



Percutaneous Intervention in Mitral Valve Disease

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Faculty Disclosure

Relationship

Manufacturer(s)

Speaker's Honoraria

Edwards Lifesciences

Consultant (Advisory Board)

Abbott,
Medtronic
Saint Jude Medical
Valtech

Percutaneous Mitral Commissurotomy

Percutaneous Mitral Valve Repair

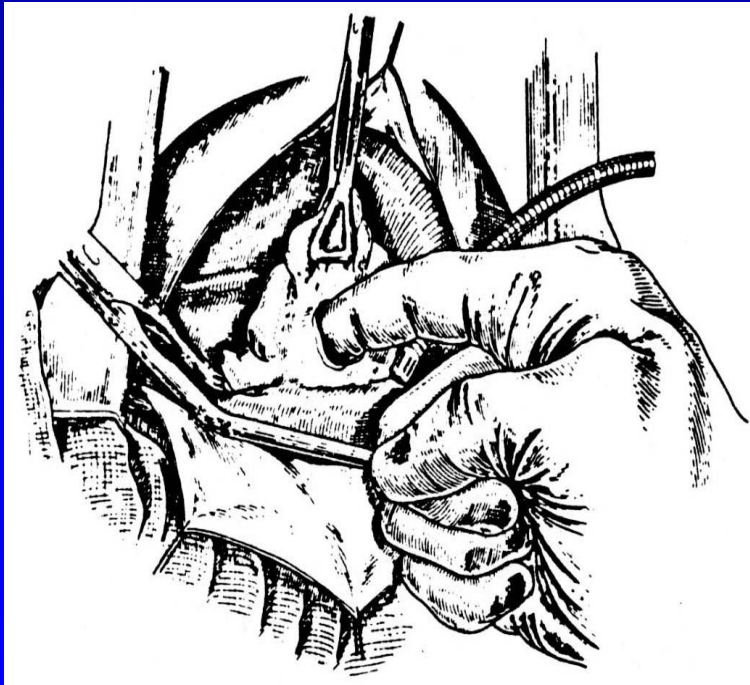
Transcatheter treatment after surgical failure

Final comments

Percutaneous Mitral Commissurotomy

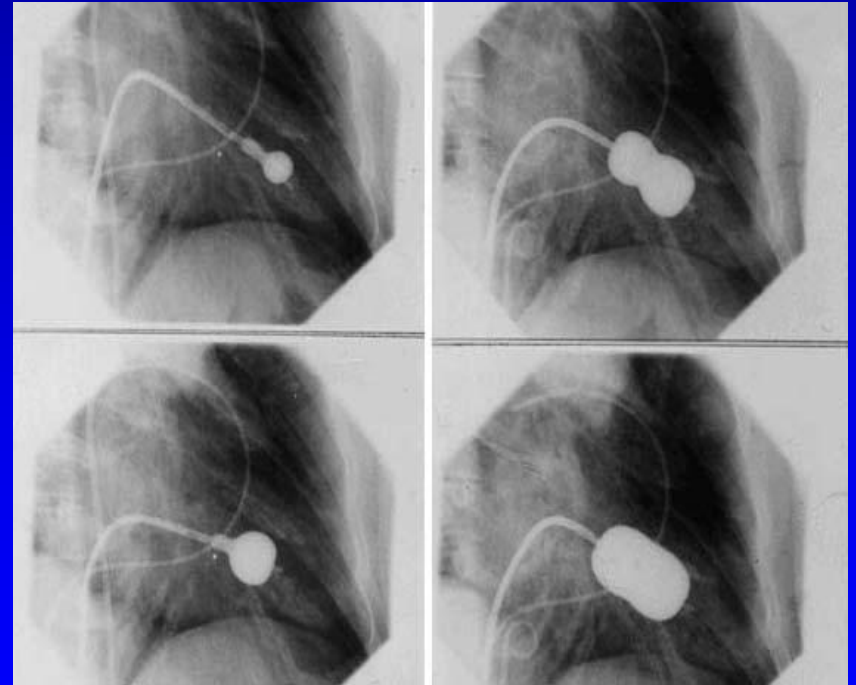
“The Proof of Concept for
Percutaneous Valve Intervention”

Surgical Comparator



(D. Harken, 1948)

Percutaneous Mitral Commissurotomy



(K. Inoue, 1984)

Follow-up

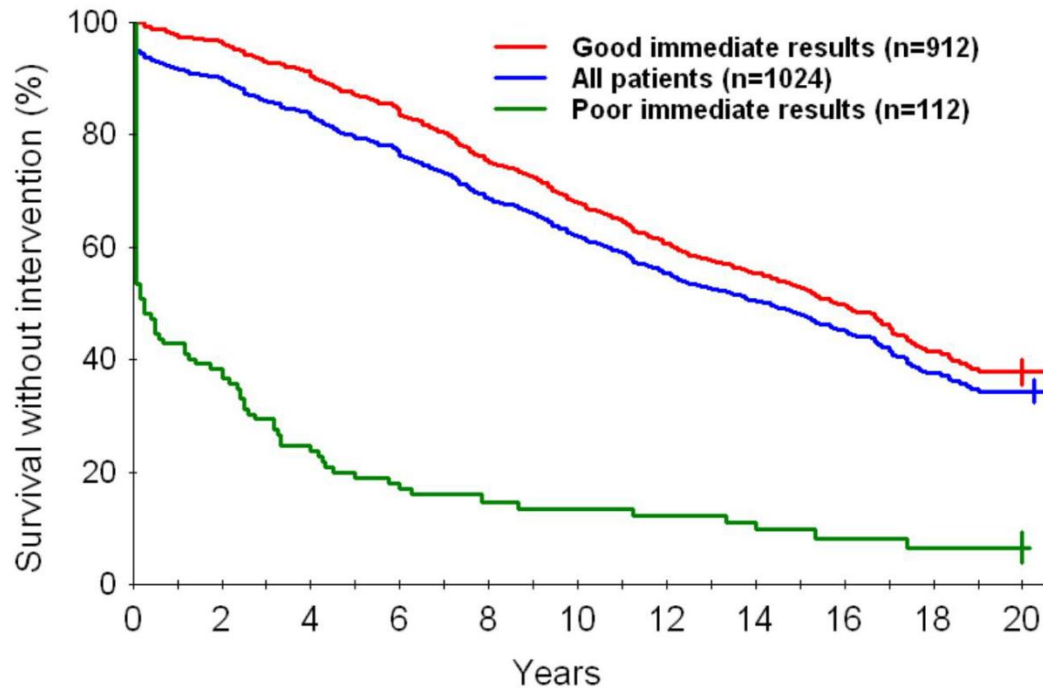
- FU was concluded in 2008
- FU was complete in 923 patients (90%)
- Median FU: 11 years [interquartile range 5 - 16]
- Clinical endpoints:
 - death
 - need for surgery or re-PMC
 - NYHA class III-IV

Good Functional Results: patient alive, not operated on, and in NYHA class I or II at last follow-up



20-Year Results

Survival without Surgery or Re-PMC



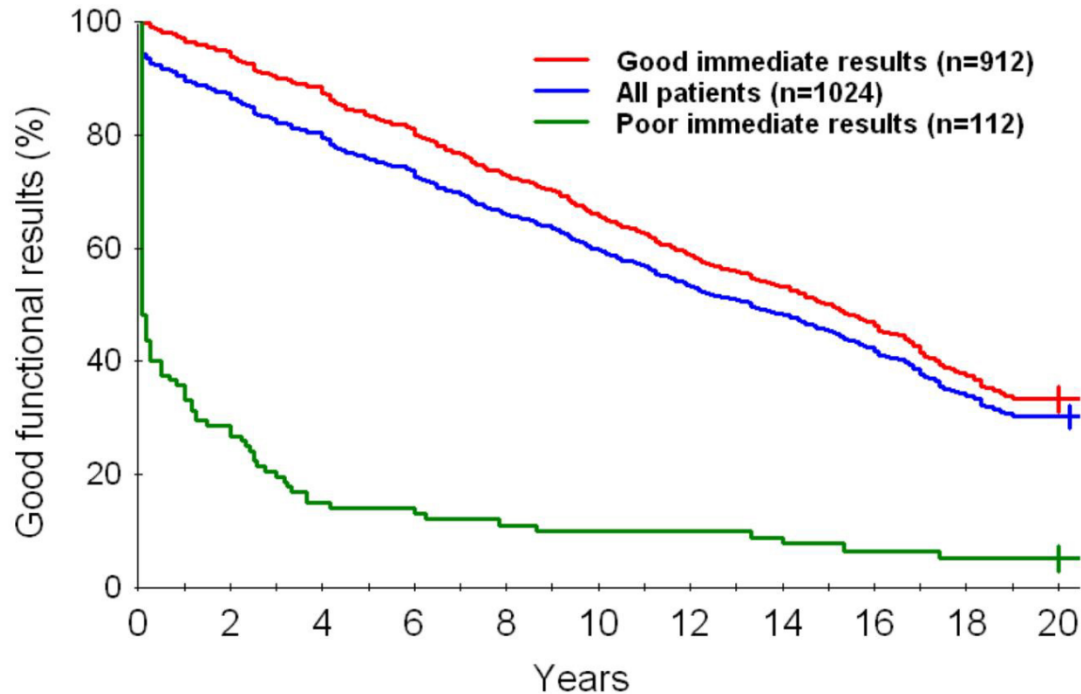
No. at Risk

Good imm. results	912	855	783	697	591	521	456	384	244	115	47
All patients	1024	898	809	715	603	532	466	393	249	118	49
Poor imm. results	112	43	26	18	12	11	10	9	5	3	2

(Bouleti et al. *Circulation* 2012;125:2119-27)

20-Year Results

Survival without Surgery or Re-PMC, and in NYHA class I or II



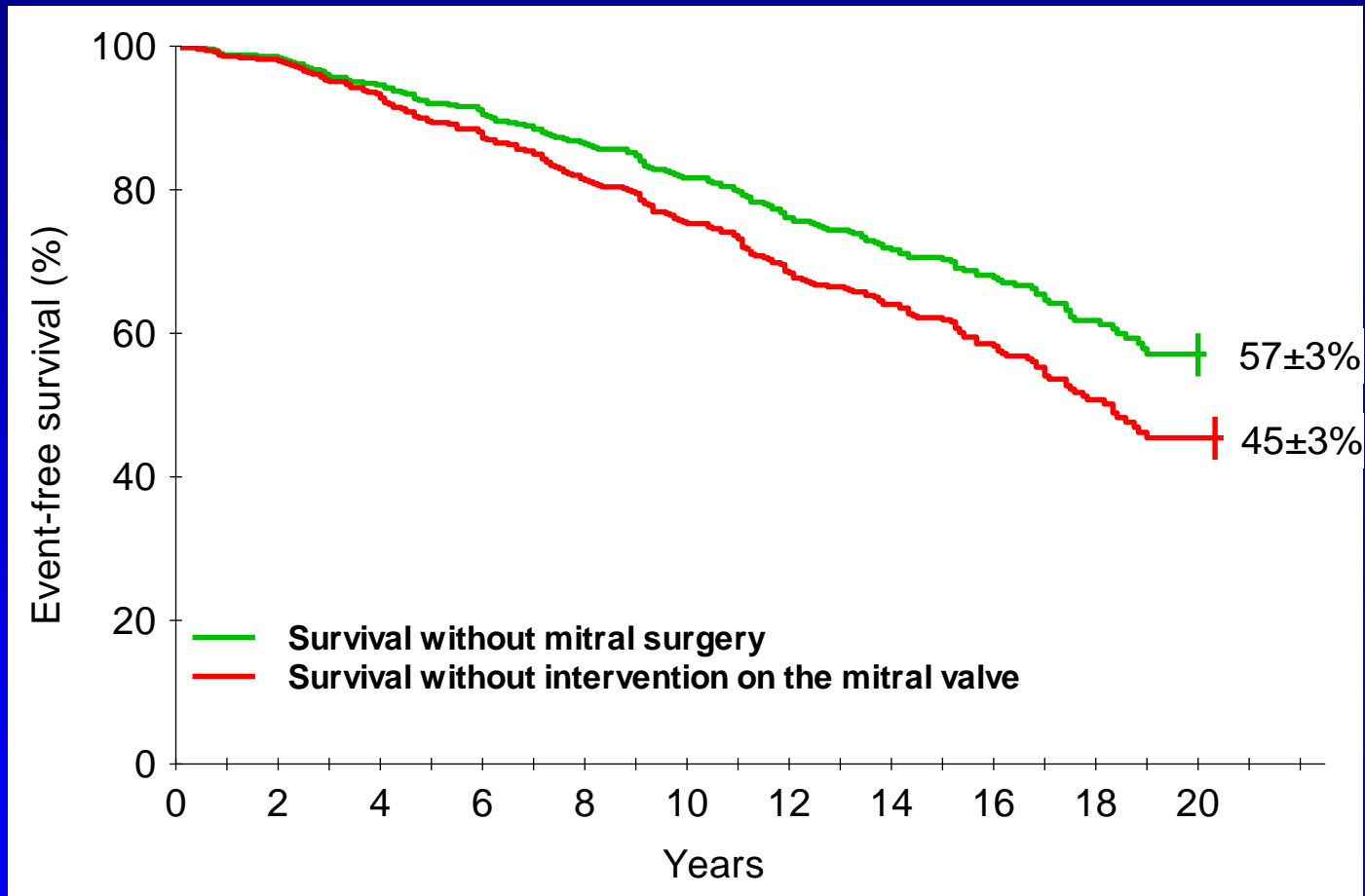
No. at Risk

Good imm. results	912	839	761	673	620	507	446	375	237	111	45
All patients	1024	870	777	687	630	516	465	383	242	114	47
Poor imm. results	112	31	16	14	10	9	9	8	5	3	2

(Bouleti et al. *Circulation* 2012;125:2119-27)

20-Year Results

Survival without re-intervention or surgery
(pts <50 years)

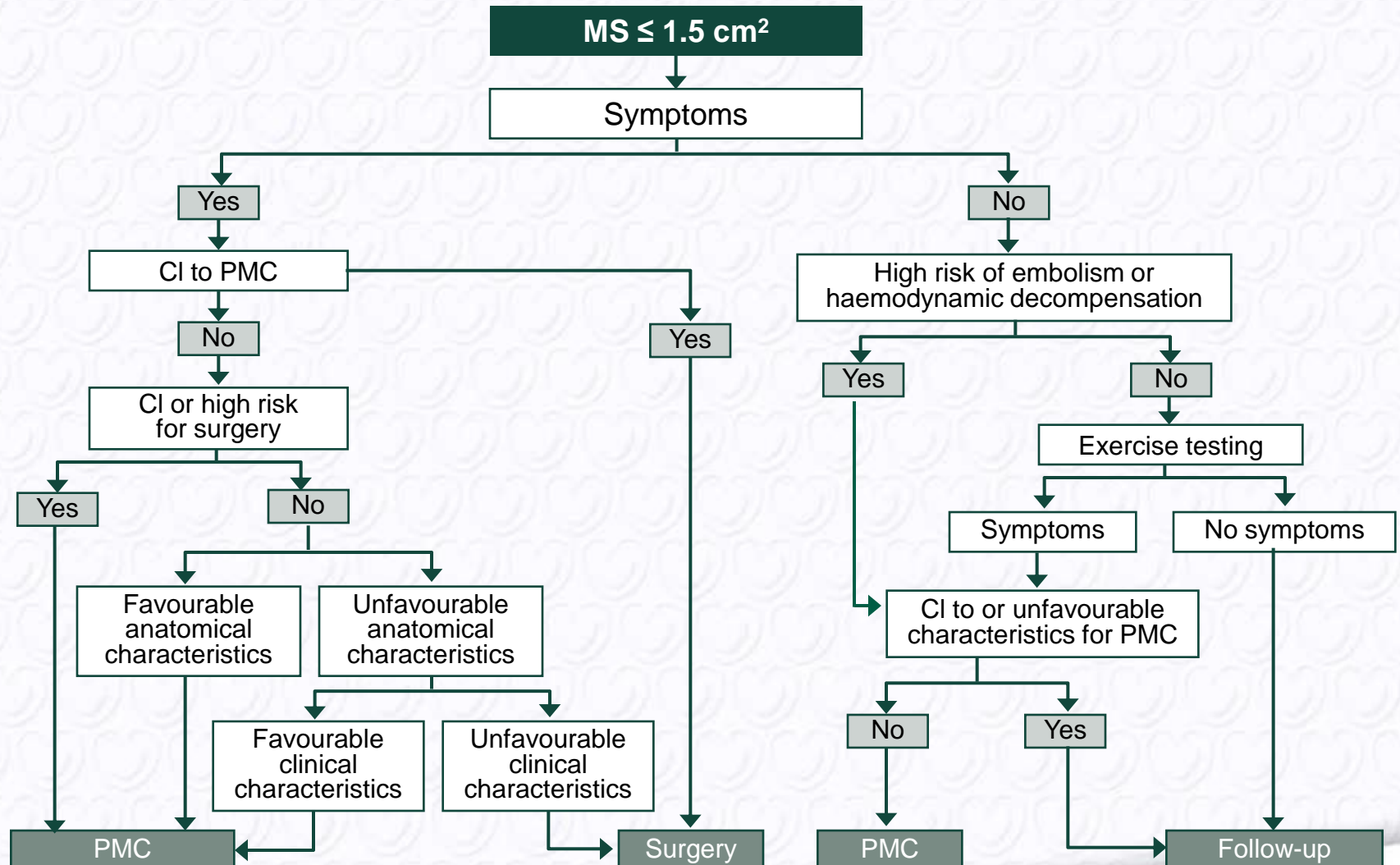


(Bouleti et al. *Circulation* 2012;125:2119-27)

Prediction of Long-Term Results of PMC

	HR [95% CI]	p	Points
Age (y) and final mitral valve area (cm²)			
<50 and MVA \geq 2.00	1		0
<50 and MVA 1.50-2.00 <i>or</i> 50-70 and MVA $>$ 1.75	2.1 [1.6-2.9]	<0.0001	2
50-70 and MVA 1.50-1.75 <i>or</i> \geq 70 and MVA \geq 1.50	5.1 [3.5-7.5]	<0.0001	5
Valve anatomy and sex			
No valve calcification	1		0
Valve calcification			
- female	1.2 [0.9-1.6]	0.18	0
- male	2.3 [1.6-3.2]	<0.0001	3
Rhythm and NYHA class			
Sinus rhythm <i>or</i> A. fib. and NYHA class I-II	1		0
Atrial fibrillation and NYHA class III-IV	1.8 [1.4-2.3]	<0.0001	2
Final mean mitral gradient (mm Hg)			
\leq 3	1		0
3-6	1.1 [1.0-1.8]	0.05	1
\geq 6	2.5 [1.8-3.5]	<0.0001	3

ESC/EACTS Guidelines : Management of clinically significant mitral stenosis



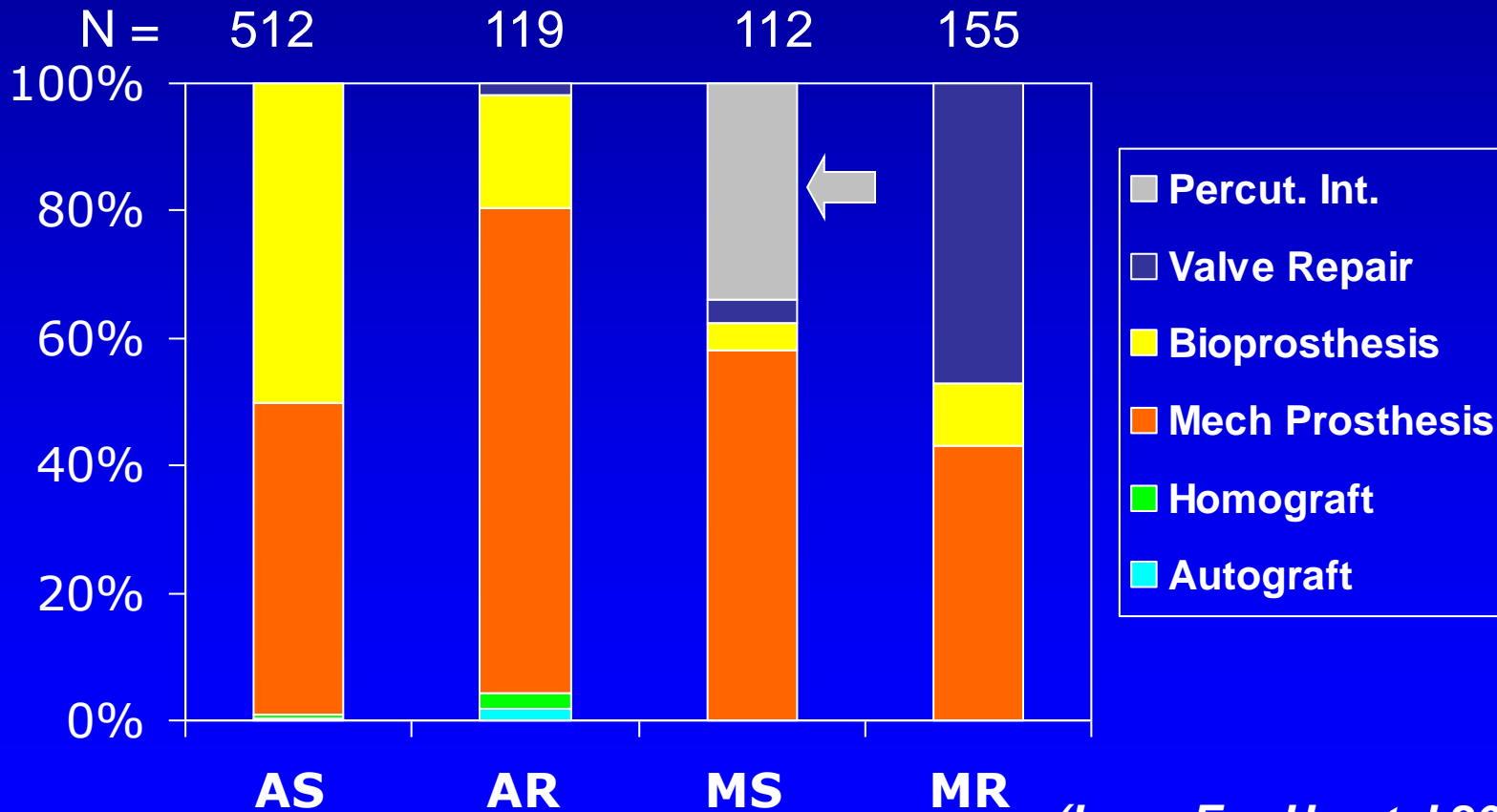
European Heart Journal 2012 - doi:10.1093/eurheartj/ehs109 &
 European Journal of Cardio-Thoracic Surgery 2012 -
 doi:10.1093/ejcts/ezs455).



The Role of PMC



5001 Patients admitted in 92 centres from April to July 2001



(lung. Eur Heart J 2003;24:1231)

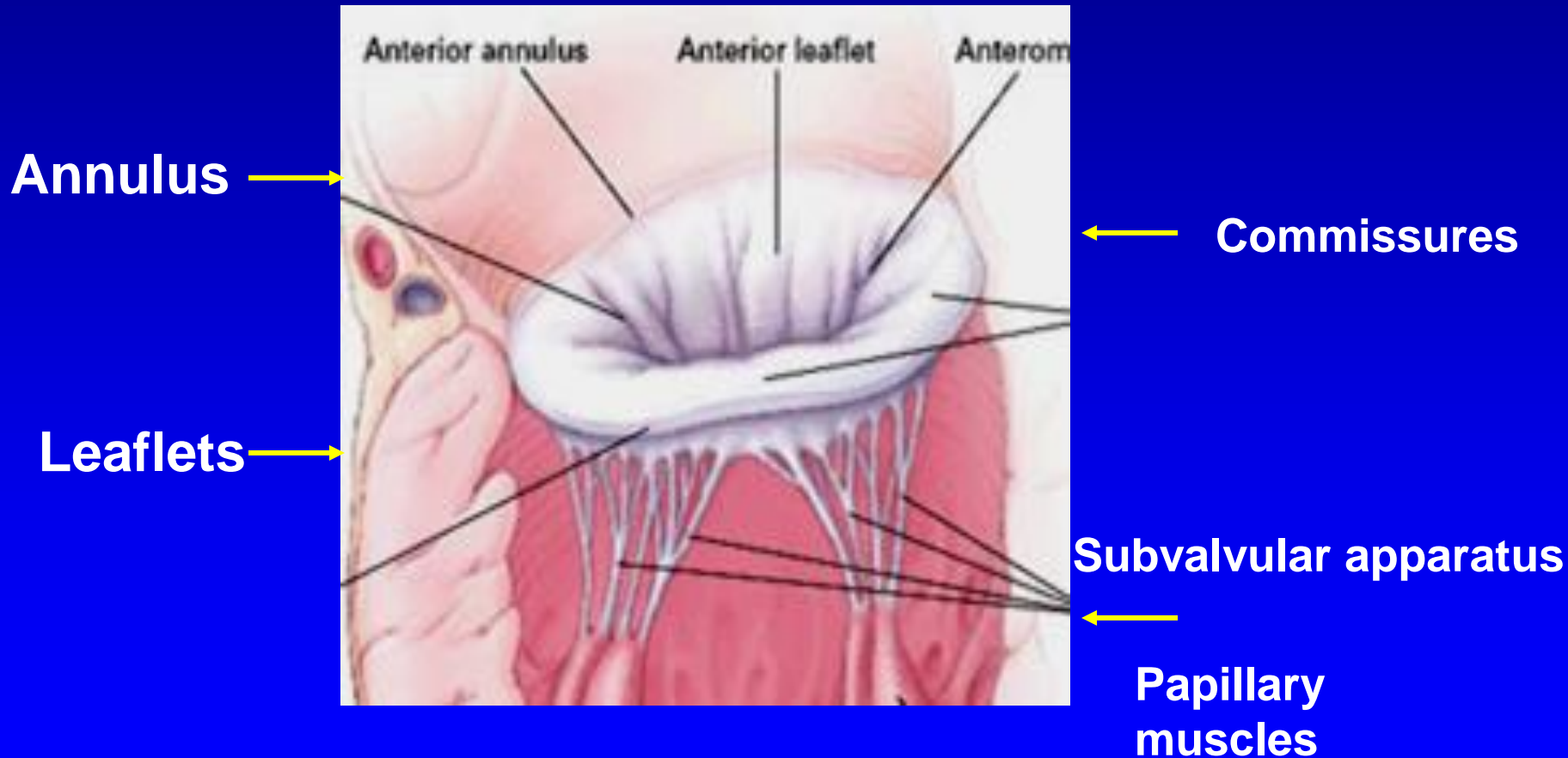
Percutaneous Mitral Commissurotomy

Percutaneous Mitral Valve Repair

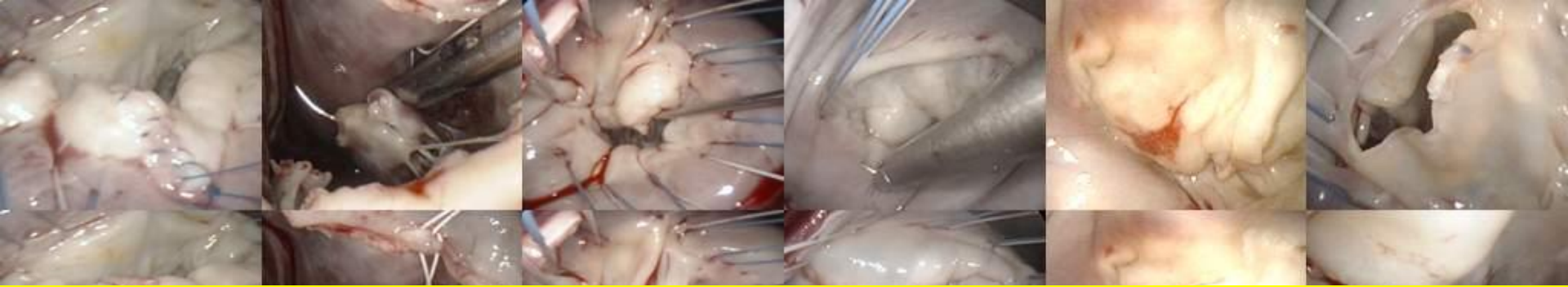
Transcatheter treatment after surgical failure

Final comments

Mitral Valve Apparatus



Complex interaction



Principles of a reconstructive valve operation

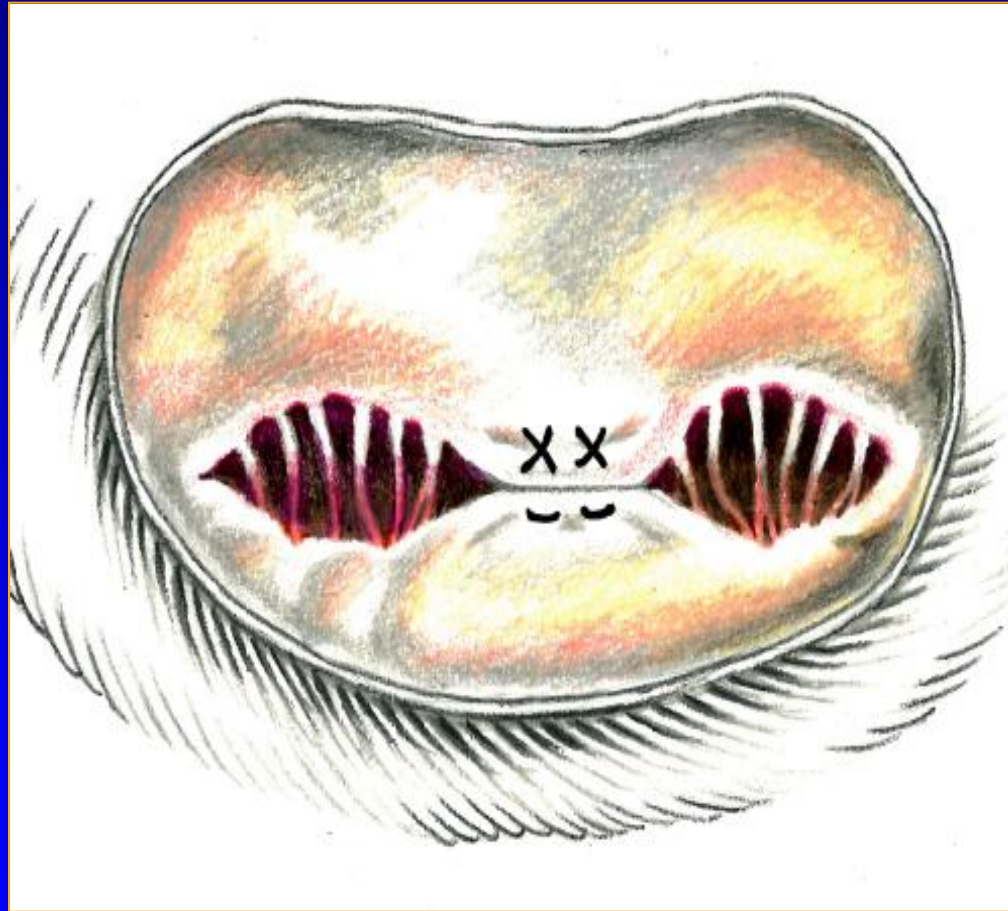
- **Preserve or restore full leaflet motion**
- **Create a large surface of coaptation**
- **Remodel and stabilise the entire annulus**



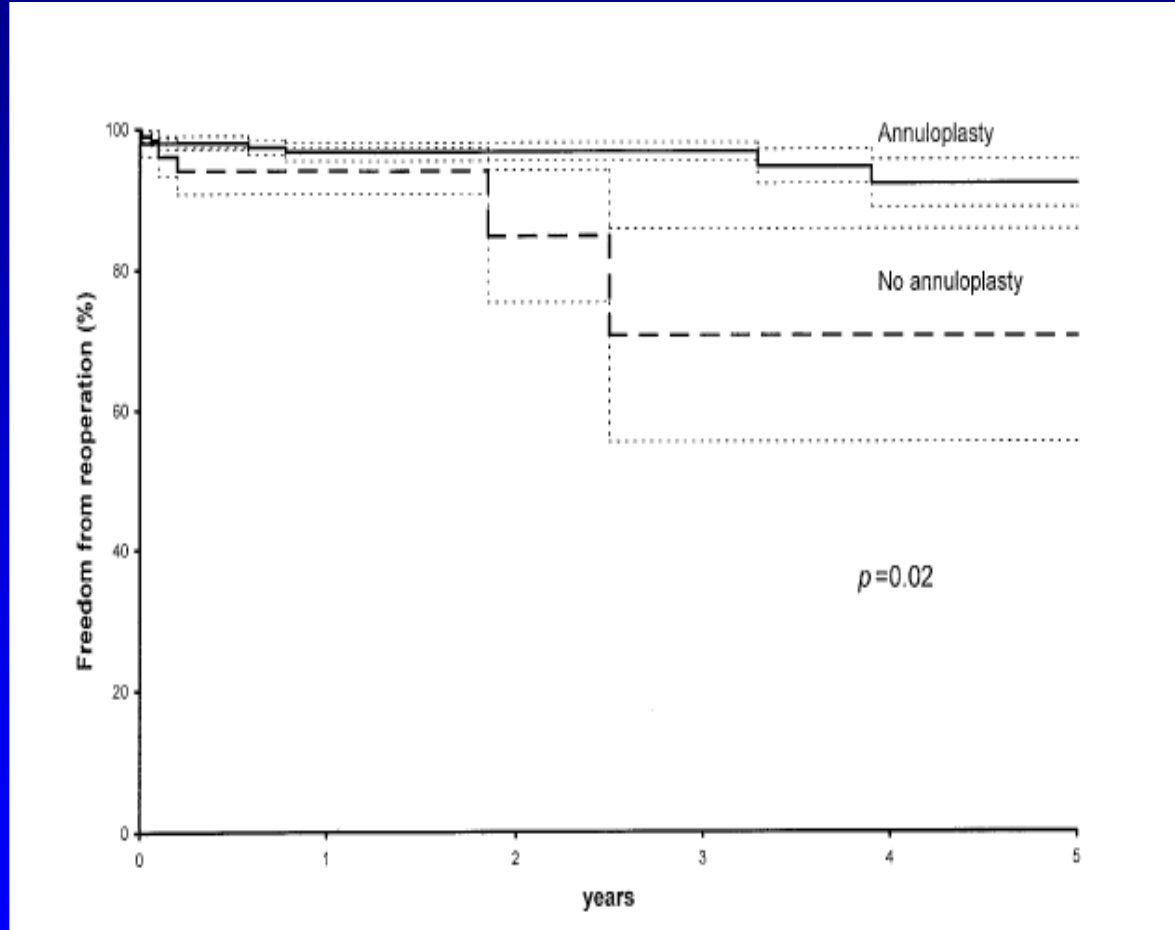
Surgery in Mitral Regurgitation

- In expert centres, in patients with primary MR, the repair rate is >90% and >90% of patients are alive and free from reoperation after 10-15 years.
- Surgery for secondary MR remains a challenge. Most studies failed to demonstrate improved long-term clinical outcome following surgical correction.

Edge-to-Edge Technique



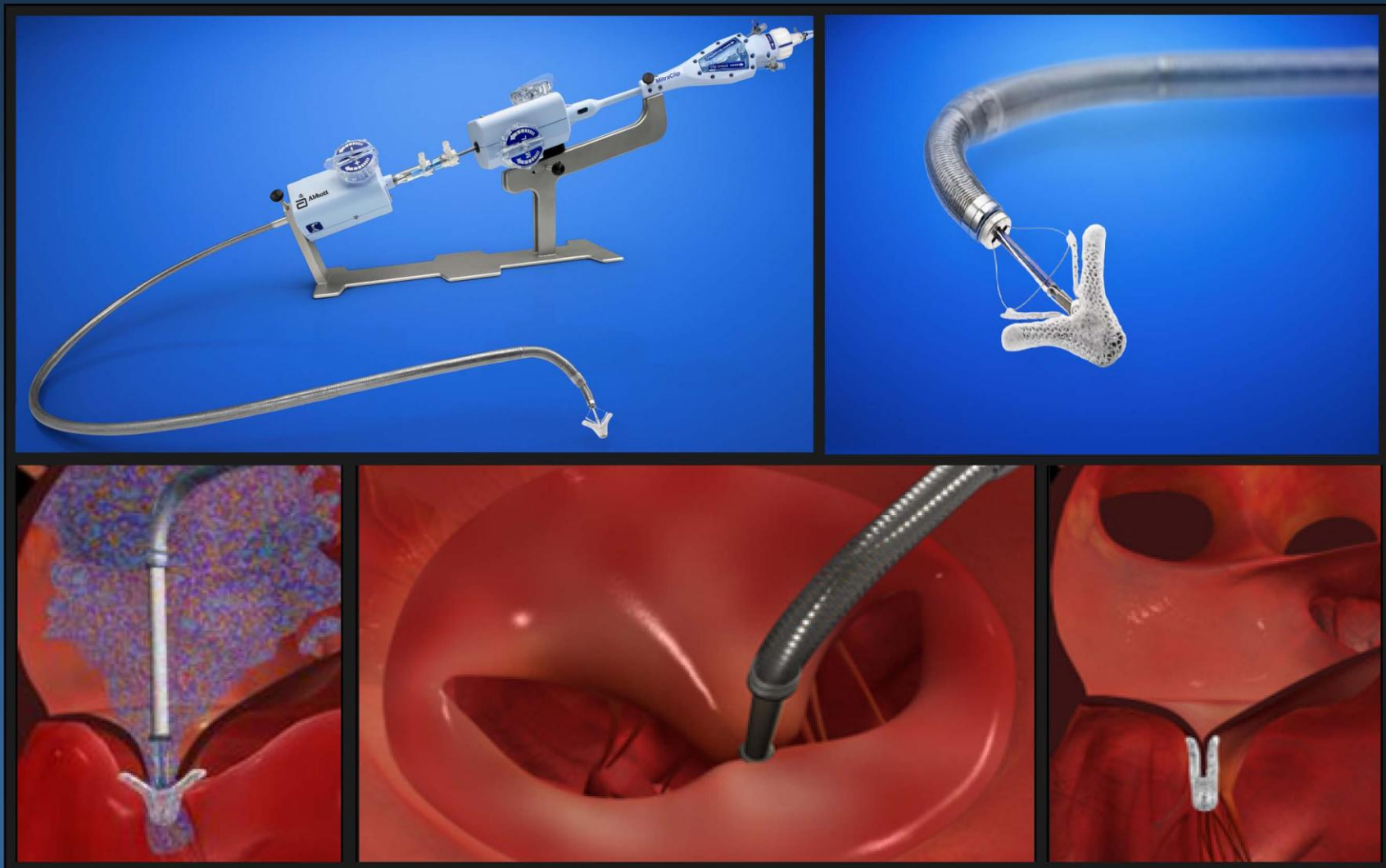
Surgical Edge-to-Edge technique



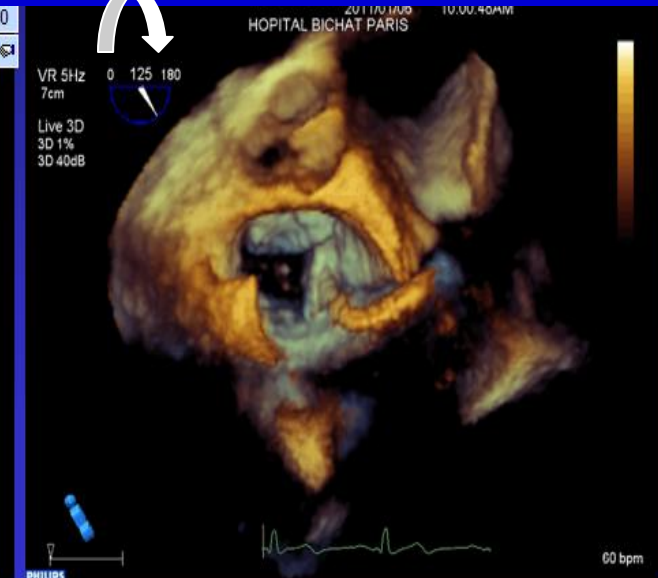
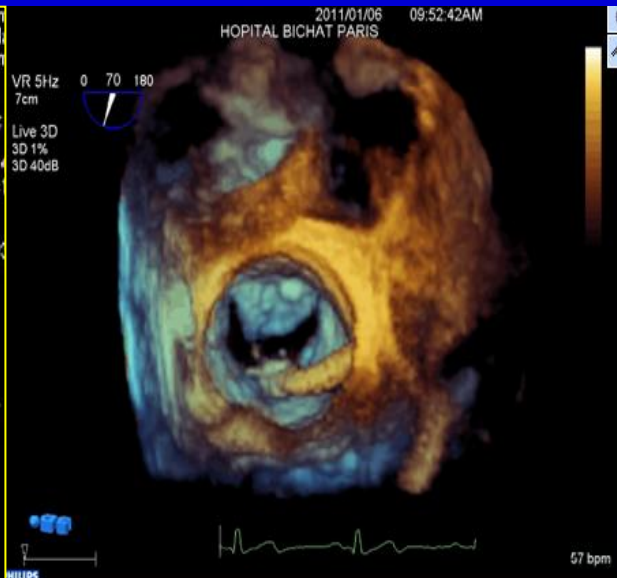
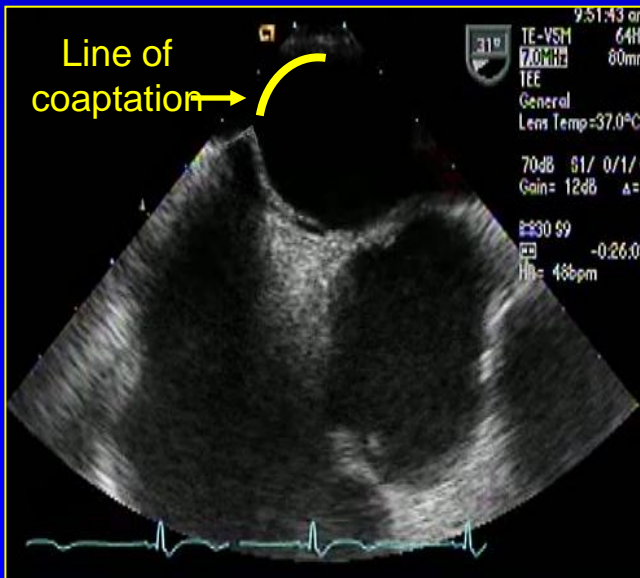
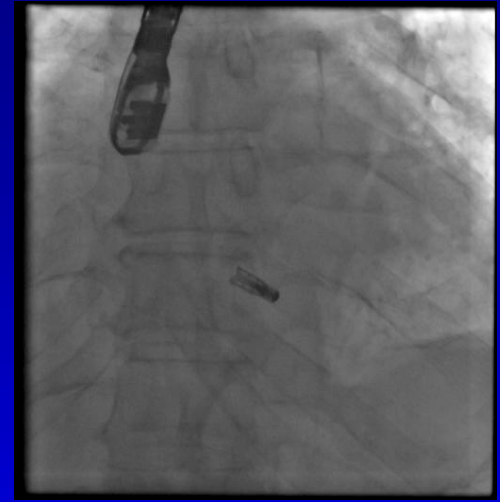
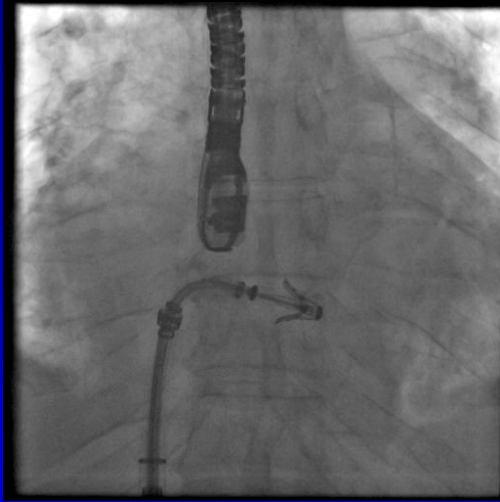
(Alfieri. J Thorac Cardiovasc Surg 2001;122:674-81)

Percutaneous Mitral Valve Repair

MitraClip® System



The Procedure



Study Design

EVEREST II Randomized Controlled Trial (RCT)

279 Patients enrolled at 37 sites

Significant MR (3+ or 4+)
Specific Anatomical Criteria

↓
Randomized 2:1

↙ ↘
Percutaneous Group
MitraClip System
N=184

↙ ↘
Surgery Group
Surgical Repair or Replacement
N=95

↓ ↓
Echocardiography Core Lab and Clinical Follow-Up:
Baseline, 30 days, 6 months, 1 year, 18 months, and
annually through 5 years

Key Inclusion/Exclusion Criteria

EVEREST II RCT

Inclusion

- Candidate for MV Surgery
- Moderate to severe (3+) or severe (4+) MR
 - Symptomatic
 - $>25\%$ EF & LVESD $\leq 55\text{mm}$
 - Asymptomatic with one or more of the following
 - LVEF 25-60%
 - LVESD $\geq 40\text{mm}$
 - Pulmonary hypertension
 - Atrial fibrillation

ACC/AHA Guidelines
JACC 52:e1-e142, 2008

Exclusion

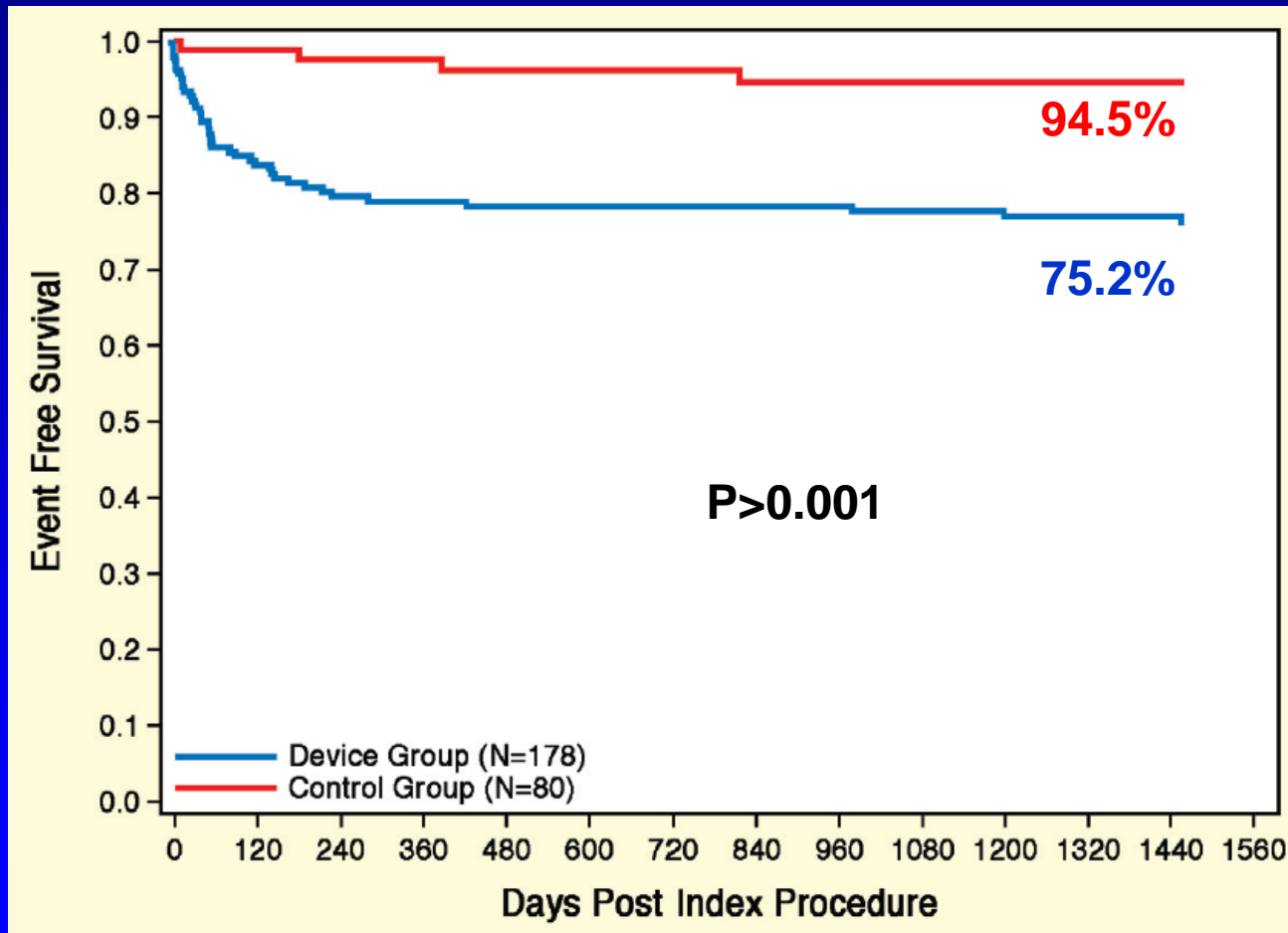
- AMI within 12 weeks
- Need for other cardiac surgery
- Renal insufficiency
 - Creatinine $>2.5\text{mg/dl}$
- Endocarditis
- Rheumatic heart disease
- MV anatomical exclusions
 - Mitral valve area $<4.0\text{cm}^2$
 - Leaflet flail width ($\geq 15\text{mm}$) and gap ($\geq 10\text{mm}$)
 - Leaflet tethering/coaptation depth ($>11\text{mm}$) and length ($<2\text{mm}$)

Safety Endpoint: 30 Day MAE

Intention to Treat

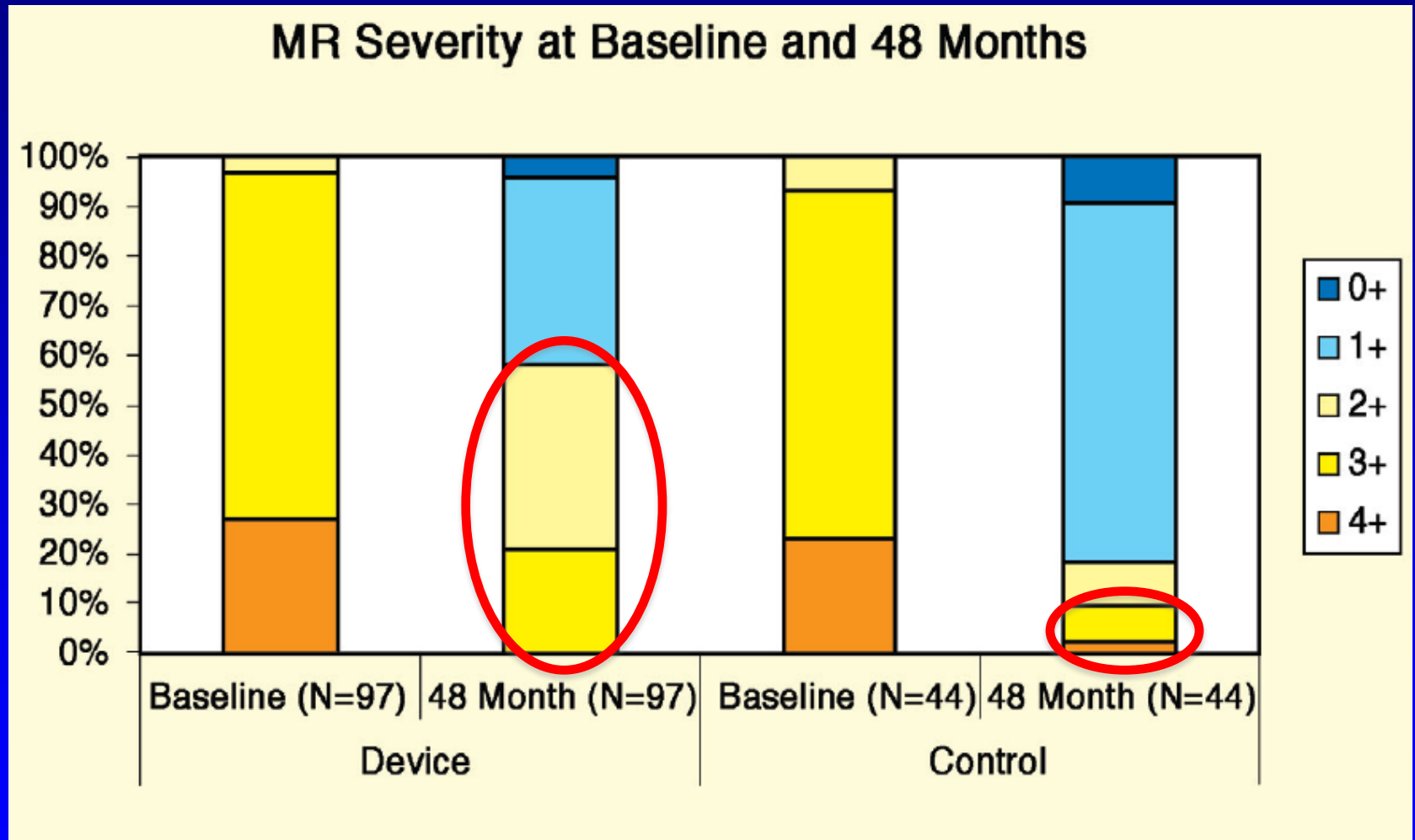
30 Day MAE	# (%) Patients experiencing event	
	Percutaneous (N=180)	Surgery (N=94)
Death	2 (1.1%)	2 (2.1%)
Major Stroke	2 (1.1%)	2 (2.1%)
Re-operation of Mitral Valve	0	1 (1.1%)
Urgent / Emergent CV Surgery	4 (2.2%)	4 (4.3%)
Myocardial Infarction	0	0
Renal Failure	1 (0.6%)	0
Deep Wound Infection	0	0
Ventilation > 48 hrs	0	4 (4.3%)
New Onset Permanent Atrial Fib	2 (1.1%)	0
Septicemia	0	0
GI Complication Requiring Surgery	2 (1.1%)	0
Transfusions ≥ 2 units	24 (13.3%)	42 (44.7%)
TOTAL % of Patients with MAE	15.0%	47.9%
	Difference (Percutaneous – Surgery) = -32.9%	
	p<0.001; (95% CI: -20.7%, -45.0%)	

Freedom from MV Surgery or Re-operation in EVEREST



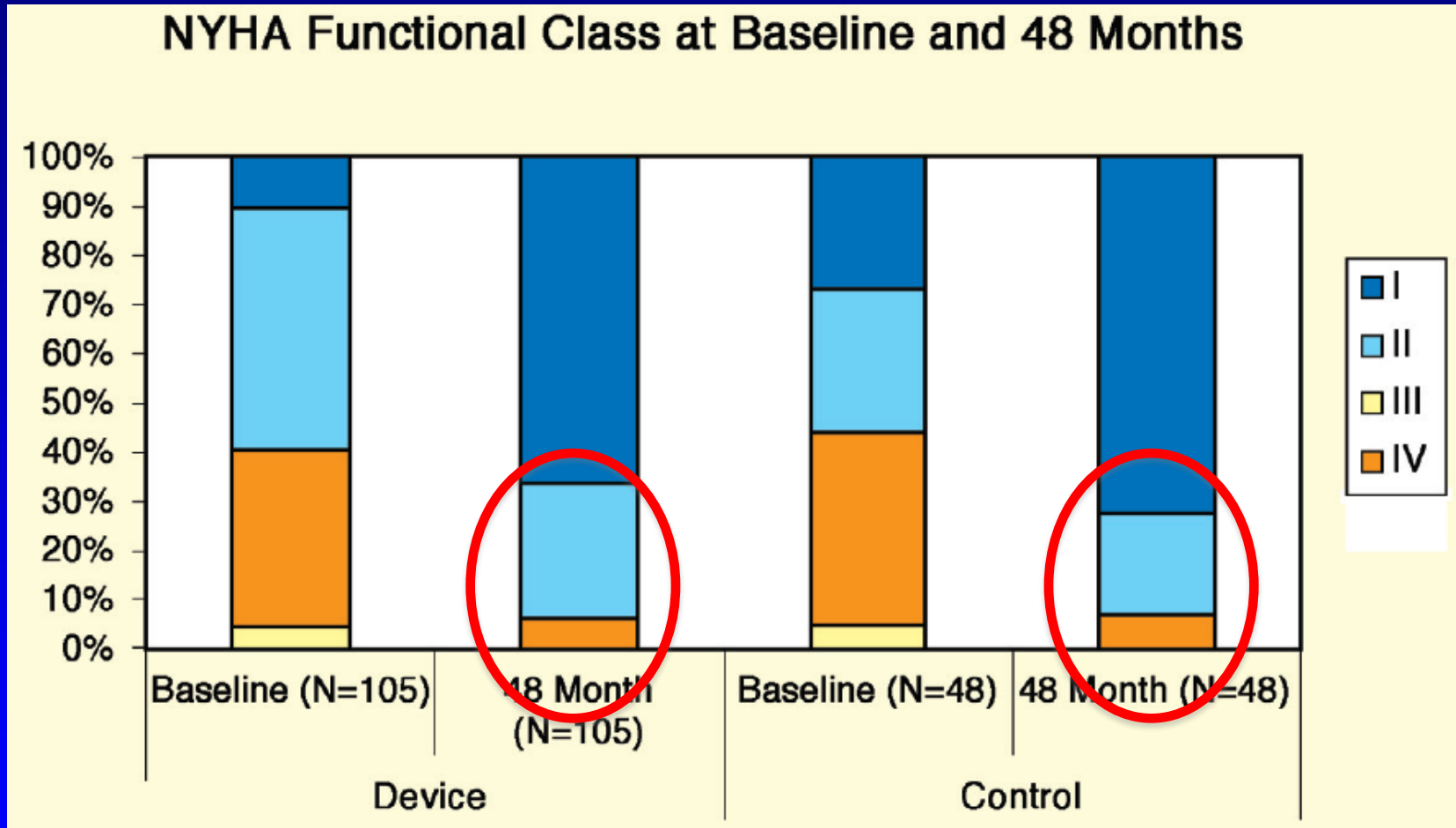
(Mauri L et al. J Am Coll Cardiol 2013. Online)

Mitral Regurgitation Severity in EVEREST



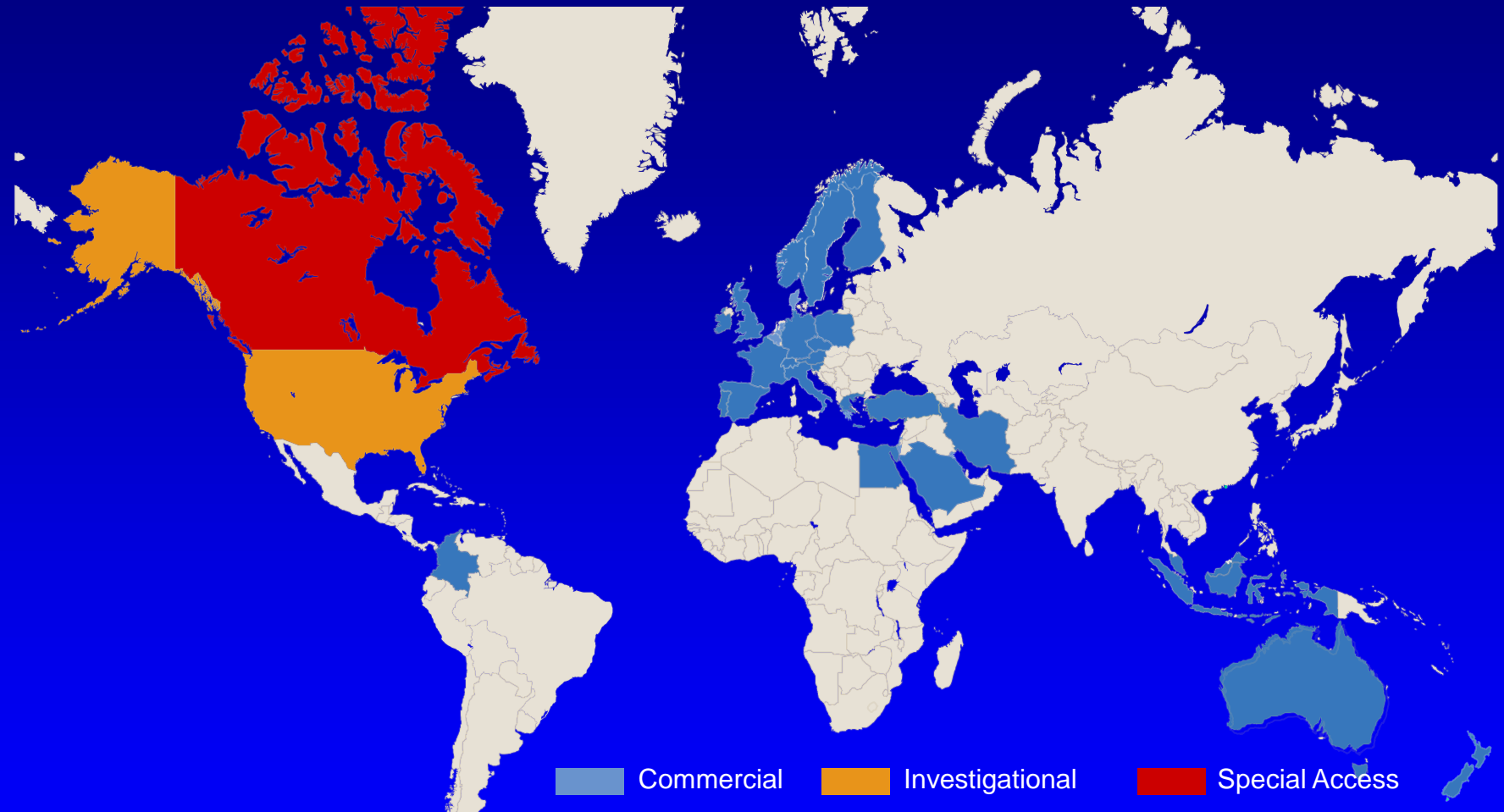
(Mauri L et al. J Am Coll Cardiol 2013. Online)

NYHA Functional Class in EVEREST



(Mauri L et al. J Am Coll Cardiol 2013.Online)

MitraClip Therapy Worldwide



Treating Centers

278

Patients

10,019

MitraClip Therapy

UHC experience

17 Sep 2008 – 31 Aug 2012

	EVEREST II	Hamburg	P
n	184	340	
Age, years	67 ± 13	75 ± 9	<0.0001
Men	55 (30%)	216 (64%)	<0.0001
Functional MR	49 (27%)	230 (68%)	<0.0001
NYHA III/IV	94 (51%)	320/333 (96%)	<0.0001
LVEF, %	60 ± 10	43 ± 16	<0.0001
Log. EuroSCORE, % [median (IQR)]	33 (18%)	22 (12 – 38)	<0.0001
Cardiomyopathy	86/183 (47%)	241/328 (73%)	<0.0001
Coronary artery disease	40/183 (22%)	218/337 (65%)	0.0031
Atrial fibrillation	59/175 (34%)	220/337 (65%)	<0.0001
Diabetes	14 (8%)	102/336 (30%)	<0.0001
COPD	27/183 (15%)	69/337 (21%)	<0.0001
MR 3+/4+	176 (96%)	340 (100%)	0.1633



80% of patients would not have fulfilled EVEREST criteria

Safety Results

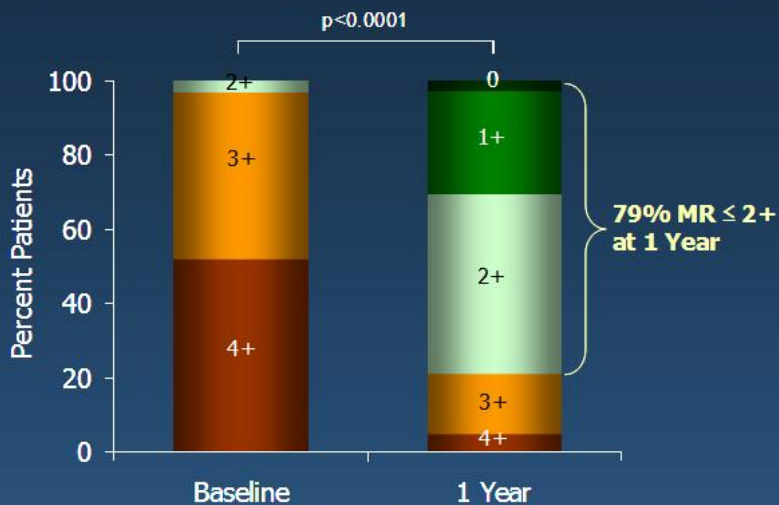
German TRAMI Registry n=1064

	(%)
Procedural Success	95.3
Patient with MACCE (death, MI, Stroke)	3.5
Death	2.9
Myocardial infarction	0.2
Stroke	0.4
Severe bleeding, transfusion	14.5
Pericardial effusion	1.4
Vascular injury	6.9
Clip embolism	0

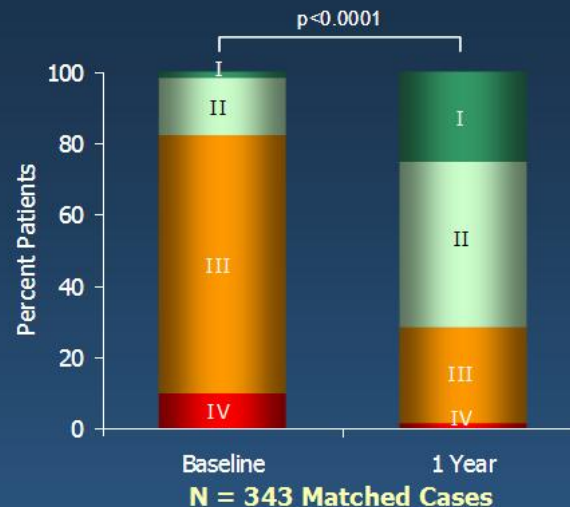
(Schillinger W et al. EuroIntervention 2013. In Press)

Efficacy Results in ACCESS EU

Mitral Regurgitation Grade*



NYHA Functional Class

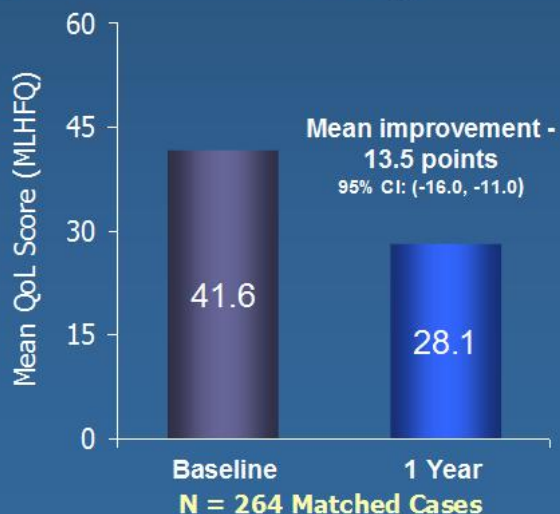


*As assessed by the sites

N = 327 Matched Cases

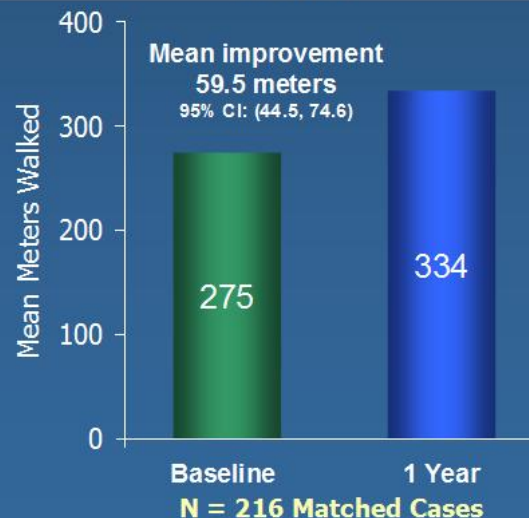
N = 343 Matched Cases

MLHFQ



N = 264 Matched Cases

6MWT



N = 216 Matched Cases

ESC/ EACTS Guidelines for the Management of Valvular Heart Disease

« The percutaneous Mitraclip procedure may be considered in symptomatic patients with severe primary or secondary MR despite optimal medical therapy, who fulfil the echo criteria of eligibility, are judged inoperable or at high risk for surgery by a heart team, and who have a life expectancy greater than one year »

(Recommendation class IIb, level of Evidence C)

« The current findings have to be confirmed in larger series with longer follow-up and with a randomized design »

European Heart Journal 2012 - doi:10.1093/eurheartj/ehs109 &
European Journal of Cardio-Thoracic Surgery 2012 -
doi:10.1093/ejcts/ezs455).

The Trials we need in Secondary MR

HF patients with Severe MR and Low EF

RESHAPE, COAPT just started
Mitra-FR will start

management

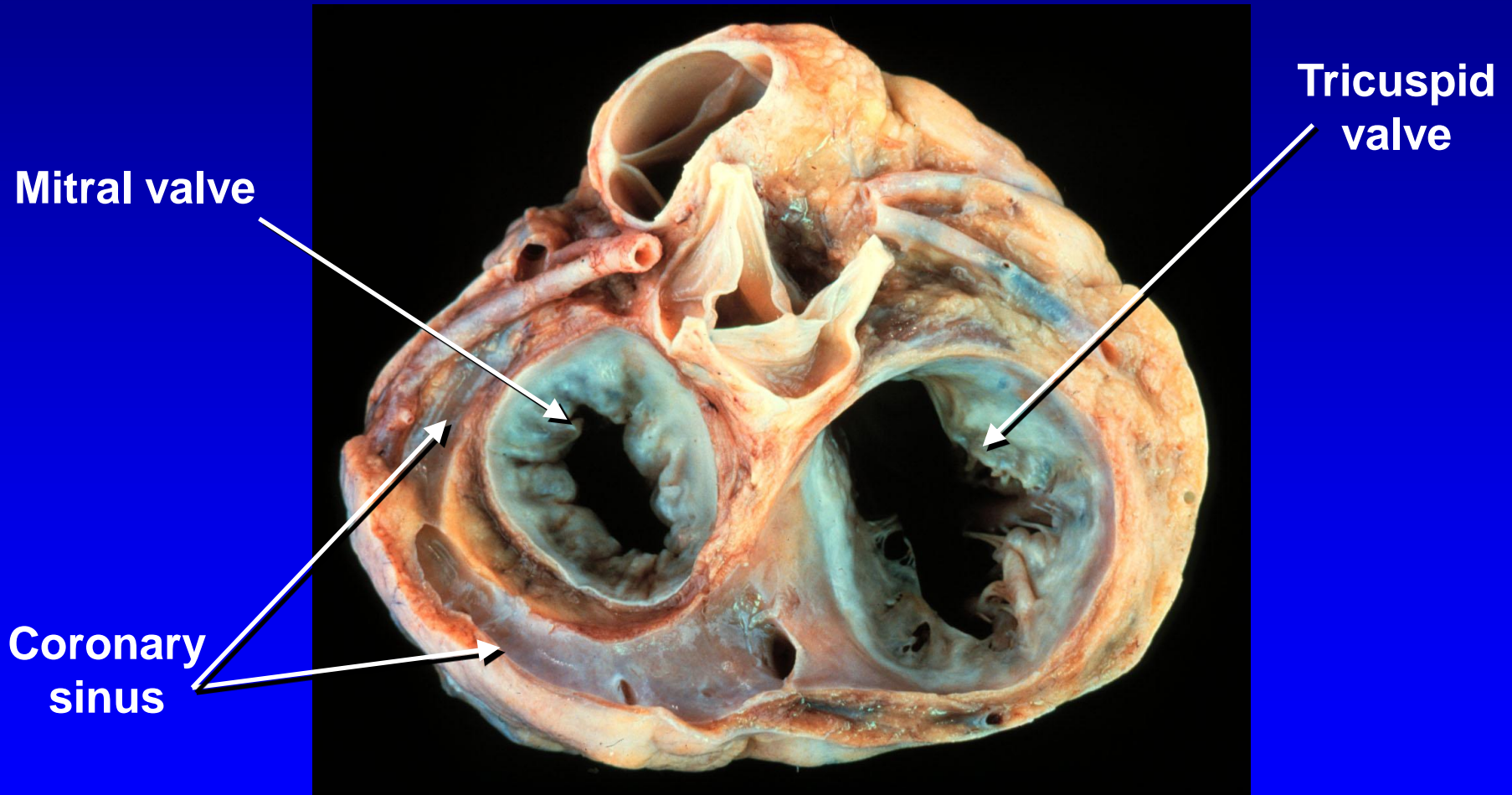
(including Revascularisation and/or CRT)

Edge-to-Edge

Medical therapy

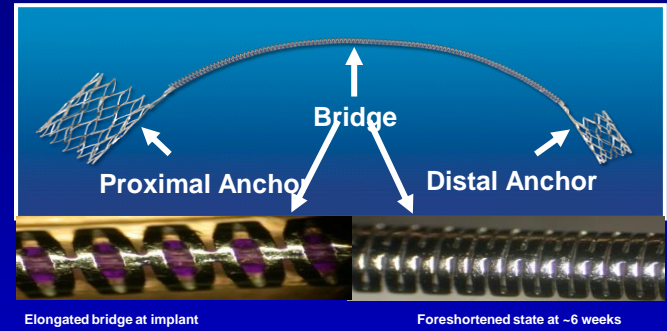
Coronary Sinus Annuloplasty

Limitations of Percutaneous Coronary Sinus Annuloplasty

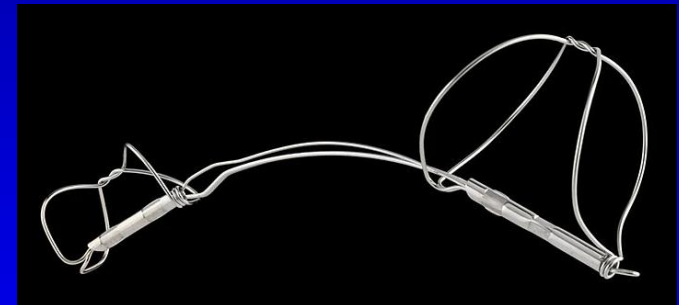


The Devices

- The Edwards MONARC system*

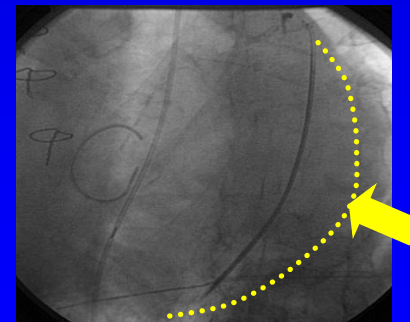


- The CARILLON device



- The PTMA Implant System*

* abandoned



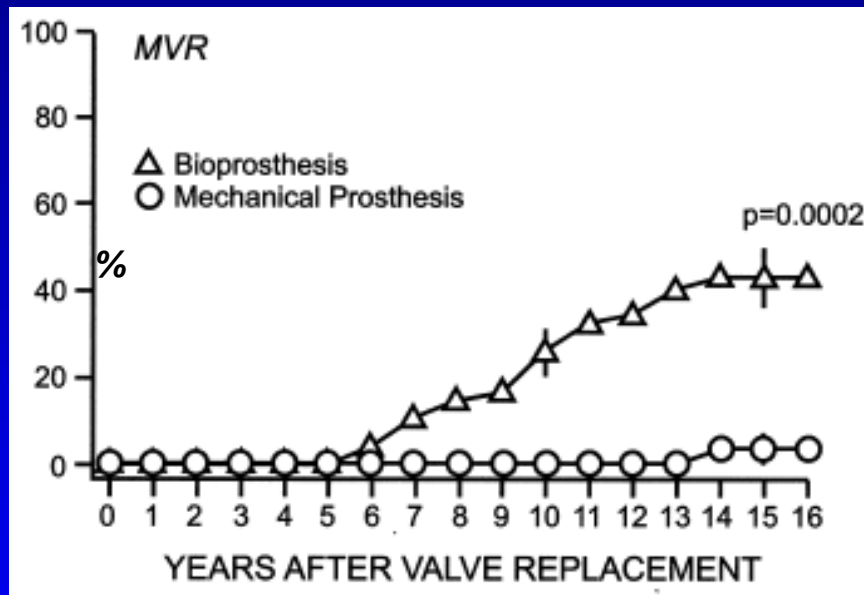
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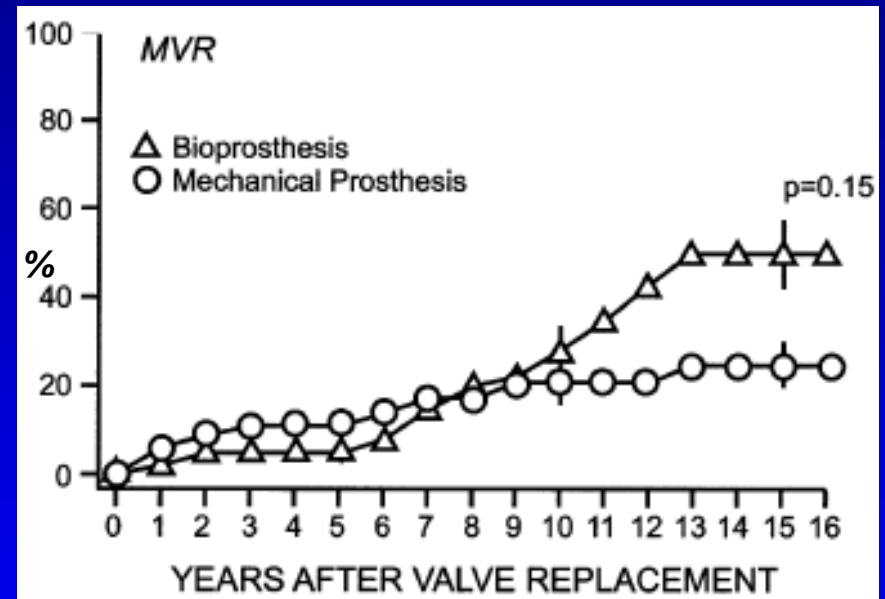
Transcatheter treatment after surgical failure

Final comments

Mitral Bioprosthesis vs Mechanical Prostheses



Primary dysfunction



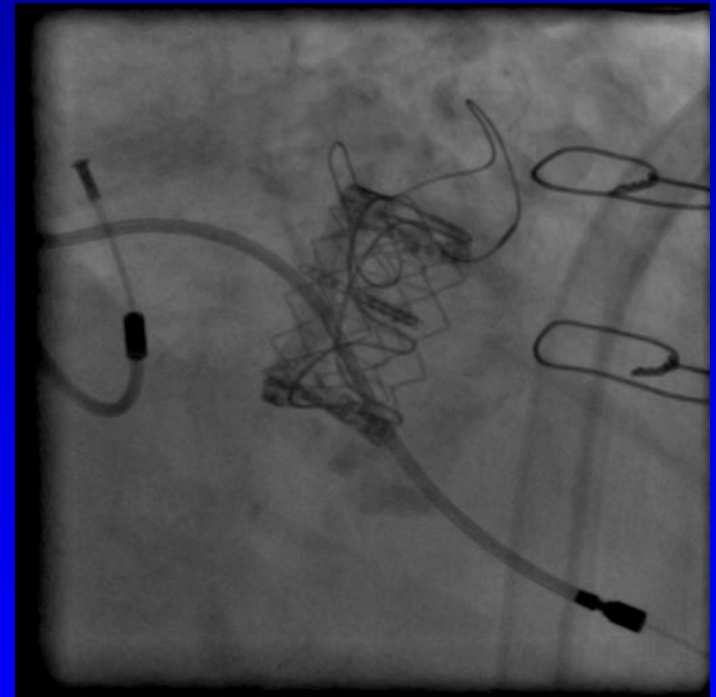
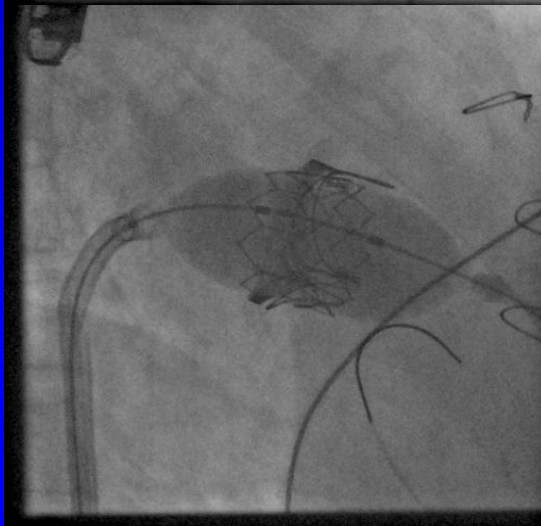
Reoperations

Transcatheter « Valve in Valve » for Mitral Bioprosthesis Failure

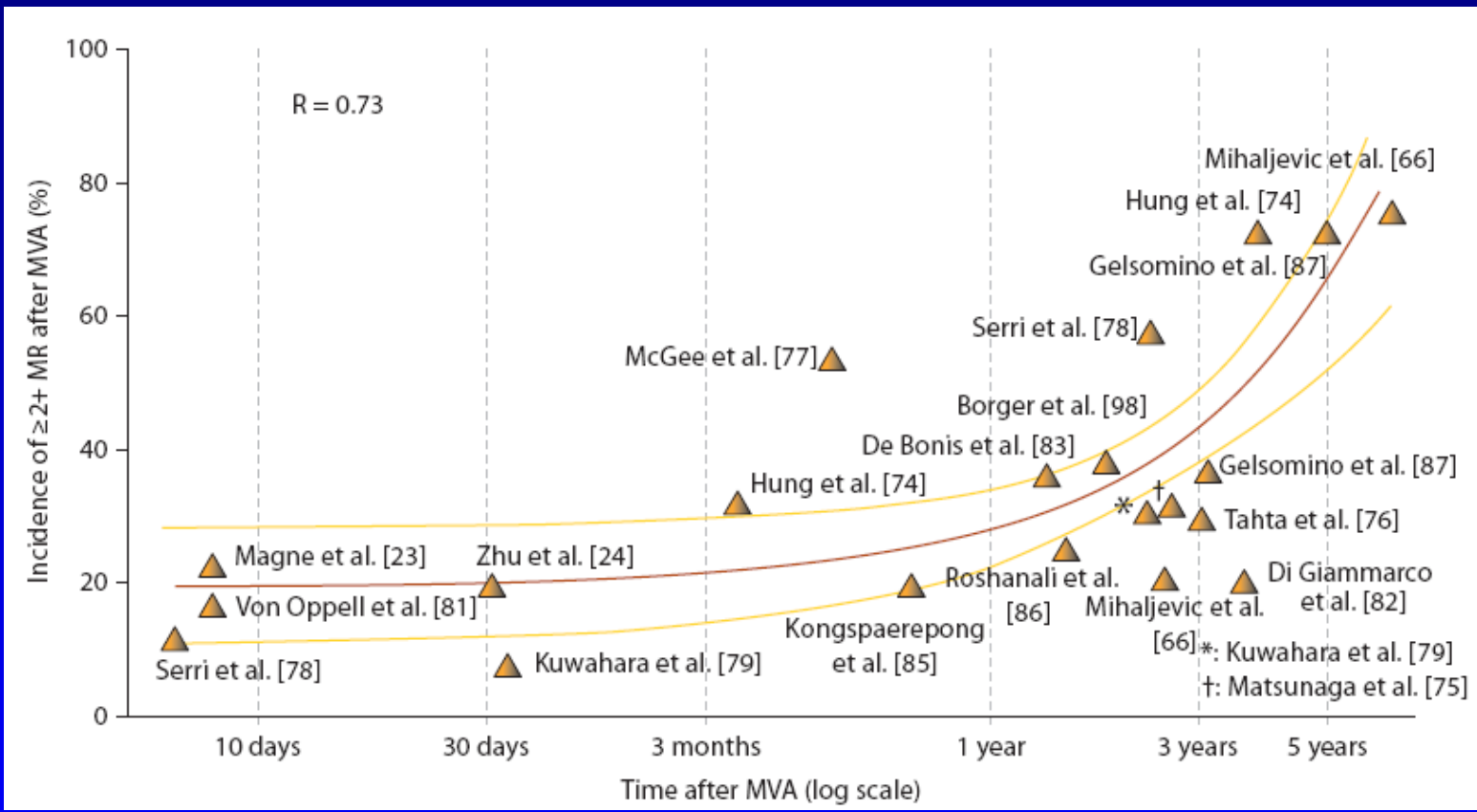
Transapical



Transseptal



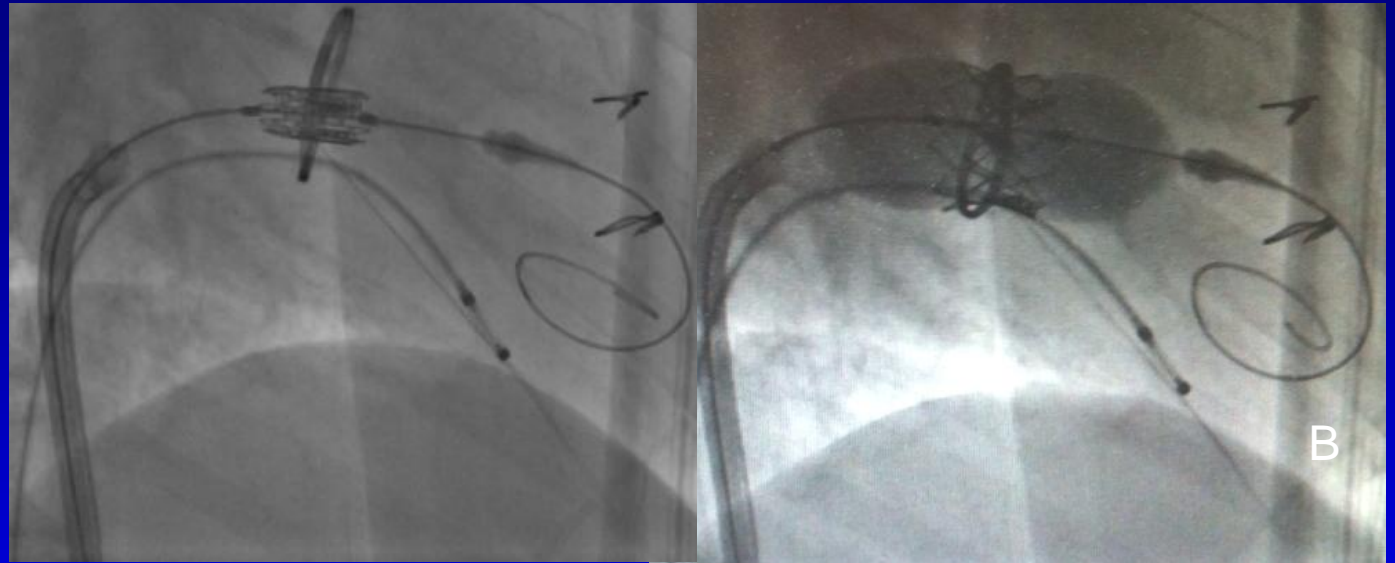
Persistence/Recurrence of MR following Restrictive Annuloplasty



(Magne et al. Cardiology, 2008)

Transcatheter « Valve in a Ring »

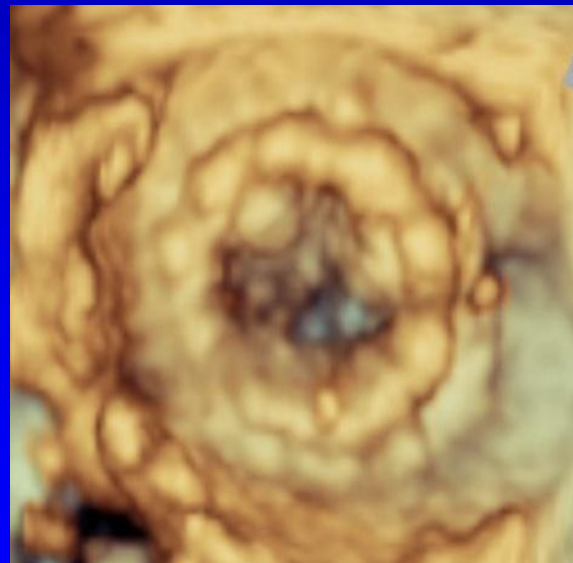
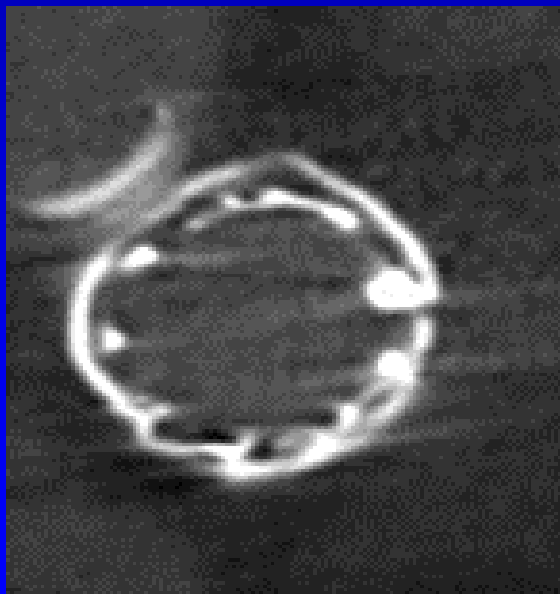
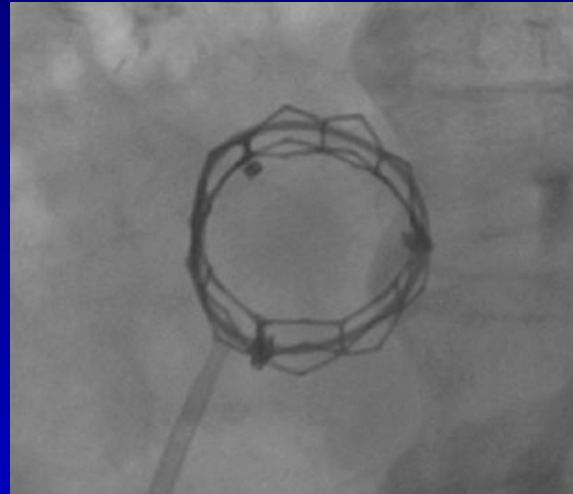
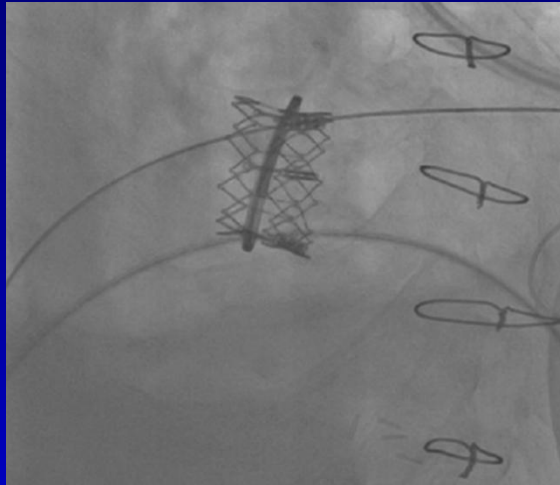
Transseptal



Transapical



Transcatheter « Valve in a Ring »



(De Weger. *Eur J Cardio-thorac Surg.* 2010.)

(D Himbert. *Circ Cardiovasc Interv* 2011;4:396-398)

(D Himbert. *J Am Coll Cardiol.* 2012;60:1205-6.)

Percutaneous Mitral Commissurotomy

Percutaneous Mitral Valve Repair

Transcatheter treatment after surgical failure

Final comments

The « Heart Team »

Surgeons

Cardiologists

Anaesthesiologists

Treatment of Mitral Valve
Disease

Other specialists:
HF, EP,
Geriatricians,...

Imaging specialists (Echo, CT, MRI)

Patient Selection for Intervention on the Mitral Valve

Medical Rx

PMVR

Surgery
(*Repair, Replacement, LVAD, Transplantation*)

« *Futility > Utility* »
Because of *cardiac*
and extra cardiac
factors

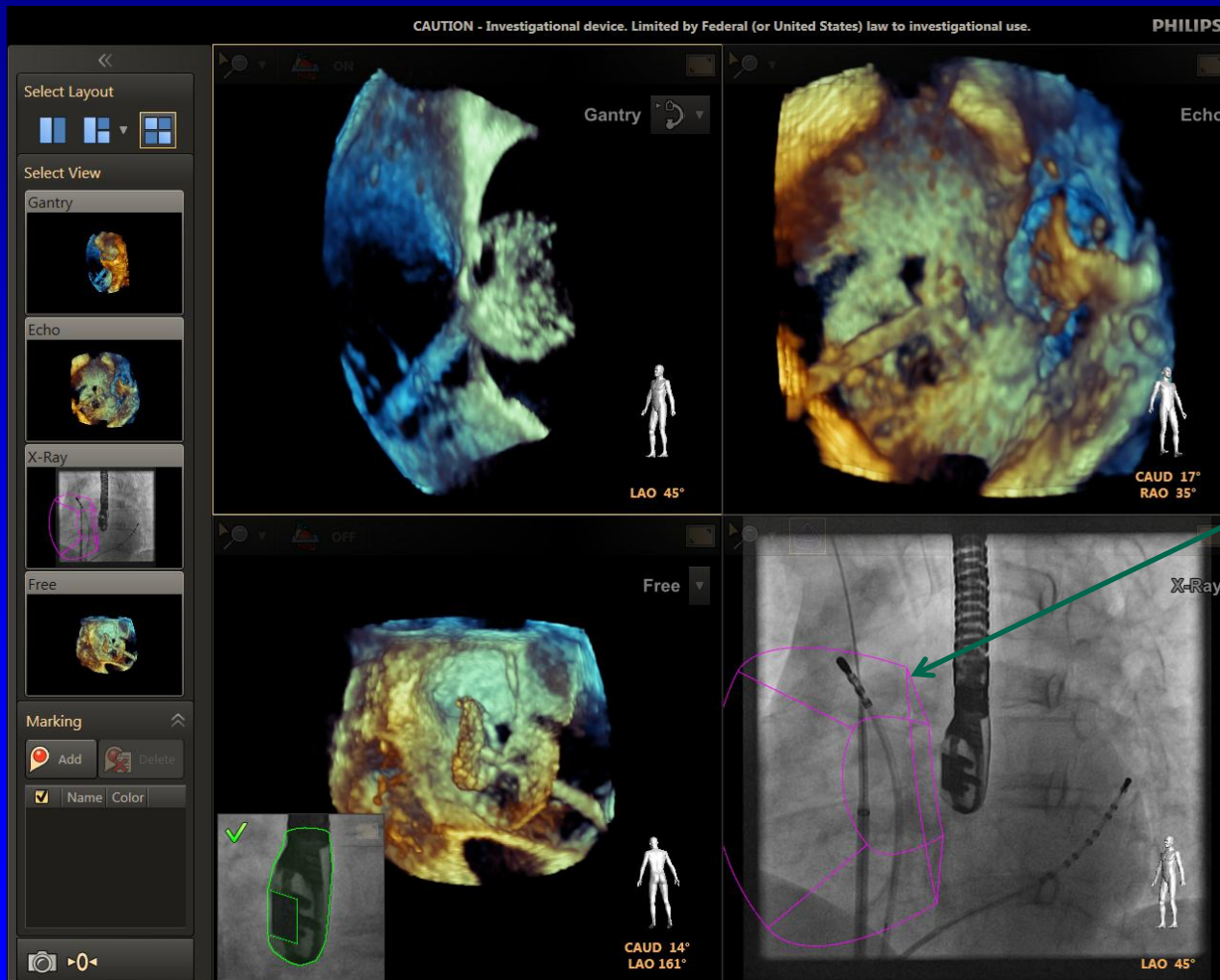
Where Shall we Perform Percutaneous Valve Intervention?

In cardiology and cardiac surgery centres



Multimodality Imaging

Linked Live 3DTEE and fluoroscopic images



Volume location of 3D Echo



Montreal

Transcatheter Mitral Valve Landscape

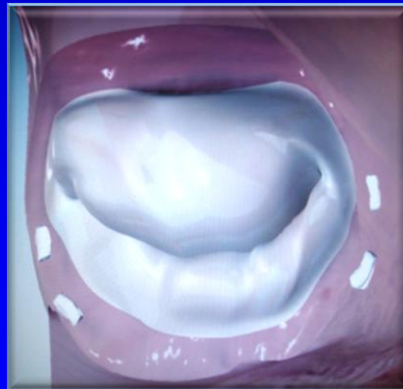
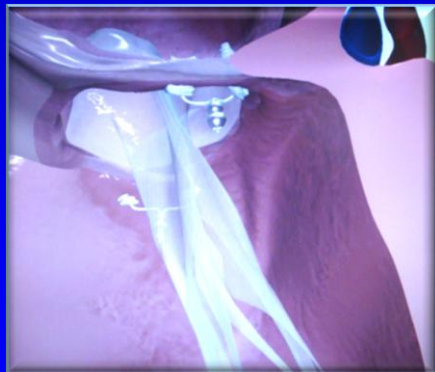
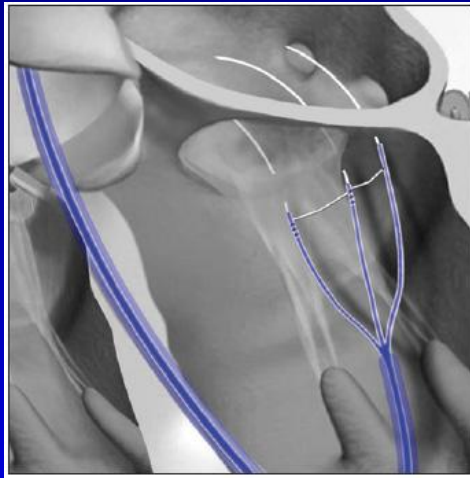


Munich

Approach	Commercial	In Development	Abandoned
Edge-to-Edge Repair			
Direct Annuloplasty		 	
Indirect Annuloplasty			
Chordal Repair			
Ventricular Remodeling		 	
Enhanced coaptation		 	
MV Replacement		 	

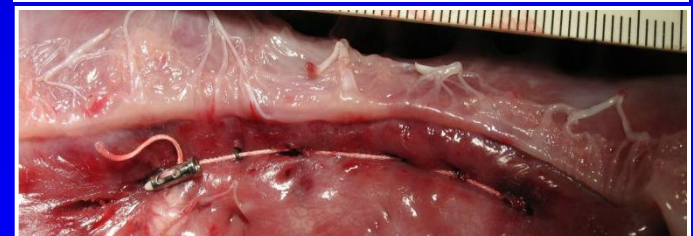
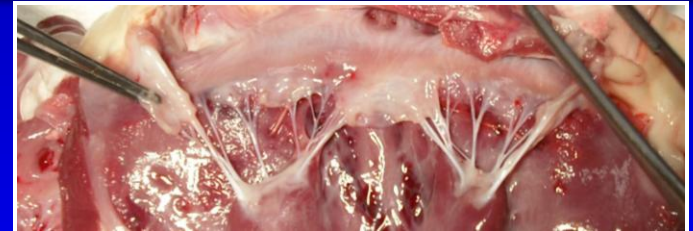
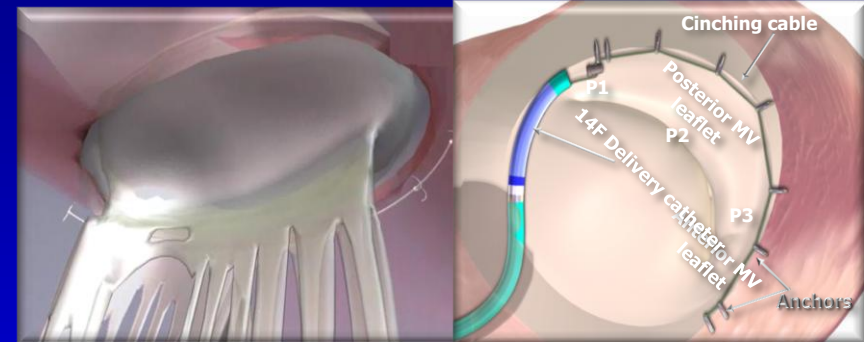
New Devices: Direct Annuloplasty

Mitralign



In clinical trial (n=40)

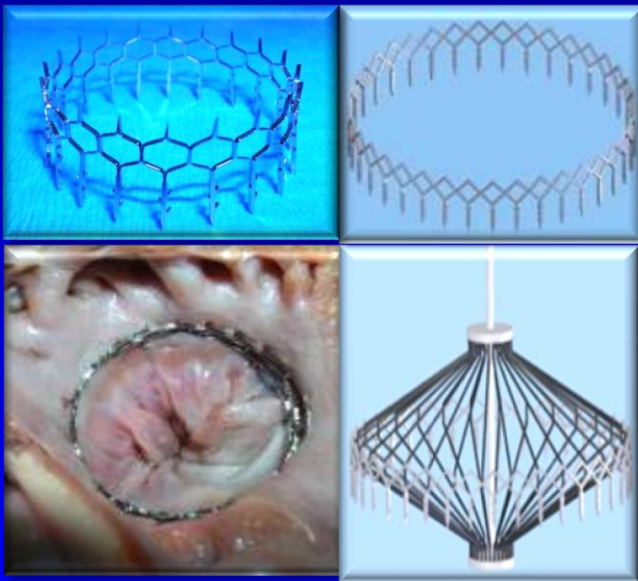
GDS



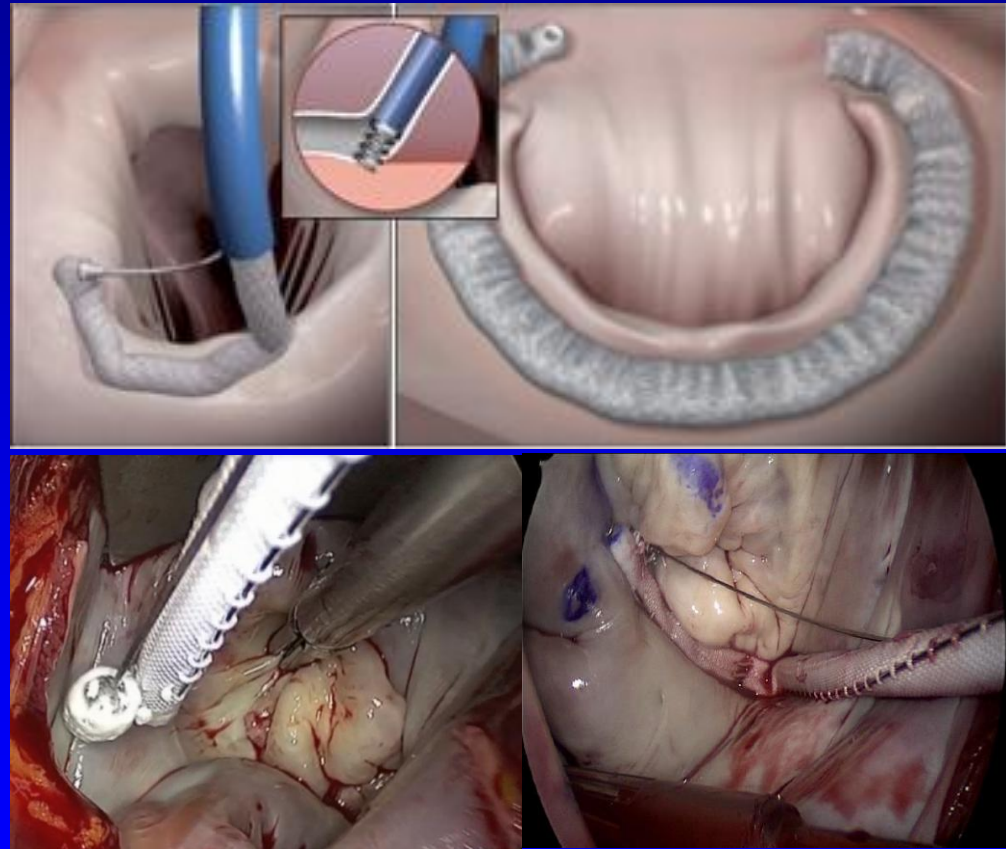
In clinical trial (n=10)

New Devices: Direct Annuloplasty

Millipede



Valtech Cardioband



In clinical trial (n=8)

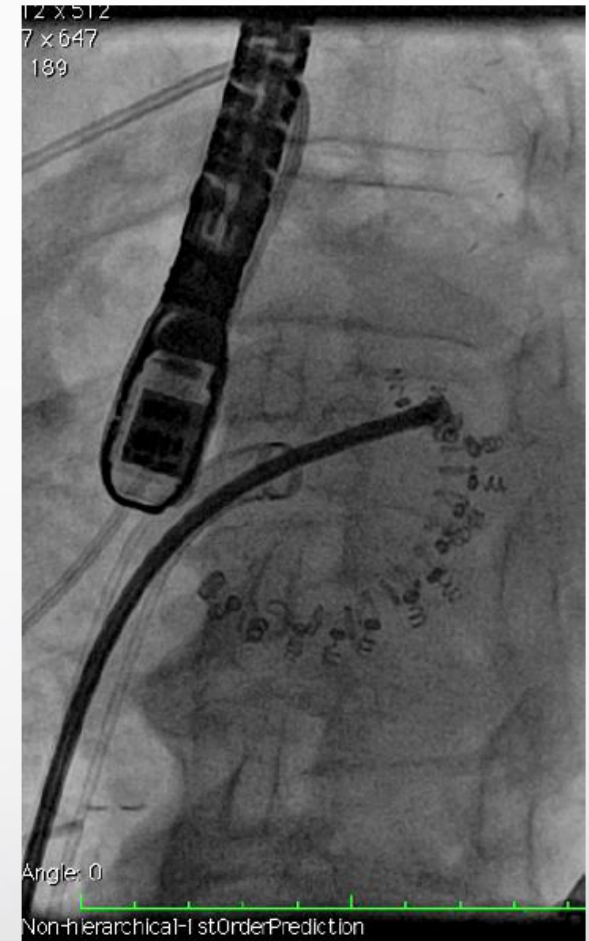
Cardioband™ Transfemoral FIM

Patient C1-05, San-Raffaele Hospital, February 19th, 2013

- 69 years old male
- NYHA Class II, underwent CABG in 2000
- Ongoing Atrial Fibrillation
- Severe MR

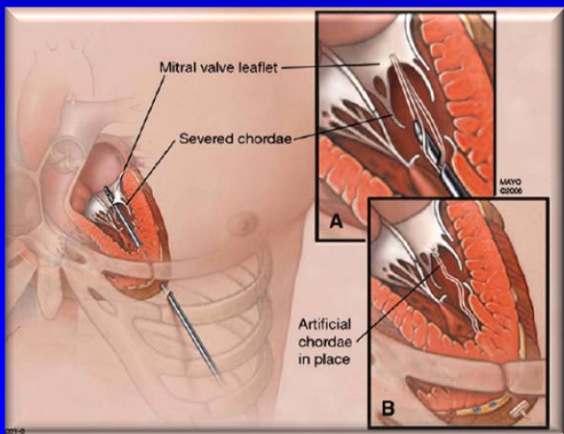
- Implanted with the Cardioband transfemoral system
- Total Procedure time: 2.5 hours
- MR Reduced to **MILD** by cinching the implant
- *Patient was discharged after 2 days with no safety issues*

	Before Adjustment	After Adjustment
MR Grade	Severe	Mild
Septo-Lateral Dimension	29.5mm	19mm (34% decrease)
Coaptation Length	7mm	9.9mm
Anterior-Posterior Dimension	35mm	30mm



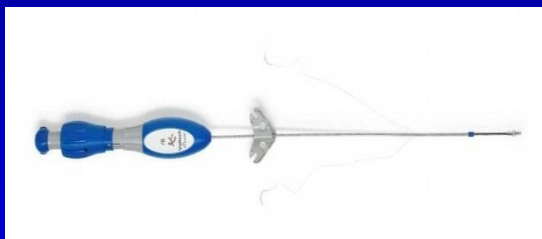
New Devices: Chordal Implant

NeoChord



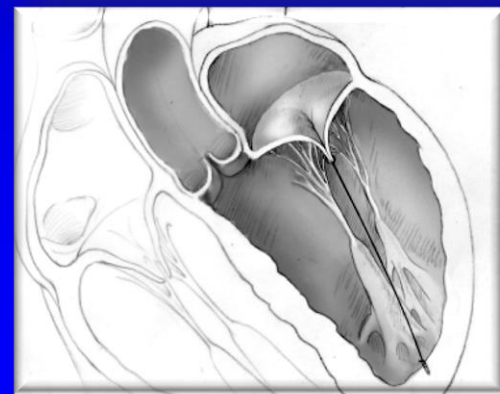
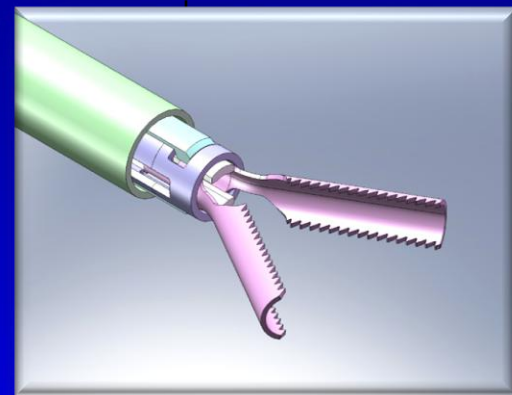
In clinical trial

Valtech V-Chordal

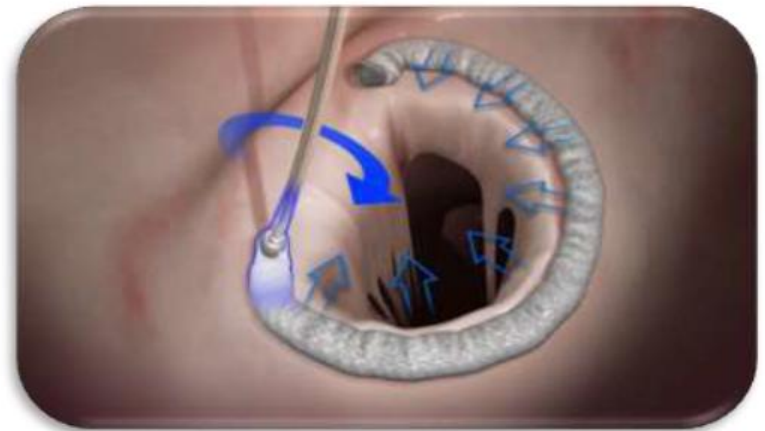
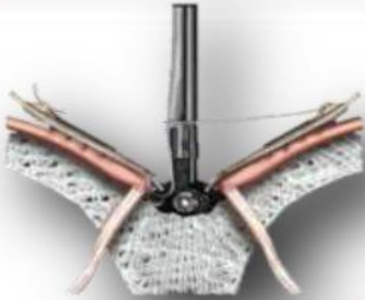


In clinical trial

MitraFlex



Combination of Techniques



Fully Percutaneous Mitral Repair

Transcatheter Mitral Valve Implantation

CardiAQ Valve Technologies

Transcatheter Mitral Valve Implantation



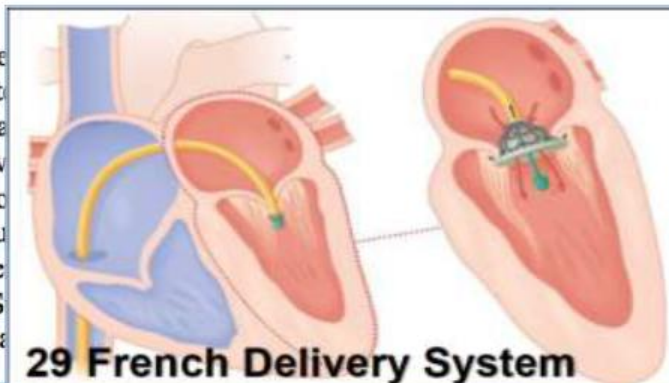
NEWS RELEASE

FOR IMMEDIATE RELEASE

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CardiAQ™ Valve Technologies reports cardiovascular medicine milestone: first-in-human nonsurgical percutaneous implantation of a bioprosthetic mitral heart valve

IRVINE, Calif., June 14, 2012—CardiAQ Valve Technologies, the world's first self-conforming and self-anchoring transcatheter mitral valve implantation (TMVI), today announced the cardiovascular medicine milestone: a bioprosthetic mitral heart valve treatment into an 86-year-old male suffering from mitral regurgitation. The breakthrough TMVI procedure was performed on June 14, 2012, at the University Hospital, Copenhagen, Denmark, by interventional cardiologist and lead investigator Dr. Hans-Jørgen Andersen, M.D., and Olaf Franzen, M.D., cardiovascular surgeon at the University Hospital, Copenhagen, Denmark, and echocardiographer Nikolaj Ihlemann, M.D., at the University Hospital, Copenhagen, Denmark.



29 French Delivery System



Transcatheter Mitral Valve Implantation

Challenges

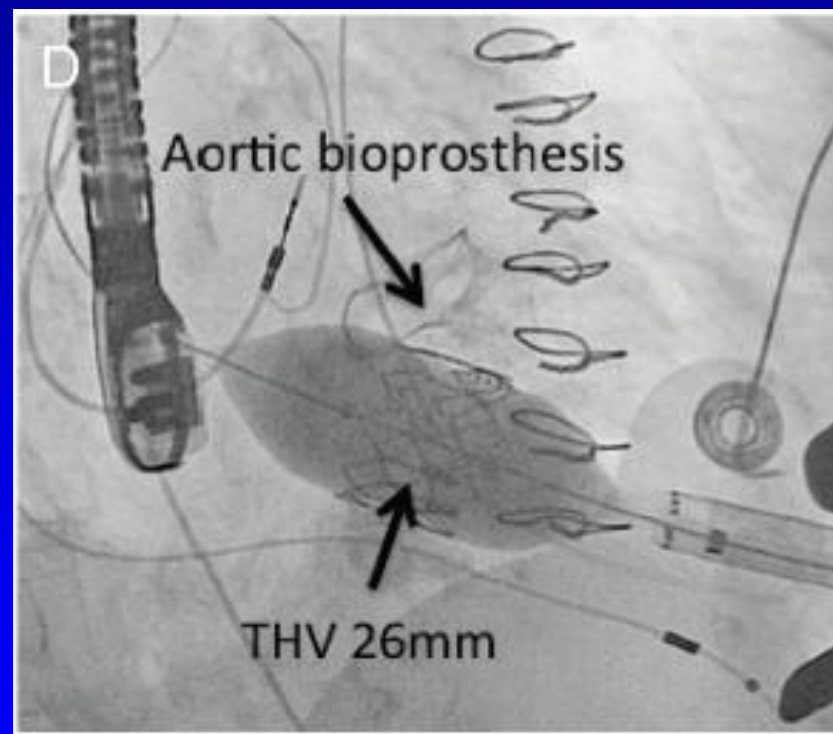
- Positioning
- Fixation
- Paravalvular leaks
- Valve gradient and LV outflow track obstruction
- Thrombosis
- Durability
- Feasibility of reintervention
-

Micro Int

Neovasc - Tiara

Lutter Valve

Transcatheter Mitral Valve Replacement in a Patient with Calcified Native Mitral Valve Stenosis



Conclusions

- ***Percutaneous Mitral Commissurotomy*** shows good immediate and long-term clinical results and carries a low risk when performed by experienced teams. Patient selection must be based on anatomy as well as other characteristics.
- The current results of ***the Edge-to-Edge technique*** suggest that it may be useful in selected high risk patients. Long- term FU and RCT in secondary MR are needed.
- The results with ***coronary sinus annuloplasty*** are disappointing
- Preliminary data on ***transcatheter treatment after surgical failure*** show that it is feasible.
- ***In the future improvement is expected from :***
 - New devices aimed at reproducing surgical techniques
 - Combination of repair techniques
 - Valve replacement

The Future of the Treatment of Mitral Regurgitation

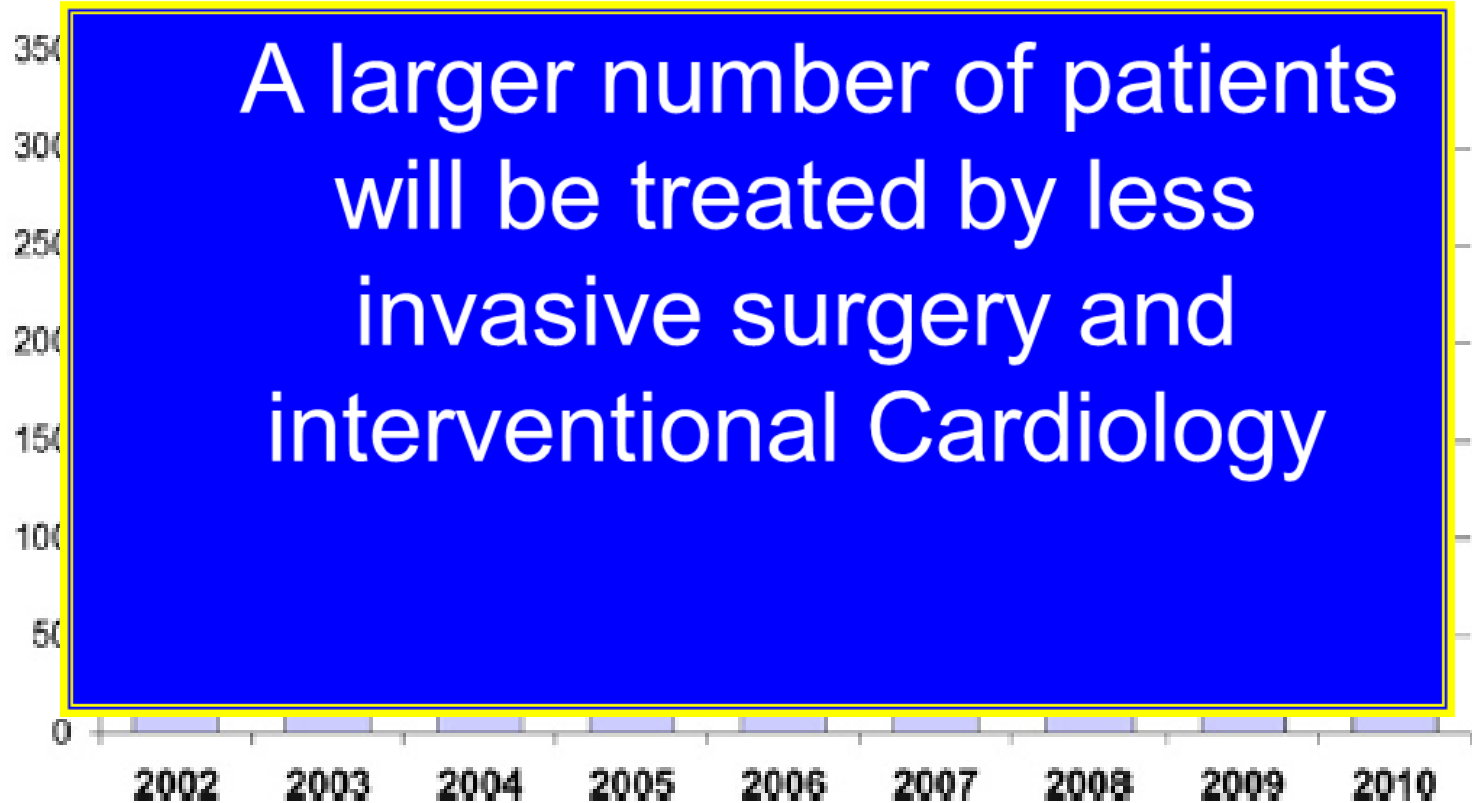


FIGURE 7. Volume of surgical and percutaneous mitral valve treatment at the University Heart Center Hamburg 2002–2010.

« We need to be sure that we do not sacrifice proven long-term effectiveness for short-term issues, such as convenience, invasiveness, or irreversible procedural complications »

C . Otto

Mitral transcatheter techniques may represent a satisfactory palliation in patients who are at high surgical risk or inoperable , however it is unlikely that they will ever reach the success of TAVI.

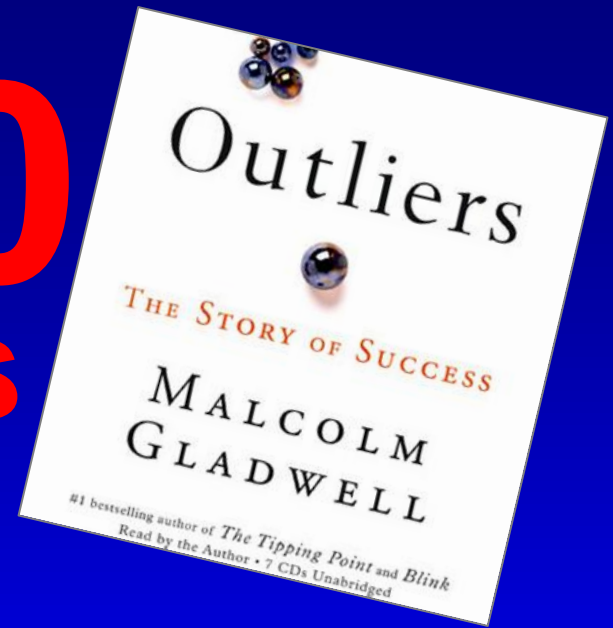


Keep the well proven

... and be open-minded for something new

(Courtesy of R Lange)

10.000
extra hours



Talent & Innovation
Engagement