Percutaneous Treatment of Mitral Regurgitation

Igor F. Palacios, M.D.
Director of Interventional Cardiology
Massachusetts General Hospital
Professor of Medicine
Harvard Medical School
Boston, MA

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New York, New York
Mechanisms of Mitral Regurgitation

- **LA cavity**
  - Posterior wall distension
  - Lack of contraction

- **Mitral Annulus**
  - Dilatation
  - Calcification

- **Leaflets**
  - Perforation
  - Cleft
  - Redundancy
  - Prolapse
  - Thickening
  - Commissural fusion

- **Chordae Tendineae**
  - Abnormal insertion
  - Elongation
  - Shortening
  - Rupture
  - Fusion
  - Thickening

- **Papillary Muscle**
  - Elongation
  - Ischemia
  - Fibrosis
  - Rupture
  - Replacement

- **LV Free Wall**
  - Lateral distension
  - Ischemia
Mitral Regurgitation: Multiple Causes

(1) Degenerative (primary MR)
(2) Functional (secondary MR)
## Organic vs. Functional MR

<table>
<thead>
<tr>
<th></th>
<th>Organic MR (Primary)</th>
<th>Functional MR (Secondary)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cause</strong></td>
<td>Disease of the <em>mitral valve leaflets</em> (i.e., myxomatous degeneration, leaflet prolapse)</td>
<td>Disease of the <em>left ventricle</em> leads to enlargement of the LV and subsequently the mitral valve annulus</td>
</tr>
<tr>
<td><strong>Standard of Care</strong></td>
<td><em>Surgical</em> mitral valve repair or replacement</td>
<td><em>Medical</em> management</td>
</tr>
<tr>
<td><strong>Emerging Technologies</strong></td>
<td>Percutaneous <em>Edge To Edge</em> repair</td>
<td>Percutaneous Valve Annulus Cinching <em>(Coronary Sinus)</em></td>
</tr>
<tr>
<td></td>
<td><em>Percutaneous Mitral Valve Replacement</em></td>
<td>Percutaneous Atrial Tethering</td>
</tr>
</tbody>
</table>

*Cardiac Dimensions*
Mitral Regurgitation 2009 U.S. Prevalence
A Largely Untreated Patient Population

Total MR Patients
1,200,000

Eligible for Treatment
(MR Grade ≥3+)
84% Untreated
Large and Growing
Clinical Unmet Need

Annual Incidence
(MR Grade ≥3+)
14% Newly
Diagnosed
Each Year

Annual MV Surgery
Only 2% Treated Surgically

Many patients are not considered appropriate candidates for mitral valve surgery

Large portion of mitral regurgitation patients are left untreated—ineligible for surgical treatment or denied surgical intervention\(^1^2\)

Factors prohibiting Surgery include\(^6\):

- Impaired LVEF
- High operative risk
- Multiple comorbidities
- Advanced age

Of surgical candidates, up to 50% of patients are not referred to surgery, even if a surgical indication exists\(^2\)

\(\text{Surgical Patients (30K)}\)
\(\text{High-Risk Patients*}^{3-5}\)
\(\text{(860K)}\)
\(\text{Surgical Candidates (850K)}\)

\* Data on file Abbott Vascular.
High Risk Eligibility Criteria (at least one)

- STS Score ≥ 8
- Prior CABG
- Hepatic Cirrhosis.
- Functional MR and LVEF < 40%
- Prior chest surgery, LVEF < 35%, and creatinine > 2.5 mg/dl
- Age > 75 and prior chest surgery and creatinine > 2.5 mg/dl
- Two (2) or more chest surgeries
Percutaneous Approaches to Structural Heart Disease

- A new field is emerging in the world of percutaneous interventional cardiology.
- The exponential growth of novel percutaneous interventions for the treatment of structural heart diseases or non-coronary cardiac diseases is overwhelming and exciting, and deserves focused attention and expertise training.
## Mitral Valve Repair Technology Summary

<table>
<thead>
<tr>
<th>Technology</th>
<th>Approach</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bowtie</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- E Valve</td>
<td>Leaflet Coupling</td>
<td>Clinical</td>
</tr>
<tr>
<td>- Edwards</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Coronary Sinus</strong></td>
<td>CS Reshaping</td>
<td>Early Clinical</td>
</tr>
<tr>
<td>- Edwards</td>
<td></td>
<td></td>
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<tr>
<td>- Viaco</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Cardiac Dimensions</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Annulus Plication</strong></td>
<td>Posterior Reshaping</td>
<td>Pre-Clinical</td>
</tr>
<tr>
<td>- Mitralign</td>
<td></td>
<td></td>
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<tr>
<td>- Guided Delivery Systems</td>
<td></td>
<td></td>
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<tr>
<td><strong>LV Shape Change</strong></td>
<td>External LA/LV</td>
<td>Clinical/Pre-Clinical</td>
</tr>
<tr>
<td>- Myocor</td>
<td></td>
<td></td>
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<tr>
<td>(Surgical/Endovascular)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PS3 Ample Medical</strong></td>
<td>Internal Direct S-L</td>
<td>Pre-Clinical</td>
</tr>
</tbody>
</table>
The double-orifice technique as a standardized approach to treat mitral regurgitation due to severe myxomatous disease: surgical technique

Francesco Maisano, Jan J. Schreuder, Michele Oppizi, Brenno Fiorani, Carlo Fino, Ottavio Alfieri

Cardiac Surgery Department, IRCCS Ospedale San Raffaele, Via Olgettina 60, 20132 Milan, Italy

Received 2 October 1999; received in revised form 30 December 1999; accepted 18 January 2000
Edge to Edge: Clinical Results
Freedom from Reoperation

Alfieri et al; 465 pts; 1991-2005

90.0 ± 3.37%
The MitraClip System is an investigational technology:
- Establishes vertical coaptation while capturing the leaflets and drawing them together
- Repositionable to allow real-time MR assessment prior to deployment
Percutaneous Mitral Valve Repair

MitraClip® System

24 French
Case Selection

- Coaptation Length: <2mm
- Coaptation Depth: >11mm
- Flail Gap: ≥10mm
- Flail Width: ≥15mm
Edge to Edge: First Case
Caracas - Venezuela
# Mitral Clip Trials

<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></td>
</tr>
<tr>
<td></td>
<td>184 MitraClip</td>
<td></td>
</tr>
<tr>
<td></td>
<td>95 Surgery</td>
<td></td>
</tr>
<tr>
<td>REALISM (Continued Access)</td>
<td>High Risk &amp; Non High Risk</td>
<td>360</td>
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<tr>
<td>European Experience</td>
<td></td>
<td>724</td>
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<tr>
<td><strong>Total</strong></td>
<td></td>
<td>1,461 MitraClip</td>
</tr>
</tbody>
</table>

Everest II Randomized Trial

Safety
Modified* Major Adverse Events
30 days

Device Group, n=180
8.3%

Control Group, n=94
42.6%

*p<0.0001

Effectiveness
Clinical Success Rate*
12 months

Device Group, n=175
66.9%

Control Group, n=89
74.2%

*p = 0.0005

* Major Bleeding Complications in place of transfusions

* Freedom from the combined outcome of death, MV surgery or re-operation for MV dysfunction >90 days post Index procedure, MR >2+ at 12 months
Freedom from MV Surgery. Everest II Randomized Trial. 2 year Results

Assessment of Device Success

51% follow-up at 2yrs

At Risk:
Device 137 136 127 122 82 56
Control 80 77 75 70 44 30
More effective reduction in MR with Surgery

Favorable LV remodeling in both groups

Better NYHA & SF-36 QOL with MitraClip
Favorable LV remodeling in both groups

Better NYHA & SF-36 QOL with Mitral Clip
Degenerative vs. Functional MR
30-day Major Adverse Cardiac Events

- DMR Device patients, n=135: 8.1%
- FMR Device Patients, n=49: 8.2%
- Control Group, n=94: 42.6%
Similar MR Reduction in Degenerative and Functional MR

DMR Cohort

Baseline
n=135

12 Months
n=87

FMR Cohort

Baseline
n=49

12 Months
n=32

2+

3+/4+

1+ 11.5%

2+ 36.8%

3+/4+ 17.2%

2+ 34.5%

1+ 21.9%

1+ 12.5%

2+ 25%
## Worldwide Experience Using the MitraClip

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>N*</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVEREST I (Feasibility)</td>
<td>Feasibility patients</td>
<td>55</td>
</tr>
<tr>
<td>EVEREST II (Pivotal)</td>
<td>Pre-randomized patients</td>
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<tr>
<td>EVEREST II (Pivotal)</td>
<td>Non-randomized patients (High Risk Study)</td>
<td>78</td>
</tr>
<tr>
<td>EVEREST II (Pivotal)</td>
<td>Randomized patients (2:1 Clip to Surgery)</td>
<td>279</td>
</tr>
<tr>
<td></td>
<td></td>
<td>184 Clip / 95 Surgery</td>
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<tr>
<td>REALISM Continued Access</td>
<td>Non-randomized patients (High Risk Patients)</td>
<td>631</td>
</tr>
<tr>
<td>REALISM Continued Access</td>
<td>Non-randomized patients (Non-High Risk Patients)</td>
<td>272</td>
</tr>
<tr>
<td>COAPT</td>
<td>Randomized patients (1:1 Clip to No Clip)</td>
<td>2</td>
</tr>
<tr>
<td>Compassionate/Emergency Use</td>
<td>Non-randomized patients</td>
<td>66</td>
</tr>
<tr>
<td>ACCESS Europe Phase I</td>
<td>Non-randomized patients</td>
<td>567</td>
</tr>
<tr>
<td>ACCESS Europe Phase II</td>
<td>Non-randomized patients</td>
<td>286</td>
</tr>
<tr>
<td>Commercial Use</td>
<td>Commercial patients</td>
<td>6,921</td>
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<tr>
<td>Total</td>
<td></td>
<td>9,122 + 95 surgery</td>
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</table>
## Patient Characteristics (first procedure only)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Commercial Patients (N=7,226)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (mean ± SD), years</strong></td>
<td>76 ± 10</td>
</tr>
<tr>
<td><strong>Male Gender, (%)</strong></td>
<td>63</td>
</tr>
<tr>
<td><strong>Etiology</strong></td>
<td></td>
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<tr>
<td>Functional MR, (%)</td>
<td>67</td>
</tr>
<tr>
<td>Degenerative MR, (%)</td>
<td>23</td>
</tr>
<tr>
<td>Mixed Etiology, (%)</td>
<td>10</td>
</tr>
</tbody>
</table>
## Left Ventricular Dysfunction

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Commercial Patients (N=7,226)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Left Ventricular Ejection Fraction (LVEF), (%)</strong></td>
<td></td>
</tr>
<tr>
<td>LVEF &lt;30%</td>
<td>33</td>
</tr>
<tr>
<td>LVEF ≥30%</td>
<td>67</td>
</tr>
<tr>
<td><strong>Left Ventricular End Systolic Diameter (LVESD), (%)</strong></td>
<td></td>
</tr>
<tr>
<td>LVESD &lt;55 mm</td>
<td>98</td>
</tr>
<tr>
<td>LVESD ≥55 mm</td>
<td>2</td>
</tr>
<tr>
<td><strong>Left Ventricular Dysfunction, (%)</strong></td>
<td></td>
</tr>
<tr>
<td>None (LVEF &gt;60% and LVESD &lt;55 mm)</td>
<td>13</td>
</tr>
<tr>
<td>Mild to Moderate (LVEF ≤60% but ≥30%, LVESD ≥40 mm but ≤55 mm)</td>
<td>48</td>
</tr>
<tr>
<td>Severe (LVEF ≤30% or LVESD ≥55 mm)</td>
<td>35</td>
</tr>
<tr>
<td>Unknown</td>
<td>4</td>
</tr>
</tbody>
</table>
Site-Reported MR Grade

Pre-Procedure

- 2+
- 3+
- 4+

Post-Procedure

- 1+

94% MR ≤ 2+ Post-Procedure
Long-term Results

Freedom from Death and Mitral Valve Surgery (Device Group) and Freedom from Death and Re-operation (Control Group), Modified ITTα (N = 258)
CONCLUSIONS

- The MitraClip device provides a non-surgical option for reduction of significant MR
- Adoption of the MitraClip therapy as a non-surgical treatment option in an underserved patient population with high risk or too high risk for surgery continues to expand, driven by procedural safety, positive patient outcomes and increasing physician experience
THE COAPT TRIAL
Clinical Outcomes Assessment of the MitraClip Percutaneous Therapy for High Surgical Risk
Purpose

- COAPT is a landmark trial to further study the MitraClip device in a FMR patient population that is too high risk to undergo mitral valve surgery
- The study will generate important clinical and economic data to support reimbursement and evidence to support the development of treatment guidelines
- COAPT is the first randomized controlled clinical trial to compare non-surgical standard of care treatment to an intervention to reduce MR
~420 patients enrolled at up to 75 US sites

- Significant FMR (≥3+ by core lab)
- High risk for mitral valve surgery
- Specific valve anatomic criteria

Randomize 1:1

- **MitraClip**
  - N=210

- **Control group**
  - Standard of care
  - N=210

Clinical and TTE follow-up:
- 1, 6, 12, 18, 24, 36, 48, 60 months
Primary Endpoints

- **Primary Effectiveness** (min 1-year FU all pts)
  - Recurrent heart failure hospitalizations
    - Superiority hypothesis (Andersen-Gill)
- **Primary Safety** (1 year)
  - Composite of all-cause death, stroke, worsening kidney function, or LVAD or cardiac transplant
    - Non-inferiority hypothesis
Secondary Endpoints

• Secondary Effectiveness
  – MR severity at 12 months
  – Change in 6MWD at 12 months
  – Change in quality of life score (KCCQ) at 12 months
  – Change in LVEDV at 12 months
  – Reduction to NYHA Functional Class I/II at 12 months

• Secondary Safety
  – Composite of death, stroke, MI, non-elective CV surgery for device related complications in Device group at 30 days
  – All-cause mortality at 12 months (non-inferiority hypothesis with 6% delta)
Key Inclusion Criteria (1)

- Functional MR $\geq 3+$ due to cardiomyopathy of either ischemic or non-ischemic etiology, confirmed by the Echo Core Lab
- Symptomatic (NYHA class II, III or ambulatory IV)
- STS mortality risk is $\geq 8$% OR Local Site Heart Team concludes that co-morbidities result in a prohibitive predicted operative risk of stroke or death.
- Subjects who do not meet the STS mortality risk criterion of $\geq 8$% can be included in the trial if the Local Site Heart Team and the Central Eligibility Committee concur and document that the subject’s predicted operative risk of stroke or death is prohibitive for open mitral valve surgery for reasons not captured by the STS risk calculator.
• The subject has had at least 1 HF hospitalization in the 12 months prior to enrollment and/or BNP ≥400 pg/ml or nT-proBNP ≥1600 pg/ml measured within 90 days prior to enrollment
• Subject adequately treated per applicable standards for CAD, LV dysfunction, MR or HF (CRT, revascularization, and/or OMT) before enrollment
• The primary regurgitant jet originates from malcoaptation of the A2 and P2 scallops of the mitral valve. If secondary MR jets exist, they must be considered clinically insignificant.
Key Exclusion Criteria (1)

- The subject has severe LV dysfunction based on an echocardiogram obtained within 6 months prior to enrollment (severe LV dysfunction is defined as LVESD >60mm or LVEF<20%)
- MV area <4 cm2
- MI in the prior 90 days
- Untreated clinically significant CAD requiring revascularization
- CVA or TIA within 6 mo or severe carotid stenosis
Key Exclusion Criteria (2)

- Any PCI, carotid or endovascular intervention or carotid surgery within 30 days, or any coronary or endovascular surgery within 6 months
- CRT and/or ICD implant or revision within 90 days
- Leaflet anatomy which may preclude MitraClip implantation, proper MitraClip positioning on the leaflets or sufficient reduction in MR
- Severe right ventricular failure or severe TR
Indirect Annuloplasty: Coronary Sinus Devices

- **CARILLON** (Cardiac Dimensions)
- **PTMA** (Viacor)
- **MONARC** (Edwards Lifesciences)
- Schematic representation of the atrial remodeling PS3 device (A)
- and the Left Ventricular remodeling iCoapsys device (B).
Direct Annular Plication Concept.

Direct Annular Plication in an Ovine Model Using the Accucinch Device.

96 patients implanted
25 extracted because of coronary compromise
11 reimplanted more proximally.
88% in Funct. Class 1-2 at 6 months
CARILLON Mitral Contour System

HEART CENTER
Theoretical Challenges of CS Approach

1) Possible compromise of circumflex artery
2) Variable distance of CS to valve annulus
The AMADEUS™ Trial

CARILLON™ Mitral Annuloplasty Device European Union Study

Cardiac Dimensions® CARILLON™ Mitral Contour System™

- Prospective single-arm multi-center trial
  - 7 European centers (6 Active); Total of 30 patients with implants

- **Primary Endpoint:** Safety of deploying and implanting the device in the coronary sinus and great cardiac vein of subjects with functional MR (30 day MAE)

- **Secondary Endpoint:** Long-term safety and effect of the device on hemodynamics and subject function @ 1, 3, and 6 months
  - Safety @ 6 months
  - NYHA Class
  - Exercise
  - MR Reduction
  - QOL
Inclusion / Exclusion

**INCLUSION:**
- NYHA Class > II
- FMR > 2+ (NYHA II with FMR 2+ not eligible)
- LVEDd > 55mm
- EF < 40%
- 6 MWT distance between 150m & 450m
- Stable on heart failure medication

**EXCLUSION:**
- Recent hospitalization for cardiac surgery, revascularization, unstable angina
- Presence of chronic atrial fibrillation
- Presence of left atrial appendage clot
- Creatinine > 2.2mg/dL
- Presence of coronary sinus pacing leads
- Life expectancy of < 1 year
## Baseline Demographics
Patients with Implants (n=30)

<table>
<thead>
<tr>
<th></th>
<th>AMADEUS™ Trial</th>
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<tbody>
<tr>
<td>Age</td>
<td>66.5 (47-81 yrs)</td>
</tr>
<tr>
<td>Gender</td>
<td>M = 86.7% (26) F = 13.3% (4)</td>
</tr>
<tr>
<td>NYHA Class</td>
<td>II - 6</td>
</tr>
<tr>
<td></td>
<td>III - 22</td>
</tr>
<tr>
<td></td>
<td>IV - 2</td>
</tr>
<tr>
<td>EF</td>
<td>31.6% avg. (12.5 – 39.9)</td>
</tr>
<tr>
<td>MR</td>
<td>2+ = 4</td>
</tr>
<tr>
<td></td>
<td>3+ = 20</td>
</tr>
<tr>
<td></td>
<td>4+ = 6</td>
</tr>
<tr>
<td>LVEDD</td>
<td>65.7mm (55 – 77mm)</td>
</tr>
<tr>
<td>History of CAD</td>
<td>72.2%</td>
</tr>
<tr>
<td>Ischemic Disease</td>
<td>57.1%</td>
</tr>
<tr>
<td>History of PTCA</td>
<td>55.6%</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>20.0%</td>
</tr>
<tr>
<td>History of Arrhythmias</td>
<td>44.4%</td>
</tr>
</tbody>
</table>
3) CS/GCV Position Relative to Annulus

**METHOD**

1) Measurements made at midpoint of each third – P1, P2, P3

2) Distances measured from edge of annulus to middle of vein lumen in x, y, z directions
1) AMADEUS™ Procedural Success
Permanent Implants

- Procedural Success = Acute MR reduction and a permanent implant
- No devices are left in unless MR is reduced at the time of the implant
- Learning curve, improved technique, device modification increased the success rate
2) Managing Coronary Arteries

**Frequency of Crossing**
- 84%
- 16%
43 Cases
- Cross Artery
- No Artery

**Implant Rate when Artery Crossed**
- 83%
- 17%
36 Cases w/Crossed Arteries
- Implant
- No Implant

- Arteries can be successfully managed with CARILLON™ System
  - Operator determines precise implant location
  - Operator determines amount of tension
  - Recapture feature allows for immediate relief of any compromise

- In AMADEUS, 11 cases of crossed arteries required “Recapture”
  - In 5 of those a 2nd device was successfully placed more proximal
Observed Intra-Procedural Complications

- **Coronary Sinus (CS) Access**
  - Trauma to CS
    - 2 perforations; 1 dissection; All patients recovered
    - Related to early experience with CS access
    - Risk minimized by introduction of a curved delivery catheter
  - Proper equipment and technique facilitate success
    - Soft-tip guidewire
    - Appropriate access catheter size and shape
    - Telescoping technique

- **Maintenance of Fluid Balance**
  - 1 case of transient pulmonary edema
  - Volume loading to support arterial pressure may have contributed
5) Acute Intra-procedural MR

- TEE was used in all patients intra-procedurally to determine acute MR reduction

- Acute MR reduction was required to leave a device
  - Visual assessment was done in all 30 patients
  - Grade $3.0 \pm 0.6$ to $2.0 \pm 0.8 \,(p<0.0001)$
5) Acute Intra-procedural MR
Quantitative MR Performed in Final 20 Patients

- Vena Contracta: 0.69 cm, 0.46 cm
- EROA: 0.33 cm², 0.19 cm²
- Regurgitant Volume: 40 ml, 24 ml
- % Area: 45%, 32%
MONARC Device

- Bioabsorbable bridge connected to self-expanding stents/anchor
- Gradual MR improvement 3-6 weeks.
- Remodels the posterior annulus by displacing it anteriorly

Nitinol Bridge with bioabsorbable spacers

Distal Anchor

Proximal Anchor

Coronary Sinus
6 Month Follow Up: Primary Efficacy
≥ 1 MR grade reduction (72 pts)
6 Month Follow Up MR Severity

**EVOLUTION I Clinical Study**
MACE = Device migration, Death, Device Embolization, Cardiac Tamponade, Coronary sinus thrombosis or Pulmonary embolism
Evolution I. Conclusions

- At 6 Month Follow Up:
  - Lower rehospitalization for cardiac events
  - 92% of patients had MR reduction > 1+
  - Device is durable with no observed fractures or separations

- At 3 year Follow up:
  - At 36 months, 64% of patients are event free.
  - Encouraging 36-mnths results compared to baseline on MR reduction and NYHA class improvement.

- Program discontinued by industry sponsor in spite of no major safety or efficacy concerns. **EVOLUTION II clinical study** at current pace would take several years to complete.
PTOLEMI II: 2.8% 30 day MACE and 90% procedural success
Stefan Sack et al on behalf of the PTOLEMI II Trial
PTOLEMI II: 2.8% 30 day MACE and 90% procedural success
Stefan Sack et al on behalf of the PTOLEMI II.
Mitraling Brident Approach

Grube et al. 12 FIM cases

- Two plications in two locations: P1-P2 and P2-P3
- Minimum permanent implants
  - 4 surgical pledgets
  - 2 locks to lock the sutures after plication

[Images of mitral valve procedures]
Mitraling Brident Approach

New Bident Design

Before Plication

Bench test

20 mm

Computer model

Bench test

12 mm

- Maximum reduction of the septo-lateral dimension can be achieved by plication of two pairs of pledgets at the P1 and P3 location of the annulus.
Mitraling Bristent Approach

Before

After
Place the guide catheter against the posterior wall
Percutaneous Septal, Sinus Shortening
Septal Sinus Shortening (The ARTO™ System) for the Treatment of Functional Mitral Regurgitation: 6-Month MAVERIC Trial Results

Marie-Claude Morice, MD
Institut Cardiovasculaire Paris Sud
Générale de Santé
Massy, France

for the MAVERIC Investigators

Andrejs Erglis, Jason H. Rogers, Martyn Thomas, Marie Claude Morice, Inga Narbute, Milana Zabunova, Thomas Hovasse, Mathieu Poupineau, Ainars Rudzitis, Ginta Kamzola, Ligita Zvaigzne, Samantha Greene, Jason H. Rogers
Magnet Tipped Catheters

MagneCath™ Delivery
# MAVERIC Trial

**MitrAL ValvE RepaIr Clinical Trial**

<table>
<thead>
<tr>
<th>Safety and feasibility</th>
<th>30 Patient, multi-center</th>
</tr>
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<tbody>
<tr>
<td>Outcome measures</td>
<td>Phase I: Riga, Latvia</td>
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<tr>
<td></td>
<td>- Andrejs Erglis, PI</td>
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<td>Phase II: add UK &amp; France</td>
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<td></td>
<td>- London - Simon Redwood, PI</td>
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<td></td>
<td>- Massy Philippe Garot, PI</td>
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<tr>
<td>Key inclusion criteria</td>
<td>Trial management</td>
</tr>
<tr>
<td></td>
<td>- Management: CERC</td>
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<td>- Core lab: CERC</td>
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<td>DSMB approved the</td>
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<tr>
<td></td>
<td>continuation of the trial</td>
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<tr>
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<td>- France &amp; Latvia approval</td>
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</tbody>
</table>

- Safety and feasibility
- Outcome measures
  - Major Adverse Event rate to 30 days and 6 months
  - Reduction of MR at 30 days and 6 months
  - Device placement success
- Key inclusion criteria
  - Refused for MV surgery
  - Optimal HF medication
  - NYHA Class II-IV Symptomatic MR ≥ 2+
### MAVERIC Safety Events

**Pt. 003 – GCV dislocation into LA at 30d**
- No clinical symptoms at 30 d f/u
  - MR = 1+ from 3+
  - NYHA = 2 from 3
- Patient well enough for sMVR on day 65

### Event Timing

<table>
<thead>
<tr>
<th>Event</th>
<th>Procedure N=11</th>
<th>1 to 30 Days N=11</th>
<th>31-180 Days N=10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Stroke</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mitral Operation/Intervention</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Bleeding Complication</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pericardial Effusion</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

**Pt. 011 – Posterior effusion on day 5**
- Surgically evacuated on day 15
- Likely caused by GW in LAA (on Coumadin with low INR)

**Pt. 011 – Atraumatic Tip Separation at 6 mo.**
- No impact to safety or efficacy
- Fullly in-grown and retained in GCV
COAPSIS LV Remodeling
Transcatheter Mitral Valve Implantation

Engineering Prototype – Sheep Implant

Animal work encouraging...
Transcatheter Mitral Valve Implantation (TMVI)

1. Transseptal Access of MV
2. Sub-Annular Positioning
3. Anchoring
Percutaneous MV Replacement

- Transseptal approach
- Valve sparing (like repair)

- Immediately function
- Repositionable

Neither design frozen
Transcatheter Mitral Valve Implantation.

Conclusions

• Percutaneous therapy has emerged as an option for treatment of mitral regurgitation for selected, predominantly high-risk patients. Most of the percutaneous approaches are modifications of existing surgical approaches.

• Catheter-based devices mimic these surgical approaches with less procedural risk, due to their less-invasive nature. Percutaneous annuloplasty can be achieved indirectly via the coronary sinus or directly from retrograde left ventricular access.
Catheter-based leaflet repair with the MitraClip is accomplished with an implantable clip to mimic the surgical edge-to-edge leaflet repair technique. A large experience with MitraClip has been reported, and several other percutaneous approaches have been successfully used in smaller numbers of patients to demonstrate proof of concept, whereas others have failed and are no longer under development.

There is increasing experience in both trials and practice to begin to define the clinical utility of percutaneous leaflet repair, and annuloplasty approaches are undergoing significant development. Transcatheter mitral valve replacement is still in early development.
Igor F. Palacios, M.D.
Director of Interventional Cardiology
Massachusetts General Hospital
Professor of Medicine
Harvard Medical School
Medical History

- **ID/CC:** 69 y/o F with diabetes, chronic renal insufficiency, dilated cardiomyopathy with LVEF 26% s/p BIV/ICD therapy and severe MR presents to clinic with increasing dyspnea on exertion.

- **HPI:**
  - Patient presented with dyspnea in 1998
    - Cardiac catheterization revealed no significant epicardial disease. TTE demonstrated dilated and diffusely hypokinetic LV with EF 25%
  
  - Over the following 15 years, patient followed with serial echocardiograms, which demonstrated continued EF < 35% with moderate-severe MR
HPI continued:

- Patient had intermittent presentations for chest pain over the following years
  - Serial stress echocardiograms were negative for ischemia
  - Catheterization in 2010 and 2011 demonstrated moderate, non-obstructive coronary artery disease

- In 2011, the patient had an AICD placed for primary prevention

- In 2012, the patient had an upgrade of her AICD to a BiV device after multiple admissions for CHF exacerbations
HPI continued:

– Patient initially did well with CRT, however she had a series of 5 admissions to the hospital in the spring of 2013 for CHF exacerbations and syncope in the setting of volume changes.

  • Titration of heart failure regimen complicated by recurrent orthostasis and syncope.

    – Lability in volume status thought to be exacerbated by severe MR

– Patient presented with dyspnea on minimal exertion (e.g. walking 1 block, walking up 3 steps, performing ADLs). She requires oxygen PRN for her symptoms.
Past Medical History
- Idiopathic Dilated Cardiomyopathy s/p BiV-ICD as detailed above
- Non-obstructive coronary artery disease
- Insulin-dependent diabetes Mellitus
- Chronic renal insufficiency (Cr 1.43)
- Hypertension
- Hypercholesterolemia
- GERD
- Asthma
- Hx of obesity s/p gastric bypass surgery in 2010
- Hx of ITP in 2010 treated with IGG and Decadron
- Vitamin D deficiency
- s/p TAH/BSO

Medications at Home
- Aspirin 325mg QD
- Advair 1 puff BID
- Albuterol inhaler PRN
- Cymbalta 30mg BID
- Ergocalciferol 1000U QD
- Gabapentin 600mg QHS
- Lantus 8U SC QHS
- Lasix 40mg QD
- Losartan 12.5mg QD
- Prilosec 40mg BID
- Simvastatin 40mg QD
- Singulair 10mg QHS
- Sucralfate 1gm TID
- Toprol XL 25mg QD
- Trazodone 25mg QD
- Vitamin B12 1000mcg QD

Social Hx: denies T/D/A
Family Hx: Denies family history of idiopathic cardiomyopathy
Baseline Echocardiogram
• Patient referred to cardiac surgery for evaluation for MVR
  – Deemed high risk for surgery (STS 6.4% without accounting for pulmonary hypertension, history of ITP and general frailty)

• Further steps considered
  – Medical Management
  – Percutaneous treatment of functional MR with MitraClip
Etiology and Epidemiology of Functional Mitral Regurgitation

- Estimated 500,000 patients in the United States suffer from functional MR

- Results from
  - Annular enlargement
  - Papillary muscle displacement
Treatment Options for Functional Mitral Regurgitation

- **Medical Therapy**
  - Medications (ACE-Inhibitors or ARBs; Beta blocker; Diuretics; Aldosterone antagonist)
  - Device Therapy with CRT

- **Surgical Therapy**
  - Usually in form of mitral annuloplasty
  - Data limited to small, single center observational studies
  - No clear evidence of long-term mortality benefit, although it may improve symptoms
  - Guidelines do not support routine isolated MVR for severe MR secondary to ventricular dilatation
Concepts Behind MitraClip System

- Based on Alfieri surgical edge-to-edge repair
  - Approximate A2 and P2 and suture together

- Pathophysiologic Effects of Edge-to-Edge Repair
  - Facilitates proper leaflet coaptation
  - Creates tissue bridge
  - Restrains LV wall
The MitraClip System
Advancing MitraClip Through the Left Atrium Mullins Introducer
3D TEE of Guide-Wire in the Left Atrium via Transseptal LHC
3D TEE of Guide Wire Parked in Left Upper PV
Crossing the Mitral Valve with the MitraClip Device
3D TEE of MitraClip Open in the Mitral Plane
3D TEE of MitraClip Open in the Mitral Plane
3D TEE of MitraClip Open in the Mitral Plane
3D TEE of MitraClip Open in the Mitral Plane
3D TEE MitraClip
Grabbing the Mitral Leaflets
Release of the MitraClip Device
Release of the MitraClip Device
Release of the MitraClip Device
Color 3D TEE Mitral Clip Deployed
Pre and post MitraClip Deployment

Pre MitraClip

Post MitraClip
One Month

Six Month

One and Six Months post MitraClip Deployment
Baseline and 1 year post MitraClip Deployment

Baseline

1 Year F/U