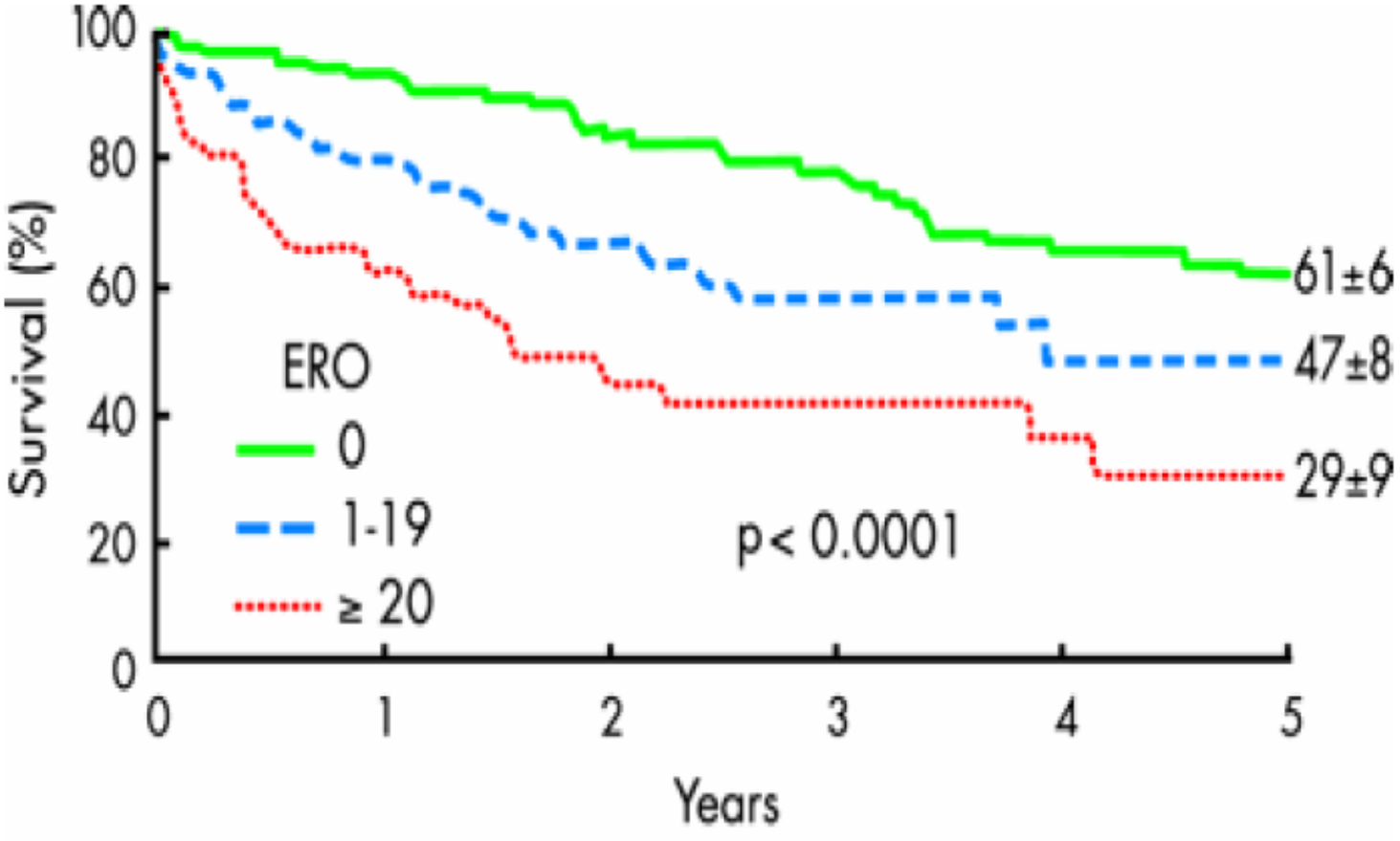
Percutaneous treatment modalities for mitral regurgitation

Nassos Manginas MD
FACC, FESC
Onassis Cardiac Surgery Center
Athens, Greece

Prognosis of Ischaemic MR



ERO < 20 mm²	1.65	0.049
ERO > 20 mm²	2.23	0.003

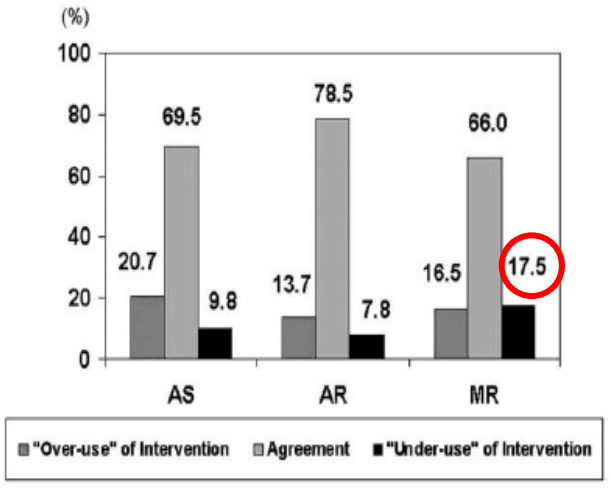
Grigioni Circulation 2001, 103; 1759

A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease

Bernard Iung[a*], Gabriel Baron[b], Eric G. Butchart[c], François Delahaye[d], Christa Gohlke-Bärwolf[e], Olaf W. Levang[f], Pilar Tornos[g], Jean-Louis Vanoverschelde[h], Frank Vermeer[i], Eric Boersma[j], Philippe Ravaud[b], Alec Vahanian[a]

Table 2 Type of valvular heart disease

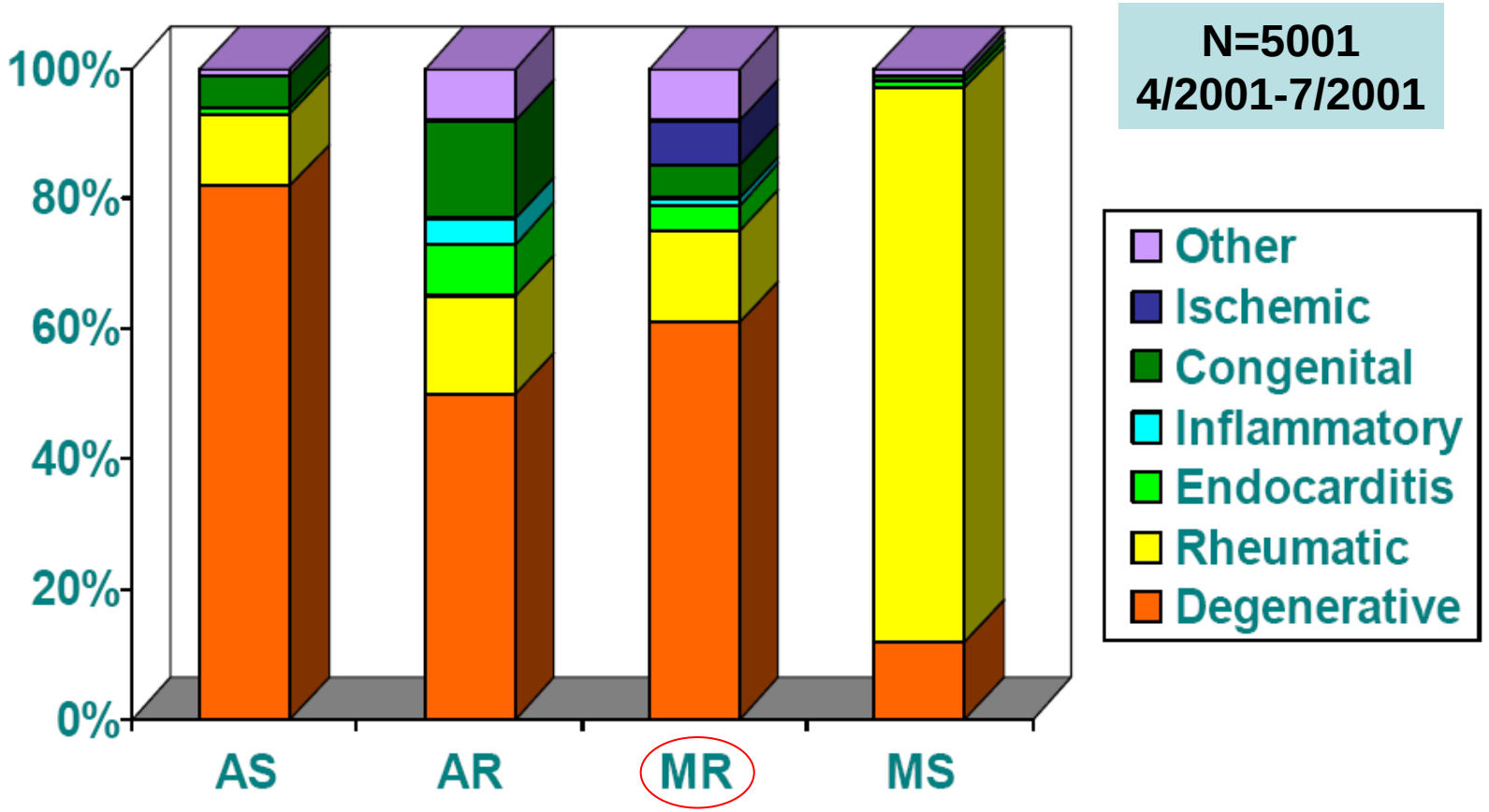
	Total population *n*=5001		Patients with intervention *n*=1269	
Native valve disease (%)	71.9		87.0	
Aortic (% native)	44.3		57.4	
Aortic stenosis (%)		33.9		46.6
Aortic regurgitation (%)		10.4		10.8
Mitral (% native)	34.3		24.3	
Mitral stenosis (%)		9.5		10.2
Mitral regurgitation (%)		24.8		14.1
Multiple (% native)	20.2		16.8	
Right (% native)	1.2		1.5	
Previous intervention (%)	28.1		13.0	
Conservative surgery (%)	18.4		28.7	
Valve replacement (%)	81.6		71.3	



European Heart Journal (2003) 24, 1231–1243

Single Native Valve Disease

Etiology

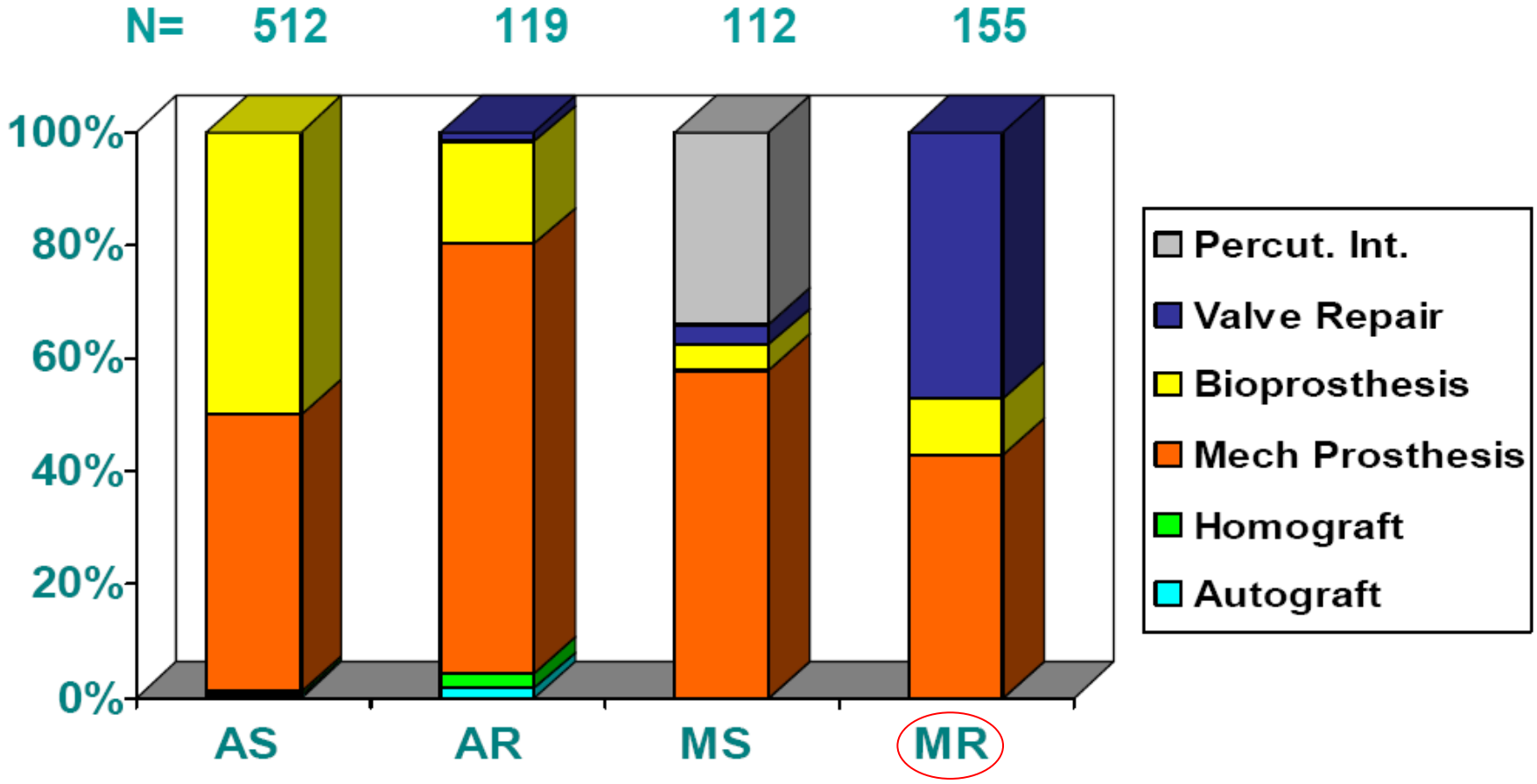


N=5001
4/2001-7/2001

Pre-operative Symptoms

	NYHA Class (%)			
	I	II	III	IV
Aortic Stenosis	**16**	**37**	39	*8*
Aortic Regurgitation	**21**	**32**	36	*11*
Mitral Stenosis	**15**	**21**	59	*5*
Mitral Regurgitation	**15**	**28**	42	*15*

Type of Intervention
Native Valve Disease



A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease

Bernard Iung[a*], Gabriel Baron[b], Eric G. Butchart[c], François Delahaye[d], Christa Gohlke-Bärwolf[e], Olaf W. Levang[f], Pilar Tornos[g], Jean-Louis Vanoverschelde[h], Frank Vermeer[i], Eric Boersma[j], Philippe Ravaud[b], Alec Vahanian[a]

Table 8 Operative mortality and morbidity of interventions according to the underlying valve disease

	Aortic stenosis *n*=512	Aortic regurgitation *n*=119	Mitral stenosis *n*=112	Mitral regurgitation *n*=155	Multiple valve disease *n*=185	Previous conservative intervention *n*=47	Previous prosthetic replacement *n*=117
Mortality (%)	3.1	3.4	0.9	3.9	6.5	2.1	6.2
Major Bleeding (%)	7.7	2.5	2.7	7.7	10.8	4.3	12.0
Tamponade (%)	2.9	1.7	0.9	2.6	4.3	0	1.7
Embolism[a] (%)	3.1	2.5	2.7	7.1	2.2	2.1	3.4
Prosthetic thrombosis[b] (%)	0.2	0	0.9	0.6	0	0	0
Myocardial infarction (%)	1.0	0	0	0.6	0.5	0	1.7
Mediastinitis (%)	0.6	0.8	0	1.3	2.2	0	0

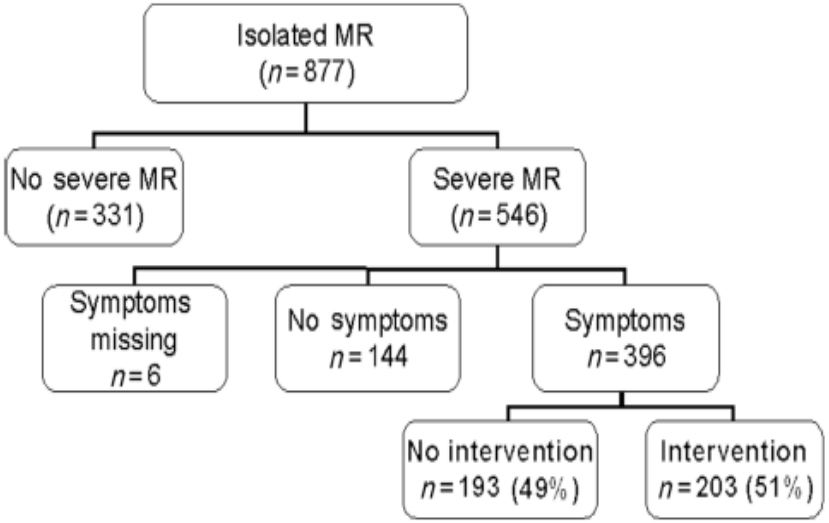
The 16 patients operated on for right-sided valve disease are not detailed. Major bleeding is defined by bleeding leading to death, surgery, or transfusion.

[a]including transient ischaemic attacks.
[b]oclusive or non-occlusive thrombosis.

European Heart Journal (2003) 24, 1231–1243

What are the characteristics of patients with severe, symptomatic, mitral regurgitation who are denied surgery?

Mariana Mirabel[1], Bernard Iung[1]*, Gabriel Baron[2], David Messika-Zeitoun[1], Delphine Détaint[1], Jean-Louis Vanoverschelde[3], Eric G. Butchart[4], Philippe Ravaud[2], and Alec Vahanian[1]



1 year survival **89,5±2,3%** **96,0±1,4%**
p=0,02

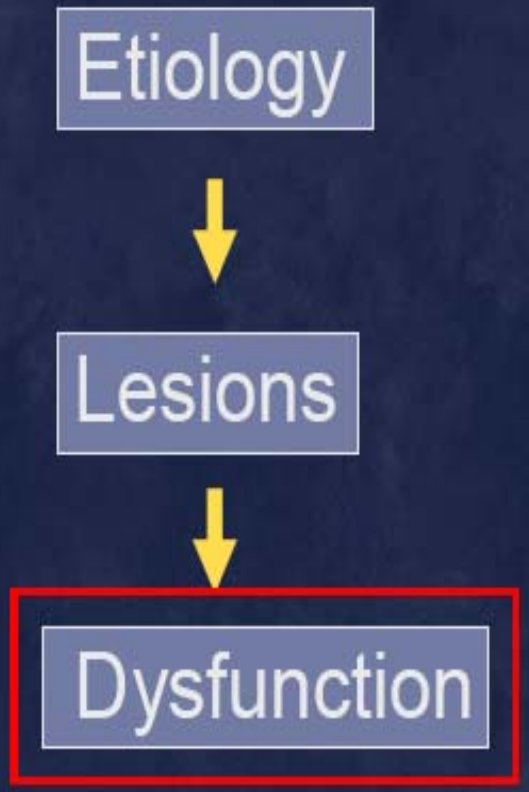
Table 3 Factors associated with a decision not to operate. Multivariable analysis

	P	Odds ratio	95% CI
LVEF (per 10% decrease)	0.0002	1.39	(1.17–1.66)
Aetiology	0.0006		
Ischaemic		1	
Non-ischaemic		4.44	(1.96–10.76)
Age (per 10-year increase)	0.001	1.40	(1.15–1.72)
Charlson comorbidity index (per 1 point increase)	0.004	1.38	(1.12–1.72)
Degree of MR	0.005		
Grade 4/4		1	
Grade 3/4		2.23	(1.28–3.29)

Hosmer-Lemeshow goodness-of-fit $\chi 2 = 9.84$ (df = 8), $P = 0.28$.

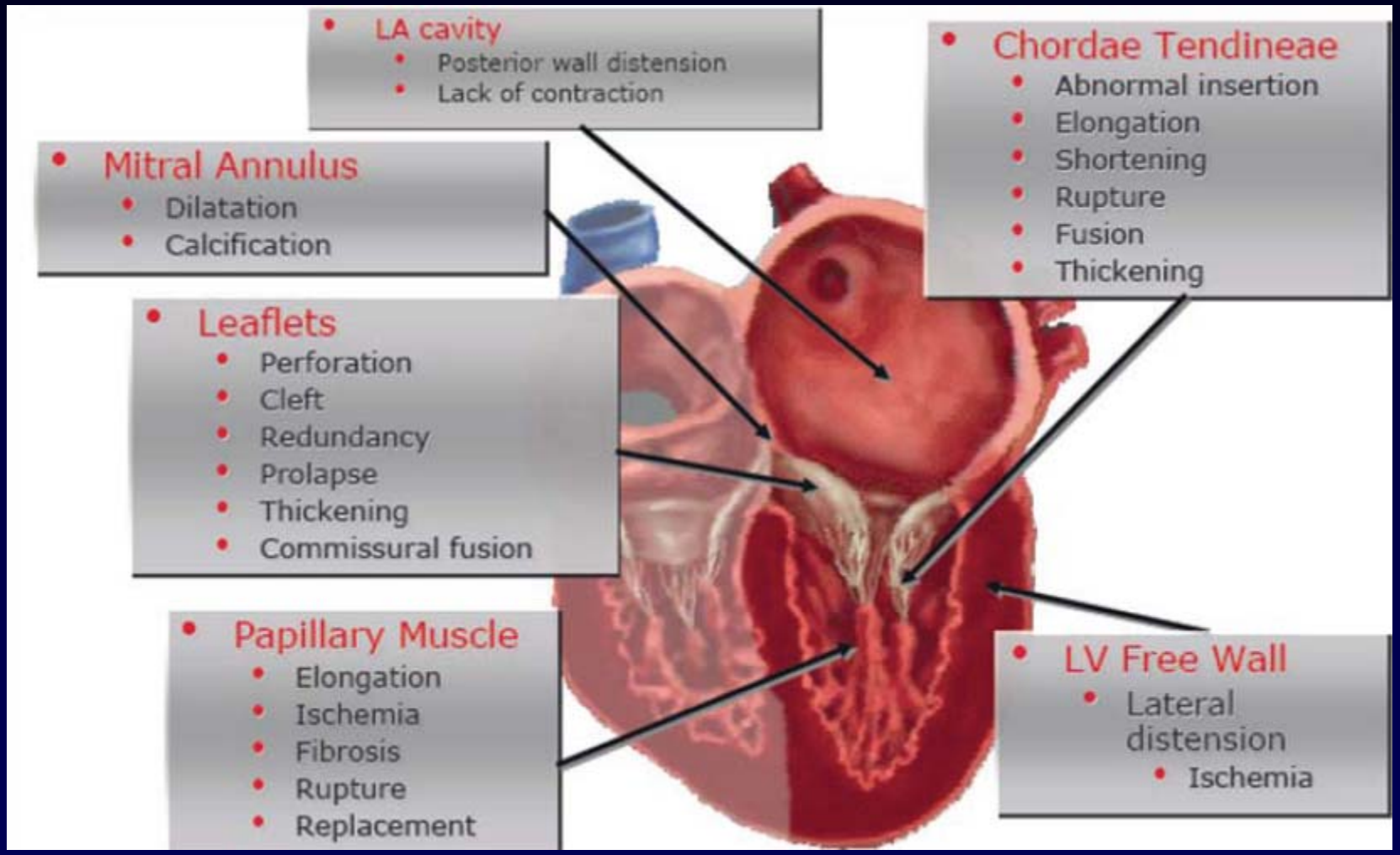
European Heart Journal (2007) 28, 1358–1365

The Pathophysiologic Triad

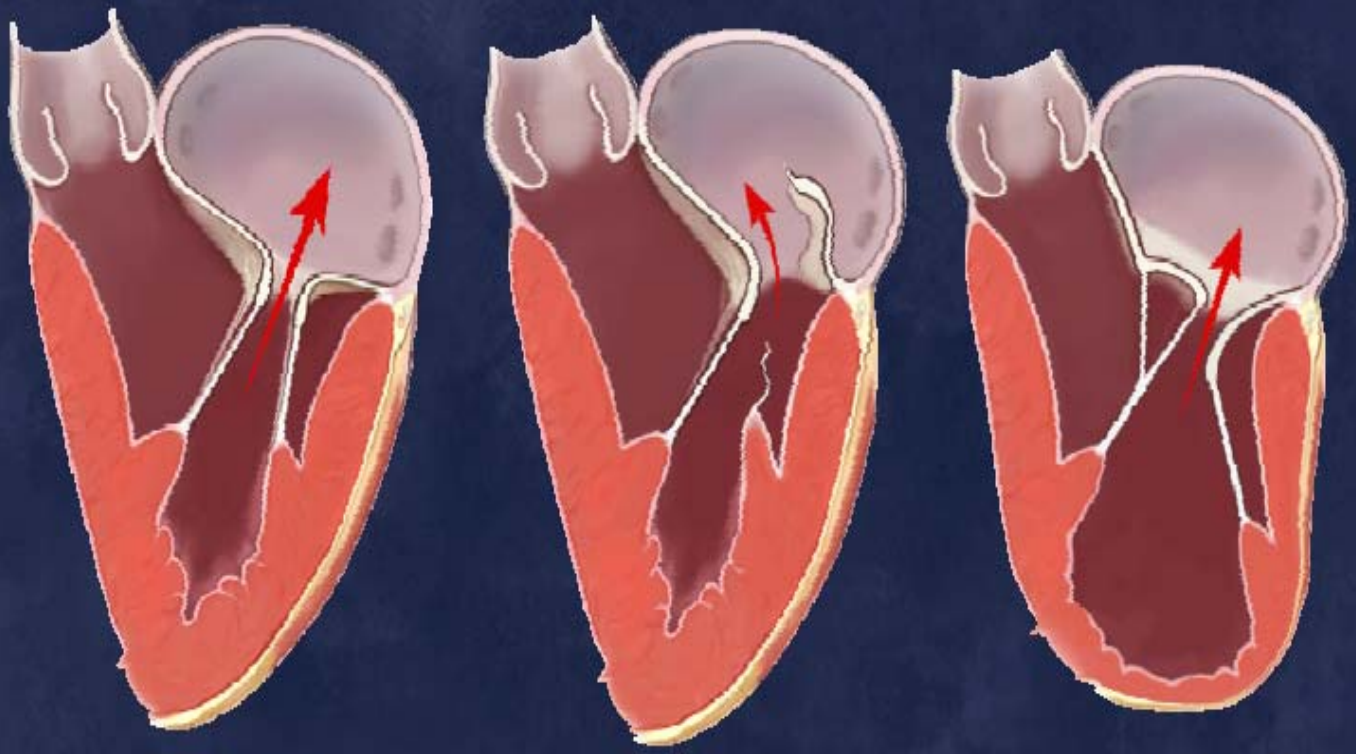


Carpentier et al. J Thorac Cardiovasc Surg 1983; 86

Lesions leading to MR



Mitral Valve Dysfunction

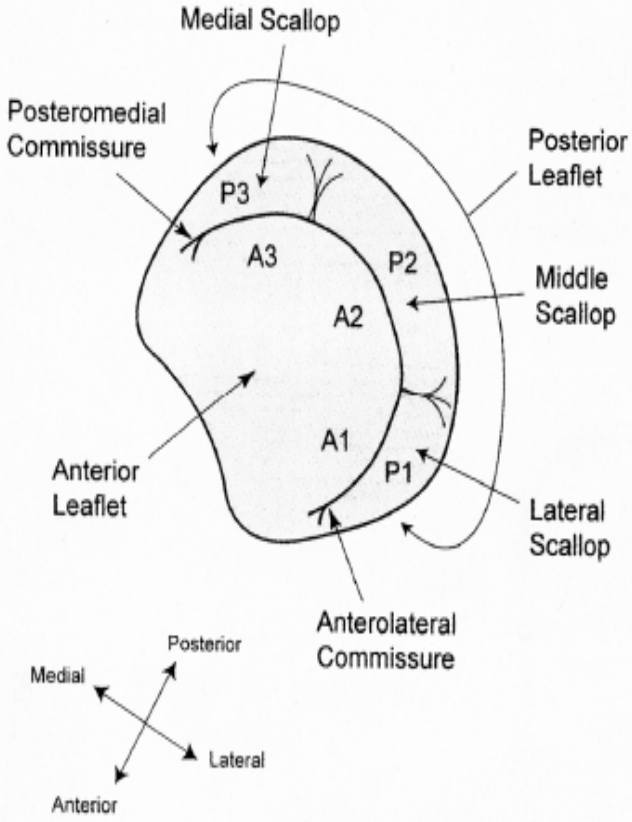


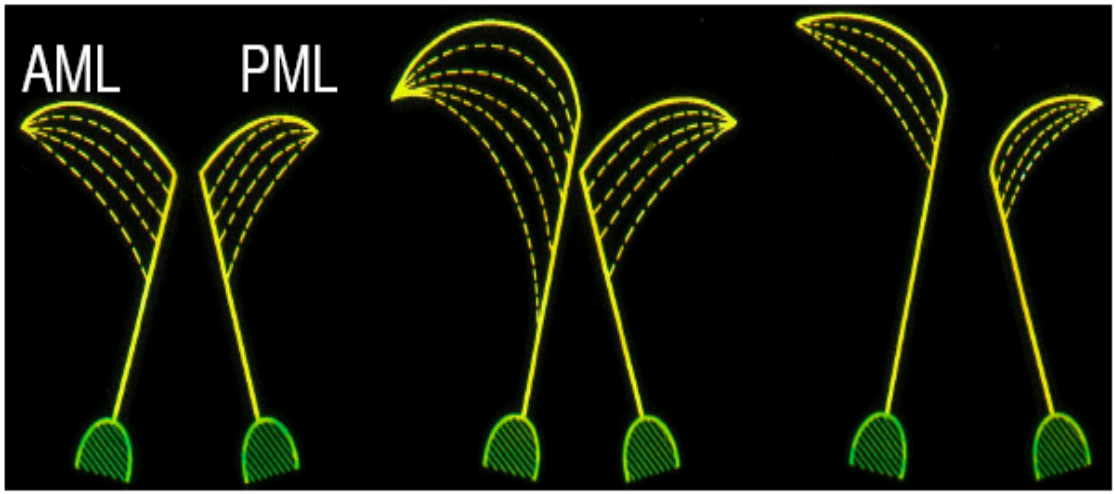
Carpentier's Valve Reconstruction; Carpentier A, Adams DH, F Filsoufi (in press)

Echo guidance

- Echo is the gold standard primary imaging modality for lesion and dysfunction diagnosis
- Needs to be reviewed by the Interventional Cardiologist
- A nomenclature is needed
- A preprocedural conference is necessary

Echographic Guidance is Key





TYPE I

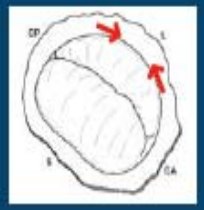
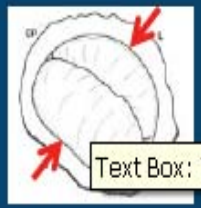
Nle Leaflet Motion

TYPE II

Prolapse

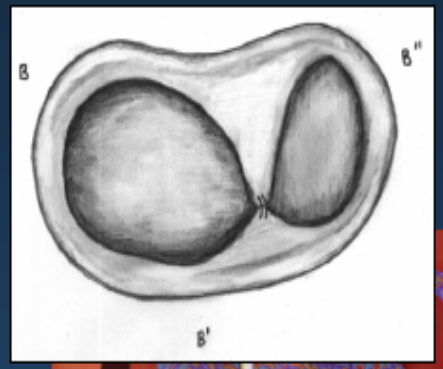
TYPE III

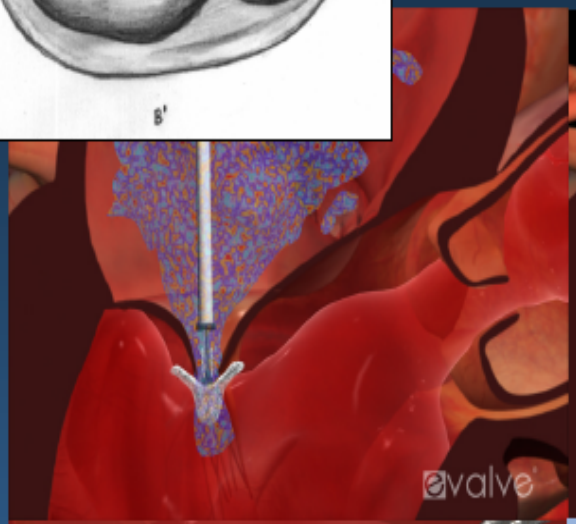
Restricted Motion

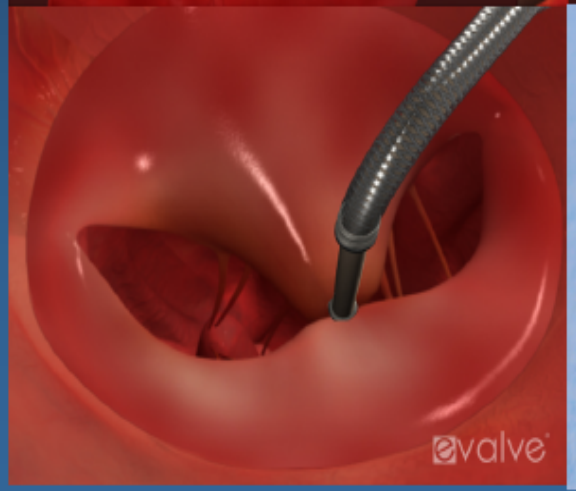
Technology	Approach		Status
Bowtie • E Valve • Edwards	Leaflet Coupling		Clinical
Coronary Sinus • Edwards • Cardiac Dimensions • Viacor	CS Reshaping		Early Clinical
Annulus Plication • Mitralign • Guided Delivery Systems	Posterior Reshaping		Pre-Clinical
LV Shape Change • Myocor (Surgical/Endovascular)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

Text Box: Technology Summary

Percutaneous Mitral Repair



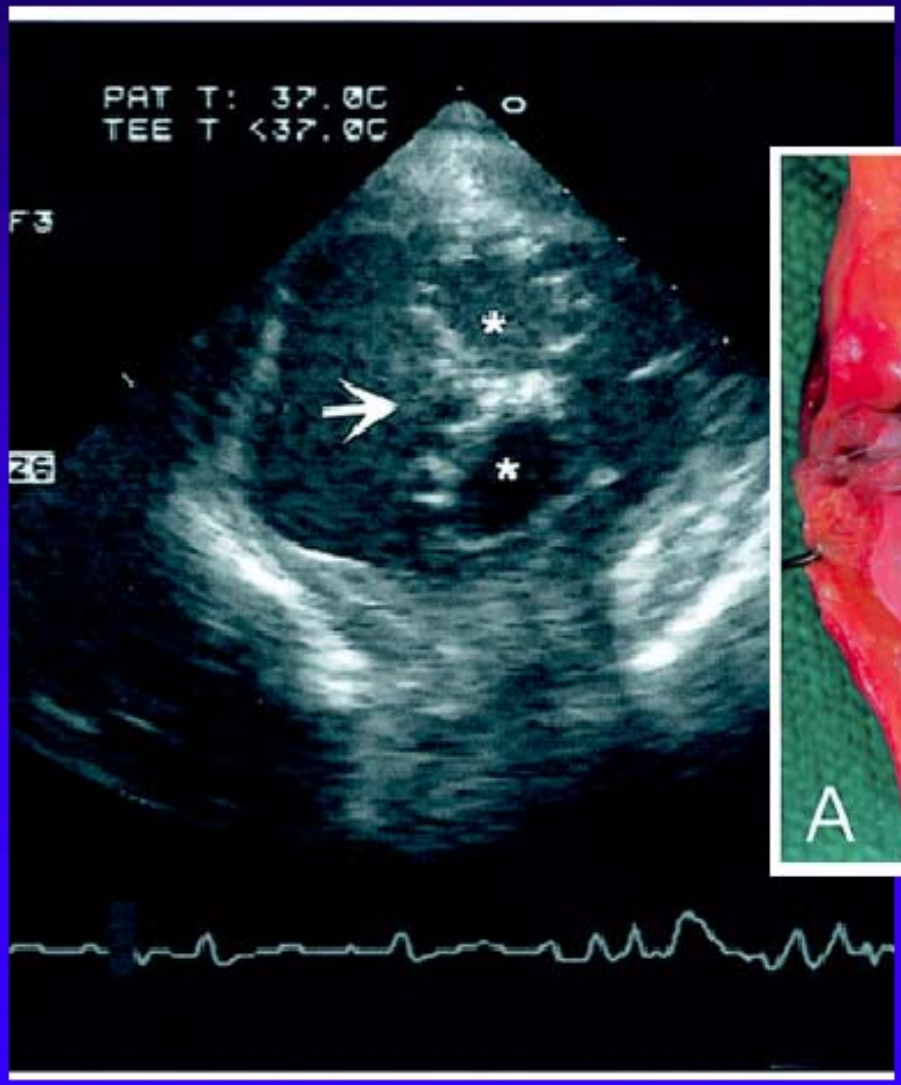


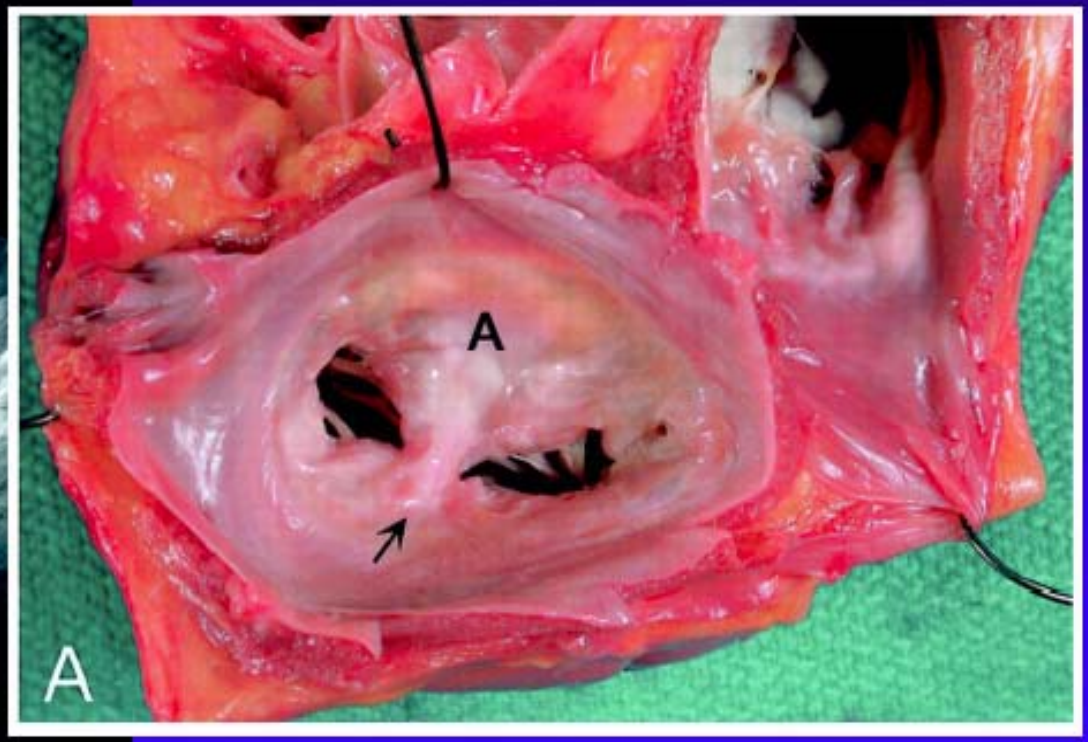


Images in Cardiovascular Medicine

Alfieri Mitral Valve Repair

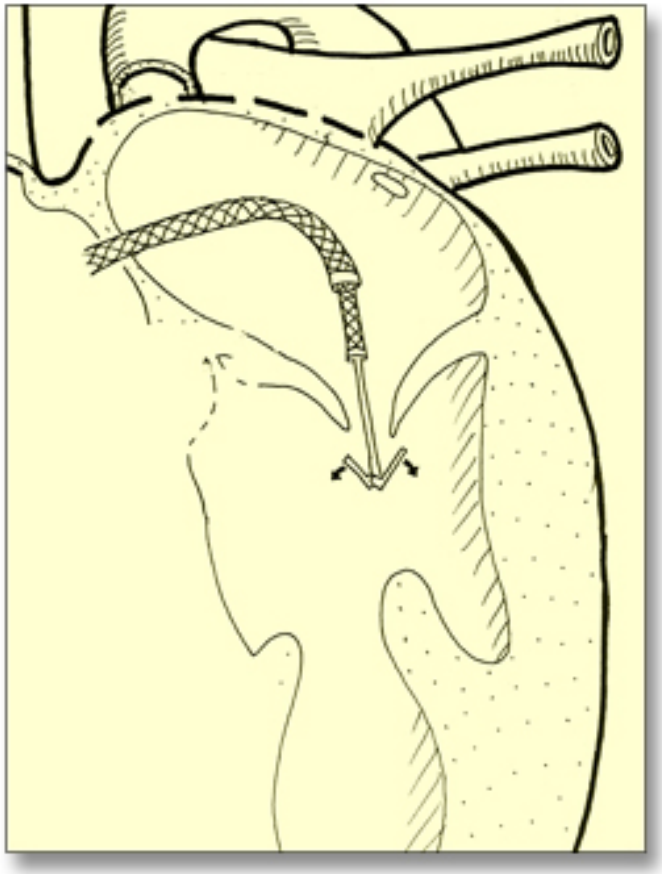
Clinical Outcome and Pathology



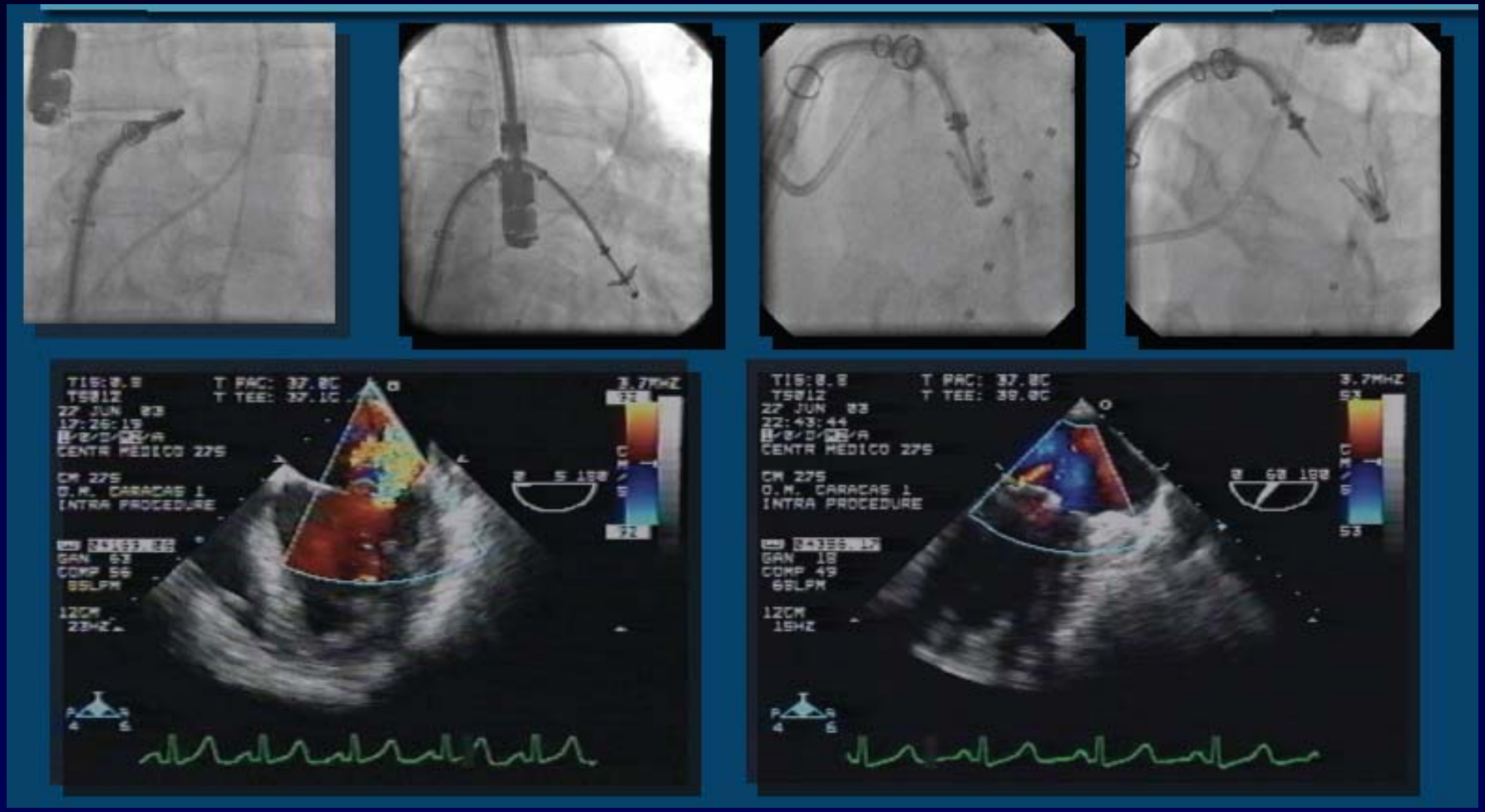


Circulation. 2002;106:e173

Clip Opened and Advanced



E-valve. First Case Performed



EVEREST Preliminary Cohort
MR Etiology
N = 107

Degenerative/Mixed	84 (79%)
Posterior Prolapse/Flail	57 (68%)
Anterior/Bi-leaflet Prolapse/Flail	27 (32%)
Functional	23 (21%)

EVEREST II: Key Echocardiographic Selection Criteria

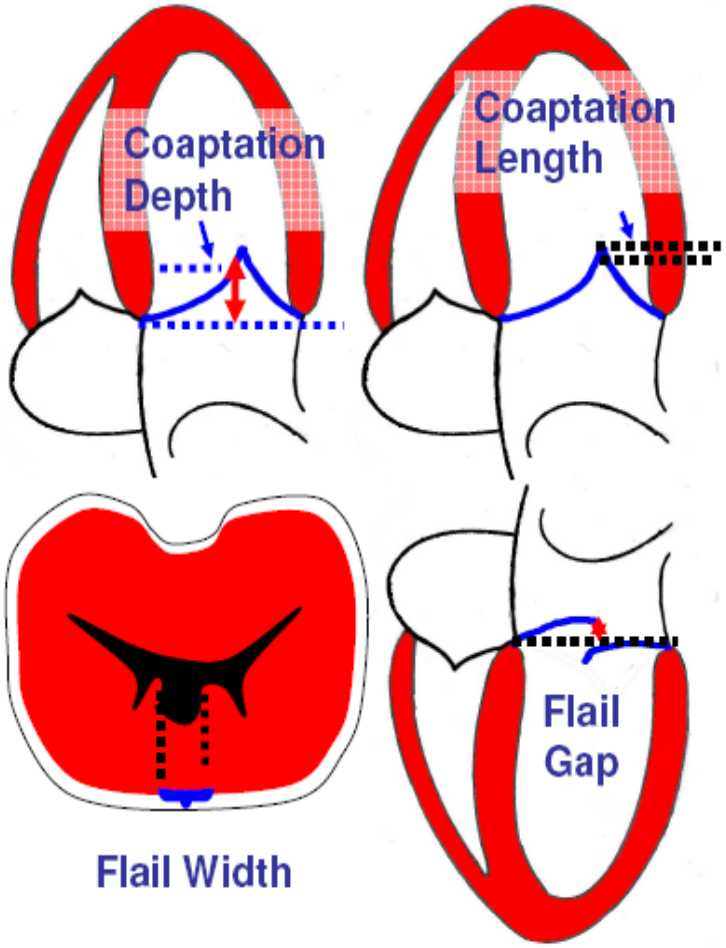
I. **A2-P2 mal-coaptation**

II. **Key exclusions:**

- A. Severe MAC and/or leaflet Ca++
- B. Flail exclusions
  1. Width in short axis > 15 mm
  2. Flail gap in long-axis view >10 mm
- C. Functional MR with leaflet tethering:
  1. Coaptation depth (below annulus) > 11 mm
  2. Coaptation length (contact) < 2 mm

III. **Knowledge based on current data**

- A. Learning continues …



EVEREST I Trial
Inclusion Criteria

- Moderate to Severe Mitral Regurgitatation.
- Experiencing symptoms (fatigue, chest pain, shortness of breath).
- Asymptomatic patients with decreased LV systolic function.
- MR originating from the central two thirds of the valve; and
- Qualify for mitral valve surgery including cardiopulmonary bypass.

EVEREST II

Key Eligibility Criteria

- Age 18 years or older
- Moderate to severe (3+) or severe (4+) MR
  - *Symptomatic*
  - *Asymptomatic with LVEF <60% or LVESD >45mm*

  ACC/AHA Task Force Guidelines JACC 1998;32:1486
- MR originates from A2-P2 mal-coaptation
- Core lab echo assessment

  ASE Guideline - JASE 2003;16:777-802
- Candidate for mitral valve surgery including CPB
- Transseptal deemed feasible
- Key Exclusions
  - *EF < 25% or LVESD > 55 mm*
  - *Renal insufficiency*
  - *Endocarditis, rheumatic heart disease*

Pivotal Study of Percutaneous Edge-to-Edge MV Repair

- Prospective, randomized, multi-center study
- Phase II evaluation of the safety & effectiveness of an endovascular approach to the treatment of MR using the Evalve Cardiovascular Valve Repair System
- 279 patients randomized 2:1
  - Up to an additional 3 roll in-patients per site
- Treatment *strategy* comparison
  - includes whether surgery can be performed safely after initial percutaneous approach

Study Power

Percutaneous treatment with the MitraClip

vs

Strategy of mitral repair or replacement surgery

EVEREST II

Primary Effectiveness Endpoint

- 12 months freedom from
  - death
  - moderate to severe (3+) or severe (4+) MR
  - surgery for valve dysfunction

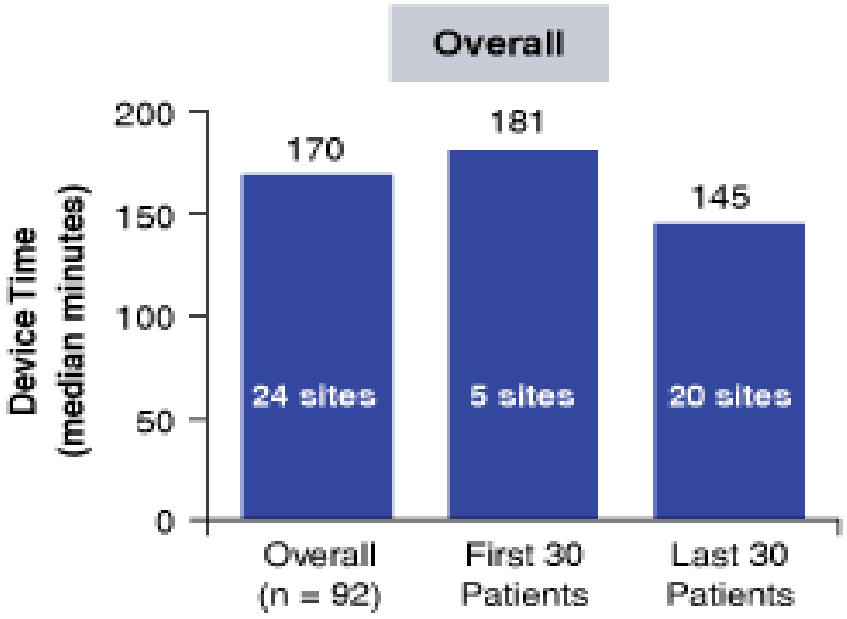
- *Valve dysfunction defined as:*
  - *3+ or 4+ MR*
  - *mitral stenosis*
  - *valve injury*
  - *clip detachment*
  - *failed surgical repair or replacement or prosthesis failure*
  - *any surgery required for further reduction in MR*

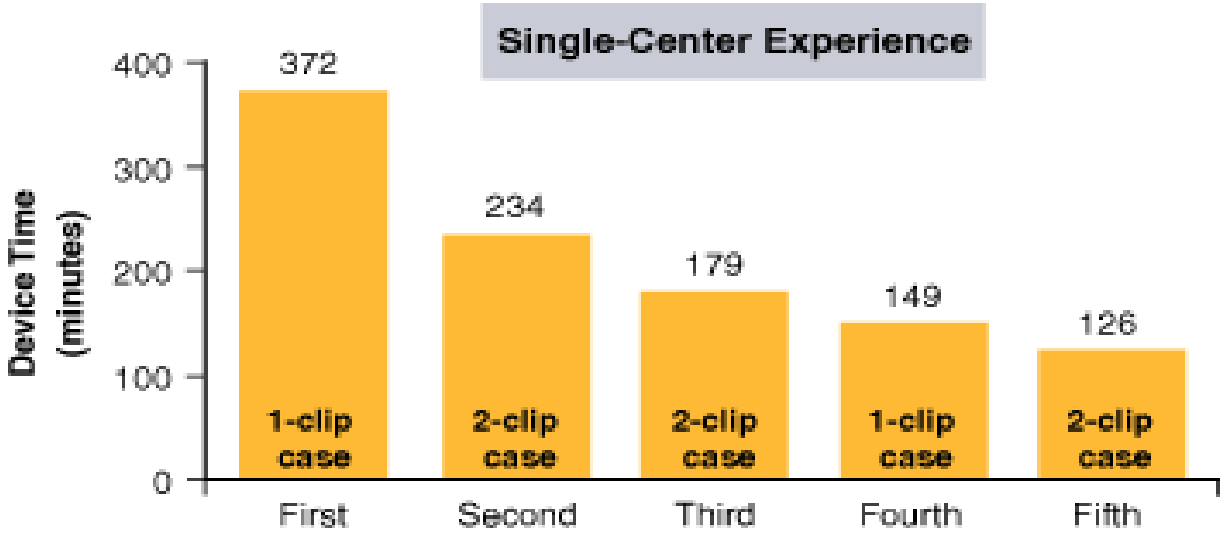
EVEREST I & II Enrollment

Randomization 8/5/2005-9/17/2008

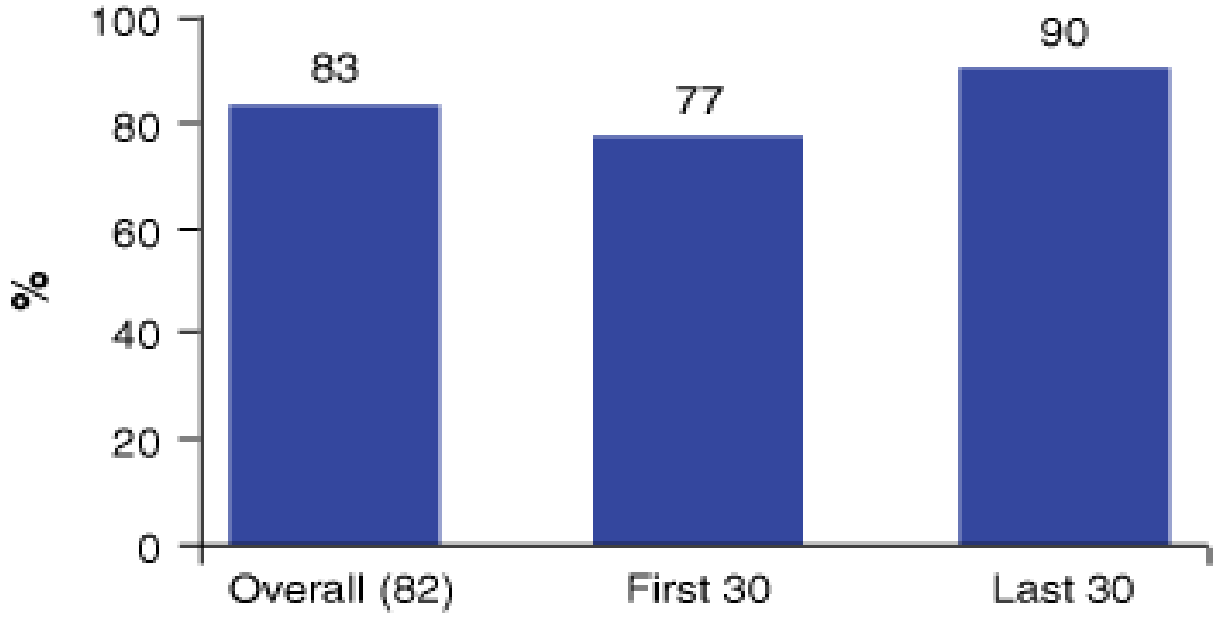
Enrollment	Population	n
EVEREST I Feasibility (1st patient 7/2/2003)	Registry patients	55
EVEREST II Randomized n=279	Roll-in	60
	Randomized Clip	184
	Randomized Surgery	95
EVEREST II	High Risk Registry	78
Total enrolled		472

EVEREST: Procedural Learning Curve



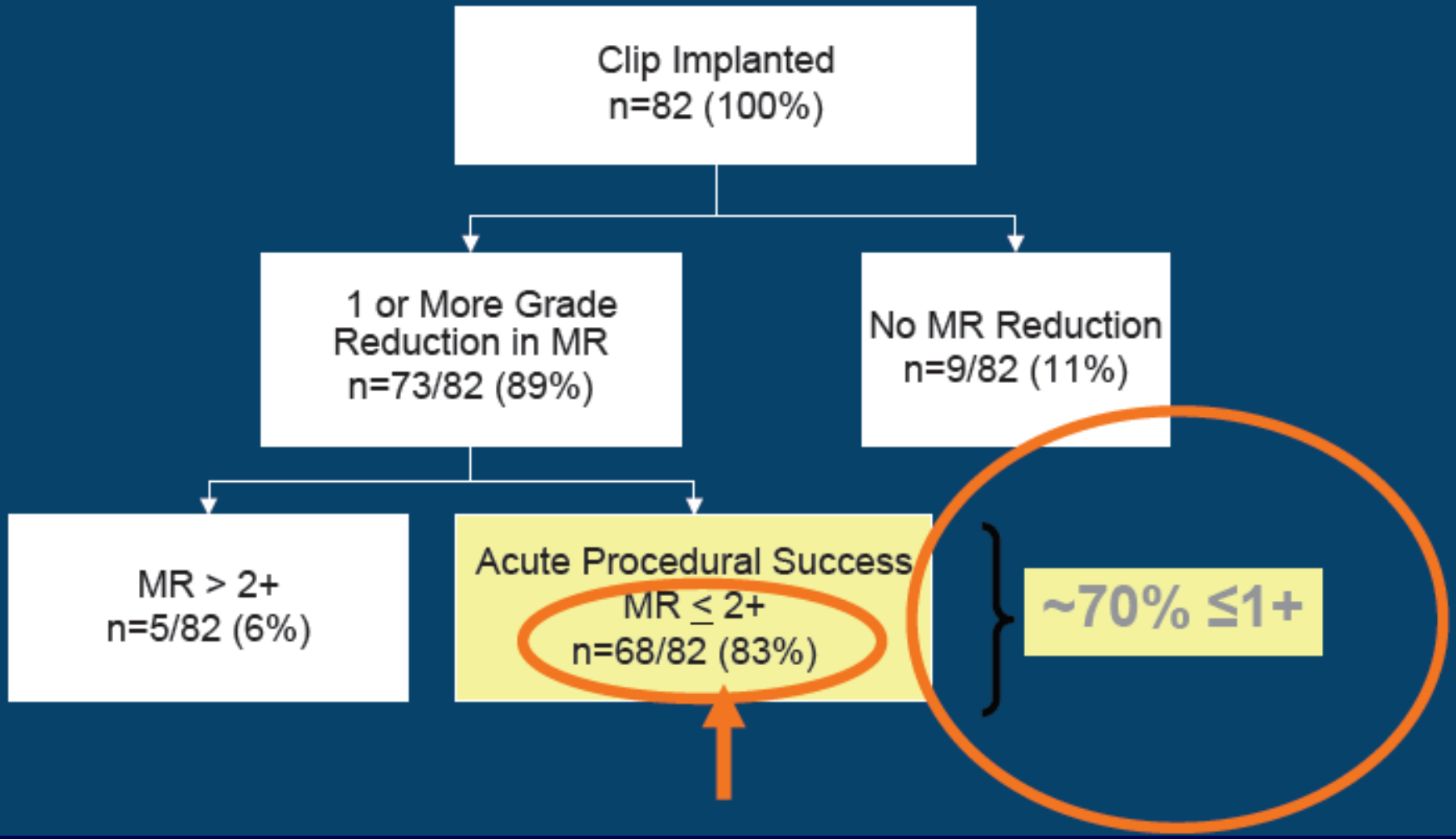


Evalve Clip Patients: Acute Procedural Success*
(n = 82)



*Defined as placement of one or more clips resulting in discharge mitral regurgitation severity of 2+ or less, as determined by core lab

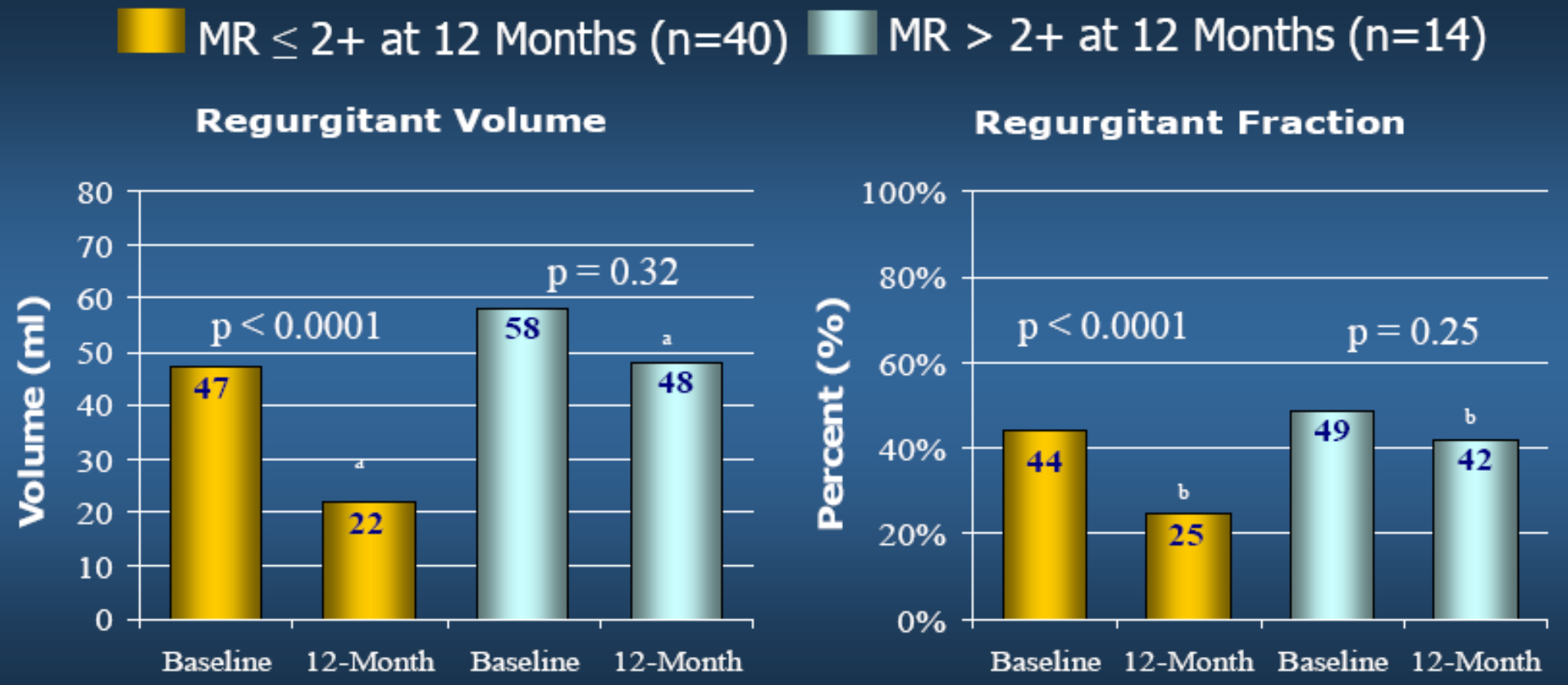
E-valve
Immediate Results



EVEREST Preliminary Cohort

LV Reverse Remodeling after 12-months

APS Patients (n = 54)



a: change from baseline
p = 0.05 vs. MR>2+ group

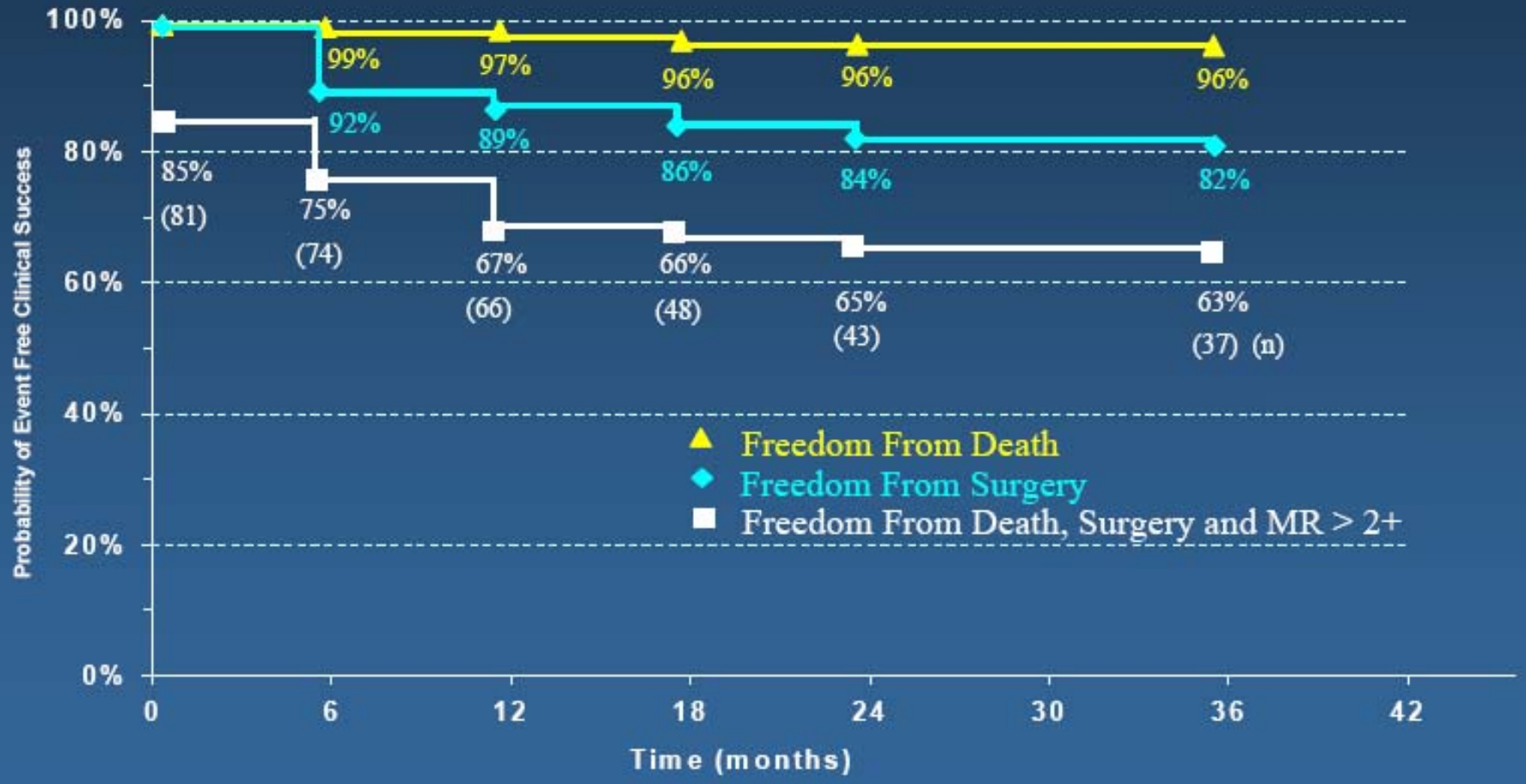
b: change from baseline
p < 0.02 vs. MR>2+ group

Evanston Hospital
NorthShore
University HealthSystem

EVEREST Preliminary Cohort

Event Free Clinical Success Kaplan-Meier

Acute Procedure Success Patients n = 81



Evanston Hospital NorthShore University HealthSystem

Freedom from death, mitral valve surgery, & MR>2

Surgical Option Is Preserved Following Evalve Clip Procedure

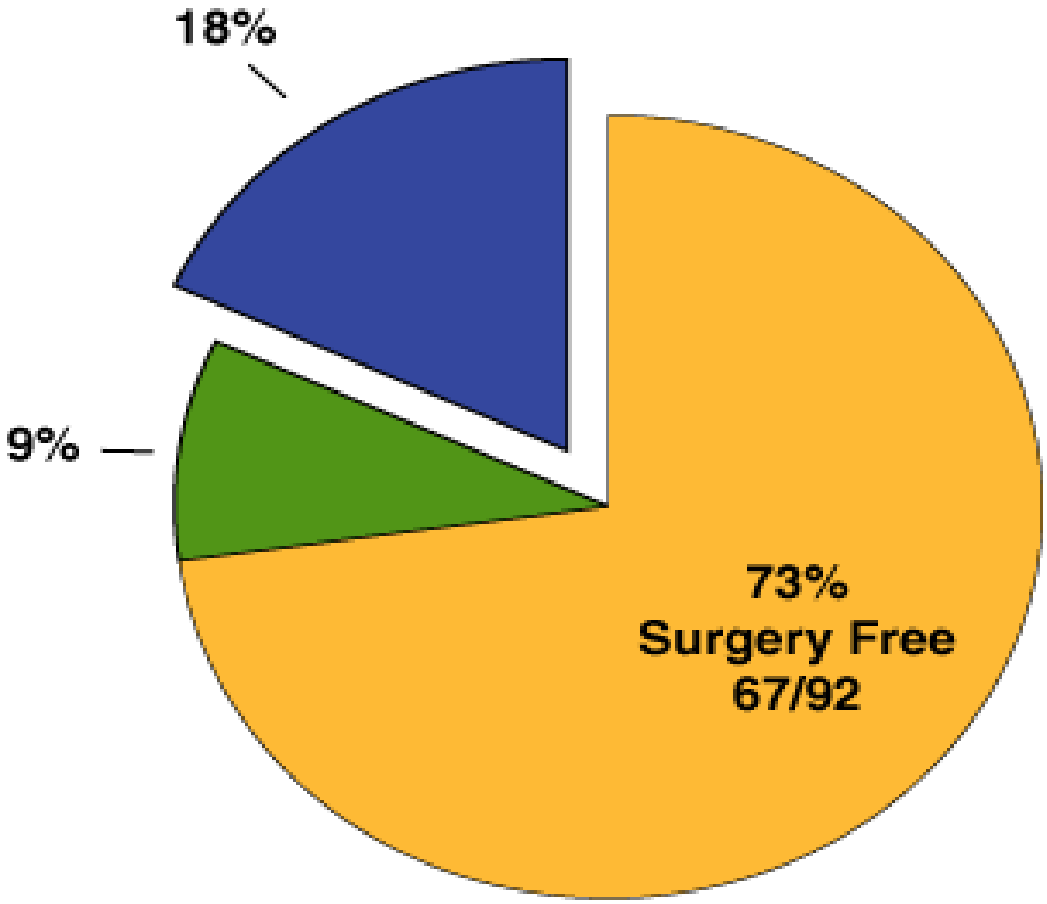
Surgery after Clip Implanted (n = 17)

- 12 Repairs (0-555 days)
- 5 Replacements

68% of surgery patients repaired

Surgery after No Clip (n = 8)

- 5 Repairs
- 3 Replacements

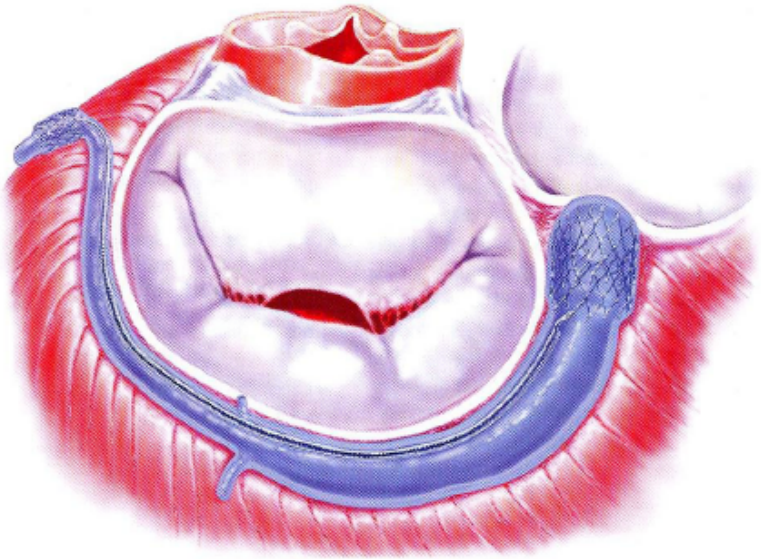


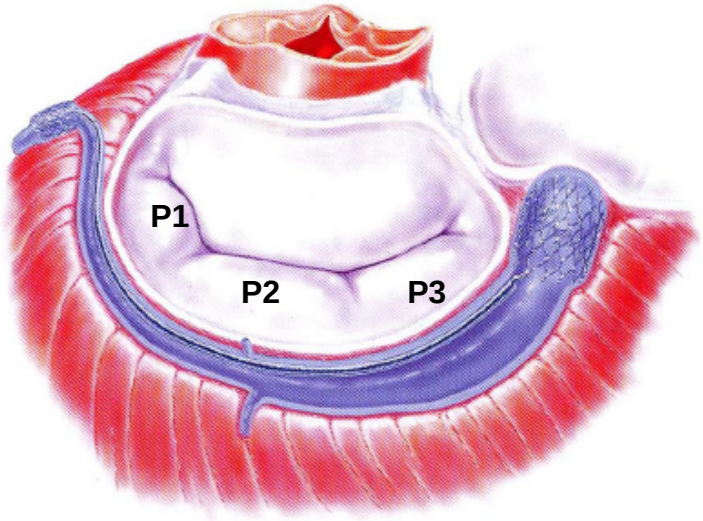
EVEREST: In-Hospital Outcomes

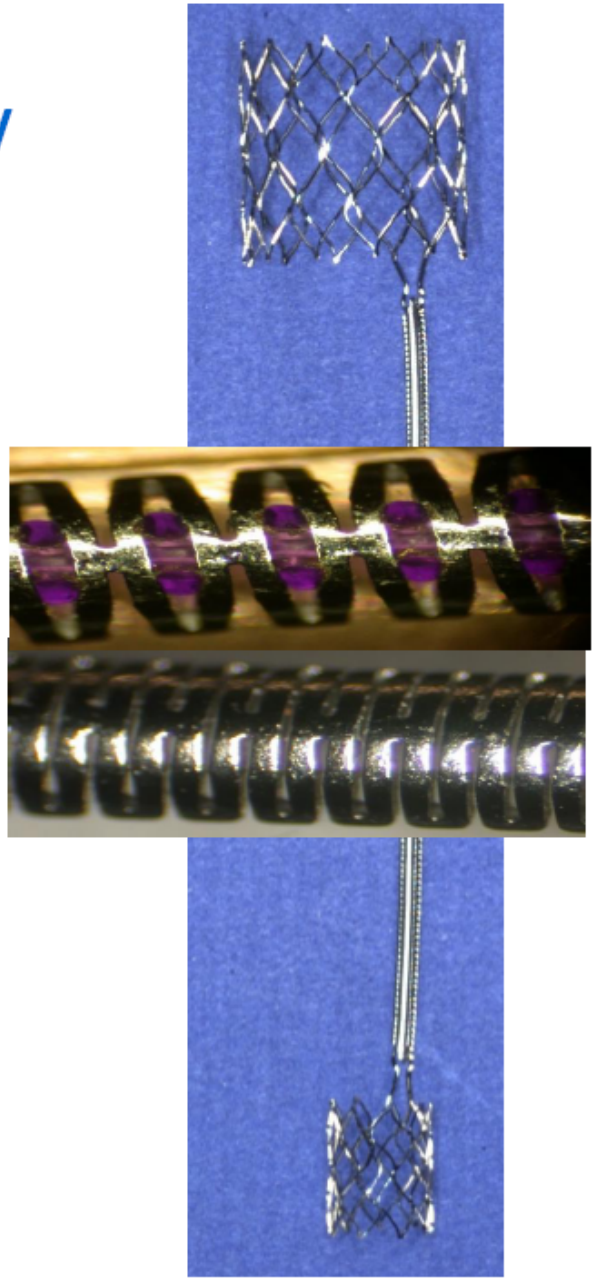
	EVEREST (n = 92)	2002 STS	
		Repair	Replacement
Death – unrelated to clip	1 (1.1%)	1.5%	6.0%
Mechanical ventilation >48 hrs	0 (0.0%)	5.0%	13%
Blood product use	2 (2.2%)	37.0%	56%
Transseptal complication requiring surgery	1 (1.1%)	na	na
Effusion requiring pericardiocentesis	1 (1.1%)	na	na
Renal failure or dialysis	0 (0.0%)	3.0%	5.0%
Post-procedural hospital stay (median days)	2.0	5	7
ICU/CCU time (median days)	1.2	na	na
Discharged home (without home health care)	90 (98%)	na	na

STS = Society of Thoracic Surgeons; ICU = Intensive Care Unit; CCU = Critical Care Unit

The MONARC system
Delayed Release-*in situ*

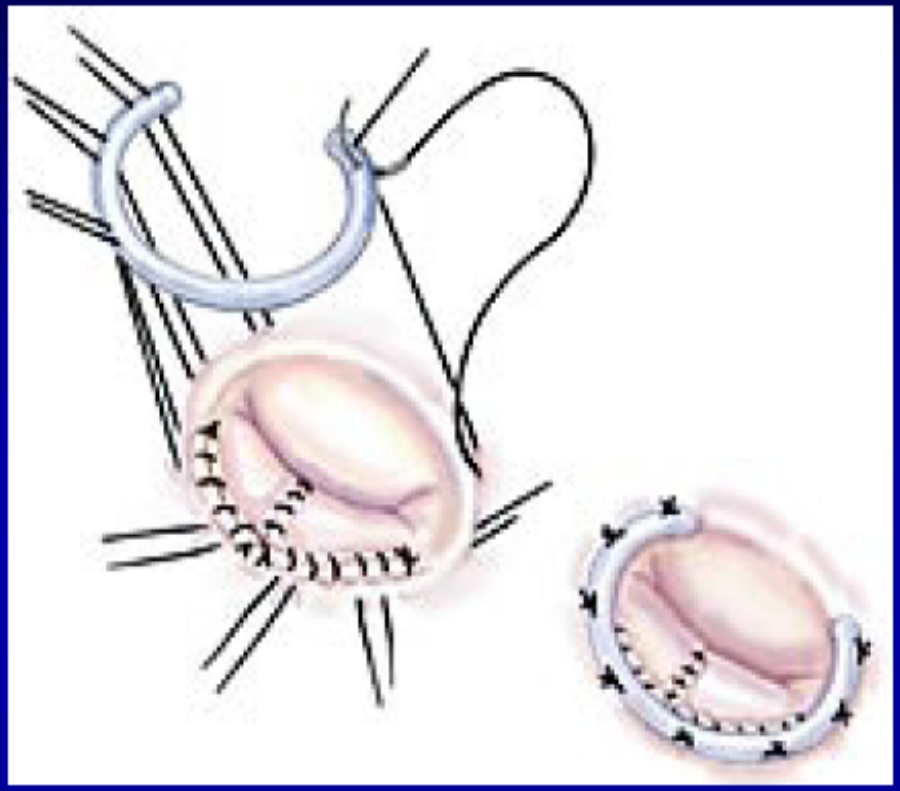






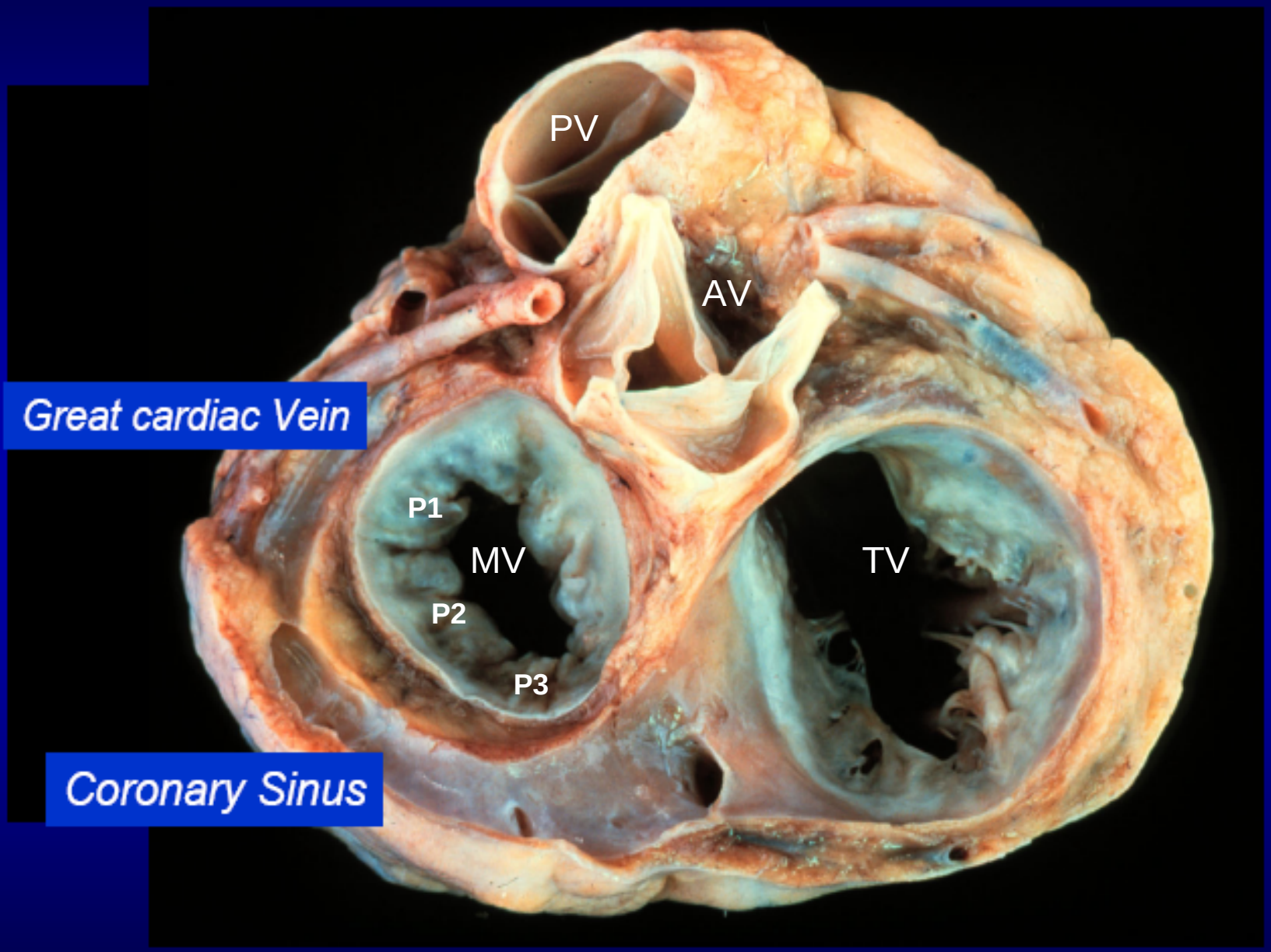
Webb et al Circulation 113:851-855, 2006

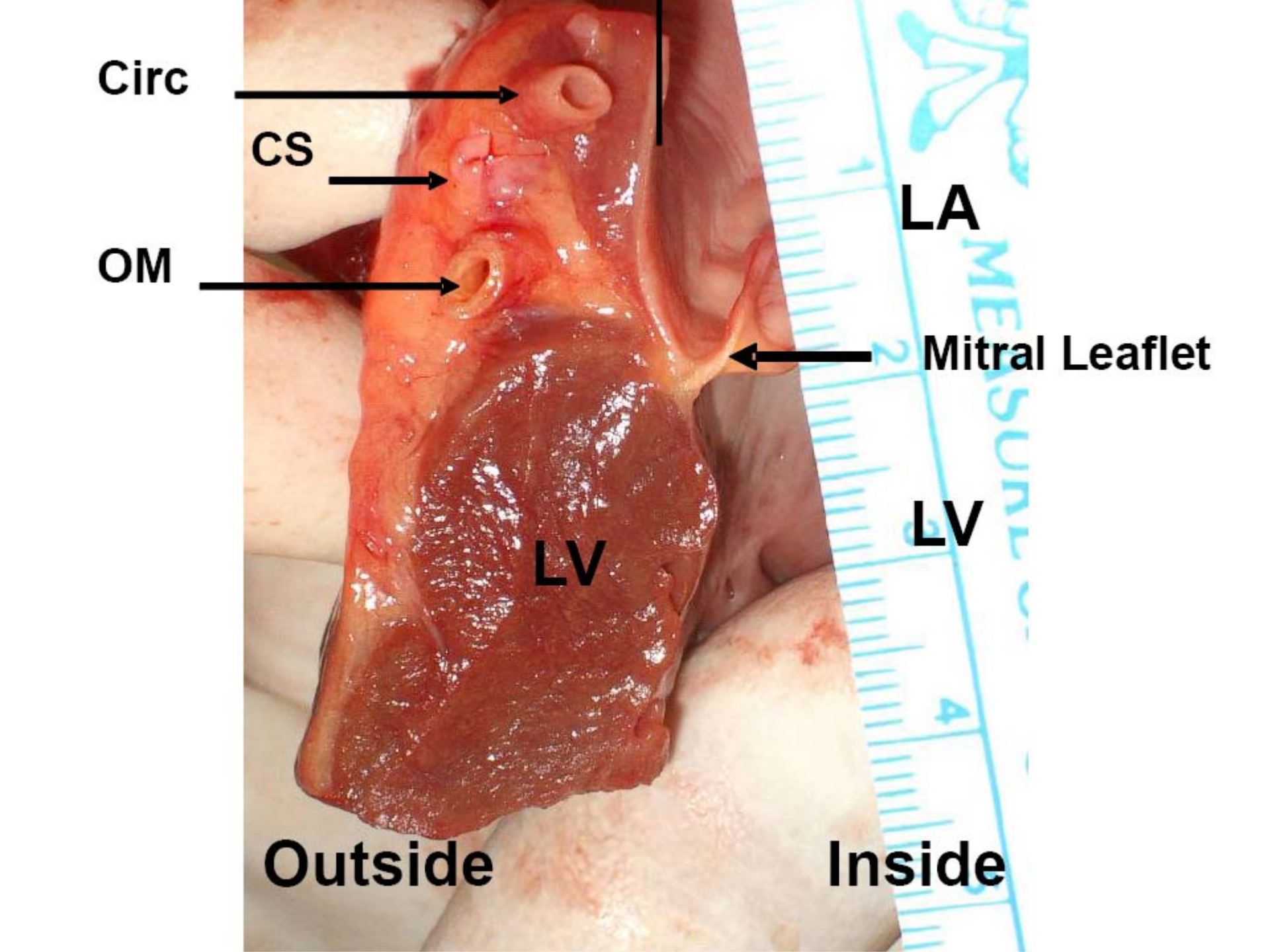
Mitral Annuloplasty



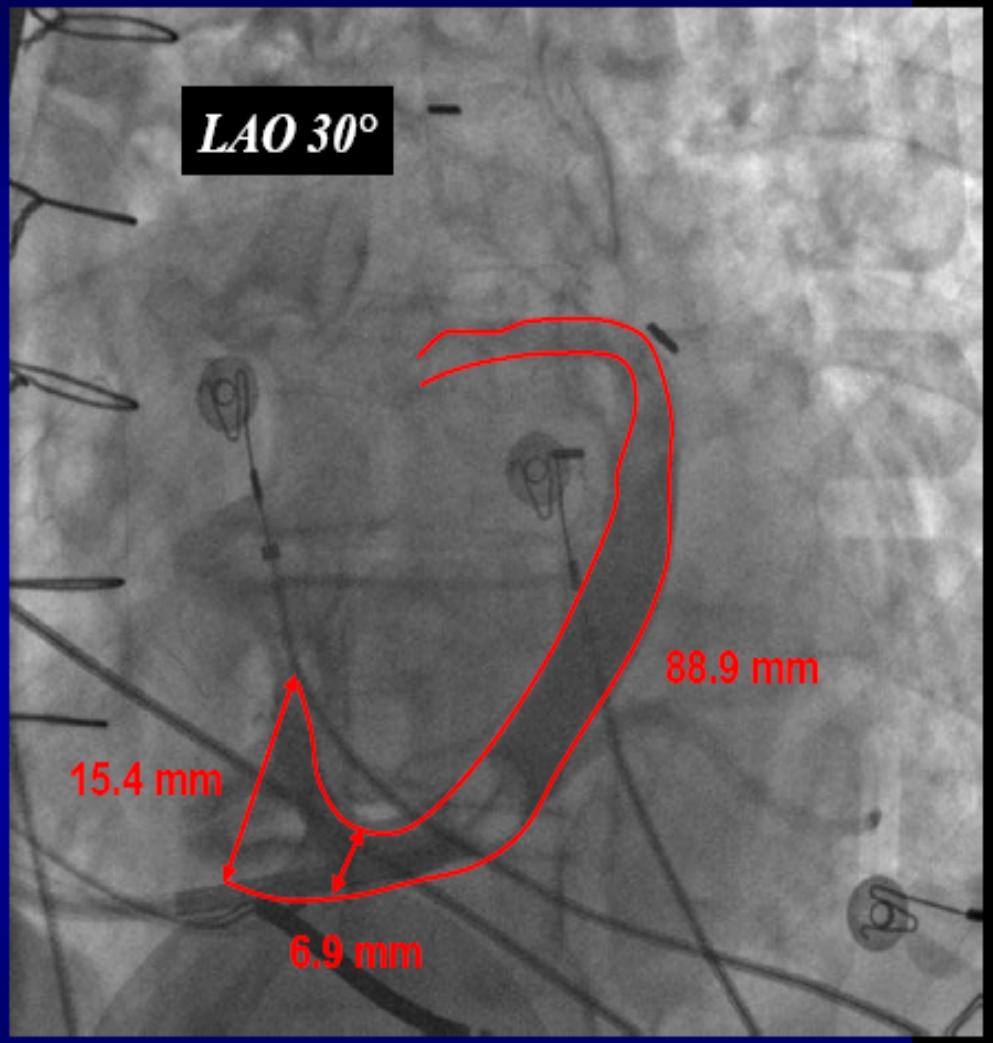
- An annuloplasty ring is sutured into the annulus to reinforce and reduce it
- Decreases septal-lateral diameter
- Improves coaptation of mitral valve leaflets
- Excellent data out to 30 years demonstrating robust efficacy

Normal Coronary Sinus (At annular Plane)

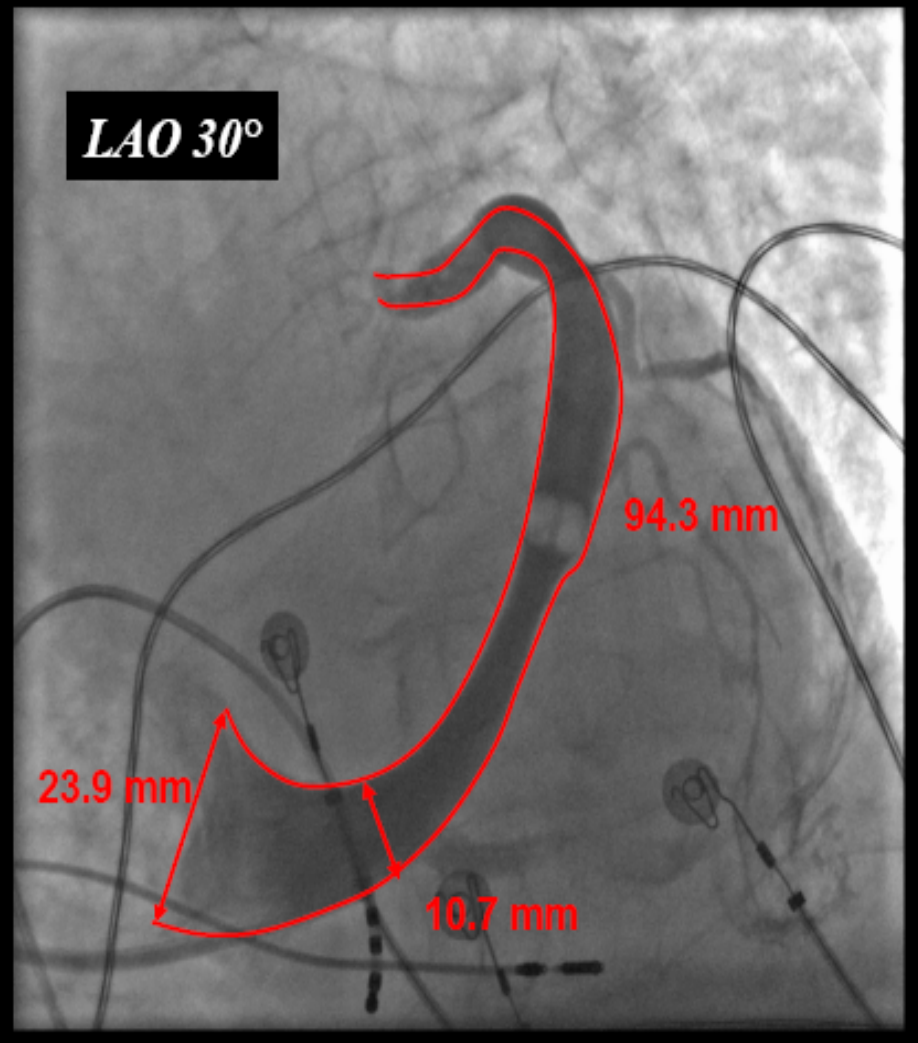



Circ
CS
OM
LA
Mitral Leaflet
LV
LV
Outside
Inside

CS dimensions and perimeter are increased in functional MR



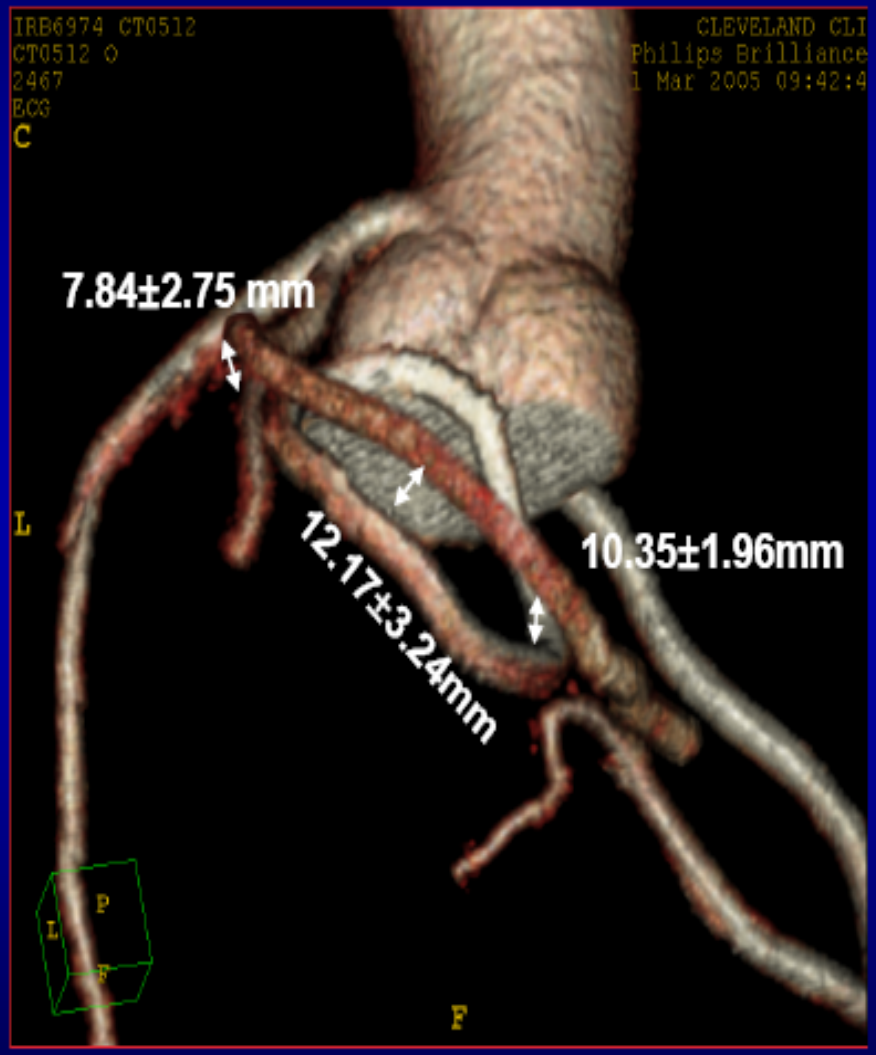
No Mitral Regurgitation



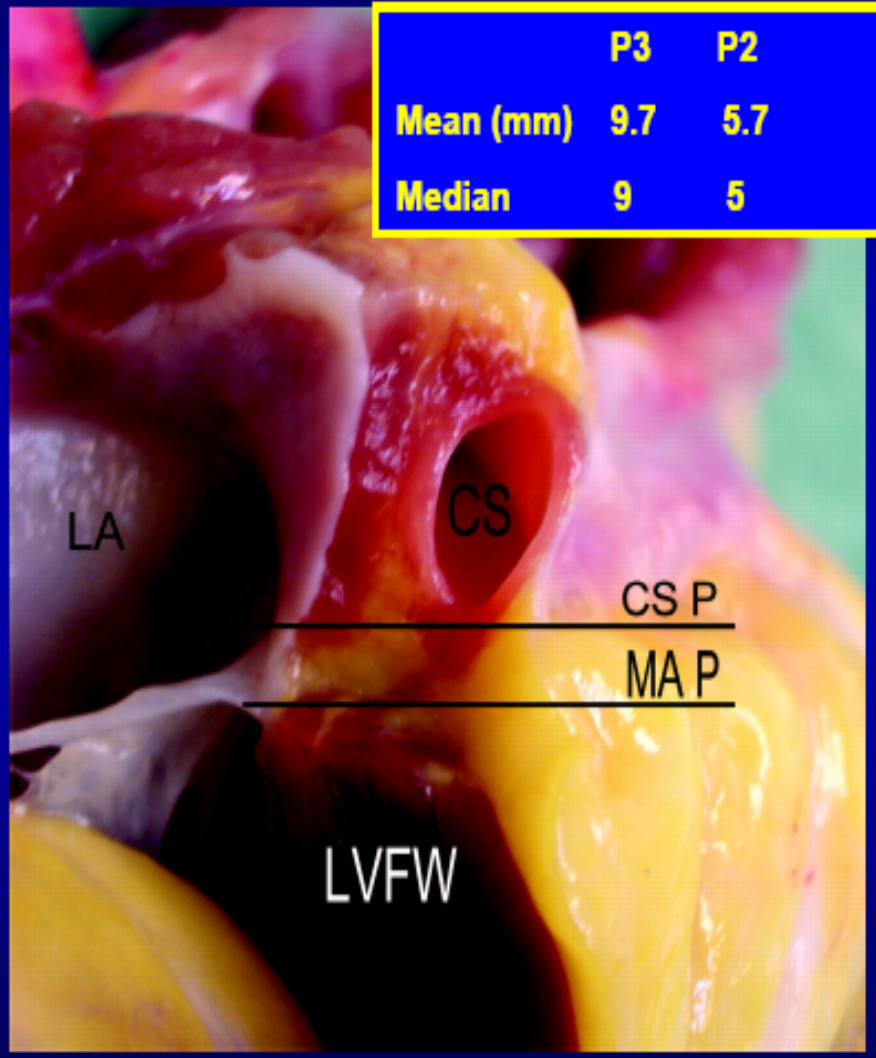
Severe Mitral Regurgitation

Lee, Makkar et al. CCI 2005

Coronary Sinus lies usually superior to the Posterior Mitral annulus in normal population



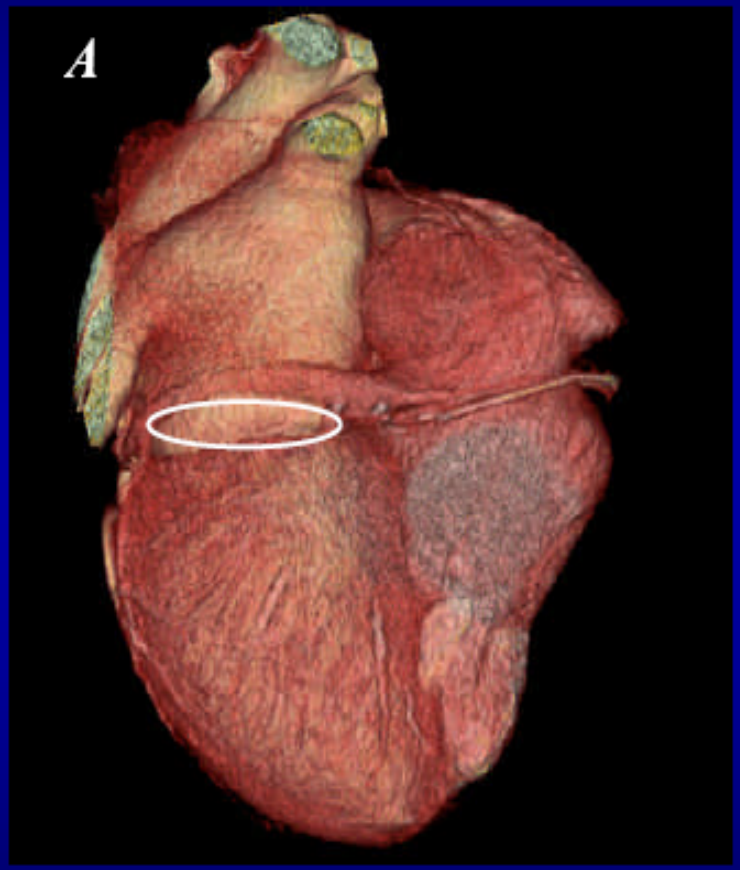
Courtesy Samir Kapadia, MD,

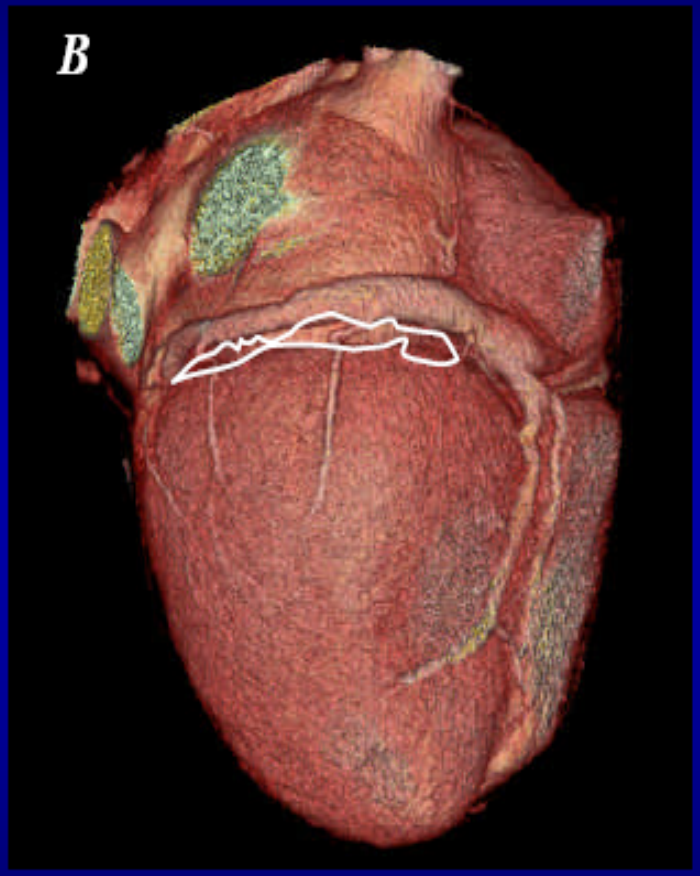


	P3	P2
Mean (mm)	9.7	5.7
Median	9	5

Maselli et al. *Circ* 2006;114:377-380

Reduction of area between CS and MA plane in dilated hearts

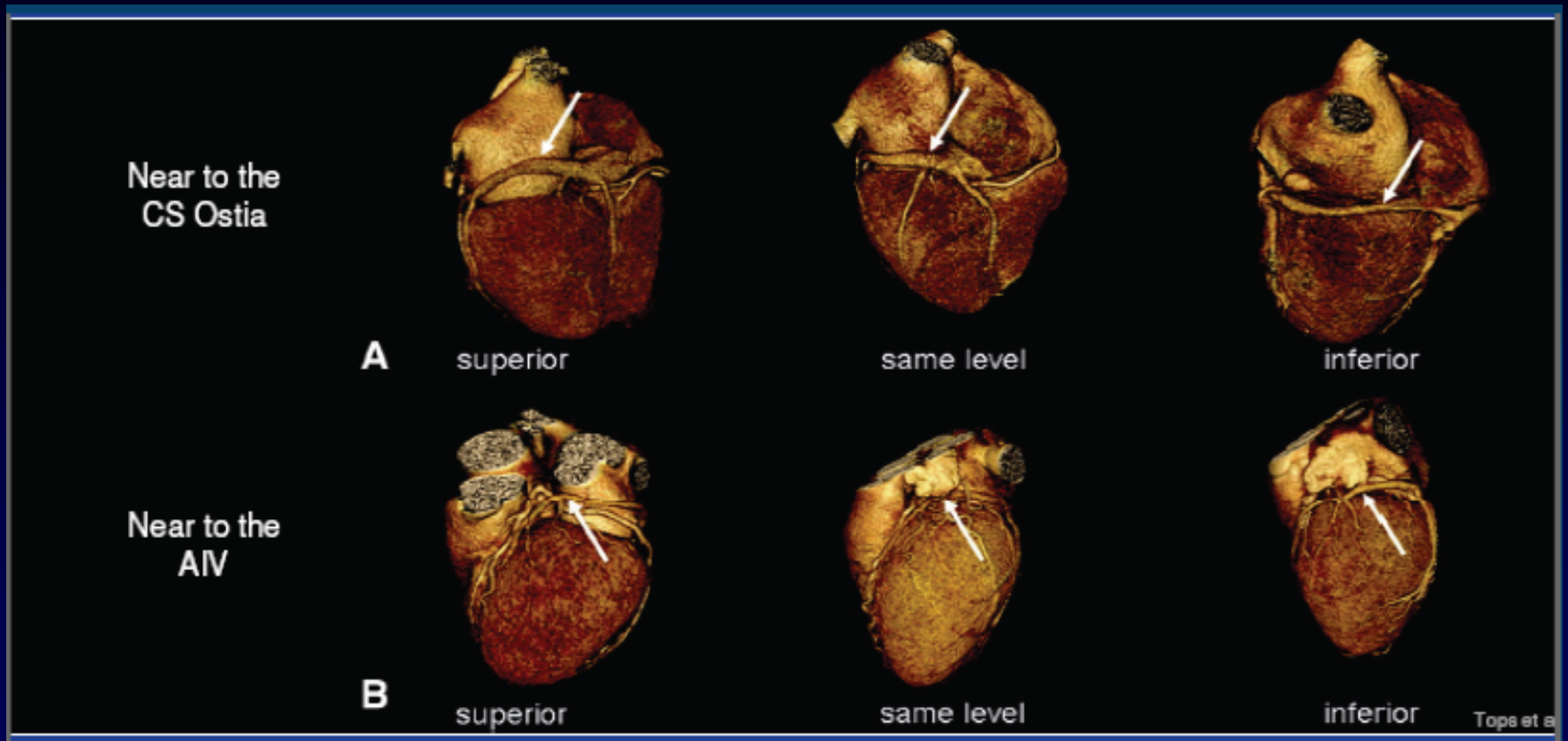




Area between CS and MA plane in normal ventricle (A) and dilated ventricle (B)

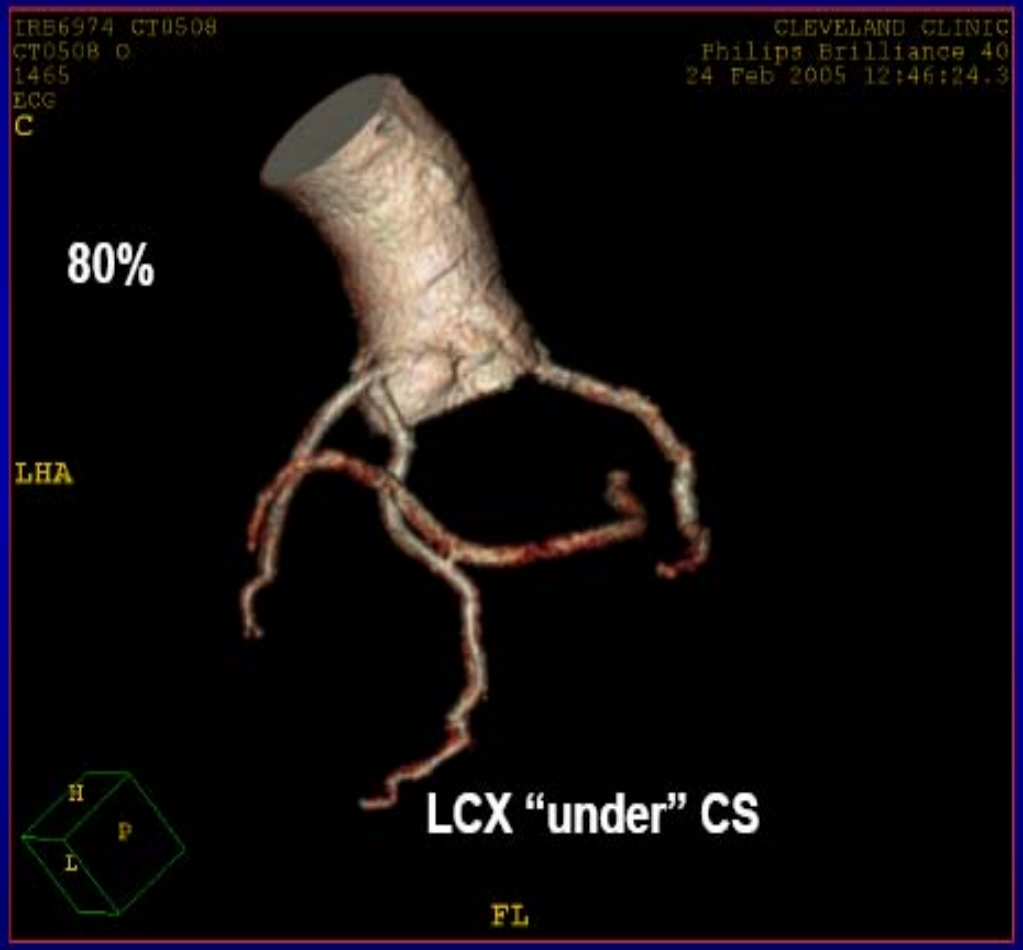
Sorgente et al, Am J Cardiol 2008;

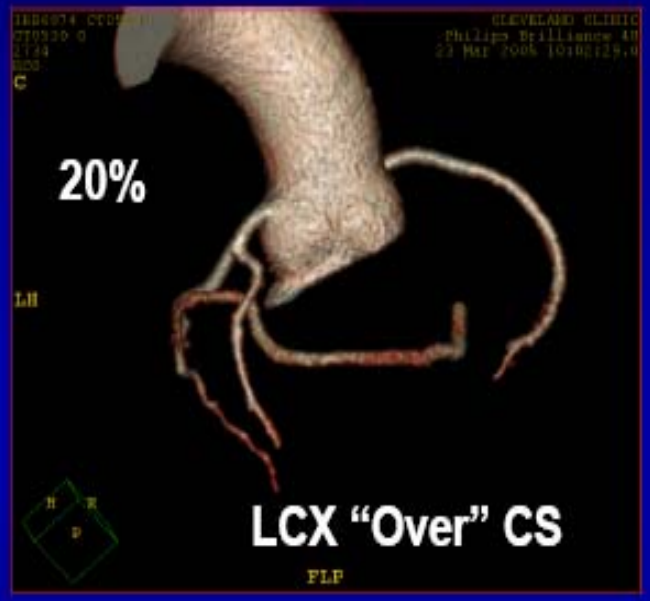
Superior or inferior location?



Choure et al. JACC 2006;48:1938-1945	(n=36)	100%	0	0
Tops et al. Circulation 2007;115:1426-1432	(n=105)	90%	1%	9%

LCX crosses under CS in 45 to 90% cases.





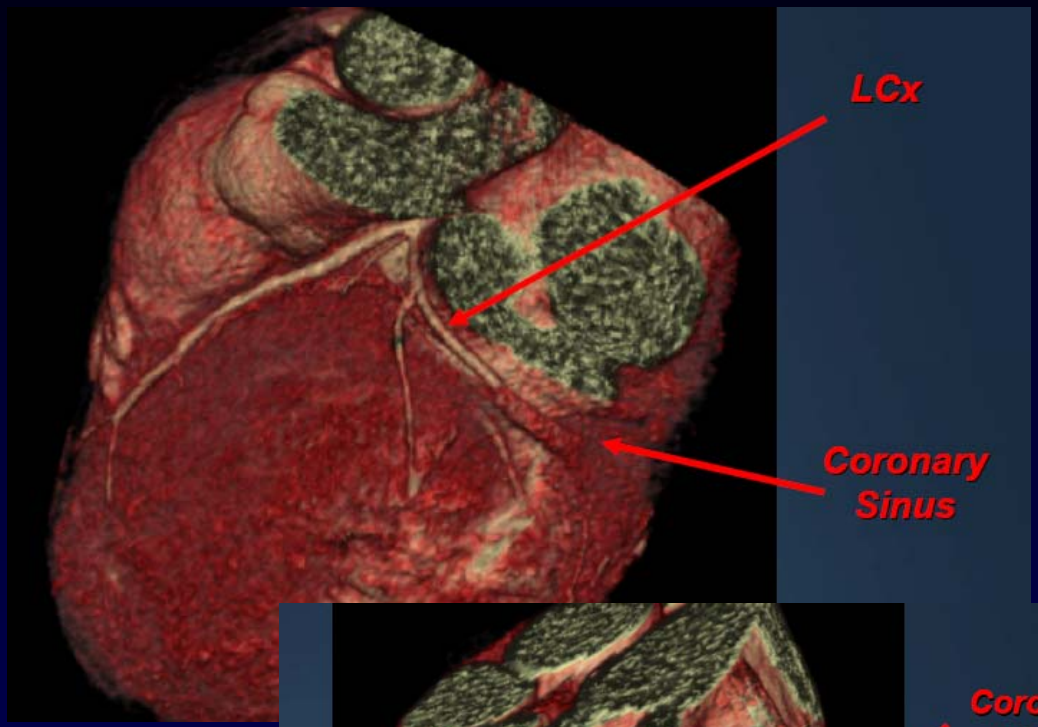
Maselli et al: *Circ* 2006;114:377-380

LCx crossed under 64%

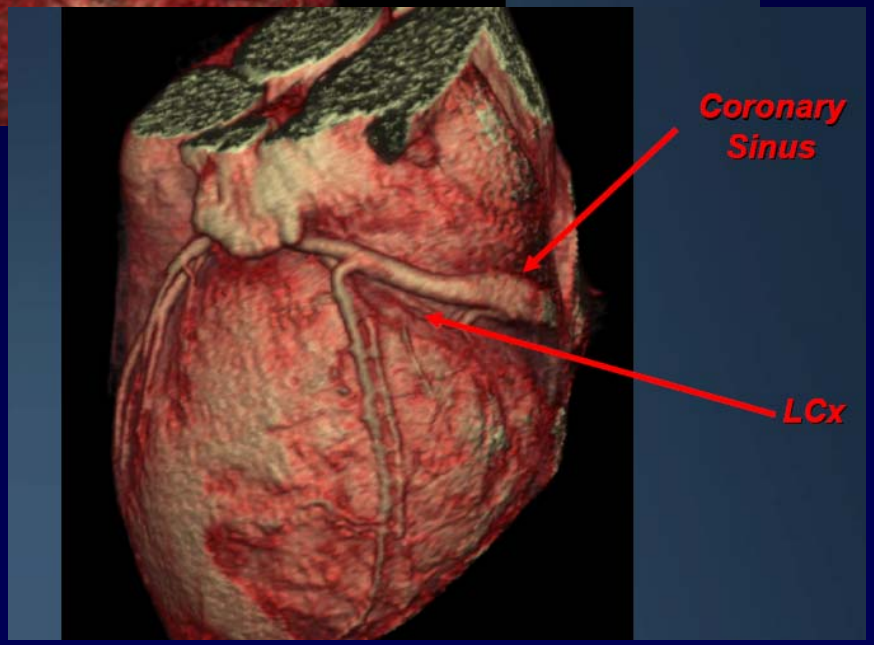
Diag / ramus 16%

Choure et al. J Am Coll Cardiol 2006

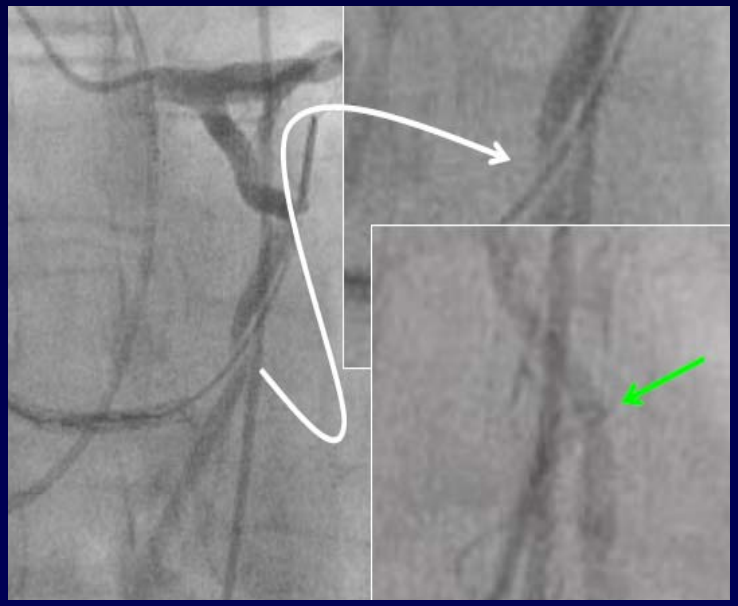
CS to LCx relation



Not at risk

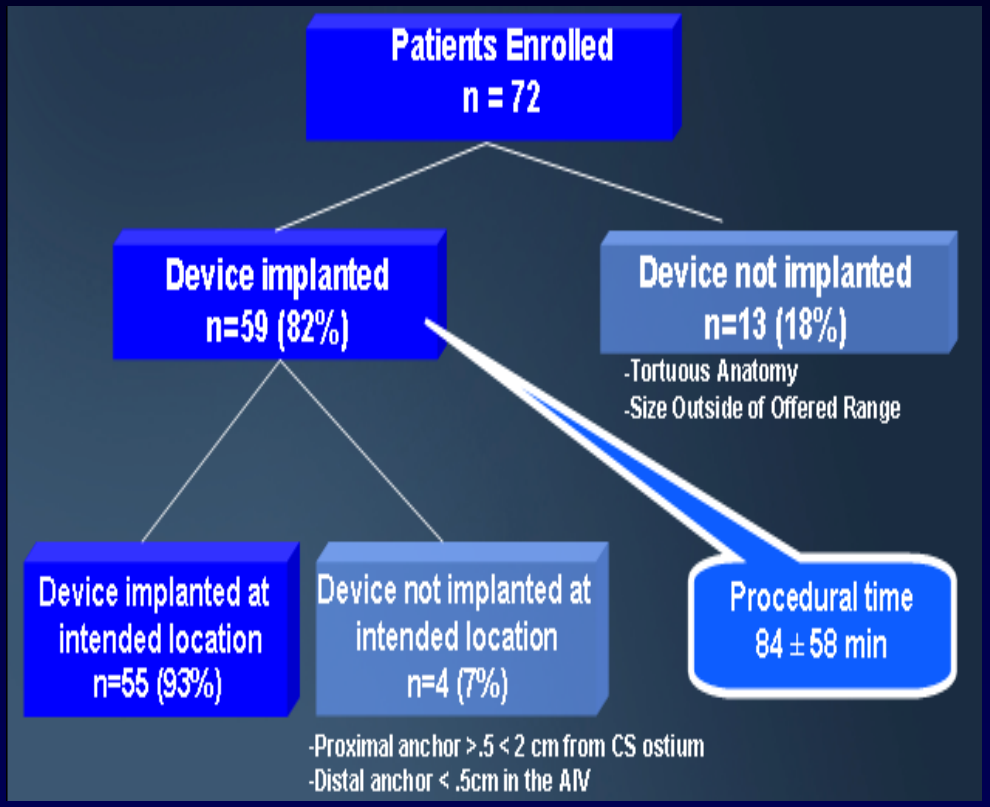


At risk



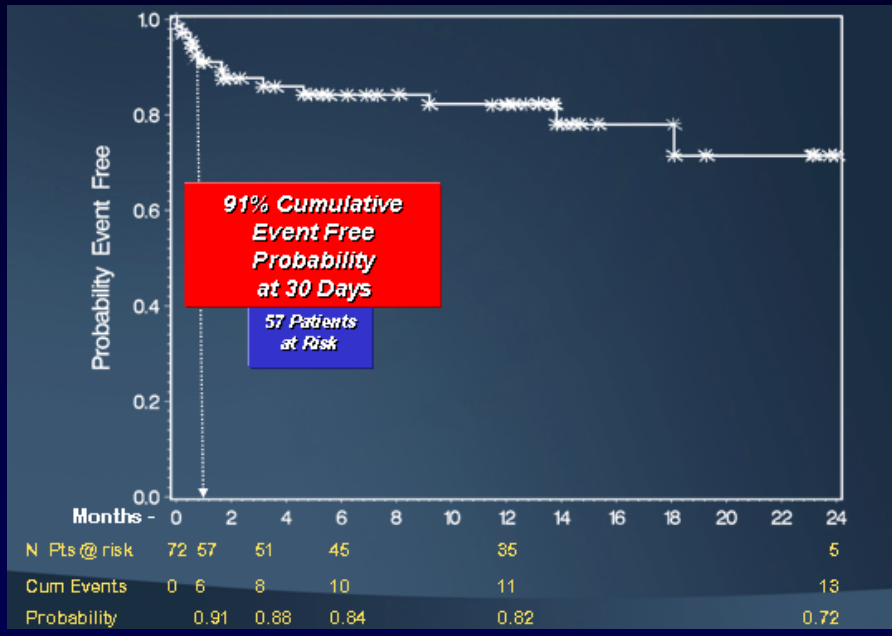
EVOLUTION

Procedural success

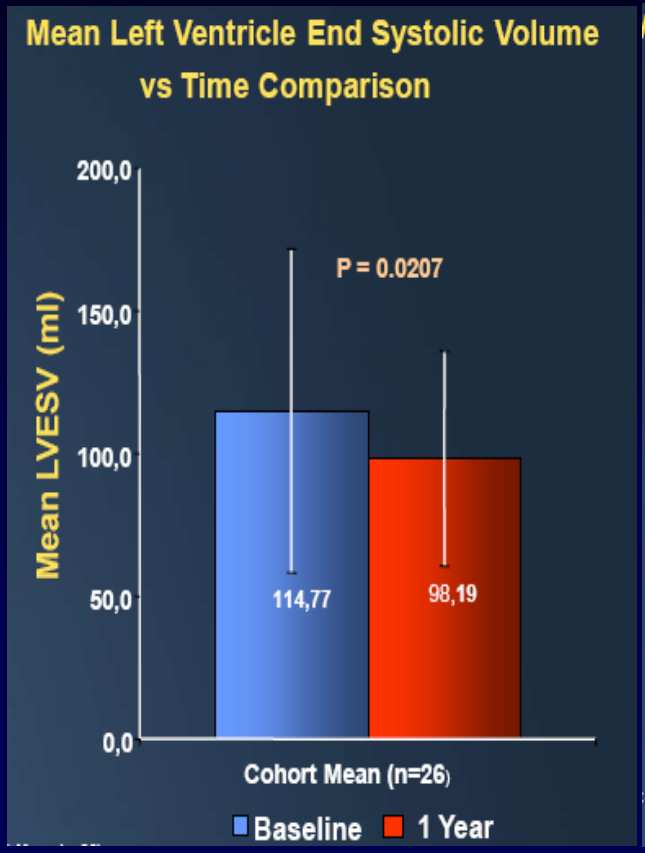


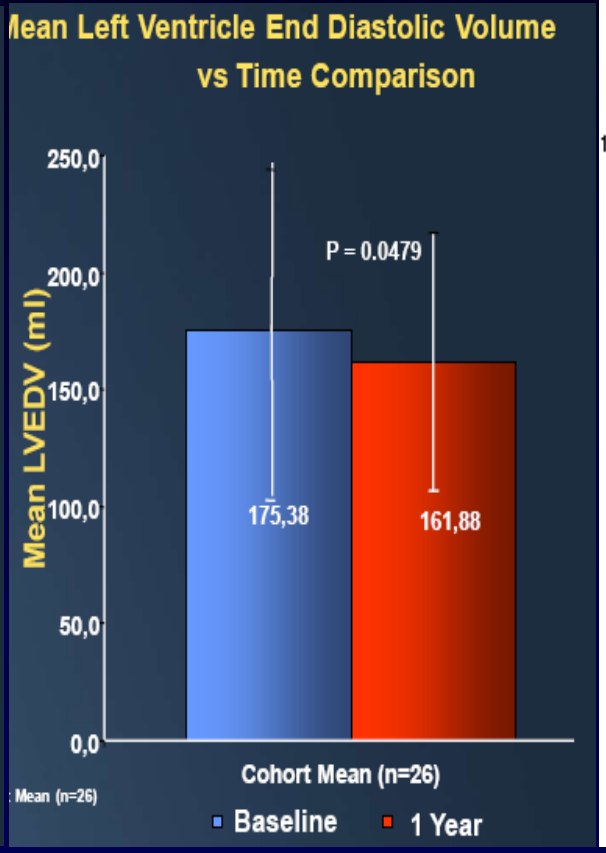
Safety

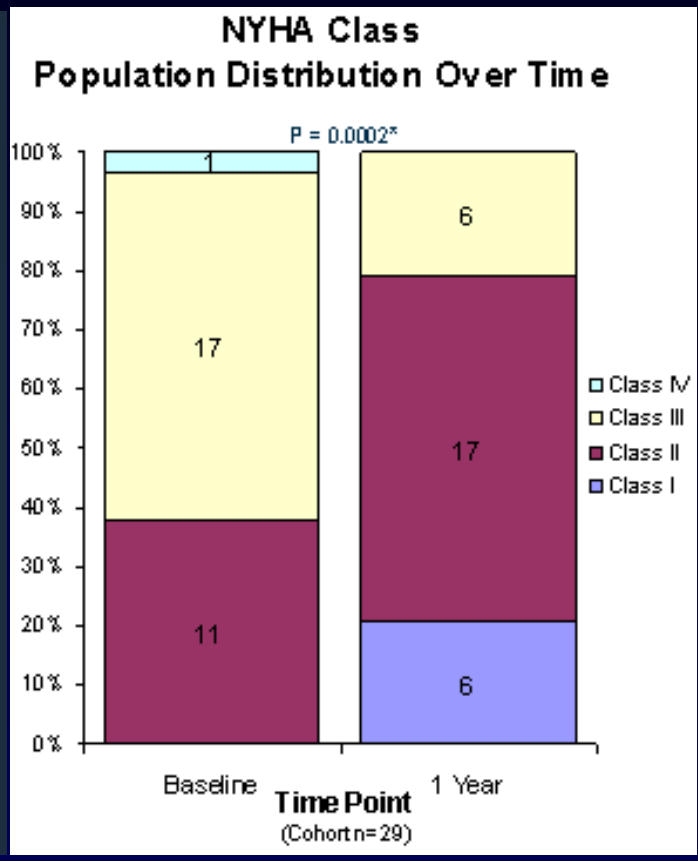
Death+MI+tamponade



EVOLUTION
1 year f/up

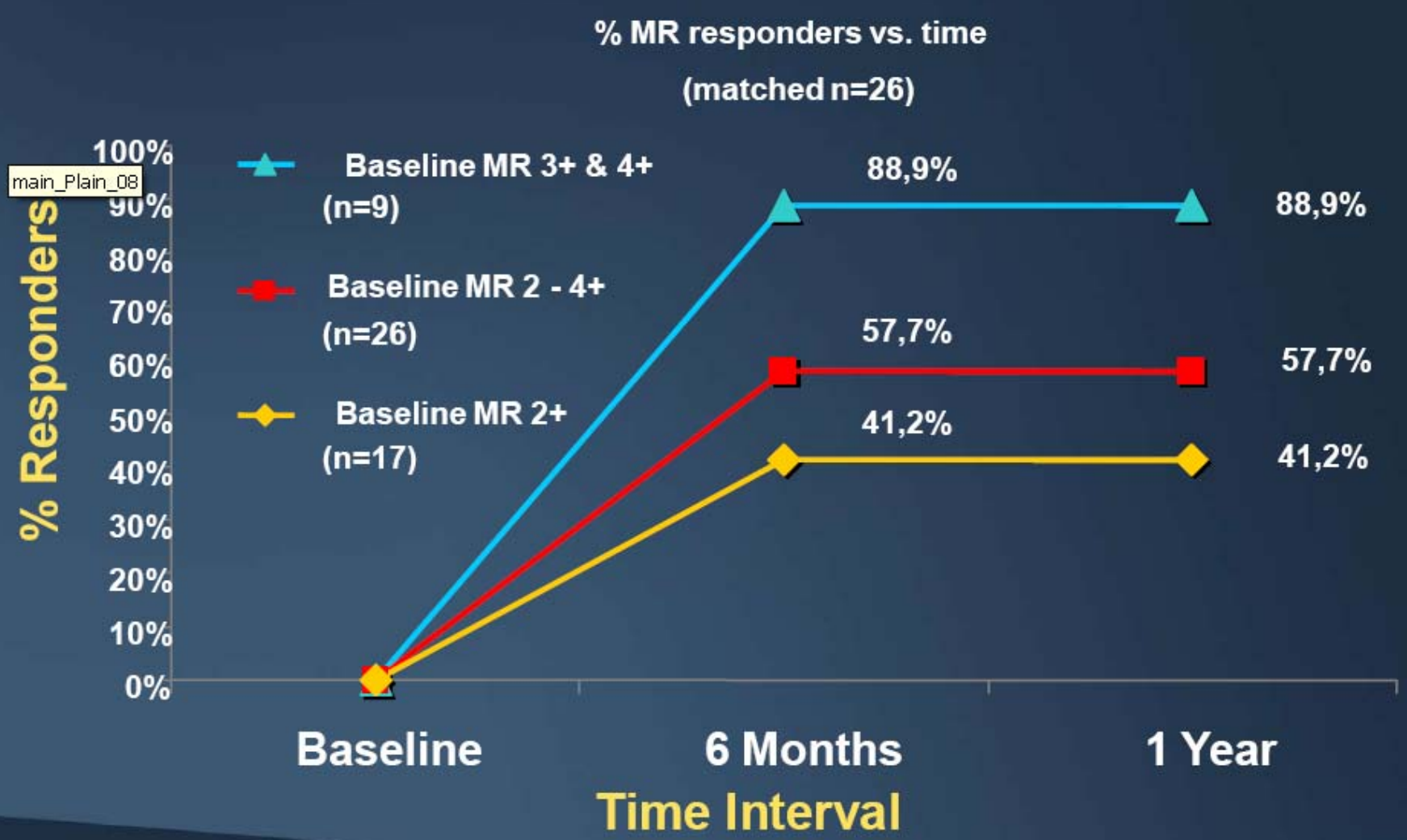




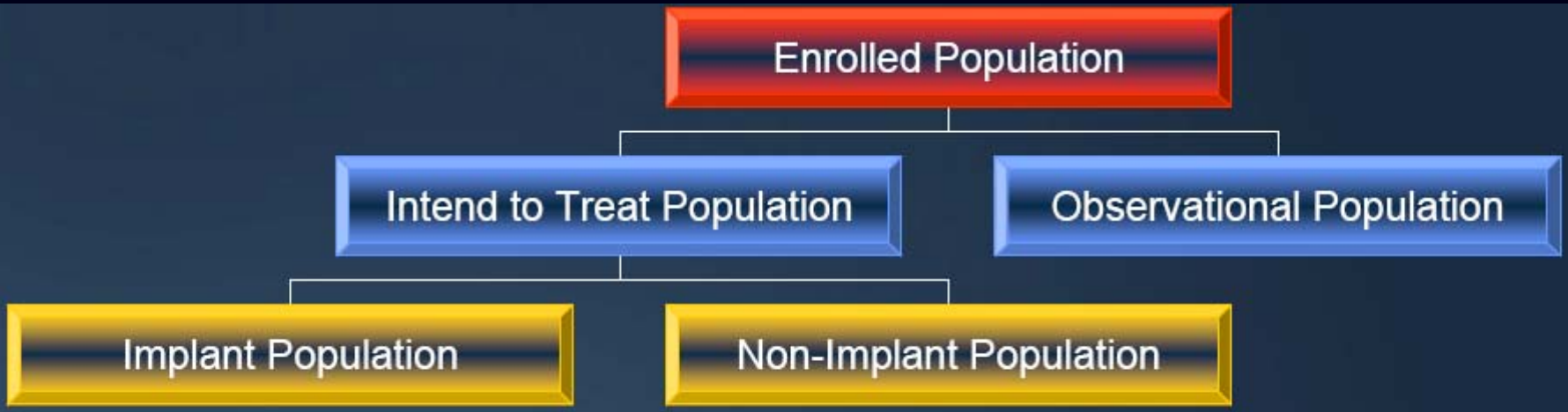


EVOLUTION

Percent responders at 6 months and 1 year

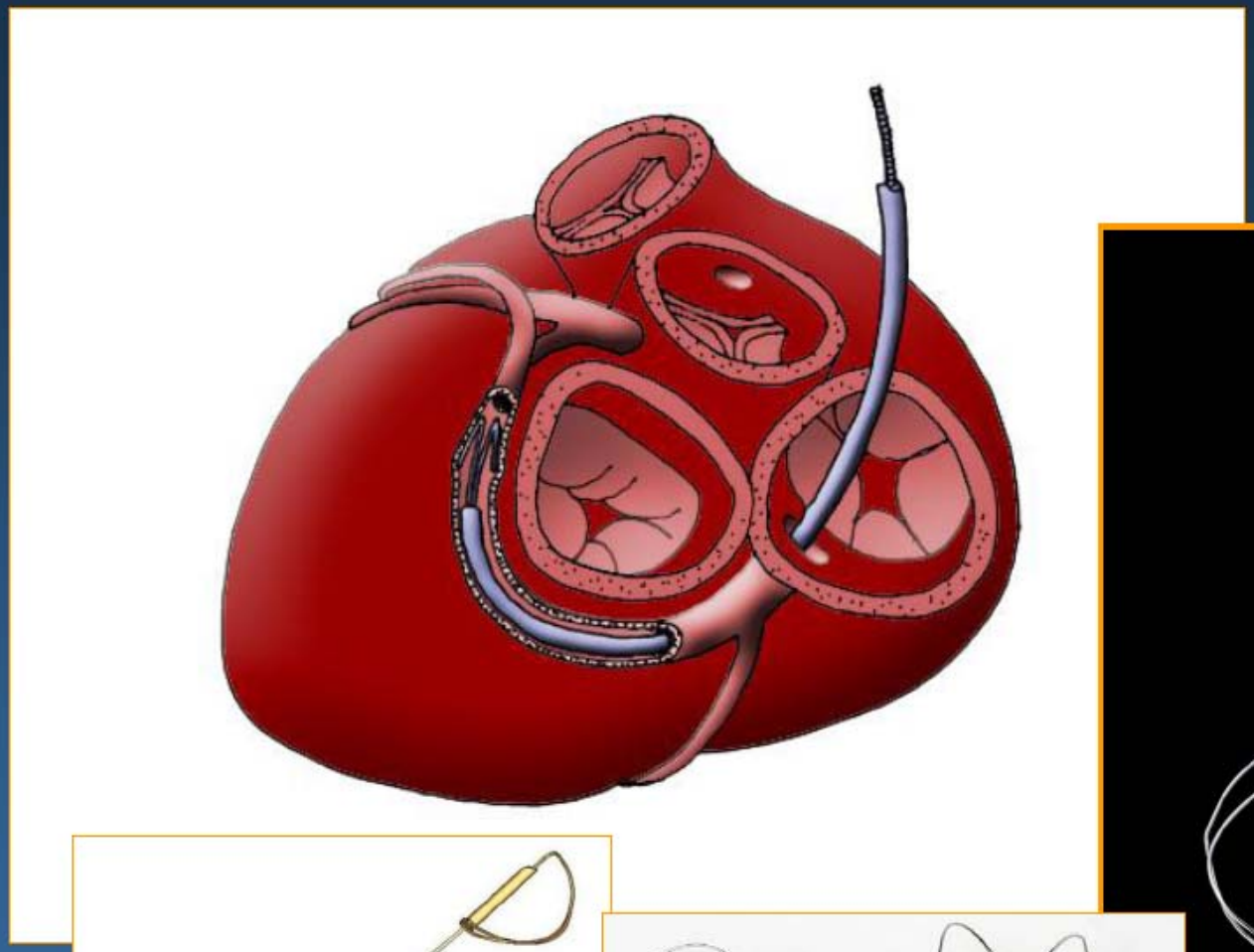


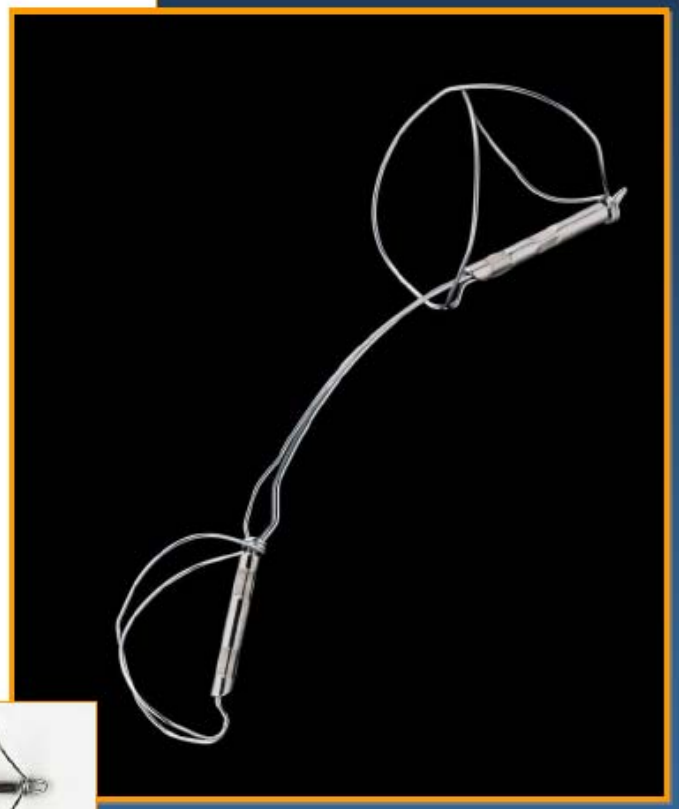
EVOLUTION II

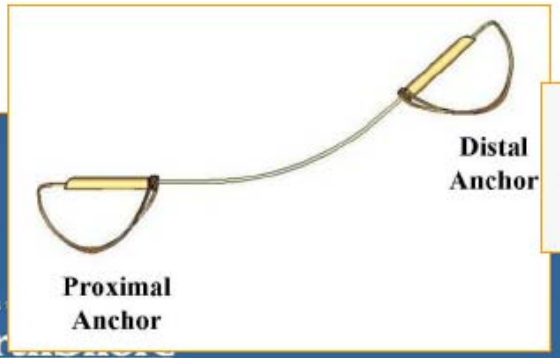


- **Implant Population**
  - **Subjects that fulfill all inclusion/exclusion criteria and are implanted with a MONARC device.**
- **Non-Implanted Population**
  - **Subjects that fulfill all of the inclusion/exclusion criteria, undergo an implant procedure but are not implanted with a MONARC device and will continue care with standard medical management.**
- **Observational Population**
  - **Subjects that fulfill all of the inclusion/exclusion criteria with the exception of vessel anatomy.**

CARILLON Mitral Contour System

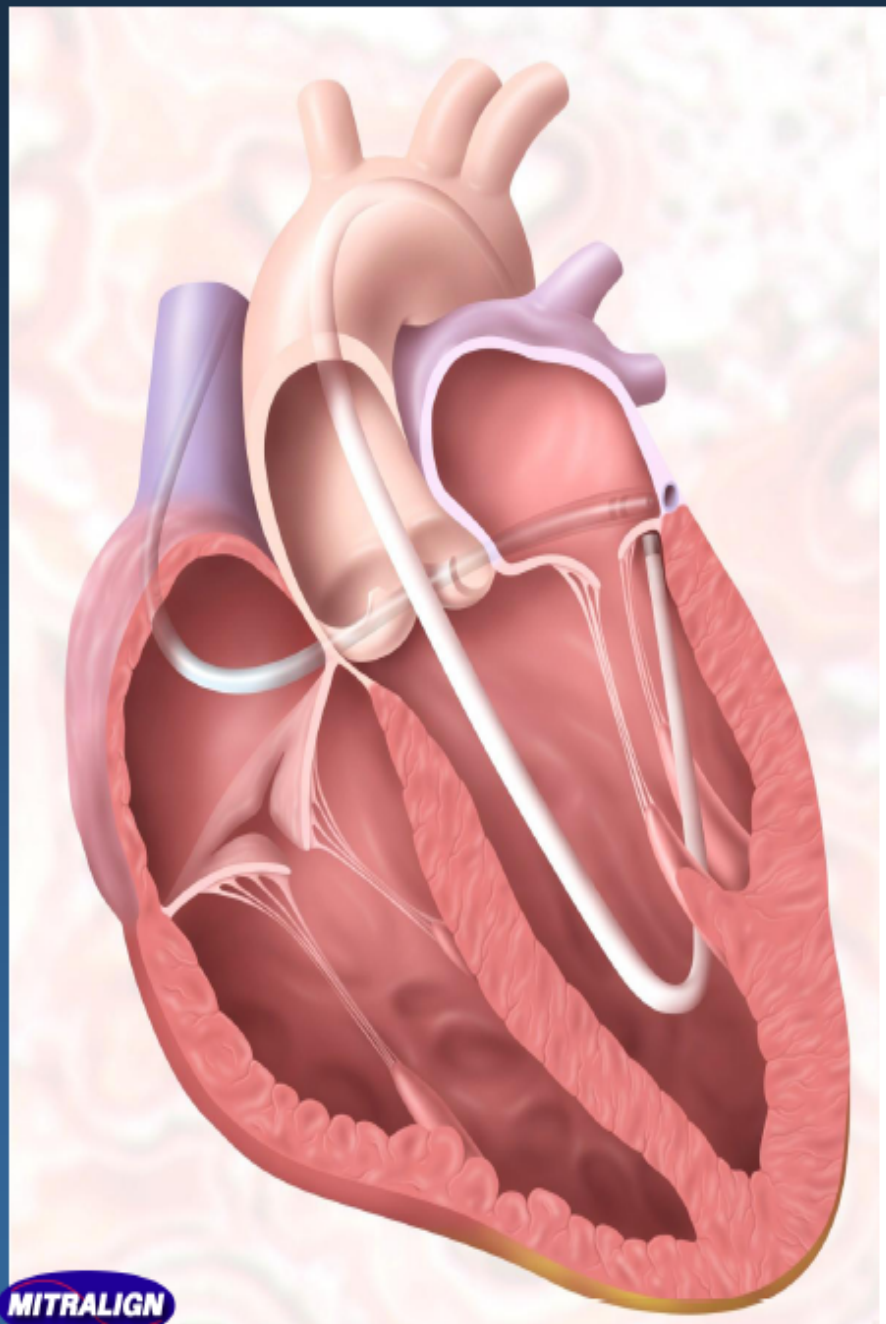


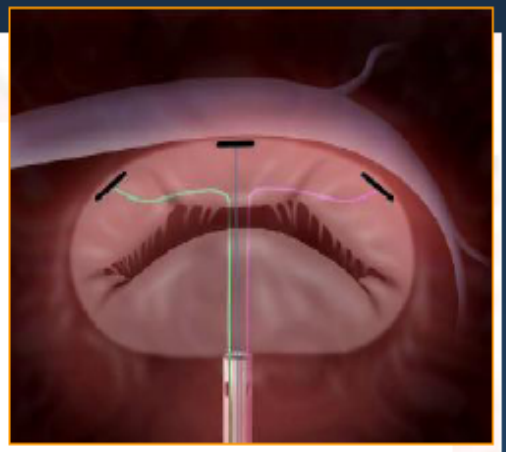


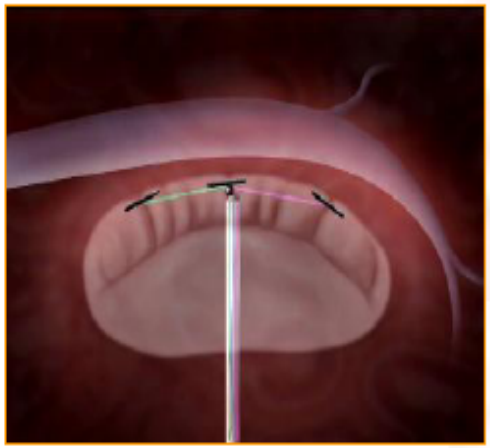


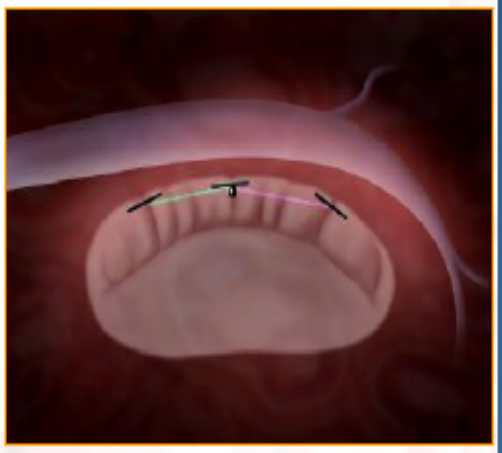
CARDIAC DIMENSIONS

Evans
Northwestern
University HealthSystem







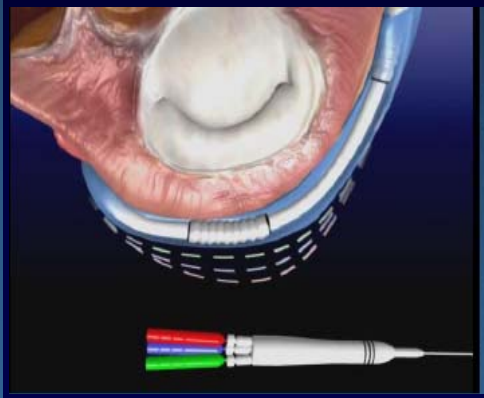


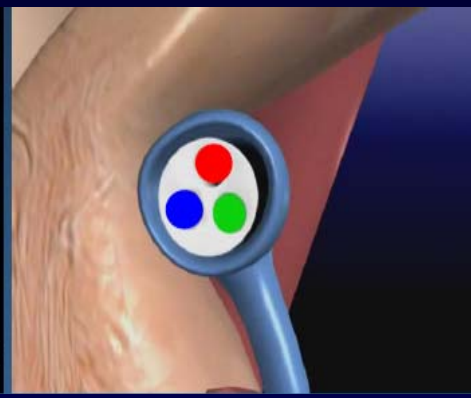
MITRALIGN

University HealthSystem

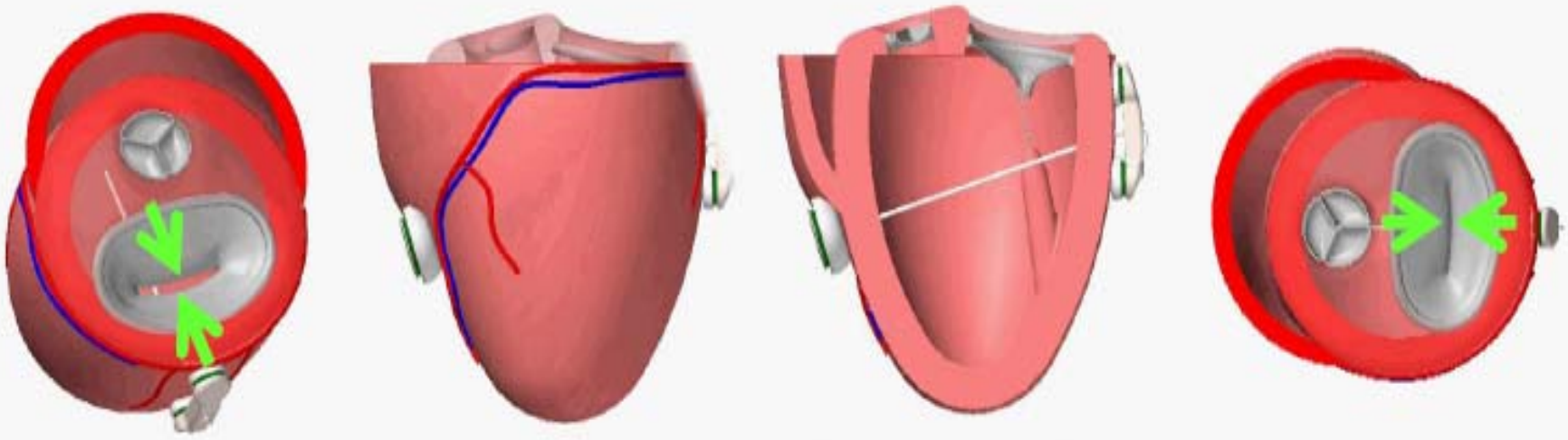
Viacor PTMA Experience

3D Echo End Diastole Annulus Tracing Data

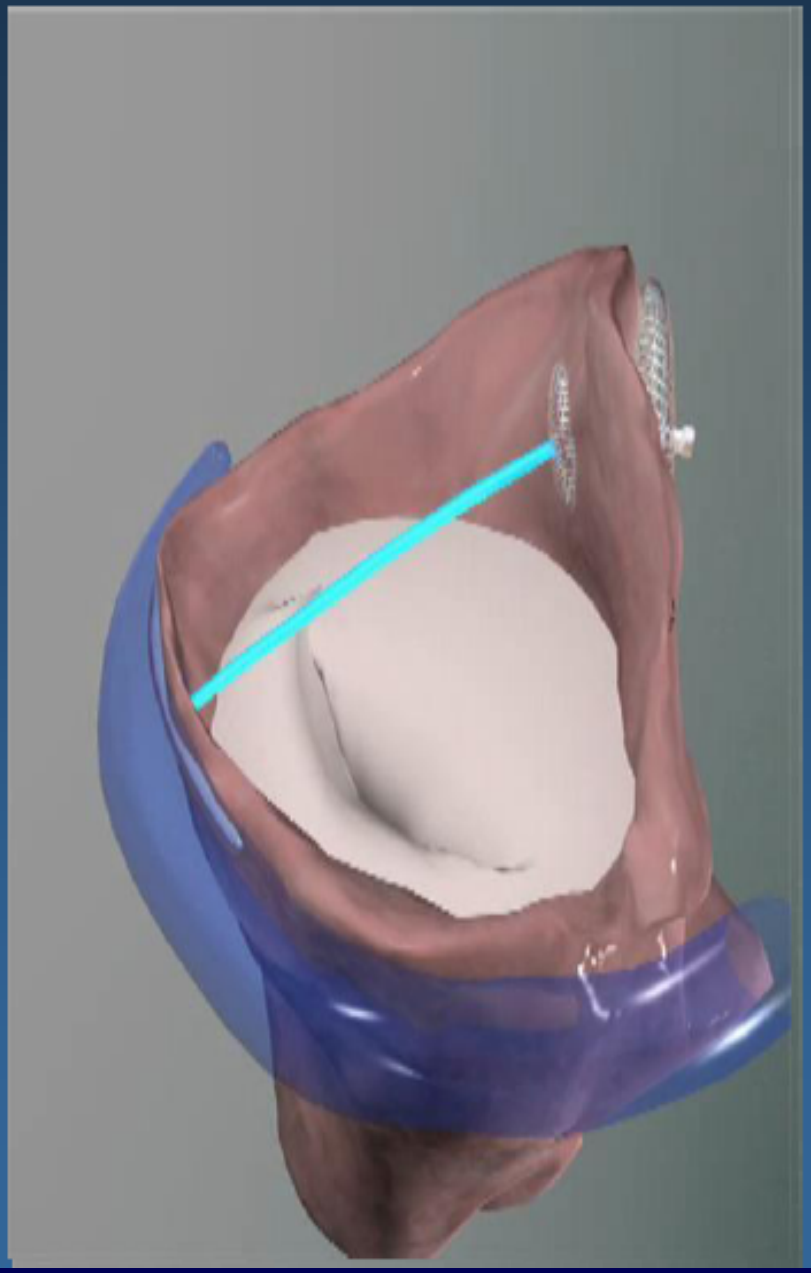


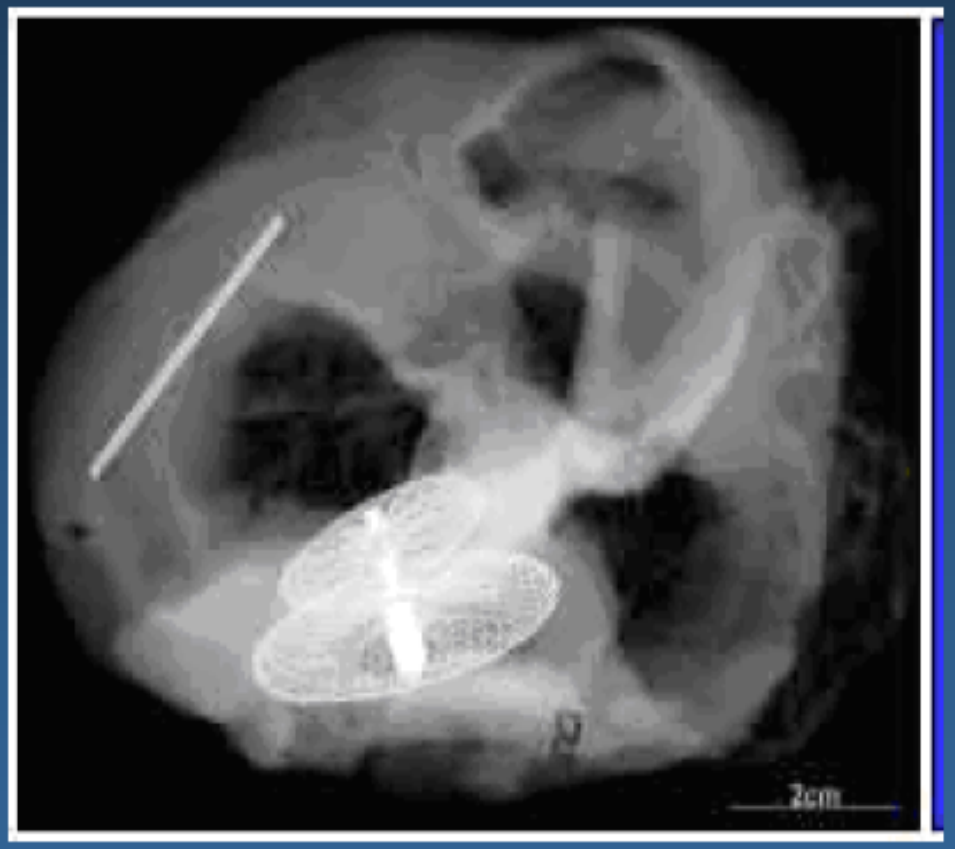


The Myocor Surgical Coapsys System

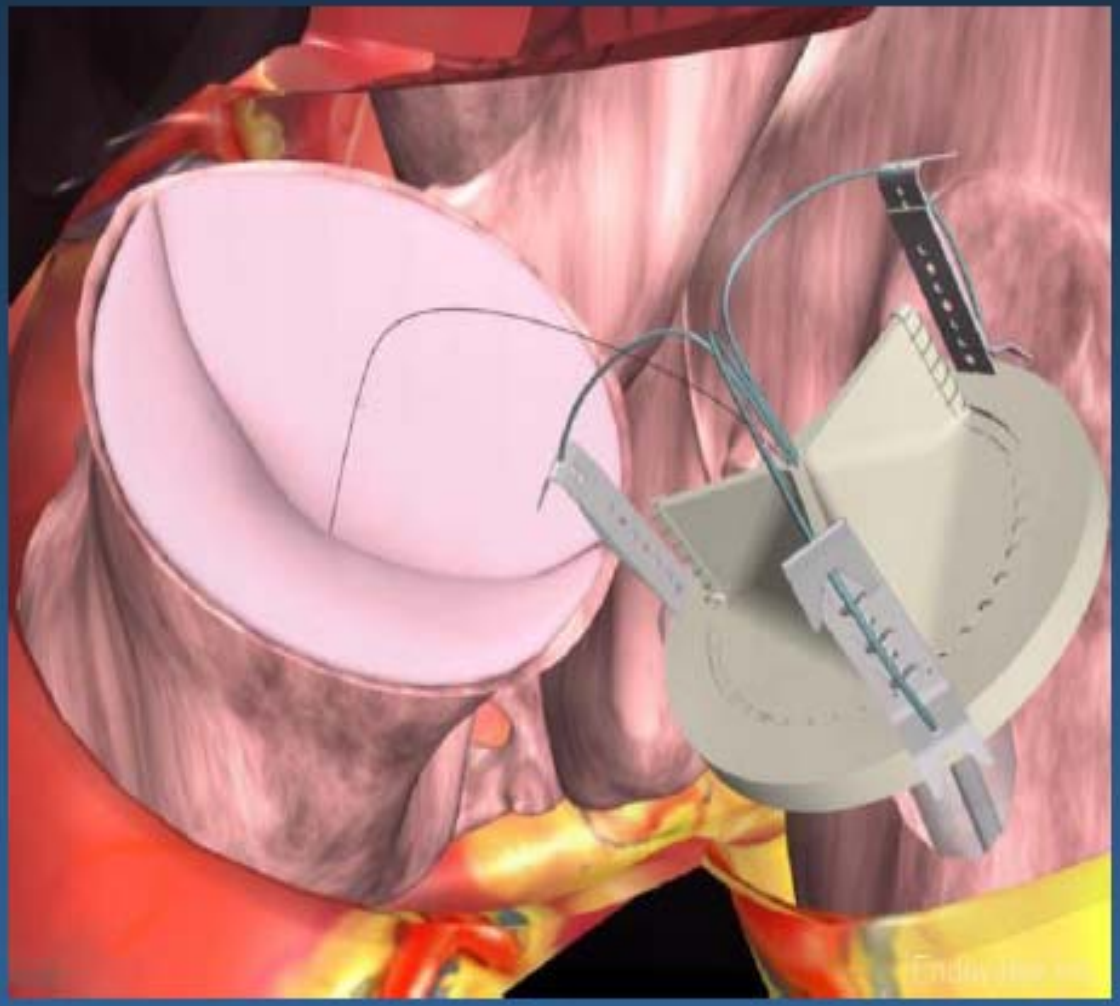


PS^3 System Components






endoValve



30-Day Mortality

Comparison with Surgical Registers

	STS 2001	UKCSR 99-2000	EHS 2001
Aortic valve replacement no CABG	3.7	3.1	2.7
Aortic valve replacement + CABG	6.3	7	4.3
Mitral valve repair no CABG	2.2	2.8	0
Mitral valve replacement no CABG	5.8	6.2	1.7
Mitral valve repair or replacement + CABG	10.1	8.6	8.2
Multiple valve replacement (with or without CABG)	7.2	11.4	6.5

Conclusions 1

- Percutaneous techniques for mitral insufficiency are feasible and safe
- Phase I results confirm the effectiveness of both E-valve and coronary sinus annuloplasty techniques, respecting the effect of learning curves
- Appropriate case selection is crucial for each class of devices

Conclusions 2

- Significant knowledge should be acquired on the evaluation of MV anatomy and dysfunction, and the proper use of echo
- It is very likely that in the future these techniques will play a significant role in the management of patients with mitral insufficiency