the suture device was used to carefully close the ASD with interrupted sutures. Each suture was tied with the knot pusher, and the thread was cut with the suture-cutting system. Finally, the heart was excised, and the success of these manipulations was confirmed. After the right atrium was incised, all sutures were cut and removed, and the ASD was reopened to determine its true area.

After the ASD was closed, the atrial shunt was graded by 2D epicardial echocardiography as described previously\textsuperscript{16} with the following scale: (1) none, no defect detected and no color Doppler disturbance on the right atrium side; (2) trivial, no defect detected and minimal color disturbance on the right atrium side (<1 mm wide at origin of color Doppler jet); (3) small, no defect detected and a 1- to 2-mm-wide color Doppler jet; (4) moderate, defect detected and >2-mm-wide color jet; and (5) large, defect detected and large and/or multiple color jets. Off-pump ASD closure was judged to have been successful when the atrial shunt was graded “none” or “trivial,” all of the sutures were tightly knotted, no massive introduction of air into the cardiac cavity was observed during the procedure, and there were no hemodynamic deteriorations except the hemodynamic changes related to ASD creation or ASD closure.

Validation Study
Because images obtained by echocardiography sometimes overestimate or underestimate the actual dimensions, we evaluated the reliability of the echocardiographic images. An experienced echocardiographer who was unaware of the true area scanned the area of the ASD by RT3DE. The images were recorded on videotape, and the echocardiographic images recorded were measured later with a digitizing tablet. All ASDs in the actual specimens were then photographed with a digital camera, and after they were transferred to a personal computer, the area of ASD was measured planimetrically and calculated by an independent, blinded observer. The
images obtained by echocardiography and by direct measurement were then compared.

**Statistical Analysis**

All values are expressed as mean±SD. Linear regression analysis was used to assess the correlation between the area of the ASD obtained by echocardiography and the area obtained by direct measurement. A Bland-Altman analysis$^{17}$ and Pitman’s test were also performed to assess agreement between the results obtained by the 2 methods. Differences were considered significant when confidence limits exceeded 95% (P<0.05).

**Results**

Small ASDs were successfully created in all animals by balloon atrial septectomy. As shown in Figure 4, the interatrial communications were successfully enlarged by biting off the rim of the ASD with a Kerrison bone punch. Enlargement of the ASDs was confirmed by 2D Doppler echocardiography. These maneuvers were easily performed in a few minutes by monitoring the spatial relationship between the ASD and peripheral structures such as the tricuspid valves and the coronary sinus by RT3DE. As shown in Figure 5, the ASD was then carefully closed with interrupted sutures with the semiautomatic suture device, each suture was tied with a knot pusher, and the thread was cut with the suture-cutting system. During the surgical procedure, the thread that had been passed through the rim of ASD was clearly visualized. No changes in blood pressure or heart rate were noted during the intracardiac manipulations, only the hemodynamic changes related to the creation and closure of the ASD.

The Table summarizes the results of the experiment. An appropriate atrial communication was observed in all animals, and there was no introduction of air through the atrial port. Residual shunts were observed by 2D Doppler echocardiography after ASD closure in the first 2 cases. They were thought to be attributable to the small number of sutures compared with the size of the ASD, and we increased the number of sutures thereafter. As a result, there were no or only trivial residual shunts after ASD closure in all of the

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Figure 2. A, Prototype semiautomatic suture device. Straight needle fixed in niche at tip of proximal jaw of device by pulling down thread with one hand can be automatically moved to distal jaw (1 through 3). B, Suture cutting device, consisting of inner and outer tubes. Inner tube has cutting edge into which thread can be inserted and cut. Handle is joined at end of shaft to turn inner tube. Thread can be cut by inserting it between inner and outer tubes (1 through 3). Units on the ruler are centimeters.
animals except the first 2. When the heart was excised and the right atrium opened, all sutures were confirmed by the independent observer to be tightly knotted. Examination of the excised heart showed that all sutures were located within a permissible range (mean distance from the rim of the ASD 2.09 ± 0.29 mm [range 1.50 to 2.65 mm]/mean distance between sutures 2.42 ± 0.49 mm [range 1.50 to 4.10 mm]), and the ASD was concluded to have been successfully closed in all animals except the first 2. The mean area of the ASD created was 82.5 ± 38.6 mm² (range 22.4 to 138.5 mm²) based on measurements of recorded RT3DE images made by an independent echocardiographer and 81.6 ± 38.2 mm² (range 23.6 to 137.1 mm²) based on direct measurements. The areas measured on RT3DE images were significantly correlated with the areas measured directly (echo measurements/1.007 × direct measurements +0.337; P<0.0001; n=12; Figure 5). Bland-Altman analysis showed a negligible difference of only 0.892 ± 2.197 between the results obtained by the 2 methods of measurement. The upper and lower limits of agreement were 7.807 and −6.024 mm², respectively. No significant correlation was observed between the differences across 2 measurements and their means (Pitman’s test of difference in variance: r=0.120, P=0.711). These results indicated excellent agreement between the 2 methods.

Discussion

Minimally invasive surgery is currently being advocated in the field of cardiac surgery.18 Median sternotomy remains the standard approach used by most cardiac surgeons, but alternative approaches such as anterolateral thoracotomy have been developed over time.19,20 The current minimally invasive approaches for ASD closure with cardiopulmonary bypass, however, are intended to make the skin incision small or less prominent for cosmetic reasons, and a truly less-invasive approach without cardiopulmonary bypass is still needed.

Although several devices have become available since the first successful attempt at per-catheter ASD closure21–23, they have all been associated with occasional complications.24 The Amplatzer Septal Occluder has recently been developed as a new device,25 and although some favorable results compared with conventional surgical closure have been reported,26–28 limitations remain, including the need for patient selection in terms of age, body weight, and type of ASD, as well as a lower success rate than that of surgical closure. If a surgical approach could be accomplished with an incision size the same as that of per-catheter techniques, a minimally invasive, off-pump surgical approach would offer significant advantage.29

2D echocardiography is widely used to examine patients with cardiovascular disease. Although a vast amount of clinically useful information can be obtained at a relatively low cost, the technique has significant limitations. Instead of providing precise quantitative information, geometric assumptions are made to calculate chamber volume, mass, and ejection fraction. Thus, many of the observations are subjective, which results in significant interobserver variation.3 To overcome such limitations, a variety of 3D echocardiographic systems have been developed during the past decade, including a system that reconstructs a series of 2D echocardiographic images.4 Nevertheless, the current system of 3D reconstruction from multiple cross-sectional echocardiographic scans is still cumbersome and time-consuming, and the reconstruction process requires a substantial learning curve.5 Imaging time is shorter with RT3DE than with 3D reconstruction techniques applied to 2D echocardiography, because
all planes are imaged simultaneously. In addition, RT3DE eliminates the need for ECG and respiratory gating. This new methodology makes it possible to obtain qualitative and quantitative information on heart disorders. Acar et al recently reported 3D echocardiographic techniques to monitor aortic valve balloon dilatation and have imaged per-catheter ASD closure before and after implantation. In addition, Cao et al demonstrated the usefulness of 2D and 3D transesophageal echocardiography in patient selection and transcatheter closure of multiple ASDs. However, RT3DE has generally only been applied to diagnostic methods. Our system is applicable to treatment as a method of monitoring surgical closure of ASD, making it possible to perform an operation that was thought to be difficult.

Surgical procedures may not be impossible with 2D images alone, but spatial relationships cannot be grasped, and the surgical procedures cannot be performed precisely, which is unacceptable to any surgeon. The present study shows that all sutures were located within a permissible range and that none of the sutures were loose. Downing et al reported a successful suture rate of 75% and a mean distance from the ideal position at the midportion of the leaflet of 8.5 ± 5.0 mm in experimental beating-heart mitral valve surgery monitored by 2D echocardiography. Apparently, this was not considered accurate and would not be acceptable in clinical situations because the target structures were small. Use of the RT3DE systems allowed the "surgeon's view" to be obtained in real time, and the surgeon could perform 3 procedures in the same manner as endoscopic surgery or ordinary surgery.

A limitation of the present study is that the frame rate and spatial resolution of the RT3DE images still need to be improved, because the frame rate we used was only 5 to 10 frames/s. A new RT3DE system and the use of a 2D array probe may be one solution to this problem. Another limitation of this study is that we did not evaluate individual variability in measurements of the area of the ASD by RT3DE, because 3D images themselves depend greatly on an appropriate opacity line and echo gain, which were decided by the echocardiographer. Further assessment will be needed to elucidate individual variability. Finally, median sternotomy was required to perform all of the surgical procedures in the present study. If the current RT3DE system is used through a small skin incision, 2 different thoracotomies would be needed because of the large echo probe. The use of

### Results

<table>
<thead>
<tr>
<th>No.</th>
<th>Size of ASD (Echo), mm</th>
<th>Echo Shunt Before Closure</th>
<th>Number of Sutures</th>
<th>Air Introduction</th>
<th>Echo Shunt After Closure</th>
<th>Closure Successful or Unsuccessful</th>
<th>Size of ASD (Direct), mm</th>
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<td>82.2</td>
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<td>Moderate</td>
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<tr>
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<td>5</td>
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<tr>
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<td>90.2</td>
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<td>5</td>
<td>34.1</td>
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<td>6</td>
<td>68.5</td>
<td>+</td>
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<td>S</td>
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<tr>
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<td>22.4</td>
<td>+</td>
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<td>9</td>
<td>132</td>
<td>+</td>
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<td>130.4</td>
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<tr>
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<td>116</td>
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<tr>
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<td>S</td>
<td>84.6</td>
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</table>

S indicates successful; US, unsuccessful.

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Figure 6. A, Correlation between areas of ASD measured on RT3DE images and areas measured directly. B, Bland-Altman analysis showing excellent agreement between measurements obtained by 2 methods (difference 0.892 mm²; upper and lower limits of agreement 7.807 and −6.024 mm², respectively).
References
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