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Percutaneous Treatment of Mitral Regurgitation

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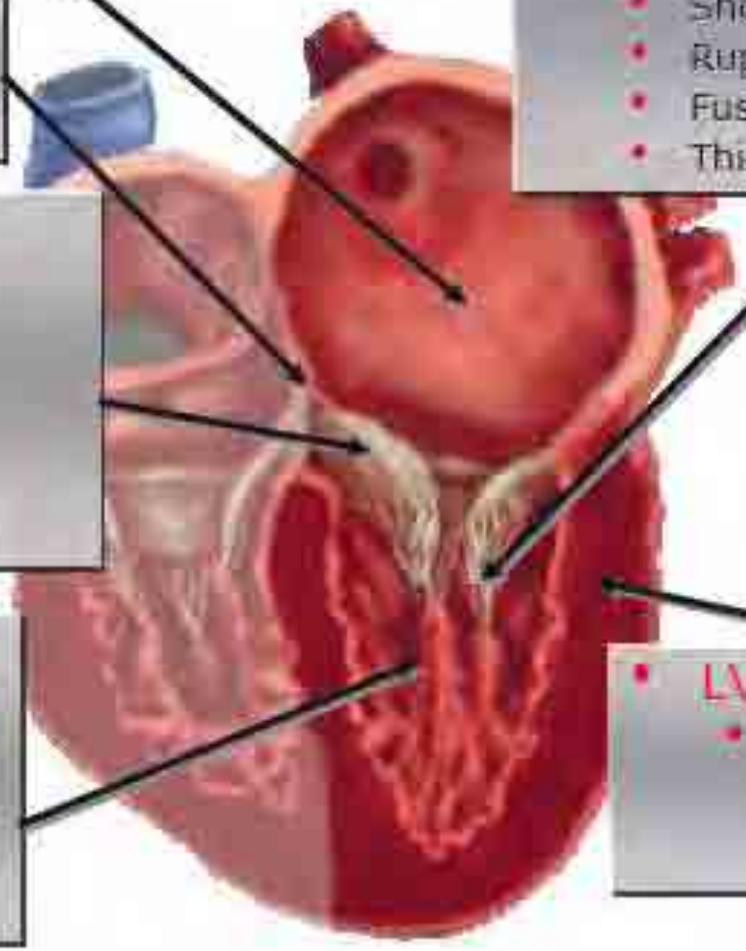
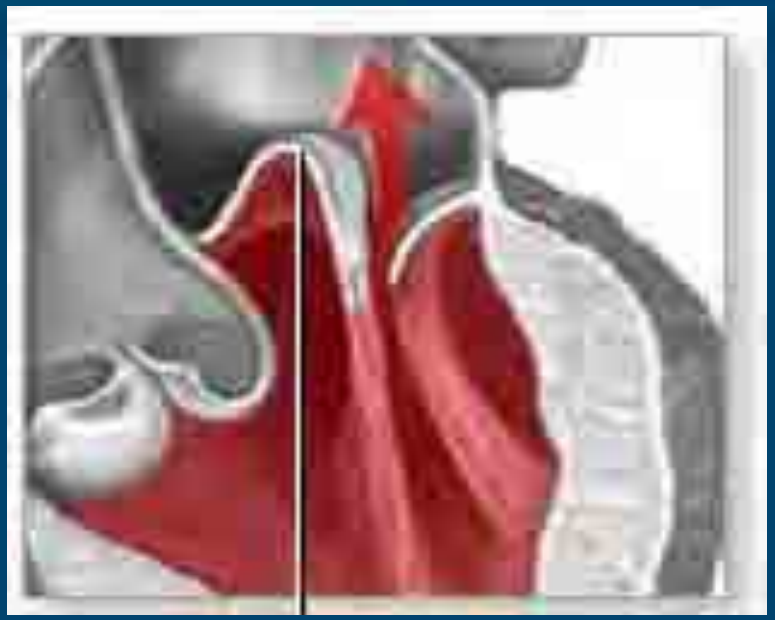
Mechanisms of Mitral Regurgitation

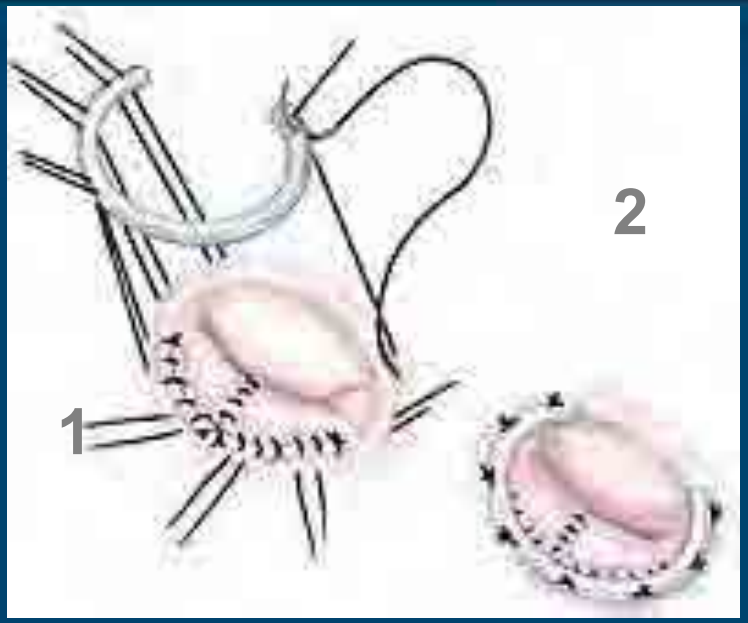
- LA cavity
  - Posterior wall distension
  - Lack of contraction
- Chordae Tendineae
  - Abnormal insertion
  - Elongation
  - Shortening
  - Rupture
  - Fusion
  - Thickening
- Mitral Annulus
  - Dilatation
  - Calcification
- Leaflets
  - Perforation
  - Cleft
  - Redundancy
  - Prolapse
  - Thickening
  - Commissural fusion
- Papillary Muscle
  - Elongation
  - Ischemia
  - Fibrosis
  - Rupture
  - Replacement
- LV Free Wall
  - Lateral distension
  - Ischemia



Degenerative Mitral Regurgitation



Mis-aligned and thickened leaflets allows backflow of blood into the left atrium

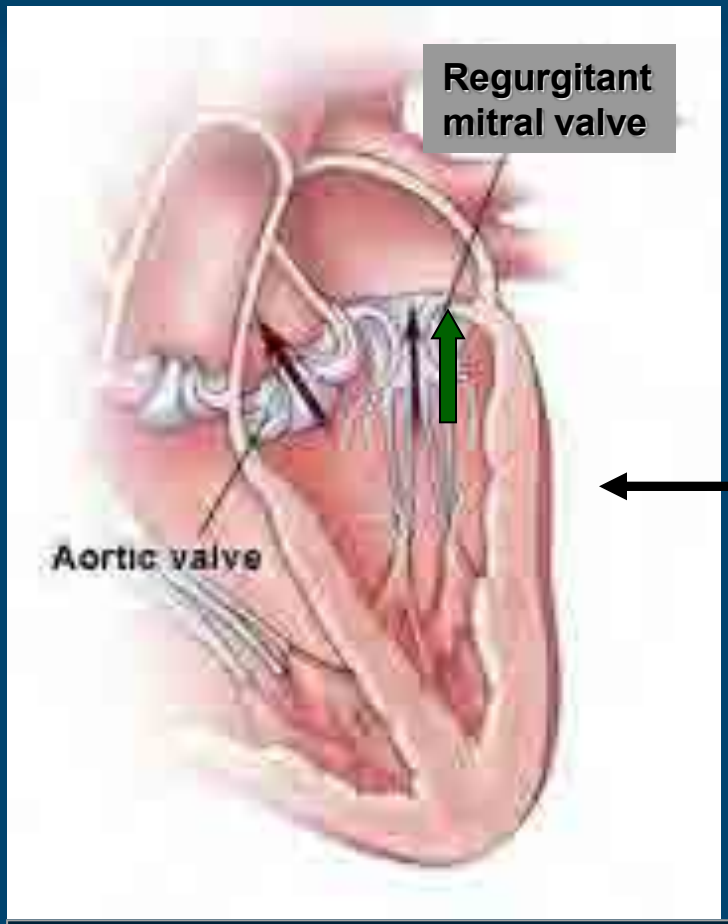


Surgical Leaflet Repair:
Excellent Outcomes
Limited to Centers of Excellence

Pts are typically referred for surgery when MR reaches 3-4+, left ventricular size has increased, functional status has become impaired, and the surgical risk is acceptable

Functional Mitral Regurgitation

MR caused by ischemic heart disease or cardiomyopathy



"MR begets MR"

Enlargement of the left ventricle leads to displacement of the papillary muscles and mitral leaflets with annular dilatation → MR

Left atrial enlargement

↓

Left ventricular dysfunction

↓

Increase in left ventricular size and remodeling

Pts are generally <u>not</u> considered for surgery, and are maintained on medical therapy for control of CHF sx

Device Landscape: Percutaneous MV Repair

Edge-to-edge (2)
- eValve Pivotal completed!
- Edwards Mobius

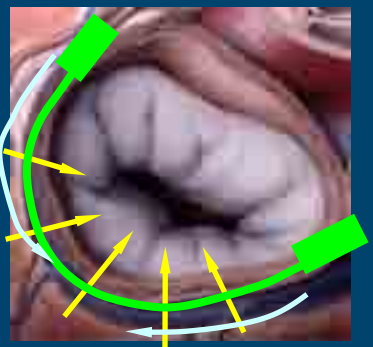
Coronary sinus annuloplasty (3)
- Edwards Monarc
- Cardiac Dimensions Carillon
- Viacor PTMA

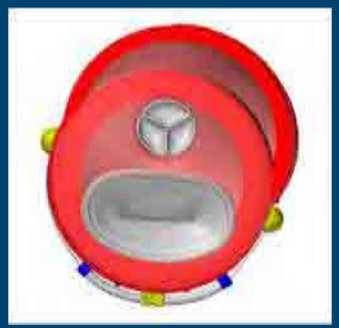
Indirect annuloplasty (3)
- Ample PS3
- Myocor i-Coapsys
- St. Jude AAR

Direct annuloplasty (5)
- Mitralign
- Guided Delivery Systems
- QuantumCor, Cordis DPA
- MiCardia, Mitral Solutions

Mitral valve replacement (1)
- Endovalve



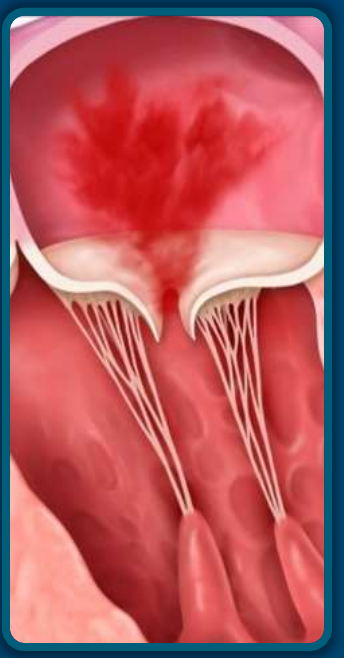
Mitral Regurgitation: Multiple Causes

Normal Mitral Valve

Degenerative MR: Prolapse

Degenerative MR: Flail

Functional MR



(1) Degenerative (primary MR)

(2) Functional (secondary MR)

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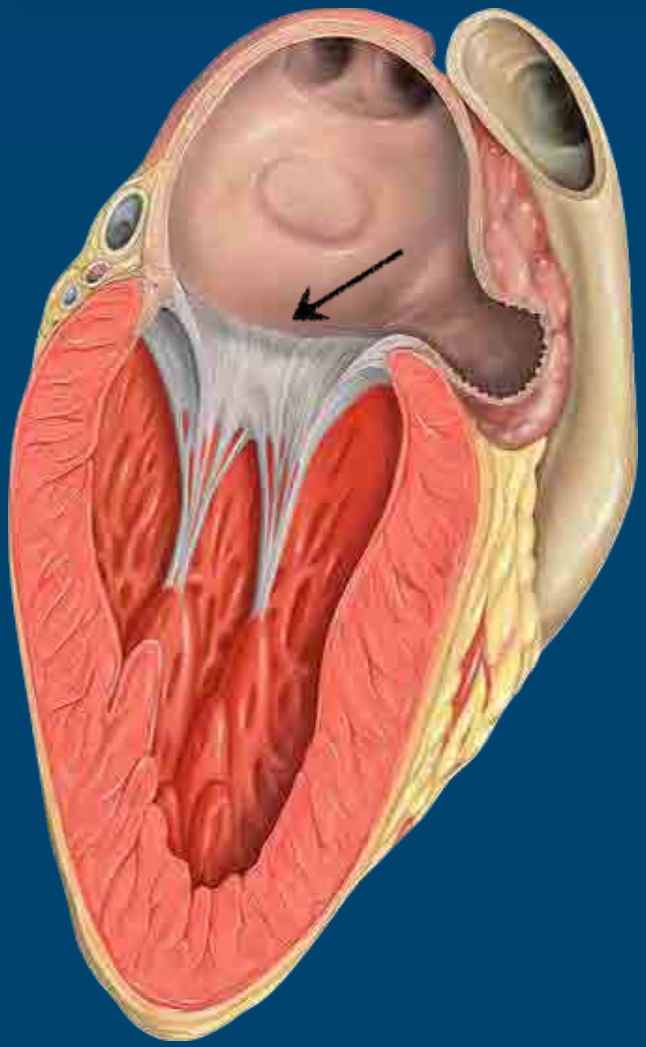
Organic vs. Functional MR

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

EDGE-TO-EDGE

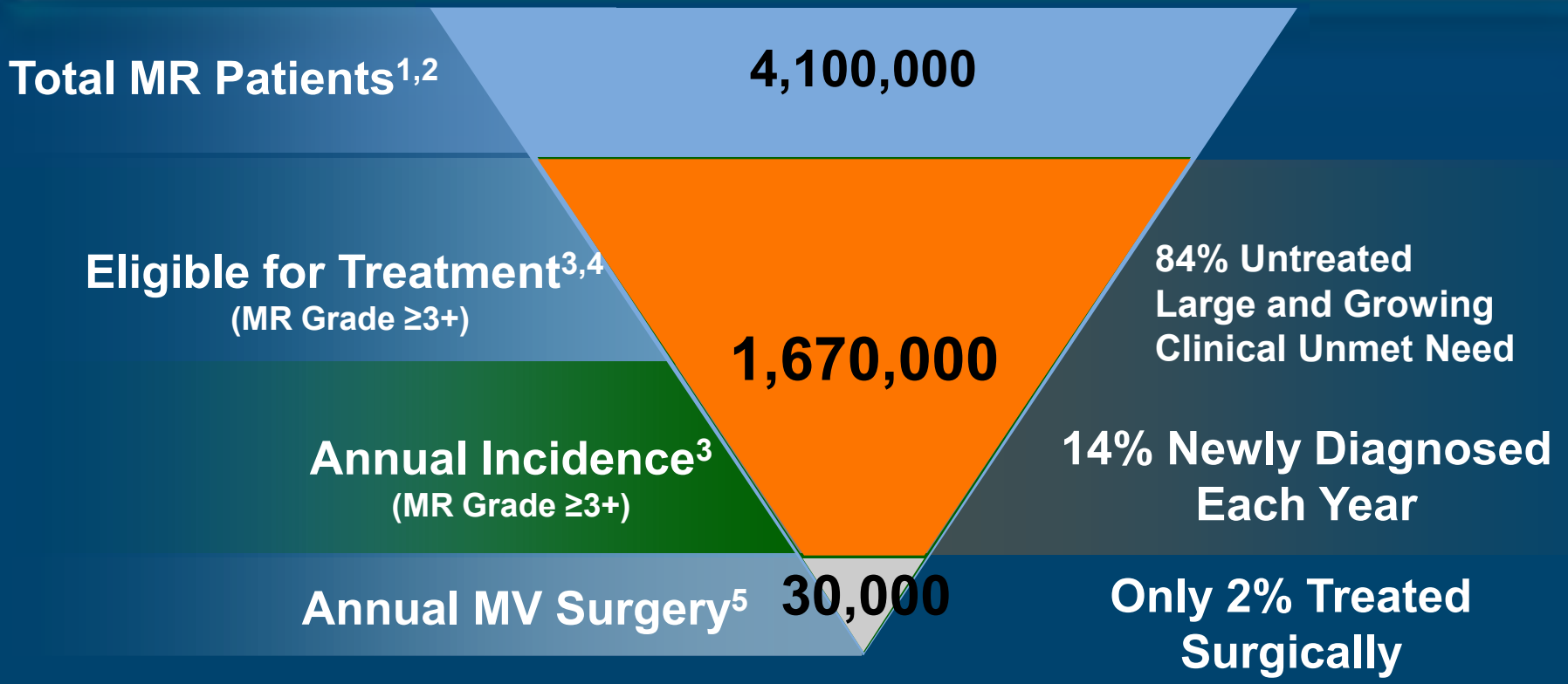


- ***MitraClip (1)***
- Status: Randomized trials
- Limitations: Durable?, MS
- ***MitraFlex***
- Status: Preclinical
- Limitations: Durable?, MS

- **LEAFLET COAPTATION**
- ***Percu-Pro (2)***
- Status: Phase 1 trial
- Limitations: thrombus formation, MS

- **LEAFLET ABLATION**
- ***Thermocool (3)***
- Status: Animal models
- Limitations: Not precise, leaflet perforation

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



1. US Census Bureau. Statistical Abstract of the US: 2006, Table 12.
2. Nkomo et al. Burden of Valvular Heart Diseases: A Population-based Study, Lancet, 2006; 368: 1005-11.
3. Patel et al. Mitral Regurgitation in Patients with Advanced Systolic Heart Failure, J of Cardiac Failure, 2004.
4. ACC/AHA 2008 Guidelines for the Management of Patients with Valvular Heart Disease, Circulation: 2008
5. Gammie, J et al, Trends in Mitral Valve Surgery in the United States: Results from the STS Adult Cardiac Database, Annals of Thoracic Surgery 2010.

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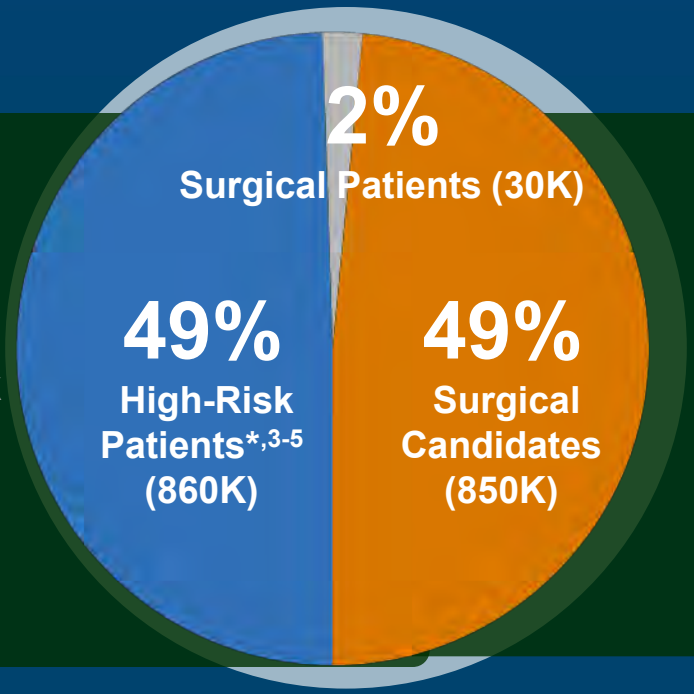
Many patients are not considered appropriate candidates for mitral valve surgery

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]

1. Lung B, et al. *Eur Heart J.* 2003;24:1231-1243.
2. Mirabel M, et al. *Eur Heart J.* 2007;28:1358-1365.
3. U.S. Census Bureau, Statistical Abstract of the U.S.
4. Nkomo et al. Burden of Valvular Heart Diseases: A Population-based Study, Lancet, 2006; 368: 1005-11.
5. Patel, et al. Mitral Regurgitation in Patients with Advanced Systolic Heart Failure, J of Cardiac Failure, 2004.
6. Rankin, et al, J of Thoracic and Cardiovascular Surgery, March 2006.

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Treatment Options in USA

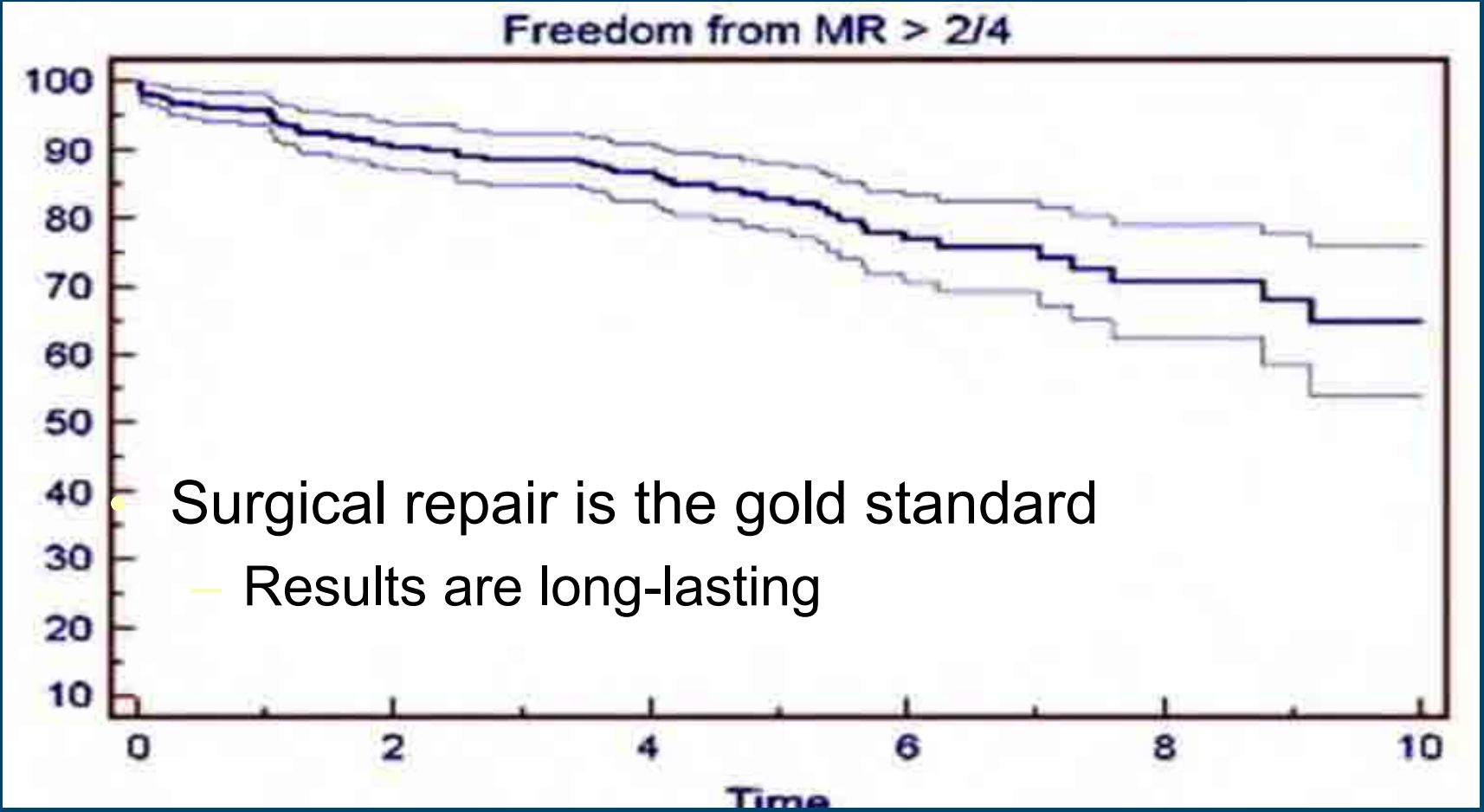
- Medical Therapy
  - First course of therapy – limited role
- Surgery
  - Repair or replacement
  - Class I indication for some
  - Proven effective

Why Percutaneous Valve Repair?

- Surgical repair is the gold standard
  - Surgical Mortality is low

NYHA Class	Mortality for Repair (%)
Class I	0.64
Class II	0.87
Class III	1.80
Class IV	3.71

Why Percutaneous Valve Repair?



- Surgical repair is the gold standard
  - Results are long-lasting

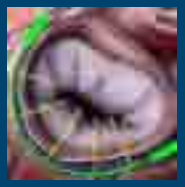
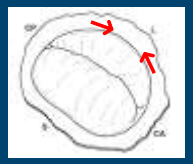
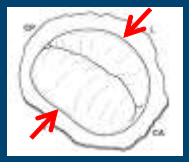
All Patients NOT Candidates for Surgery

- Multiple, serious co-morbidities increase risk of surgical mortality and morbidity
- Benefits of surgery do not outweigh risks
- In the USA, these patients are left with no other treatment option
- Physicians struggle with the management of these high surgical risk patients

High Risk Eligibility Criteria (at least one)

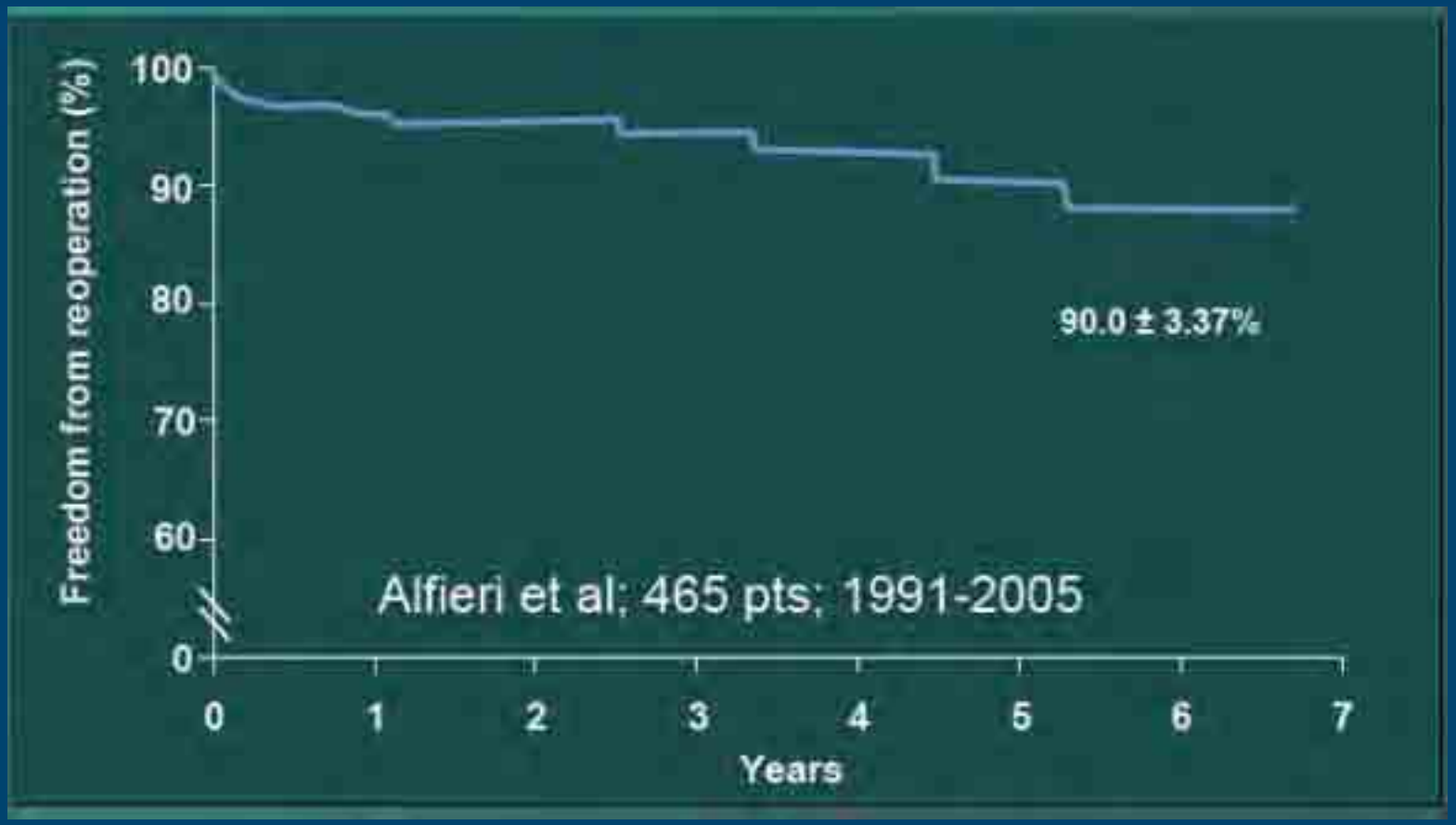
- STS Score ≥ 8
- Prior CABG
- Hepatic Cirrhosis.
- Functional MR and LVEF < 40%
- Prior chest surgery, LVEF < 35%, and creatinine > 2.5 mg/dl
- Age > 75 and prior chest surgery and creatinine > 2.5 mg/dl
- Two (2) or more chest surgeries

Mitral Valve Repair Technology Summary

Technology	Approach		Status
Bowtie • E Valve • Edwards	Leaflet Coupling		Clinical
Coronary Sinus • Edwards • Viaco • Cardiac Dimensions	CS Reshaping		Early Clinical
Annulus Plication • Mitralign • Guided Delivery Systems	Posterior Reshaping		Pre-Clinical
LV Shape Change • Myocor (Surgical/Endovascular)	External LA/LV		Clinical/ Pre-Clinical
PS3 Ample Medical	Internal Direct S-L		Pre-Clinical

The Alfiere Operation - 2000

Edge to Edge: Clinical Results
Freedom from Reoperation



MitraClip System

- 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

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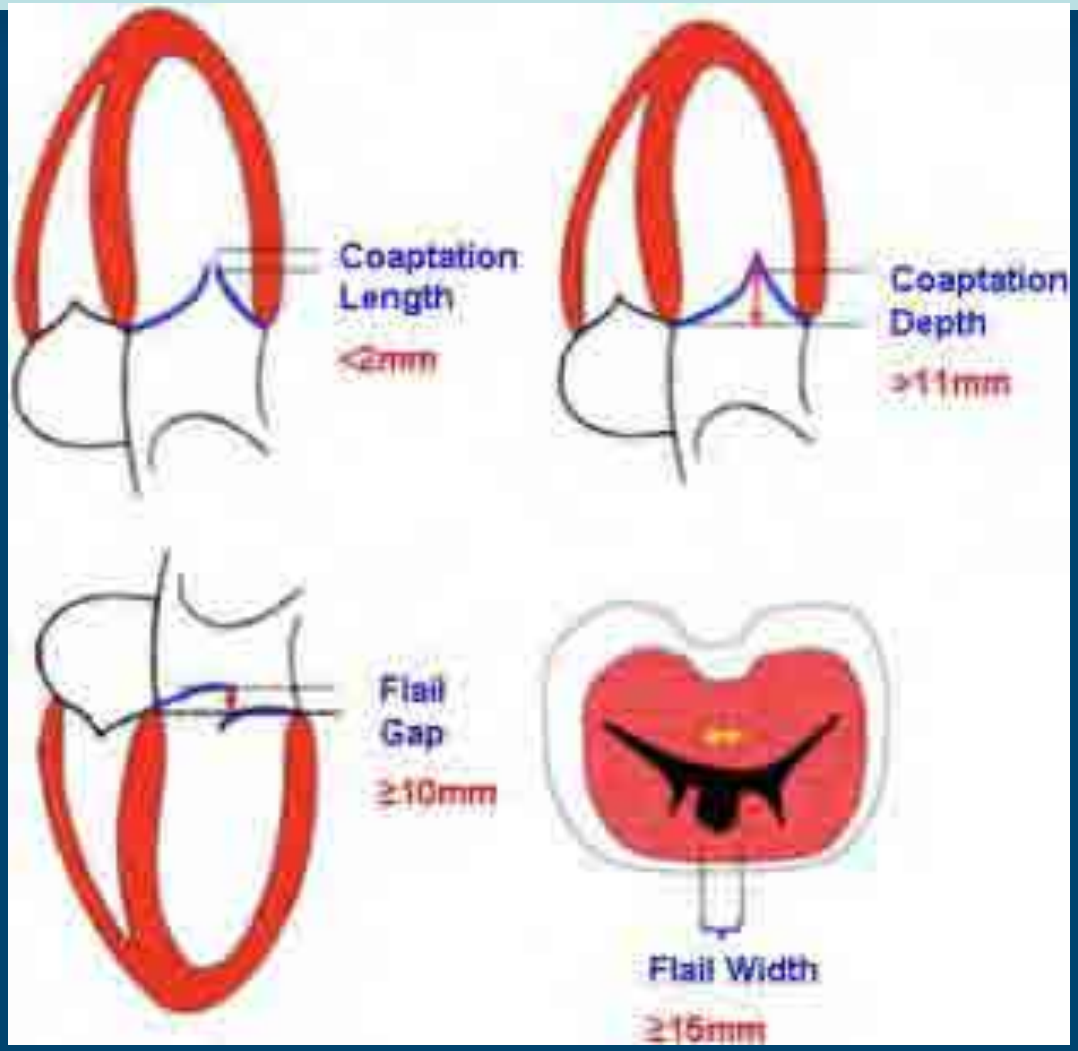
Case Selection

Case Selection



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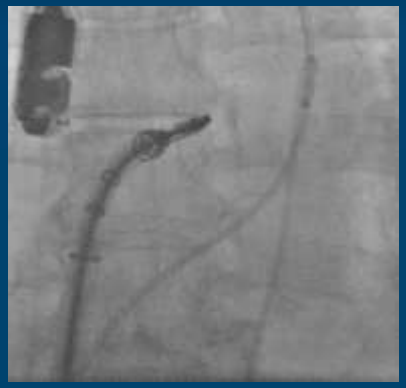
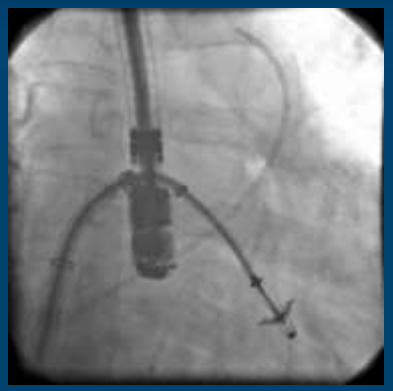
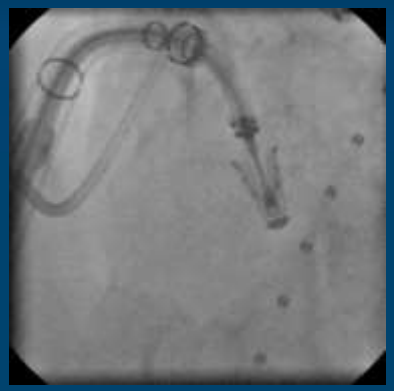
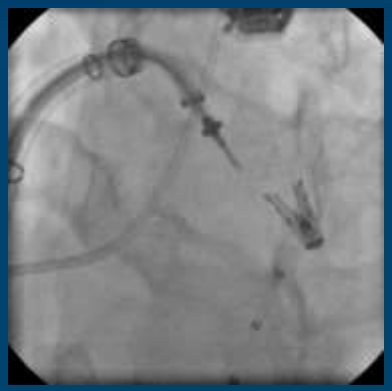
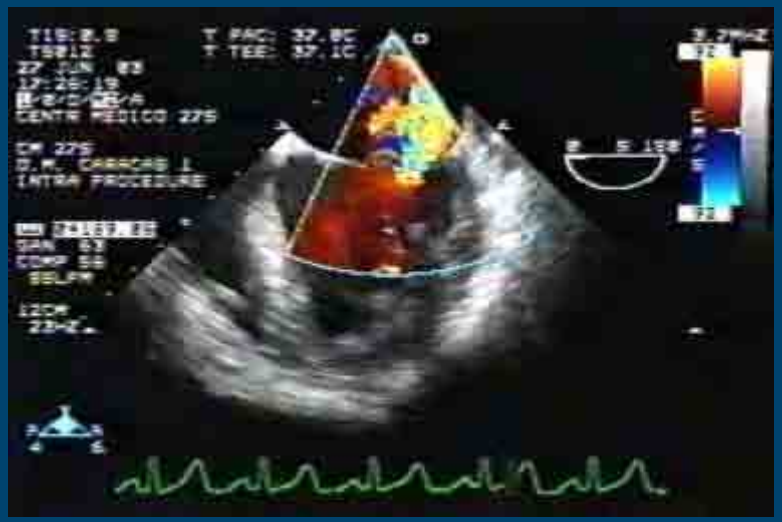
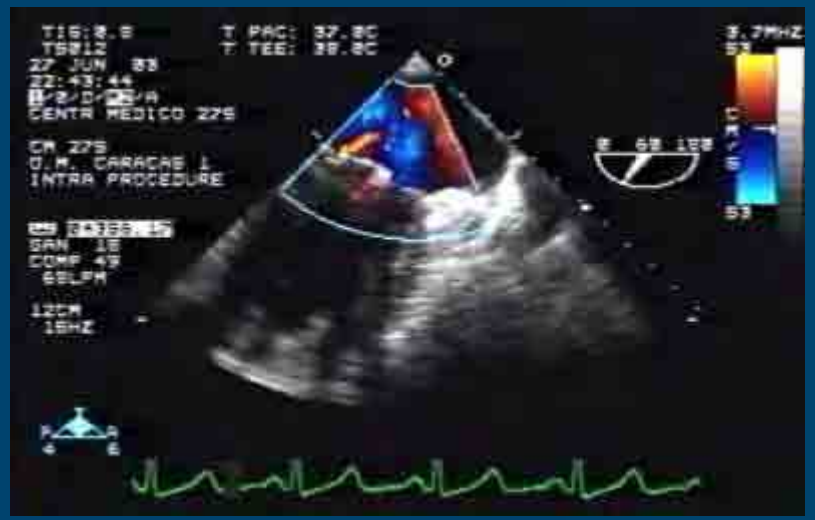
Edge to Edge: First Case
Caracas - Venezuela





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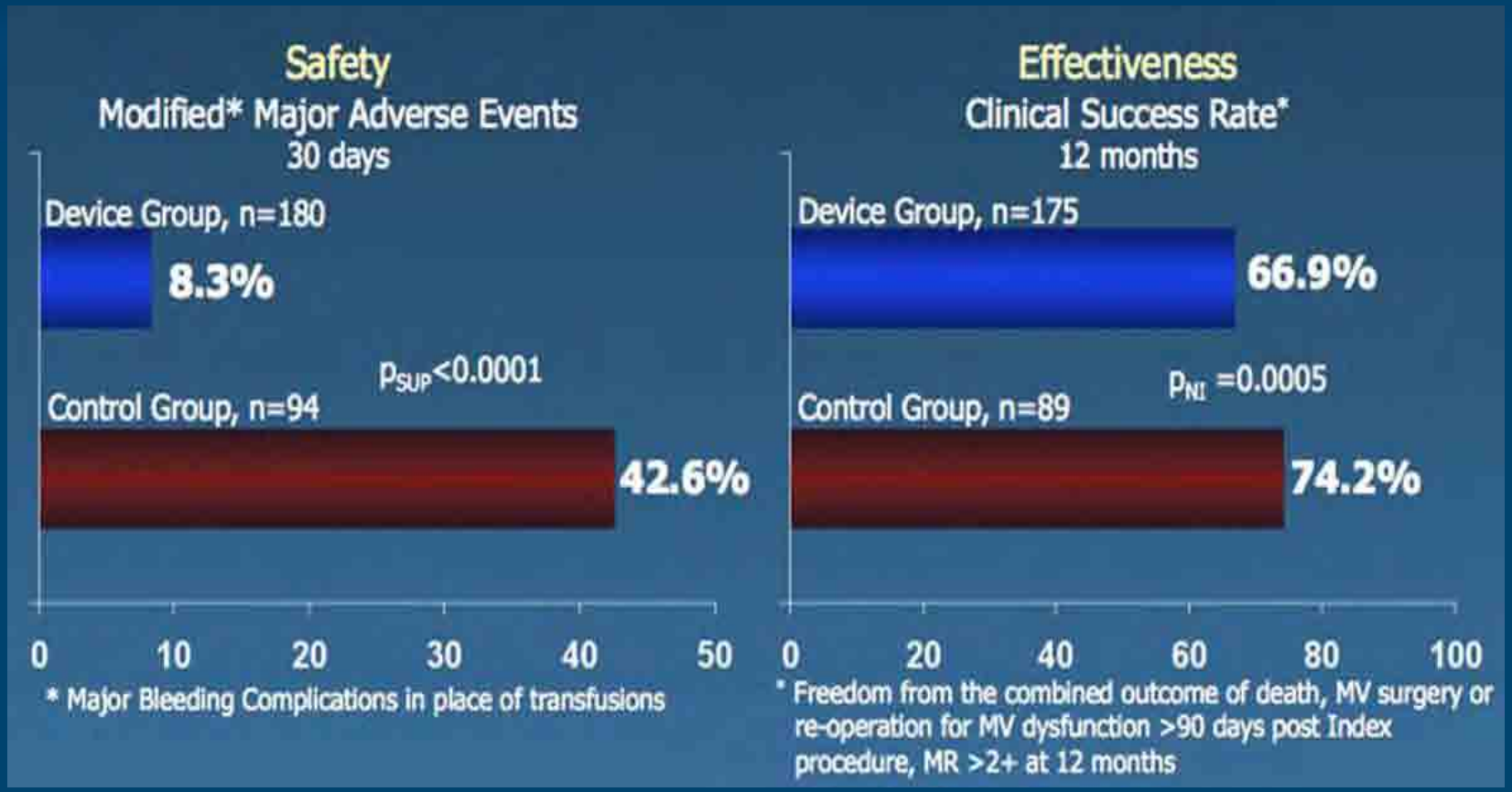
Mitral Clip Trials

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	360
European Experience		724
	Total	1,461 MitraClip

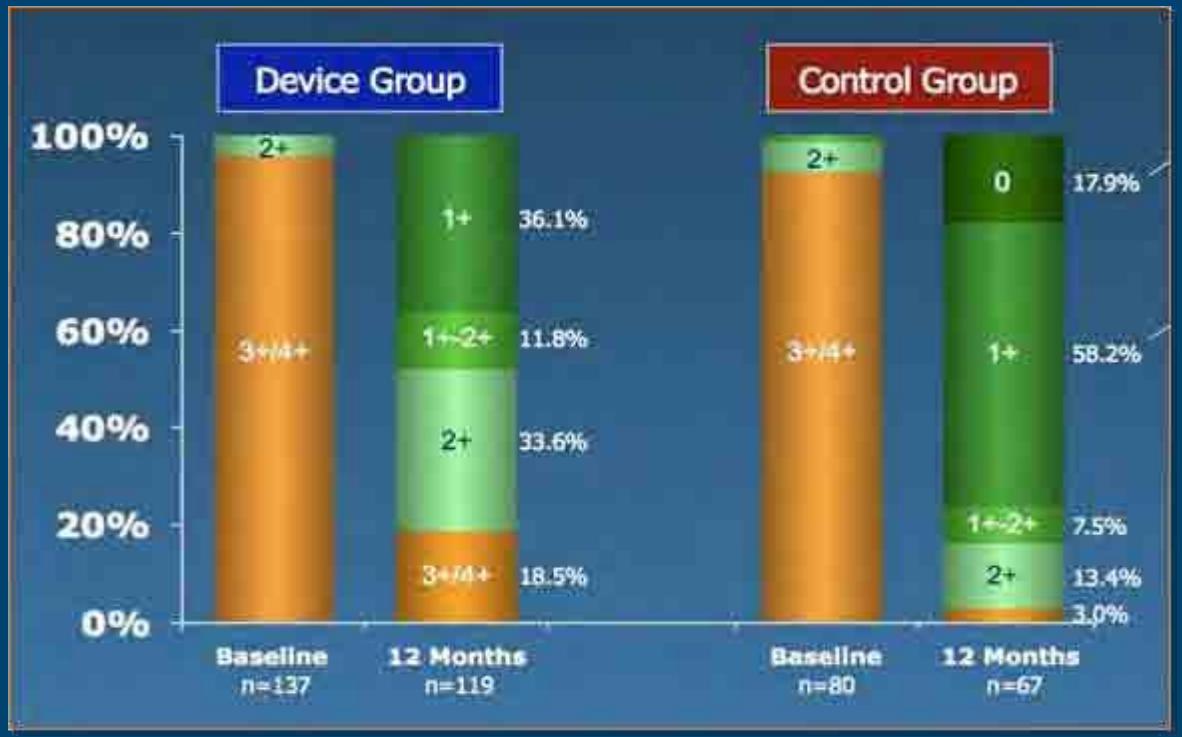
*Percutaneous Mitral Valve Repair Using the Edge-to-Edge Repair: Six months Results of the EVEREST Phase I Clinical trial, JACC 2005;46:2134-2140.
Percutaneous Mitral Repair with the MitraClip System: Safety and Midterm Durability in the Initial EVEREST Cohort, JACC 2009; 54:686-694.

Everest II Randomized Trial



More effective reduction in MR with Surgery

More effective reduction in MR with surgery



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

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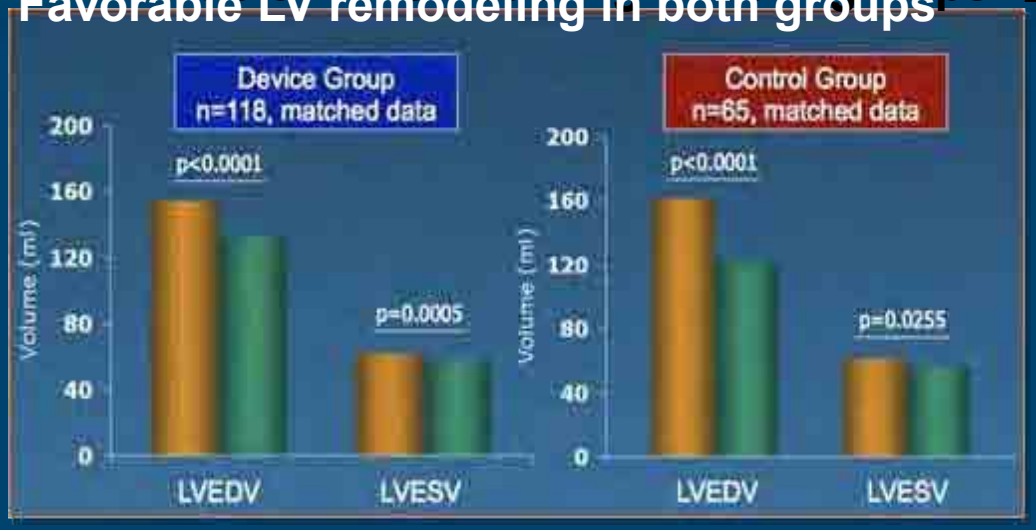
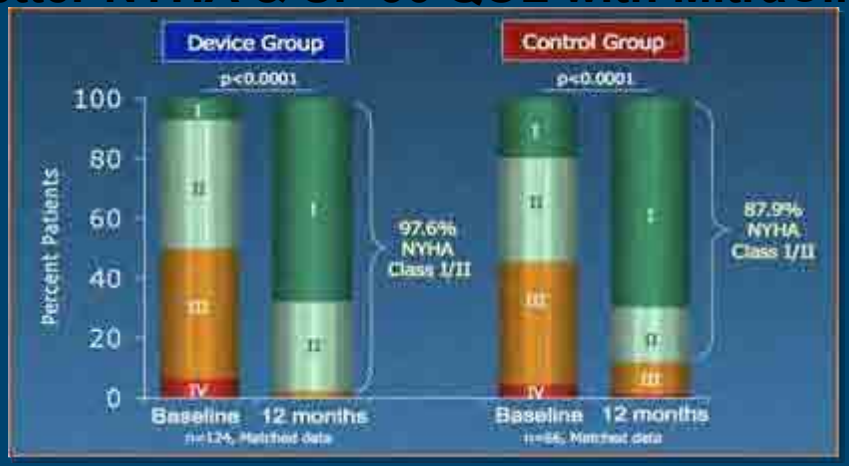
effective reduction in MR with surgery

EVEREST II Final Results

Favorable LV remodeling in both groups



Better NYHA & SF-36 QOL with Mitral CLip



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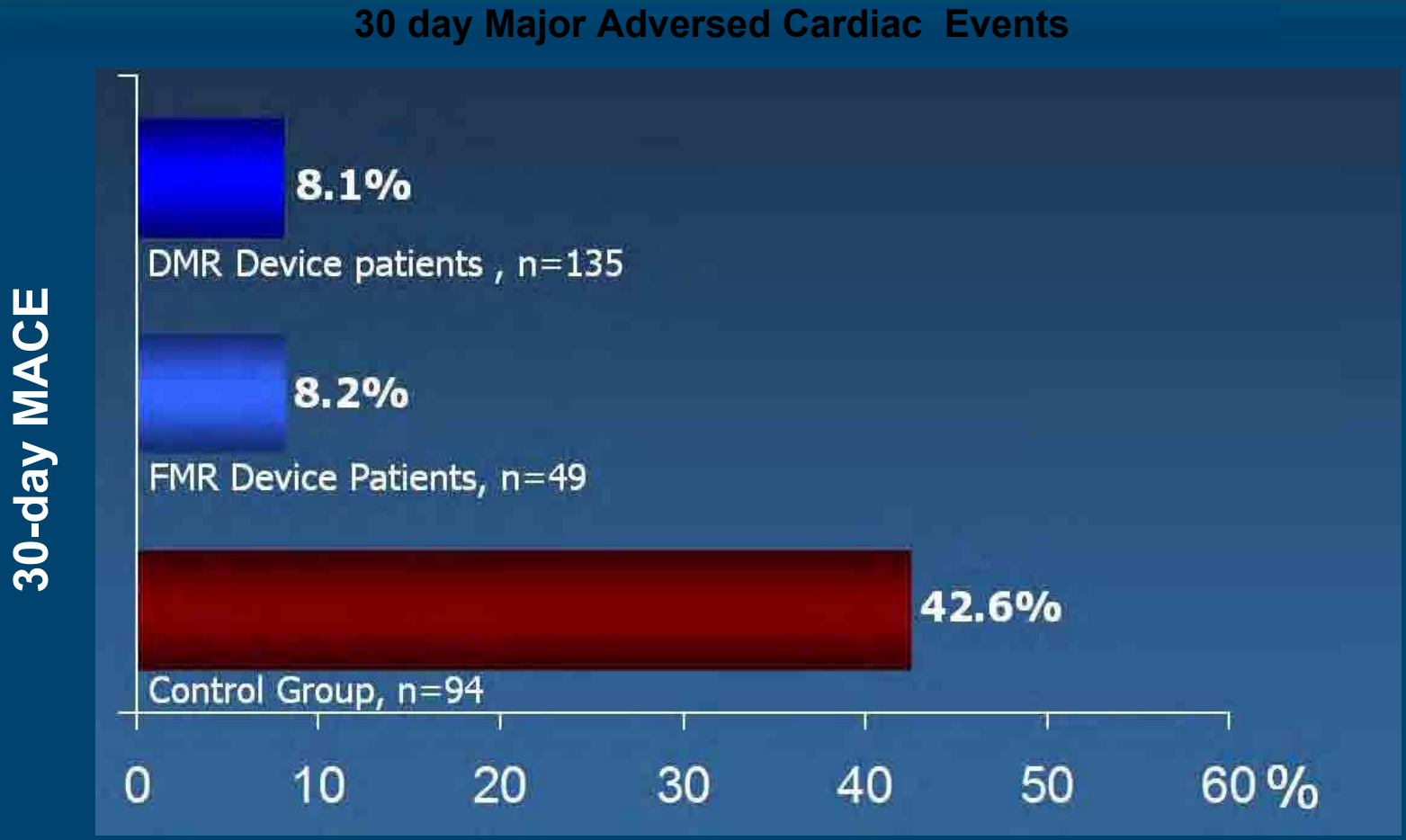
Degenerative vs. Functional MR
30-day Major Adverse Cardiac Events



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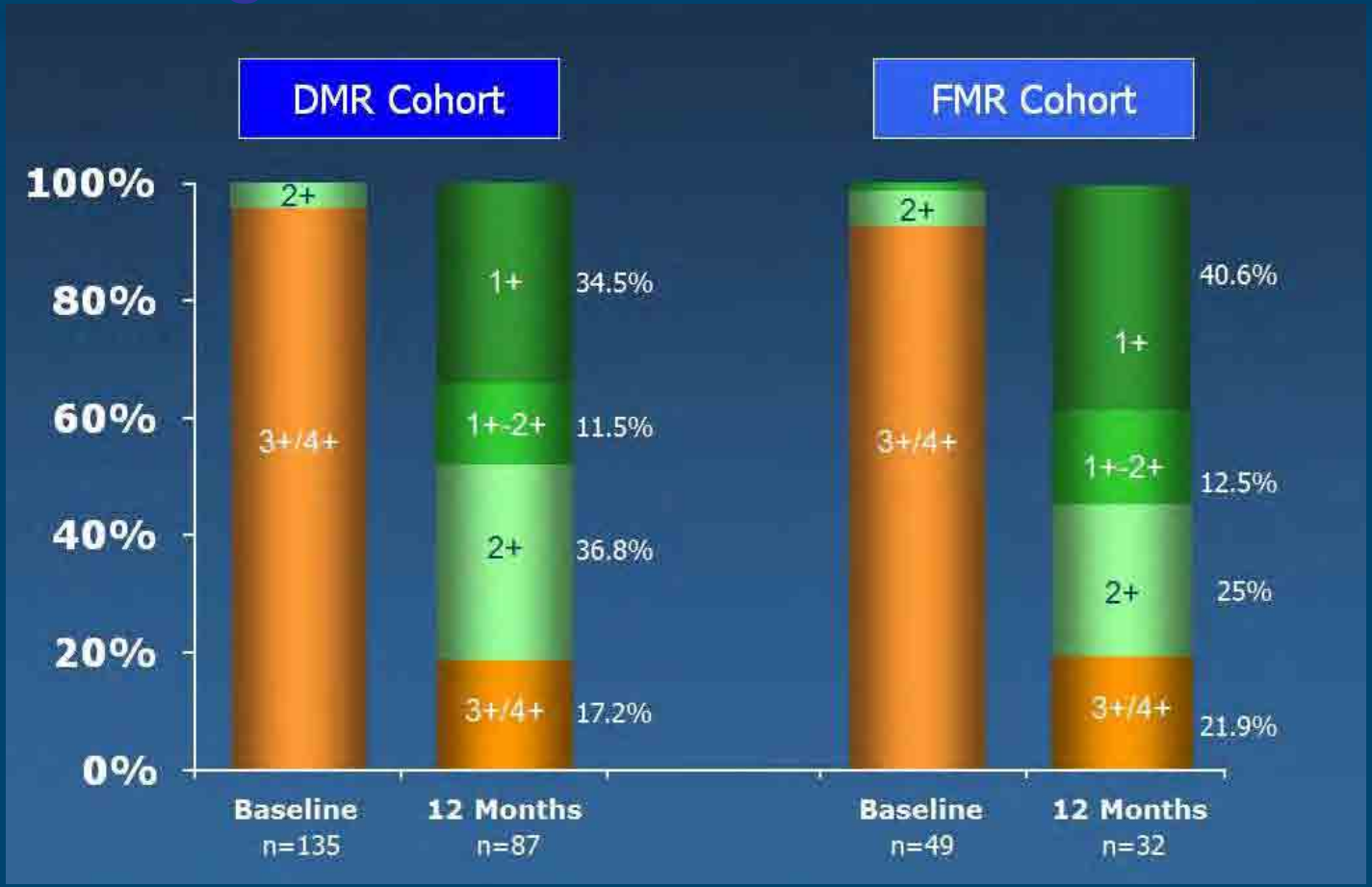
Similar MR Reduction in Degenerative and Functional MR



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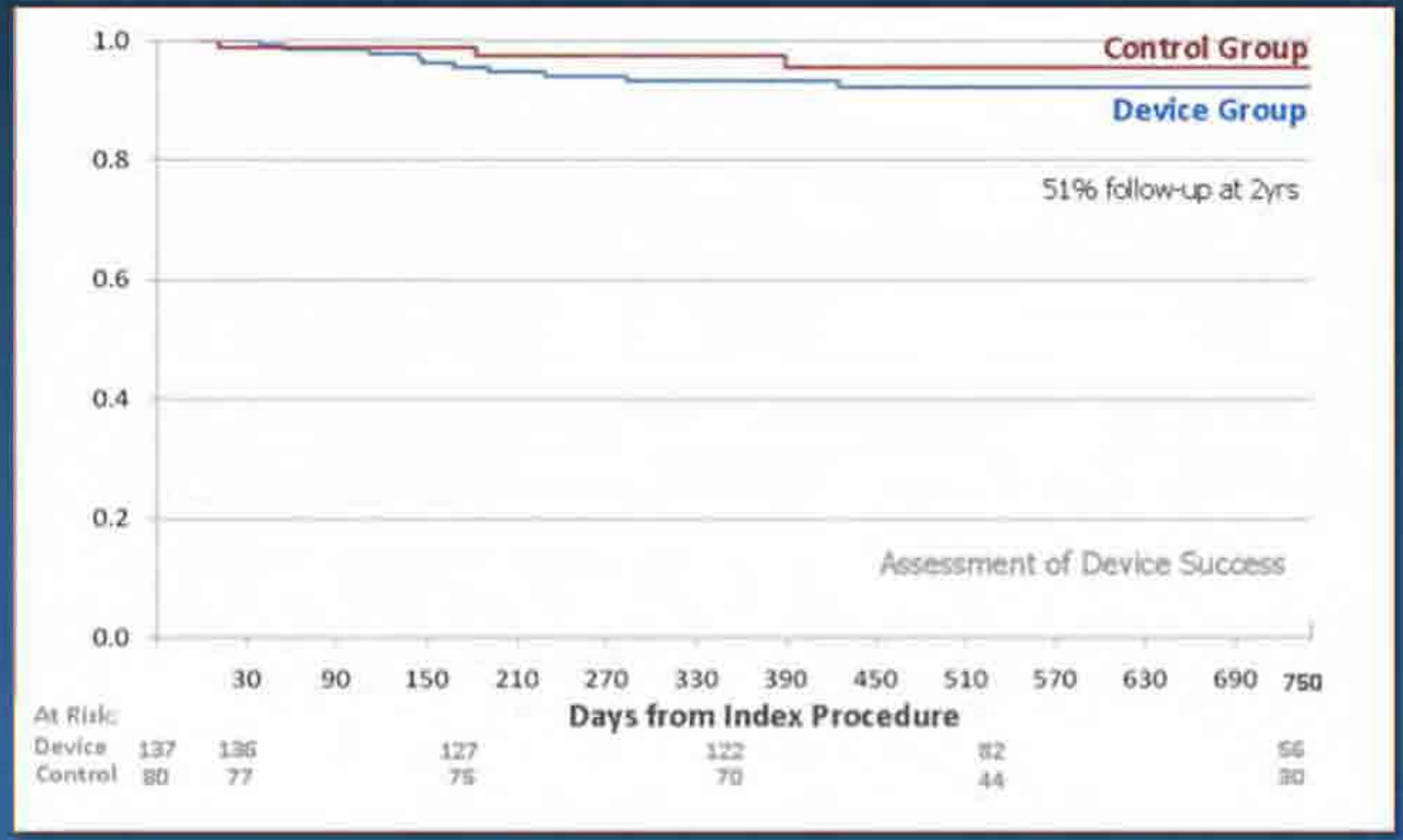
Freedom from MV Surgery.

Everest II Randomized Trial. 2 year Results



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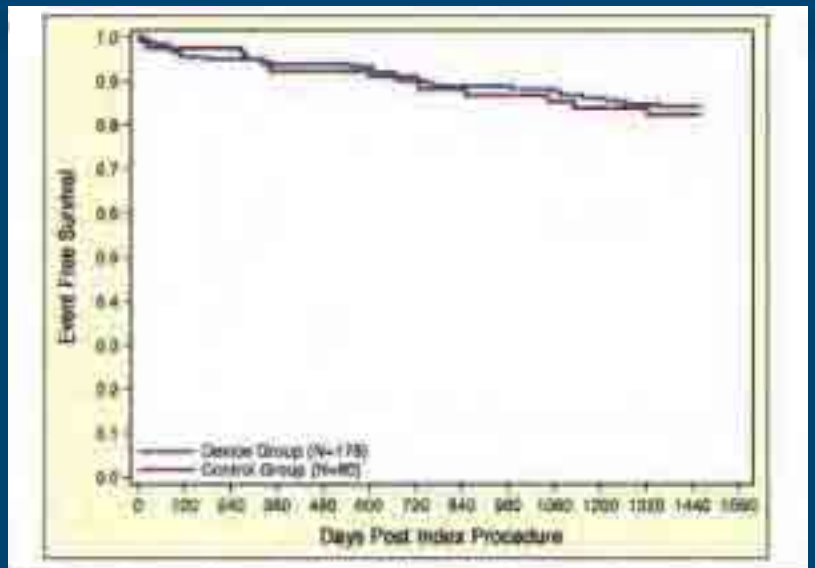
4-Years Follow-Up of the EVEREST II Trial



Mauri et al, JACC 2013; 62: 317-328.

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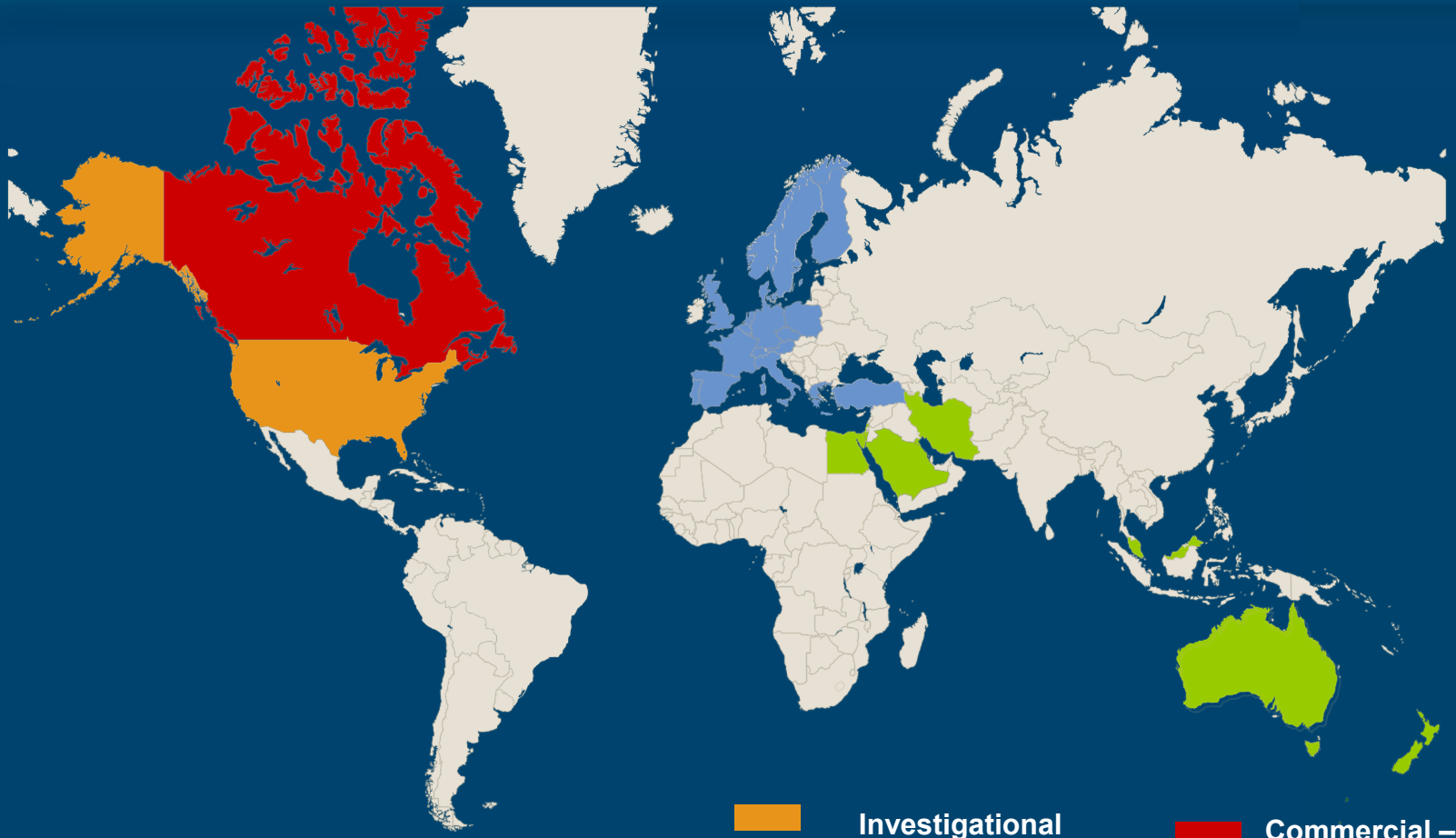
Worldwide Experience Using the MitraClip

Study	Population	N*
EVEREST I (Feasibility)	Feasibility patients	55
EVEREST II (Pivotal)	Pre-randomized patients	60
EVEREST II (Pivotal)	Non-randomized patients (High Risk Study)	78
EVEREST II (Pivotal)	Randomized patients (2:1 Clip to Surgery)	279 184 Clip / 95 Surgery
REALISM Continued Access	Non-randomized patients (High Risk Patients)	631
REALISM Continued Access	Non-randomized patients (Non-High Risk Patients)	272
COAPT	Randomized patients (1:1 Clip to No Clip)	2
Compassionate/Emergency Use	Non-randomized patients	66
ACCESS Europe Phase I	**Non-randomized patients**	**567**
ACCESS Europe Phase II	**Non-randomized patients**	**286**
Commercial Use	**Commercial patients**	**6,921**
Total		**9,122 + 95 surgery**

MitraClip Therapy
Current Global Adoption



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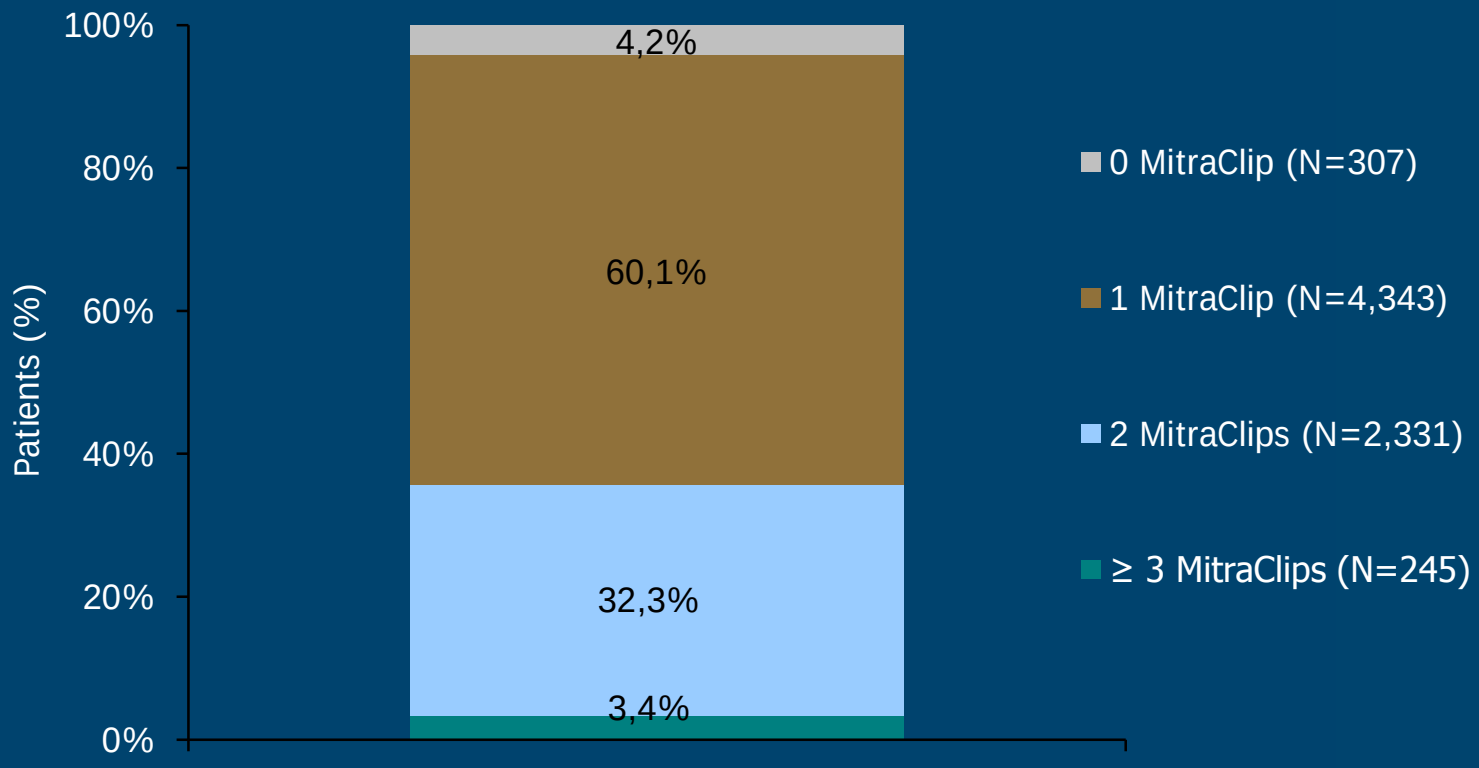
Patient Characteristics (first procedure only)

Characteristics	Commercial Patients (N=7,226)
Age (mean ± SD), years	76 ±10
Male Gender, (%)	63
Etiology	
Functional MR, (%)	67
Degenerative MR, (%)	23
Mixed Etiology, (%)	10

Left Ventricular Dysfunction

Parameters	Commercial Patients (N=7,226)
Left Ventricular Ejection Fraction (LVEF), (%)	
LVEF <30%	33
LVEF ≥30%	67
Left Ventricular End Systolic Diameter (LVESD), (%)	
LVESD <55 mm	98
LVESD ≥55 mm	2
Left Ventricular Dysfunction, (%)	
None (LVEF >60% and LVESD <55 mm)	13
Mild to Moderate (LVEF ≤60% but ≥30%, LVESD ≥40 mm but ≤55 mm)	48
Severe (LVEF ≤30% or LVESD ≥55 mm)	35
Unknown	4

Number of MitraClips Implanted and Implant Rate



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Site-Reported MR Grade

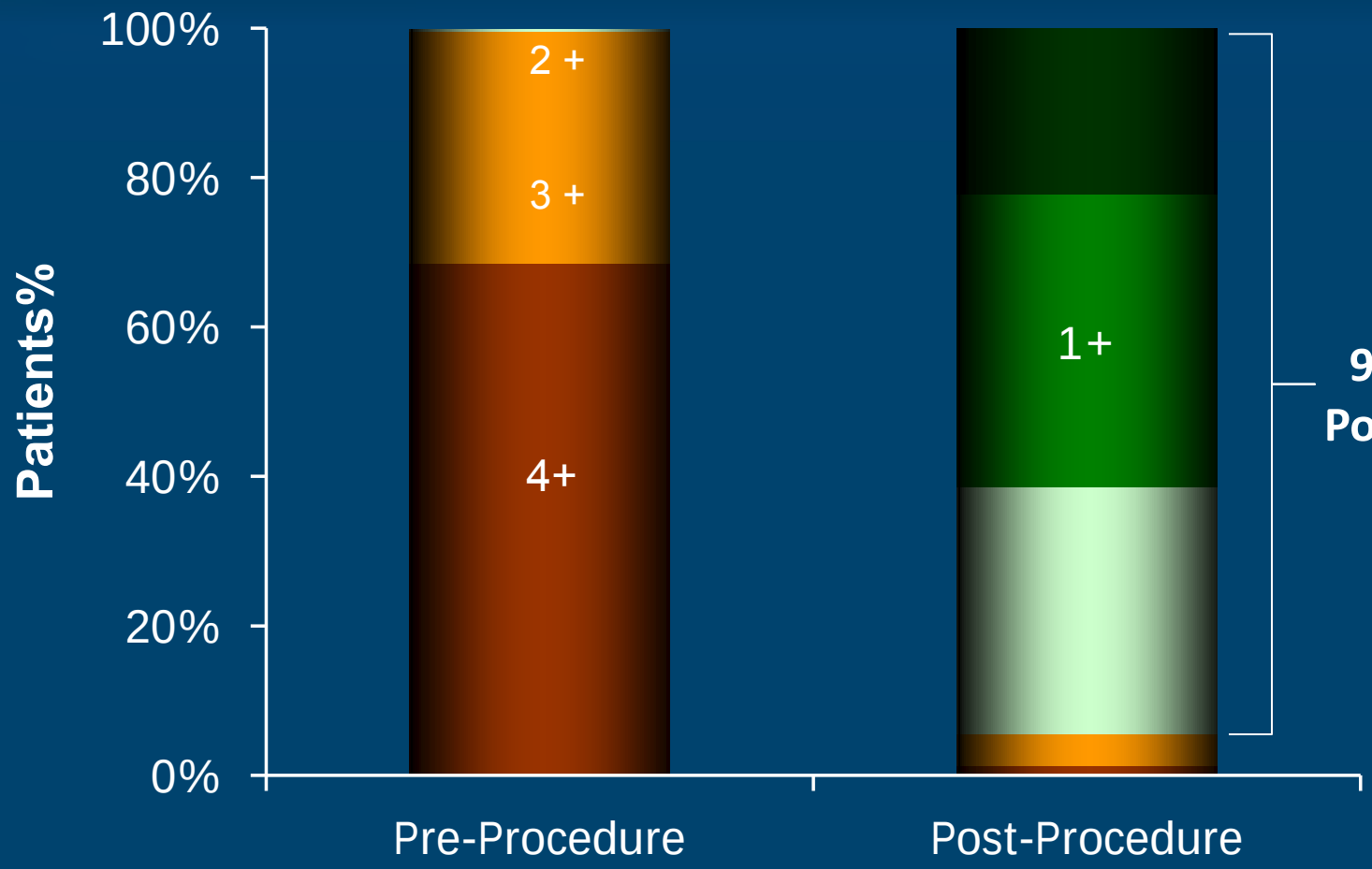

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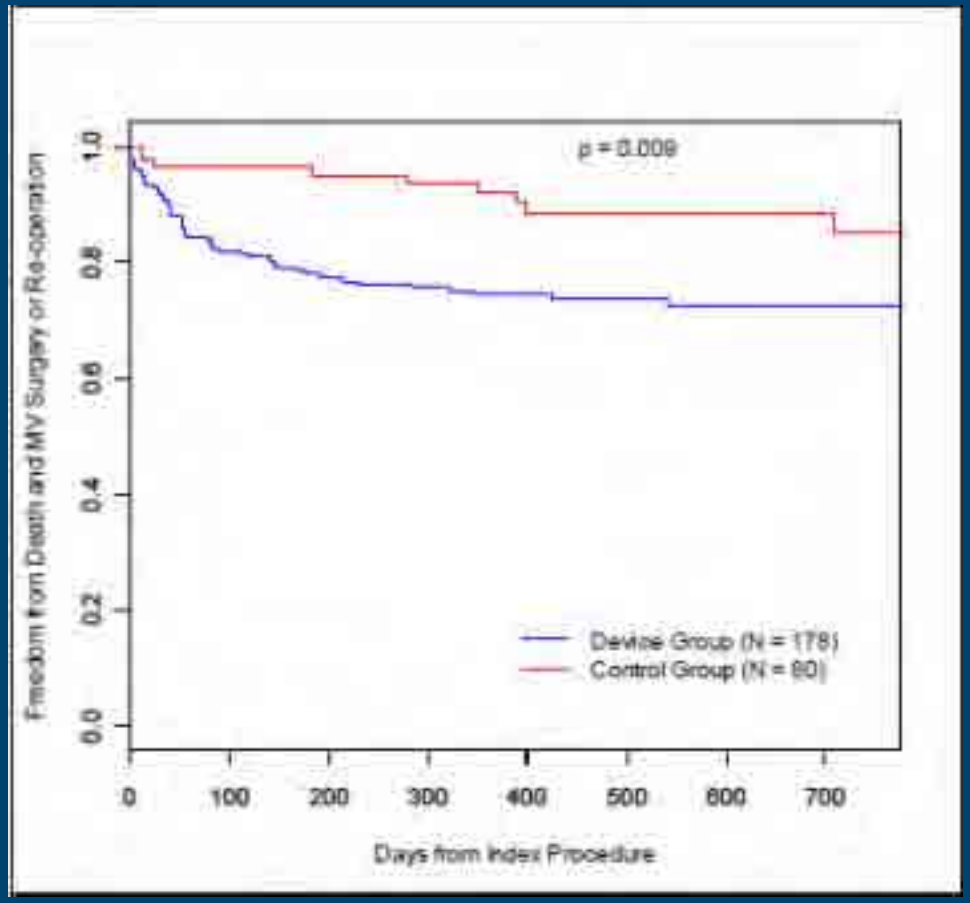
Figure 2: Kaplan-Meier Freedom from Death and Mitral Valve Surgery (Device Group) and Freedom from Death and Re-operation (Control Group), Modified ITTa (N = 258)



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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

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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

Trial design

COAPT TRIAL

~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

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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 ≥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 ≥ 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 ≥ 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

Key Inclusion Criteria (2)

- 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)

COAPT TRIAL

- 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)

COAPT TRIAL

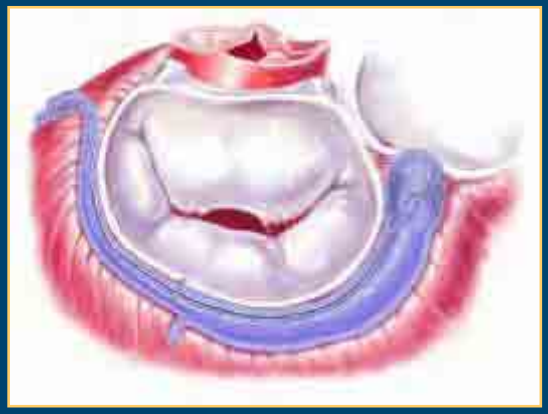
- Any PCI, carotid or endovascular intervention or carotid surgery within 30 days, or any coronary or endovascular surgery within 6 months
- CRT and/or ICD implant or revision within 90 days
- Leaflet anatomy which may preclude MitraClip implantation, proper MitraClip positioning on the leaflets or sufficient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

Indirect Annuloplasty: Coronary Sinus Devices

CARILLON
(Cardiac Dimensions)

PTMA
(Viacor)

MONARC
(Edwards Lifesciences)



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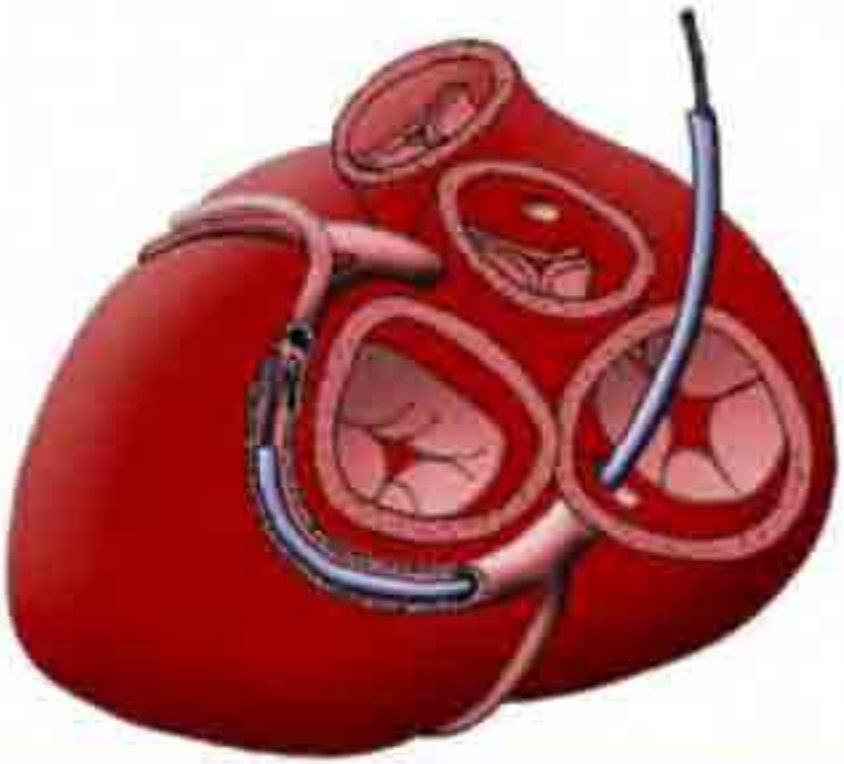
CARILLON Mitral Contour System



AMADEUS

Prospective, single-arm, 30 patient, multi-center feasibility study in patients with HF and PMR @ 1 & 6 months (CARILLON TE implant)

TITAN

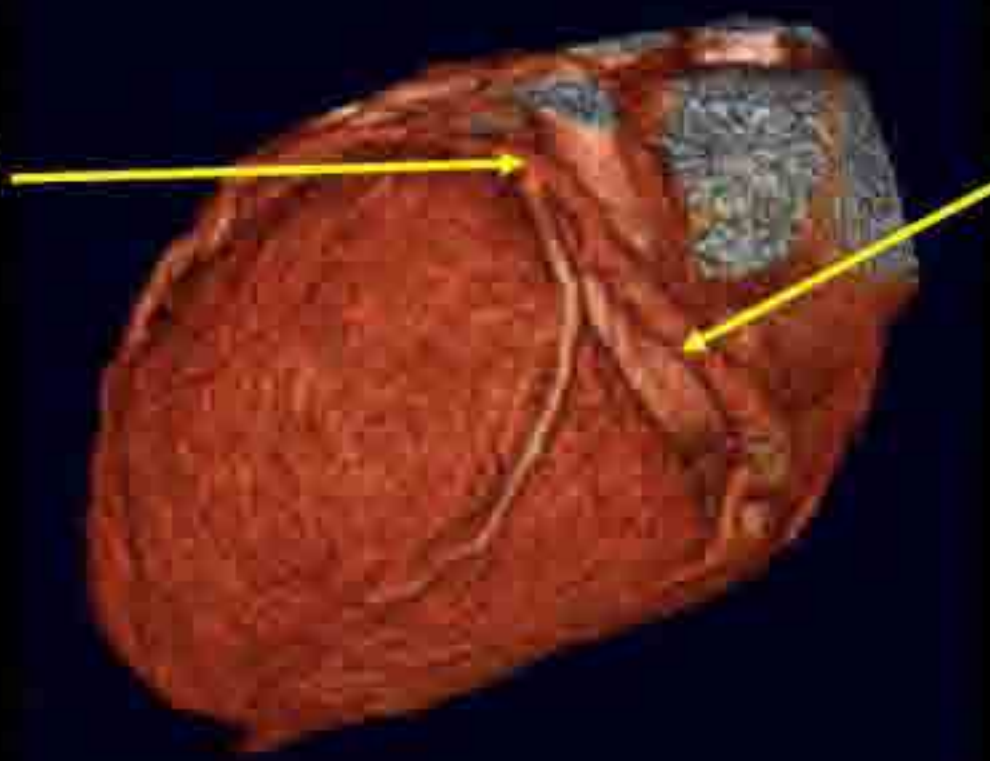
Prospective, single-arm, 30 patient, multi-center feasibility study in patients with HF and PMR @ 1, 6, 12, 18 & 24 months (CARILLON XLO implant)

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

CARDIAC DIMENSIONS

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

Cardiac Dimensions

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

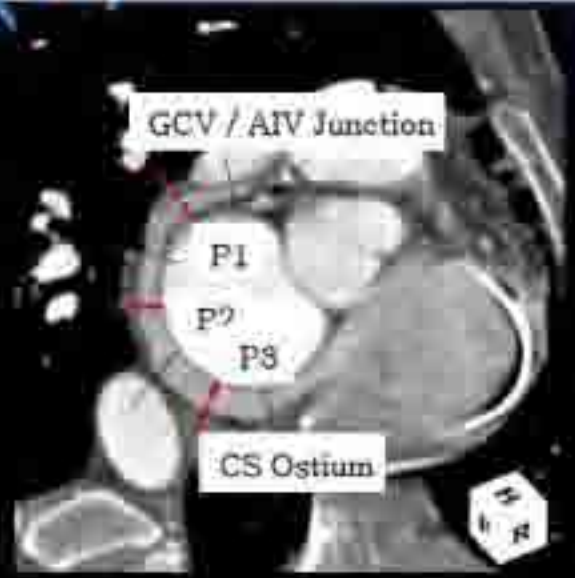
EXCLUSION:

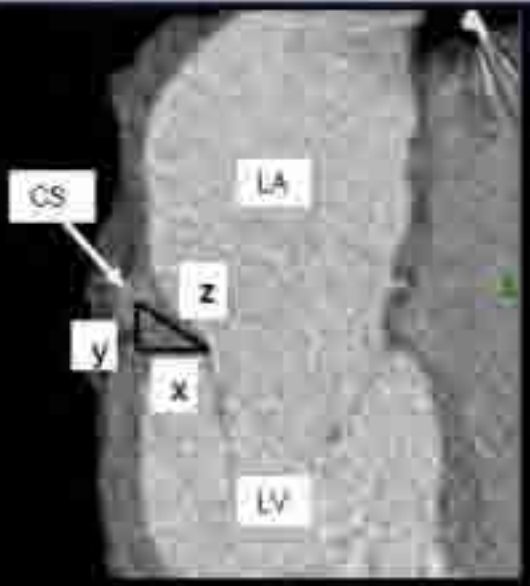
- Recent hospitalization for cardiac surgery, revascularization, unstable angina
- Presence of chronic atrial fibrillation
- Presence of left atrial appendage clot
- Creatinine > 2.2mg/dl

Baseline Demographics
Patients with Implants (n=30)

	AMADEUS™ Trial
Age	66.5 (47-81 yrs)
Gender	M = 86.7% (26) F = 13.3% (4)
NYHA Class	II - 6 III - 22 IV - 2
EF	31.6% avg. (12.5 – 39.9)
MR	2+ = 4 3+ = 20 4+ = 6
LVEDD	65.7mm (55 – 77mm)
History of CAD	72.2%

3) CS/GCV Position Relative to Annulus





METHOD

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

2) Distances measured from edge of annulus to middle of vein lumen in x, y, z directions

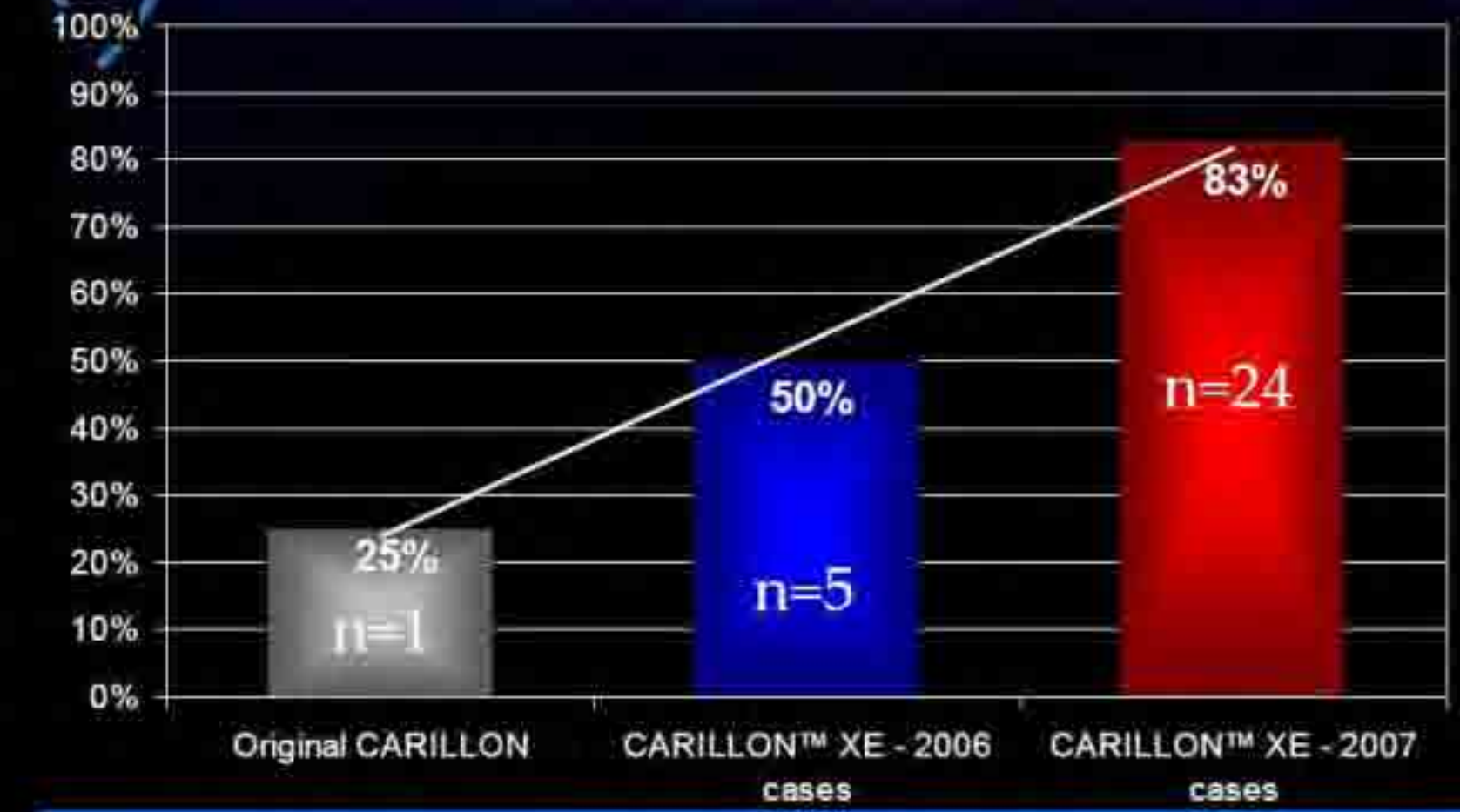
Anterior

Lateral

Posterior

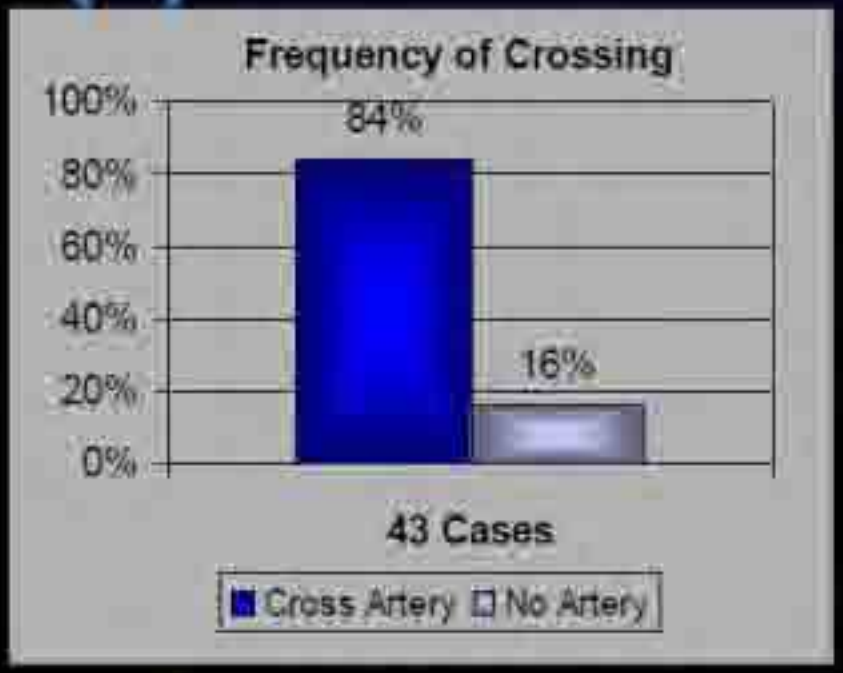
1) AMADEUS™ Procedural Success

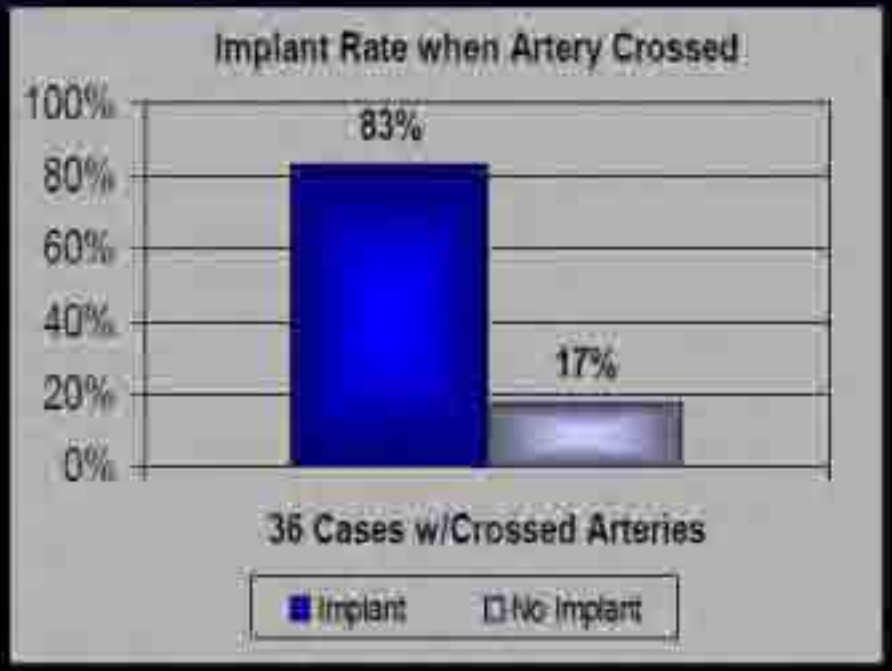
Permanent Implants



- Procedural Success=Acute MR reduction and a permanent implant
- No devices are left in unless MR is reduced at the time of the implant

2) Managing Coronary Arteries





- 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

ensions

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

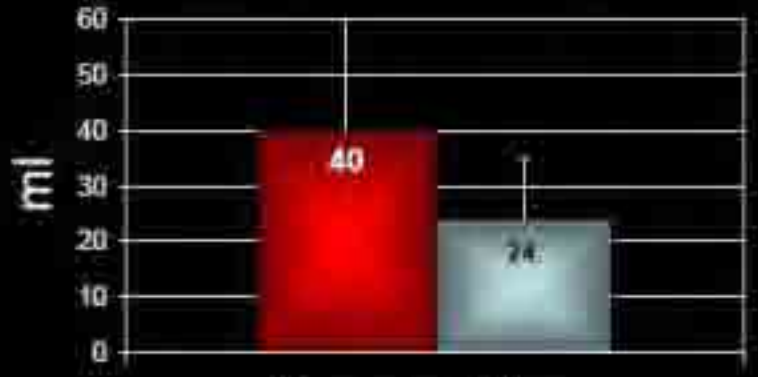
- TEE was used in all patients intra-procedurally to determine acute MR reduction
- Acute MR reduction was required to leave a device
  - Visual assessment was done in all 30 patients
  - Grade 3.0 ± 0.6 to 2.0 ± 0.8 ($p<0.0001$)

5) Acute Intra-procedural MR

Quantitative MR Performed in Final 20 Patients

Vena Contracta

EROA



Regurgitant Volume

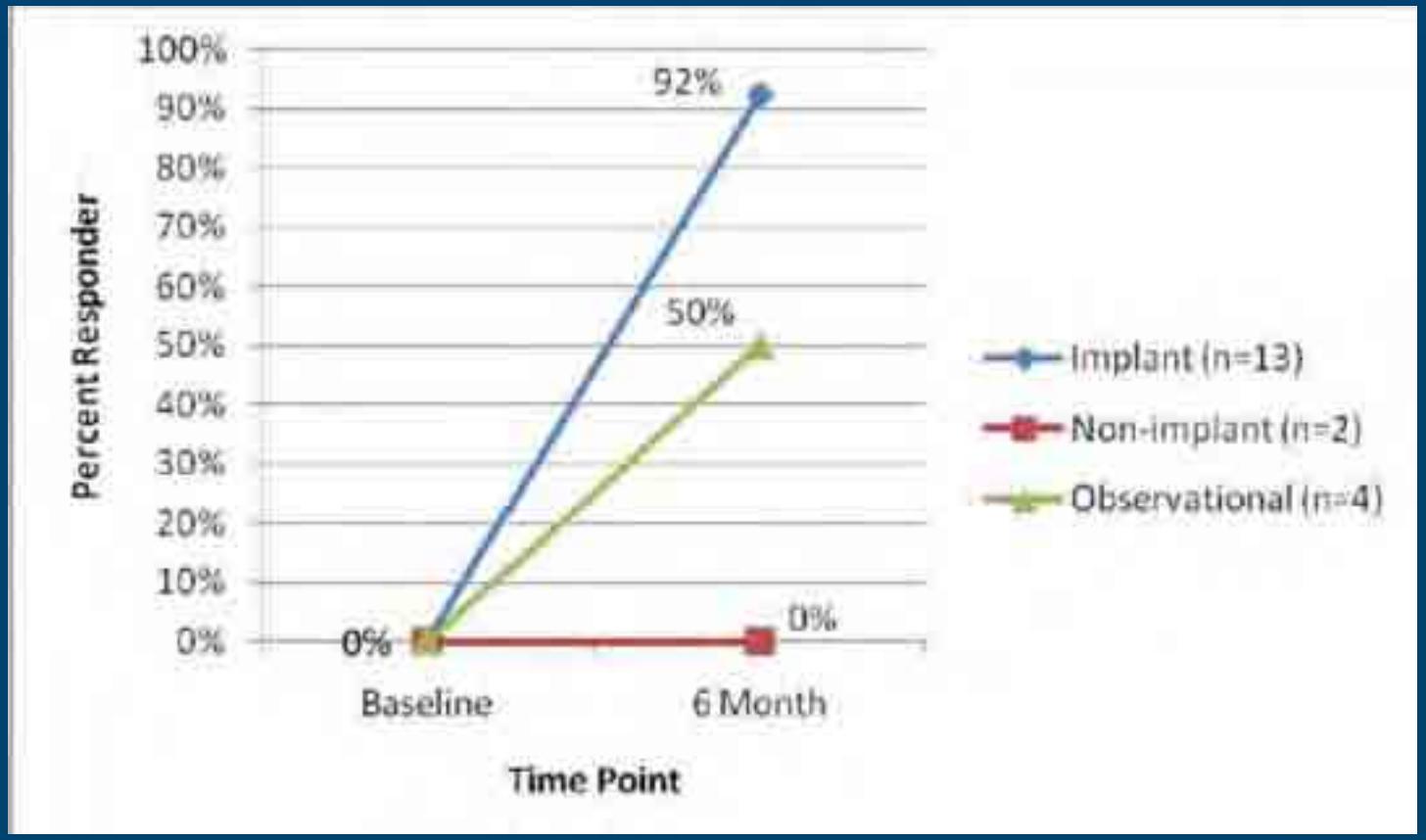
MR Jet/LAA

Cardiac Dimensions

MONARC Device

EVOLUTION I Clinical Study

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



EVOLUTION I Clinical Study

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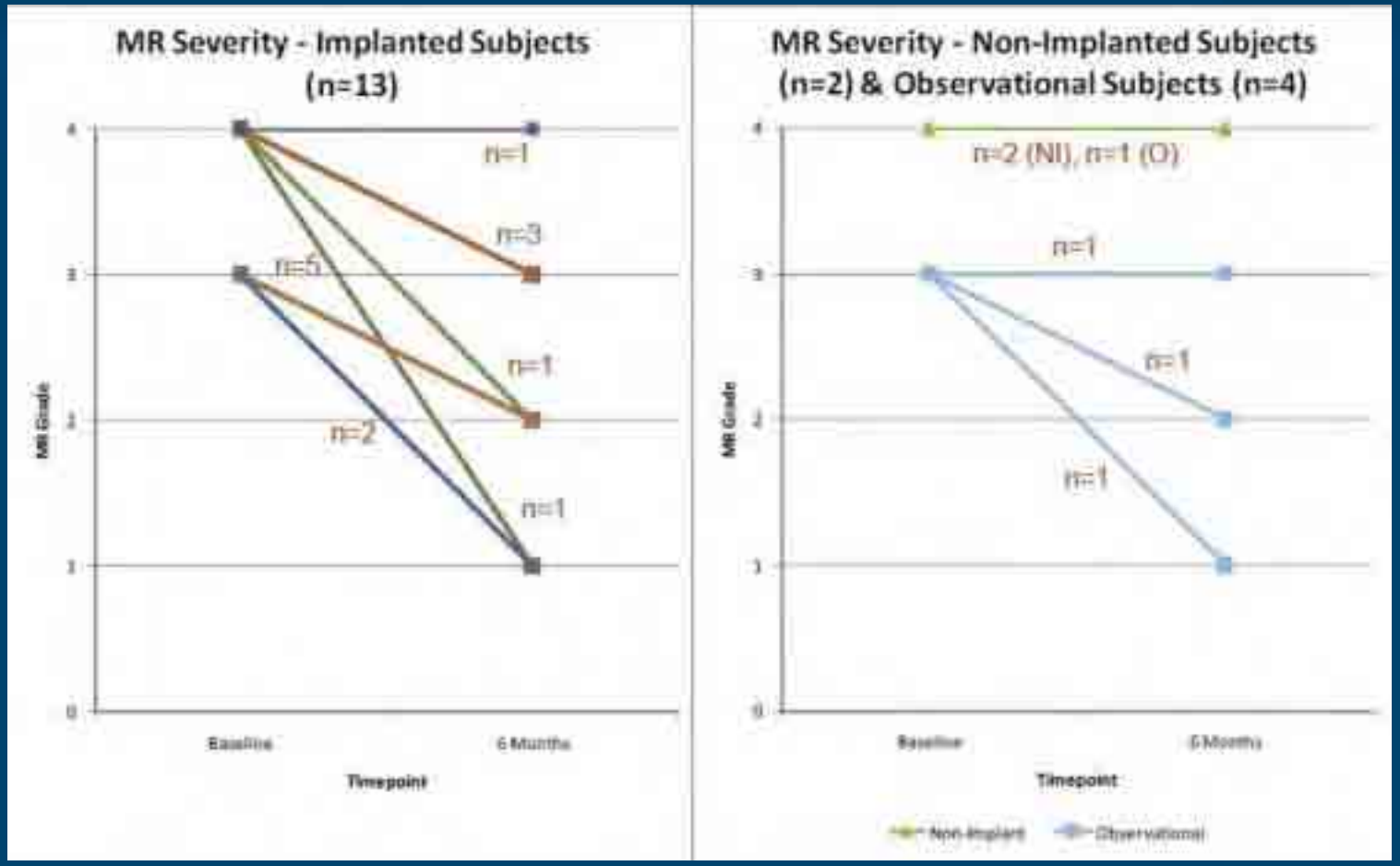
HEART CENTER

6 Month Follow Up MR Severity



EVOLUTION I Clinical Study

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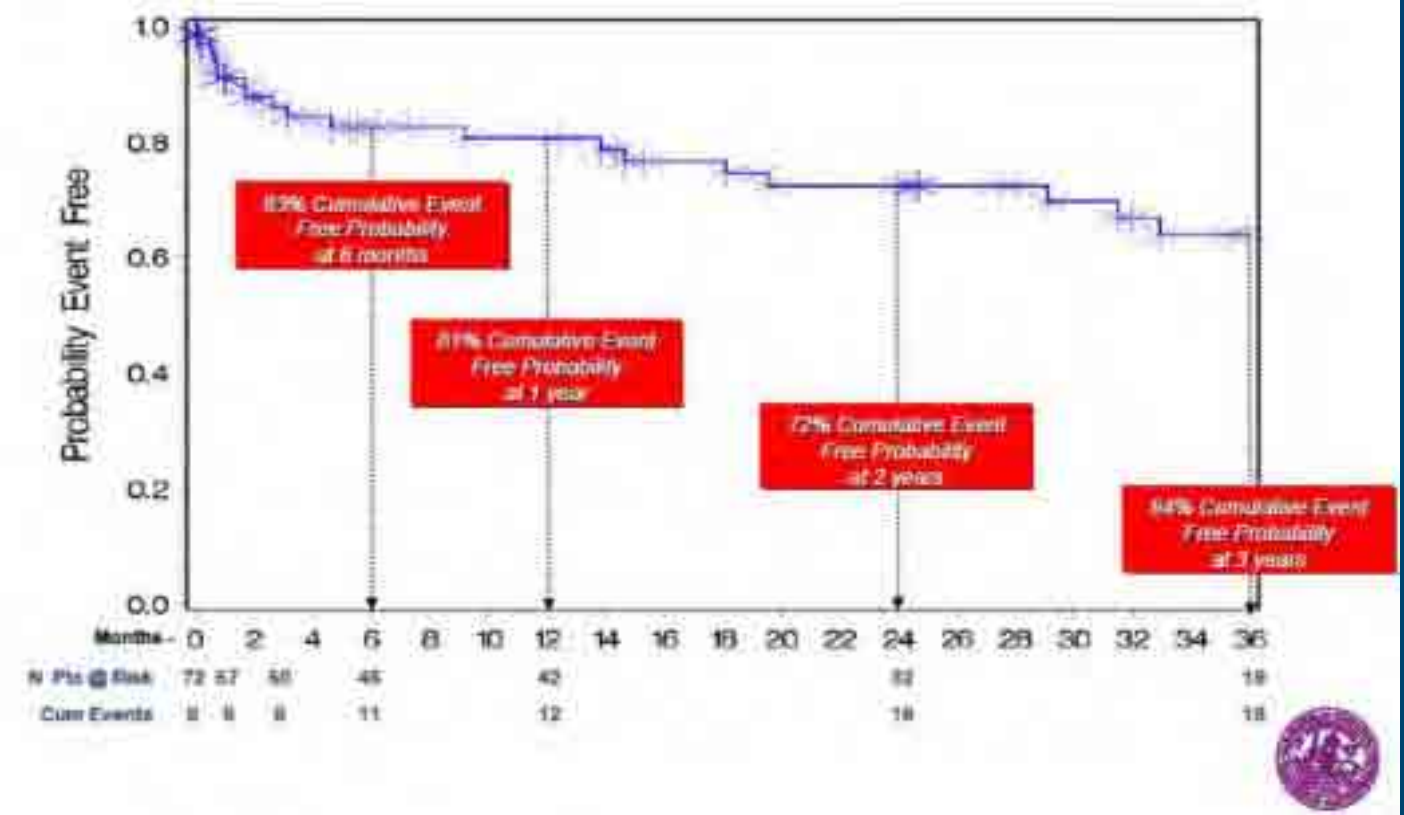
EVOLUTION I Clinical Study

Cumulative Safety



MACE= Device migration, Death, Device Embolization, Cardiac Tamponade, Coronary sinus thrombosis or Pulmonary embolism

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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.

Viacor PTMA Coronary Sinus Device. Ptolemy II Trial

PTOLEMI II: 2.8% 30 day MACE and 90% procedural success
Stefan Sack et al on behalf of the PTOLEMI II.

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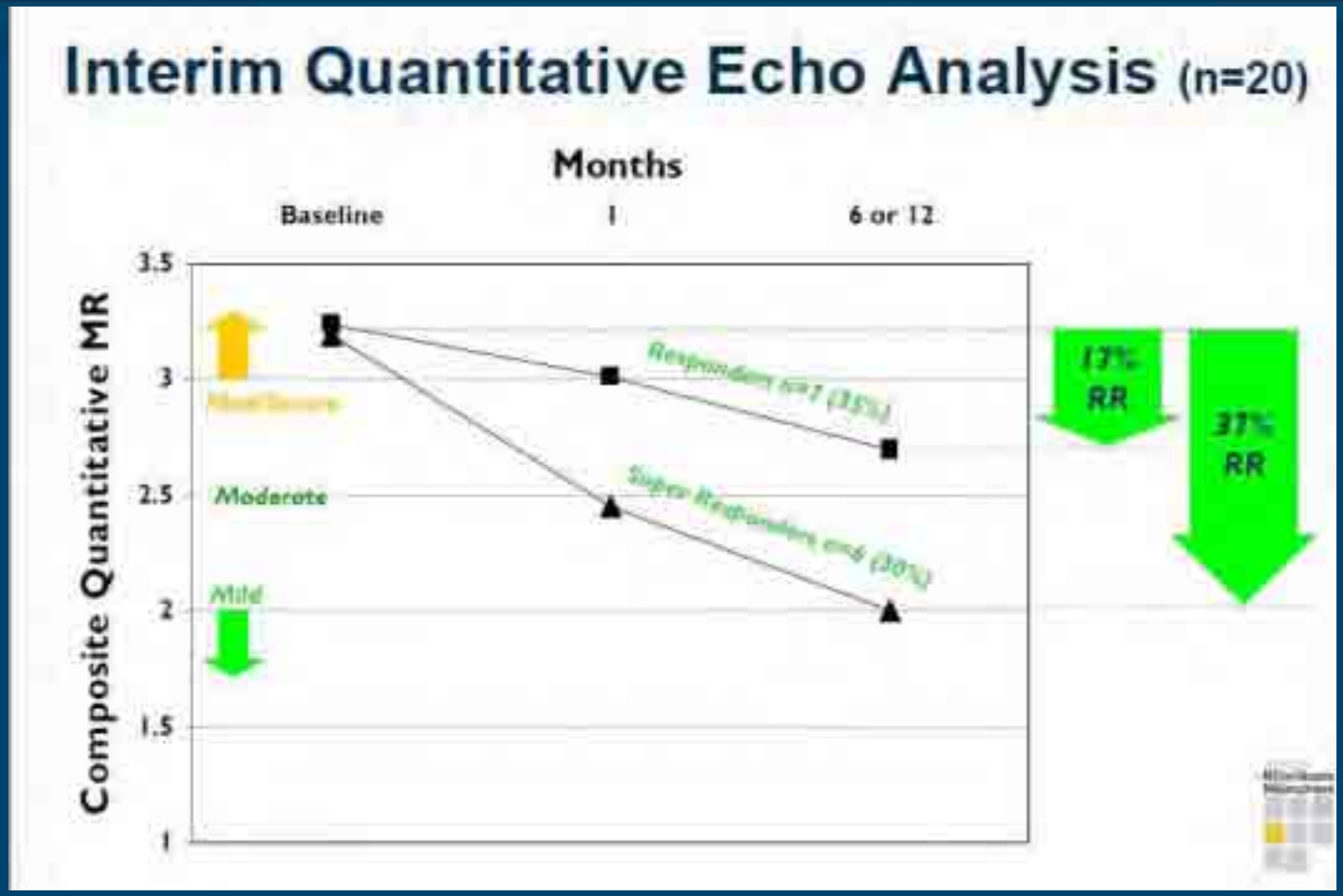
Viacor PTMA Coronary Sinus Device. Ptolemy II Trial



PTOLEMI II: 2.8% 30 day MACE and 90% procedural success
Stefan Sack et al on behalf of the PTOLEMI II.

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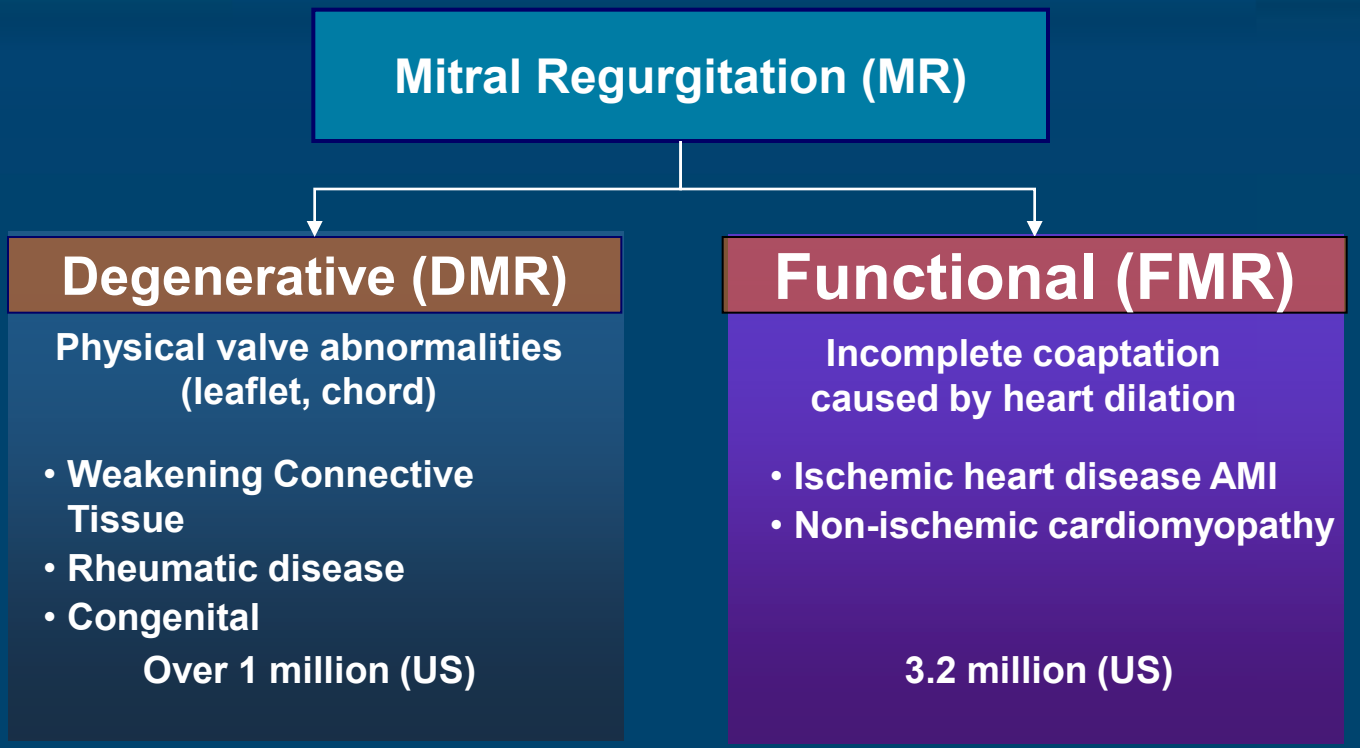
Mitralign: Key Points

- **Within the Mitral Valve space, Mitralign is an emerging leader**
- **Our procedure has been shown feasible, repeatable and durable**
- **Mitral CE Mark study more than halfway completed**
- **Mitral US feasibility study scheduled to initiate Q3 _13**
- **Tricuspid FIM planned for Q4 _13**
- **Overall, Mitralign positioned well for multiple indications**

Mitral Regurgitation: Two Main Etiologies



Mitralign is Intended to Treat Functional Mitral Regurgitation (FMR)

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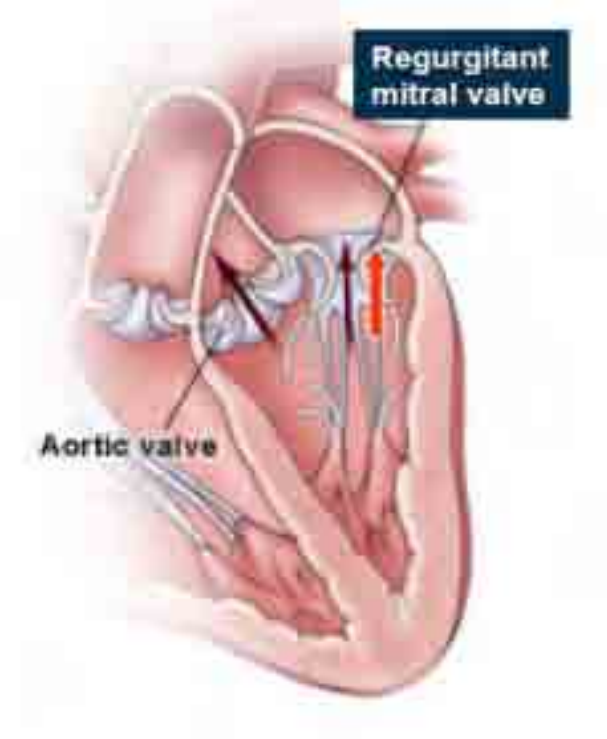
Percutaneous Mitral Valve Therapy: Role in DMR and FMR May be Different

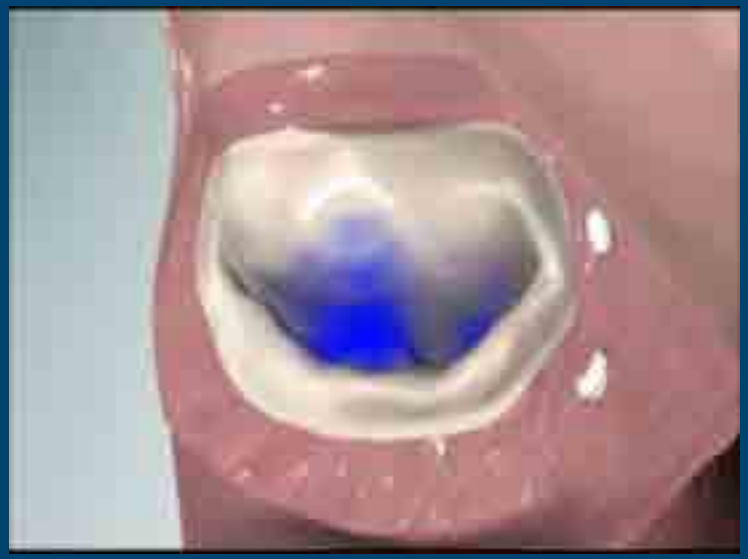
- In DMR, there is something physically wrong with the valve apparatus
- MitraClip is a viable treatment for DMR
- The use of MitraClip in DMR, may limit future ability to place a percutaneous rep. valve, complicating the choice of therapy
- In general, repair and replacement are options, but repair options should allow for future percutaneous replacement
- Replacement overall may play an earlier role in DMR, depending upon the effectiveness of repair options

Percutaneous Mitral Valve Therapy: Role in DMR and FMR may be different

- In FMR, the leaflets have separated due to dilation of the heart, but the valve apparatus remains essentially normal
- To outright replace a normal valve apparatus in a patient that may be on average 10 years younger than a TAVR patient, may not be the first consideration
- Percutaneous repair technologies, if they are safe and leave open all future clinical options can work well and may be considered a first line option
- Replacement likely to be a “later stage” option in FMR

Mitralign TAMR
Transcatheter Annuloplasty for Mitral Repair





Objective: Reduction of the posterior mitral annulus to coapt the leaflets and thereby initiate LV remodeling, improve QoL and decrease repeat hospitalizations

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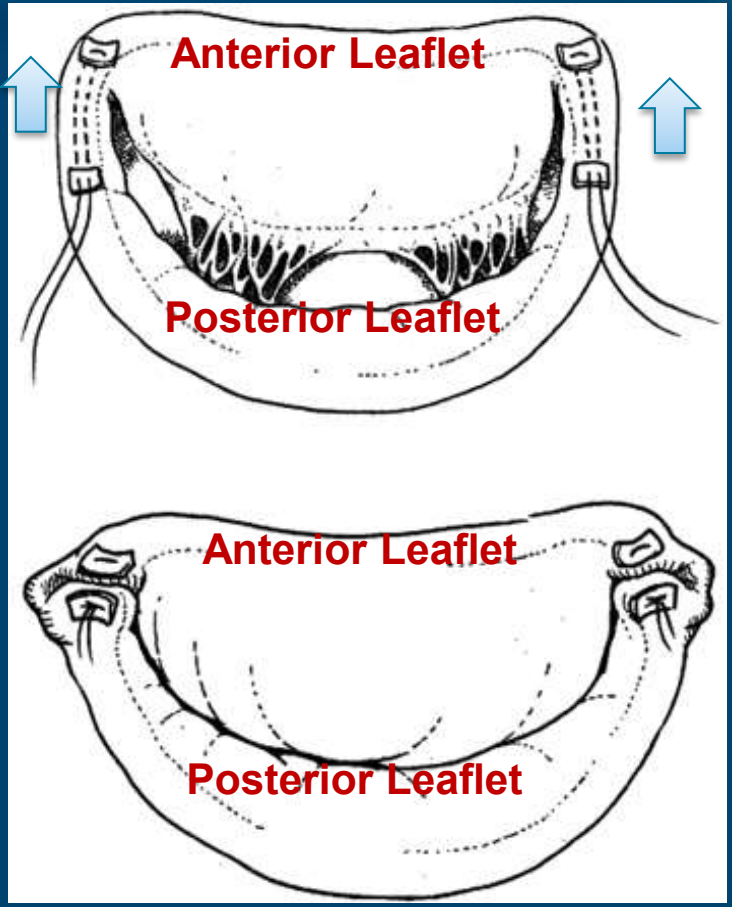
The Mitralign Procedure
Similar to Modified Kay Annuloplasty

- **The Kay annuloplasty was a successful surgical procedure, the precursor to the ring.**
- **Pledget and suture with plication**
- **Shorten the posterior mitral annulus by bring posterior leaflet towards the anterior leaflet**



Annals of Thoracic Surgery. 2007; 84 Issue 6, 2007: 2059–2065

Mitralign Procedure: Main Steps

Wire Delivery

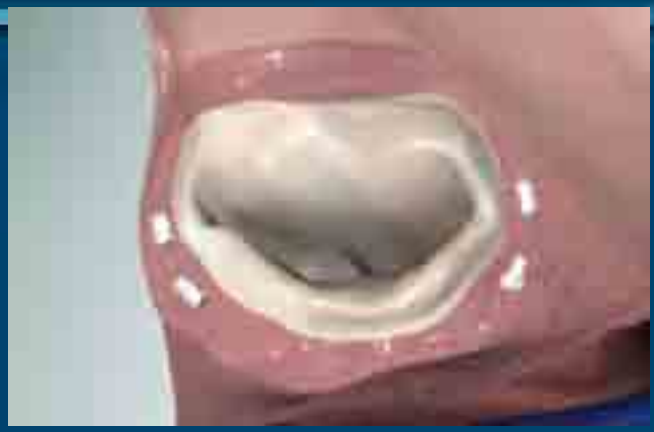
Pledget Delivery

Plication & Lock

The Mitralign Procedure

Transcatheter Annuloplasty for Mitral Repair (TAMR)

- **Polyester pledgets delivered percutaneous via the left ventricle thru the posterior mitral annulus**
- **Pledgets are plicated and locked in targeted location**
- **Currently using one or two implants**
- **US study will allow up to three implants**



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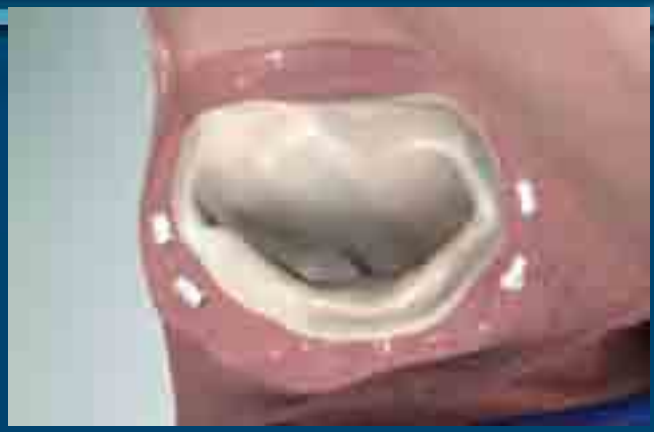
The Mitralign Procedure

Therapeutic Options Remain Open

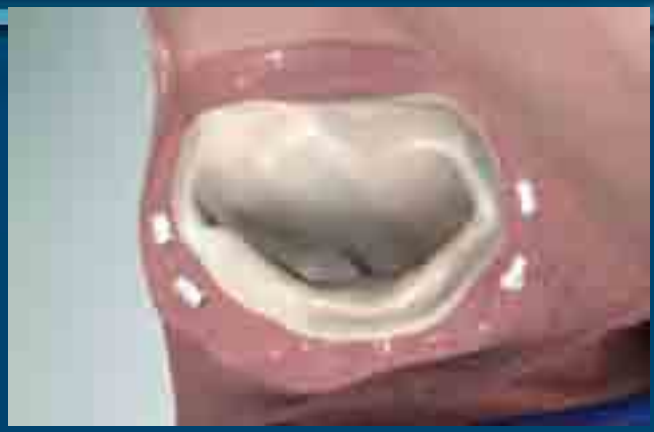
- Once implanted, the pledget pairs rapidly encapsulate into the annulus
- Open for future repair options: MitraClip, 2nd Mitralign, surgical
- Open for future replacement options
- Tighter annulus may facilitate replacement technologies



The Mitralign Procedure

Customized Therapy for a Complex Condition

- Mitral disease is complex and lends itself to some customization
- Potential to use 1, 2 or 3 implants
- Customize the location of the implant “reinforce” the infarcted area
- Customize the amount of plication to match the heart size, extent of MR



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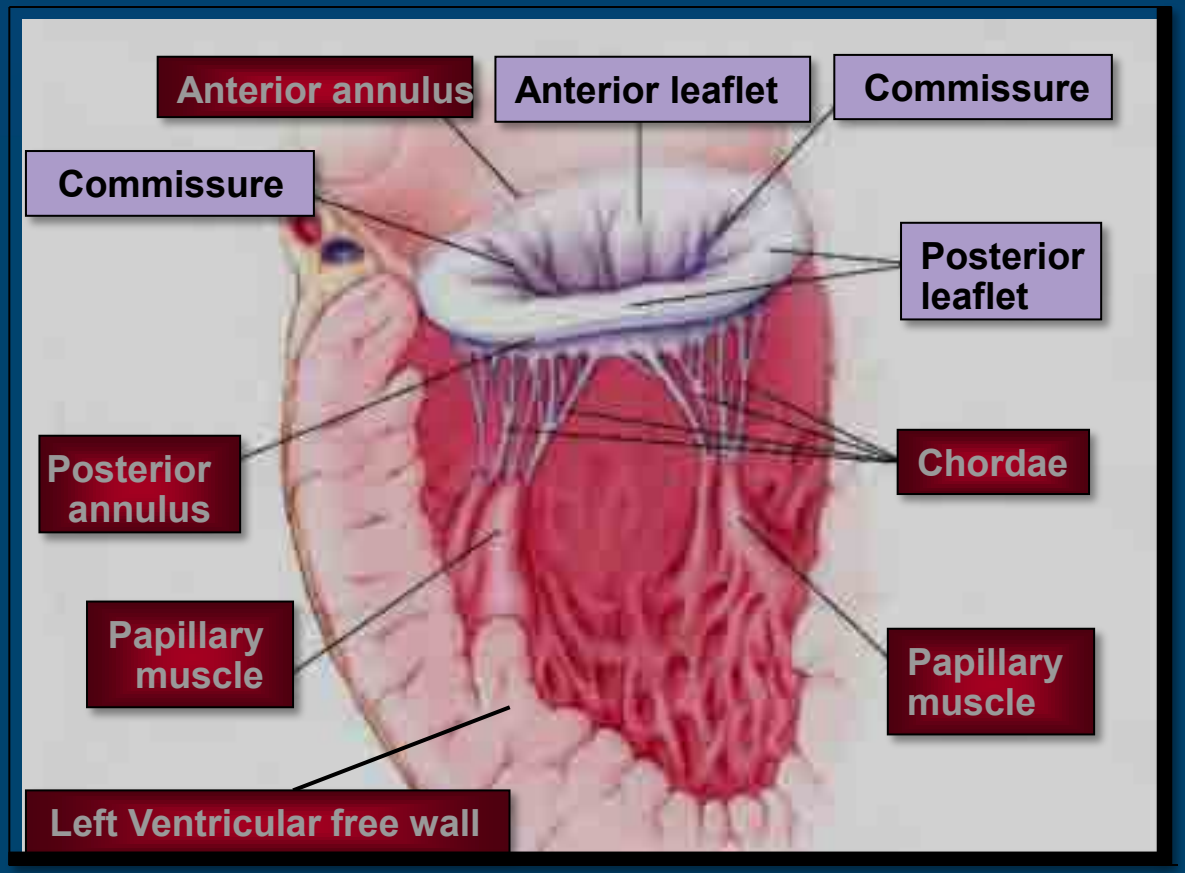
Focused on Functional Mitral Regurgitation Mitralign Repair as First Line Therapy



- Left Ventricle free wall —falls away"
- Leaflets are dislocated but remain normal
- For first line therapy, better to repair than replace a normal valve, especially if one can preserve future clinical options

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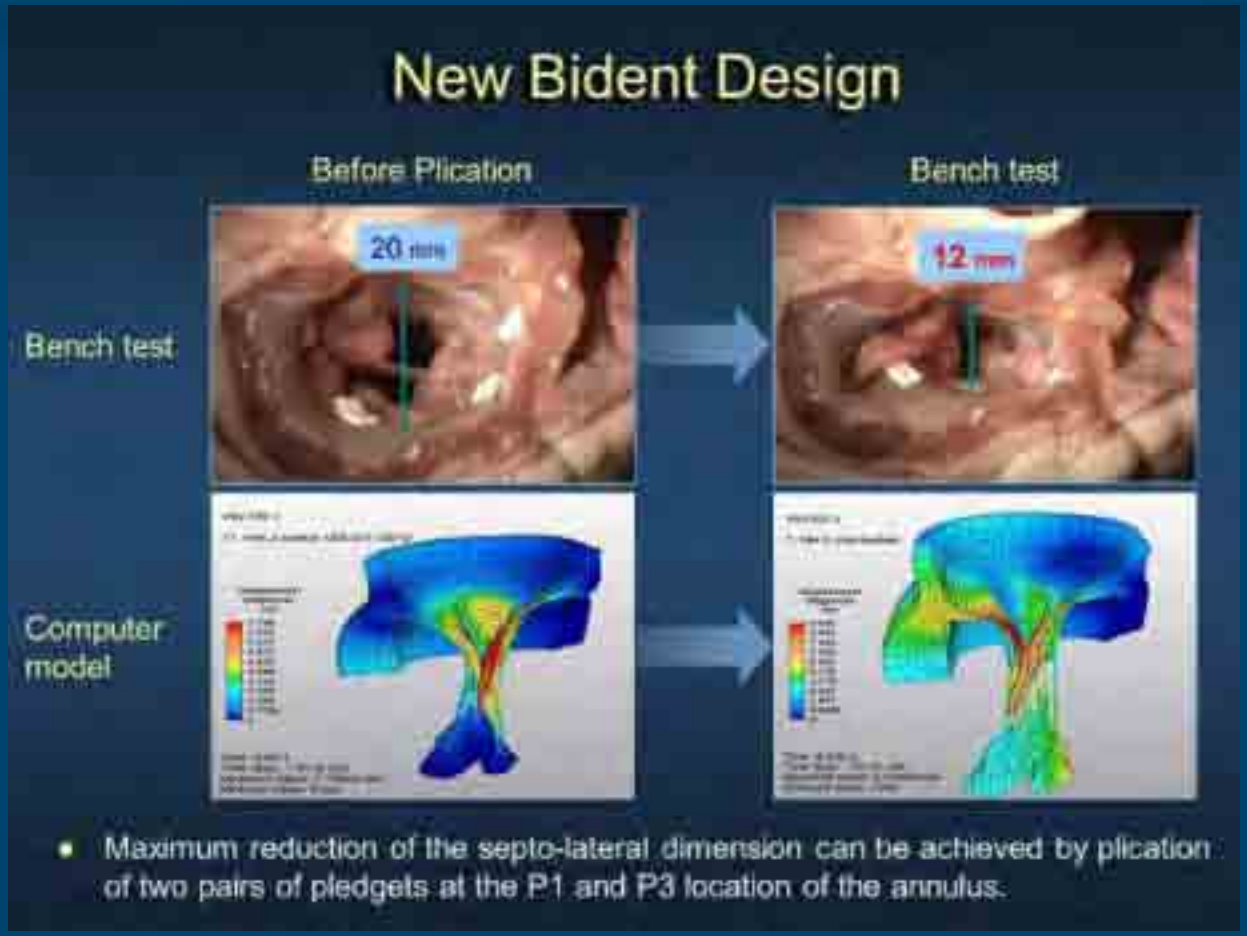
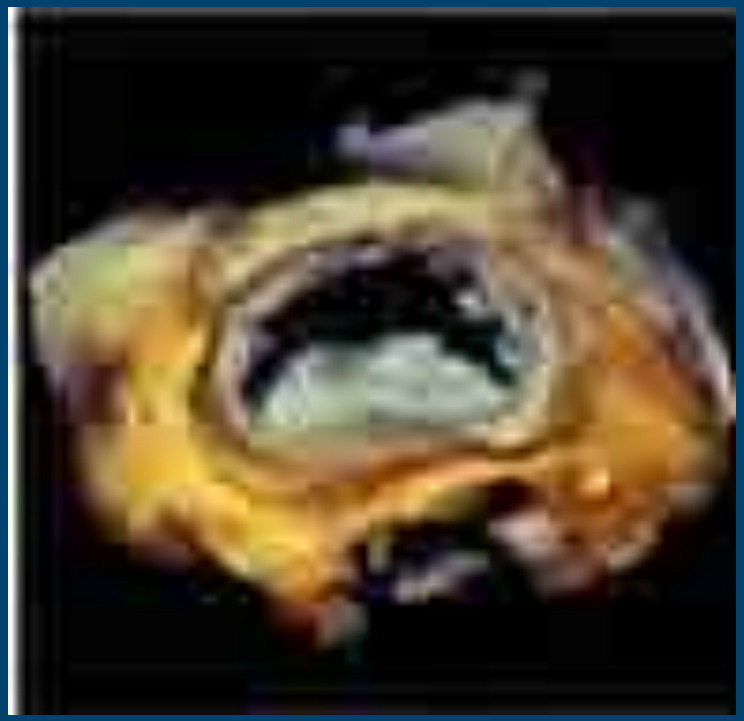
Mitraling Brident Approach

Grube et al. 12 FIM cases

Mitraling Brident Approach



Mitraling Brident Approach



Before

After

The Mitralign Procedure

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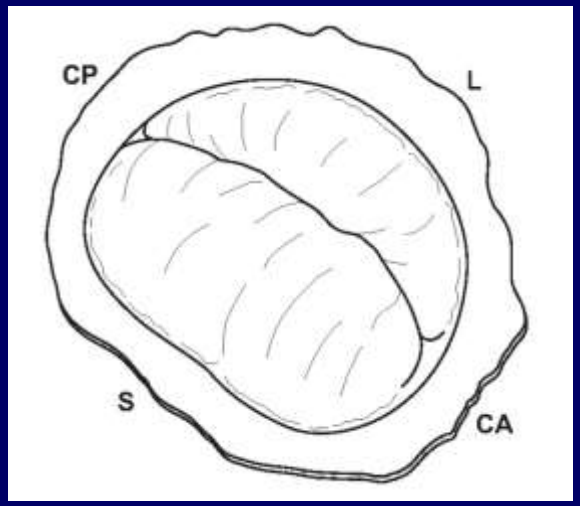
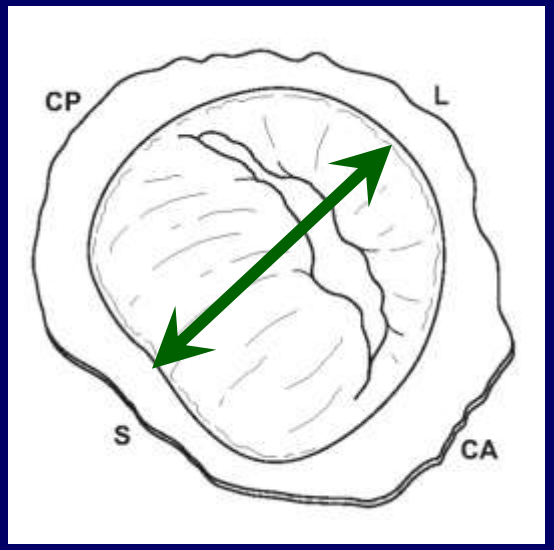
S-L Expansion Causes FMR

Mitral Regurgitation in CHF

Normal



Diseased



- Sheep CHF/FMR Model Strong Surrogate for Human Condition

Dagum, Miller, et. al., J. Thoracic Card Surg, 2001

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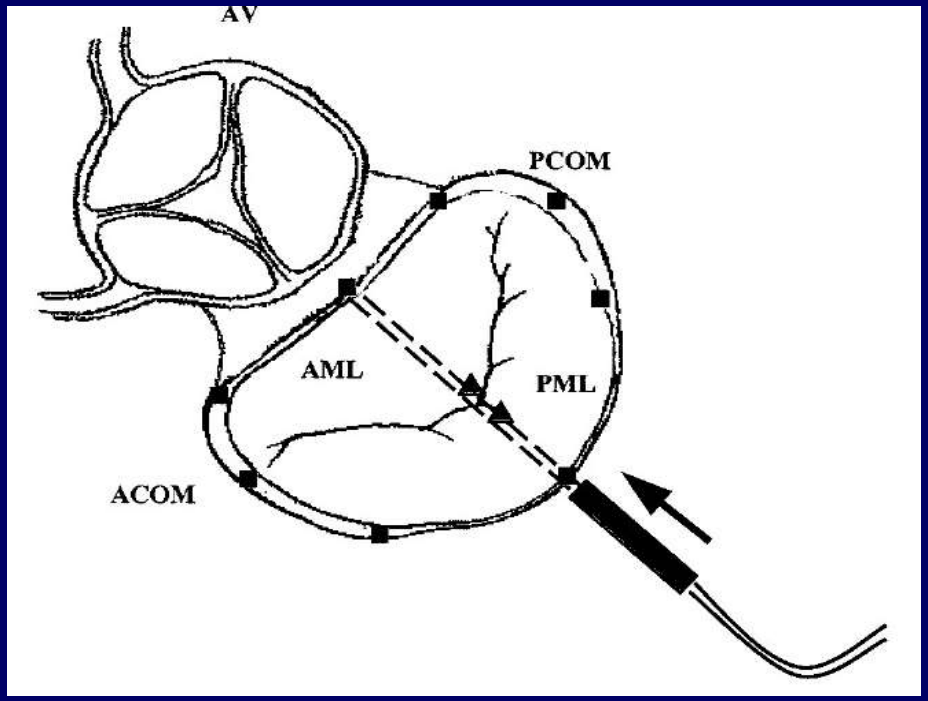
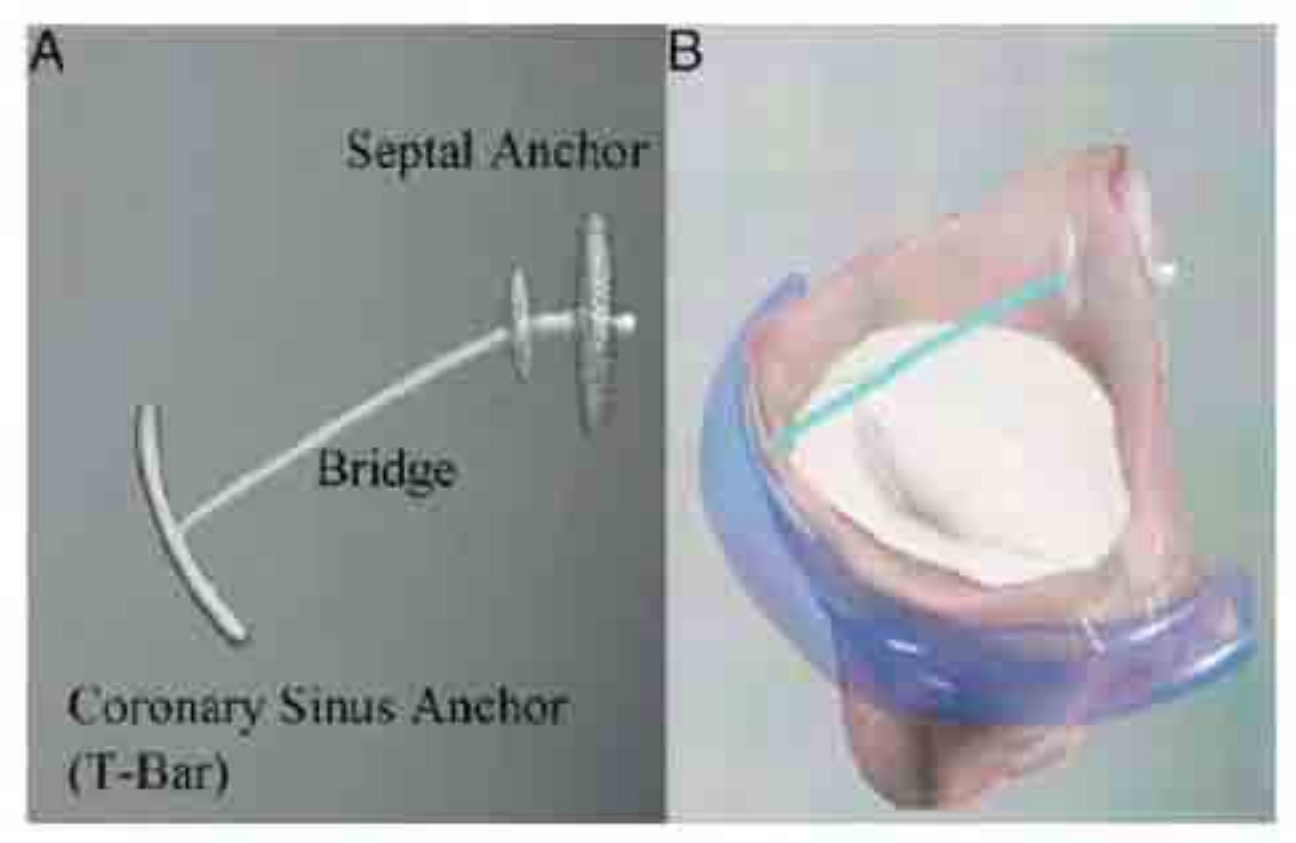
Direct S-L Shortening Stops FMR

FMR Ameliorated By Restoring S-L to Normalcy



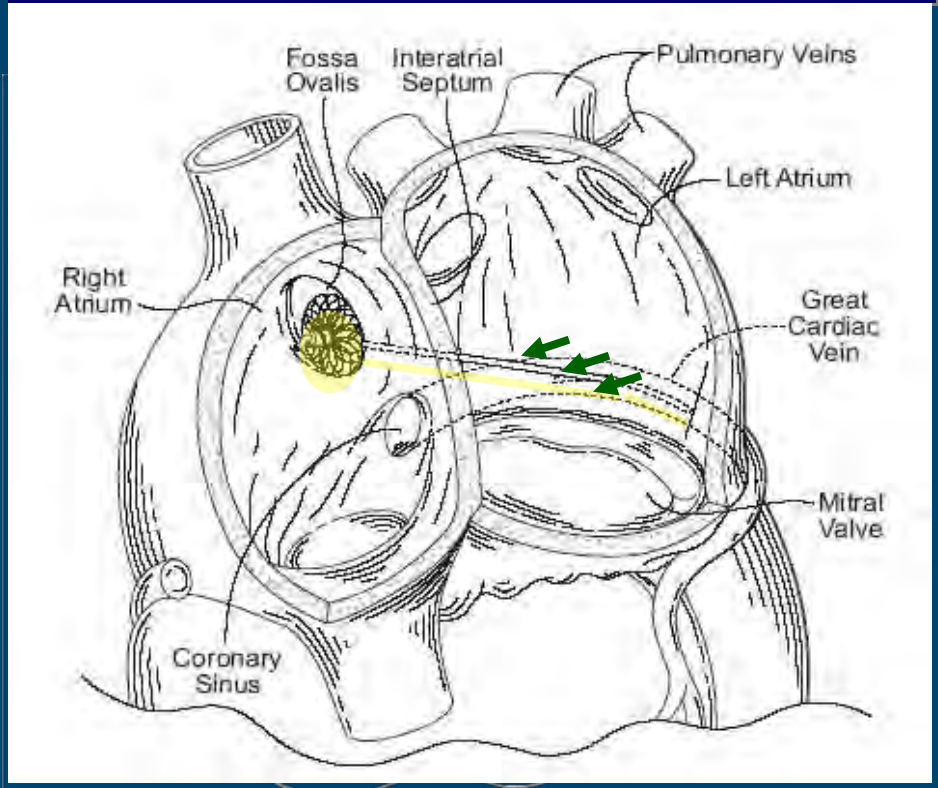
Timek, Miller, et. al., J. Thorac Cardiovasc Surg, May 2002

Percutaneous Septal, Sinus Shortening



The PS^3 System

Percutaneous Septal-Sinus Shortening



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Rogers JH, Palacios, IF. Circulation. 2006;113:2329-2334.

Ample PS3 FIM Studies in Caracas - Venezuela

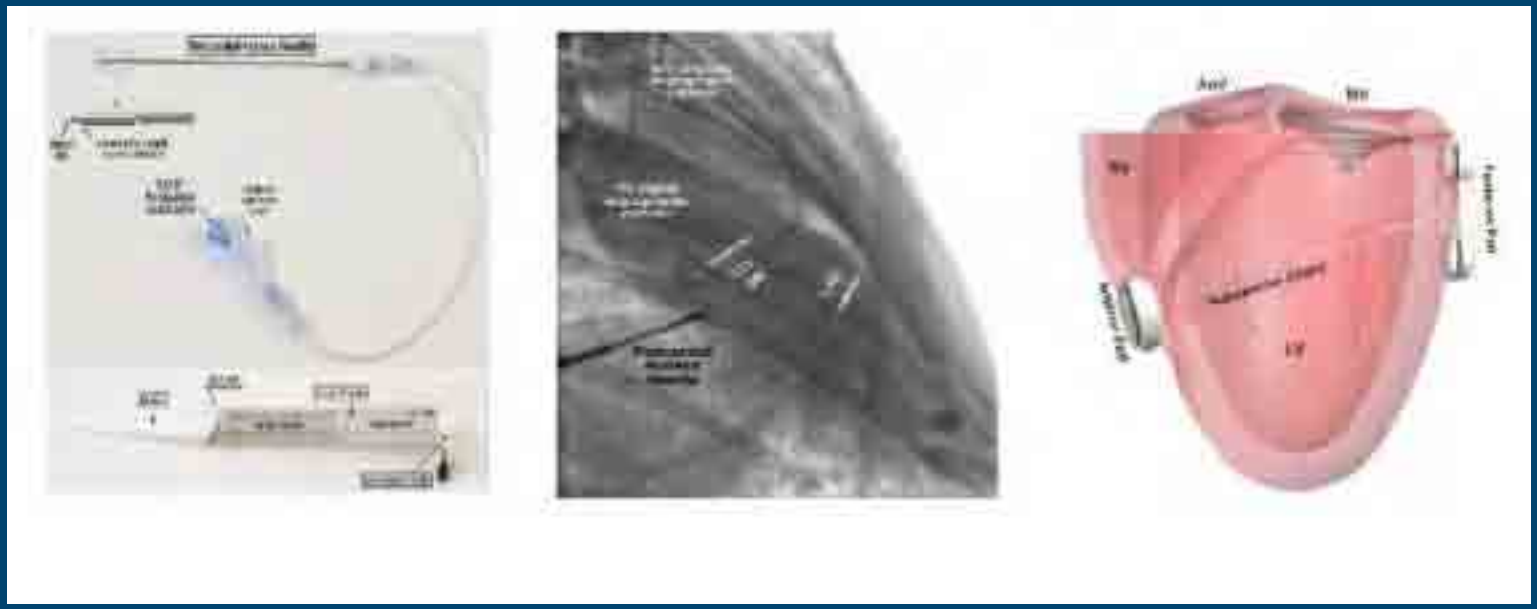
Phase I Surgical

- FIM experience in two patients with severe MR scheduled for cardiac surgery.
- Safety and efficacy issues
- ⇨Significant changes in the PS dimensions and MR

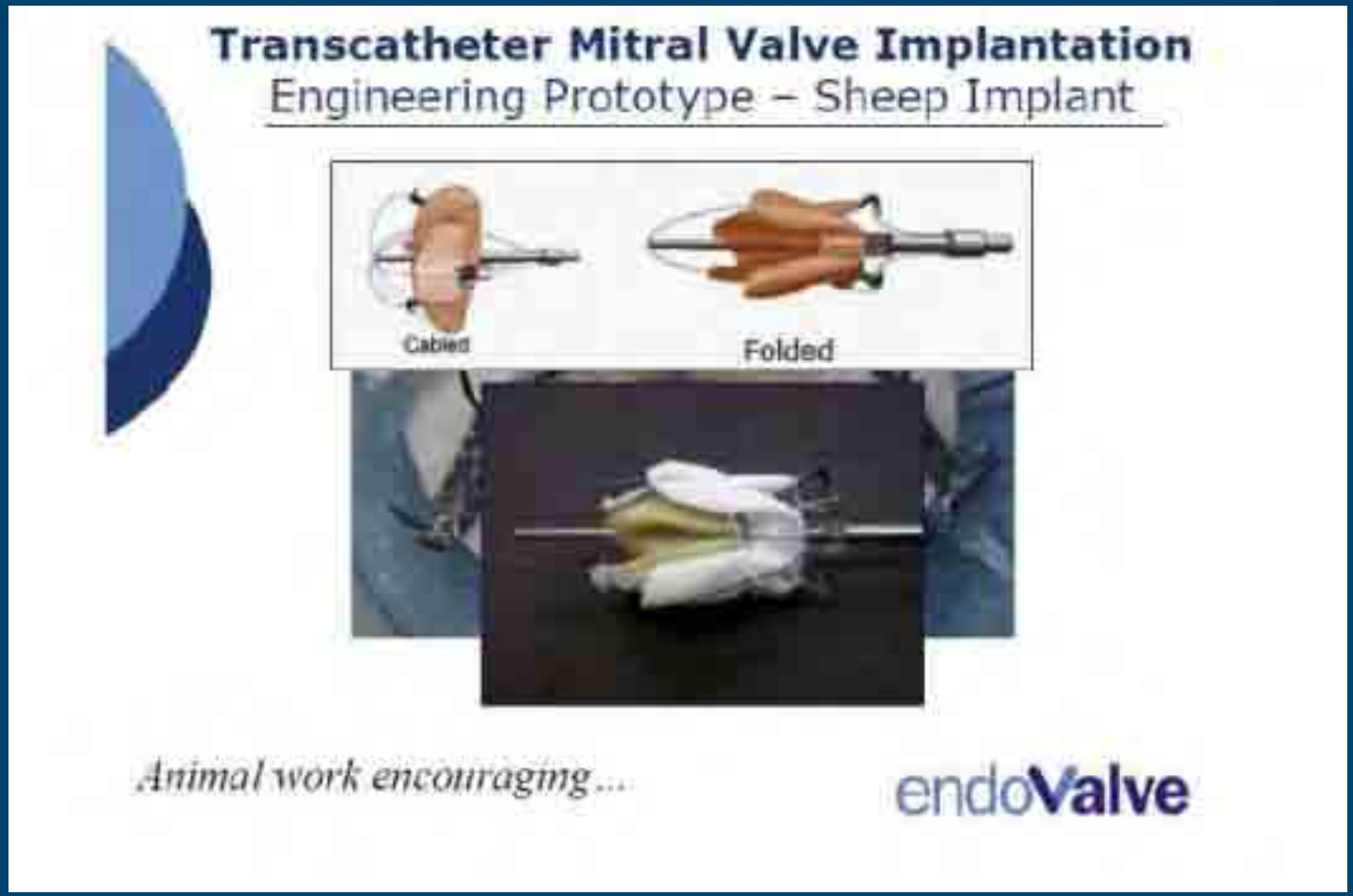
Phase II Café Trial

- To assess the feasibility and safety of the chronically implanted Ample PS3 device in patients with FMR
- 40 pts to be enrolled at 3 hospitals in Venezuela. Three patients initially done.
- Study restarted on May 2014

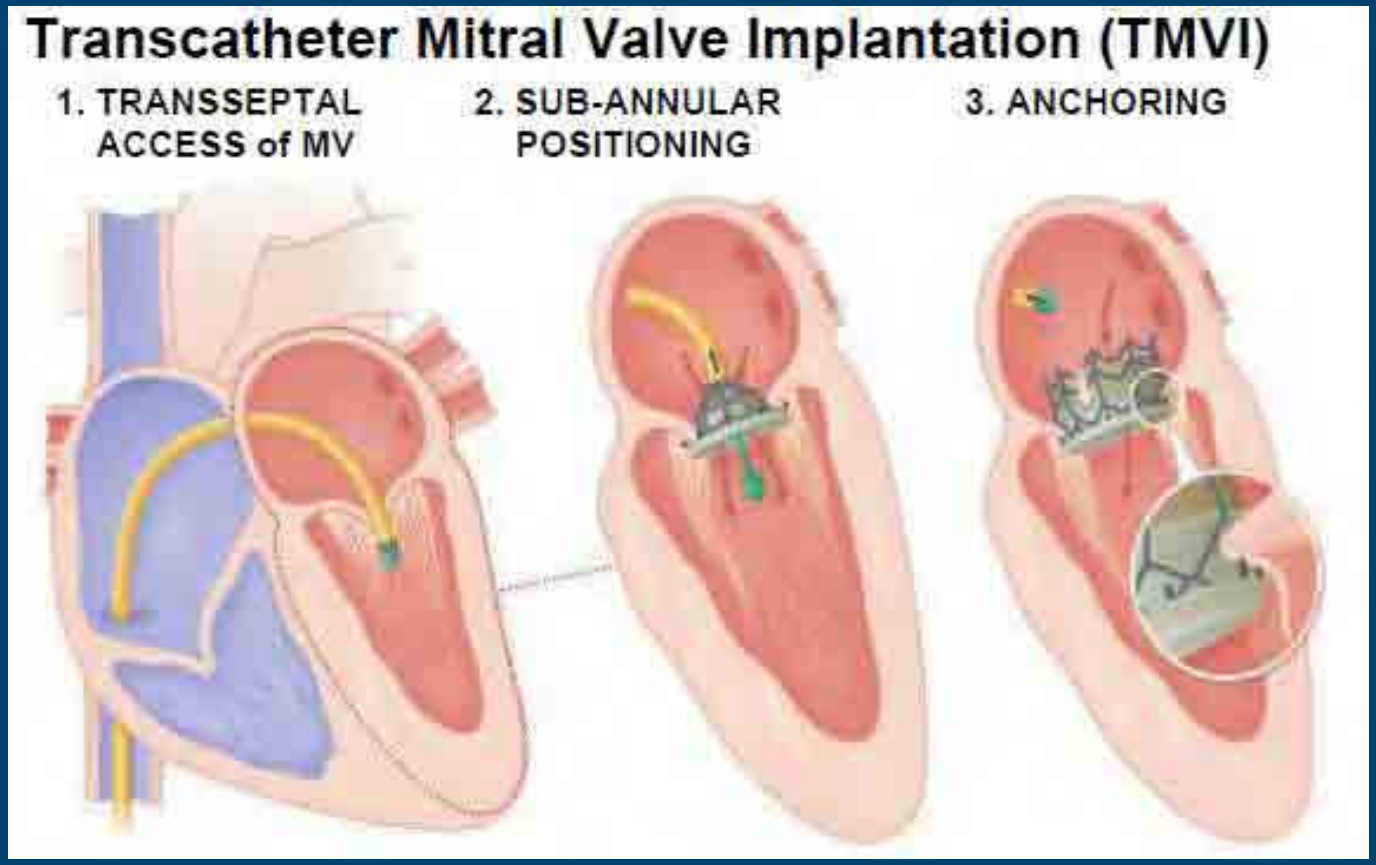
COAPSIS LV Remodeling



Transcatheter Mitral Valve Implantation



CardiAQ Valve Technologies



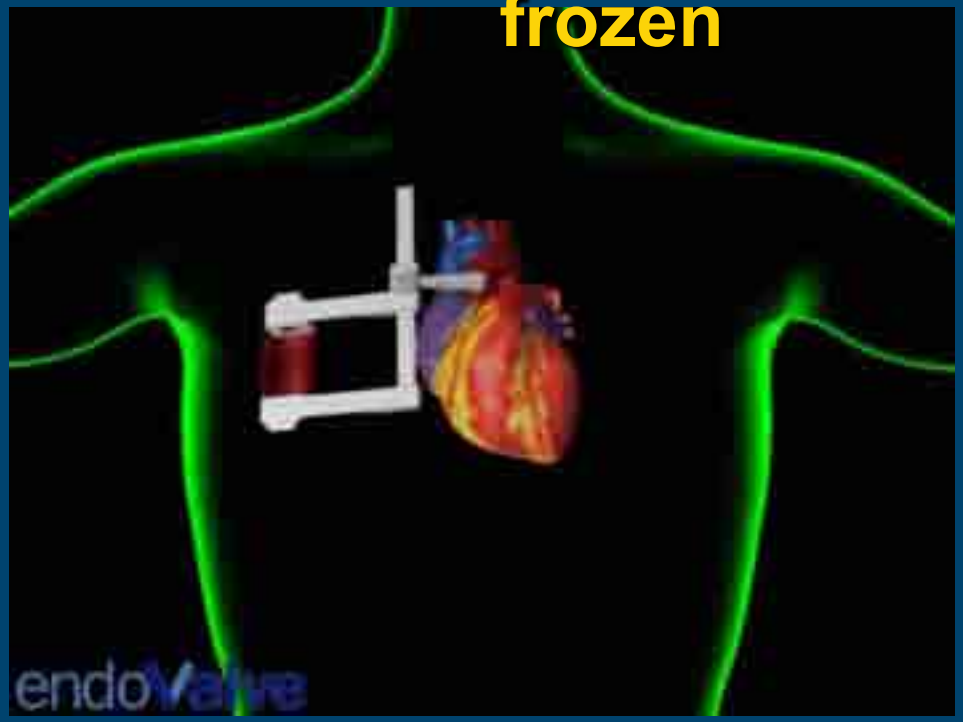
Percutaneous MV Replacement

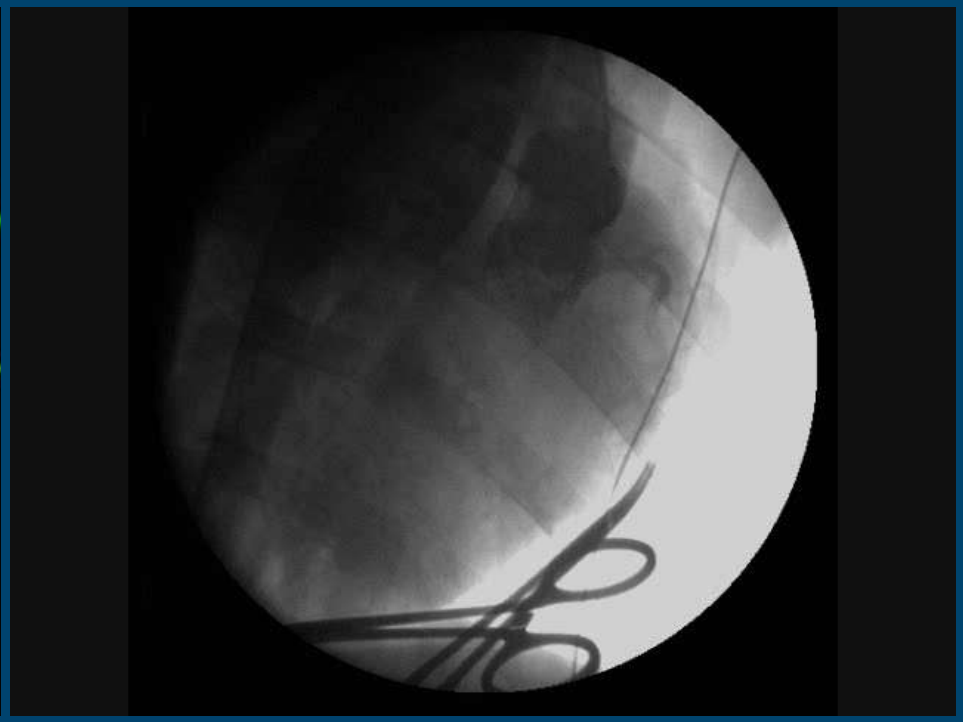
- Transseptal approach
- Valve sparing (like repair)
- Immediately function
- Repositionable

endoValve

CardiAQ Valve Technologies

Neither design frozen





Percutaneous Treatment of MR - Conclusions

- Mitral valve repair for organic MR has been performed successfully with the use of a leaflet plication method to create a double-orifice mitral valve.
- Reduction in the degree of MR and improvement of symptoms have been achieved with this catheter-based, non-surgical approach.
- Initial experience with experimental devices to treat FMR are encouraging but further development are needed to treat ischemic and functional MR.