ASD Device Closure Erosions!

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Atrial Septal defects

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Ideal Device For Catheter Closure

1. User friendly "Simple mechanics"
2. Retrievable or repositionable.
3. Effective/high complete closure rate.
4. Small delivery system.
5. Low profile within the heart.
6. Durability until full endothelialization.
7. Non-thrombogenic.
8. Preservation of flow & function despite embol.
9. Lack of ongoing morbidity.
10. Economical.

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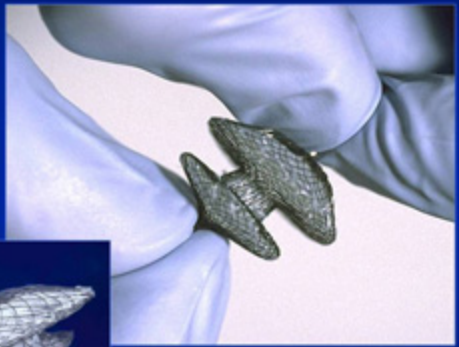
Approved Devices in US

0.004-0.0075” Nitinol
Two Flat Disks
4mm Waist
Dacron Mesh
4-40 mm Sizes
Delivery Cable
7-12F



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The Gore Helex Device

- Low profile, double-disk.
- Expanded polytetrafluoroethylene membrane bonded to a single nitinol wire frame

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Evidence Based Medicine

"a set of principles and methods intended to ensure that to the greatest extent possible, medical decisions, guidelines, and other types of policies are based on and consistent with good evidence of effectiveness and benefit"

Eddy, D. (2005) Evidence-Based Medicine: A Unified Approach. Health Affairs: Vol 24: 9-17

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ASD Device Closure

Classification of Recommendations

Intervention is useful and effective

Weight of evidence/opinion is in favor of usefulness/efficacy

Usefulness/efficacy is less well established by evidence/opinion

Intervention is not useful/effective and may be harmful

Level of Evidence

A Data from many large, RCTs

B Data from fewer, smaller RCTS, careful analyses of nonrandomized studies, observational registries

C Expert consensus

Figure 5. Classes of recommendations and level of evidence used in ACC/AHA clinical practice guidelines. RCT indicates randomized controlled trial.

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Un-operated ASDs: To Close or Not to Close?

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Closure (catheter or Surgical) in ASD Patients
Class I

1. RAE & RVVO with or without symptoms: Level B
2. Sinus venosus, coronary sinus, primum ASDs: surgery: Level B

Warnes CA, Williams RG, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease. Circ 2008;118:2395-2451

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Closure (catheter or Surgical) in ASD Patients
Class II a

1. Surgery of ASD during concomitant surgery for tricuspid valve or device closure is not feasible: Level C

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Closure (catheter or Surgical) in ASD Patients Class II a

1. Surgery/device of ASD in the presence of:
a. Paradoxical embolism: Level C
b. Orthodeoxia-platypnea: Level B

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Closure (catheter or Surgical) in ASD Patients Class II b

1. Concomitant Maze may be considered for Afib: Level C
2. Net L-R shunt, PAP <2/3 systemic, PVR<2/3 systemic: Level C

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Closure (catheter or Surgical) in ASD Patients Class III

Irreversible PAH and no evidence of L-R shunt should not have their ASD closed: Level B

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Possible Advantages of Transcatheter vs Surgical Closure

- Minimizes pain and discomfort
- Avoids incisional scar
- No exposure to cardiopulmonary bypass.
- Unlikely to require blood or blood product transfusion
- Reduction in hospital stay
- Rapid return to normal activities
- Results in cost savings

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Possible Complications

- Embolization
- Arrhythmias/CHB
- Thrombus formation
- Air Embolism
- TIA/Stroke
- Erosions/PE/Tamponade/Death
- SBE
- Frame Fracture
- Headaches/Migraines

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Vol. 39, No. 11, 2002

Comparison Between Transcatheter and Surgical Closure of Secundum Atrial Septal Defect in Children and Adults

Results of a Multicenter Nonrandomized Trial

Zhong-Dong Du, MD,* Ziyad M. Hijazi, MD, MPH, FACC,* Charles S. Kleinman, MD, FACC,† Norman H. Silverman, MD, FACC,‡ Kinley Lamtz, PhD,¶ for the Amplatzer Investigators

Chicago, Illinois; Orlando, Florida; San Francisco, California; and Minneapolis, Minnesota

OBJECTIVES This study sought to compare the safety, efficacy and clinical utility of the Amplatzer septal occluder (ASO) for closure of secundum atrial septal defect (ASD) with surgical closure.

BACKGROUND The clinical utility of a device such as the ASO can only be judged against the results of contemporaneous surgery.

METHODS A multicenter, nonrandomized concurrent study was performed in 29 pediatric cardiology centers from March 1998 to March 2000. The patients were assigned to either the device or surgical closure group according to the patients' option. Baseline physical exams and echocardiography were performed preprocedure and at follow-up (6 and 12 months for device group, 12 months for surgical group).

RESULTS A total of 442 patients were in the group undergoing device closure, whereas 154 patients were in the surgical group. The median age was 9.8 years for the device group and 4.1 years for the surgical group ($p < 0.001$). In the device group, 395 (89.4%) patients had a single ASD; in the surgical group, 124 (80.5%) ($p = 0.008$) had a single ASD. The size of the primary ASD was 13.3 ± 5.4 mm for the device group and 14.2 ± 6.3 mm for the surgery group ($p = 0.099$). The procedural attempt success rate was 95.7% for the device group and 100% for the surgical group ($p = 0.006$). The early, primary and secondary efficacy success rates were 94.8%, 98.5% and 91.6%, respectively, for the device group, and 96.1%, 100% and [illegible] for the surgical group. [illegible] for the device group and 3.4 ± 1.2 days for the surgical group ($p < 0.001$).

CONCLUSIONS The early, primary and secondary efficacy rates of transcatheter closure of ASD were not statistically different; however, the complication rate was lower and the length of hospital stay was shorter for device closure than for surgical repair. Appropriate patient selection is an important factor for successful device closure. Transcatheter closure of secundum ASD using the ASO is a safe and effective alternative to surgical repair. (J Am Coll Cardiol 2002;39:1836–44) © 2002 by the American College of Cardiology Foundation

Complication rate was 7.2% for the device Group and 24% for the surgical group (P<0.001)

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Safety & Efficacy of ASO

Technical Success – Successful deployment of the device, or the successful completion of the surgical procedure

Table 5. Principal Effectiveness and Safety Results – Pivotal Study

	AMPLATZER Patients*	Surgical Control Patients	90% Confidence Interval
Technical success	423/442 (95.7%)	154/154 (100%)	(-0.084, -0.010)
Procedure success	413/423 (97.6%)	154/154 (100%)	(-0.059, +0.008)
Early (≤ 30 days) composite success	401/442 (90.7%)	148/154 (96.1%)	(-0.096, +0.019)
12-month composite success	331/362 (91.4%)	146/154 (94.8%)	(-0.153, -0.033)
24-hour closure success	404/418 (96.7%)	154/154 (100%)	(-0.073, -0.001)
6-month closure success	376/387 (97.2%)	154/154 (100%)	(-0.068, +0.003)
12-month closure	326/331 (98.5%)	149/149 (100%)	(-0.052, 0.017) [Presumably, second value should be +]
Principal Safety Measures			
Major adverse events 12 months	7/442 (1.6%)	8/154 (5.2%)	(-0.090, -0.002)
Minor adverse events 12 months	27/442 (6.1%)	29/154 (18.8%)	(-0.200, -0.070)
12-month composite success (K-M)	0.934	0.938	[-0.044, +0.036]
Survival at 30 days (K-M)	0.939	0.956	[-0.052, +0.036]
Survival at 180 days (K-M)	0.936	0.947	[-0.048, +0.026]

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Safety & Efficacy of ASO-<20 yrs age

Table 6. Principal Effectiveness and Safety Results – Patient Age Less Than 20 Years

	AMPLATZER Patients	Surgical Control Patients	90% Confidence Interval
Technical success	315/328 (96.0%)	149/149 (100%)	(-0.086, -0.005)
Procedure success	306/315 (97.1%)	149/149 (100%)	(0.074, +0.005)
Early (≤ 30 days) composite success	295/328 (89.9%%)	143/149 (95.9%)	(-0.124, -0.007)
12-month composite success	256/281 (91.1%)	142/149 (95.3%)	(-0.108, +0.013)
24-hour closure success	301/310 (97.1%)	149/149 (100%)	(-0.075, +0.005)
6-month closure success	270/278 (97.1%)	149/149 (100%)	(-0.077, +0.006)
12-month closure	246/251 (98.0%)	149/149 (100%)	(-0.068, +0.014)
Principal Safety Measures			
Major adverse events 12 months	6/328 (1.8%)	7/149 (4.7%)	(-0.086, +0.008)
Minor adverse events 12 months	16/328 (4.9%)	29/149 (19.5%)	(-0.221, -0.085)
12-month composite success (K-M)	0.930	0.944	[-0.055, +0.027]
Survival at 30 days (K-M)	0.933	0.954	[-0.059, +0.017]
Survival at 180 days (K-M)	0.930	0.954	[-0.062, +0.014]

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Safety & Efficacy of Gore Helex

Table 4 Number of Subjects by Category of Major Adverse Events, Successful Device Delivery, or Surgical Closure Events Reported Through 12-Month Follow-up

	Device Non-Training	Surgical Controls	p Value*
Subjects evaluable for safety	119	128	
Subjects with 1 or more major adverse events	7 (5.9%)	14 (10.9%)	0.176
Cardiac	2 (1.7%)	10 (7.8%)	0.036
Bleeding (treatment required)	-†	1 (0.8%)	1.000
Embolization (post-procedure)	2 (1.7%)	Na‡	
Pulmonary edema	-	1 (0.8%)	1.000
Post-pericardiotomy syndrome	Na	8 (6.3%)	
Integument	1 (0.8%)	-	0.482
Allergic reaction	1 (0.8%)	-	0.482
Neurologic	2 (1.7%)	-	0.231
Migraine (new)	2 (1.7%)	-	0.231
Paresthesia	1 (0.8%)	-	0.482
Pulmonary (respiratory)	-	1 (0.8%)	1.000
Stridor	-	1 (0.8%)	1.000
Vascular	1 (0.8%)	1 (0.8%)	1.000
Hemorrhage (treatment or intervention required)	1 (0.8%)	1 (0.8%)	1.000
Wound	-	2 (1.6%)	0.499
Hernia	-	1 (0.8%)	1.000
Scarring or scar related	-	1 (0.8%)	1.000
Device (HELEX septal occluder)	3 (2.5%)	Na	
Allergic reaction	1 (0.8%)	Na	
Device size inappropriate	2 (1.7%)	Na	
Other	-	1 (0.8%)	1.000
Anemia	-	1 (0.8%)	1.000

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Safety & Efficacy of Gore Helex

Table 6 Clinical Success End Point

	Device Non-Training	Surgical Controls	Difference (90% CI)*	p Value†
Evaluable subjects with successful delivery/surgical closure	117	124		
Clinical success end point				
Subjects evaluated	109	86		
Clinical success	100 (91.7%)	72 (83.7%)	−8.0% (−15.9%, −0.2%)	<0.001
Clinical failure	9 (8.3%)	14 (16.3%)		
Major device/procedure adverse event‡	7 (6.4%)	14 (16.3%)		
Significant leak on final core lab evaluation	2 (1.8%)	0 (0.0%)		
Subjects not evaluated	8	38		
Lost to follow-up prior to evaluation	2	18		
Final defect evaluation missing	6	20		

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Outcome Comparison with OHS

STS Data

2000-2009, N=365

Mortality: Zero

Complications: 20% (arrhythmias 7.7%, pleural effusions 1.6%, pneumonia 3.3%,
mechanical ventilation >7 days 0.6%; bleeding requiring reoperation i 0.6%.

Mascio CE et al. Outcomes in adult congenital heart surgery: Analysis of the Society of Thoracic Surgeons Database. J Thorac Cardiovasc Surg 2011;142:1090-7

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Outcome Comparison with OHS

Non Congenital adult cardiac surgeons
Inn-hospital mortality of 2.1% for isolated ASD
5% if combined with another procedure

Mascio CE et al. Outcomes in adult congenital heart surgery: Analysis of the Society of Thoracic Surgeons Database. J Thorac Cardiovasc Surg 2011;142:1090-7

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Outcome Comparison with OHS

13 original non-randomized studies (3,082 patients) of surgery/device.

One death was reported in the surgical group (0.08%.

Complications 31% in surgical patients vs 6.6% for device.

OR for surgery *vs.* catheter-based closure for total complications was 5.4 (95% CI 2.96-9.84; p<0.0001), significantly in favor device.

Major complication 6.8% surgery vs 1.9% device.

Butera G et al. Percutaneous versus surgical closure of secundum atrial septal defects: a systematic review and meta-analysis of currently available clinical evidence. EuroInterven 2011;7:377-85

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Long-term Outcome

1. Dr. King's first patients from 1975
2. Sadiq et al: 1999-2009, N=205 patients. No mortality, no thromboembolic events, no erosions. Afib in 1.5%.
3. Post Surveillance Study: 876 patients, 2 erosions!

Sadiq M, Kazmi T, Rehman AU, et al. Device closure of atrial septal defect: medium-term outcome with special reference to complications. Cardiol in Young 2012;22(1):71-78

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Long-term Outcome

4. Krumsdorf et al. 1000 patients. Clot formation 0% for ASO; 0.8% for Helex. No thromboembolic events.

krumsdorf et al. Incidence and clinical course of thrombus formation on atrial septal defect and patient foramen ovale closure devices in 1,000 consecutive patients. JACC 2004 Jan 21;43(2):302-9

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Long-term Outcome

Kutty et al: Long-term outcome of SC vs PC of ASD. They concluded both methods are excellent with no significant differences were found between device and surgical closure with regard to survival, functional capacity, atrial arrhythmias, or embolic neurologic events.

Kutty S et al. Long-Term (5- to 20-Year) Outcomes After Transcatheter or Surgical Treatment of Hemodynamically Significant Isolated Secundum Atrial Septal Defect. Am J Cardiol. 2012 Feb 13. [Epub ahead of print].

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Long-term Outcome

Device Fracture
Zero for ASO
0-5.5% for Helex: usually larger devices (30 or 35mm); no significant clinical sequlae.

Smith BG, Wilson N, Richens T, Knight WB. Midterm follow-up of percutaneous closure of secundum atrial septal defect with Helex septal occlude. J Interven Cardiol 2008;21:363-68

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Mechanism of Erosion

Multi-factorial:

- Rim deficiency
- Patient characteristics
- Defect shape
- Device size

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FDA MAUDE

11 & 12/2011 had 27 reports of significant adverse events. All occurred in 2011 except 4 which occurred in 1998, 2006, 2007 and 2008 all of which were adjudicated as erosions. In all there were 6 erosions but in two of these the device was left in place with limited management. Only one erosion from 2006 was unexplained based on the data presented. The vast majority of the remaining MAUDE reports noted device embolizations primarily related to operator error or efforts to undersize t device to avoid erosion. This limited sample of MAUDE r suggest:

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FDA MAUDE

1. That erosions are extremely rare when operator error and frank device oversizing are excluded. (Only one erosion from 2006 was unexplained).
2. That operator technical errors and inexperience are frequently the cause of most ASO adverse events.
3. There are more device embolizations and retrieval surgery reported which occur primarily to avoid potential liability by under-sizing the device.

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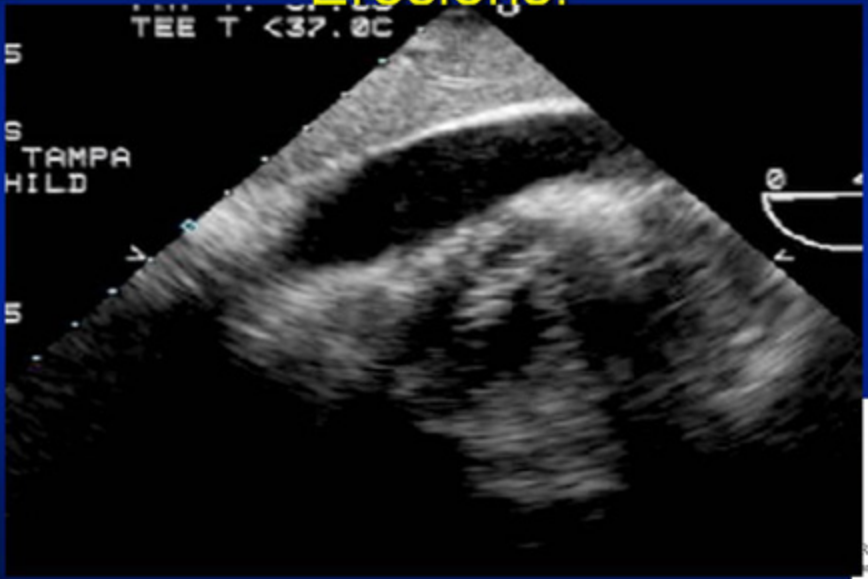

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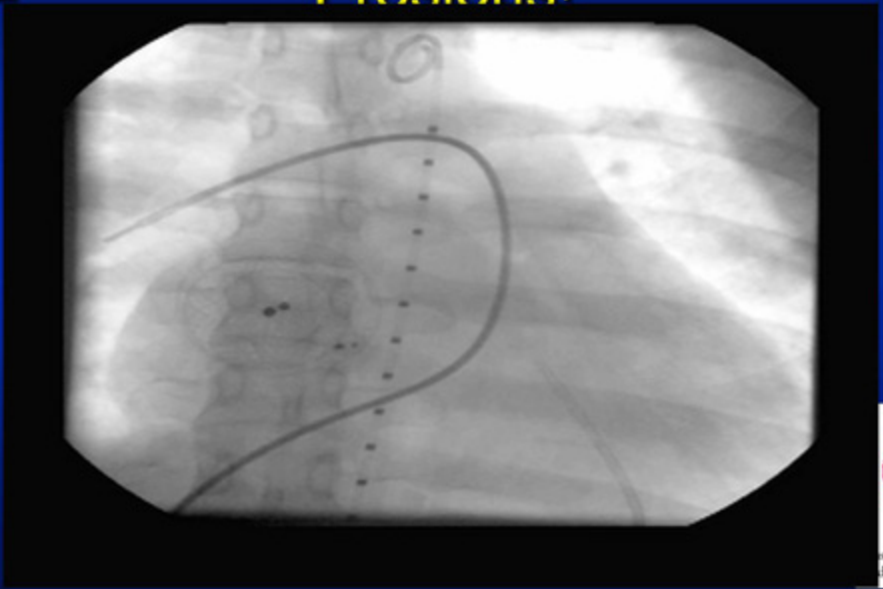

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History of Erosions

First erosion case reported in US 2002

2004: IFU updated for device sizing

2009: IFU updated about sizing with additional warning.

2011: SJM/FDA agreed to change IFU to include contra indications in patients with deficient ant/sup rim.

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Numbers of Erosions as of 3/2012

Source	Potential Erosions (n=202)	Confirmed -- Not Erosion Events (n=105)	Confirmed Erosions (n=97)
Literature	44	28	16
Field Event Report-MAUDE	122	46	76
PAS Investigator Query	10	7	3
PAS	26	24	2

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FDA and SJM agreed upon symptoms and/or outcomes that potentially indicate an erosion:

- Perforation
- Pericardial effusion with or without required drainage
- Pericardial tamponade
- Hemopericardium
- Tissue erosion
- Aortic to Atrial Fistula
- Death due to erosion
- Death due to erosion or tamponade
- Penetration
- Puncture
- Laceration
- Fissure

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ROOT CAUSE ANALYSIS-Data Analyzed

Incidence of erosion events was investigated across the following factors:

- age (pediatric ≤18 years, adult >18 years),
- rim sufficiency (specifically anterior-superior rim),
- erosion event description,
- explant status,
- gender,
- geography,
- outcome,
- oversized devices and
- time from implant to erosion event.

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Confirmed Erosion Events By Year

Year	US	OUS	Total
1998	0	1	1
1999	0	0	0
2000	0	1	1
2001	0	2	2
2002	6	4	10
2003	6	3	9
2004	1	6	7
2005	3	3	6
2006	5	5	10
2007	5	6	11
2008	4	4	8
2009	6	5	11
2010	6	6	12
2011	2	3	5
2012	2	0	2
unknown	2	0	2
total	48	49	97

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EROSION ANALYSIS

- Hemodynamic presentation(n=97)
  - Aortic atrial fistula – 16 (16.5%)
  - Tamponade with a hemo PE -68 (70.1%)
  - PE or Hemo PE or tamponade – 13(13.4%)
- Site of erosion
  - LA – 47(28 involving the Ao)
  - RA – 26(22 involving the Ao)
  - RA & LA – 9
  - Unknown - 15

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EROSION MORTALITY RATE

	Number of Deaths from Erosion	Mortality Rate
SJM (WW)	8	0.004-0.015%
SJM (US)	6	0.008-0.016%

- No deaths occurred in patients younger than 15 ye
- All reported deaths occurred within 16 months of i plant.
- Each event confirmed presence of device oversizi deficient anterior superior rim, or both

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EROSION ANALYSIS

- **Management**
  - –Explanted 74
  - –Not explanted 21
    - Repair of the erosion site
    - Pericardiocentesis alone
  - –Unknown – 2

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ROOT CAUSE ANALYSIS SUMMARY

97 Worldwide erosion cases have been identified in association with the on-label use of the AMPLATZER ASO device from December 1998 to March 2012:

- **48 US/49 OUS**
- **40% Pediatric**
- **70% Female**
- **75% involved device sizes > 18mm**
- **87.6% occurred within the first year of implants**
- **57% of pediatric erosion events occurred <72 hours**
- **35% of adult erosions occurred <72 hours**

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ROOT CAUSE ANALYSIS SUMMARY

The most frequently observed relationship to erosion was oversizing and deficient anterior superior rims

- 40% of all erosion events were oversized
  - 31% pediatric
  - 46% adult
  - Declining from earlier reported 50%
- 90% of all erosion cases had anterior-superior rim deficiency
  - 100% pediatric
  - 84% adult
- Every erosion case except 2 had either a deficient ante[illegible] superior rim or were oversized

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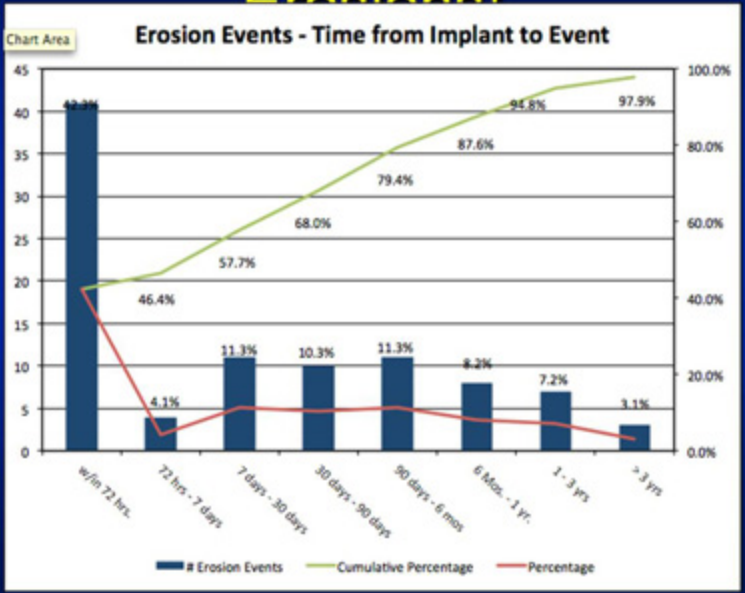

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EROSION INCIDENCE RATE

	# of Erosions	Sales	With Cards	Incidene
SJM (WW)	97	223,965	55,000	0.04-0.17%
SJM (US)	48	72,566	38,000	0.07- 0.11%
	Number of Erosions	Number of Implants	Incidence	
Pivotal Trial	0	452	0%	
PAS	2	970	0.23%	

Note: PAS erosion events are included in the 48 US erosion events

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Long –Term Outcome

- Generally safe!
- Would not discharge patient completely from clinic!
- RV remodeling!
- Watch out for ?arrhythmias
- Watch out for erosions!!!

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Conclusions

Most secundum ASDs are amenable for device closure.

The two available devices and many other devices OUS are safe and effective.

There are certain indications to close ASDs.

Long-term outcome is good, however, there are rare long-term complications.

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Acknowledgment

William E. Hellenbrand, MD

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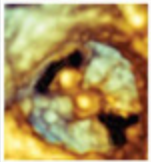

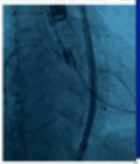

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SAVE THE DATE

JANUARY 19–22

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MIAMI 2013

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