Future Directions:
Structural Heart Disease Interventions

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Structural Heart Interventions

- **Shunts**
  - ASD and PFO closure
  - VSD closure
  - Fistula closure
- **Valvular heart disease**
  - Valvuloplasty
  - Paravalvular leak closure
  - Valve repair
  - Valve replacement
- **Cardiomyopathies**
  - Dilatation and stent implantation of sub- and supravalvular obstructions
  - Septal ablation
- **Left atrial appendage closure**
- **Heart failure**
  - Catheter treatment of LV aneurysms
  - LV remodeling
  - Monitoring
- **Some extracardiac diseases**
  - Patent ductus closure
  - Angioplasty/stenting of coarctation
  - Stenting of pulmonary artery stenoses
  - Stenting of pulmonary vein stenoses
  - Pulmonary AV Fistula closure
- **"Exotic interventions"**
Structural Heart Interventions

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Future Directions in PFO Closure

• Indications, reimbursement and use in daily clinical practice will depend on the results of the randomized trials
  - CLOSURE I to be presented at AHA
  - PC Trial 2011
  - If these trials are positive, PFO closure will become one of the most frequent structural heart interventions
  - If these trials are negative, the same will happen

• Technically, there is a trend towards defect anatomy specific closure techniques
  - For example in-tunnel devices

• Bioresorbable devices and closure techniques without a device are under development
Paravalvular Leak Closure
Paravalvular leaks after surgical valve replacement

- Are frequent
  - 12% echo incidence for mitral prostheses
  - 5% aortic prostheses requiring replacement
- May cause severe symptoms
  - Hemolysis, valve insufficiency
- Difficult to treat
  - Mortality for 1\textsuperscript{st} redo around 12%
  - 2\textsuperscript{nd} redo 15%
  - 3\textsuperscript{rd} redo 35%
  - Freedom from recurrence less likely with each repeat redo operation
What about device closure?

Experience is very limited
Devices

• Clamshell, Cardioseal-/Cardioseal-Starflex
  • Difficult!
  • Not retrievable
  • Bad results with Starflex due to the micro-springs
Devices

- Amplatzer
  - VSD Occluder
  - PDA Occluder
What are the Problems?

- Difficulties to cross the defect
- Difficulties to introduce the sheath due to friction
- Device may cause valve leaflet obstruction
- Residual leak due to shape of defect
- Hemolysis
- Delayed tissue covering
- Endocarditis
What are the future directions?
We now have

- Steerable sheaths

Agilis NxT
We now have

• Steerable sheaths
• Improved imaging
  - intra-cardiac echocardiography
    • Trans-venous
    • Trans-arterial
  - the first generation of 3D TEE
• A dedicated device for paravalv leaks
  - and there are more new devices to follow
With 3D TEE shape and size of defects can be visualized directly.

- Round
- Oval
- Crescentic
- Slit-like
- Crescentic cutting edge
Amplatzer Vascular Plug III

- Oval-shaped
- Thinner wires
- More wires
- Multiple layers

- Smaller pore size
- Improved surface contact
- Faster occlusion
Guiding of the Procedure

Opening of LA disc…

After rotation..still suboptimal

This could not be imaged with 2D TEE…
iCi 2010
July 7, 2010
Frankfurt, Germany

INTERVENTIONAL IMAGING:
A KEY ROLE FOR SUCCESS

www.ici-congress.org
Even with these new technologies, paravalvular leak closure is still a difficult and demanding procedure.

However, procedural complications are rare …

… they usually can be managed by catheter techniques …

… and re-do surgery can still be performed if necessary …
For these reasons catheter closure will become the primary treatment option.
Transcatheter Valve Repair

- Almost the past in the US
  - the FDA may need years
- Present in Europe
  - Almost routine in selected centers
- Future in Asia
July 8 – 10, 2010 | Frankfurt, Germany

CSI – Catheter Interventions in Congenital & Structural Heart Diseases

www.csi-congress.org
1. **Grasping**

MR decreases during clip closure
before

after
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%

Control Group, n=79
57.0%

Effectiveness
Clinical Success Rate*
12 months

Device Group, n=134
72.4%

Control Group, n=74
87.8%

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%

* 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

T. Feldman, ACC 2010
What does that mean?

• The catheter technique is as good as surgery
• Complications are 5 x less frequent as with surgery and less severe
• This is true for surgical candidates, not only for high surgical risk patients
• Without question high surgical risk patients will benefit even more from the catheter approach
Surgeons usually combine mitral valve leaflet repair with anuloplasty.

- Reduces diameter of annulus
- Pushes posterior leaflet forward for better coaptation
Percutaneous Mitral Repair

- Annuloplasty approaches
  - Coronary sinus annuloplasty
    - Edwards Monarc
    - Cardiac Dimensions Carillon
    - Viacor Shape Changing Rods
    - NIH-Cerclage
    - St. Jude Medical
    - Ample PS3
  - Direct annuloplasty
    - Mitralign Suture-based Plication
    - Guided Delivery AccuCinch
    - Cordis Direct Plication Annuloplasty
    - ReCor Medical
    - QuantumCor RF Annulus Remodeling
    - MiCardia variable size ring (hybrid)
    - Mitral Solutions (hybrid)
Annuloplasty Techniques

• Initially problems
  - Low efficacy
  - Complications due to compression of LCX

• Improved results with
  - better patient selection
  - increased operator experience
  - new devices
The PTMA Implant System

- Percutaneous subclavian access
- Permanent catheter in the coronary sinus
- Nitinol rods are progressively inserted
- Treatment effect is induced by re-shaping the coronary sinus
- Implant can be adjusted or removed
- Device action is one of bending rather than cinching between fixed anchors
Procedural MR Reduction by TEE
(PTOLEMY-1 Trial: n=13)

- No adverse events with sequelae
- < 2 hours procedure time
- MR reduction in 11/13 patients

Circulation Cardiovascular Interventions, 2009; 2:227-284 (Sack et al)
A balloon catheter is advanced via transseptal access into the left atrium.

Balloon is inflated with contrast-water and positioned at the mitral annulus.

High Frequency Ultrasound (HIFU) is delivered circumferentially to produce tissue heating.

5 applications with 80–130 W for 40-60s.

FIM 25. Feb 2010.
ReCor
Balloon position in 3D
Babic

- Percutaneous implantation of artificial chordae tendineae
Babic

Pre-implant

Post-implant
Lutter Mitral Valve Prosthesis

- Stent mounted valve
- Transapical
- Animal tests are ongoing
- Current trial:
  - Accurate positioning in 4/5 pigs
  - 4 pigs completed 7 days follow-up
  - After 7 days:
    - Correct valve position
    - Only small transvalvular and LVOT gradients
    - No migration or embolism
    - No LVOT obstruction
... and the future of mitral valve interventions?

- We will have to find out which of the many different approaches do work best
- Those will need improvement and refinement
- We will have to combine different techniques like the surgeons do
- At the end, transcatheter techniques will replace surgery as the primary approach not in all but in many patients
Aortic Valve Implantation
CoreValve & Edwards

- Already daily routine in Europe
- > 6000 patients
- Completely percutaneously
- Procedural mortality in many centers < 3%
- Excellent mid-term results
Next generation aortic valves

• Repositionable
• Retrievable
• Low profile (< 18 F sheath)
Heart Leaflet Technologies

<16 Fr retrievable

FIM 2009
Jena Valve

Unique design:
Prosthesis is "grabbing" the native leaflets

Self-expanding
Repositionable
Porcine, equine or bovine

Transapical human implantations have been performed
... and the future of transcatheter aortic valve implantation?

We will be able to (almost) completely replace conventional surgery!

And I hope very much that we can do this together with and not against the surgeons
Structural Heart Interventions in Heart Failure Patients

- Acute heart failure
  - Assist devices
- Chronic heart failure
  - Monitoring
  - Percutaneous treatment
    - Cardiac assist devices
    - Epicardial techniques
    - Intraventricular approaches
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Heart Failure: Monitoring Can Reduce Hospitalizations

Medtronic COMPASS Trial: 274 pts, Class 3 & 4

<table>
<thead>
<tr>
<th>Measure</th>
<th>p&lt;sup&gt;(a)&lt;/sup&gt;</th>
<th>% Decline</th>
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<tr>
<td>Reduction in heart failure hospitalizations and ER Visits</td>
<td>p=0.33</td>
<td>↓ 21%</td>
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<tr>
<td>Reduction in heart failure hospitalizations</td>
<td>p=0.03</td>
<td>↓ 36%</td>
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<tr>
<td>Reduction in heart failure hospitalizations: Class 3 patients</td>
<td>p=0.06</td>
<td>↓ 36%</td>
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(a) p values less than 0.05 are considered statistically significant.
CardioMEMS
Delivery System and Sensor Design

- Implantable sensor
- Measures the pressure in the pulmonary artery

HF Sensor Design:
Length: 15mm
Width: 3.5mm
Height: 2.0mm
Wire Loops: 1cm diameter
Total Length with Loops: 4.5cm
Wire Loop Function:
- Maintain alignment with vessel
- Prevent distal embolization
Patient Home Electronics Unit
Patient Data Viewed on Secure Web

Discrete Data

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<tr>
<th>Parameter</th>
<th>Value</th>
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<tr>
<td>Systolic</td>
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<tr>
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<tr>
<td>Mean</td>
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<td>Cardiac Output</td>
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<td>Signal Average</td>
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<tr>
<td>Signal Minimum</td>
<td>93</td>
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- Real-time
- Daily access
- Physician alerts
- Home transmissions
Structural Heart Interventions in Heart Failure Patients

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  - Percutaneous treatment
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Mardil’s BACE System

- Silicone band with inflatable chambers placed around LV
- Surgically implanted (minimal invasive or open chest)
- Can be remotely adjusted after implantation
- Can be removed
- FIM:
  - N = 11
  - Mean reduction in MR > 2.5
  - Improvement in heart failure
  - No device related AEs
Dor Procedure
Aneurysm Resection

- Reduces the LV size
  - reduces LV wall stress
- Improves contractility of remote myocardium

Athanasuleas CL et al, JACC 2004
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
- Two sizes (75/85mm)
- Introduced through a 14 F sheath
Case Example

BALLOON INFLATION TO EXPAND DEVICE

FULL DEPLOYMENT
Efficacy: NYHA Class

P<0.01

before

6 months

2.4

1.3
Efficacy: Six-Minute Walk

P<0.02

Before: 367
6 months: 394

CAUTION: Investigational device. Limited by US law to Investigational Use.
This Material Copyrighted and Confidential.
Left Atrial Appendage Closure
Watchman Device

- Nitinol frame
- PET membrane
- row of fixation barbs around the mid perimeter
- 21, 24, 27, 30, 33 mm

CE mark
Protect AF
(System for Embolic PROTECTion in Patients with Atrial Fibrillation)

- Multicenter
- Prospective randomized
- WATCHMAN vs coumadin 2:1
- Non-inferiority trial
- 800 pts (enrollment closed June 2008)
- > 900 patient-years
Primary Efficacy Endpoint
Freedom from Stroke, Death, Systemic Embolization

LAA closure not inferior to anticoagulation
All Stroke

Warfarin: 3.2 Events/100 patient years

LAA Closure: 2.3

P < 0.05

28%
Hemorrhagic Stroke

Events/100 patient years

Warfarin

LAA Closure

P<0.05

1.6

0.1

94%
Mortality

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<th>Events/100 patient years</th>
<th>P&lt;0.05</th>
<th>38%</th>
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<td>Warfarin</td>
<td>4,8</td>
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<tr>
<td>LAA Closure</td>
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Future Directions?
Most of us did not realize yet that this was a trial with patients who can take anticoagulation.

Left atrial appendage closure will become the primary treatment in patients with atrial fibrillation.
70 Million worldwide