Experimental Atrial Septal Defect Closure With a New, Transcatheter, Self-Centering Device

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**Background.** Despite two decades of research, a transcatheter atrial septal defect closure device is not available for clinical use. We have designed a new superelastic Nitinol-Dacron, double-disk, self-centering, atrial septal defect closure device and studied its efficacy in a canine model of atrial septal defects.

**Methods and Results.** Atrial septal defects were created surgically in 20 adult dogs using either a 7.5-mm or 10-mm punch. Percutaneous transcatheter closures were attempted using a new device. The device sizes used were 20 mm in 6 dogs, 22 mm in 9, and 25 mm in 5 (22.1±1.9 mm, mean±SD). The stretched atrial septal defect diameter was 10.5±1.3 mm, and the device to stretched atrial septal defect diameter ratio was 2.1±0.3. Closures were successful in 19 studies and unsuccessful in 1. Angiography showed a left-to-right shunt in all 20 dogs before closure. Immediately after closure (n=19), there were no shunts in 17 and trivial shunts in 2. Six dogs were followed for a period of 4.7±3.0 months (range, 2 to 8 months). The trivial shunt present in 1 animal immediately after closure had closed by the time of the repeat study. Spontaneous embolization of the device was not seen during follow-up. A solitary wire fracture was found 8 months after closure in 1 device. Light microscopy at 8 weeks in 3 dogs showed the devices to be covered by smooth endocardium, enmeshed in mature collagen tissue, with a minimal mononuclear cell infiltration. Retrievalability was assessed by deliberately embolizing 4 devices in 2 dogs into the right atrium (n=1) and pulmonary artery (n=3). All devices were successfully retrieved with a snare.

**Conclusions.** This feasibility study demonstrates that this new self-centering atrial septal defect closure device has a number of design features that permit effective and safe closures in a canine model. These results support the investigation of this device in human clinical trials. (*Circulation.* 1993;88[part 1]:1754-1764.)

**Key Words** • atrial septal defect • transcatheter closure • implants, artificial

Transcatheter closures of atrial septal defects were performed for the first time in experimental animal models and humans by King and Mills. This early device and a later device developed by Rashkind never found widespread clinical use because of the large size of the delivery sheath (23F) in the former and the presence of tethering hooks in the Rashkind single-disk device, which made proper centering and implantation difficult. The two devices currently undergoing evaluation, the Lock “clamshell” device and the Sideris “buttoned” device, are essentially umbrella-like devices with metallic struts radiating from the center for support of the fabric patches, with the two disks or the left atrial (LA) disk and a right atrial (RA) counteroccluder being joined together at a central hub or “button.” Problems with the clamshell device include spontaneous device embolization, persistent residual shunts in as many as 26% of patients, and wire fractures in up to 33% of patients on follow-up. With the buttoned device, a cumbersome implantation technique with a 26% failure rate, structural failure characterized by “unbuttoning” in 10%, residual leaks in 39%, and embolization are obvious drawbacks. Despite two decades of research, a transcatheter technique for closure of atrial septal defects is not clinically available, and it is still an investigational technique. To overcome the drawbacks of these devices, we have designed a new device with a novel mechanism of closure, and we studied its efficacy in the closure of surgically created atrial septal defects in a canine model. The study protocol was approved by the Animal Care Committee of the University of Minnesota and conforms to the guiding principles of the American Physiological Society.

**Methods**

**Device and Delivery System**

The device (Fig 1) consists of two square frames made of superelastic Nitinol wire (0.010-in. diameter) with a radiopaque marker wire of platinum wound around it. Each square frame has four "legs" that are interconnected by flexible eyelets at the corners. At the midpoint of each leg there is a flexible eyelet. The eight eyelets in each square frame function as torsion springs and permit the frame to be collapsed to load the device into
the delivery catheter. The wire frames are covered by Dacron (polyester) fabric that has been specially developed for this device to have an element of elastic stretch. The fabric is stretched taut and sewn onto the frames. A circular hole, whose diameter is approximately half the size of the disk, is punched out from the right atrial disk. The margin of this orifice is sewn onto the fabric of the left atrial disk to form a conjoint ring (Fig 1). The radial tension of the superelastic Nitinol wire frames and the apposed taut fabric sewn together along the conjoint ring keep both the disks closely apposed to each other. Each square frame can be collapsed by folding it so that the four corner eyelets are drawn close to each other (Fig 2). The device is available in a range of sizes from 18 to 40 mm.

A special delivery system was designed to permit precise and reliable deployment of the device. It consists of a control handle (Fig 3) connected to a 10.5F delivery catheter. A “Y” connector interconnects the two to permit the delivery catheter to be flushed continuously with saline. A coaxial pusher runs inside the delivery catheter to its tip, and this is connected within the control handle to a rotary thumbscrew, which permits the tip to be drawn in or pushed out by rotating the thumbscrew. At the tip of the coaxial pusher, a short length of stainless steel tubing is incorporated (Fig 4) with a notch cut out. Within the lumen of this tube and the coaxial pusher runs a 0.014-in.-diameter Nitinol wire, from the tip all the way back to the control handle, where it is interconnected to a spring-loaded release trigger. To prevent accidental activation of the release trigger, a safety screw, which has to be loosened first, has been incorporated. On withdrawing the trigger, the Nitinol wire is drawn back in the notch of the release fixture. One of the corner eyelets of the right atrial disk (Fig 1) is positioned within the notch and the Nitinol wire is slid back through the eyelet, locking it in the release fixture, akin to a sliding bolt. The device frame is then collapsed (Fig 2) and loaded into the tip of the delivery catheter by turning the thumbscrew to draw the tip release fixture and device into the delivery catheter. The basic mechanism of closure with this device is illustrated in a schematic manner in Fig 5. The delivery catheter, with the collapsed device loaded, is positioned across the atrial septal defect. The LA disk is opened in the LA and pulled against the atrial septum. The RA disk is then deployed in the RA. The release of the RA disk causes the superelastic Nitinol frames to stretch out the conjoint ring. The conjoint ring is drawn against the margins of the atrial septal defect, stretching it, centering the device around it, and tightly occluding it. On bench testing in an acrylic atrial septal defect model this was found to occur repeatedly and reliably.

Surgical Creation of Atrial Septal Defects

Atrial septal defects were surgically created under general anesthesia, without cardiopulmonary bypass,
FIG 2. Photograph: The left atrial disk has been collapsed by folding the frame so that the four corners are brought close to each other and held together. The right atrial disk is open. Note the two eyelets in the middle of each side of the frame of the open disk.

using a modification of the technique of May\textsuperscript{13} and adapted for creation of atrial septal defects. A total of 23 adult dogs weighing 27±2 kg (range, 24 to 30 kg) underwent surgery for the creation of atrial septal defects. Two dogs died intraoperatively (both developed ventricular fibrillation; 1 during endotracheal intubation).

FIG 3. Photograph: The control handle of the delivery system is connected to a 10.5F delivery catheter through a “Y” connector (arrow). A coaxial pusher runs within the delivery catheter from its tip to the handle, where it is connected to a rotary thumbscrew (•). A release trigger on top of the handle (double arrows) releases the device on being pulled back. A safety screw (open arrow) has to be loosened before activating the release trigger.
and 1 during surgery), and 1 dog died on the second postoperative day of pulmonary atelectasis. Twenty dogs survived the surgery.

The animals were anesthetized by administering sodium pentobarbital (20 mg/kg) intravenously. They were intubated and mechanically ventilated with a Harvard ventilator. A right thoracotomy was performed, and the heart was exposed. A vertical incision was made in the pericardium, anterior and parallel to the right phrenic nerve with a T extension anteriorly. The right atrial appendage was clamped, a purse string suture was applied, and the tip of the appendage was excised. A second purse string suture was applied to the right atrial wall. The punch was introduced through the right atrial wall through the purse string suture. The left index finger was passed through the right atrial appendage and was used to palpate the fossa ovalis and correctly position the punch. The trocar of the punch was extruded outside the protective barrel on rotation of the screw knob by an assistant. This was then forcibly pushed across the atrial septum, and the atrial septum was seated in the slot of the trocar. On rotating the screw knob and returning the trocar to its original position, a clean circular hole was punched out in the atrial septum (Fig 6). We used either a 10-mm or 7.5-mm punch in all the studies, and this permitted the creation of atrial septal defects of precise sizes. The purse string sutures were tied off, the pericardial incision was repaired, and the chest was closed in layers. The atrial septal defects created in this manner are approximately the same diameter as the punch. To establish the validity of this model, 8 dogs underwent transcatheter atrial septal defect closure 5.1±1.9 months (range, 0.5 to 7 months) after surgery, when all were found patent.

**Catheterization and Defect Closure Protocol**

After obtaining vascular access percutaneously from the right femoral vein, the atrial septal defect was crossed with an 8F NIH catheter (USCI, CR Bard Inc, Tewksbury, Mass). An LA angiogram was performed to demonstrate and document the atrial septal defect. The atrial septal defect was recrossed with an end hole catheter. Over an exchange wire, a 7F wedge pressure

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**Fig 4.** Photograph: The tip of the pusher is seen after it has been extruded out of the tip of the delivery catheter by rotating the thumbscrew. The tip has a release fixture, a short length of stainless steel tubing with a notch (open arrow) cut into it. A 0.014-in.-diameter Nitinol wire (arrow) runs from the tip of the release fixture through the lumen of the coaxial pusher and is attached to the release trigger in the control handle.

**Fig 5.** Schematic illustration of the mechanism of closure. Panels A to D are sectional views; panel E is a frontal view. A, The delivery sheath is positioned across the atrial septal defect (ASD). DC indicates delivery catheter; P, pusher. B, The left atrial disk (LADsk) has been deployed. Fab. indicates fabric. C, The right atrial disk (RADsk) has been deployed with the frame (Fr.) attached to the release fixture (RF). D, The released implanted device. Note the increase in the diameter of the ASD. RS indicates radial stretch. E, The conjoint ring (CR) has been opened. Radial arrows illustrate the direction of the radial stretch due to the square superelastic wire frame. CE indicates corner eyelet; IAS, interatrial septum.
balloon catheter (Arrow International Inc, Reading, Pa) or a 7F Fogarty catheter (American Edwards Laboratories, Anasco, Puerto Rico) was used to cross the atrial septal defect and size the defect. An 11F, 76-cm-long delivery sheath (USCI, CR Bard Inc) was then passed over the exchange wire, and the tip of the sheath was positioned in the left atrium. The device sizes were selected to achieve a device to stretched atrial septal defect diameter (D/D) ratio of approximately 2:1. The device, preloaded in its 10.5F delivery catheter, was introduced into the long sheath through the Touhy Borst adapter and passed to the tip of the outer sheath in the left atrium (Fig 7, panel A). By rotating the thumbscrew, the LA disk was then extruded (Fig 7, panel B) until the disk opened fully, and the whole sheath assembly was gently pulled back until the LA disk snagged on the atrial septum. While gentle traction was applied to the delivery catheter, the thumbscrew was rotated until the RA disk was extruded and deployed. The safety screw of the release trigger was loosened, and the trigger was activated to release the device. The implanted device self-centers around the atrial septal defect because of the conjoint ring, and both disks are tightly apposed to the atrial septum (Fig 7, panels C and D). Right atrial angiography was then performed, with follow-through of the pulmonary levo phase to opacify the left atrium and evaluate any left-to-right shunt.

Acute studies. Fourteen animals underwent acute studies. These were performed either immediately after the surgical creation of the atrial septal defect (n=12) or after 6 months of follow-up (n=2). In these animals after transcatheter closure and angiography, the dogs were killed by injection of 400 mEq IV potassium chloride bolus. The chest was opened, and the heart was excised. The atria were opened, and the seating of the device and closure of the atrial septal defect were examined.

Survival studies. In 6 animals, device closures were performed 5.1±2.2 months (range, 0.5 to 7 months) after the surgical creation of atrial septal defects. After device closure, these animals were allowed to recover and were followed for 4.7±3.0 months (range, 2 to 8 months).

Follow-up Evaluation

The follow-up studies in chronic models were performed at variable intervals. Three dogs were restudied 2 months after atrial septal defect closure. After angiography was performed, the dogs were euthanized, both atria were opened for gross examination, and the devices and surrounding atrial septum were subjected to histopathological examination. To study the effects of long-term implantation, 3 dogs were restudied at 7, 7, and 8 months after atrial septal defect closure. In 1 dog, angiography was performed at 8 months to evaluate a trivial shunt that had been present immediately after closure. Cinefluoroscopy was performed in the 2 other animals when initial closures were complete. The cinefilms were studied to evaluate device position and for
any evidence of wire fractures. These 3 dogs are alive and are to be prospectively followed up for a period of 2 years.

Retrieval Studies
To assess the retrievability of these devices, 4 devices (22-mm sized) were released into the RA of 2 normal adult dogs. Three of these devices were dislodged with a catheter and embolized to the pulmonary artery. All these devices were attempted to be retrieved with a snare device (Amplatz gooseneck snare, Microvena Corporation, Minneapolis, Minn).

Results
Percutaneous Atrial Septal Defect Closures
This was attempted in 20 dogs surviving surgery (Table). The stretched atrial septal defect diameter on balloon sizing was found to be 10.5±1.3 mm (range, 8 to 13 mm). The device size used for closure of these defects was 22.1±1.9 mm (range, 20 to 25 mm) with a D/D ratio of 2.1±0.3 (range, 1.5 to 2.5). Deployment and implantation was successful in 19 studies where D/D ratios of 1.7 or larger were used. To determine the smallest D/D ratio that could reliably close a defect, a device with a D/D ratio of only 1.5 was used. This closure was unsuccessful, and the device immediately embolized to the pulmonary artery. In the 19 successful studies, the device was deployed optimally in 18 dogs with the LA disk opened fully in the LA and the RA disk opened fully in the RA. In the first study, the delivery system did not have a safety screw, and after the LA disk was deployed and was being drawn against the atrial septum, the release trigger was accidentally released, causing the RA disk to be prematurely released. One corner of the RA disk straddled the atrial septal defect, with the other three in the RA. Nevertheless, the fully open LA disk occluded the defect and closed the shunt. The device was stable and did not embolize. After the first study, a safety screw was incorporated in the release trigger, and this problem has not recurred.

Angiography
Angiographic left-to-right shunts were present in all the 20 dogs before the closures. In the 19 successful closures, trivial residual shunts were seen in only 2 instances, immediately after closure. One of the 2 animals was followed chronically. Angiography after 8 months showed no shunt.

Complications
One study of the 20 was associated with complications. This was characterized by transient, generalized, ST segment depression and T wave inversions on the ECG, when the delivery catheter was being introduced coaxially into the long delivery sheath. The exact cause was not clear but probably was due to air embolism through the long sheath. In subsequent studies, with meticulous attention to clamping of sheaths with a rubber-shod hemostat and continuous flushing of the sheath and delivery catheter with saline, similar complications have not been encountered.
Results of Transcatheter Atrial Septal Defect Closures

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ASD indicates atrial septal defect; N/A, not applicable; and F+, fracture of a leg at its middle eyelet.

*Premature release of right atrial disk, leading to one corner of right atrial disk straddling ASD; †long-term survival study models to be followed up for 2 years; ‡cinéfluoroscopy only; §device embolized to pulmonary artery; ‖transient generalized ST depression.

Acute Studies, Gross Findings

In 13 of the 14 acute studies, closures were successful. The hearts were examined, and both the RA and LA were opened to examine the device and its deployment. In 12 of these the device deployment was optimal with the LA disk fully open in the LA and RA disk fully open in the RA, with none of the corners straddling the atrial septal defect. The disks were closely apposed to the atrial septum with the atrial septal defect fully obscured and not visible from either side. On lifting up the corners of the devices, they were found well centered around the defects, with the conjoint ring tightly apposed to the margins of the defects. In 1 of the 13 successful studies, 1 corner of the RA disk straddled the atrial septal defect. Three of the corners were open in the RA. The LA disk was fully open in the LA and occluded the defect. The device was seated in a stable manner. None of the devices occluded the pulmonary veins or the coronary sinus or impinged upon the mitral or tricuspid valves. The fabric was soaked with blood and clotted; however, there were no lumps of clot seen on the fabric that could have dislodged.

Follow-up Studies and Histopathology

In the 6 survival studies, 3 dogs underwent angiography 8 weeks after closure and then were euthanized. There were no residual shunts, embolization of devices, or wire fractures. On opening the atria, the devices were found to be covered by a glistening, smooth, grayish endocardium, which was smoothly continuous with the surrounding atrial wall. There were no thrombi seen adherent to the device or on the atrial wall. The fabric patches and frames were intimately adhered to the atrial septum and could not be separated from the septum (Fig 8). The atrial septum was excised with the device in place, and wedges of tissue including the implant and normal adjacent atrial septum were cut out and subjected to histopathological examination. This showed a smooth continuation of the endocardium from the atrial wall onto the surface of the patch. The luminal surface of the patch was covered by a thick layer of dense mature collagenous tissue underlying the endocardium (Fig 9). The fabric fibers were seen with large diameters, pale staining, and enmeshed in collagen tissue (Fig 10). There was a minimal inflammatory reaction to these fibers characterized by a few mononuclear inflammatory cells. There was no inflammatory response around the wires of the frame.

Three dogs have been followed for a period of 7, 7, and 8 months. In one of them a wire fracture of one leg at its middle eyelet was seen at 8 months, and angiography showed no left-to-right shunt. In the other two dogs, cinéfluoroscopy showed no embolization of the devices or wire fractures.
Retrieval Studies

Four 22-mm devices were embolized to the RA (n=1) and pulmonary artery (n=3) in two normal adult dogs through a 12F introducer sheath placed in the right internal jugular vein. A 35-mm gooseneck snare was passed through a right femoral vein access site; the device in the RA was snared and then drawn down to the right femoral vein and removed through a venotomy. Snare was then passed through femoral vein access sites to the pulmonary artery, and the devices in the pulmonary artery were similarly retrieved. During retrieval of one of these devices, while it was being pulled through the right ventricle, a right bundle branch block transiently induced. None of the devices were snagged in the tricuspid valve apparatus, and all of them could be successfully retrieved.

Discussion

In this study, we have designed and developed a new transcatheter atrial septal defect closure device with a novel "conjoint ring" that permits self-centering of the device and effective closure. Its feasibility was established in a canine model of atrial septal defects.

Design Features of the Present Device

The device evaluated in this report was designed with the principal aims of overcoming the problems of centering of the device in the atrial septal defect and for the device to be tightly self-occluding. To achieve this, three features were incorporated: (1) oversize LA and RA disks, (2) both disks being closely apposed to the atrial septum after deployment, with no potential spaces between the disks and atrial septum, and (3) a conjoint ring between the fabric disks. The conjoint ring plays a very important role. If a D/D ratio of 2 is used, the conjoint ring diameter is approximately equal to the stretched diameter of the ASD. On deployment of both disks, the radial tension of the superelastic wire frames stretches out the fabric and opens the conjoint ring. The ring approximates the edges of the defect and stretches the atrial septal defect to permit a tight and effective seal. In addition, the conjoint ring self-centers the device. Since it self-centers in the defect, small D/D ratios of up to 1.7 are effective. This is a potential advantage in the closure of large defects in children.

To make the deployment process reliable, the device was designed with a number of features. The first was to prevent "coning" of the deployed LA disk due to the axial traction used when it is drawn against the atrial septum. This prevents the device from being pulled through the defect because of a reduction in the D/D ratio during the process of coning. In this device, axial traction does not readily cause the frame to collapse. By design, due to the orientation of the eyelets, radial forces can more easily collapse the frame than axial traction, and no radial forces are actually involved in the deployment process. In addition, once the LA disk is deployed, the connection to the RA disk and delivery system is by elastic fabric. When the LA disk is drawn against the atrial septum, it snags, and any further traction draws the tip of the delivery catheter...
away from the LA disk by stretching the elastic fabric. This again prevents the frame from being collapsed and instead, the elastic fabric stretches out. On releasing tension, the tip of the delivery catheter, with the RA disk still in the catheter, moves back to approximate the LA disk because of the elastic fabric. In addition, the delivery system has been so designed that the entire deployment process is controlled from the control handle, enabling the deployment of the device to be precise and controlled.

The frame is made of superelastic Nitinol. Nitinol is a nickel titanium alloy composed of almost equal parts of the two metals and is available in a thermal shape memory alloy form or a superelastic form, depending on the exact composition of the alloy. The thermal shape memory alloy wire is currently used in the Simon vena cava filter and was earlier used as coil stents in animal models. The thermal shape memory permits the metal to be extremely pliable at low temperatures and returns to its annealed shape on rewarming to a temperature just above the phase-change temperature (at body temperature) with great rapidity and considerable force. In the high temperature phase, the wire is rigid. However, the introduction of these devices requires the perfusion of ice cold saline through the delivery sheath, and rewarming occurs on release into the warm blood stream. To simplify the implantation procedure, we chose to use the superelastic form of Nitinol wire. After annealing at 500°C on a preformed jig for 30 minutes and cooling to room temperature, the wire can be deformed to any shape but immediately returns to its preprogrammed annealed shape on release. The biocompatibility of Nitinol alloy as an implant material has been established in experimental studies, and no problems have been encountered in the Simon inferior vena cava filter, which is made of Nitinol. Nitinol has characteristics of resistance to corrosion, oxidation, and abrasion, reasons for its biocompatibility.

The fabric used for this device is Dacron (polyester), specially knit to permit elastic stretch. The inert nature of Dacron with a minimal inflammatory reaction, excellent healing by 8 weeks, and the ability of the elastic Dacron to stretch from a small constrained size to its fully open state are reasons why we have chosen this fabric. In addition, the extensive use of Dacron patches for surgical closures of septal defects has firmly established its biocompatibility. One of the potential advantages of the design of this device is that the two disks are held together by elastic Dacron and are not affixed at a rigid central point. Thus, it would be possible for the disks to be implanted on both sides of thick ventricular septa for closure of muscular ventricular septal defects or across long patent ductus arteriosi, with the fabric stretching to conform to the required shape without altering the shape or size of the Nitinol frame. In addition, the two disks can be out of plane in relation to each other, which is potentially useful in the closures of such defects.

**Design-Related Problems in Clinical Trials of Atrial Septal Defect Closure Devices**

This device was designed primarily to overcome the limitations of the devices currently undergoing clinical
trials. The implantation success rate with the buttoned device has been reported to be only 74%,\textsuperscript{12} with 26% of devices being either removed at implantation because of an unstable position or being removed within 24 hours of implantation because of unbuttoning of the devices or embolization. In addition, the technique of closure is cumbersome because the LA disk has to be opened first in the LA, the barlike counteroccluder opened in the RA, and finally both “buttoned” to each other. The implantation success rate with the clamshell device was 94% in its initial clinical use,\textsuperscript{7} with two instances of early device embolization; in closures of smaller patent foramen ovale after presumed paradoxical embolization resulting in strokes, it has been 100%.\textsuperscript{11} On implantation of devices where the two disks are interconnected at a central hub or button, it is very likely that the central point would be off center in the atrial septal defect and settle at its most dependent portion. Even though the Lock device becomes cone-shaped on traction and would potentially self-center, it would require the left atrial cone to be pulled exactly perpendicular to the plane of the atrial septum to self-center. Traction of the device at an angle would not permit self-centering, and the device would be seated off center. In the initial study of Rome et al (with Lock),\textsuperscript{7} 6-month follow-up showed small residual leaks (<3 mm) around the devices in 26% and that the defect was completely closed in patients with a larger D/D ratio of 4.3±2.2, as compared with a smaller D/D ratio of 1.8±0.8 (P<.01) in those with residual leaks. Even when this device has been used to close small patent foramen ovale,\textsuperscript{11} 18% of patients followed for approximately 8 months had residual leaks. By considerable oversizing of a centrally interconnected double-disk device, off centering can be overcome, but in large defects there is a limitation as to the extent by which one can oversize the device primarily because of a narrow rim of the surrounding atrial septum. In single-disk devices like the Sideris device with the barlike RA counteroccluder, leaks are seen in as many as 39%\textsuperscript{12} of patients on follow-up, reflecting the difficulties of a single-disk device to tightly occlude the defect.

With the buttoned device, 10% of the devices after initial successful closure “unbuttoned,” and 3 of 4 of them had to be surgically removed.\textsuperscript{12} While no serious complications have been reported, so far, as a consequence of “unbuttoning” of the LA disk and its “counteroccluder,” such catastrophic structural failure remains as an area of concern with this device. While structural failure of this nature does not occur with the Lock device, follow-up of patients has revealed an incidence of late fractures of one or more arms of the device in 30%. This has led to the discontinuation of the use of this device for closure of atrial septal defects,\textsuperscript{11} and the device is currently being modified.\textsuperscript{21} No clinical sequelae of arm fractures have been reported. Presumably because of the late occurrence of fractures after adequate collagenization, scar formation, and endothelialization, embolization of the device or any significant complications do not occur.

**Results and Limitations of the Present Study**

The present study was designed primarily to assess the feasibility and safety of this novel device and delivery system in a canine model and to gather preliminary information about its efficacy. The feasibility of this device has been clearly established by the successful deployment of the device in 19 of 20 attempted closures. The design of this device permits stable seating of the device, and none of the devices with D/D ratios of 1.7 or larger spontaneously embolized on release of the device or on follow-up. There were no deaths caused by the procedure or major complications, attesting to its safety. The demonstration of the retrievability of embolized devices is another positive feature of this study.

The data about the efficacy of the device in occluding defects can only be considered preliminary because of certain limitations of this study. The present study has been performed in only small to moderate-sized defects in a canine model. Our experience with an earlier pentagonal prototype showed us that devices 30 mm in size are difficult to deploy in the relatively small atria in dogs;\textsuperscript{22} hence, we confined this study to 25-mm devices or smaller. In addition, the technique used to evaluate the closure was RA angiography with follow-through of the pulmonary levo phase to delineate LA opacification and left-to-right atrial shunting. This technique may underestimate the degree of shunting. We chose not to perform conventional oximetry saturation determinations and pulmonary angiography with levophase follow-through, as experimental studies with the clamshell device\textsuperscript{6} have shown that manipulation of catheters in the region of a deployed device can dislodge the device. In the clinical use of the clamshell device,\textsuperscript{7} these two techniques are not used, and RA angiography and echocardiography have been used. We did not use transthoracic and transesophageal echocardiography because in our earlier experience\textsuperscript{22} we found that because of the surgical thoracotomy performed to create the atrial septal defects, a significant amount of air is present in the mediastinum and pleural cavities in the acute studies. This resulted in a poor quality of images that was considered suboptimal for assessing small shunts. Hence, we performed RA angiography with follow-through of the pulmonary levo phase in both acute and chronic studies to use the same technique in both groups. The opacification of the LA was found to be good, with a reasonable assessment of left-to-right shunting. Interestingly, the demonstration of complete closures of small atrial septal defects in 100% of the experimental studies with the buttoned device,\textsuperscript{8} using transesophageal echocardiography, was not a predictor of the results in further clinical evaluations.\textsuperscript{12} Where residual shunts after closure of larger defects have been reported in as much as 39% of cases. Hence, because of inherent limitations of the animal model that we have used, the small size of atrial septal defects occluded, and limitations of the technique of evaluation of closures used, the efficacy of closure in larger atrial septal defects can only be established in clinical trials.

In the present study, no structural failure of this device was encountered because the two fabric disks are firmly sewn to each other. There was a solitary instance of a wire fracture of one of the devices during the period of follow-up. The more muscular atria seen in dogs presumably subjects these devices to a greater degree of stress than is likely to be seen in humans. Nitinol has excellent resistance to fatigue,\textsuperscript{14} and the elasticity of superelastic Nitinol is nearly 100%.\textsuperscript{15} With a quality control step to exclude nicked or flawed wire frames and
the use of a thicker wire (0.012 in.) in humans with a more compliant atrial septum, it is probable that wire fractures will be rare.

The drawback of this device is that it is currently delivered through an 11F delivery sheath and hence cannot be used in children less than 8 kg in weight. With improvements in its design and construction, it may be possible to further miniaturize the device and the delivery system to use smaller-size sheaths.

**Conclusions**

The initial results of the transcatheter closure of atrial septal defects in an animal model with this new device compare favorably with the initial results in experimental studies of both the clamshell device and the buttoned device. This study has established the feasibility and safety of this device and delivery system and has provided preliminary information about the efficacy of closures. These results support the institution of clinical trials to investigate the efficacy of this device in humans.

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**References**

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