The CardioSEAL Septal Occlusion System
Instructions For Use
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Instructions For Use

The CardioSEAL Septal Occlusion System

Federal law (USA) restricts this device to sale by or on the order of a physician (or properly licensed practicioner).

1. HUMANITARIAN USE DEVICE: Authorized by Federal law for use in patients with a complex ventricular septal defect (VSD) of a significant size to warrant closure, but that based on location, cannot be closed with standard transatrial or transarterial approaches. The effectiveness of this device for use in this indication has not been demonstrated.

2. PRODUCT DESCRIPTION:

The CardioSEAL Septal Occlusion System consists of two primary components:

- The CardioSEAL (Occluder), which is constructed of a metal (MP35N) framework to which polyester fabric is attached, and
- The Delivery Catheter, a coaxial polyurethane catheter designed specifically to facilitate attachment, loading, delivery and deployment of the CardioSEAL to the defect.

3. INDICATION FOR USE:

The CardioSEAL Septal Occlusion System is authorized by Federal law as a Humanitarian Use Device for use in patients with a complex ventricular septal defect (VSD) of a significant size to warrant closure, but that based on location, cannot be closed with standard transatrial or transarterial approaches.

The effectiveness of this device in this indication has not been demonstrated.

4. CONTRAINDICATIONS:

Presence of thrombus at the intended site of implant, or documented evidence of venous thrombus in the vessels through which access to the defect is gained.

Active endocarditis, or other infections producing a bacteremia.

Patients whose vasculature, through which access to the defect is gained, is inadequate to accommodate the appropriate size sheath.

Patients whose defect is too small to allow the 11 F sheath to cross the defect.

Anatomy in which the CardioSEAL size required would interfere with other intracardiac or intravascular structures, such as valves or pulmonary veins.

Patients with coagulation disorders who are unable to take Aspirin, Heparin, Coumadin, or other anticoagulants.

5. WARNINGS:

This device should only be used by those physicians trained in transcatheter defect closure techniques, and by those physicians prepared to provide long term follow up patient monitoring.

Physicians attempting to recover an embolized device should be limited to those that have completed appropriate device retrieval technique training.

Embolized CardioSEAL devices should be removed. Dislodged CardioSEALs have embolized to the pulmonary and systemic vasculature.

Embolized CardioSEALs may disrupt critical cardiac functions. Physicians must be prepared to deal with urgent requirements to extract or move embolized CardioSEALs that result in critical hemodynamic compromise.

Embolized CardioSEALs should not be withdrawn through intracardiac structures unless they have been adequately collapsed within a sheath. Devices that are not adequately collapsed within a sheath may entangle with valvular or other cardiac structures.

Do not attempt to repair or reuse damaged product. Do not reuse or resterilize product. Return to manufacturer.

Surgical support should be readily available if needed.

Transient hemodynamic compromise may be encountered during device placement, which may require fluid replacement or other medications as determined by the physician.

6. PRECAUTIONS:

6.1 CardioSEAL – Handling Precautions

Do not use the system if, during loading of the CardioSEAL, difficulty is encountered in transferring the CardioSEAL into the loader or from loader to the pod of the delivery catheter.

Do not modify the delivery catheter or CardioSEAL. Modification may result in damage that can result in complications such as embolism, framework fracture, failure to release, and improper seating at the target defect.

6.2 CardioSEAL – Sizing Precautions

The use of a compliant balloon catheter to determine defect localization is recommended.

Accurate defect sizing is criticial to CardioSEAL selection. Defect sizing methods, such as contrast angiography, echocardiography and – or balloon sizing should be considered as procedural alternatives. The defect and surrounding structures should be fully examined in multiple planes to assure proper sizing of the CardioSEAL.

The anatomic area surrounding the target defect should have enough contiguous structure to support the CardioSEAL.

6.3 CardioSEAL – Procedural Precautions

The ability of the patient to remain still during implantation must be weighed against the need for "conscious" sedation versus general anesthesia. The decision to use general anesthesia in any individual patient is subject to physician judgement.

Patients should be fully heparinized throughout the procedure using adequate dosing so as to keep the ACT greater than 200 msec.

Antibiotic therapy periprocedurally is recommended to reduce the risk of perioperative infection.

The use of Transesophageal Echocardiography (TEE) should be considered as a potential aid in placing the CardioSEAL. If used, the patient's esophageal anatomy must be adequate for placement and manipulation of the TEE probe.

Placement of the CardioSEAL requires the use of fluoroscopic X-ray guidance. The risk of increased x-ray exposure for patients who are pregnant must be weighed against the potential benefits of the technique.

The patient's vasculature should be sufficient to accommodate the 11 F sheath required to deliver the CardioSEAL.

Introducer sheaths longer than 80 cm will prohibit the complete extrusion of the CardioSEAL from the sheath during delivery to the defect.

A delivery catheter of equivalent or larger pod size must be used with the CardioSEAL to avoid damage to the implant during loading and deployment.

Malpositioned CardioSEALs may interfere with cardiac, vascular or valvular structures, depending on patient anatomy. Physicians should consider removing malpositioned CardioSEALs in these patients.

6.4 CardioSEAL – Post Implant Precautions

The time course of endothelialization of the device is unknown. Patients should receive appropriate endocarditis prophylaxis for the six months following implantation. The decision to continue prophylactic treatment after six months is subject to physician judgement.

Patients should be treated with antiplatelet/anticoagulation therapy, such as Aspirin (see Section 8 Clinical Studies for the dosage used in the High-risk study) for six-months following implant. The decision to continue medical treatment beyond six months is subject to physician judgement.

All CardioSEALs are non-ferromagnetic. Independent studies of CardioSEAL in a 1.5 Tesla magnetic field demonstrate no movement of the CardioSEAL. However, MRI image quality may be compromised in the area of the implant.

7. ADVERSE EVENTS

7.1 Observed Adverse Events:

A total of 63 patients requiring closure of a VSD were enrolled in a 292 patient multi-center High risk study.

Four patients died within 4 months of device placement, for an overall mortality rate of 7.7% among patients receiving a device to occlude a ventricular septal defect. All four deaths were reviewed by an independent Safety and Data Monitoring Committee. One of the deaths in a small infant was classified as due to the catheterization procedure. In this patient, the cardiac catheterization procedure was complicated by complete heart block induced by the catheters. Two days after the procedure, the patient was taken to the operating room for placement of a pacing wire. During this procedure the patient suffered a cardiac arrest and could not be resuscitated. The remaining three deaths were attributed to the patient's underlying cardiac (2) or medical (1) condition.

A total of 194 adverse events were recorded among the 63 patients enrolled in the study for closure of their VSD. These adverse events were classified as Serious (23), Moderately Serious (75), Not Serious (92), or Unknown Seriousness (4) and were linked to either the device, the implant procedure, the catheterization procedure, or other causes, such as a pre-existing condition. Adverse events (7.1) that were classified as Serious or Moderately Serious and definitely or probably related to the device, the implant procedure or the catheterization are shown in Table 1.

Adverse Events – Table 1 VSD (n=63)				
	Moderately Serious		Serious	
	Early Event*	Late Event**	Early Event*	Late Event**
Device Related				
Device Malposition	1	0	0	0
Ventricular premature beats	1	1	0	0
Endocarditis	1	0	0	0
Hemolysis	1	0	0	0
Ventricular tachycardia	3	0	0	0
Supraventricular tachycardia	1	0	0	0
Non-sustained ventricular tachycardia	1	0	0	0
Implant Procedure Related				
Arterial pulse loss, requiring heparin	1	0	0	0
Atrial flutter	1	0	0	0
Blood loss requiring transfusion	0	0	1	0
Congestive heart failure	1	0	0	0
Air embolism	1	0	0	0
Heart block (3 ^{0})	0	0	5	0
Hypotension requiring intervention	1	0	1	0
Perforation of the heart	1	0	0	0
Transient bradycardia	0	1	0	0
Valve regurgitation-aortic	0	0	1	0
Valve regurgitation-mitral	2	2	0	0
Valve regurgitation-tricuspid	1	0	0	0
Venous thrombosis (suspected)	1	0	0	0
Ventricular tachycardia	1	0	1	0

Adverse Events - Table 1 (cont.) VSD (N= 63)				
	Moderately Serious		Serious	
	Early Event*	Late Event*	Early Event*	Late Event*
Catheterization Procedure Related				
Acute renal failure	0	0	1	0
Blood loss requiring transfusion	13	0	0	0
Cyanosis	1	0	0	0
Fever	2	0	0	0
Heart block (3 ^{0})	0	0	1	0
Hypotension requiring intervention	6	0	0	0
Multi organ failure	0	0	1	0
Perforation of vessel	1	0	0	0
Phlebitis	1	0	0	0
Pseudoaneurysm	1	0	0	0
Pulmonary edema	1	0	0	0
Respiratory insufficiency	2	0	0	0
Sinus tachycardia	1	0	0	0
Stridor	1	0	0	0
Hypercyanotic episode	1	0	0	0
Upper respiratory infection	1	0	0	0
Ventricular tachycardia	0	0	2	0
Wheezing	1	0	0	0

* = Early event is $\leq$ 30 days from implant. Total =67 early events.

** = Late event is > 30 days from implant. Total =4 late events.

7.2 Potential Adverse Events:

Placement of the CardioSEAL involves using standard interventional cardiac catheterization techniques. Complications commonly associated with these procedures include, but are not limited to:

Air Embolus
Allergic dye reaction
Anesthesia reactions
Apnea
Arrhythmia
Death
Fever
Headache / Migraines

Hematoma and/or Pseudoaneurysm including blood loss requiring transfusion
Hypertension; Hypotension
Infection including Endocarditis
Perforation of Vessel or Myocardium
Stroke / Transient Ischemic Attack
Thromboemobolic events
Valvular regurgitation.

Fractures of the framework have been reported in some implanted patients. The risk of fracture appears to be related to the size Occluder selected relative to the size of the heart chamber it was implanted in. Two reports of palpitations have been the only complications observed with the CardioSEAL Septal Occluder. These complications did not occur in the VSD population. In the independent, multicenter clinical trial sponsored by Children's Hospital, Boston Massachusetts, the arm fracture rate was 18.1% in the Ventricular Septal Defect population.

7.3 Observed Device Malfunctions:

There were three reports of a delivery system malfunction in which the physician had difficulty releasing the implant from the delivery catheter, one report of a kink in the delivery system, identified during the device placement, and three reports of a kink in the delivery system during loading of the device. There were no clinical sequelae associated with any of these device malfunctions.

8. CLINICAL STUDIES:

Study Design/Objective: The multi-center clinical trial conducted by Children's Hospital, Boston, Massachusetts, is a prospective, non-randomized trial studying the use of the CardioSEAL® Septal Occlusion system to close a variety of hemodynamically significant defects. The risks of surgical closure for the patients enrolled in this trial were considered sufficient to justify the known and potentially unknown risks of transcatheter closure with the CardioSEAL device. The study (referred to as the High-risk study) is ongoing and is summarized below. Data from patients undergoing VSD closure were extracted from this study.

Patient Entry: Patients were eligible for enrollment in the High risk study if they had a defect(s) of sufficient size to require closure, but were considered to be at high risk for surgical closure, due to either complex medical or cardiac disease. An independent peer review group determined whether a patient should be enrolled into the trial based on the following criteria:

- the patient had a type of defect that was technically difficult or impossible to close surgically, such that the surgical risks were sufficient to justify the known and potential unknown risks of the device, or

- the patient's overall medical condition was such that the surgical risks were sufficient to justify the known and potential unknown risks of the device.

Methods: After enrollment, patients underwent cardiac catheterization. Position and size of the defect were confirmed by angiography. A hemodynamic assessment was performed pre-implant, and after test occlusion of the defect with a balloon. When these data suggested that the defect contributed to unfavorable hemodynamics and was feasible for transcatheter closure, device placement proceeded. Patients received aspirin, 1mg/kg/day, rounded to the nearest half tablet of 80 mg size, for at least six months following the procedure.

Patients were seen for follow up assessments as described in Table 2:

Timing of Evaluations – Table 2

	Pre-Implant	Pre-D/C	1 month F/U	6 month F/U	12 month F/U	24 month F/U
Cardiac HX/PE	X	X	X	X	X	X
Chest X-Ray	X	X	X	X	X	
Fluoroscopy				X		X
Echo/Doppler	X	X	X	X	X	X
O_2 Saturation	X	X	X	X	X	X
Clinical Status Evaluation	X	X	X	X	X	X
EKG (rhythm)	X	X	X	X	X	X
Severity of illness	X	X	X	X	X	X

Primary Endpoints: A 5-category ordinal scale (Severity of Illness scale) was used to measure clinical status. Patients were grouped by their physiologic condition into three broad classes (right to left shunt, left to right shunt, or valvular / paravalvular leak). The scale took values from 1 to 5, and was constructed so that an improvement by one category (e.g., from category 1 to category 2, or from 2 to 3) would be considered clinically meaningful (refer to Table 3). Any patient who died during the study would receive a value of 0. Data used in the construction of the scale were measured objectively by diagnostic laboratory tests, documented clinical status, or echocardiography. The data were collected prospectively before device implantation, at discharge from the hospital, and at each follow-up visit, so that patient classification at each time point could be implemented using a computer algorithm.

The major criteria by which severity was categorized for patients undergoing device placement for VSD closure was left to right shunting. The Severity of Illness scale for VSDs is shown in Table 3.

Severity of Illness Scale[1] - Table 3

Physiologic Condition	1	2	3	4	5
L → R shunt	More than small residual flow and dependent on ventilator, balloon pump, or left ventricular assist device	More than small residual flow by Doppler and Requires IV inotropes or NYHA Class III or IV	More than small residual flow by Doppler	Small residual flow by Doppler	Trivial to absent residual flow by Doppler

[1]A deceased patient is rated as 0 on the Severity of Illness Scale.

Clinical Status Scale

The Clinical Status Scale was developed to improve ability to discriminate clinically important changes among patients. While the Severity of Illness scale grouped patients into three broad classes of physiologic condition, the Clinical Status Scale grouped patients into seven different categories (right to left shunt, left to right shunt, systemic embolic, hemodynamic compromise not due to shunt, arrhythmia, elevated PVR, and medical illness). A patient could be placed in multiple categories of the clinical status scale, as applicable to their clinical status.

The left to right shunt category was the category most closely related to the patient's indication for device closure of the VSD. This scale is shown in Table 4.

Clinical Status Scale[2] – Table 4						
Category	0	1	2	3	4	5
L to R shunt	Ventilator dependent and/or intractable CHF	Heart failure, symptomatic	Left ventricular volume overload, significant/ large shunt	moderate shunt	small shunt	trivial or no shunt

[2]A deceased patient is rated as -1 on the Clinical Status Scale.

Patients with prior placement of a pulmonary artery band to limit the degree of left to right shunting are categorized, where possible, according to the estimated anatomic size of the defect.

Additionally an assessment of the echocardiographic closure status was made at each time point both at the evaluating facility, and by an unaffiliated core laboratory. Residual flow was assessed using Doppler color flow mapping, and graded using the following guidelines:

> **"Trivial" to "Absent":** barely detectable or no detectable residual color flow through the defect. If flow is present, it is a single color flow jet, well-circumscribed, with a proximal jet width measuring less than 1 mm in diameter in all views.
>
> **"Small":** single color flow jet, well-circumscribed, and measuring 1-2mm (maximal proximal width) in all views in infants and children weighing less than 20 kg, or between 1 and 3 mm in diameter in larger children and adults.
>
> **"More than small":** single color flow jet, well-circumscribed, measuring greater than 2 mm in diameter in all views in infants and children weighing less than 20 kg, or greater than 3 mm in diameter in all views in larger children and adults.

Results: At the time the VSD data was analyzed, 63 patients with no additional anatomic lesions were enrolled in the study for closure of a VSD. Enrollment occurred at one investigational site. Ten of these patients did not have a device implant attempted because the defect was smaller than anticipated.

Device placement was successful in 52 of 53 patients (98.1%) in whom an implant was attempted. One patient had an unfavorable anatomy which precluded device placement. Multiple procedures were performed in 7 patients, and multiple devices were implanted in 24 patients for a total of 98 implanted devices. None of the devices embolized.

The types of VSD defects closed with a CardioSEAL device were: congenital muscular (25); post-operative (24); and post-infarction (3). Sixteen patients (25.4%) had previously undergone placement of a pulmonary artery band; 4 had been debanded.

Among the 52 patients treated with a CardioSEAL device, there were 20 (38.5%) males and 32 (61.5%) females. The age of the patients ranged from 0.3 years to 79 years, with a median age of 4.4 years.

Three devices were explanted, 2 at the time of a heart transplant, and 1 during a Fontan surgery performed after a failed septation.

The following tables present the combined results of the effectiveness measures for all VSD defect types. The available data column presents the number of patients with data available (numerator) and the number of patients who were expected to be seen at the respective visits (denominator).

Table 5 reflects the number of patients observed within each Severity of Illness category at each visit.

Severity of Illness – Table 5							
		Category					
Time point	**0**	**1**	**2**	**3**	**4**	**5**	**Available Data**
Initial	0	3	6	26	10	0	45/50
Discharge	0	1	1	5	15	14	36/48
1 Month	2	0	0	1	11	19	33/47
6 Month	2	0	1	1	13	13	30/40
12 Month	0	0	0	3	5	8	16/31
24 Month	0	0	0	0	2	8	10/10

Table 6 reflects the number of patients observed within each Clinical Status category at each visit.

		Clinical Status –Table 6						
		Category						
Time Point	**-1**	**0**	**1**	**2**	**3**	**4**	**5**	**Available Data**
Initial	0	5	13	10	21	3	0	52/52
Discharge	0	1	2	1	6	25	12	47/48
1 Month	2	0	0	0	3	23	13	41/47
6 Month	2	0	0	1	0	18	11	32/40
12 Month	0	0	0	0	1	16	7	24/31
24 Month	0	0	0	0	1	6	7	14/14

Table 7 reflects the number of patients observed within each Echo closure category at each visit.

Echo Closure Status – Table 7				
		Category		
	None - Trivial	Small	More than small	Available Data
Initial	0	10	37	47/52
Discharge	15	13	5	33/52
1 Month	19	10	2	31/50
6 Month	15	14	1	30/41
12 Month	11	4	2	17/32
24 Month	7	2	0	9/9

9. HOW SUPPLIED:

The implant and delivery system are packaged separately. The delivery system is size matched to the implant. Both components are provided sterile. Product is sterilized via ETO.

10. DIRECTIONS FOR USE:

A. Detailed Product Description:

The CardioSEAL Septal Occlusion System consists of two primary components. The CardioSEAL (Occluder) is comprised of a metal alloy (MP35N) framework to which polyester fabric material has been attached.

From the center of the CardioSEAL, a small wire with a pin at its end extrudes out at approximately 90 degrees to the plane of the CardioSEAL. The CardioSEAL is attached to sutures through a loading funnel. The loader should always be connected via sutures to the side of the CardioSEAL opposite the side from which the pin wire extrudes.

The delivery catheter is comprised of a coaxial catheter shaft through which a spring guide travels, connected to a solid control rod. At the proximal end of the control rod, a control handle is connected to an inner control wire, which courses through the spring guide to the distal end of the catheter shaft, where it terminates within a small tubular sleeve. The control wire terminates at the distal end in a pin, for attachment to its mate on the CardioSEAL. When retracted, the pin slides inside the sleeve. The distal end of the catheter terminates in a pod. Retraction on the control rod moves the sleeve into the pod. Refer to figure 1 for an illustration of the delivery system and CardioSEAL.

B. CardioSEAL Size Selection and Inspection:

Selection of an appropriately sized CardioSEAL(O) should be based upon measuring the defect diameter through the use of a sizing balloon (stretched defect diameter – SDD), procedural angiography and/or Transesophageal echocardiography, unless the size of the defect is known from the medical record. It is recommended that the CardioSEAL to Stretched Defect Diameter ratio (O:SDD) be 1.7-2.0:1, and that the area containing the target defect be large enough to allow the CardioSEAL to fully deploy. The defect and surrounding structures should be fully examined in multiple planes to assure proper sizing of the CardioSEAL.

The Right Femoral Vein or Right Internal Jugular vein is recommended for vascular access although physicians should consider the VSD location and the route of introducer sheath travel relative to the potential for access in selecting the venous access site.

An 11F, 75cm long, hemostasis control introducer sheath with NIH type curve is recommended for CardioSEAL delivery. Sheath curve shape may need modification based on individual patient conditions and defect location. As the use of long sheaths represents a potential risk of air embolus, care should be taken to insure adequate irrigation and 'backfilling' of the sheath with saline during removal of the dilator in order to avoid air entry.

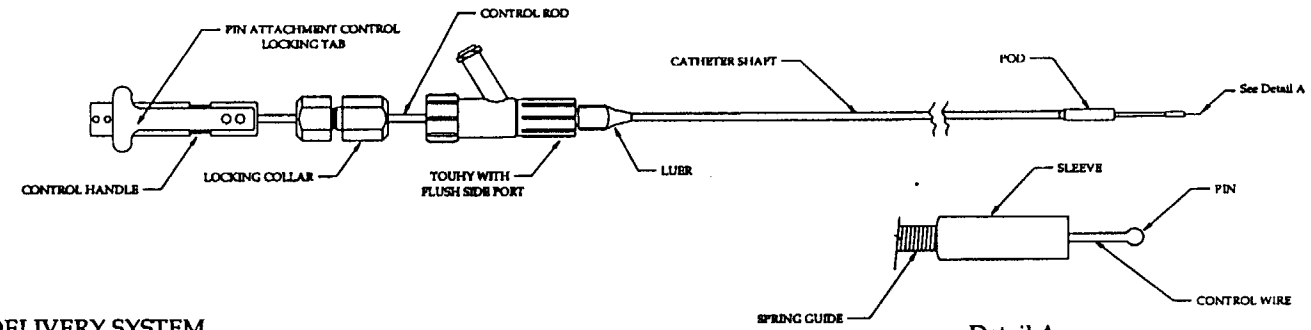
A 14F or 16F short introducer sheath may be placed coaxially over the long introducer sheath prior to long sheath insertion if the physician believes the circumstances of the case raise the potential for device retrieval after attempted placement.

Prior to use, inspect the delivery system and CardioSEAL for signs of damage, such as kinks or bends in delivery wire or framework of the CardioSEAL. Check for secure attachment of the fabric to the framework.

Manipulate the delivery system and actuate the control handle to ensure that the attach release pin exits and retracts into the sleeve, and that the spring guide wire exits and retracts into the pod.

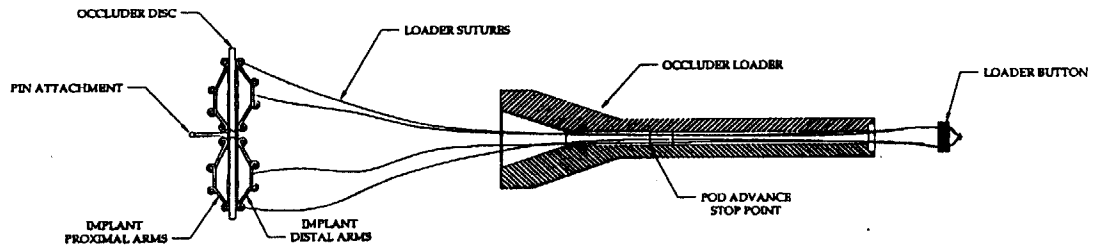
The delivery catheter system and CardioSEAL are packaged separately. Each is a component of the system, however, and each implant requires an equivalently sized or larger delivery catheter for appropriate use.

The CardioSEAL™ Septal Occlusion System



DELIVERY SYSTEM

Detail A



OCCLUDER

FIGURE #1

C. Preparation for Delivery:

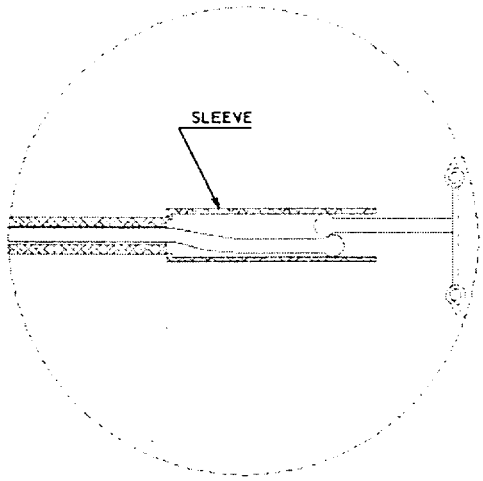
Attaching the CardioSEAL to the Delivery Catheter:

NOTE: Attachment and loading of the CardioSEAL *into the delivery catheter should not occur until*

a. *the defect has been determined to be of appropriate size and position to accomodate the CardioSEAL, and*
b. *access to the defect with an appropriate French size and length introducer sheath has been obtained.*

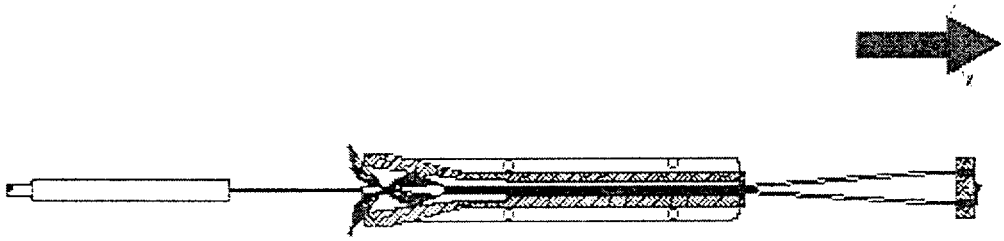
1. Loosen the black locking collar on the delivery catheter and advance the control rod until the sleeve exits from the pod. Pull gently upward on the pin control locking tab on the control handle. Push the rear section of the control handle in, extruding the pin from the sleeve about 3 – 4 mm.

2. Place the pin of the CardioSEAL into the sleeve, behind the pin extruding from the sleeve. Draw both pins into the sleeve by lifting up on the control handle tab and pulling the rear section of the control handle out. Seat control tab into slot on control handle, and test for secure attachment of CardioSEAL to delivery system with a gentle to and fro motion of the CardioSEAL.

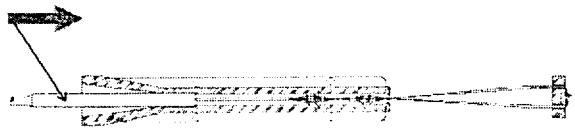


3. Submerge the loader/ CardioSEAL assembly in sterile saline and thoroughly soak the CardioSEAL. Make sure inner lumens of loader are wet. This will decrease friction between CardioSEAL and loader during loading.

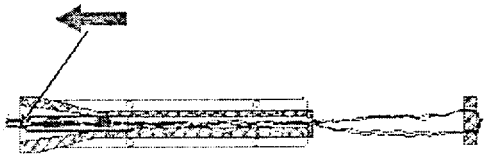
4. Carefully draw the CardioSEAL into the smallest section of the loader by pulling on the loader button. Do not attempt to force CardioSEAL into funnel section of the loader unless all four arms on each side of the CardioSEAL are appropriately retracted into the collapsed position.

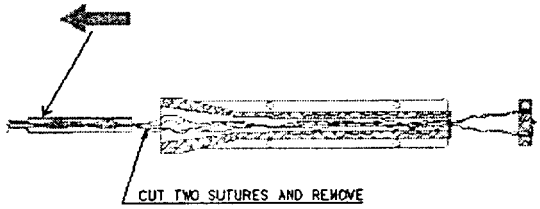


5. With the CardioSEAL fully collapsed in the smallest section of the loader, use the control rod to advance the pod into the loader until the pod contacts the stop point.



6. Holding the pod firmly in the loader, retract CardioSEAL into the pod through the use of the control rod. Once in the pod, remove pod from loader, snip sutures one at a time, and remove from the CardioSEAL. Discard loader, sutures and loader button.





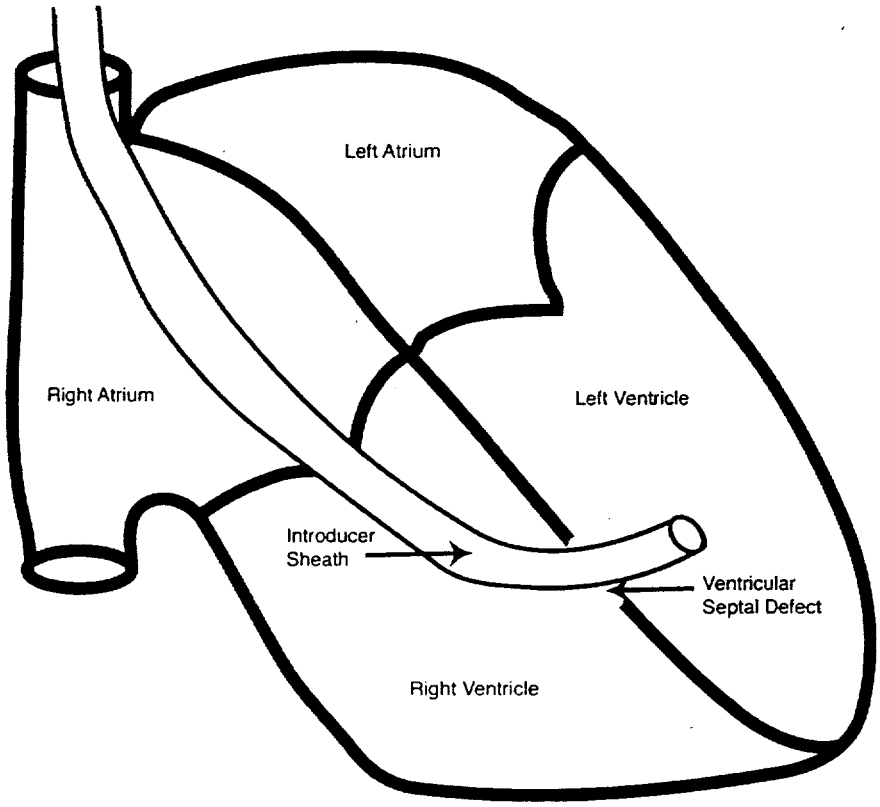
7. Loosen locking collar and advance it up to the Y-body. Tighten locking collar and flush the delivery system with normal saline several times to remove all air from the system. The CardioSEAL is now ready for delivery to the defect.

D. Insertion

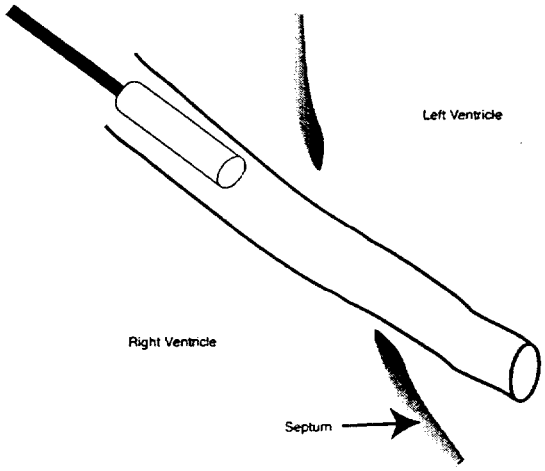
NOTE: As previously discussed in Section C, Preparation, Note B, an introducer sheath of sufficient French size (11F) for the CardioSEAL and of adequate length to reach the target defect should have been placed via the venous system across the defect.

1. Reposition sheath across the VSD so that the distal tip of the sheath is approximately 1cm into the distal side of the VSD. Thoroughly irrigate the previously placed introducer sheath to minimize risk of air entry and air embolus.

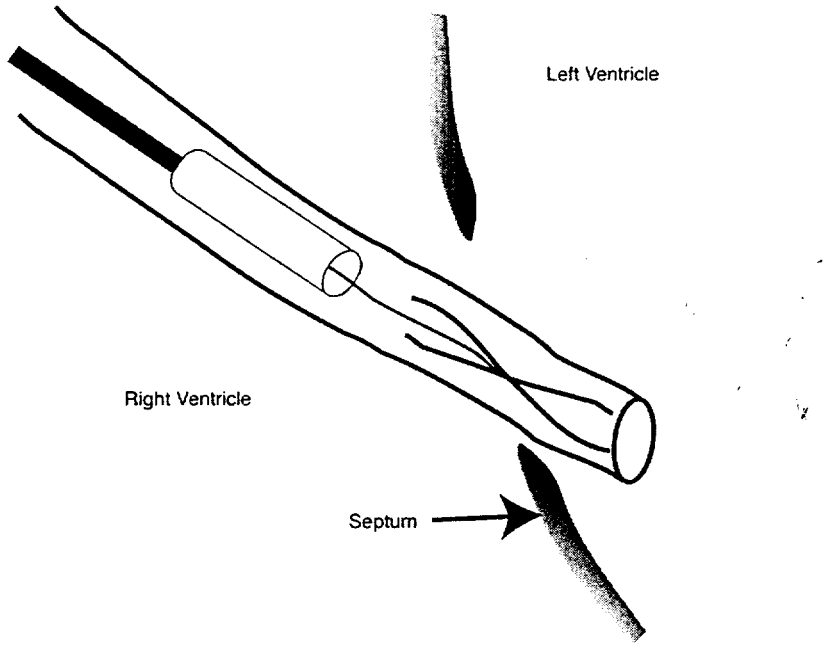
NOTE: ALL DIAGRAMS IN THIS SECTION SHOW AN APPROACH TO THE V.S.D. FROM THE RIGHT INTERNAL JUGULAR VEIN.



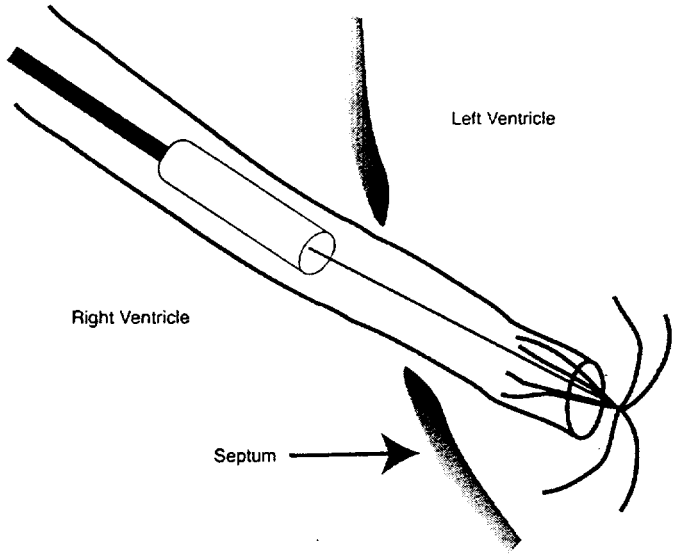
2. Insert the pod of the delivery system into the sheath, and advance until the pod is no closer than 5 to 10 cm from the tip of the sheath, or until sheath curve course resistance is met within the sheath. Resistance may be met in some patients as the curve of the sheath becomes to tight for the pod to pass through without dislodging the sheath from it's transseptal position through the defect. In either case, the pod should be in the fluoroscopic field of view.



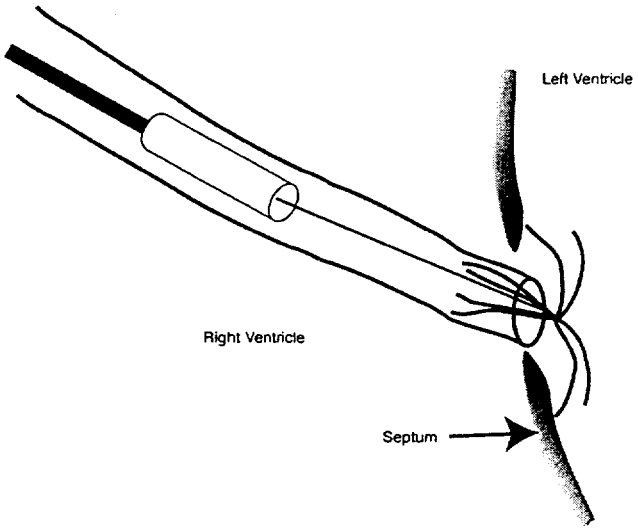
3. Loosen the locking collar nut and advance the collapsed CardioSEAL out of the pod and into the sheath. The CardioSEAL will remain collapsed within the sheath, with the sheath serving as an extension of the pod. Continue to advance the CardioSEAL until it is within 1-2mm of the tip of the sheath.



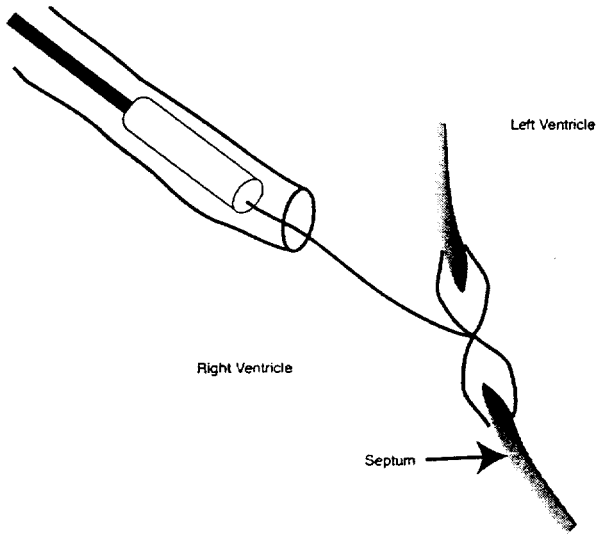
4. Recheck sheath tip position to verify location on distal side of VSD. Holding the sheath and catheter steady, advance the distal set of CardioSEAL arms out of the sheath by moving the control rod forward. Alternatively, open distal set of CardioSEAL arms by retracting sheath off of the distal arms. Under fluoroscopy and transesophageal echo, ascertain that all four distal CardioSEAL arms have fully deployed and are intact.



5. Holding the sheath and catheter steady, retract entire sheath – catheter - CardioSEAL until the distal CardioSEAL arms approximate or engage the distal wall of the VSD.

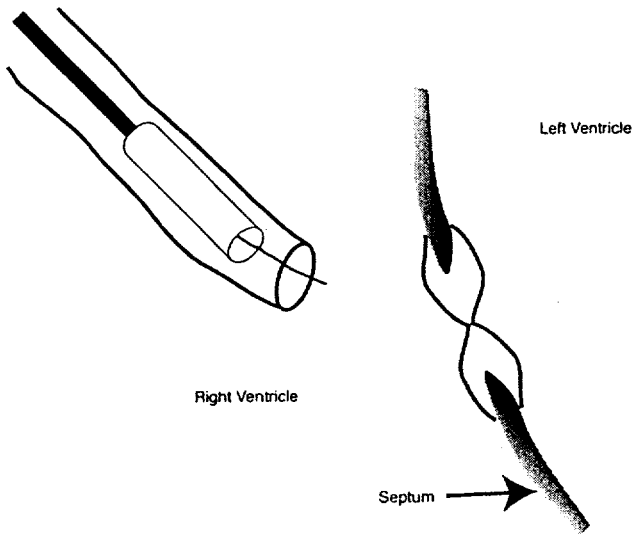


6. Once approximated or engaged, retract CardioSEAL further to slightly flex the CardioSEAL arms. Retract sheath off of proximal CardioSEAL arms while maintaining position in the VSD. This will release the proximal arms of the CardioSEAL to engage the proximal VSD wall.



7. Allow delivery catheter and sheath to assume a neutral (i.e. no retraction) position and confirm correct placement of all arms on appropriate sides of the VSD.

8. Once proper positioning is confirmed, advance the pin from the sleeve using the control handle at the proximal end of the delivery system. This will release the CardioSEAL from the delivery system.



9. Remove delivery system from sheath.

11. PATIENT INFORMATION:

The following counseling information should be provided to the patient:

Patients should be reminded of the importance of adhering to their aspirin and endocarditis prophylaxis regimens.

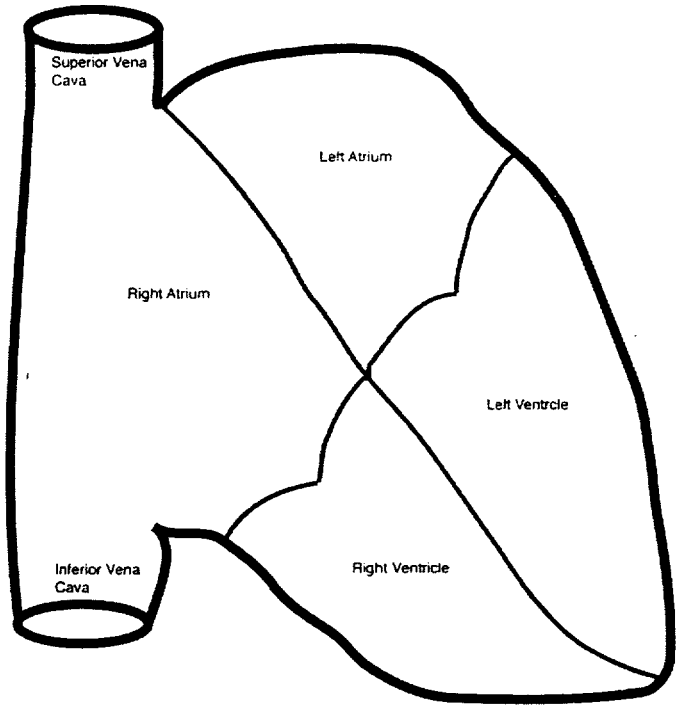
If an MRI is required, the patient should inform MRI staff of the presence of the CardioSEAL.

Patients should be encouraged to contact their physician if they have any questions or concerns

A patient brochure is available and is entitled: "A Patient's Guide to Transcatheter Hole Closure of a Ventricular Septal Hole using The CardioSEAL® Septal Occlusion System."

PL#: 0252.00

A Patient's Guide to Transcatheter Hole Closure of a Ventricular Septal Hole using The CardioSEAL® Septal Occlusion System



Basic Diagram of the Normal Heart

Humanitarian Use Device

Authorized by Federal law for use in the treatment of patients with a complex ventricular septal hole of a significant size to warrant closure, but that based on location, cannot be closed with standard surgical transatrial or transarterial approaches. The effectiveness of this device for use in this indication has not been demonstrated.

Introduction:
You (or your child) has been diagnosed with a hole in the heart called a Ventricular Septal Hole, which is an abnormal hole between the two main pumping chambers of the heart, the left and right ventricle. (see diagram below)

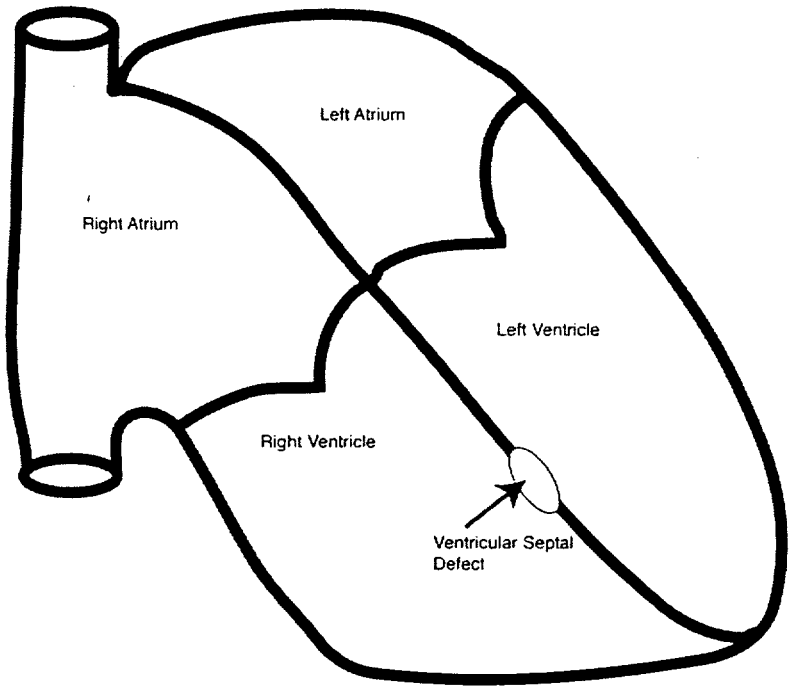
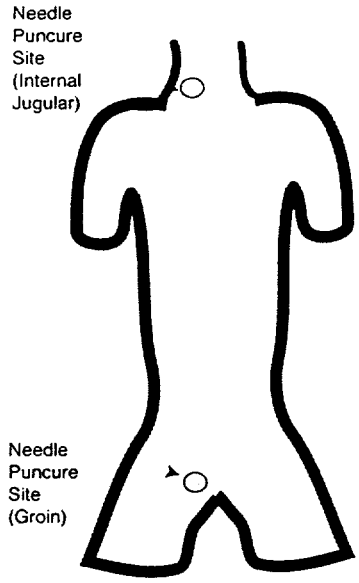


Diagram of a remote Ventricular Septal Defect

Your (or your child's) physician has recommended that this hole should now be closed using an implant. The implant is placed in the heart using a catheter. This procedure is called Transcatheter Hole Closure. It is an alternative to open heart surgery. The physician believes that the risks of open heart surgery presents an unusually high risk to you (your child). Transcatheter closure is a procedure that avoids the need for open heart surgery. As a less invasive procedure, it is believed to present fewer risks since open heart surgery is avoided.

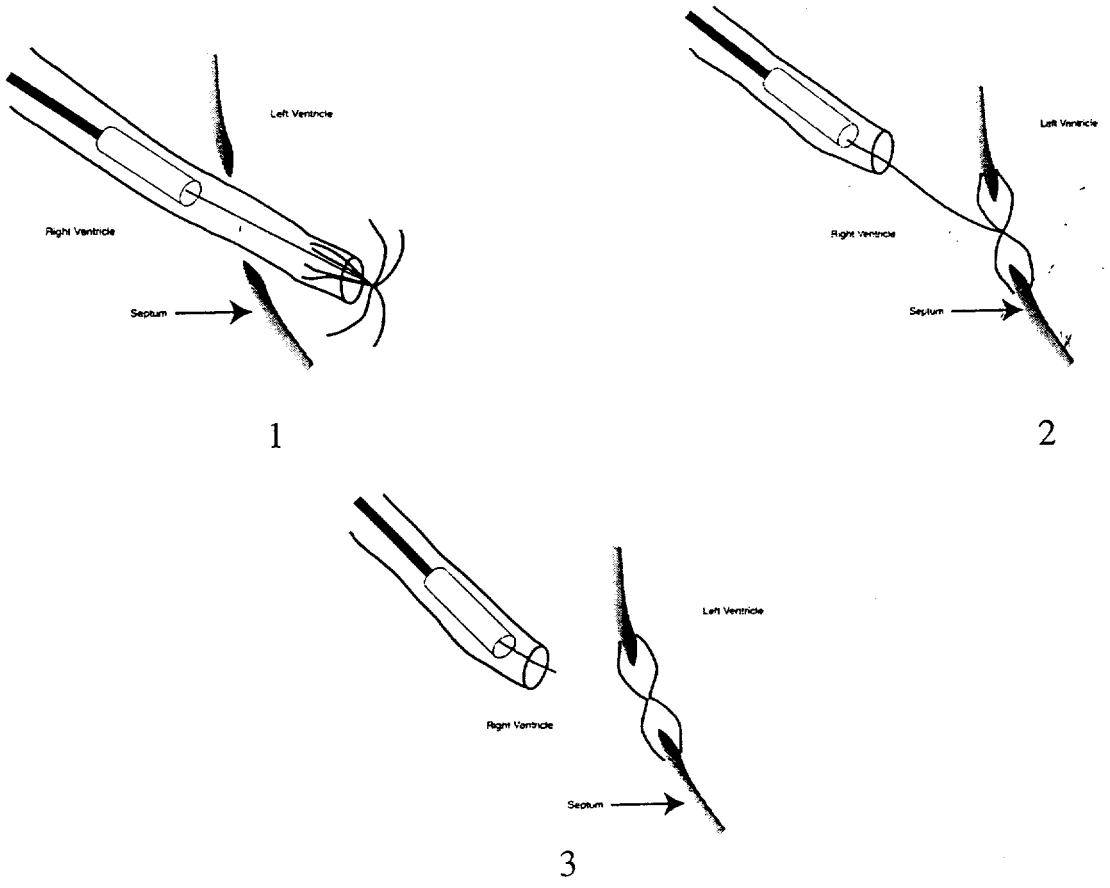
How does Transcatheter closure work?

Transcatheter closure is performed in the Cardiac Catheterization Laboratory by a Doctor. The Doctor will gain access to your (your child's) heart by getting access to a major vein in the groin or internal jugular vein.



This is done by a needle puncture. Various catheters will be advanced from the groin or arm into the heart. Moving pictures, called angiograms, will be taken to better visualize the heart and the hole. The Doctor may use a special ultrasound device, called TransEsophageal Echocardiography (TEE). This is another way to better see the heart and the hole. The TEE involves putting a probe into the esophagus, the tube between the mouth and stomach. These tests are used to determine which sized implant the physician will use to close the hole.

The appropriate size implant is attached and collapsed for placement into a special catheter. The catheter is then advanced to the site of the hole. The Doctor re-expands the implant so that part of it sits on each side of the hole. In effect the hole is gently sandwiched between the two sides of the implant. The implant is then released from the catheter. The catheter is removed and the procedure completed.

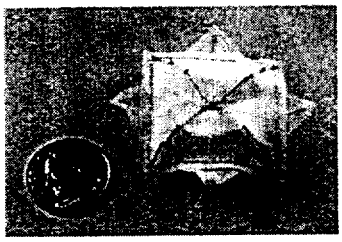


Diagrams showing the basic steps of the procedure.

Will I be awake during the procedure?
This is up to the physician. Many patients are put under general anesthesia for this procedure. A local anesthetic is used to numb the groin or arm (the location where the catheters are inserted).

How does the implant stay in place?
CardioSEAL is made from two, small diameter wire frameworks. The framework has a special fabric attached to it. The device looks like two little umbrellas set edge to edge. Each umbrella framework has special springs. This allows the umbrellas to spring towards the hole. This very slight tension, along with the blood in the heart, holds the device in place. Over time, tissue grows into the fabric and the implant becomes part of the heart.

What does the Implant look like?
CardioSEAL comes in several sizes. The smallest (17mm measured diagonally) is about the size of a dime, the largest is about the size of a half- dollar. This picture shows one of the larger implants placed next to a dime. This may give you some perspective of the size. The framework is made from a metal frequently implanted in the body during other surgeries. The fabric is the same fabric the surgeon would use if open heart surgery was performed.



What are the risks?
The risks are similar to those associated with other heart catheterization procedure. There are additional risks associated with the implant. Examples include:

- dislodgement
- incomplete sealing of the hole
- abnormal heart rhythms
- bruising at the groin or arm
- changes in blood pressure
- air embolus
- hemolysis
- apnea
- headache/migraine
- infection including endocarditis
- perforation of vessel or myocardium
- thromboembolus
- stroke or TIA

The implanting physician usually insures that the risks associated with heart catheterization and the implant are reviewed with each patient.

Will the procedure hurt?
Usually not. After the procedure, some patients report tenderness at the groin or arm. Some also complain of a sore throat from the TEE probe. Patients cannot "feel" the implant.

What is the special care after the procedure?

- bed rest for a period of time (this allows the implant to firmly stabilize)
- restriction from heavy lifting or other physical activities for a period of time
- take a blood thinning product, such as Aspirin, every day, for a period of time (perhaps several months or longer)
- take antibiotics to prevent infection (this may be required when going to the dentist or having a minor surgical procedure)
- follow the doctor's instructions precisely
- call the doctor if there are any questions

What about follow up visits?

All patients are asked to see their doctor for follow up visits. The Doctor will provide specific instructions for follow-up care.

Does the Implant stay in for the rest of my life?

Yes, it is intended to stay in forever.

Can I go through metal detectors, or have an M.R.I?

Yes. The implant will not set off metal detectors. The metal framework is not magnetic. It will not be affected by an MRI, but the picture taken by the MRI might have a fuzzy quality. If an MRI is needed, the MRI staff should be informed about the presence of the implant.

What are the options or alternatives to this treatment?

Having open heart surgery to close the hole. Or, you may elect to have no treatment of any kind.

What are the contraindications to this treatment?

- presence of blood clots in the vein used to introduce the catheter
- the vein needed to introduce the catheter is too small for the catheter to fit
- presence of an active infection
- patient unable to take aspirin or other blood thinning medication

Glossary of technical terms

- **Abnormal heart rhythms** – abnormal heart beats.
- **Air embolus** – an air bubble in the blood stream.
- **Angiogram** – a test involving moving pictures of the heart.
- **Apnea** – a transient cessation of breathing.
- **Atrium** – the upper two chambers (right and left) of the normal heart.
- **Cardiac Catheterization Laboratory** – a room in the hospital dedicated to accessing the heart using catheters and X-ray guidance.
- **Catheter** – a sterile tube for insertion into a vessel to permit injection or withdrawal of fluids or to pass material through.
- **Dislodgement** – moving from its intended position.
- **Endocarditis** – an inflammation of the lining of the heart and its valves.
- **Esophagus** – the part of the body which connects the mouth to the stomach.
- **Heart catheterization** – a less invasive way (compared to open heart surgery) to access the heart using the arteries of veins.
- **Hemolysis** – when the red blood cells break.
- **Implant** – a medical device, which is put into the body.
- **MRI** – Magnetic Resonance Imaging--a type of test used to visualize body tissue that uses a magnetic field.
- **Native** – refers to a condition that was (or is) naturally present to the body at birth.
- **Perforation of vessel or myocardium** – a tear in a blood vessel or the heart.
- **Pulmonary Arteries** – major blood vessels that direct blood from the heart to the lungs.
- **TEE** – an ulstrasound (sound waves) test to visualize the heart and hole.
- **Thromboembolus** – a blood clot within a blood vessel.
- **TIA** – (transient ischemic attack) a transient lack of oxygen to the brain.
- **Transcatheter Hole Closure**- a less invasive procedure (compared to open heart surgery) used to close heart holes using catheters.
- **Ventricle** – the lower two chambers (right and left) of the normal heart.

This guide was prepared by Nitinol Medical Technologies, Inc. It is based on input and guidance from Physicians and Clinical Staff throughout the United States. NMT wishes to thank them for their contributions. However, this guide is not a replacement for speaking with your physician. We recommend you write down questions for your doctor on a separate piece of paper.