The AMPLATZER® Duct Occluder 180° Delivery System Instructions for Use

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AMPLATZER® Duct Occluder 180° Delivery System

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

1. BRIEF DEVICE DESCRIPTION

The AMPLATZER Duct Occluder is a self-expandable device made from a Nitinol wire mesh. A retention skirt on the aortic side provides secure positioning in the ampulla of the ductus. As the occluder is implanted, it expands outward and the wires push against the wall of the ductus. Polyester fabric is sewn into the occluder with polyester thread. The fabric induces thrombosis that closes the communication. Refer to Section 11 for detailed description of the device.

The AMPLATZER 180° Delivery System is comprised of a delivery sheath, dilator, loading device, plastic vise and delivery cable. 180° indicates the curve of the delivery sheath.

2. INDICATIONS AND USAGE

The AMPLATZER Duct Occluder is a percutaneous, transcatheter occlusion device intended for the non-surgical closure of patent ductus arteriosus (PDA).

3. CONTRAINDICATIONS

3.1 Patients weighing less than 6 kgs.

3.2 Patients less than 6 months of age.

3.3 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.

3.4 Active endocarditis or other infections producing bacteremia.

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

3.6 Patients with pulmonary hypertension with pulmonary vascular resistance of > 8 Woods units or Rp/Rs of > 0.4.

4. WARNINGS

4.1 The device should be removed if >3mm extends into the pulmonary artery, or if more than half of the left pulmonary artery lumen is occupied by the device.

4.2 Patients allergic to nickel may suffer an allergic reaction to this device.

4.3 There is limited clinical data for patients over 40 years of age.

4.4 The AMPLATZER Duct Occluder and 180° Delivery System should only be used by those physicians trained in transcatheter defect closure techniques.

4.5 Physicians must be prepared to deal with urgent situations which require removal of embolized devices that result in critical hemodynamic compromise. This includes the availability of an on-site surgeon.

4.6 Embolized devices must be removed. Embolized devices should not be withdrawn through intracardiac structures unless they have been adequately collapsed within a sheath.

4.7 Do not use if the sterile barrier has been compromised in any way.

4.8 Do not release the AMPLATZER Duct Occluder from the delivery cable if the device does not conform to its original configuration or if the device position is unstable. Recapture the device and redeploy. If still unsatisfactory, recapture the device and replace with a new device.

5. PRECAUTIONS

5.1 Handling

- The AMPLATZER Duct Occluder and 180° Delivery System are for single use only. Do not reuse or resterilize.

5.2 Sizing

- Accurate defect sizing is crucial and mandatory for AMPLATZER Duct Occluder device selection. Refer to Section 11.3 for Sizing instructions.

5.3 Post-Implant

- Endocarditis prophylaxis is carried out for 6 months according to the recommendation of the American Heart Association. The decision to continue endocarditis prophylaxis beyond six months is at the discretion of the physician.
- Any patient who has a residual shunt will undergo an echo cardiographic evaluation of the residual shunt until complete closure of the defect has been confirmed.
- Lung perfusion scan should be completed if flow through is > 3M/sec, or if the Z-score is–2 for the left pulmonary artery diameter.
- Caution should be used if an MRI is performed with a magnetic field > 1.5 Tesla.

5.4 Use in Specific Populations

- *Pregnancy* – Care should be taken to minimize the radiation exposure to the fetus and the mother.

- *Nursing Mothers* – There has been no quantitative assessment of the presence of leachables in breast milk.

6. ADVERSE EVENTS

6.1 Clinical Summary

The AMPLATZER Duct Occluder was evaluated in a multi-center, non-randomized, pivotal study evaluating the clinical performance for PDA closure. 435 patients received 435 devices with a total device exposure of 371.9 years. Individual patient exposure to the device averaged 10.4 months (ranging from 0.0 to 28.5 months).

6.2 Deaths

There was one death reported five months post-procedure. The Data Safety Monitoring Board members reviewed this adverse event and were unable to determine if the death was device related.

6.3 Observed Adverse Events

Table 1 - Adverse Events Summary

Adverse Event Definition[1,2]	Number of Patients	95% Upper Confidence Bound
Serious Adverse Event		
Death	1 / 393 (0.3%)	
Major Adverse events		
Device Embolization with percutaneous removal	1 / 393 (0.3%)	
Thrombus on Device	1 / 393 (0.3%)	
Partial Obstruction of Pulmonary Artery	1 / 393 (0.3%)	
Pseudoaneurysm	1 / 393 (0.3%)	
Total Serious and Major Adverse Events	5 / 393 (1.2%)	2.7%
Minor Adverse Events		
Hematoma of the groin	7 / 393 (1.7%)	
Other[3]	6 / 393 (1.5%)	
Loss of peripheral pulse	4 / 393 (1.0%)	
Cardiac arrhythmia requiring cardioversion or medication	2 / 393 (0.5%)	
Any Adverse Event	23 / 393 (5.9%)	8.2%

[1] One patient had a Major and Minor Adverse event. 23 patients had 24 adverse events.
[2] Patients less than 6 months of age, and less than 6 kgs. are not included in this analysis.
[3] Air embolism, allergic reaction, blood loss/no transfusion, laryngospasm, respiratory arrest, and thrombus on device.

Definitions:

Death – death during or after the procedure due to complications of the procedure.
Device embolization – embolization with transcatheter removal.
Thrombus – thrombus on device with or without embolization.

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Partial Obstruction of Pulmonary Artery -- increase in the pressure gradient of > 10mmHg and a lung perfusion scan with >30% flow to the LPA.
Pseudoaneurysm – false aneurysm of the femoral hematoma requiring treatment.
Loss of peripheral pulse – transient or requiring only heparin therapy.
Cardiac arrhythmia – requiring cardioversion or medication.

6.4 Potential Adverse Events

Placement of the AMPLATZER Duct Occluder involves using standard interventional cardiac catheterization techniques. In addition to the above observed adverse events, the following are potential adverse events listed in alphabetical order that were not observed in the clinical study. The following events might occur from either the catheterization procedure or from the device:

- Air Embolus
- Allergic dye reaction
- Allergic drug reaction
- Anesthesia reactions
- Apnea
- Arrhythmia
- Bacterial endocarditis
- Bleeding
- Brachial plexus injury
- Chest pain
- Delivery system failure
- Fever
- Headache/Migraine
- Hyper/Hypotension
- MI
- Perforation of vessel or myocardium
- Peripheral Embolism
- Stroke / TIA
- Thrombus
- Valvular regurgitation
- Vascular access site complications

7. CLINICAL STUDIES

Purpose: The purpose of the trial was to evaluate the safety and effectiveness of the AMPLATZER Duct Occluder for the non-surgical closure of patent ductus arteriosus (PDA).

Conclusions: In selected patients, use of the AMPLATZER Duct Occluder demonstrated effective defect closure and acceptable rates of adverse events when compared to Objective Performance Criteria (OPC).

Design: The AMPLATZER Duct Occluder was evaluated in a multi-center, non-randomized, pivotal study evaluating the clinical performance for PDA closure. The OPC formulated the following specific outcome measure criteria as guidelines for safety and efficacy of the AMPLATZER Duct Occluder:

- Primary Efficacy Outcome measure (complete closure) greater than 85% at 12 months,
- Clinical examination closure (absence of continuous heart murmur) greater than 95% at 12 months,
- Serious and Major adverse event rate less than 6%.

Attempt to treat was initiated in 441 patients. Enrolled patients had angiographic or echocardiographic evidence of patent ductus arteriosus and body weight ≥ 5 Kilograms. Exclusion criteria included:

- Pulmonary vascular resistance above 8 Woods units or a Rp/Rs>0.4.
- Additional cardiac or non-cardiac abnormalities that could reasonably be expected to significantly affect the patient's health adversely in the next two years, i.e.; cancer, Eisenmenger's syndrome, other serious congenital heart disease.
- Pelvic vein or inferior vena cava thrombosis.
- Sepsis (local/generalized) or any type of infection that could not be successfully treated prior to device placement.
- History of repeated pulmonary infection
- Demonstrated intracardiac thrombi on echocardiography.

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- Inability to obtain informed consent.

A total of 441 patients were enrolled in the clinical study. Of the 441 patients, 6 patients were acute procedure failures and did not receive the device, 42 patients were less than 6 kgs. in weight or were younger than 6 months of age. Thus 393 patients were evaluated for effectiveness and safety in the following tables. Note that significantly higher serious and major adverse event rates and 12-month composite failure rates were observed for patients less than 6 months of age. In addition, acute procedure success and pre-discharge efficacy was significantly lower for patients less than 6 kgs in weight. These patients were excluded from the analysis and are contraindicated for device placement.

Demographics: Factors evaluated included age (mean 7.0 +/- 12.2 years; range 0.5-70.7) gender (68% female; 32% male) and weight (mean 21.9 +/- 22.3 kilograms; range 6.1 -164.5) and presence of continuous murmur (94.4%).

Methods: Patients with clinical symptoms of patent ductus arteriosus who were being evaluated for PDA closure underwent physical examination, an electrocardiogram, a chest x-ray, and an echocardiogram to assess the presence of ductus and to assess left pulmonary artery stenosis.

Device placement was attempted in 441 patients. The patients underwent baseline evaluations and pre-closure angiographic measurements. 435 patients received devices. No patient had two devices implanted.

The patients were instructed to avoid strenuous activity for a period of one month. Endocarditis prophylaxis was carried out for 6 months according to the recommendation of the American Heart Association. Additionally, patients were examined and a Transthoracic Echocardiogram (TTE) was conducted at 24 hours, 6 months and 1 year.

Results: A total of 390/393 (99.2%) of patients were successfully implanted with the AMPLATZER Duct Occluder. There were 5/393 (1.3%) patients with serious and major adverse events reported, and 19/393 (4.8%) patients experiencing a minor adverse event. Overall, 23/393 (5.8%) of enrolled patients experienced an adverse event. Complete closure of the ductus was 98.4% at the 6-month interval and 98.6% at the 12-month interval. The composite success rate at 12-months was 96.7%. Please refer to Table 2 for all Principal Safety and Efficacy Results.

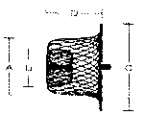
Table 2 - Principal Safety and Efficacy Results

Principal Efficacy	Patient	Percent	95% Lower Confidence Bound
Acute Procedure Success	390/393	99.2%	98.0%
Acute Efficacy	308/393	78.4%	74.7%
Pre Discharge Efficacy	354/392	90.3%	87.5%
6 Month Efficacy	312/317	98.4%	96.7%
12 Month Efficacy	205/208	98.6%	96.3%
Heart Murmur Success	201/201	100.0%	98.5%
Composite Success	205/212	96.7%	93.9%
Extended Efficacy	265/268	98.9%	97.1%
Carry Forward Efficacy	383/390	98.2%	96.7%
Principal Safety (Adverse Events)[1,2,3]			
Serious	1 / 393	0.3%	1.2%
Major	4 / 393	1.0%	
Total Serious and Major	5 / 393	1.3%	2.7%
Minor	19 / 393	4.8%	
Any Adverse Event	23 / 393	5.8%	8.2%

[1] One patient had a Major and Minor Adverse event. 23 patients had 24 adverse events.
[2] Definitions for Adverse events can be found in Table 1.
[3] Patients less than 6 months of age, and less than 6kgs. are not included in this analysis.

Acute Procedure Success - Of the number of patients where the device was attempted, those who successfully received a device.
Acute Efficacy – Of the number of patients where the device was attempted, those who had complete closure of the ductus at procedure.
Pre-Discharge Efficacy - Complete closure of the ductus at pre-discharge in the attempted patients.
6 Month Efficacy - Complete closure of the ductus at the 6 month visit in the attempted patients.
12-month Efficacy - Complete closure of the ductus as measured by echocardiography at the 12 month visit.

Heart Murmur Success – Clinical closure of the PDA as measured by absence of continuous heart murmur at the 12 month visit.
Composite Success - Device attempt with successful placement without a serious or major adverse event, surgical reintervention, embolization, or residual shunt at the 12-month visit.
Extended Efficacy – Complete closure of the ductus at the 12 month or longer visit in the attempted patients.
Carry Forward Efficacy – Complete closure of the ductus at the last visit.



8. PATIENT INFORMATION

Refer to the *Patient's Guide to Transcatheter Closure of a Patent Ductus Arteriosus Using the AMPLATZER® Duct Occluder System.*

9. HOW SUPPLIED

The AMPLATZER Duct Occluder is packaged separately from the AMPLATZER Delivery System. Refer to Table 3 in the following section for the recommended Delivery System sizes.

10. DIRECTIONS FOR USE

10.1 Storage Conditions
Store in a cool dry place.

10.2 Complete Device Description

10.2.1 AMPLATZER Duct Occluder

The AMPLATZER Duct Occluder is a self-expandable device made from a Nitinol wire mesh. A retention skirt on the aortic side provides secure positioning in the ampulla of the ductus. As the occluder is implanted, it expands outward and the wires push against the wall of the ductus. Polyester fabric is sewn into the occluder with polyester thread. The fabric induces thrombosis that closes the communication.

A = Device Diameter at Descending Aorta
B = Device Diameter at Pulmonary Artery
C = Retention Skirt
D = Length

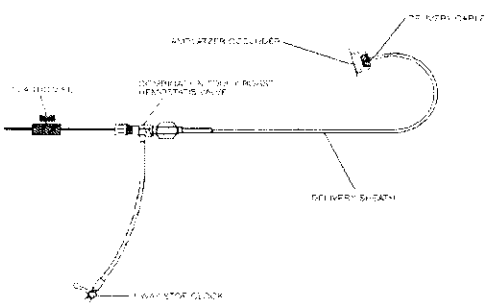
Figure 1 – AMPLATZER Duct Occluder

Table 3 -Device Specifications/Recommended sheath sizes

Order Number	A* Device Diameter at Descending Aorta	B* Device Diameter at Pulmonary Artery	C* Retention Skirt	D* Length	Recommended Sheath Size
9-PDA-003	5 mm	4 mm	9 mm	5 mm	5-6 F
9-PDA-004	6 mm	4 mm	10 mm	7 mm	5-6 F
9-PDA-005	8 mm	6 mm	12 mm	7 mm	6 F
9-PDA-006	10 mm	8 mm	16 mm	8 mm	6-7 F
9-PDA-007	12 mm	10 mm	18 mm	8 mm	6-7 F

*Refer to Figure 1.

10.2.2 AMPLATZER 180° Delivery System



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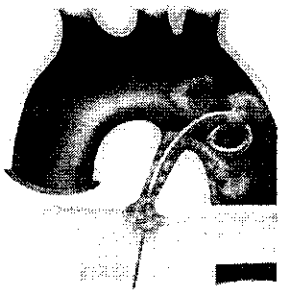


The AMPLATZER 180° Delivery System includes:

- Delivery Sheath with Touhy-Borst Adapter - used to deliver the device. 180° indicates the curve of the delivery sheath.
- Dilator – used to ease penetration of tissue.
- Loading Device – used to introduce the AMPLATZER Duct Occluder into the delivery sheath.
- Plastic Vise – facilitates direction control and serves as the "handle" for disconnecting (unscrewing) the delivery cable from the device.
- Delivery Cable – the device is screwed onto the distal tip of the delivery cable, which allows for placement (and if necessary, retrieval) of the device.

10.3 Directions for Use

- Perform a right heart catheterization in routine fashion. There are two options for angiographic demonstration of the patent

ductus arteriosus. The first is to introduce an exchange guidewire through the ductus and pass a pigtail catheter with side holes in the communication. Perform a biplane angiogram to opacify the PDA (Figure 2). The second option is to pass a pigtail catheter into the proximal descending aorta via the femoral artery and perform the biplane angiogram to opacify the PDA (Figure 3).

Figure 2

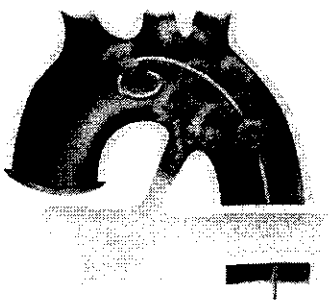


Figure 3

- Angiographic appearance of the patent ductus arteriosus are classified according to the categories that Krichenko et al [1] previously described. Figure 4 lists the 9 types of PDAs.

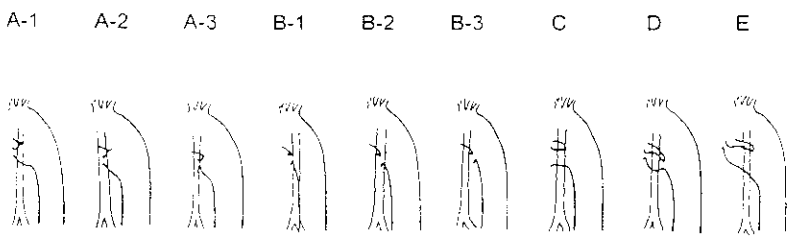


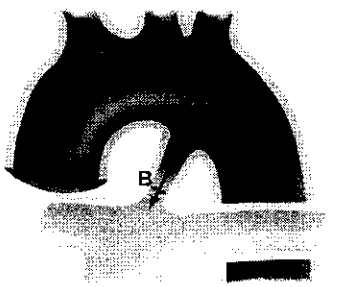
Figure 4

- Select an AMPLATZER Duct Occluder based on the smallest diameter measured in the PDA (refer to Figure 5 "B" measurement). It is recommended to select a device so that the smaller end of the device is at least 2-mm larger than the narrowest portion of the PDA. The device size is a two-digit number. For example in the 8/6 device, the 8 refers to the diameter inside the retention skirt of the device, and the 6 refers to the opposite smaller end of the device. If the "B" measurement in the ductus is 4 mm, select the AMPLATZER Duct Occluder with the smaller end of at least 6 mm. Therefore, the 8/6 device would be selected.

A = Length
B = Smallest Diameter

Figure 5

- Introduce an exchange J-tipped guidewire. Remove the



catheter. Advance the introducing sheath with dilator over the exchange wire into the aorta and position the sheath in the descending aorta while removing the dilator. (Figure 6). Position can be confirmed by a test injection of contrast medium.

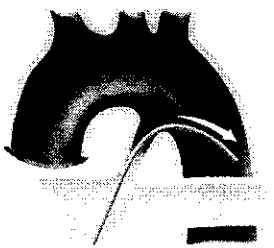


Figure 6

- Pass the delivery cable through the loader and screw the AMPLATZER Duct Occluder clockwise onto the tip of the delivery cable (Figure 7).

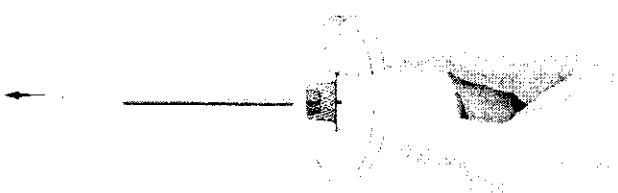


Figure 7

- Immerse the device and the loader in saline solution and pull the AMPLATZER Duct Occluder into the loader.
- Introduce the loader into the delivery sheath and without rotation, advance the device into the descending aorta (Figure 8).

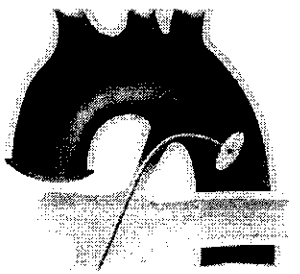


Figure 8

- Deploy the retention skirt only and pull firmly against the orifice of the patent ductus arteriosus. This can be observed by fluoroscopy, or it can be clearly felt as a tugging sensation in synchrony with the aortic pulsation. The position of the device is confirmed with repeated angiograms in the aorta using the pigtail catheter. The device can be adjusted until the retention skirt is well seated in the ampulla. Retract the delivery sheath and deploy the cylindrical portion of the device securely in the patent ductus arteriosus while applying slight tension (Figure 9).

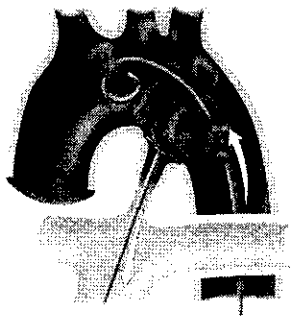


Figure 9

- Perform an aortogram to verify correct position of the device. Perform and record on cine a power injection through the catheter using 1 cc per kilogram of contrast at 12 ml per second at 400 psi. To have optimal visualization of the anatomy, angulate the AP camera at 35 degrees LAO and 35 degrees cranial, and the lateral camera straight. These views will allow you to delineate the length of the device protruding into the pulmonary artery lumen.

  WARNING: Remove the device if >3mm extends into the pulmonary artery, or if more than half of the left pulmonary artery lumen is occupied by the device. In questionable cases, perform transthoracic echocardiography before release of the device with Doppler measurement of left pulmonary artery flow velocity. The device should be removed if left pulmonary artery flow is >3.0 M/s (or >75% greater than the LPA velocity before cardiac catheterization).

- If position is not satisfactory, recapture the device into the sheath by pulling back on the delivery cable.

  NOTE: Do not release the device from the delivery cable if the device does not conform to its original configuration or if device position is unstable. Recapture the device and redeploy. If still unsatisfactory, recapture the device and replace with a new device.

- Screw the plastic vise on the delivery cable and detach the device by rotating the cable counter clockwise as indicated by the arrow on the vise. (Figure 10). Repeat aortogram.

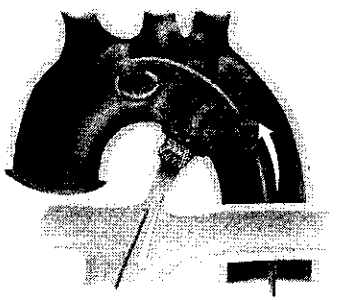


Figure 10

11. POST PROCEDURE PATIENT REGISTRATION/ INFORMATION

- **Peel Off Labels** – Peel off labels are provided for the patient's chart. These labels specify the size, lot and serial number of the device.

- **Registration Card** – An Implant Registration Form is located in each device box. Complete the patient information section and send the form to AGA Medical Corporation.

[1] Krichenko A, Benson LN, Burrows P, et al: Angiographic classification of the isolated, persistently patent ductus arteriosus and implications for percutaneous catheter occlusion. Am J of Card 1989;63:877-80.