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Associate Chief of Cardiology,
Washington Hospital Center, Washington DC

Structural Heart Disease Interventions
“New Opportunities to the Interventional Cardiologist with Structural Heart Disease”

Ron Waksman, MD, FACC, FSCAI
Professor of Medicine, Georgetown University,
Associate Chief of Cardiology,
Washington Hospital Center, Washington DC
Ron Waksman, MD

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

• Grants/Contracted Research
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 Disease is the MOST EXCITING new development in the field of interventional cardiovascular therapeutics!!!
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

- **Secundum**
- **Fossa Ovalis**
- **Limbus**
- **PFO Tunnel**
- **RA**
- **LA**
- **Primum**

- **Arrhythmogenic Right Ventricular Dysplasia**
- **Atrial Fibrillation**
- **Atrial Septal Defect**
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

- 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

**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**

<table>
<thead>
<tr>
<th>Genl</th>
<th>Cryptg</th>
<th>Migraine</th>
<th>Obstr</th>
<th>Sleep</th>
<th>Apnea</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>25%</td>
<td>50%</td>
<td>75%</td>
<td>100%</td>
<td>0%</td>
</tr>
</tbody>
</table>

**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

**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

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
Using radiofrequency

Septum primum and septum secundum are coapted mechanically

Then energy is applied

Thereafter, the device is removed leaving nothing behind
BioSTAR (NMT)

- CardioSEAL® framework
- STARFlex® self-centering mechanism
- Bioresorbable collagen matrix, heparin coating
- The metallic framework is not bioresorbable
BioTREK™ Bioabsorbable Septal Repair

- 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

6 months

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

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- Stenting of coarctation
- Heart failure treatment
- Valves
  - Mitral valve repair
  - Aortic valve implantation
## Transcatheter VSD Closure using the AGA Device

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

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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

### DELIVERY SYSTEM REQUIREMENTS

<table>
<thead>
<tr>
<th>Order No.</th>
<th>Diameter (mm)</th>
<th>Device Length (mm)</th>
<th>Sheath Minimum Size (inches)</th>
<th>Guide Catheter Minimum Size (inches)</th>
<th>Maximum Length (cm)</th>
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</thead>
<tbody>
<tr>
<td>9-AVP2-003</td>
<td>3</td>
<td></td>
<td></td>
<td>4 Fr</td>
<td>100</td>
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<tr>
<td>9-AVP2-004</td>
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<td>4 Fr</td>
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<td>9-AVP2-006</td>
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<td>4 Fr</td>
<td>100</td>
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<tr>
<td>9-AVP2-008</td>
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<td></td>
<td>4 Fr</td>
<td>100</td>
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<td>9-AVP2-018</td>
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<td></td>
<td></td>
<td>7 Fr</td>
<td>100</td>
</tr>
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<td>9-AVP2-020</td>
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<td>16</td>
<td></td>
<td>7 Fr</td>
<td>100</td>
</tr>
<tr>
<td>9-AVP2-022</td>
<td>22</td>
<td></td>
<td></td>
<td>7 Fr</td>
<td>100</td>
</tr>
</tbody>
</table>
Structural Heart Interventions

- ASD, PFO closure
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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
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

Non-inferiority criteria met
Safety

Freedom from device embolization, pericardial effusion, Severe bleeding

Mostly pericardial effusion without sequelae

Mostly stroke and bleeding

Days

WATCHMAN

Control

0 365 730 1,095

0.8 0.9 1.0
Other significant findings

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.
Structural Heart Interventions

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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

Not FDA approved
Dor Procedure
Aneurysm Resection

Athanasuleas CL et al, JACC 2004
VPD Implant
CT Scan

before
6 months
EF - Echo (%)  
n=13  

P<0.05
Structural Heart Interventions

- ASD, PFO closure
- VSD closure
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- 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.

What Causes It?

Two Distinct Etiologies

Primary

Intrinsic leaflet abnormalities
- Myxomatous degeneration
- Rheumatic disease
- Congenital

Functional

Incomplete coaptation caused by heart dilation
- Ischemic heart disease
- Non-ischemic cardiomyopathy
- Acute MI

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

How is it Treated?

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Primary</th>
<th>Functional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annuloplasty ring</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Edge-to-edge</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Leaflet resection</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Chordal transfer</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>LV reshaping</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>
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

- Distal Anchor
- Foreshortening Bridge
- Coronary Sinus
- Proximal Anchor
- Ostium
Catheter-Based Mitral Valve Repair

MitraClip® System

Investigational Device only in the US; Not available for sale in the US
## Clinical Experience

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVEREST I (Feasibility)*</td>
<td>Non-randomized</td>
<td>55</td>
</tr>
<tr>
<td>EVEREST II*</td>
<td>Pre-randomization</td>
<td>60</td>
</tr>
<tr>
<td>EVEREST II</td>
<td>High Risk Registry</td>
<td>78</td>
</tr>
<tr>
<td>EVEREST II (Pivotal)</td>
<td>Randomized patients (2:1 MitraClip to Surgery)</td>
<td>279</td>
</tr>
<tr>
<td></td>
<td></td>
<td>184 MitraClip 95 Surgery</td>
</tr>
<tr>
<td>REALISM (Continued Access)</td>
<td>High Risk &amp; Non High Risk</td>
<td>266</td>
</tr>
<tr>
<td>European Experience</td>
<td></td>
<td>472</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>1,115</strong> MitraClip</td>
</tr>
</tbody>
</table>


Data as of 2/15/2010.
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
EVEREST II RCT: Primary Endpoints
Per Protocol Cohort

Safety
Major Adverse Events
30 days

- Device Group, n=136
  - 9.6%
  - \( p_{\text{SUP}} < 0.0001 \)
- Control Group, n=79
  - 57.0%

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

Effectiveness
Clinical Success Rate*
12 months

- Device Group, n=134
  - 72.4%
  - \( p_{\text{NI}} = 0.0012 \)
- Control Group, n=74
  - 87.8%

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

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

**LCB** = lower confidence bound
**UCB** = upper confidence bound

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.

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

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

Onset of symptoms marks a critical point in the pathology.

How is it Treated?
Surgery is critical at the onset of symptoms.

Follow-Up (yrs)
Survival (%)
0 1 2 3 4 5
100% 80% 60% 40% 20% 0

Valve replacement
No surgery

MAJOR RISK FACTORS:
- Male
- Elderly
- LDL/HTN
- Diabetes
- Smoking

Survival (%)
Years of Age
Asymptomatic latent period
Onset of symptoms

Follow-Up (yrs)
Survival (%)
0 1 2 3 4 5
100% 80% 60% 40% 20% 0

Valve replacement
No surgery

p < 0.01
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
Sadra Lotus™ Valve System

- Sheath-based delivery; flexible, 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