

# "le futur du traitement percutané de la valve mitrale"

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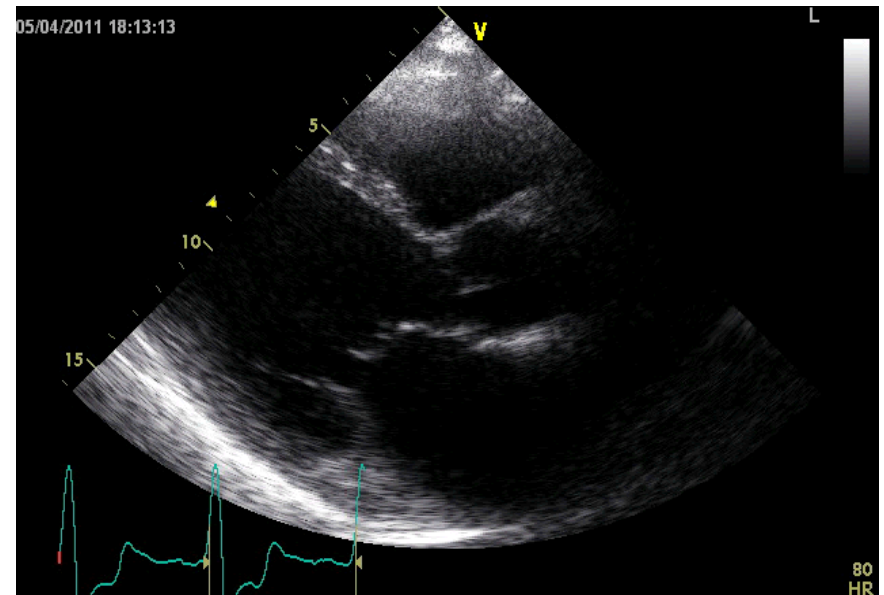
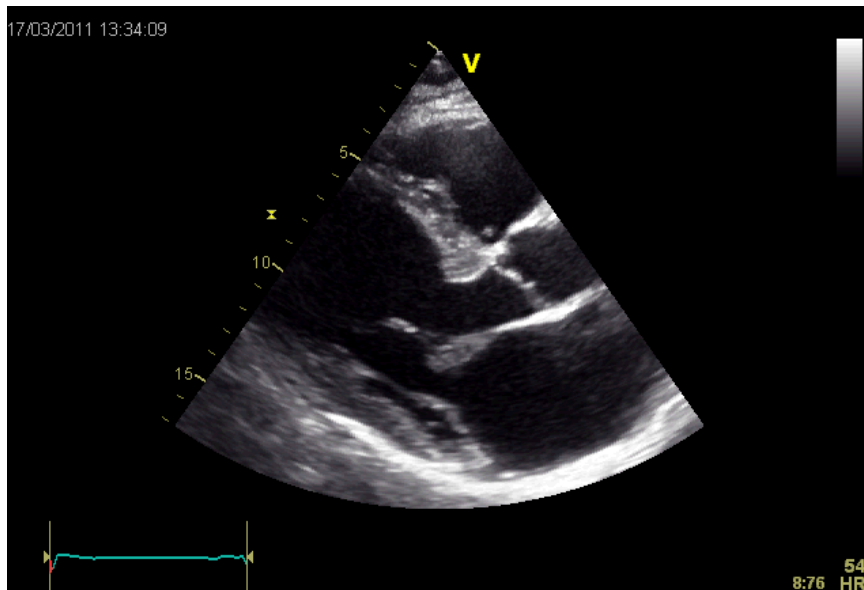
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- Consulting Fees/Honoraria
- Major Stock Shareholder/Equity
- Royalty Income
- Ownership/Founder
- Intellectual Property Rights
- Other Financial Benefit

### Company

- Lilly
- AstraZeneca
- Actelion
- Abbott Vascular

# MR Percutaneous treatment

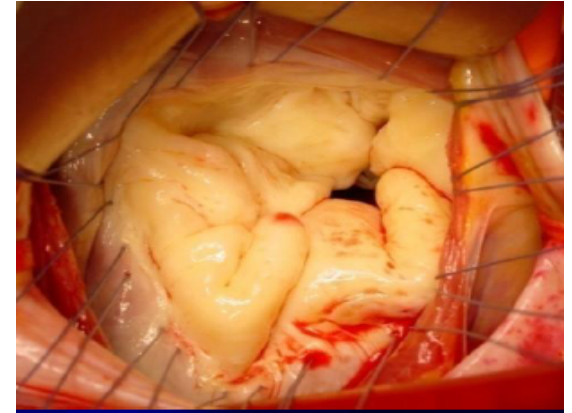
- MR: Second most frequent valve disease requiring surgery in Europe
- Good results of valve repair.
- Primary or secondary, according to the mechanism of MR



# Introduction

## Indications for surgery in Primary MR

- **Severe primary MR**
- **Symptomatic** patients with  
LVEF >30% and LVESD <55 mm
- **Asymptomatic** patients with  
LV dysfunction  
(LVESD  $\geq$ 45 mm and/or LVEF  $\leq$ 60%).



## Surgery

- Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC), European Association for Cardio-Thoracic Surgery (EACTS), Vahanian A, Alfieri O, Andreotti F, Antunes MJ, et al. Guidelines on the management of valvular heart disease (version 2012). Eur Heart J. oct 2012;33(19):2451-2496.
- David TE, Armstrong S, McCrindle BW, Manlhiot C. Late outcomes of mitral valve repair for mitral regurgitation due to degenerative disease. Circulation. 9 avr. 2013;127(14):1485-1492

# Introduction

## Indications for surgery in Secondary MR

### Indications for mitral valve surgery in chronic secondary mitral regurgitation

	Class <sup>a</sup>	Level <sup>b</sup>
Surgery is indicated in patients with severe MR <sup>c</sup> undergoing CABG, and LVEF >30%.	I	C
Surgery should be considered in patients with moderate MR undergoing CABG. <sup>d</sup>	IIa	C
Surgery should be considered in symptomatic patients with severe MR, LVEF <30%, option for revascularization, and evidence of viability.	IIa	C

	Class <sup>a</sup>	Level <sup>b</sup>
Surgery may be considered in patients with severe MR, LVEF >30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and have low comorbidity, when revascularization is not indicated.	IIb	C

- Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC), European Association for Cardio-Thoracic Surgery (EACTS), Vahanian A, Alfieri O, Andreotti F, Antunes MJ, et al. Guidelines on the management of valvular heart disease (version 2012). Eur Heart J. oct 2012;33(19):2451-2496.
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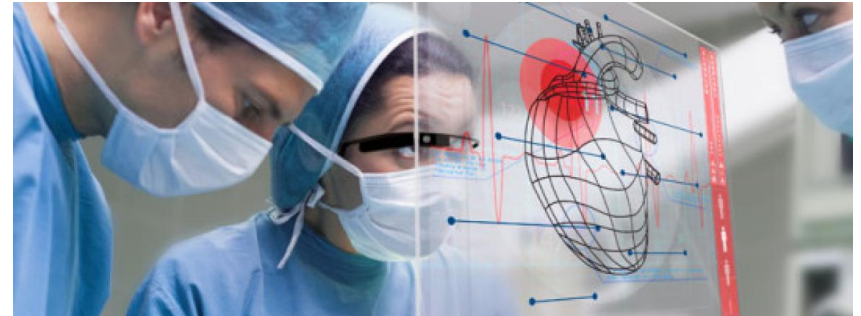
# Mitral valve repair

**What is the futur of percutaneous techniques ?**



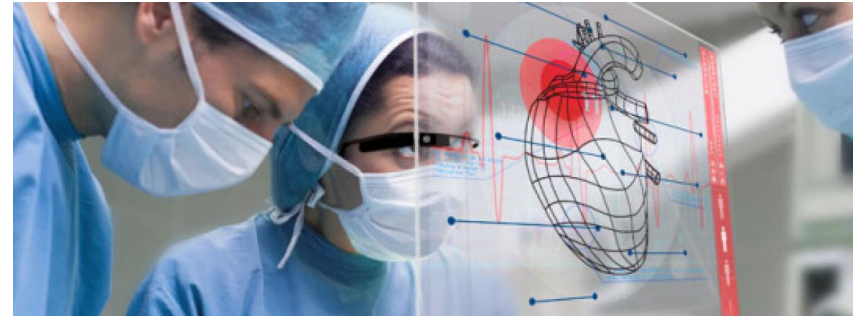
Because 50% of patients will not be operated

## The futur of mitral valve repair could be...



- Leaflets : Edge to edge repair
- Mitral valve annulus repair
- Chordae repair
- Percutaneous mitral valve replacement
- Imaging

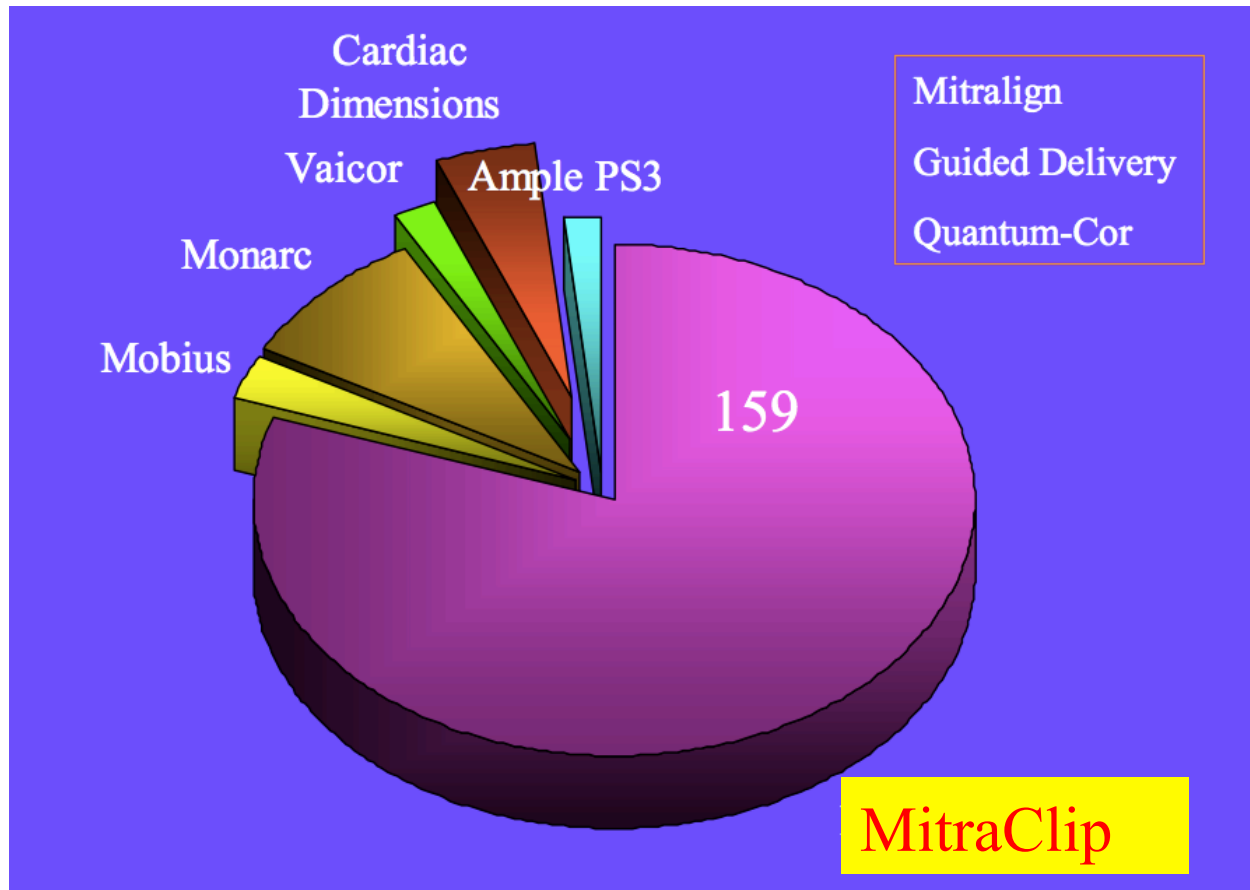
# The futur of mitral valve repair could be...



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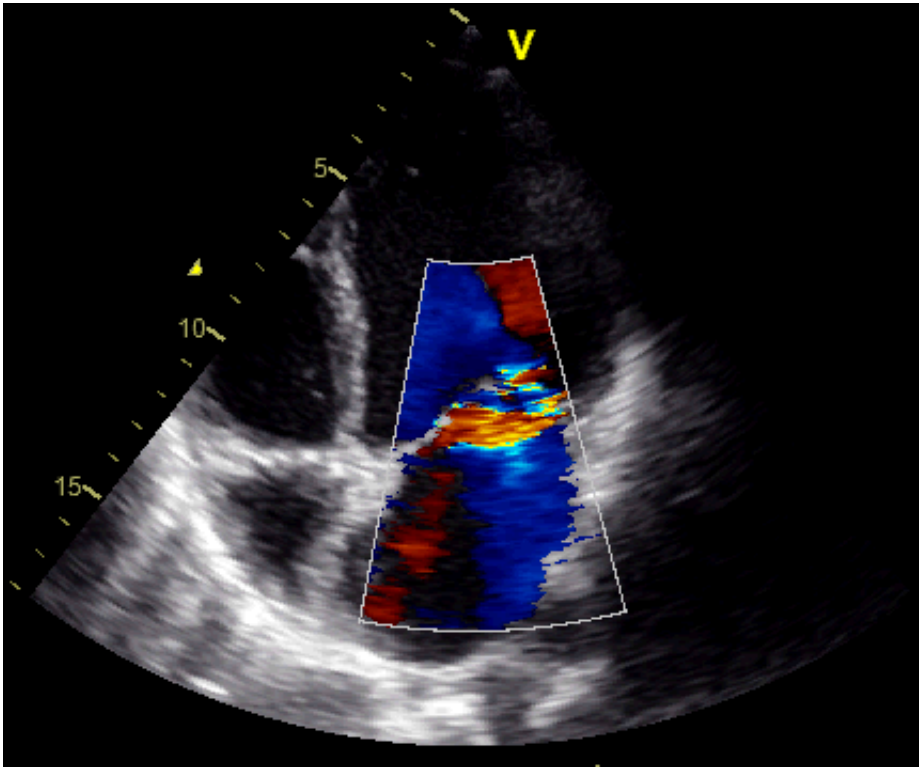


## Which percutaneous treatments for MR ?



# Principle

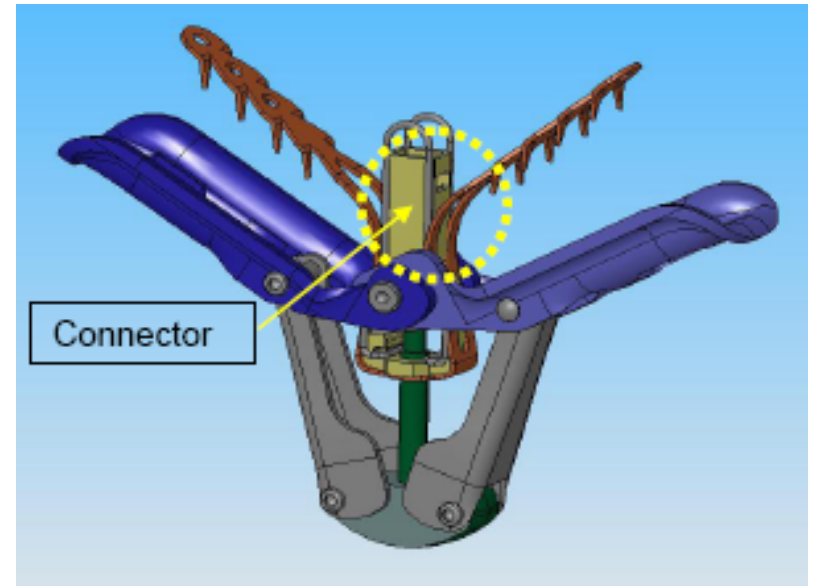
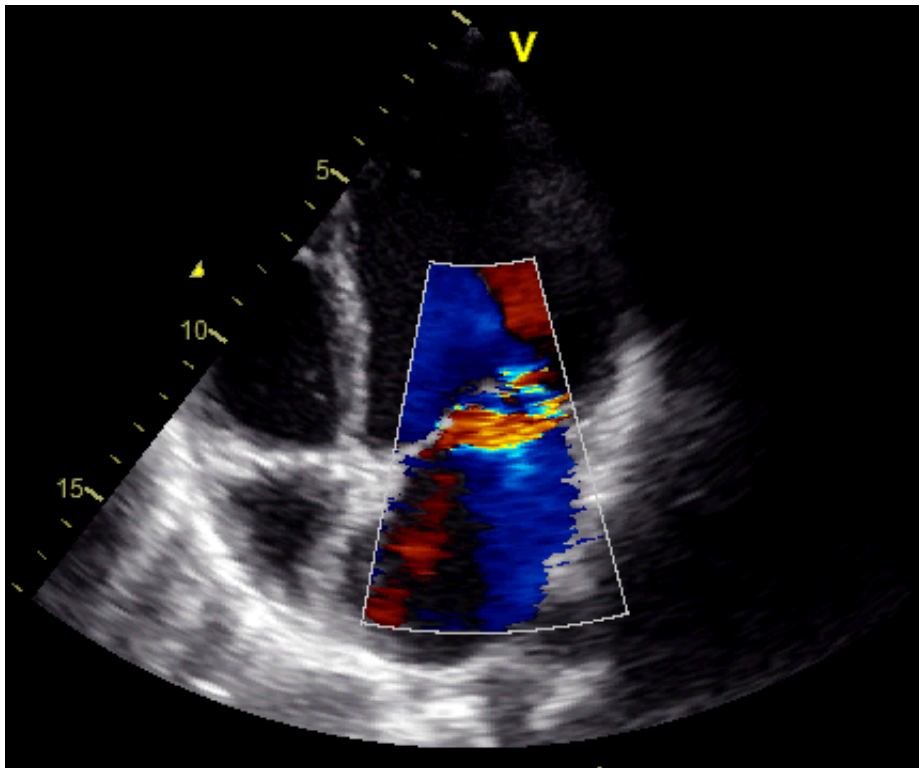
Regurgitant orifice



Regurgitant orifice closure

# Principle

Regurgitant orifice



Regurgitant orifice closure

## Just a regurgitant orifice closure ?

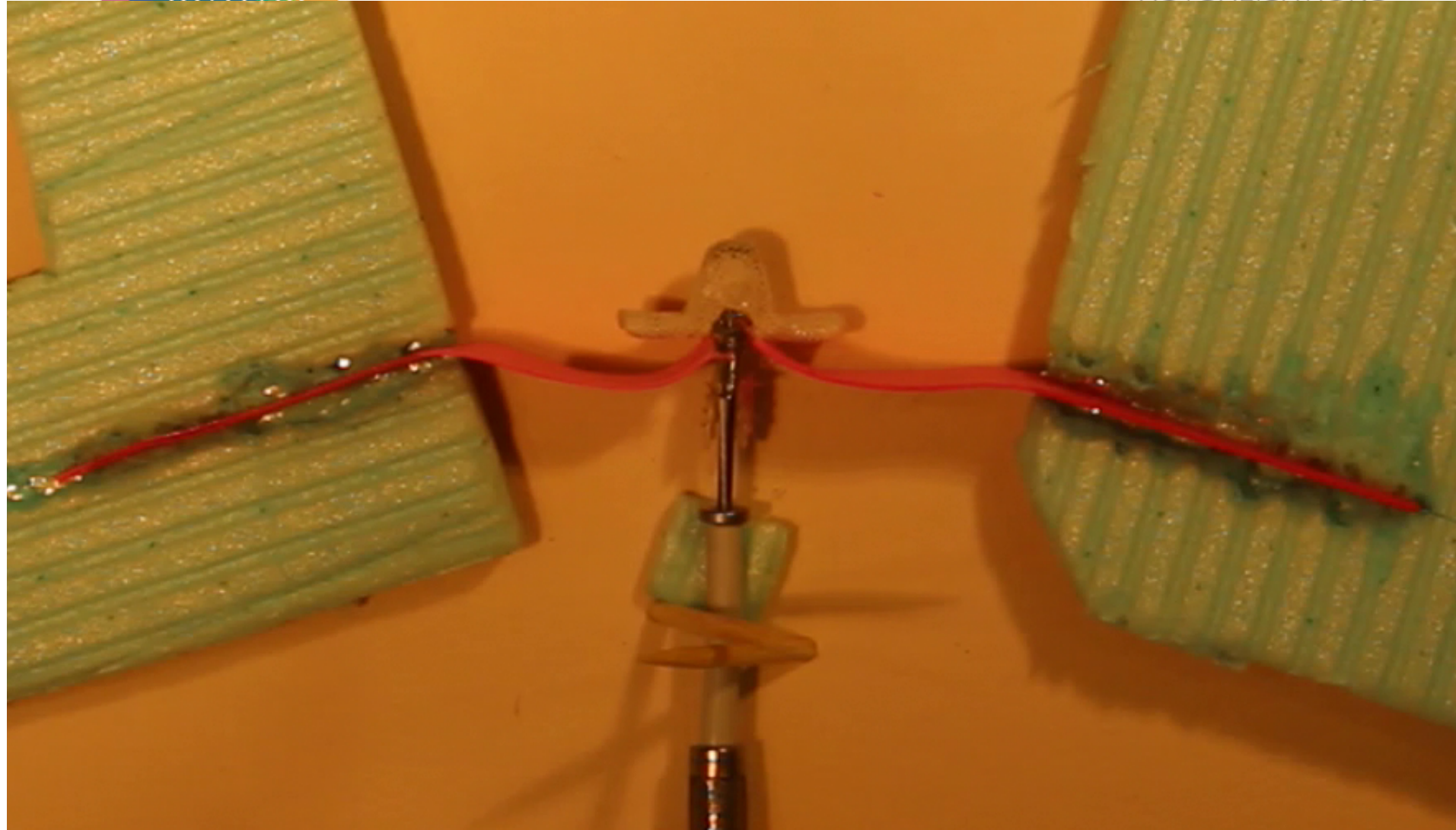


- Regurgitant orifice closure



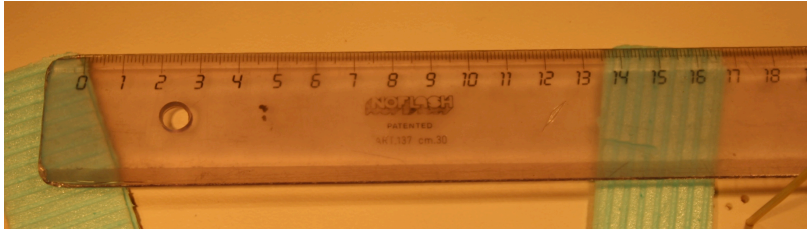
- And restriction of antero-posterior annulus diameter ?

Just a regurgitant orifice closure ?

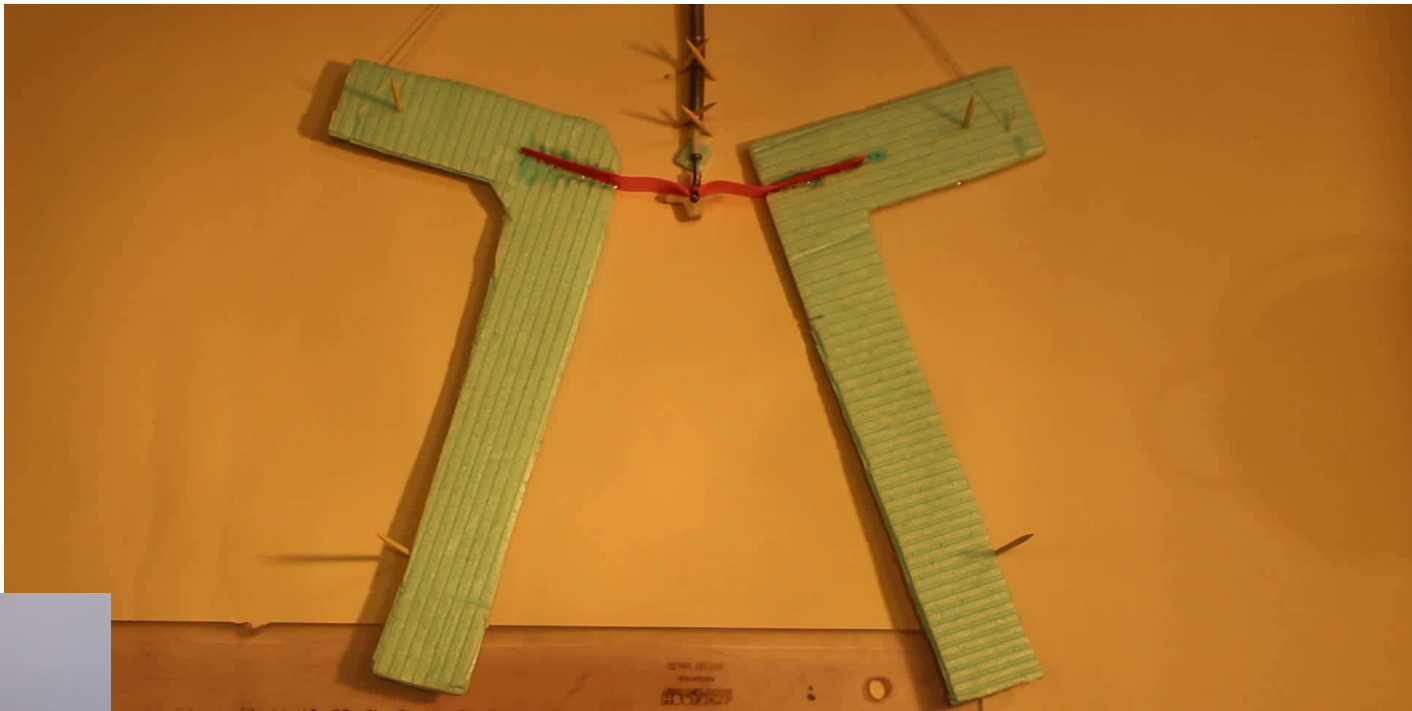


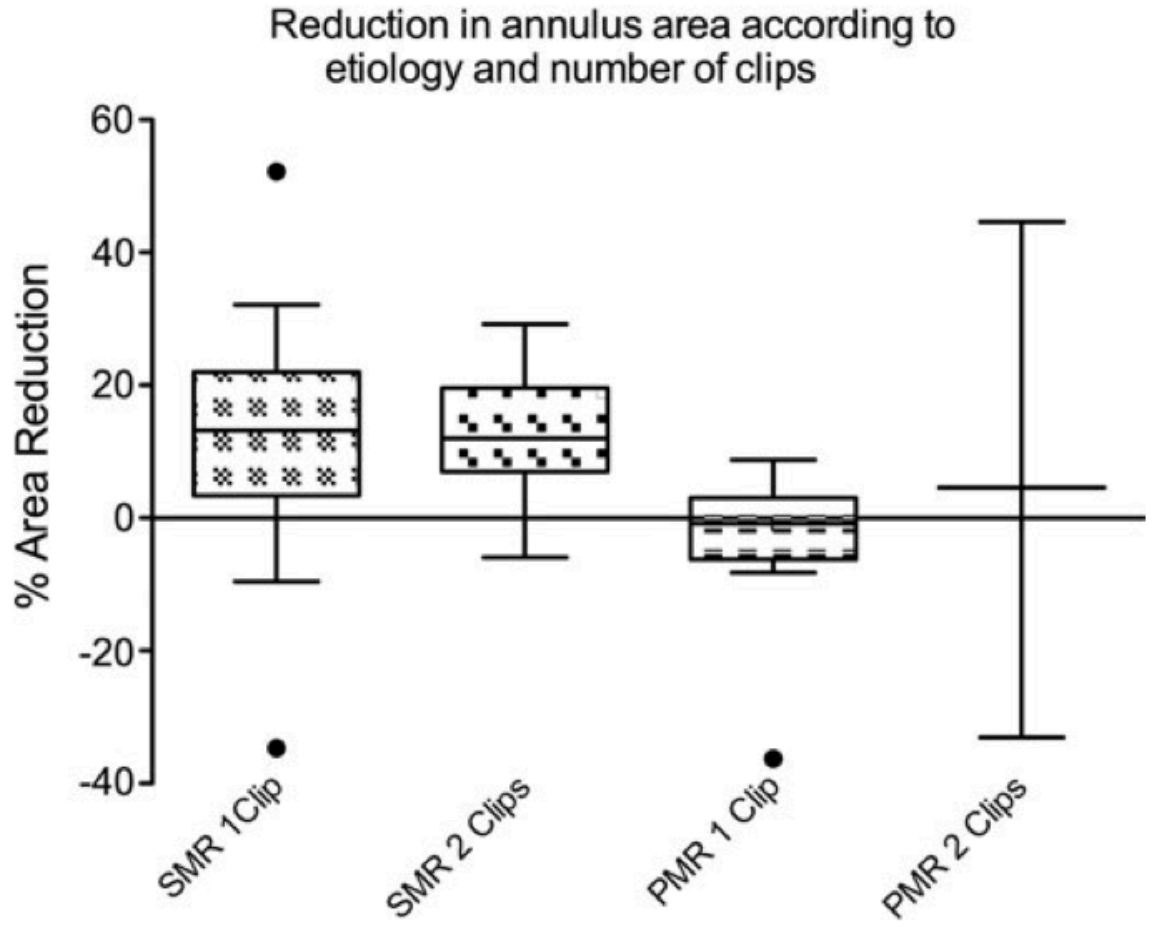
# Just a regurgitant orifice closure ?

14 cm



7 cm



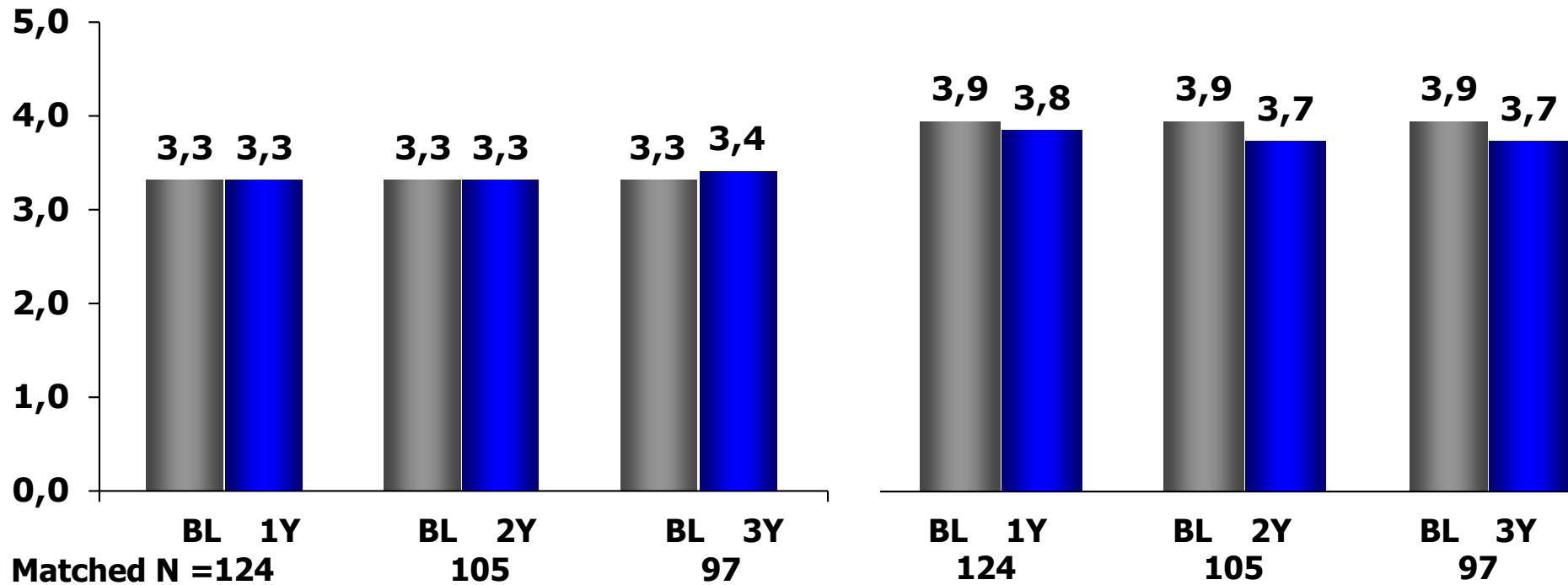


**Figure 4** Relative reduction of mitral annulus area with 1 and 2 clips given as boxplot (Tukey Method)

# Septal Lateral Annular Dimensions (AD)

Mean Systolic Septal Lateral AD (cm)  
MitraClip (N=178)  
Systolic Septal Lateral AD Stable

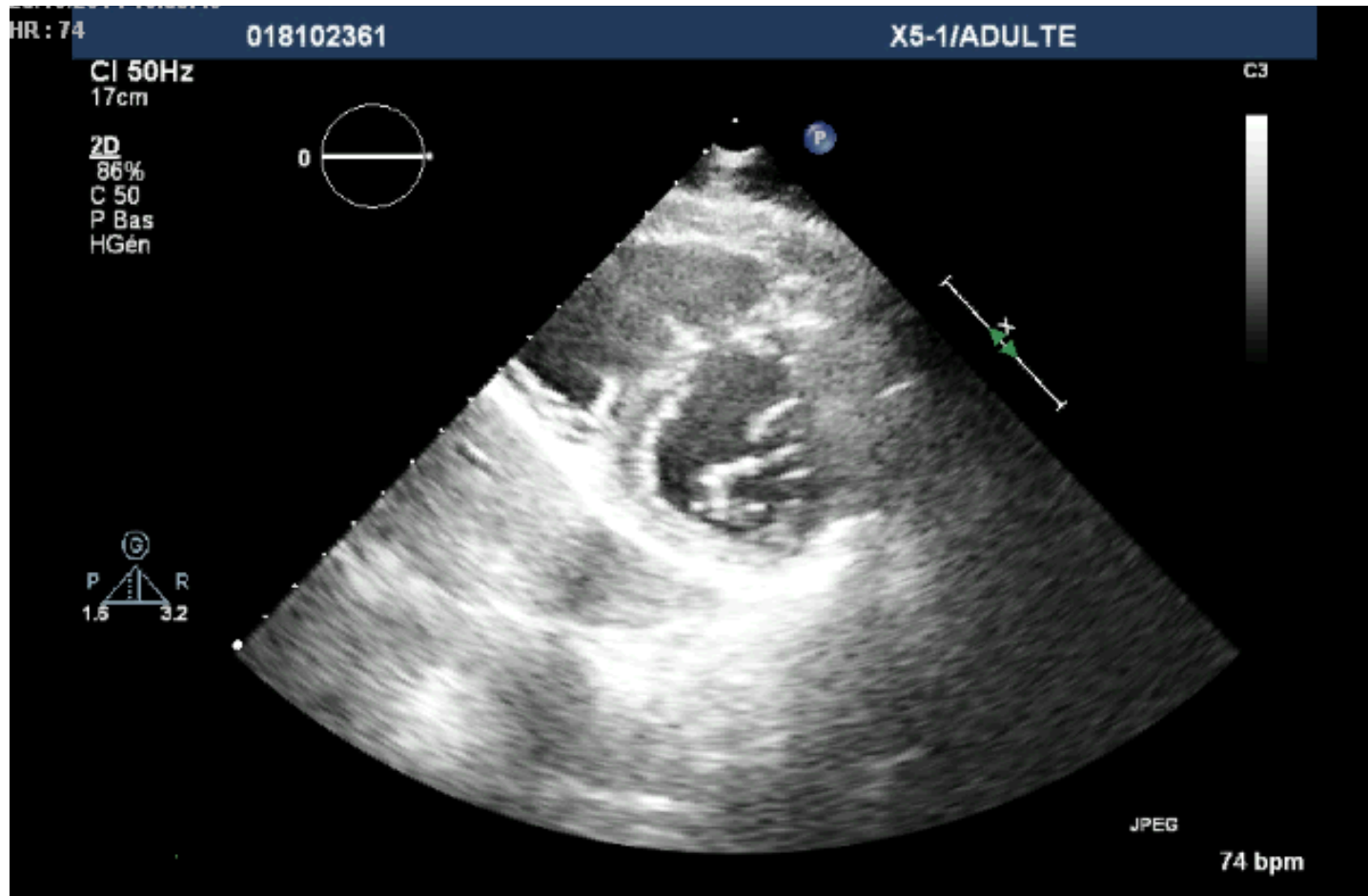
Mean Diastolic Septal Lateral AD (cm)  
MitraClip (N=178)  
Diastolic Septal Lateral AD Stable



$p = \text{NS}$  for changes from Baseline within groups

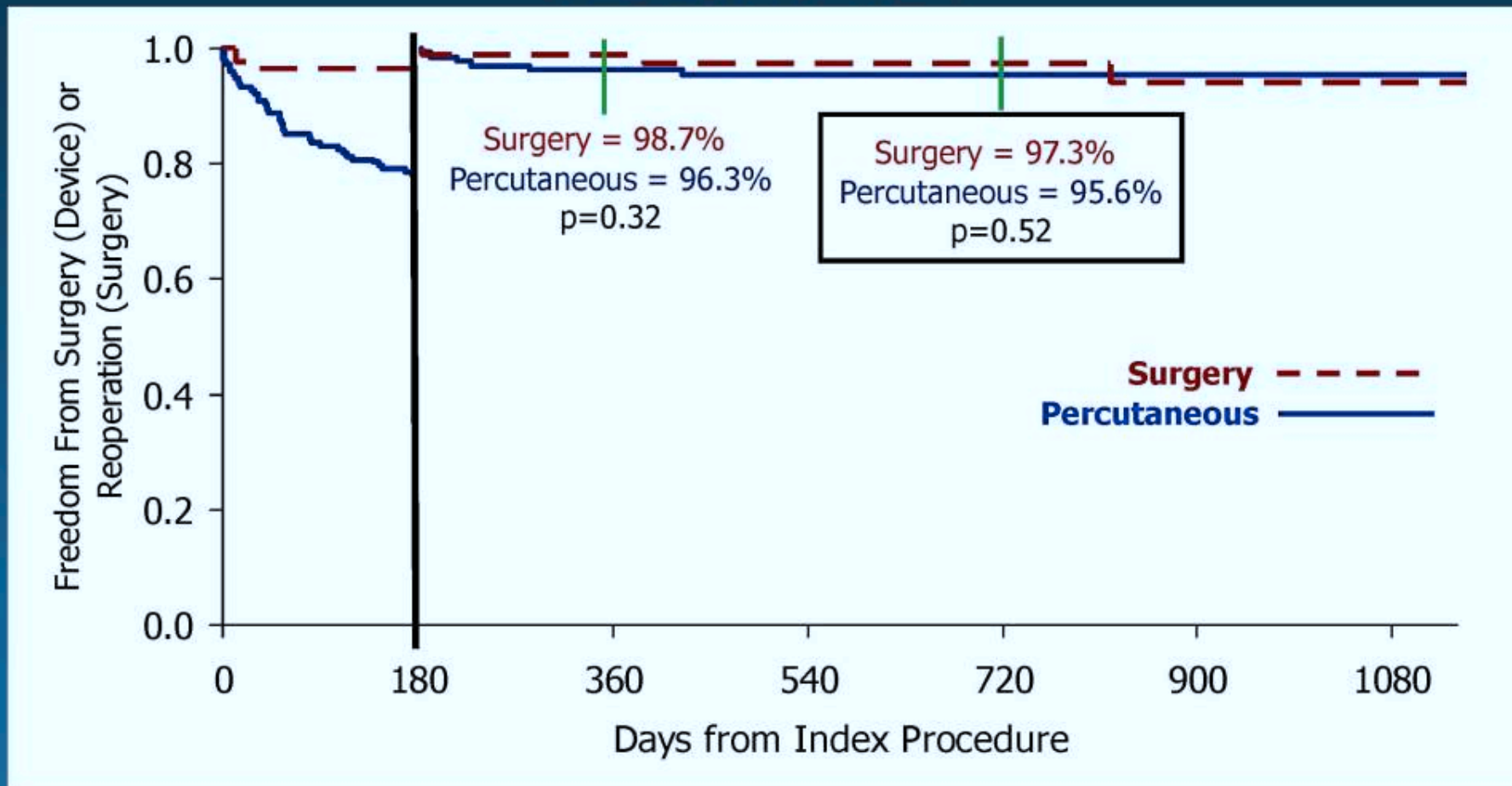


# Double orifice mitral valve ?



# Landmark Analysis of Kaplan-Meier

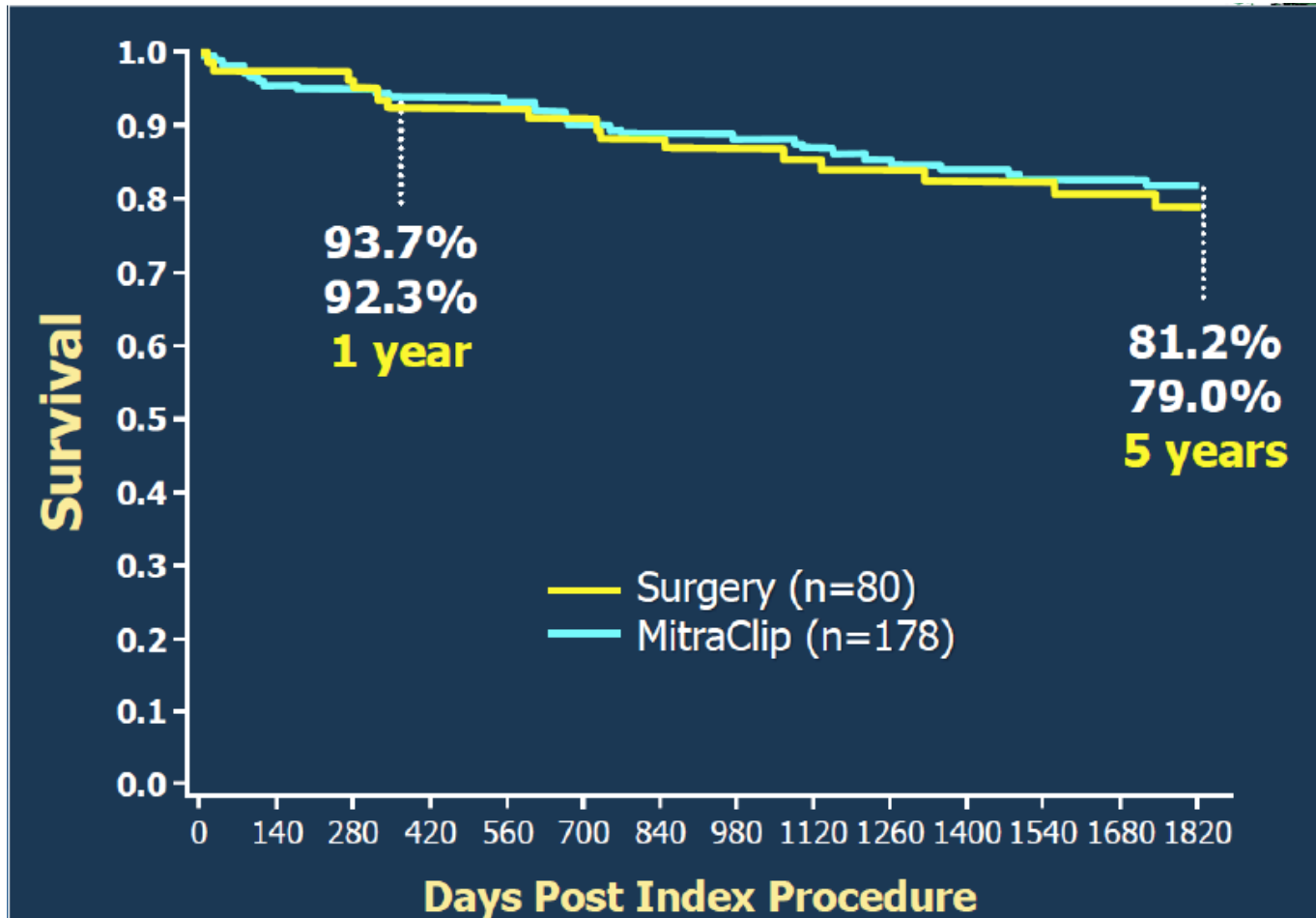
## Freedom from MV Surgery (Percutaneous)/Re-operation (Surgery) Intention to Treat



At Risk:	0 Days	6m	1yr	1.5yr	2yr	3yr
Percutaneous	184	138	131	124	109	44
Surgery	95	77	72	69	61	24

# Results

## Evrest 5 years follow up



# ESC indications

## Management of Valvular Heart Disease

**Guidelines on the management of valvular heart disease (version 2012)**

The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Authors/Task Force Members: Alec Vahanian (Chairperson) (France)\*, Octavio Alfieri (Chairperson)† (Italy), Felicità Andreotti (Italy), Manuel J. Antunes (Portugal), Gonzalo Barón-Esquivias (Spain), Helmut Baumgartner (Germany), Michael Andrew Borger (Germany), Thierry P. Carrel (Switzerland), Michele De Bonis (Italy), Arturo Evangelista (Spain), Volkmar Falk (Switzerland), Bernard Jung (France), Patrizio Lancellotti (Belgium), Luc Pierard (Belgium), Susanna Price (UK), Hans-Joachim Schäfers (Germany), Gerhard Schuler (Germany), Janina Stepinska (Poland), Karl Swedberg (Sweden), Johanna Takkenberg (The Netherlands), Ulrich Otto Von Oppell (UK), Stephan Windecker (Switzerland), Jose Luis Zamorano (Spain), Marian Zembala (Poland)

### Indication for primary MR

“Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary MR who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a ‘heart team’, and have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).” *page 21*



**Table 1. Indications for surgery in aortic regurgitation**

Indication	Class	Level of Evidence
Severe aortic regurgitation with aortic root diameter ≥ 5.0 cm	I	A
Severe aortic regurgitation with aortic root diameter ≥ 4.5 cm and aortic annulus diameter ≥ 4.5 cm	IIa	B
Severe aortic regurgitation with aortic root diameter ≥ 4.0 cm and aortic annulus diameter ≥ 4.0 cm	IIb	C
Severe aortic regurgitation with aortic root diameter ≥ 3.5 cm and aortic annulus diameter ≥ 3.5 cm	IIb	C
Severe aortic regurgitation with aortic root diameter ≥ 3.0 cm and aortic annulus diameter ≥ 3.0 cm	IIb	C
Severe aortic regurgitation with aortic root diameter ≥ 2.5 cm and aortic annulus diameter ≥ 2.5 cm	IIb	C
Severe aortic regurgitation with aortic root diameter ≥ 2.0 cm and aortic annulus diameter ≥ 2.0 cm	IIb	C
Severe aortic regurgitation with aortic root diameter ≥ 1.5 cm and aortic annulus diameter ≥ 1.5 cm	IIb	C
Severe aortic regurgitation with aortic root diameter ≥ 1.0 cm and aortic annulus diameter ≥ 1.0 cm	IIb	C
Severe aortic regurgitation with aortic root diameter ≥ 0.5 cm and aortic annulus diameter ≥ 0.5 cm	IIb	C

**Text box:** Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary MR who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a ‘heart team’, and have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).

### Indication for secondary MR

“The percutaneous mitral clip procedure may be considered in patients with symptomatic severe secondary MR despite optimal medical therapy (including CRT if indicated), who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a team of cardiologists and cardiac surgeons, and who have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).” *page 25*



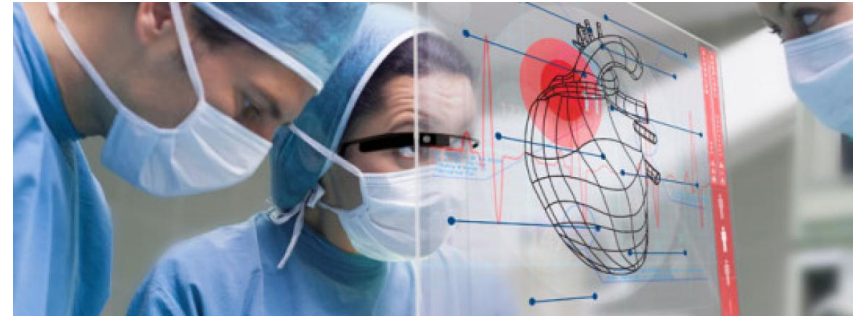
**Table 1. Indications for surgery in mitral regurgitation**

Indication	Class	Level of Evidence
Severe mitral regurgitation with aortic root diameter ≥ 5.0 cm	I	A
Severe mitral regurgitation with aortic root diameter ≥ 4.5 cm and aortic annulus diameter ≥ 4.5 cm	IIa	B
Severe mitral regurgitation with aortic root diameter ≥ 4.0 cm and aortic annulus diameter ≥ 4.0 cm	IIb	C
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Severe mitral regurgitation with aortic root diameter ≥ 2.5 cm and aortic annulus diameter ≥ 2.5 cm	IIb	C
Severe mitral regurgitation with aortic root diameter ≥ 2.0 cm and aortic annulus diameter ≥ 2.0 cm	IIb	C
Severe mitral regurgitation with aortic root diameter ≥ 1.5 cm and aortic annulus diameter ≥ 1.5 cm	IIb	C
Severe mitral regurgitation with aortic root diameter ≥ 1.0 cm and aortic annulus diameter ≥ 1.0 cm	IIb	C
Severe mitral regurgitation with aortic root diameter ≥ 0.5 cm and aortic annulus diameter ≥ 0.5 cm	IIb	C

**Text box:** The percutaneous mitral clip procedure may be considered in patients with symptomatic severe secondary MR despite optimal medical therapy (including CRT if indicated), who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a team of cardiologists and cardiac surgeons, and who have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).



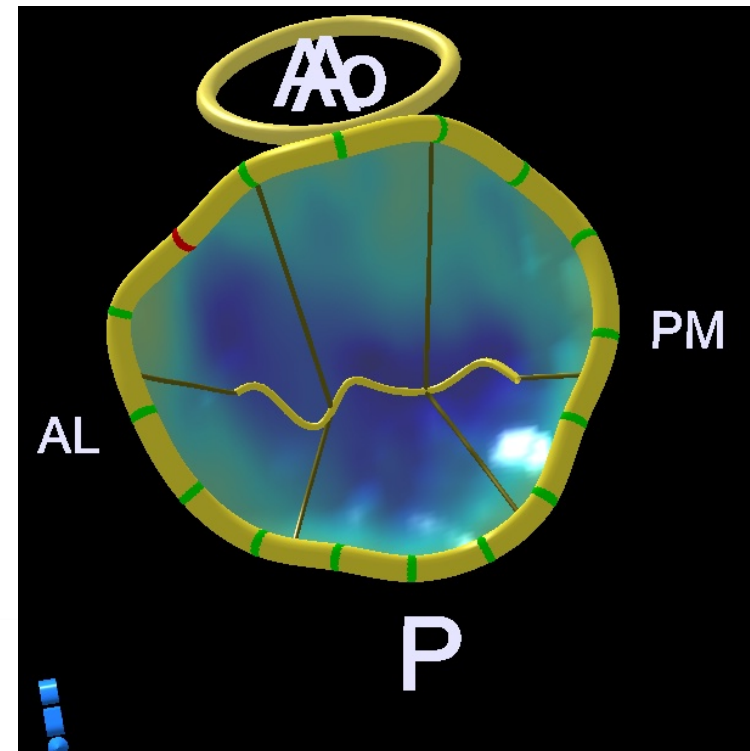
# The futur of mitral valve repair could be...



- Leaflets : Edge to edge repair
- **Mitral valve annulus repair**
- Chordae repair
- Percutaneous mitral valve replacement
- Imaging

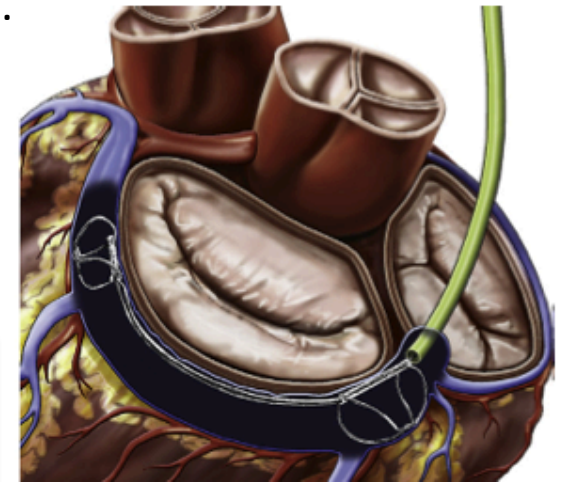
# Mitral valve annulus repair

- ***Indirect annuloplasty (Coronary sinus annuloplasty):***
  - Edwards Monarc
  - Carillon
  - Viacor Shape Changing Rods
  - St. Jude Annulus Reshaping ...
- ***Direct annuloplasty***
  - Mitralign.
  - Guided Delivery Anchor-Cinch Plication
  - QuantumCor RF Annulus Remodeling.
  - MiCardia variable size ring...
- ***Left ventricle annuloplasty***
  - Myocor iCoapsys, Ample PS3 ...



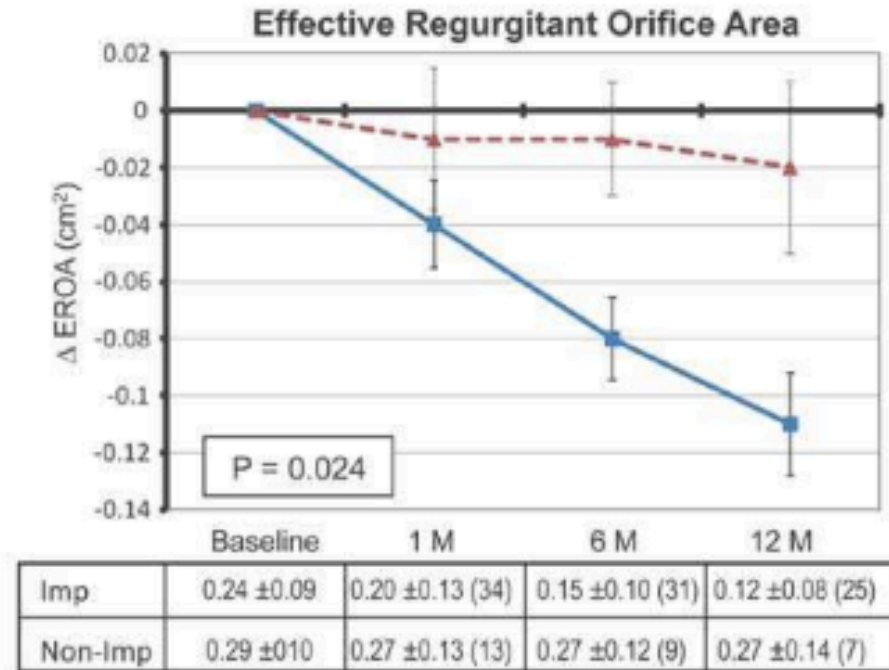
## The Carillon Mitral Contour System (Cardiac Dimension, Inc., Kirkland, Washington)

- Implanted via the internal jugular vein
- 9-F delivery catheter
- Nitinol device
- Proximal and distal anchor connected by a ribbon
- The distal anchor is released deep in the coronary sinus
- The proximal anchor resides near the coronary sinus ostium.
- Direct tension is placed on the delivery system.
- Can be repositioned or removed.



# The Carillon Mitral Contour System (Cardiac Dimension, Inc., Kirkland, Washington)

- **AMADEUS** (safety and efficacy)
  - Functional MR, 24 months
  - Significant reduction in mitral annular diameter
  - Improvement in functional class and quality of life
  
- **TITAN**
  - prospective, nonrandomized study
  - Functional MR, 12 months
  - 53 patients
  - 36 success of permanent device implantation.
  - Significant benefit in
    - regurgitant volume and effective
    - regurgitant orifice area
    - favorable changes in LV remodeling
  - improvement in
    - 6-min walk test,
    - Functional class
    - quality of life
  
- The Carillon device received CE mark approval in Europe in 2011.



**CE mark approval in Europe in 2011**

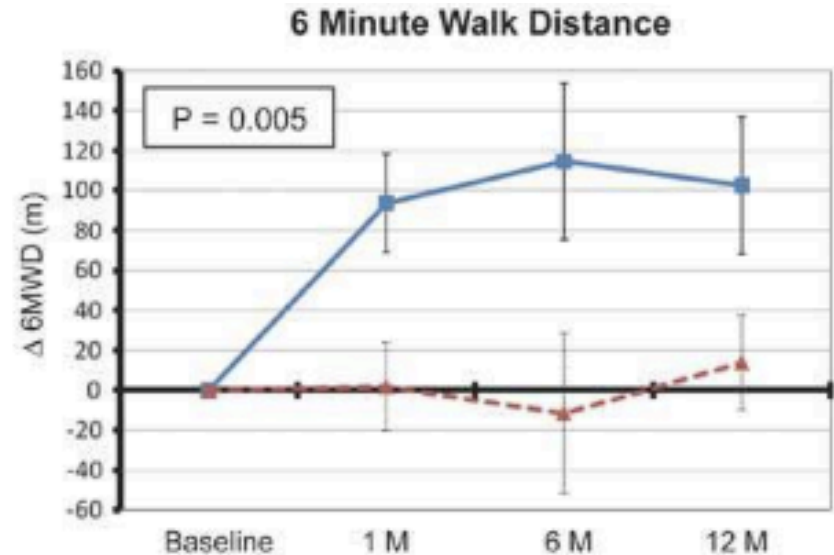
*Schofer et al. Circulation 2009; 120:326–33.*  
*Siminiak et al. Eur J Heart Fail 2012; 14:931–8.*



# The Carillon Mitral Contour System (Cardiac Dimension, Inc., Kirkland, Washington)

## • TITAN

- In 17 of the 53 patients, the device could not be permanently implanted, due to
  - difficulty cannulating the coronary sinus,
  - Ineffective reduction in MR,
  - or compression of a coronary artery (cx).  
 (17% (Amadeus) and 15% (TITAN))



**CE mark approval in Europe in 2011**

*Schofer et al. Circulation 2009; 120:326–33.*  
*Siminiak et al. Eur J Heart Fail 2012;14:931–8.*

## Direct annuloplasty

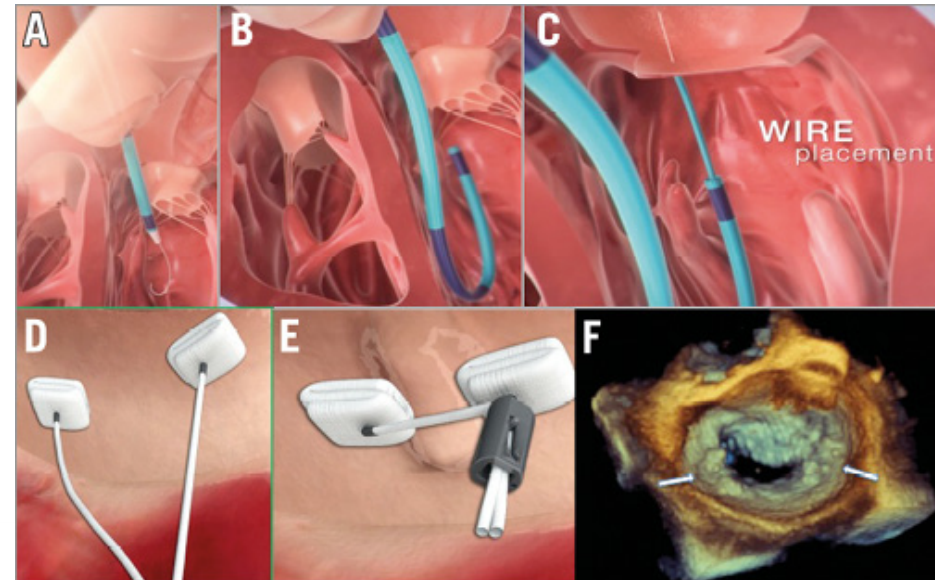
- **Retrograde transventricular approach**
  - Mitralign (Mitralign, Inc., Tewksbury, Massachusetts)
  - Accucinch (Guided Delivery Systems, Santa Clara, California)
- **Transseptal atrial access:**
  - Valtech CardioBand system (Valtech Cardio, Or Yehuda, Israel)
  - Cardiac Implant's Mitral Restriction Ring (Cardiac Implant Solutions LLC, Jacksonville, FL, USA)

## Direct annuloplasty, retrograde transventricular approach

**Mitralign** (Mitralign, Inc., Tewks- bury, Massachusetts)

- Retrograde transventricular approach
- Radiofrequency energy
- Pairs of pledgets are implanted in the posterior mitral annulus near A1-P1 and A3-P3
- Pledgets are cinched together by a suture
- Reduce the size of the mitral annulus
- Hence mitral orifice area.

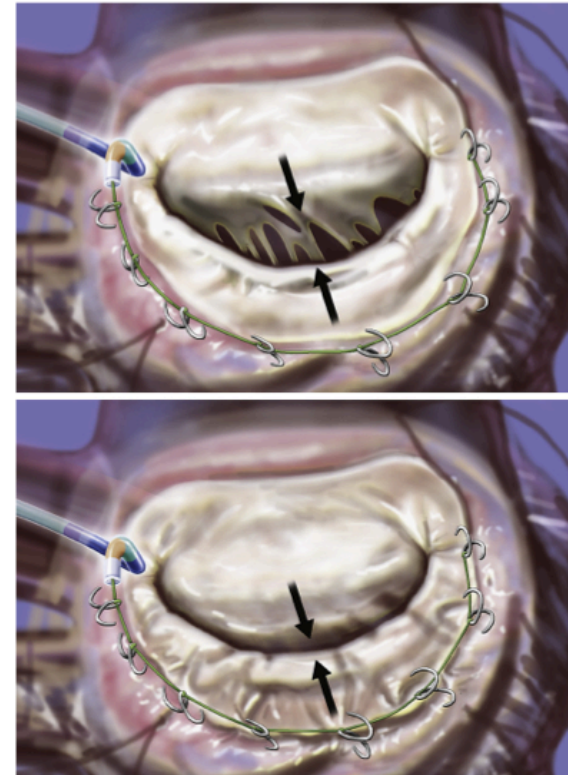
*Mandinov et al. Interventional Cardiology Review 2011;6:170–2.*



## Direct annuloplasty, retrograde transventricular approach

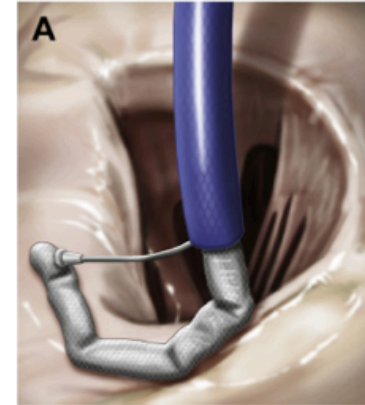
*Mandinov et al. Interventional Cardiology  
Review 2011;6:170–2.*

- **The Accucinch System**
- (Guided Delivery Systems, Santa Clara, California)
- Retrograde transventricular approach
- Anchors are implanted beneath the MV in the basilar LV.
- Anchors are connected by a nitinol wire
- Tethering the cord cinches the basal LV and mitral annulus
- Accucinch System also causes remodeling of the basal portion of the LV



## Direct annuloplasty. transseptal atrial access

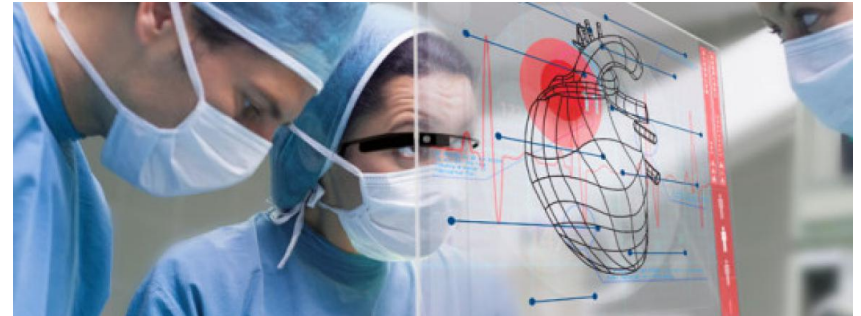
- Valtech CardioBand System  
(Valtech Cardio, Or Yehuda, Israel)
- Delivered via transseptal atrial access
- Implanted in the atrial side of the mitral annulus.
- Screw anchors are deployed from the posteromedial commissure to the anterolateral commissure
- Circumference is reduced by controlling tension on the band,
- Thereby reducing the degree of MR.
- Early animal studies demonstrated safety and feasibility in the device
- Several patients have had successful percutaneous implants



*Maisano et al. Eur J Card Thorac 2012;42:524–9.*

*Maisano et al. EuroPCR 2014, Paris, France.*

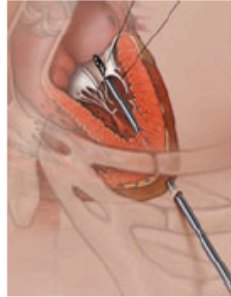
## The futur of mitral valve repair could be...



- Leaflets : Edge to edge repair
- Mitral valve annulus repair
- **Chordae repair**
- Percutaneous mitral valve replacement
- Imaging

# Chordae repair

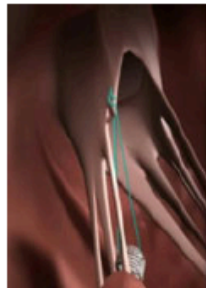
NeoChord (NeoChord DS1000)  
 Chordal repair



CE Mark approval  
 gained

- Instrumentation used to enable beating heart, transapical approach, mitral valve repair by artificial chordae implantation
- Designed for leaflet prolapse

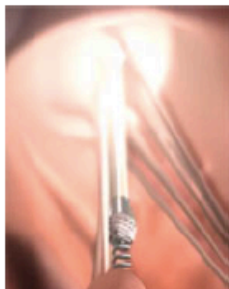
V-Chordal-Off Pump (Valtech)  
 Chordal repair



First-in-man study  
 complete

- Sutureless implantation of neochordae on the leaflets under direct surgical exposure
- Off-pump, the chordal length can be adjusted under live echo guidance, on beating heart

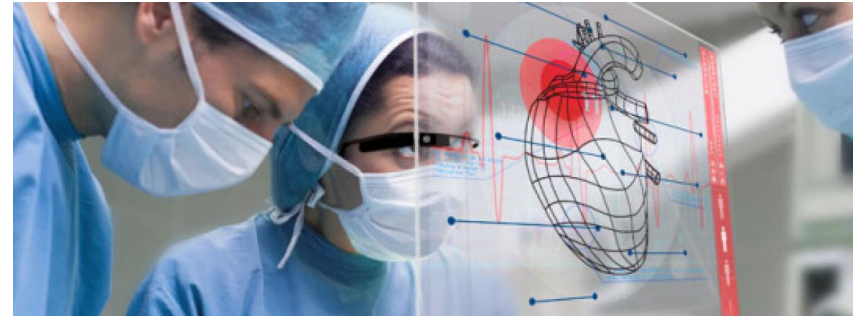
V-Chordal-Transfemoral  
 (Valtech)  
 Chordal repair



Preclinicals underway

- Transfemoral chord repair performed via transfemoral approach that is off-pump on a beating heart

# The futur of mitral valve repair could be...



- Leaflets : Edge to edge repair
- Mitral valve annulus repair
- Chordae repair
- Percutaneous mitral valve replacement
- Imaging



# Quid of percutaneous mitral valve replacement ?

**Table 1. Challenges for Percutaneous TMVR Devices**

## Valve position

To be deployed in the left AV position, making a truly percutaneous, transfemoral delivery a challenge—because of the requirement for transeptal (or transaortic retrograde) access to the LA or LV and the need for a multidimensional, highly curved catheter course (which is challenging with a large delivery system and limits the precision with which tension and traction are transmitted to the operating end of the system)

Possible access routes: transapical, transeptal, transatrial

## Valve anatomy

Should fit an asymmetrical saddle-shaped mitral annulus

There is no stable calcified structure for anchoring (unlike for TAVR) in most cases\*

The mitral valve is a complex structure composed of leaflets, annulus, chordae tendineae, and papillary muscles—preservation of the subvalvular apparatus is mandatory to preserve LV geometry

There is an irregular geometry of the mitral valve leaflets

## Dynamic environment

There are dynamic changes in mitral annular geometry (shape/size) during the cardiac cycle, resulting in an overall reduction of annular area up to 30% and a reduction of annular circumference of up to 15%<sup>30</sup>

The device should be resistant to displacement or migration while enduring continuous cyclic movements of the annulus and LV base, as well as high transvalvular gradients (high dislodgment forces)

## Device requirements

The device should have a balanced radial stiffness to resist the dynamic environment and avoid frame fracture, whereas at the same time its stiffness should not cause perforation of adjacent structures.

Valve materials must be durable enough to withstand the loads generated

The device should not obstruct the left ventricular outflow tract, occlude the circumflex coronary artery, compress the coronary sinus, or cause major conduction system disruption

Because of the large annular size, there is a need for large delivery systems

## Hemodynamic performance

Paravalvular leak (PVL) should be minimized because regurgitation is poorly tolerated in the mitral position as a result of the higher pressure gradient across the valve. Moreover, PVL may result in hemolysis.

The TMVR should restore unidirectional flow while minimizing the risks associated with the procedure

## Other issues

Thrombogenicity of a bulky device implanted in the left AV position

Possibility of reoperation or TMVR-in-TMVR is still unclear

# Quid of percutaneous mitral valve replacement ?

**Table 1. Challenges for Percutaneous TMVR Devices**

Valve position

To be deployed in the left AV position, making a truly percutaneous, transfemoral delivery a challenge—because of the requirement for transseptal (or transaortic retrograde) access to the LA or LV and the need for a multidimensional, highly curved catheter course (which is challenging with a large delivery system and limits the precision with which tension and traction are transmitted to the operating end of the system)

- Valve positioning (atrial or transaortic way...)
- Valve anatomy
- Dynamic environment
- Device requirements
- Hemodynamic performance
- Thrombogenicity
- Possibility of reoperation

system disruption

Because of the large annular size, there is a need for large delivery systems

Hemodynamic performance

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# Percutaneous mitral valve replacement

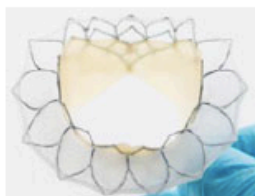
Fortis (Edwards Lifesciences)



First-in-man study underway

- Mitral valve replacement technology designed to minimize *para*-valvular leak
- Initial version being studied in first-in-man has a transapical delivery system

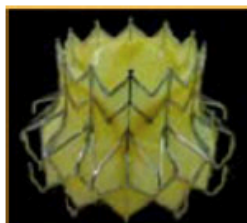
Tiara (Neovasc)



First-in-man study underway

- Self-expanding bovine pericardial, D-shaped trileaflet mitral valve implanted using a transapical delivery system
- It is anchored to the mitral annulus
- A transfemoral delivery system is also in development

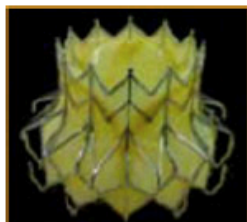
TMVI-TA (CardiAQ)



First-in-man study completed

- Self-positioning, self-anchoring, and self-conforming system for transcatheter mitral valve implantation through transapical approach

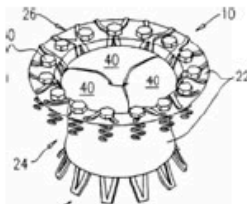
TMVI-TF (CardiAQ)



First-in-man study completed

- Self-positioning, self-anchoring, and self-conforming system for transcatheter mitral valve implantation
- 2nd-generation device has been developed; this profile covers transfemoral version

Caisson TMVR (Caisson)

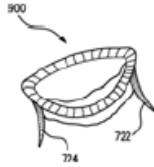


Preclinical studies underway

- Mitral valve replacement system with a transfemoral delivery system

# Percutaneous mitral valve replacement

MitraCath (Emory University)



In development

- Technology that enables the placement of a stent-mounted bioprosthesis in the mitral position

HighLife Mitral Valve Replacement (HighLife)



Preclinical underway

- Percutaneous mitral valve replacement technology with a transatrial delivery system

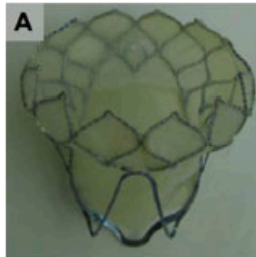
Medtronic TMVR (Medtronic)



Preclinical underway

- Self-expanding nitinol scaffold and a bovine pericardium valve with three cusps
- Designed for fixation with the native mitral annulus

MitrAssist Valve (MitrAssist)



Preclinical underway

- A mitral valve that fits into the existing mitral valve
- Delivered through a small-diameter catheter
- For all forms of mitral regurgitation

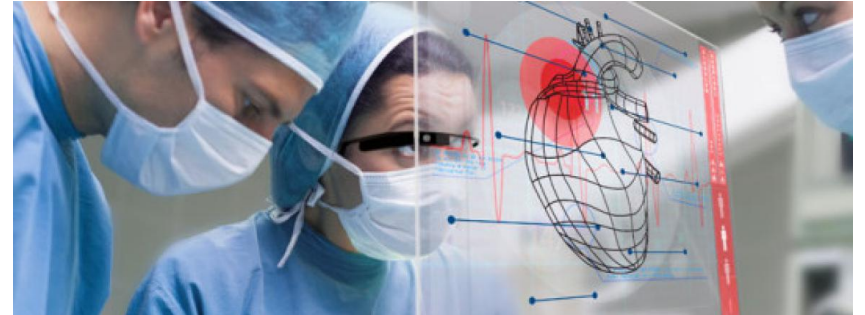
Navigate TMVR (NCSI)



Clinical implants have occurred

- Self-expandable mitral valve replacement device featuring a nitinol stent and dehydrated tissue for treatment of functional mitral regurgitation
- Transatrial, transapical, and transseptal versions are also in development

# The futur of mitral valve repair could be...



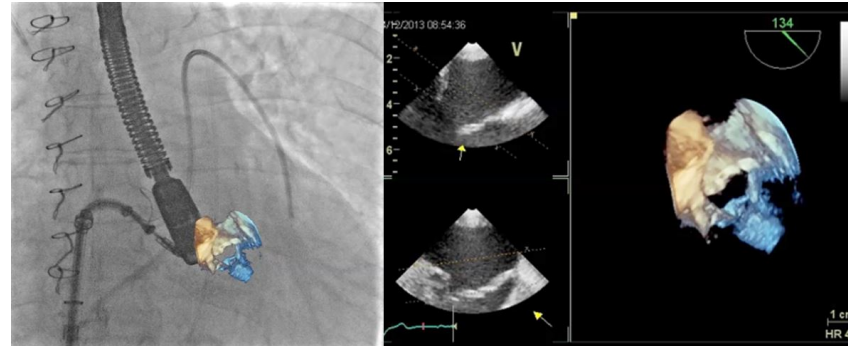
- Leaflets : Edge to edge repair
- Mitral valve annulus repair
- Chordae repair
- Percutaneous mitral valve replacement
- **Imaging**

# Imaging

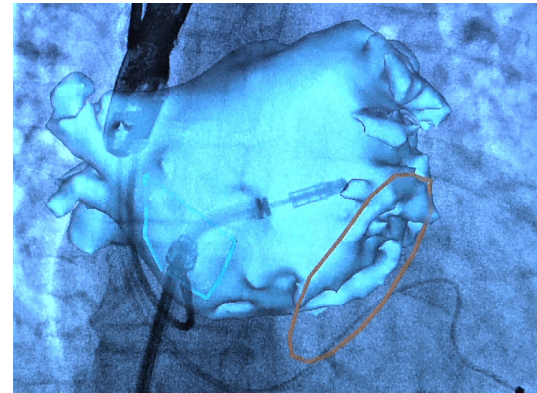
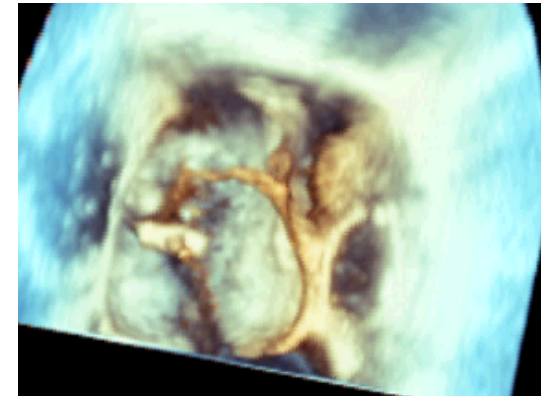
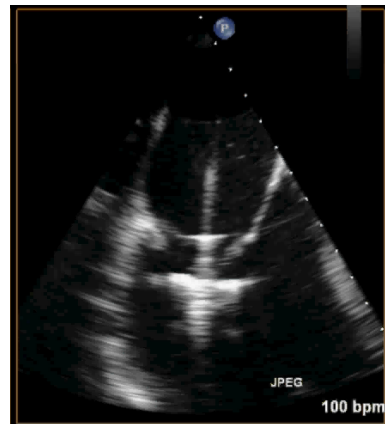


- Limits between cardiac surgery and interventional cardiology are more and more unclear
- One of the most important differences between interventional cardiologists and cardiac surgeons is the view of the operating field
- The exposure of the operating field is fundamental and enhances the safety of operating actions and renders them more precise and safe.
- Imaging techniques are the future because they could become the eyes of the operator

# Imaging



- ETT, ETO, 3D.
- Fusion d'images
  - Fusion scanner
  - Fusion IRM
  - Fusion ETO
  - Fusion ETO 3D scanner ?
  - Etc...





# "le futur du traitement percutané de la valve mitrale"

Ce qui paraît certain :

- nous sommes sur la route du traitement percutané de la mitrale : c'est parti !
- L'imagerie sera un élément clé et décisif, potentiellement limitant.

Ce qui n'est pas clair :

- Va t'on vers le remplacement valvulaire mitral percutané
- ou plutôt vers la réparation comme l'ont fait les chirurgiens avant nous ?
  - Associations de gestes (Ex : Mitraclip ou néo cordages et anneau mitral ?)



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Merci

