Structural Heart Disease Interventions

"New Opportunities to the Intervetional Cardiologist with Structural Heart Disease"

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DISCLOSURES

Ron Waksman, MD

- **Consulting Fees**
  - Abbott Vascular, Biotronik, Medtronic CardioVascular, Inc, Boston Scientific Corporation

- **Grants/Contracted Research**
  - Abbott Vascular, Biotronik, Boston Scientific Corporation, The Medicines Company, GlaxoSmithKline, Schering-Plough, sanofi-aventis U.S. LLC

CRT2011

FEBRUARY 27-MARCH 1, 2011

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CORONARY

ENDOVASCULAR INTENSIVE

TECHNOLOGY

NURSE & TECH

SCIENCE

Interventional Cardiologists never had so Many tools and opportunities to treat Structural Heart Disease

But !!!

You need to know the anatomy

The Physiology

The Tools and strategy

The Data

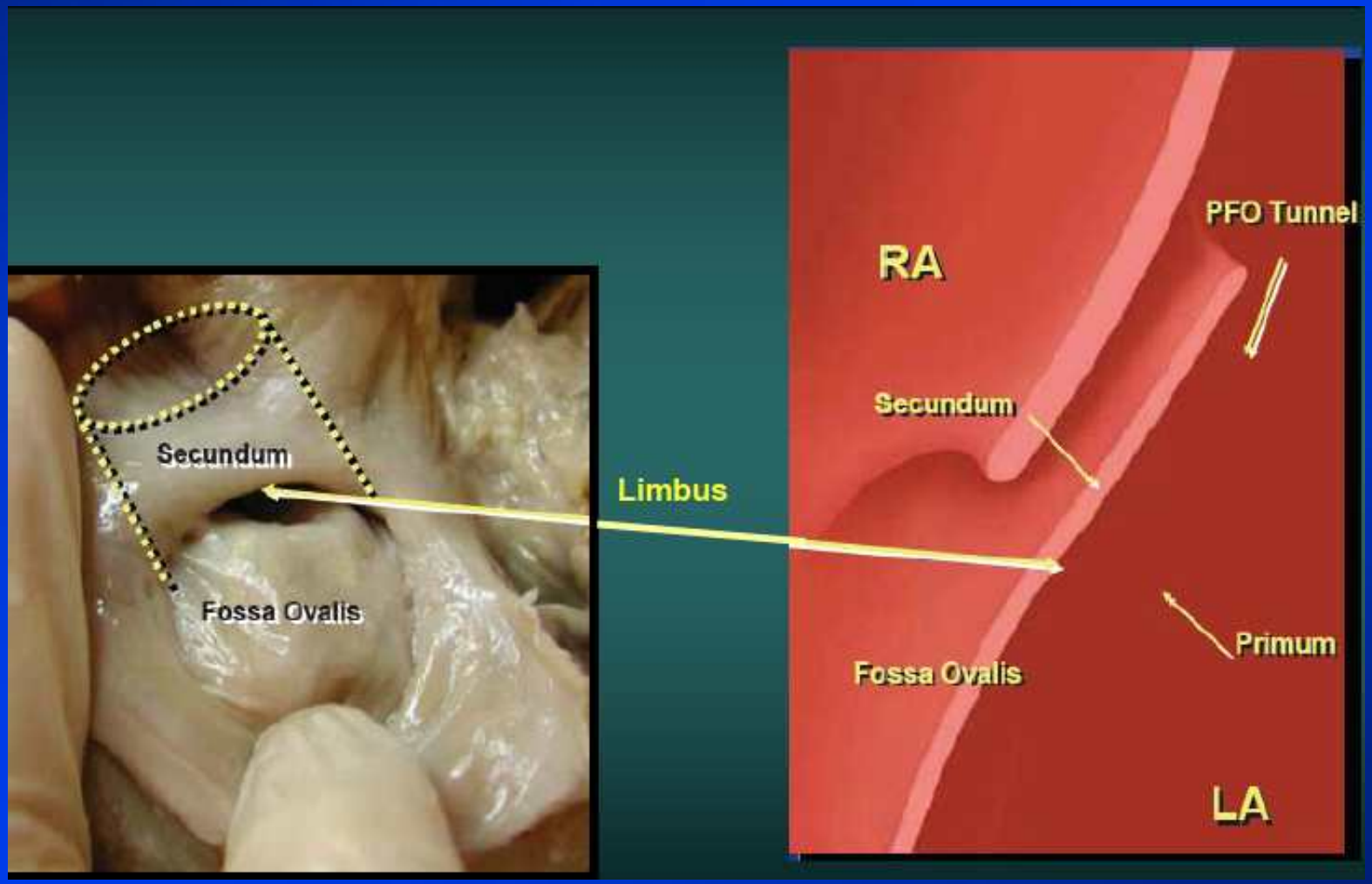
Echo

Team approach

Structural Heart Interventions

- ASD, PFO closure
- VSD closure
- Patent ductus closure
- Left atrial appendage closure
- Paravalvular leak closure
- Stenting of coarctation
- LV apical aneurysm treatment
- Valves
  - Mitral valve repair
  - Aortic valve implantation

The Atrial Septum



Atrial Septal Defect (ASD) Closure

- Prevalence
  - Common and may present at any age
  - Female predominance (65-75%) of secundum defects
  - Magnitude of shunt depends on
    - Size of defect
    - Relative diastolic compliance of LV and RV (all 4 chambers in common communication during diastole)
  - Normally, RV compliance < LV compliance so flow is L to R
    - May be transient R to L flow at onset systole
    - Older patients more symptomatic due to decrease in LV compliance and atrial arrhythmias

CURRENT ASD OCCLUSION DEVICES IN U.S.

ASD Closure Devices

- **Amplatzer ASD Occluder**

(AGA Medical Corporation)
Approval Status: First FDA approved for ASD Closure 12-2001

NEW !
Sept. 2006

Amplatzer Cribriform ASD Occluder

(AGA Medical Corporation)
Approval Status: IDE FDA Approved 8-2006

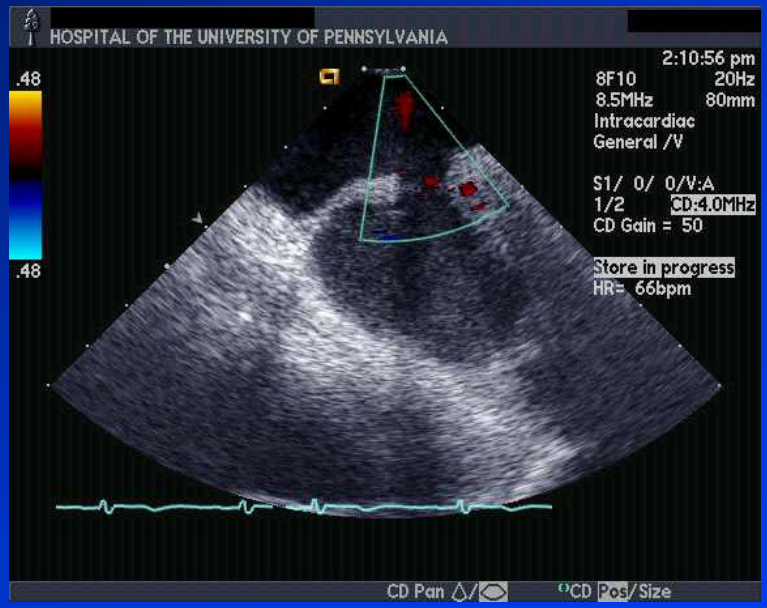
- **CardioSEAL/StarFlex septal occluder**

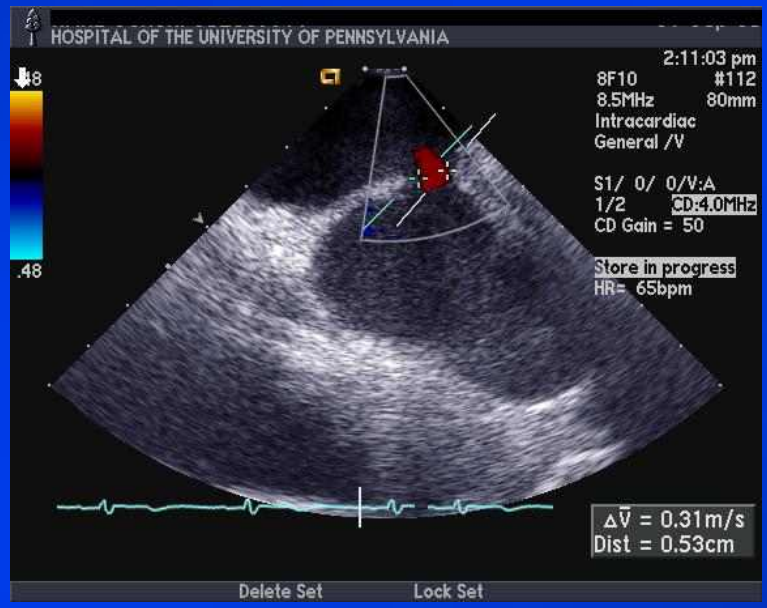
(Nitinol Medical Technologies)
IDE approval high risk muscular VSDs)

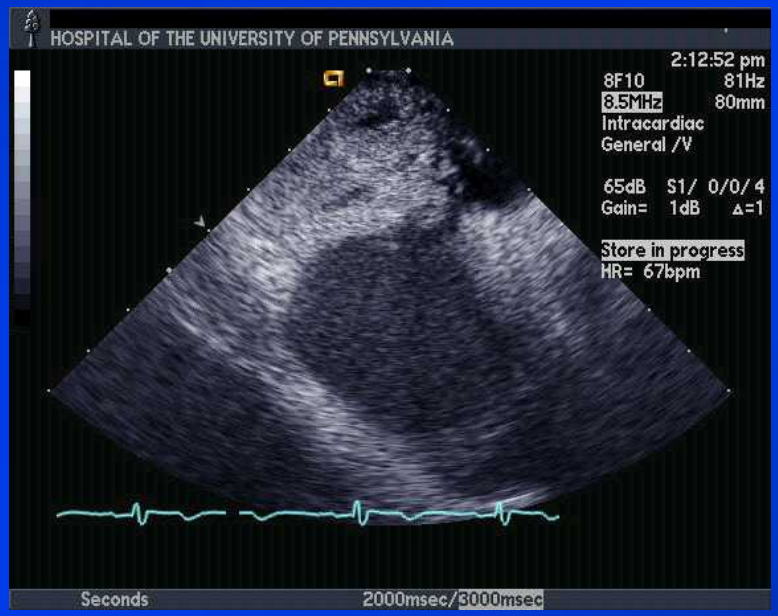
- **Helex septal occluder**

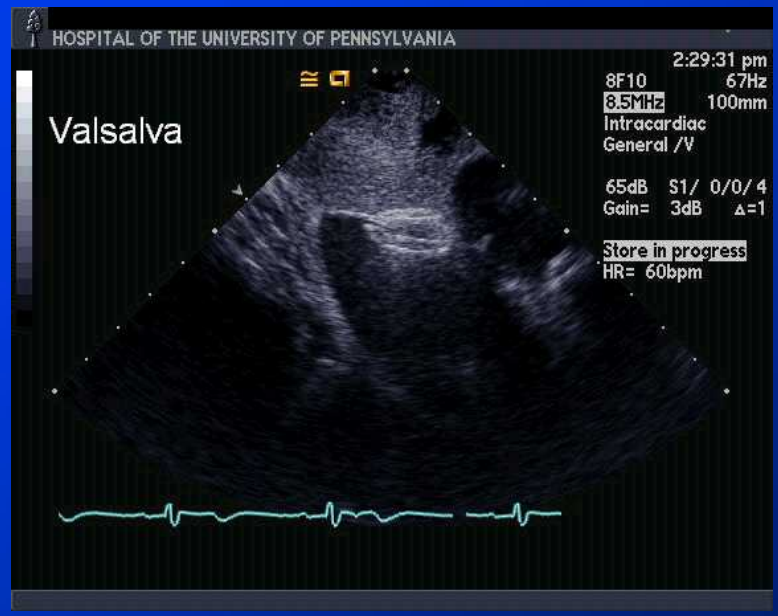
(WL Gore & Associates)
Approval Status: IDE FDA Approved 10-2006
*ASDs < 20 mm diameter

Paradoxical Embolism via ASD in a 57 yo Man

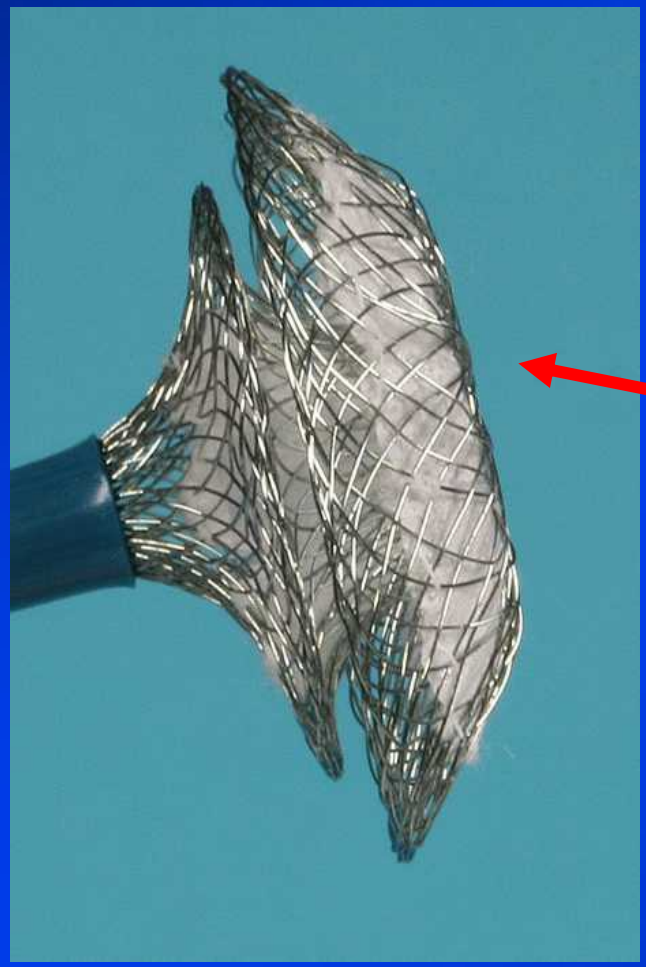






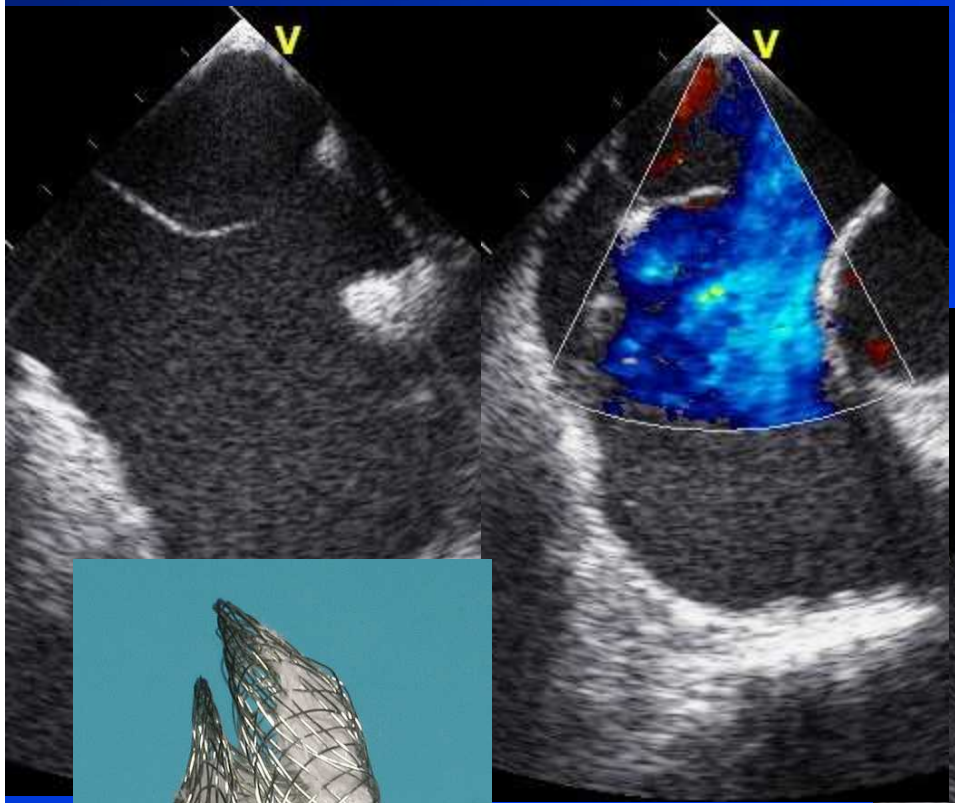


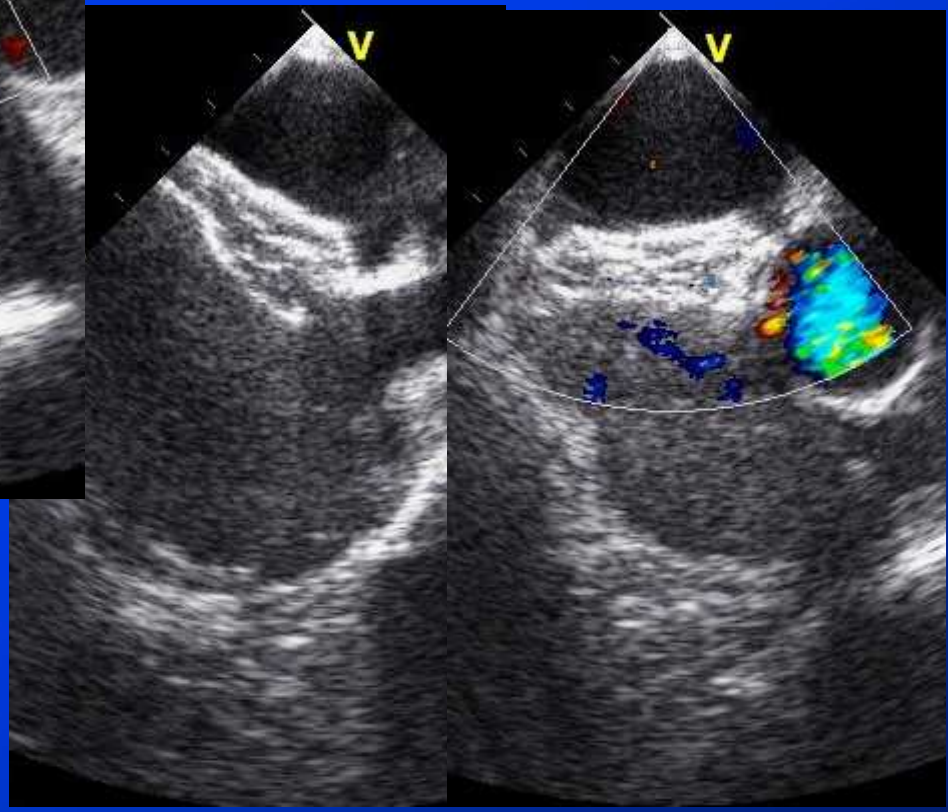
Occlutech ASD Occluder



- Similar to the Amplatzer ASD Occluder
- No left atrial hub

Occlutech ASD





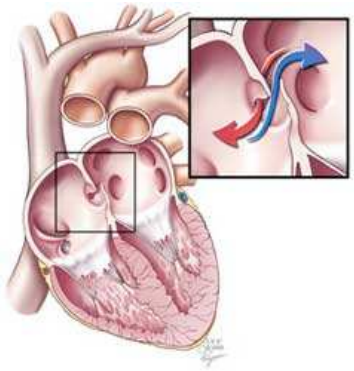
CE Mark

PFO: Overview

What is It?

Patent Foramen Ovale defined as

Incomplete closure of atrial septum resulting in valve-like opening in septal wall, permitting right-to-left shunts



Link b/w PFO & Events?

Most patients with PFO remain asymptomatic

Most important clinical manifestation of PFO is ischemic stroke due to paradoxical embolism

There is no causal link, only associative relation between:

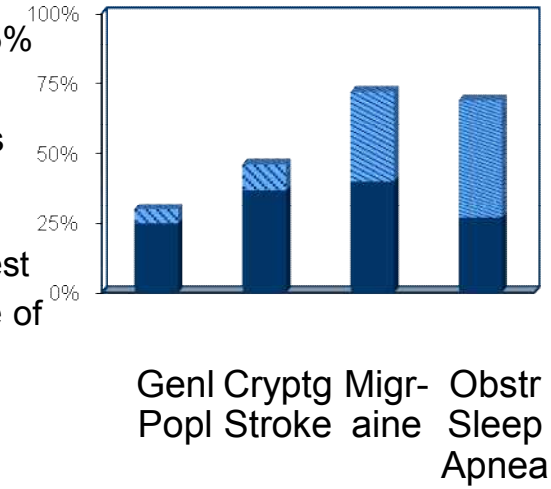
1. PFO & stroke
2. PFO & migraine
3. PFO & sleep apnea

Prevalence?

PFO is present in ~25% population, noting prevalence decreases with age

Varying reports suggest increasing prevalence of PFO in select pathologies ⇨

Prevalence of PFO



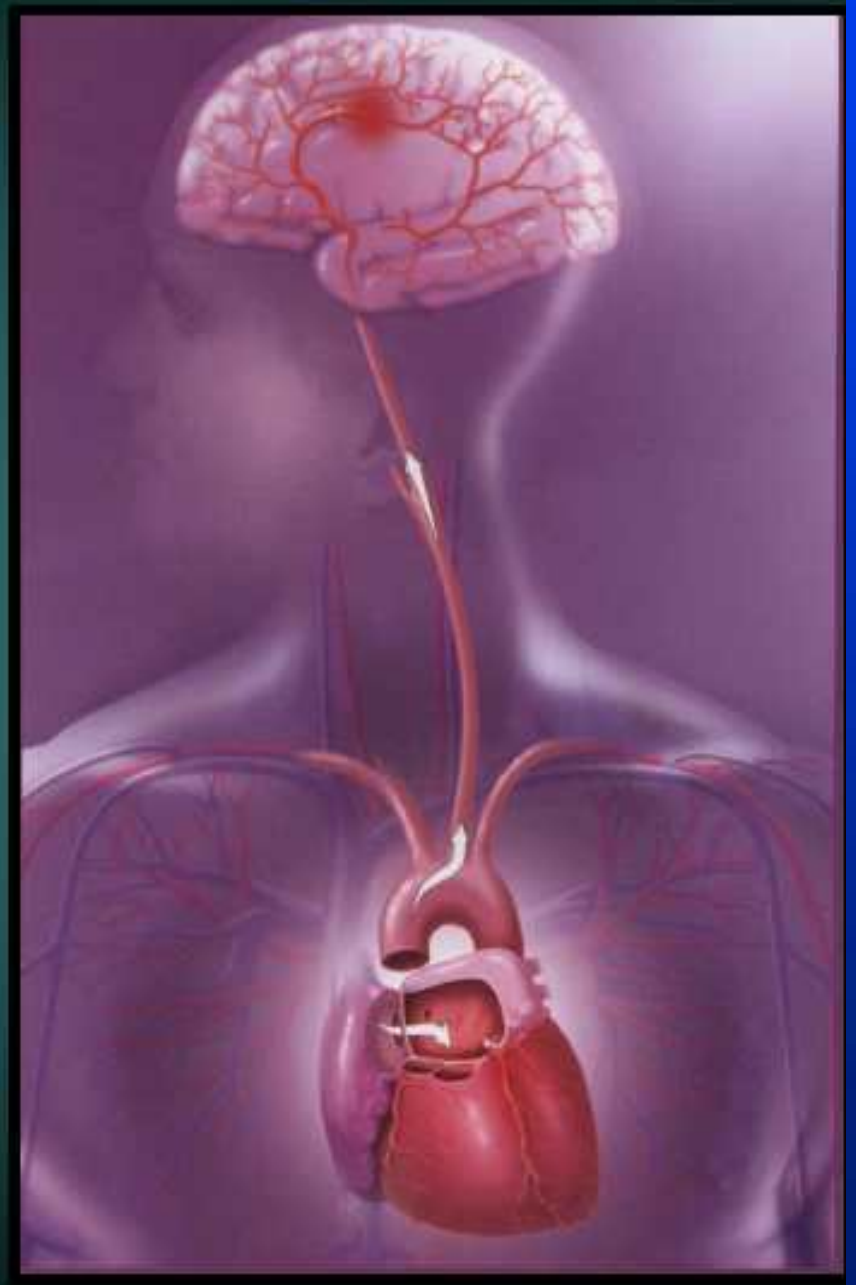
State of Evidence?

PFO & Stroke	• No level I evidence; RCTs ongoing • Case & obsvl studies demonstrate strong but non-signf benefit for closure vs. mtx
PFO & Migraine	• No level I evidence; 4 RCTs started: 1 failed, 2 terminated, 1 ongoing • Observ'l studies suggest possible benefit (~75% resolved/improved) but confounded
PFO & Sleep Apnea	• Limited to single case series (n~1) • Pts demonstrated complete resolution of symptx & discontinued cPAP usage

Sources: Up-To Date, Schwedt 2008, Silver 2007, Agnoletti 2005

Patent Foramen Ovale Association with Disease States

- CVA and TIA
- Peripheral embolization
- Decompression illness
- Migraine with/out aura
- Myocardial infarction
- Refractory hypoxemia
- Platypnea-orthodeoxia syndrome
- Major orthopedic surgery
- Obstructive sleep apnea



Transcatheter PFO Closure Devices

Helex (WL Gore)
Low profile circular disks
Components
Metal :Single nitinol strand
Fabric: ePTFE membrane

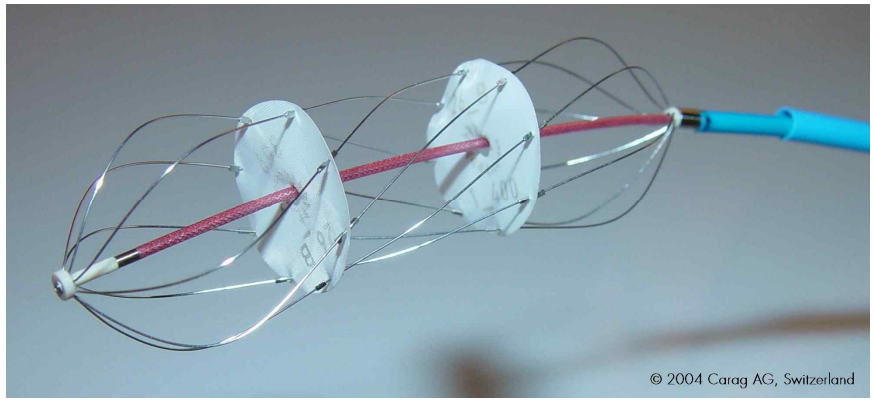
CardioSEAL (NMTI)
Double umbrella design
Components
Metal frame : MP35N
Fabric: Dacron

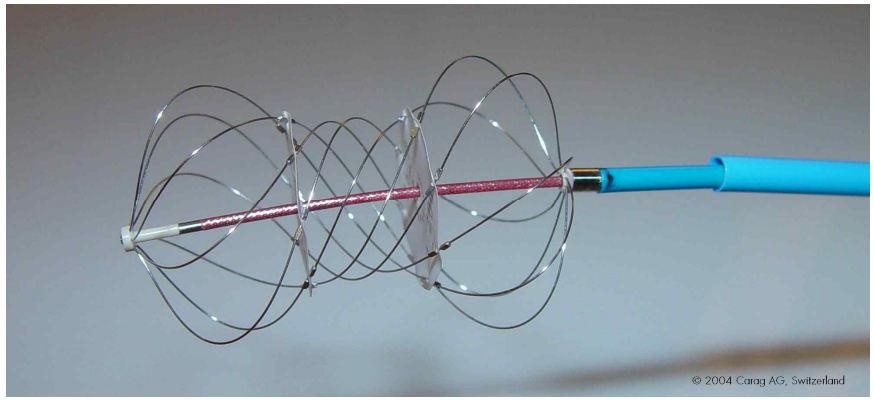
Amplatzer (AGA Medical)
Double circular disks
Components
Metal: Nitinol wire mesh
Fabric: Polyester

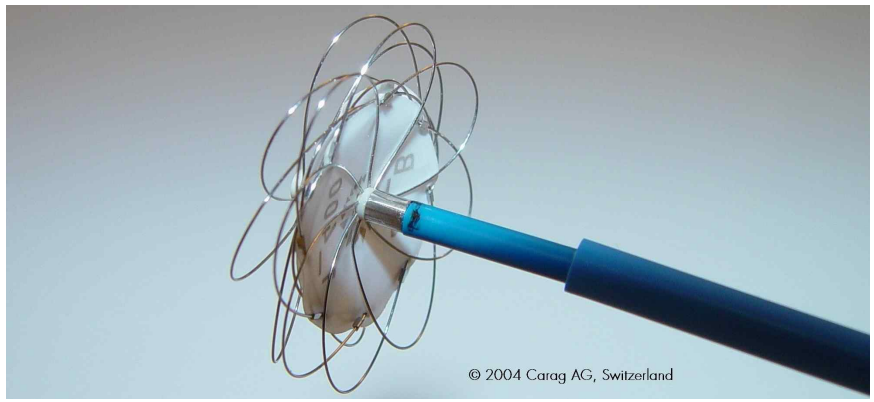
Devices available in U.S

Solysafe®

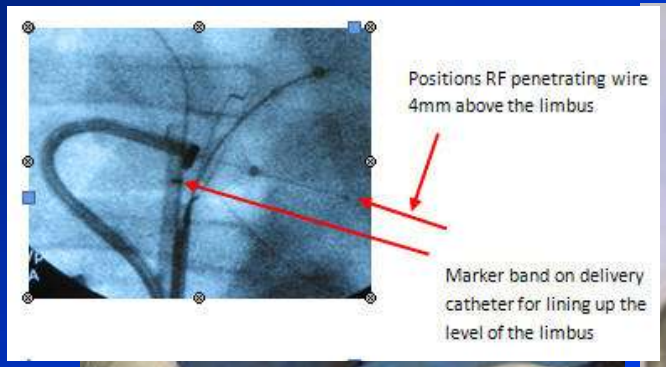
- Self-centering
- Phynox wires
- Polyester patches
- In the defect, wire-holders are moved towards each other
- Clicking mechanism keeps the wire-holders together
- Short 10 F introducer

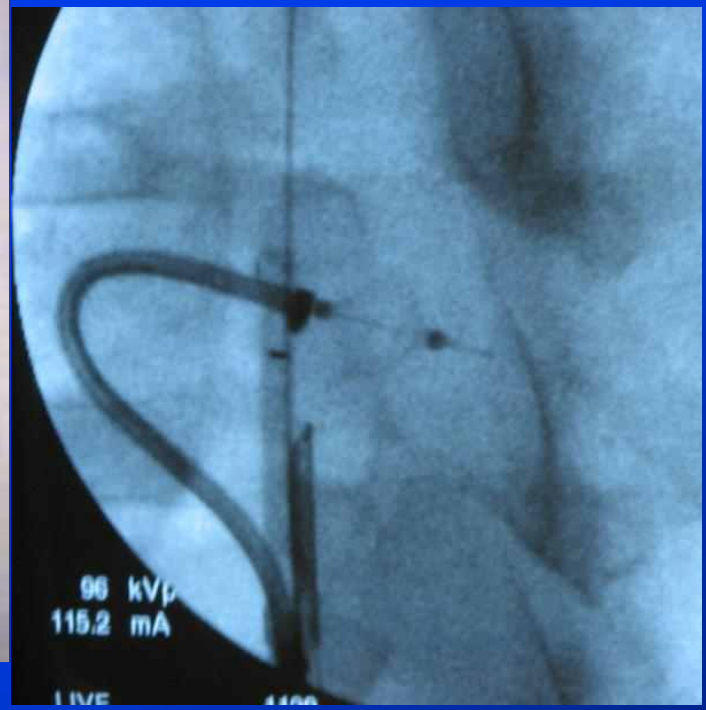






CoAptus Solution





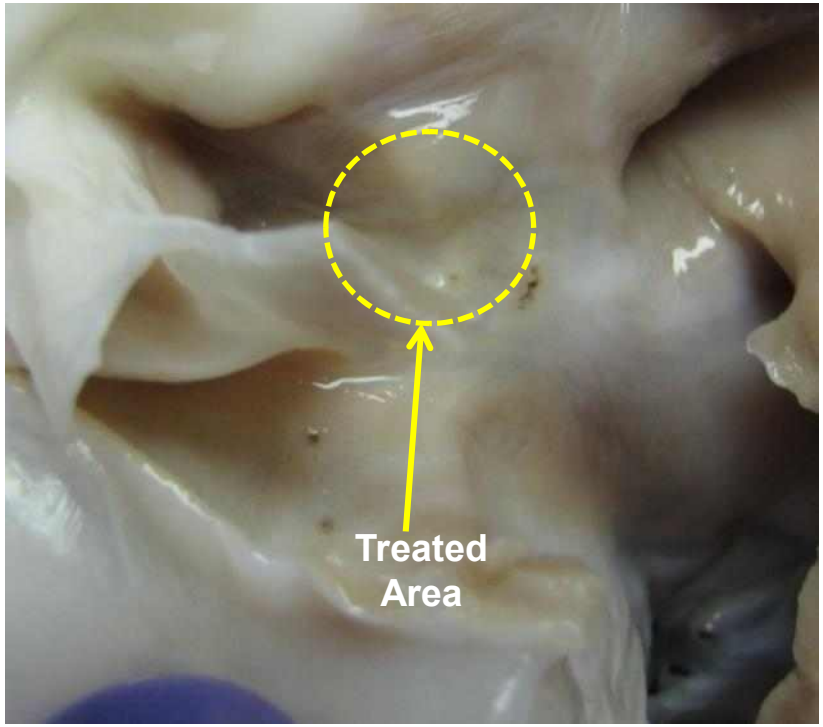
Using radiofrequency

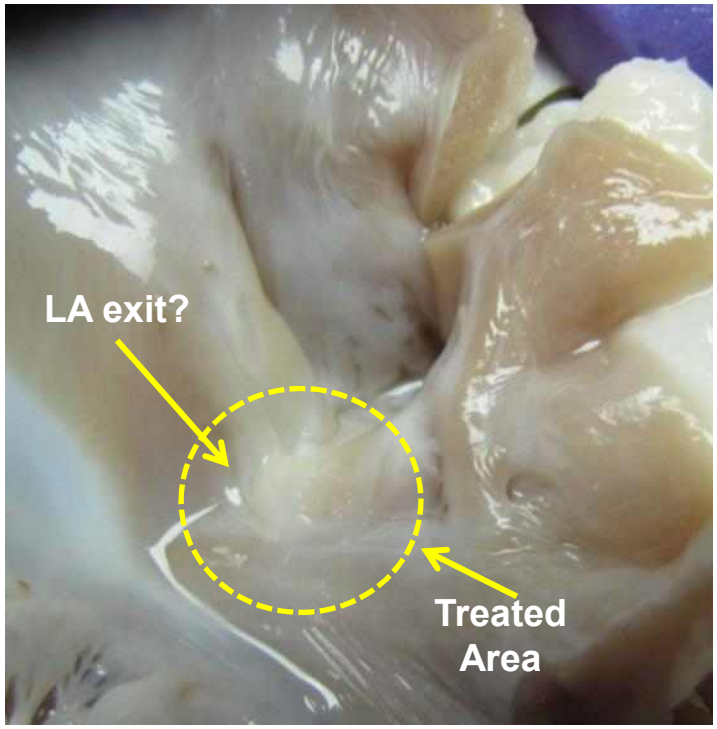
Septum primum and septum secundum are coapted mechanically

Then energy is applied

Thereafter, the device is removed leaving nothing behind

28 day

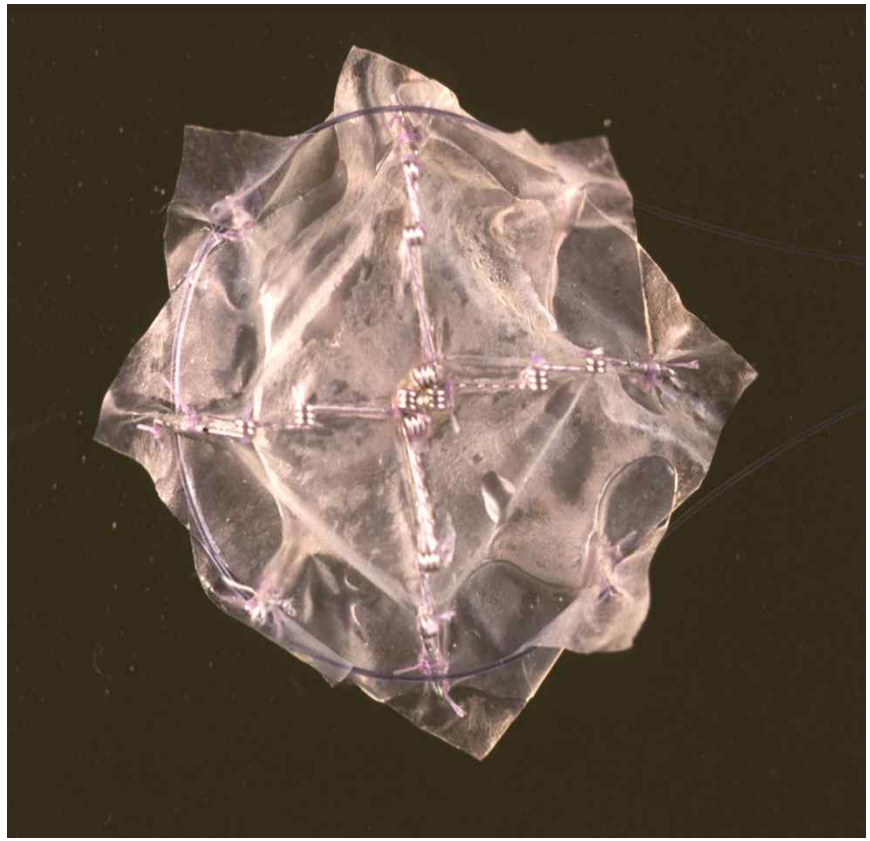




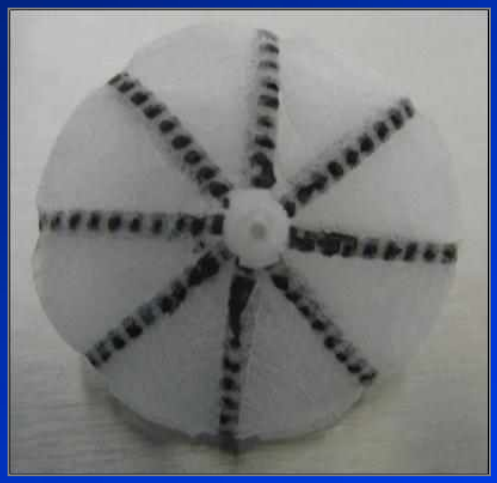
RA **LA**

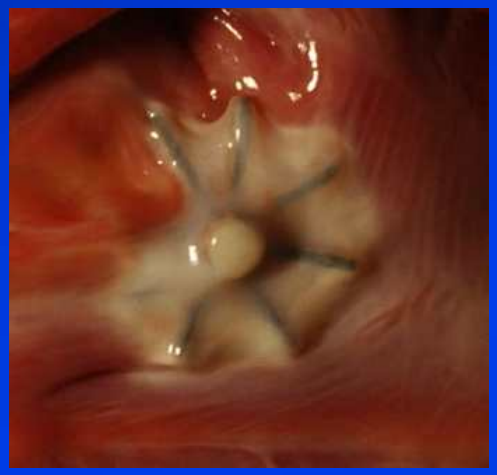
BioSTAR (NMT)

- CardioSEAL® framework
- STARFlex® self-centering mechanism
- Bioresorbable collagen matrix, heparin coating
- The metallic framework is not bioresorbable



BioTREK™ Bioabsorbable Septal Repair



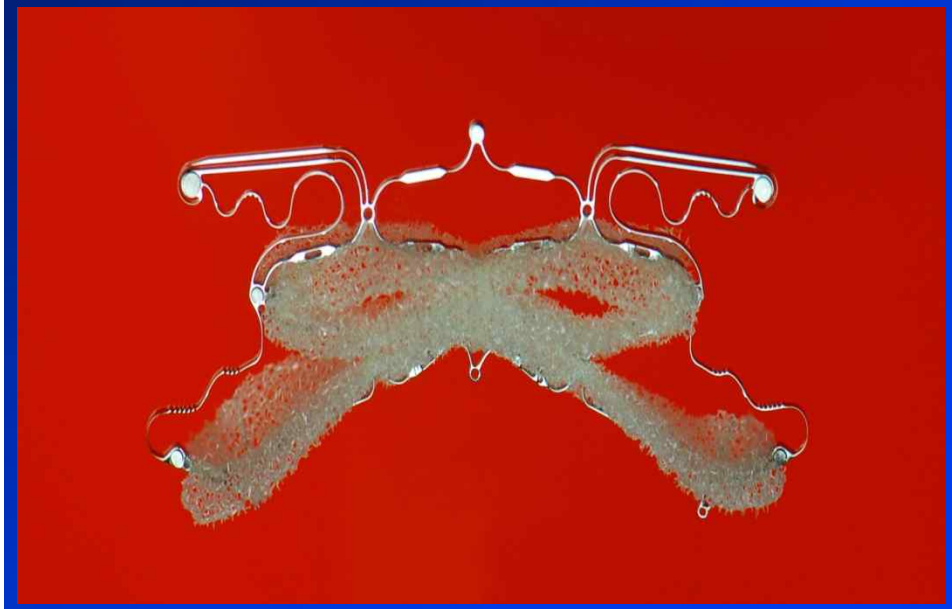


6 months

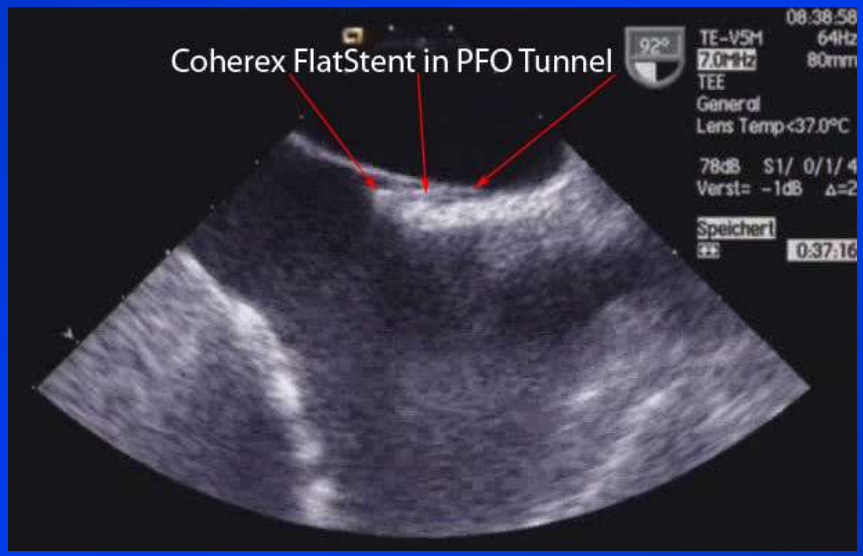
- 100% absorption over time
- novel bioabsorbable polymer (P4HB)
  - absorbs as a non-inflammatory natural metabolite
- easily repositionable and retrievable
- radiopaque and echogenic
- currently in pre-clinical studies

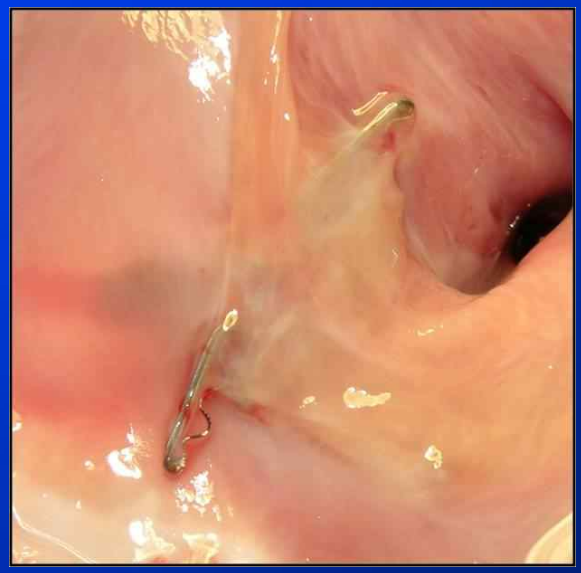
Explant photo courtesy of Aaron V. Kaplan, MD and Ebo D. de Muinck, M.D. Ph.D., Dartmouth Medical School (USA)

Coherex FlatStent EF™



- Intra tunnel device
- Early data very positive
  - Low residual shunts
  - Low complications
- Easy deployment
- Will m/p require Imaging
- Tunnel morphology will need further evaluation





Structural Heart Interventions

- ASD, PFO closure
- VSD closure
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- Stenting of coarctation
- Heart failure treatment
- Valves
  - Mitral valve repair
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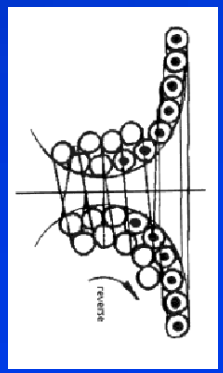
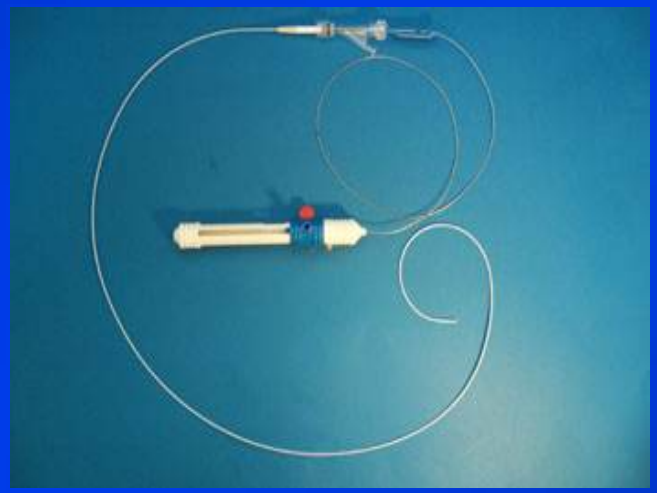
Transcatheter VSD Closure using the AGA Device

Courtesy TP Le

Study	n	Success	Residual Shunt (6 Mon FU)	Transient AV-Block	Persistent AV-Block	TR	AI
Li et al, 2005	68	91.5%	0%	16.5%	3%	8%	2.6%
Sun et al, 2005	89			12%	3.5%		
Anil et al, 2005	26	81%	9.5%	9.5%			0
Carminati et al,2005	122	97.5%	4%	7.5%	2.6%	2.6 %	2.6%
Fu et al, 2006	35	91%			2.8%	2.8 %	
Dajer et al,2006	7	85.5%	14%		14%		

The PFM VSD Coil





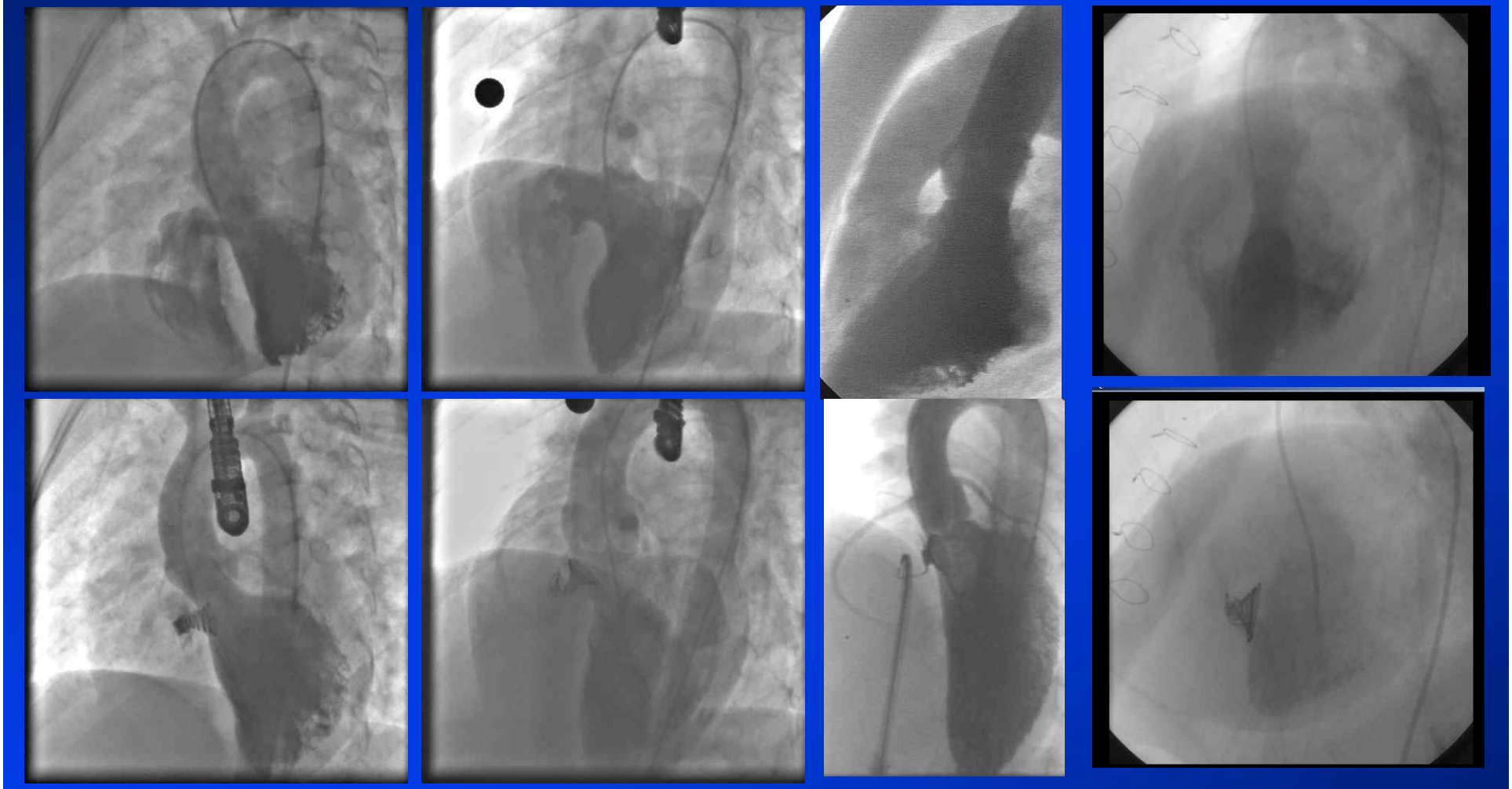
- Novel attachment mechanism
- Stiff distal loops, covered with polyester filaments

ACT: 200 - 250 sec.

5.5F delivery catheter; Distal Coil Diameter: 8,10,12,14 mm

Courtesy TP Le

Occlusion of VSD using the PFM VSD Coil



> 150 patients → No AV Block

Courtesy TP Le

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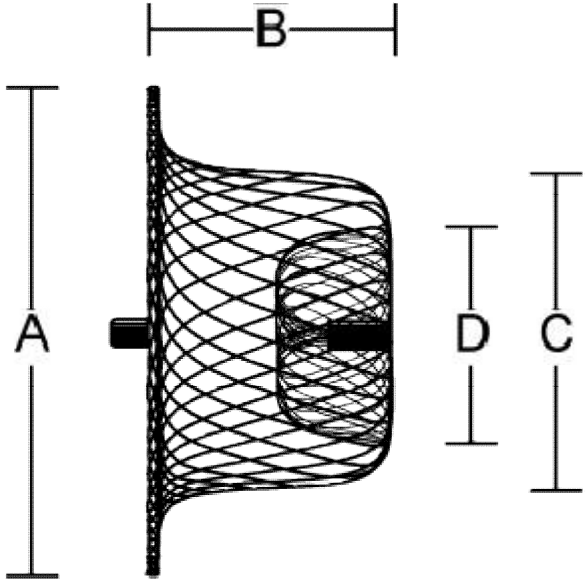
Amplatzer Duct Occluder ADO

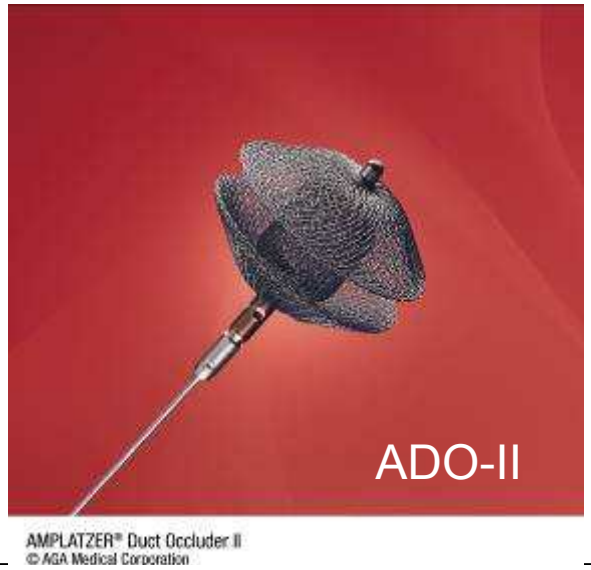


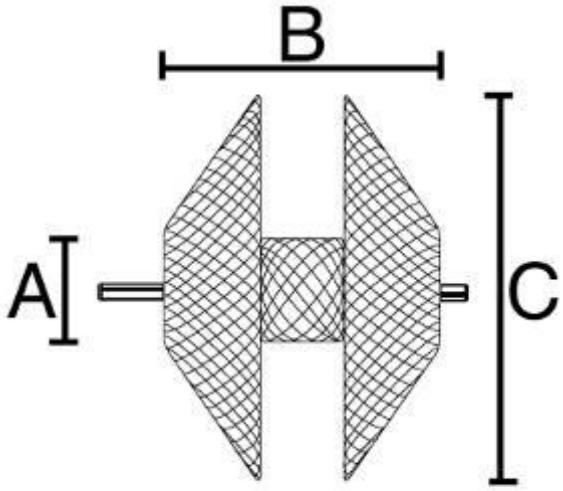
ADO-I

C: 4 to 14 mm

B: 5 to 8 mm

Sheath: 5 to 7 Fr





ADO-II

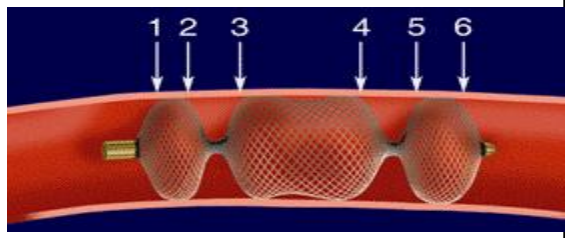
A: 3 to 6 mm

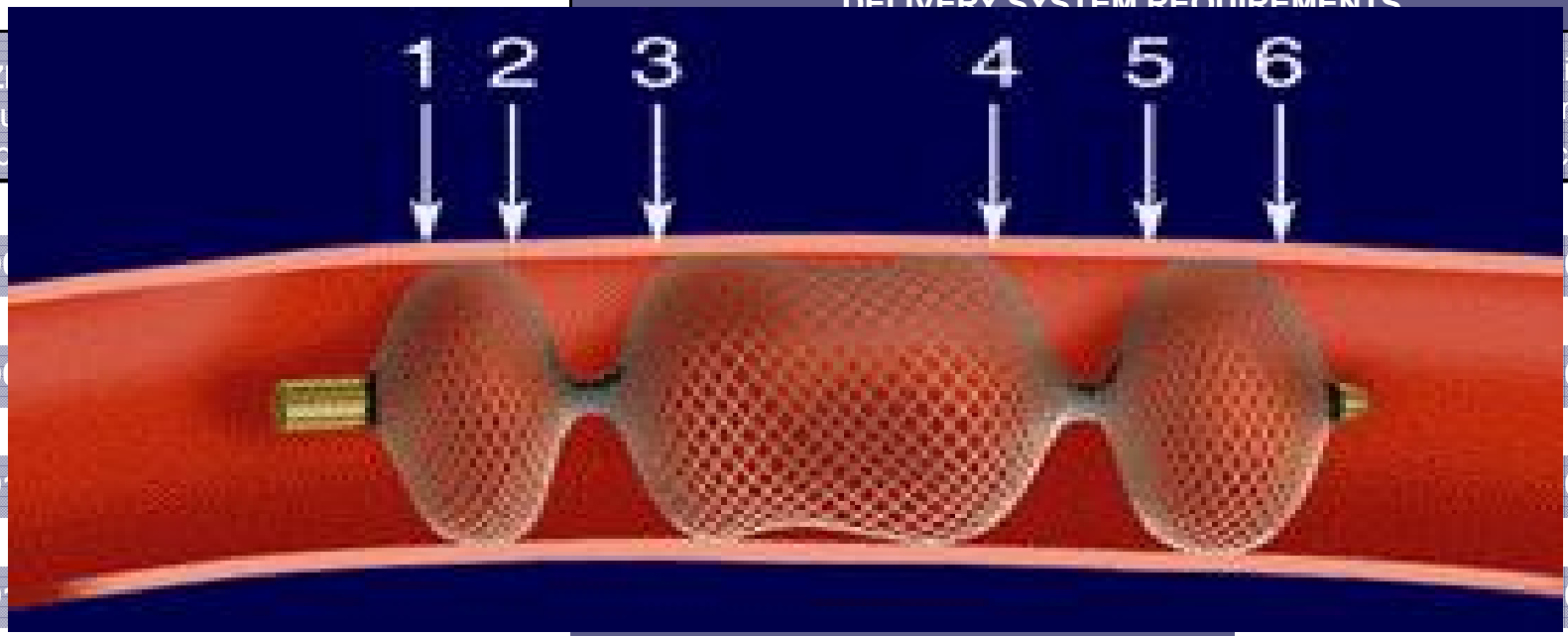
Sheath: 4 to 5 Fr

CE Mark

AMPLATZER® Vascular Plug II (AVP II)

- **Multi-layered mesh design with increased density**
- **Eleven sizes from 3mm to 22mm**
- **Three lobes**
  - **provide six planes of cross sectional coverage**
  - **allow better conformity to a landing zone**





AMPLATZ... Vascular Plu... Order No...			DELIVERY SYSTEM REQUIREMENTS			...imum ...ngth ...m)
9-AVP2-0...						...00
9-AVP2-0...						...00
9-AVP2-0...						...00
9-AVP2-0...						...00
			7 Fr	9 Fr		
9-AVP2-020	20	16	7 Fr	9 Fr	0.098	100
			7 Fr	9 Fr		

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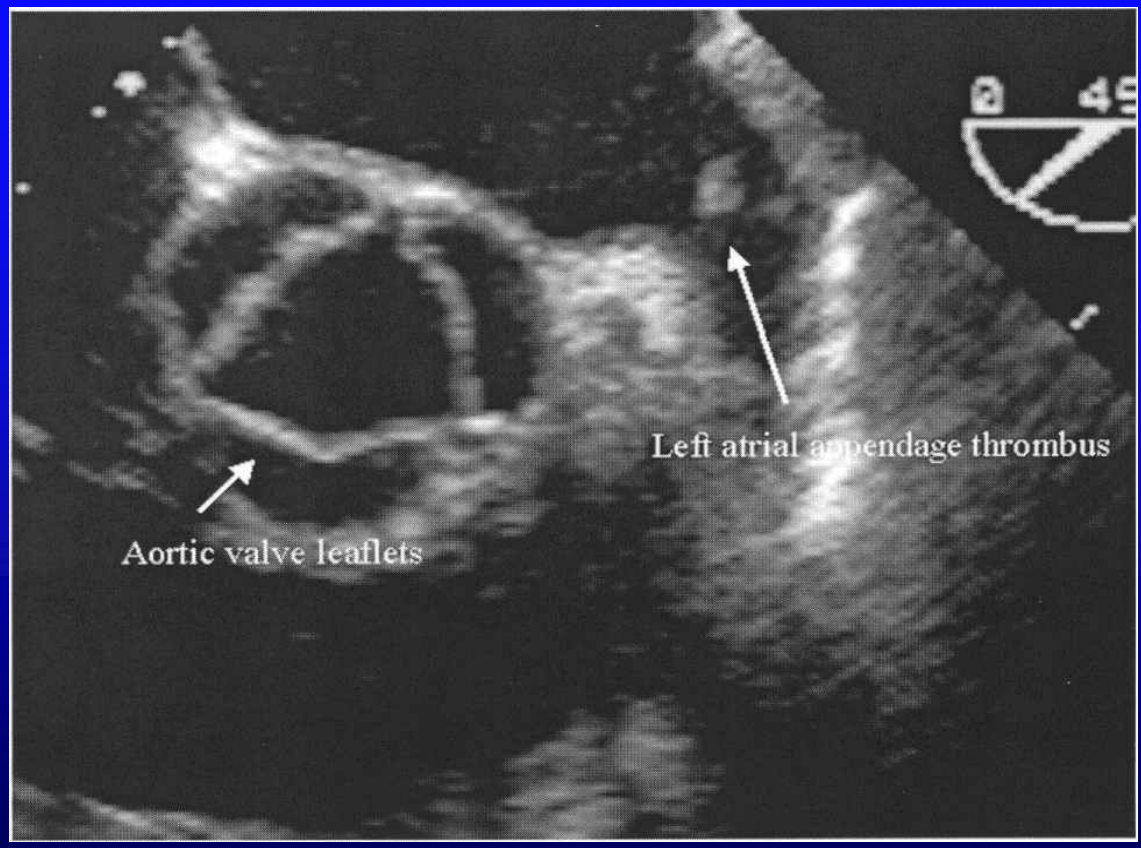
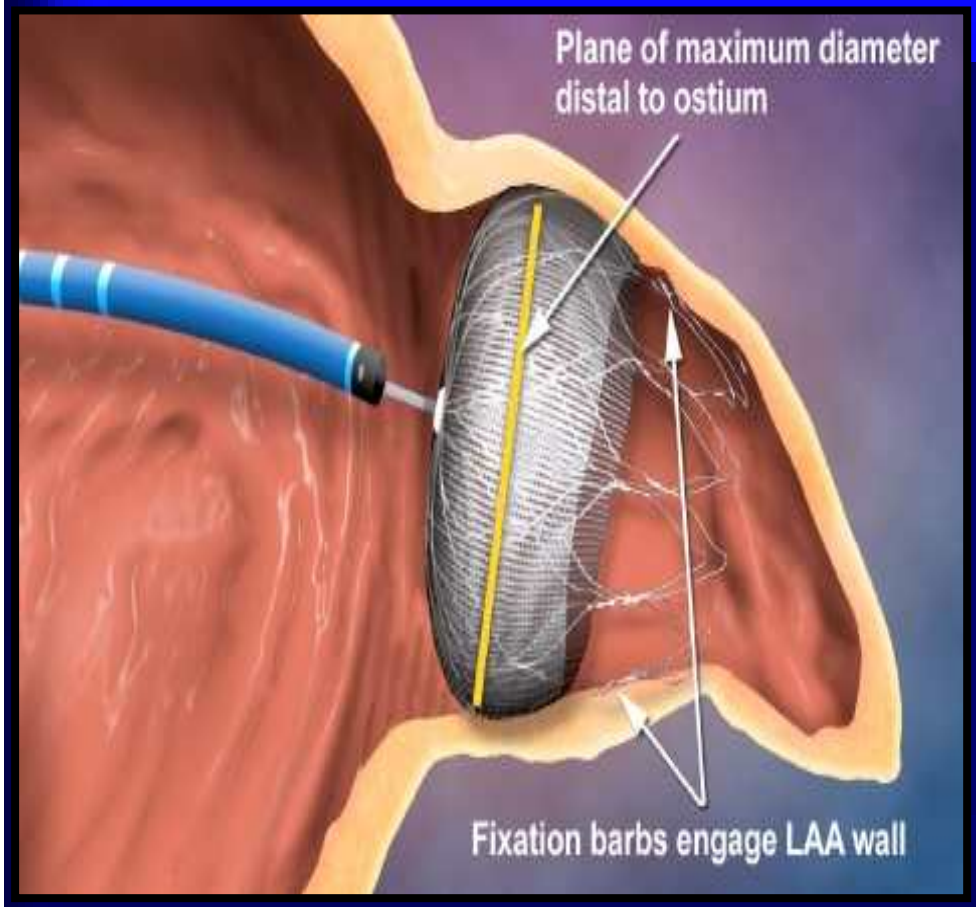
Atrial Fibrillation

- Is a major cause of stroke
- Thrombi develop in the left atrial appendage (LAA)
- LAA occlusion could be an alternative to lifelong anticoagulation

Thrombi Formation in the LAA



WATCHMAN® LAA closure system



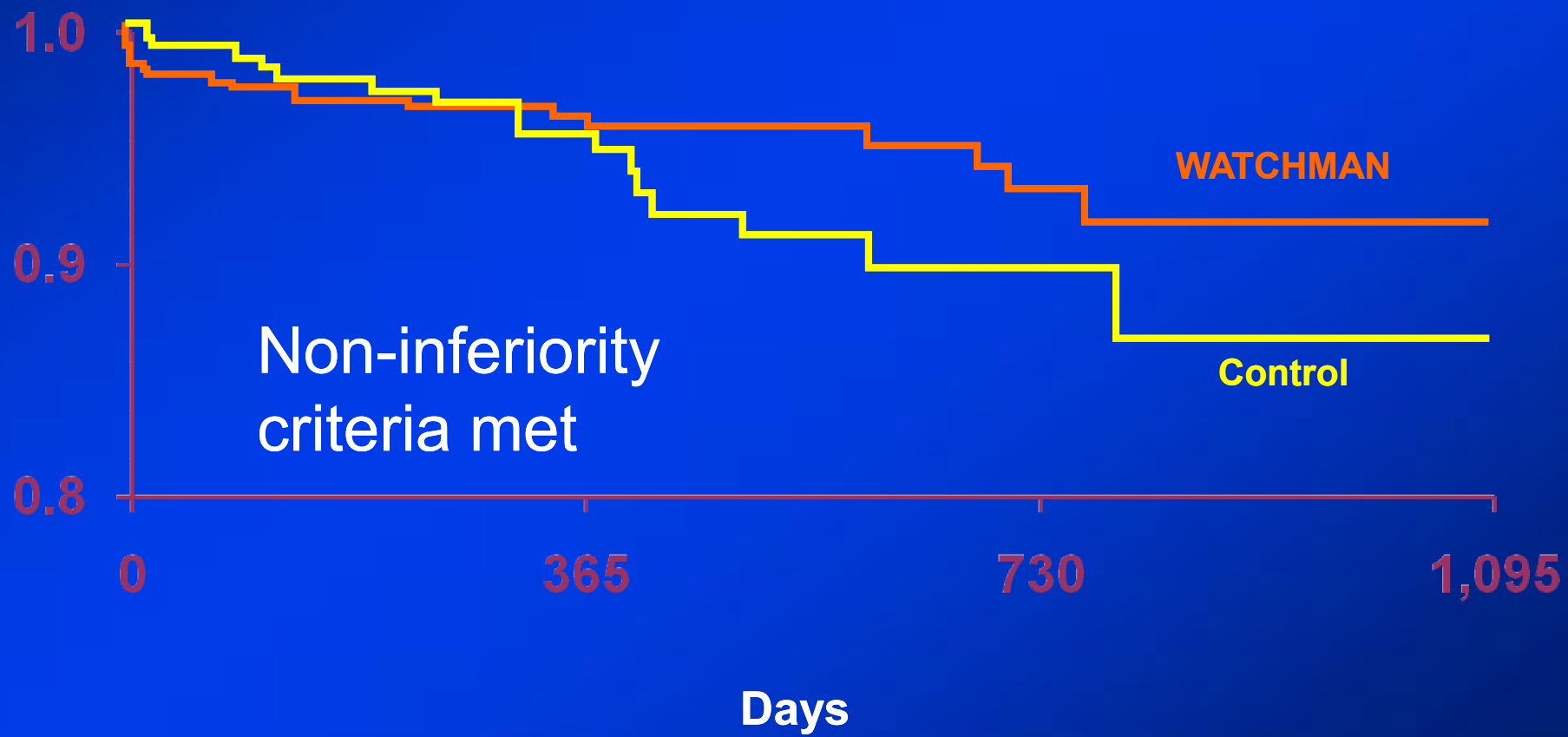
Procedure consists of percutaneous placement via transseptal of a filter device just distal to the ostium of the left atrial appendage to keep harmful sized emboli from exiting.

PROTECT AF Trial Endpoints

- Primary Efficacy Endpoint
  - All stroke
  - Cardiovascular and unexplained death
  - Systemic embolization
- Primary Safety Endpoint
  - Device embolization requiring retrieval
  - Pericardial effusion requiring intervention
  - Cranial bleeds and gastrointestinal bleeds
  - Any bleed that requires ≥ 2uPRBC

Primary Efficacy Endpoint

Freedom from Stroke, Death, Systemic Embolization



Safety

Freedom from device embolization, pericardial effusion, Severe bleeding

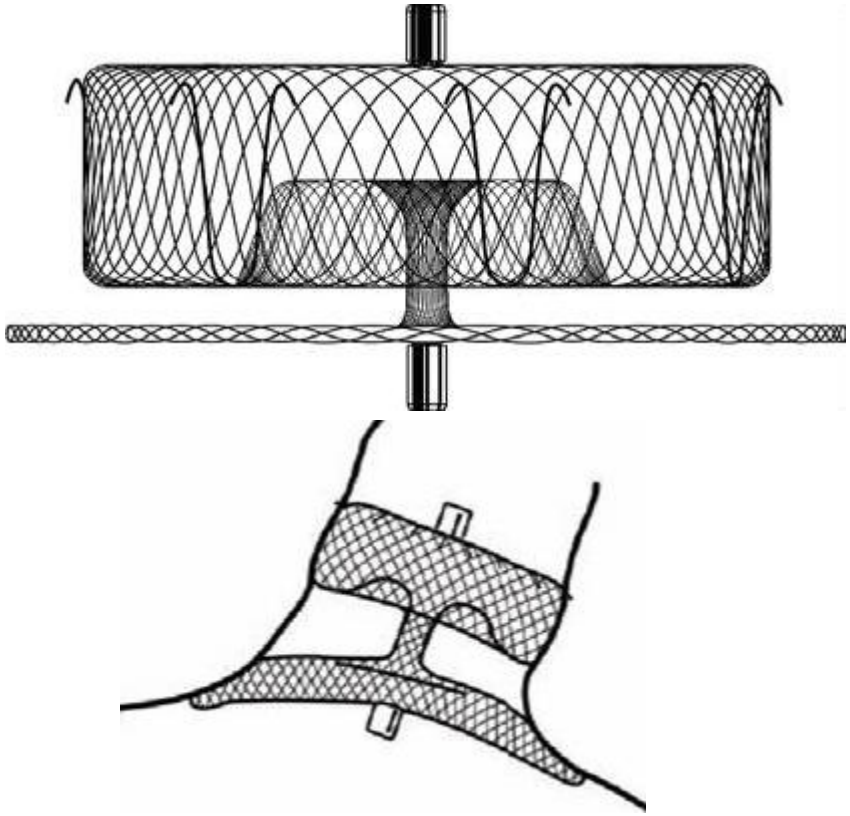
Other significant fndings

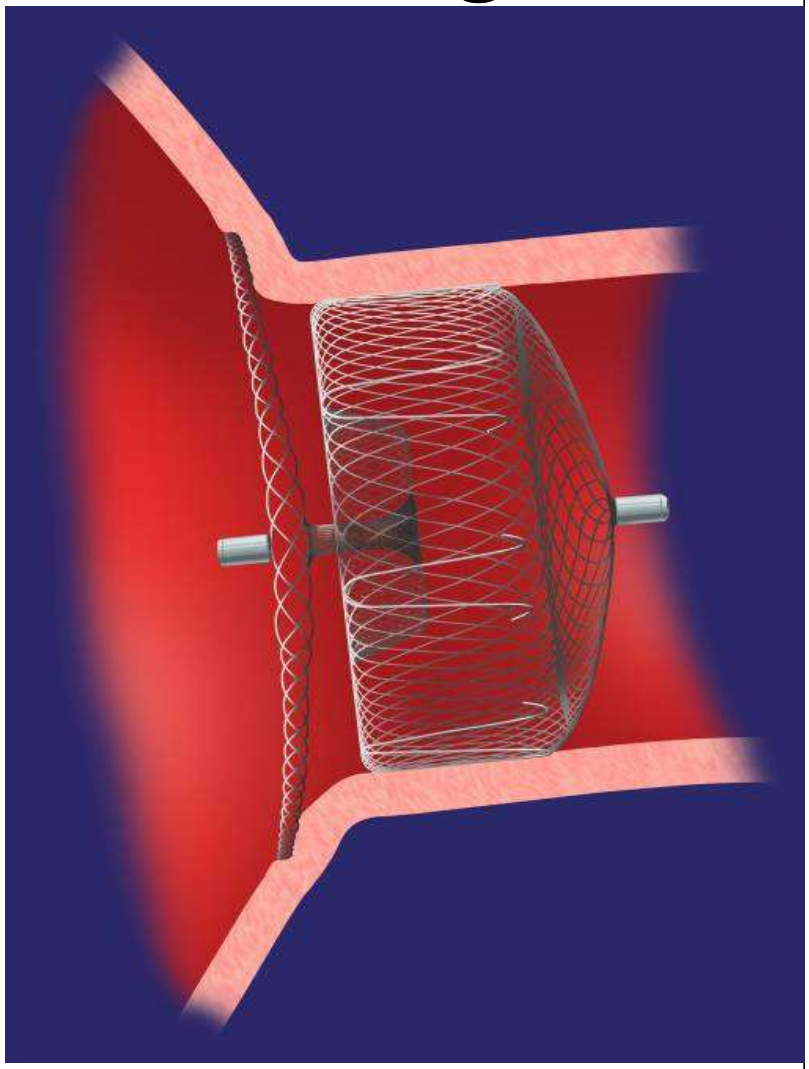
- Noninferiority for all strokes
  - 26% lower in device group
- Superiority for hemorrhagic stroke
  - 91% lower in device group
- Noninferiority for mortality
  - 39% lower rate in device group
- Most events in the device group were procedural effusions that decreased over the course of the study

New Device for LAA Closure Amplatzer Cardiac Plug

- CE mark in Dec 2008
- The only new medical device which received CE-mark before FIM

Amplatzer Cardiac Plug





- Nitinol mesh and polyester patch
- Lobe and a disc connected by a central waist
- Disc is self-orienting
- Available in 8 diameters sizes, 16, 18, 20, 22, 24, 26, 28, and 30 mm.

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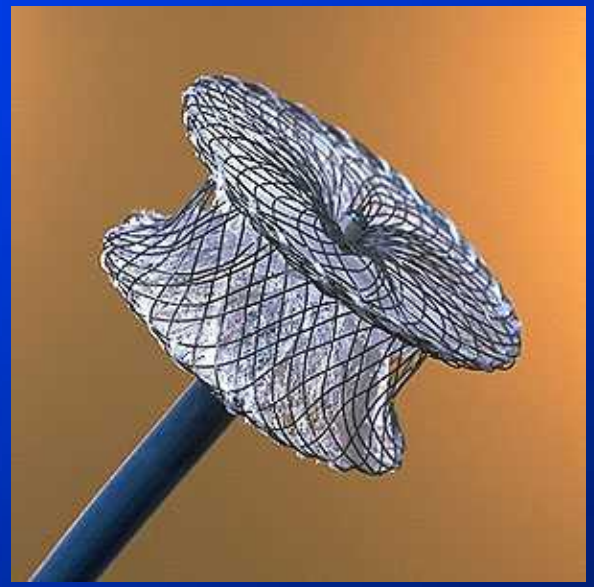
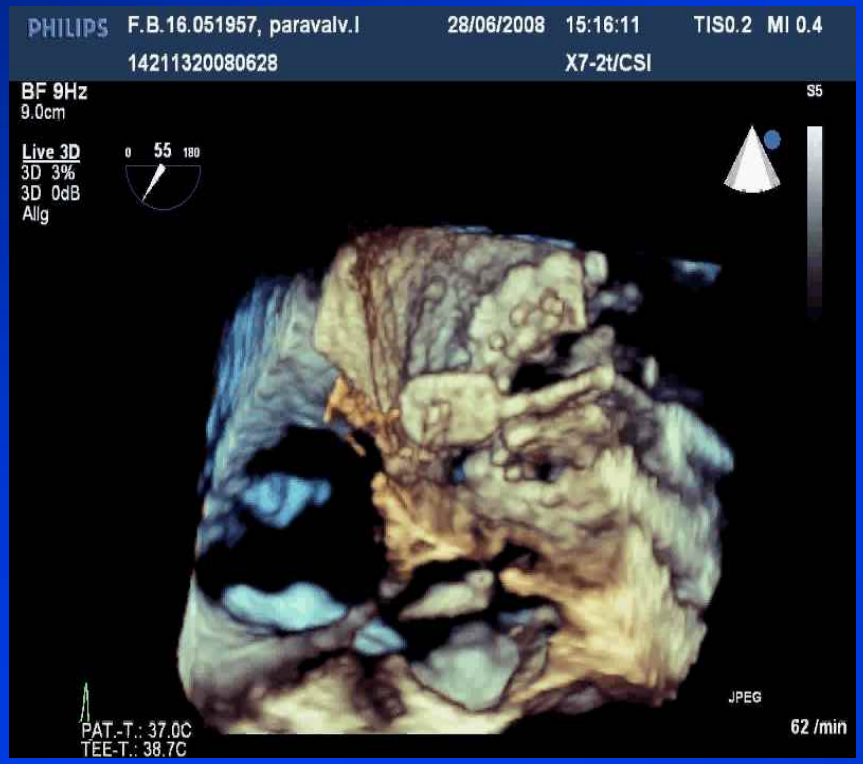
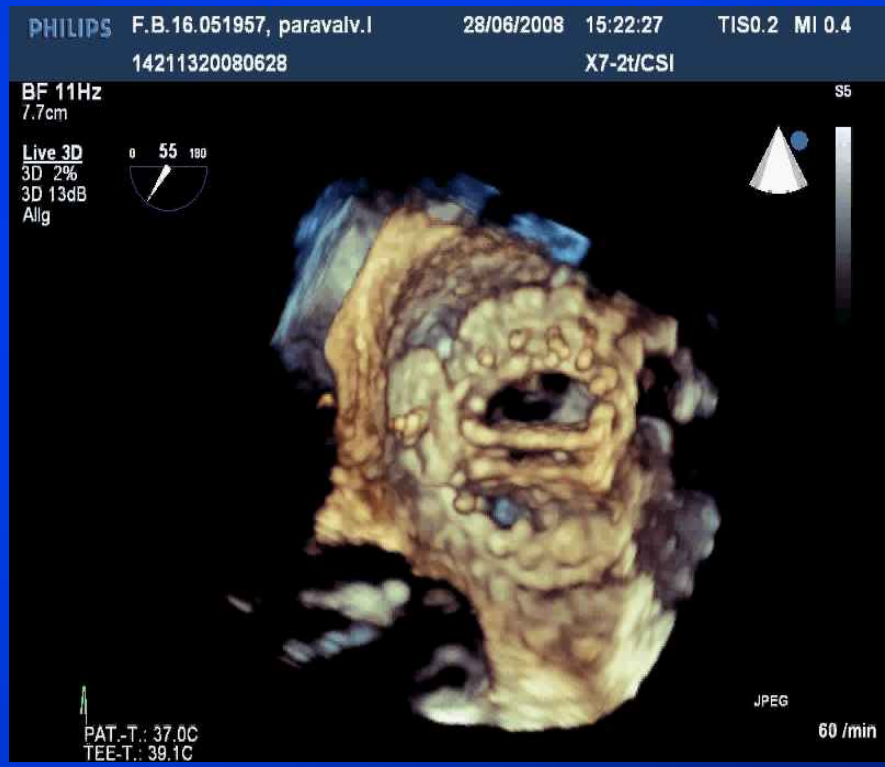
Paravalvular Leak Closure

- Amplatzer
  - ASD Occluder
  - VSD Occluder
  - PDA Occluder



Paravalvular leak closure





AVP III

Structural Heart Interventions

- ASD, PFO closure
- VSD closure
- Patent ductus closure
- Left atrial appendage closure
- Paravalvular leak closure
- Stenting of coarctation
- Heart failure treatment
- Valves
  - Mitral valve repair
  - Aortic valve implantation

Atrium™ Covered stent to prevent rupture and aneurysm

Multicenter clinical trial has started

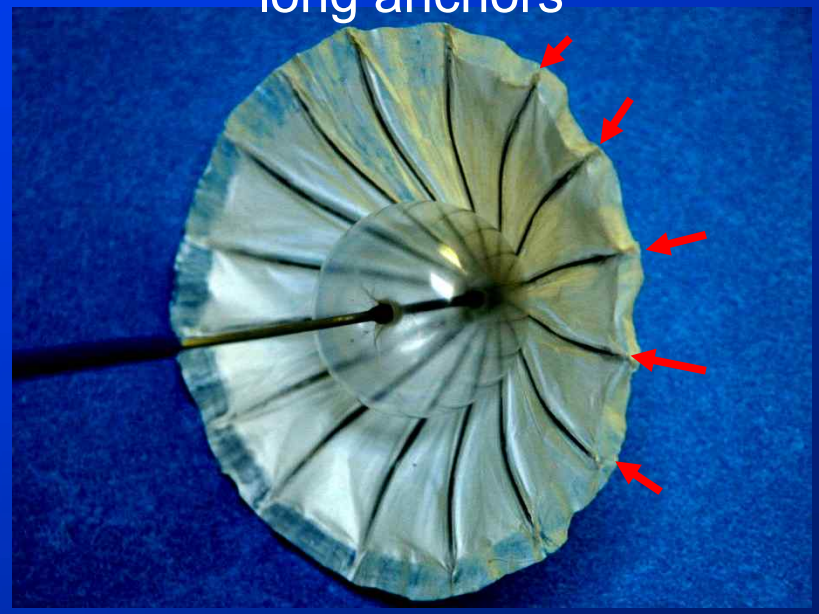
Structural Heart Interventions

- ASD, PFO closure
- VSD closure
- Patent ductus closure
- Left atrial appendage closure
- Paravalvular leak closure
- Stenting of coarctation
- LV Apical aneurysm treatment
- Valves
  - Mitral valve repair
  - Aortic valve implantation

VPD-Implant

- First device designed to treat LV wall abnormalities by catheter techniques
- Umbrella-like occlusive membrane with a nitinol frame
- 2 mm long anchors

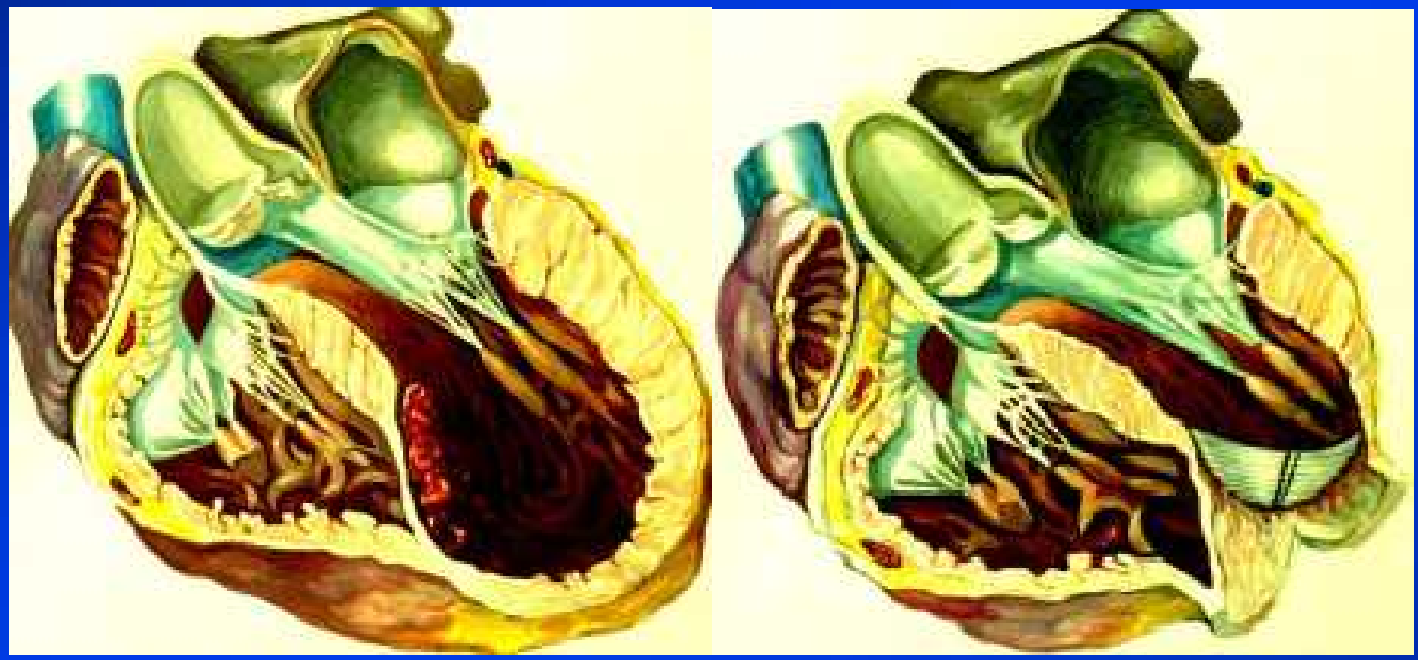
16 struts with 2mm long anchors



Not FDA approved

Dor Procedure

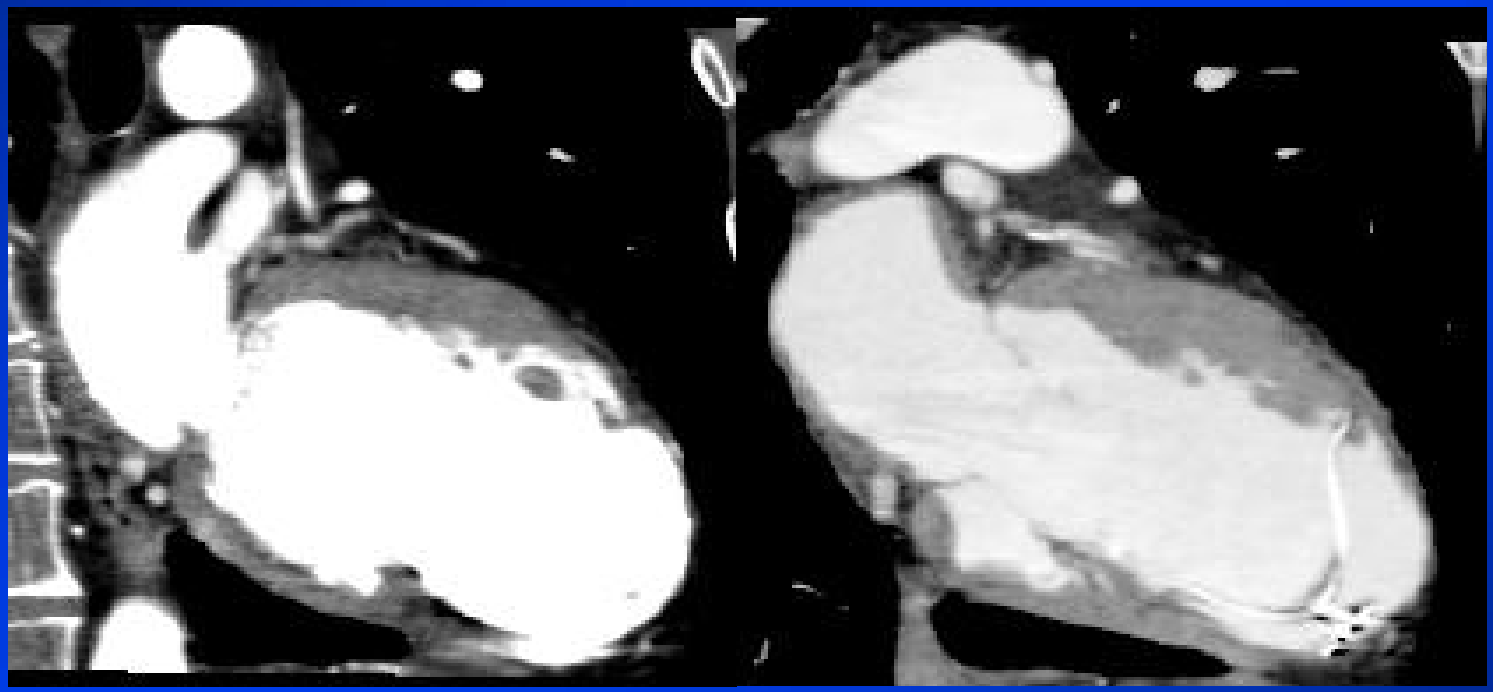
Aneurysm Resection



Athanasuleas CL et al, JACC 2004

VPD Implant

CT Scan

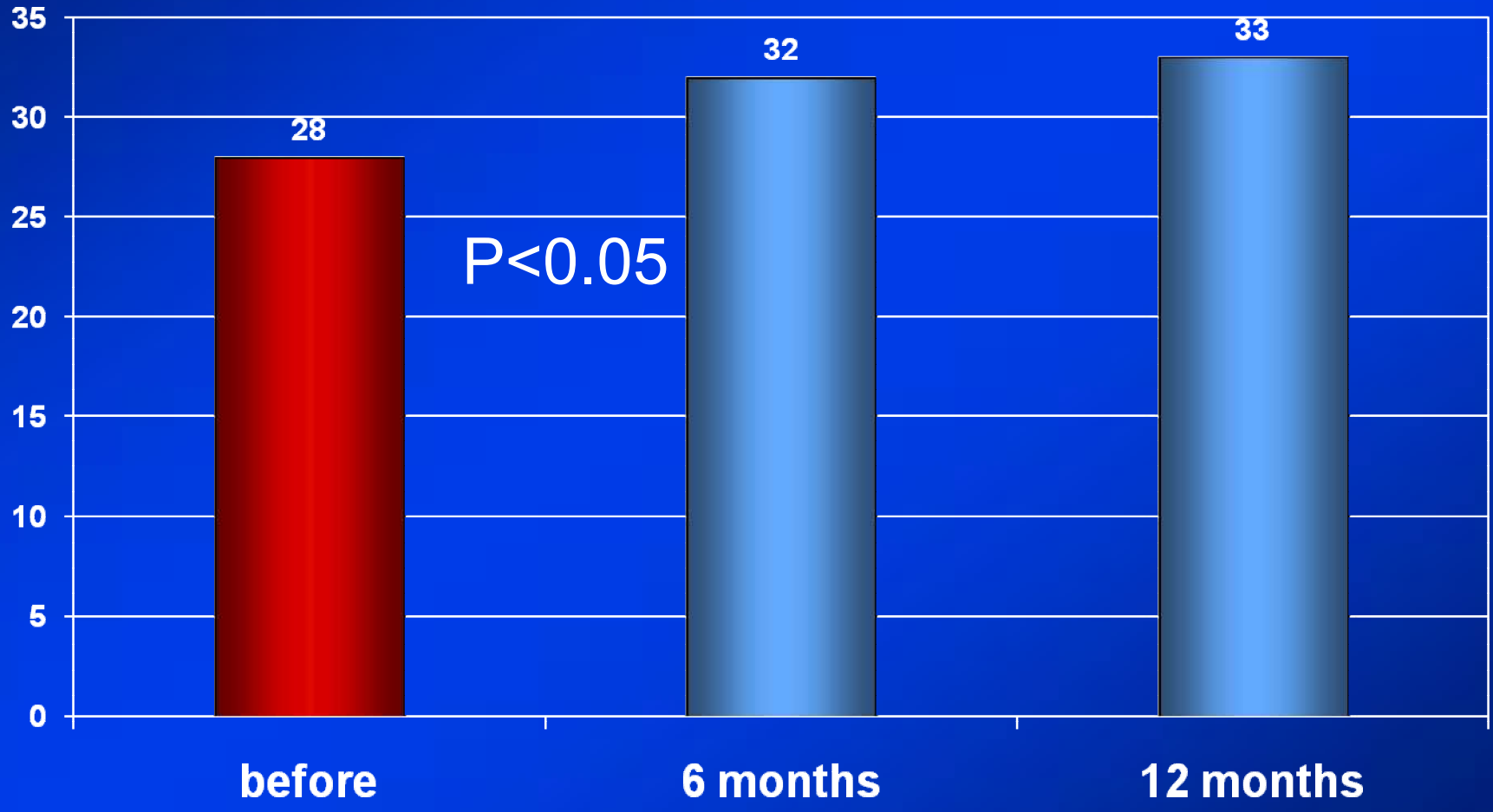


before

6 months

EF - Echo (%)

n=13



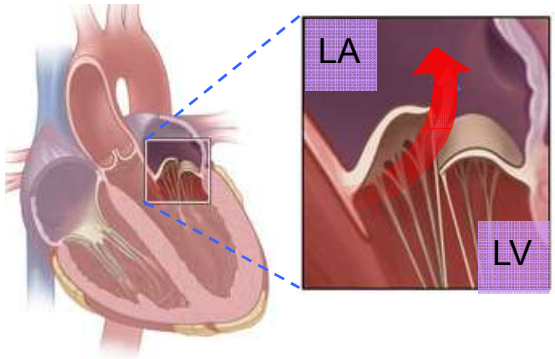
Structural Heart Interventions

- ASD, PFO closure
- VSD closure
- Patent ductus closure
- Left atrial appendage closure
- Paravalvular leak closure
- Stenting of coarctation
- Heart failure treatment
- Valves
  - Mitral valve repair
  - Aortic valve implantation

Mitral Regurgitation

What is It?

LV to LA Regurgitation



Incomplete leaflet coaptation or leaflet prolapse results in LV blood regurgitating into LA resulting in increased load and stress in the LV

Risks?

May initiate or exacerbate heart failure

Muscle Damage/Loss

Increased Load/Stress

LV Remodeling/ Enlargement

Mitral Annulus Enlargement Causing Increased MR

Self perpetuating, MR begets MR

What Causes It?

Two Distinct Etiologies

Primary

Intrinsic leaflet abnormalities

- Myxomatous degeneration
- Rheumatic disease
- Congenital

1 million

Functional

Incomplete coaptation caused by heart dilation

- Ischemic heart disease
- Non-ischemic cardiomyopathy
- Acute MI

2.6 million

How is it Treated?

		Primary	Functional
Annuloplasty ring		✓	✓
Edge-to-edge		✓	
Leaflet resection		✓	
Chordal transfer		✓	
LV reshaping			✓

Percutaneous MV Repair

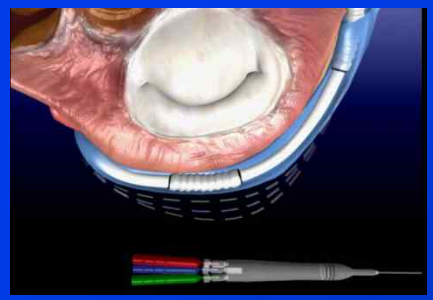
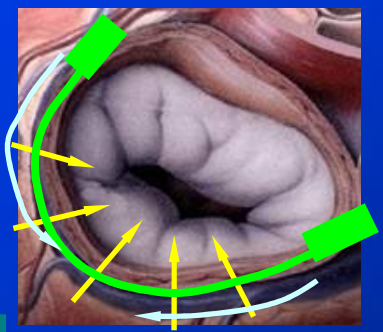
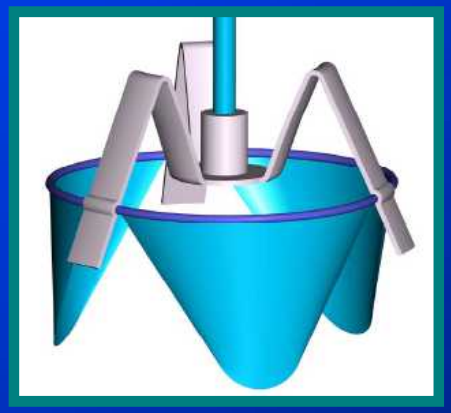
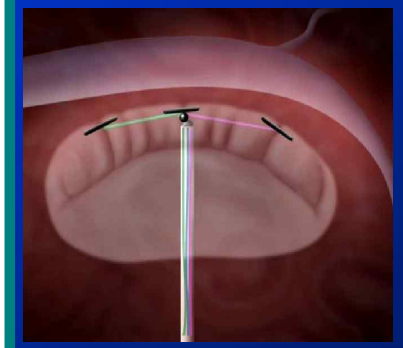
Edge-to-edge
- eValve
- Edwards Mobius

Coronary sinus annuloplasty
- Cardiac Dimensions
- Edwards Monarc
- Viacor

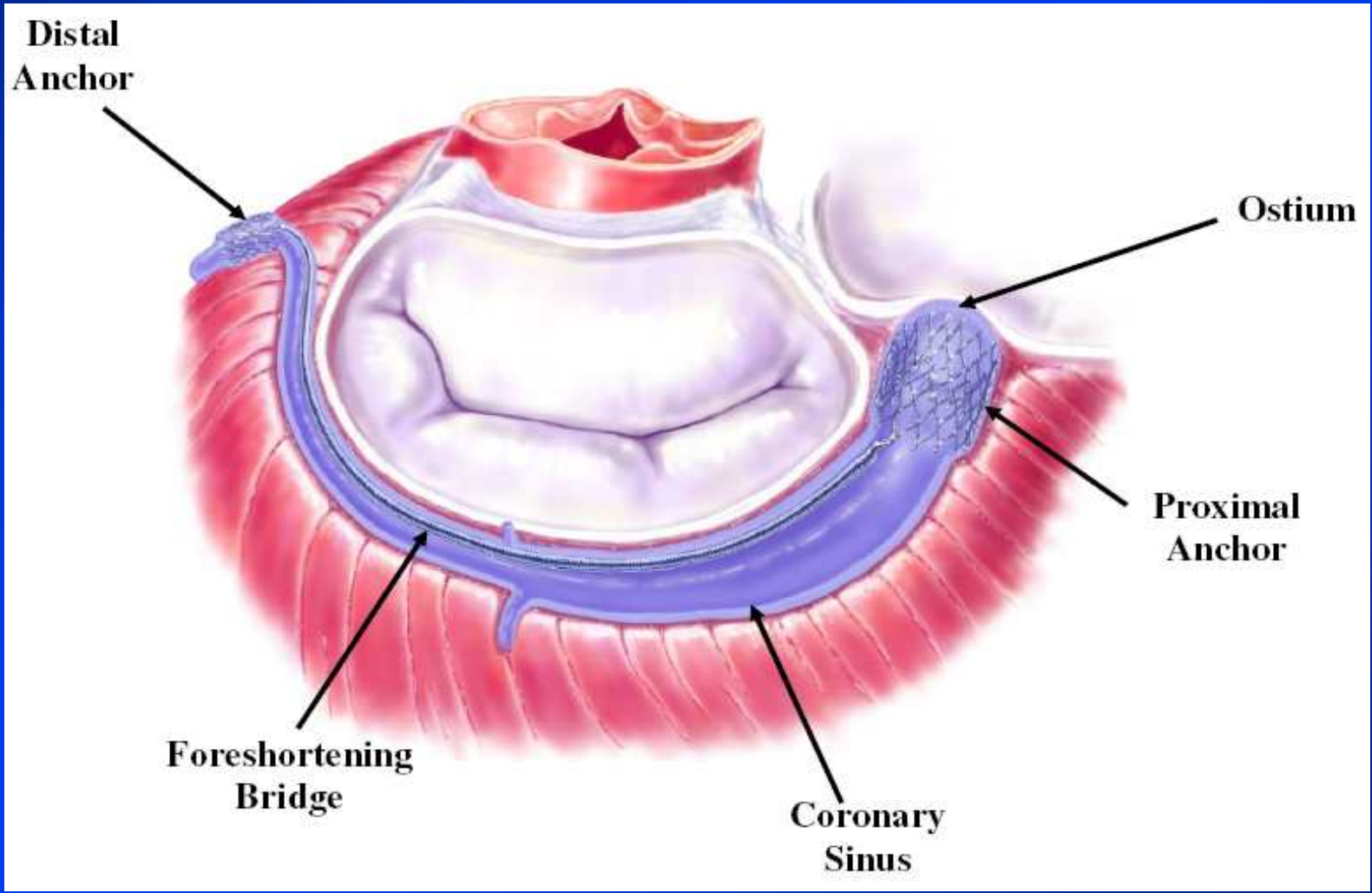
Indirect annuloplasty
- Ample PS3
- i-Coapsys

Direct annuloplasty
- Mitralign
- Guided Delivery Systems
- QuantumCor
- MiCardia



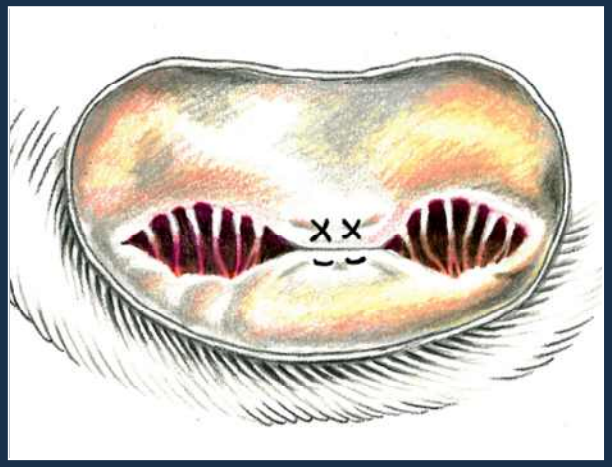





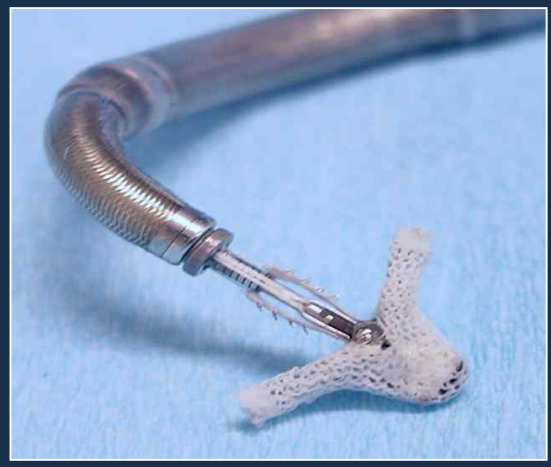
Coronary Sinus Annuloplasty

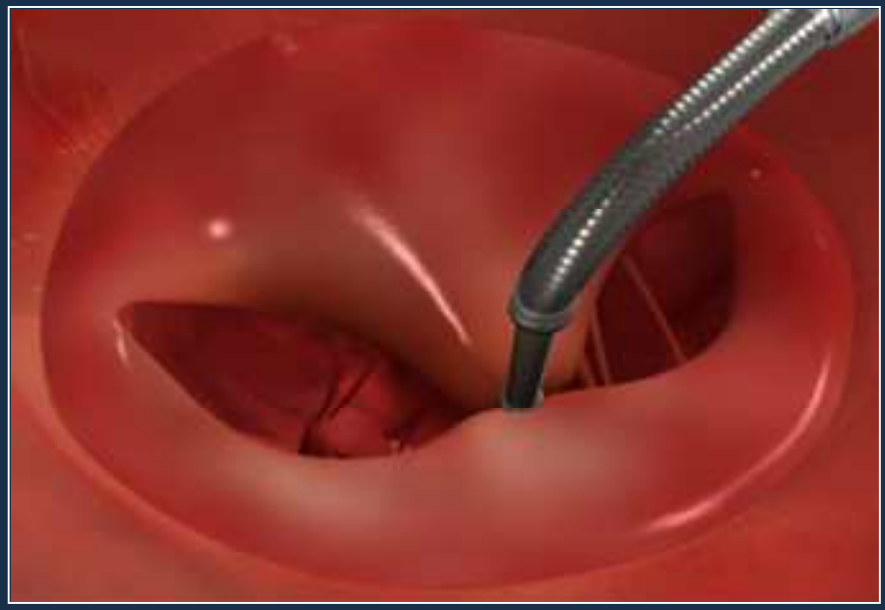


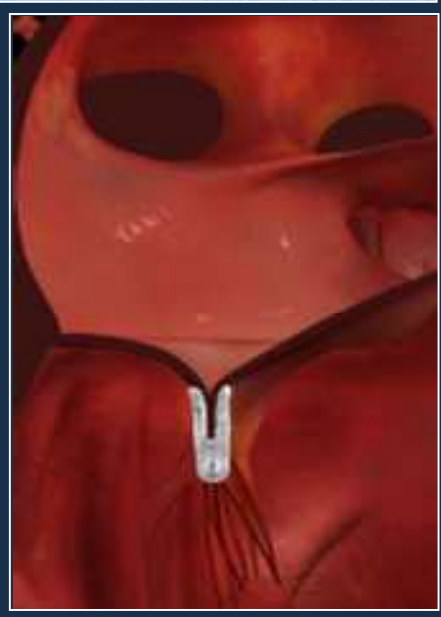
Catheter-Based Mitral Valve Repair

MitraClip® System









Evanston Hospital NorthShore University HealthSystem

Investigational Device only in the US; Not available for sale in the US

Clinical Experience

Study	Population	n
EVEREST I (Feasibility)*	Non-randomized	55
EVEREST II*	Pre-randomization	60
EVEREST II	High Risk Registry	78
EVEREST II (Pivotal)	Randomized patients (2:1 MitraClip to Surgery)	279 184 MitraClip 95 Surgery
REALISM (Continued Access)	High Risk & Non High Risk	266
European Experience		472
	Total	1,115 MitraClip

*Percutaneous Mitral Valve Repair Using the Edge-to-Edge Repair: Six months Results of the EVEREST Phase I Clinical trial, JACC 2005;46:2134-2140.
Percutaneous Mitral Repair with the MitraClip System: Safety and Midterm Durability in the Initial EVEREST Cohort, JACC 2009; 54:686-694.

Evanston Hospital NorthShore University HealthSystem

Data as of 2/15/2010.

Investigational Device only in the US; Not available for sale in the US

EVEREST II Randomized Clinical Trial

Study Design

279 Patients enrolled at 37 sites

Significant MR (3+-4+)
Specific Anatomical Criteria

↓

Randomized 2:1

↙ ↘

Device Group
MitraClip System
N=184

Control Group
Surgical Repair or Replacement
N=95

↓ ↓

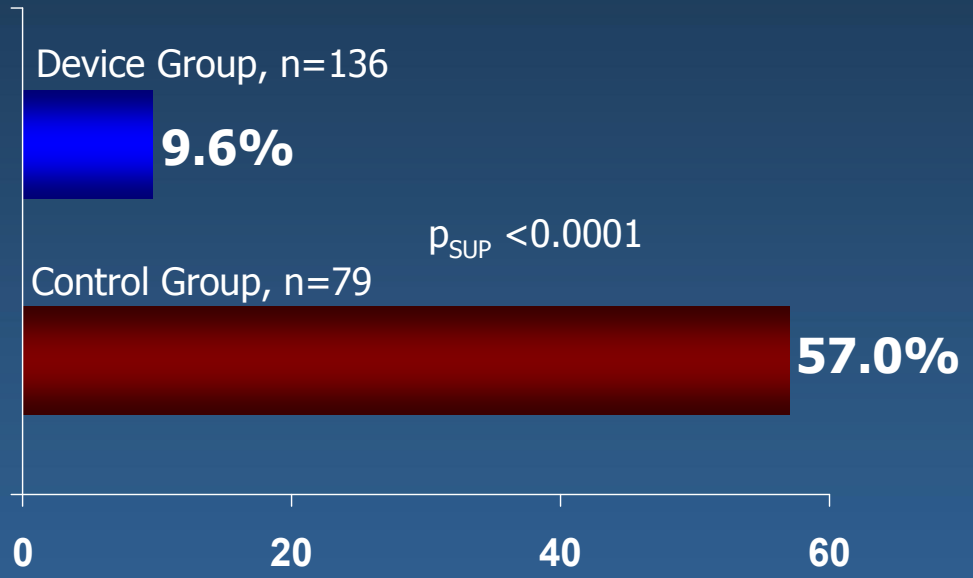
Echocardiography Core Lab and Clinical Follow-Up:
Baseline, 30 days, 6 months, 1 year, 18 months, and annually through 5 years

Evanston Hospital NorthShore University HealthSystem

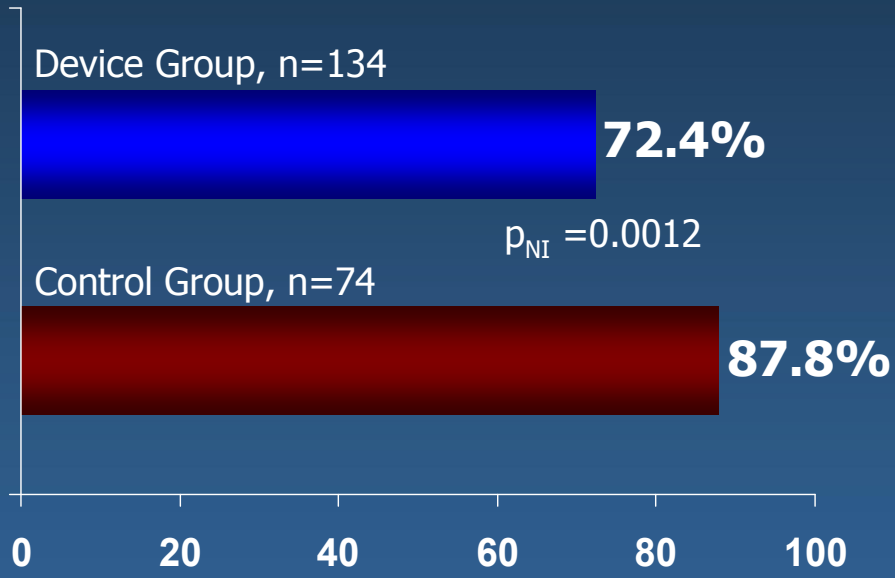
Investigational Device only in the US; Not available for sale in the US

EVEREST II RCT: Primary Endpoints
Per Protocol Cohort

Safety
Major Adverse Events
30 days



Effectiveness
Clinical Success Rate*
12 months



Met superiority hypothesis
- Pre-specified margin = 6%
- Observed difference = **47.4%**
- 97.5% LCB = 34.4%

Met non-inferiority hypothesis
- Pre-specified margin = 31%
- Observed difference = **15.4%**
- 95% UCB = 25.4%

LCB = lower confidence bound
UCB = upper confidence bound

* Freedom from the combined outcome of death, MV surgery or re-operation for MV dysfunction, MR >2+ at 12 months

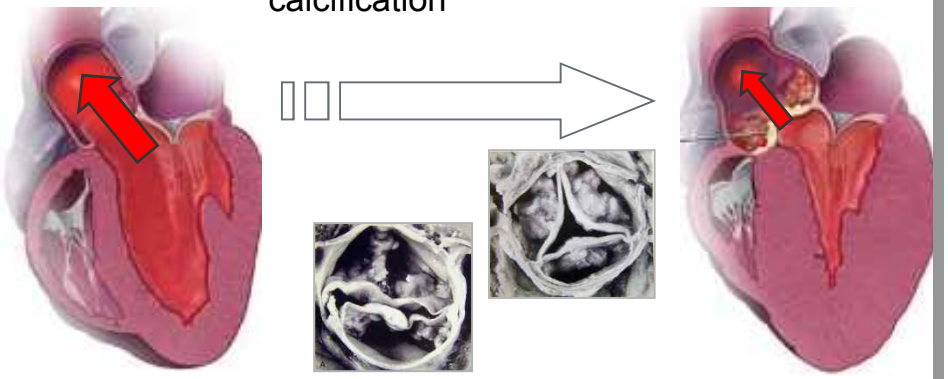
Evanston Hospital NorthShore University HealthSystem

Investigational Device only in the US; Not available for sale in the US

Aortic Stenosis

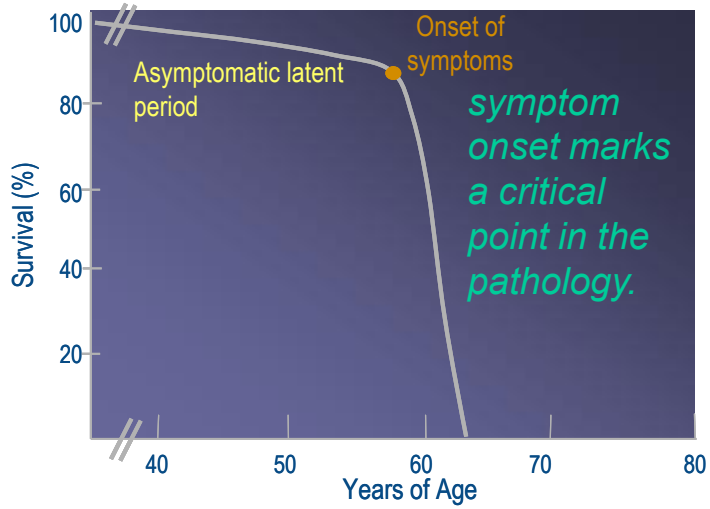
What is It?

Aortic stenosis causes obstruction of blood ejection from the left ventricle, is primarily caused by degeneration or calcification



Risk?

Aortic stenosis is a slow-progressing disease with a long asymptomatic period.



What Causes It?

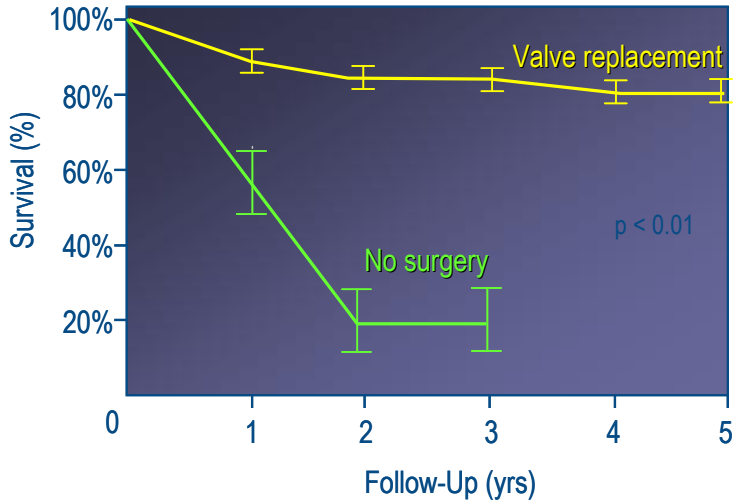
- Degeneration and calcification of aortic leaflets prevents complete opening of valves
- Congenital condition (e.g., biscupid valve – earlier onset)
- Rheumatic fever (rare in industrialized countries, >AR)

MAJOR RISK FACTORS:

Male	Elderly
LDL/HTN	Diabetes
Smoking	

How is it Treated

Surgery is critical at the onset of symptoms



Approved TAVI Devices

CoreValve Revalving System™ : self-expandable

Nitinol frame

Porcine pericardial lealfet

26 and 29 mm inflow

Edwards SAPIEN™ THV : balloon expandable

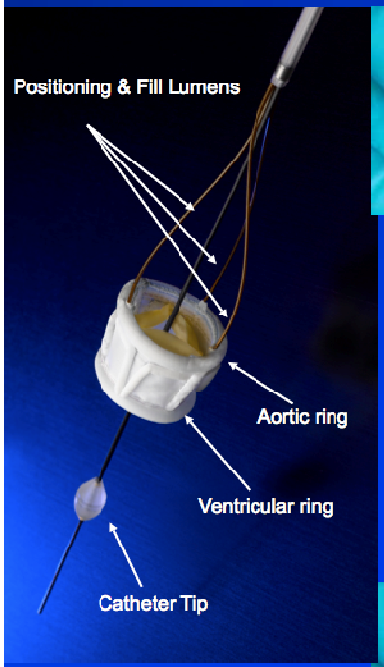
Stainless steal frame

Bovine pericardial lealfet

23 and 26 mm

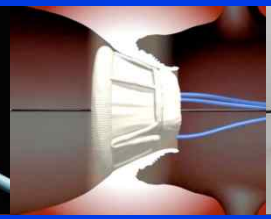
Direct Flow Medical - Percutaneous Aortic Valve

- Challenges - Profile, deliverability, repositionable, retrievable

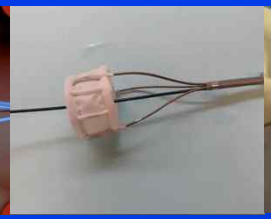


22 French

Loaded Valve



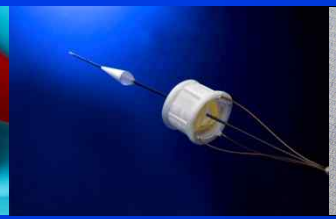
Distal Ring Inflated

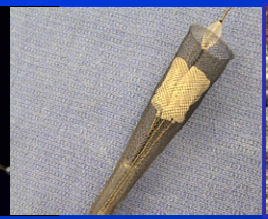


Positioning

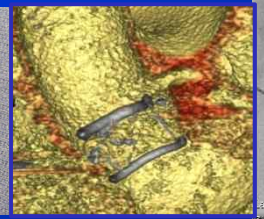
Both Rings Inflated

18 French - Next Generation

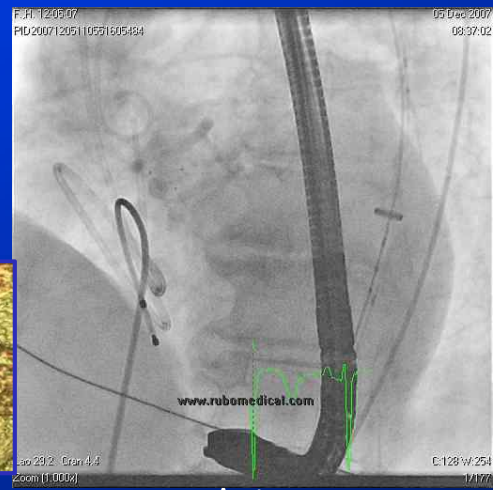




Retrieval

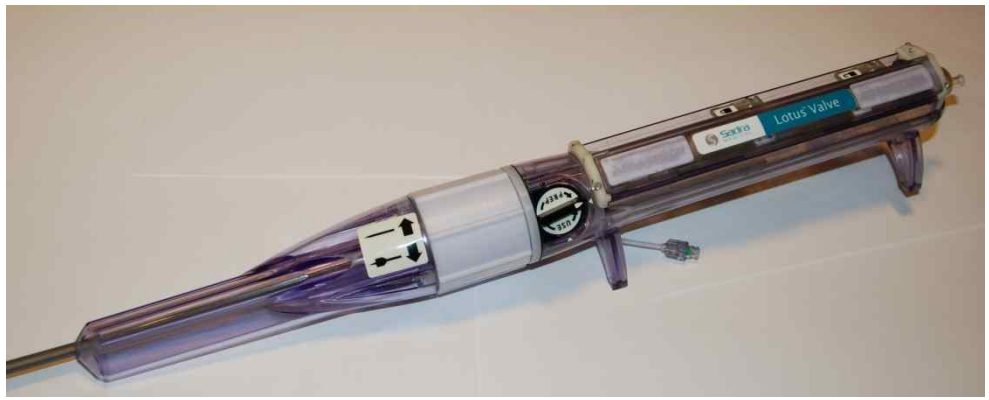


CT



Aortogram

Sadra Lotus™ Valve System

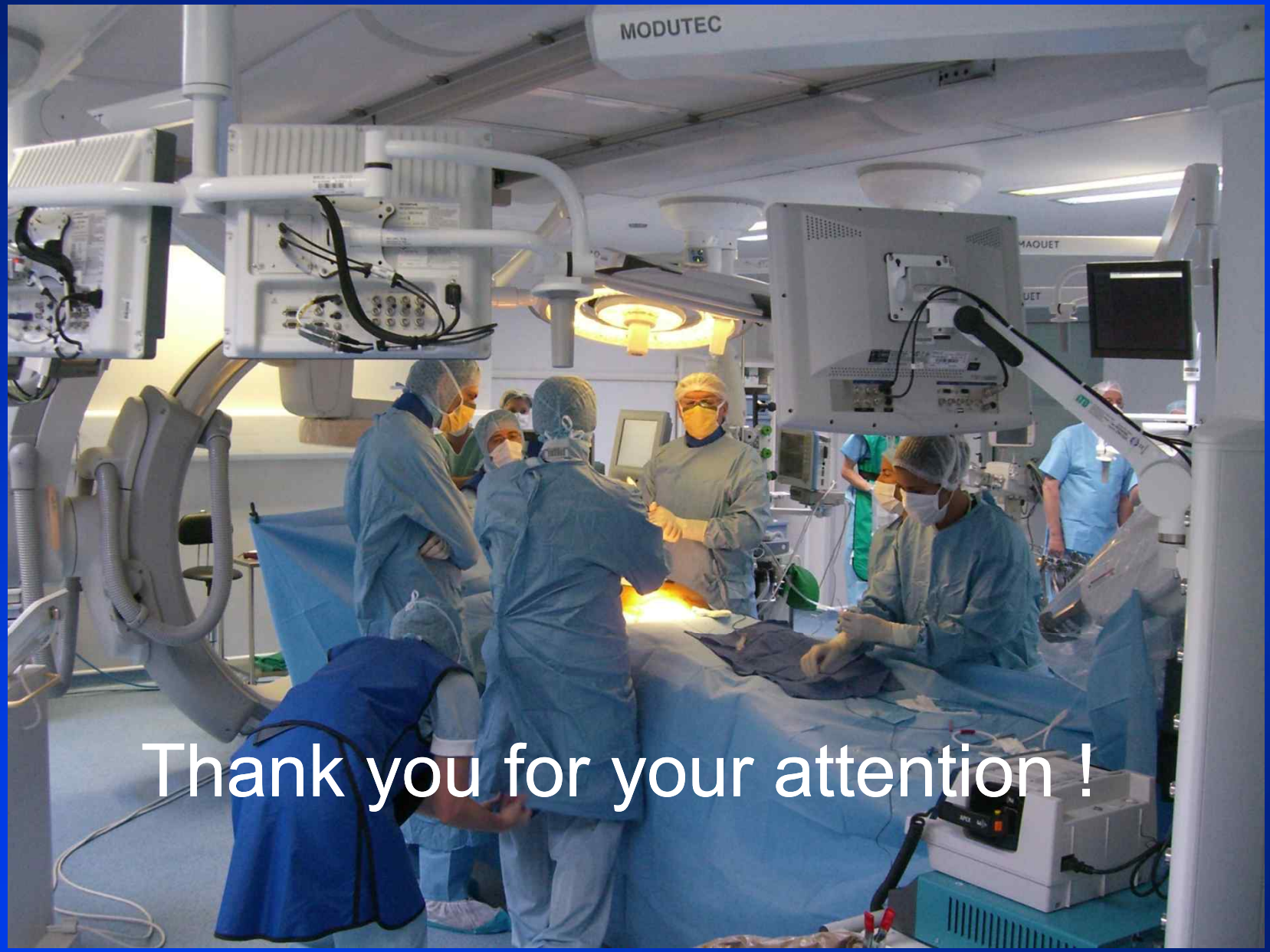


- Sheath-based delivery; flexibile, trackable, and easy AV crossing
- Adaptive “short” nitinol frame with high radial force (doesn’t obstruct CAs or MV apparatus)
- Durable bovine pericardial valve
- Controlled deployment with self-centering design facilitates accurate placement
- Early valve function ensures patient stability and excellent final trans-valvar hemodynamics
- Easily re-captured and re-positioned
- Adaptive external seal minimizes peri-valve AR

Structural Heart Disease Intervention

New Opportunities

- **We are entering a new exciting era: lesser-invasive *transcatheter treatment of Structural heart disease*.**
- **There is a *clear unmet clinical need* – many patients with structural heart disease are poorly served with either surgery or medical therapy**
- **The explosion of *innovative devices and concepts* enable us to provide a wide array of minimal invasive solutions to structural disease**
- **Multidisciplinary team approach and innovative devices are key to the success of this program**



Thank you for your attention !

Hybrid Room