# MITRA CLIP
# IN THE MANAGEMENT OF MITRAL REGURGITATION

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Oct 7, 2017

# No conflict of interest in relation to this presentation

# Mitral Valve Disease and Mitra Clip

## Anatomy and Mitral Regurgitation

Treatment Options

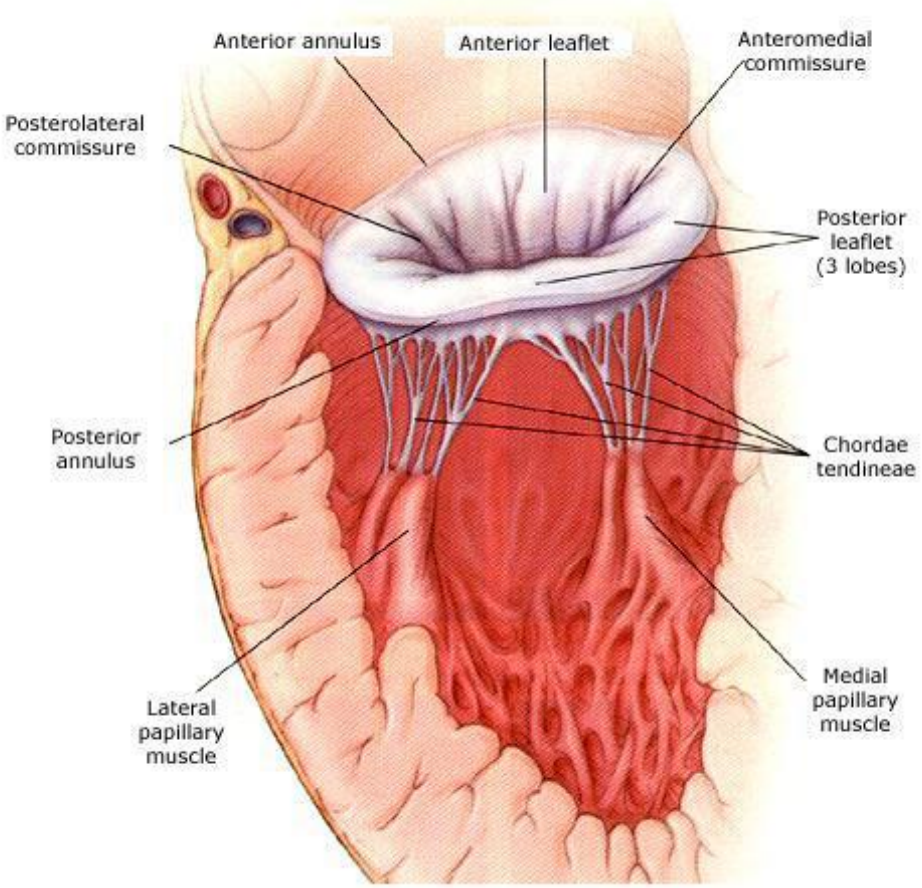
Mitra Clip technology

Clinical Trials

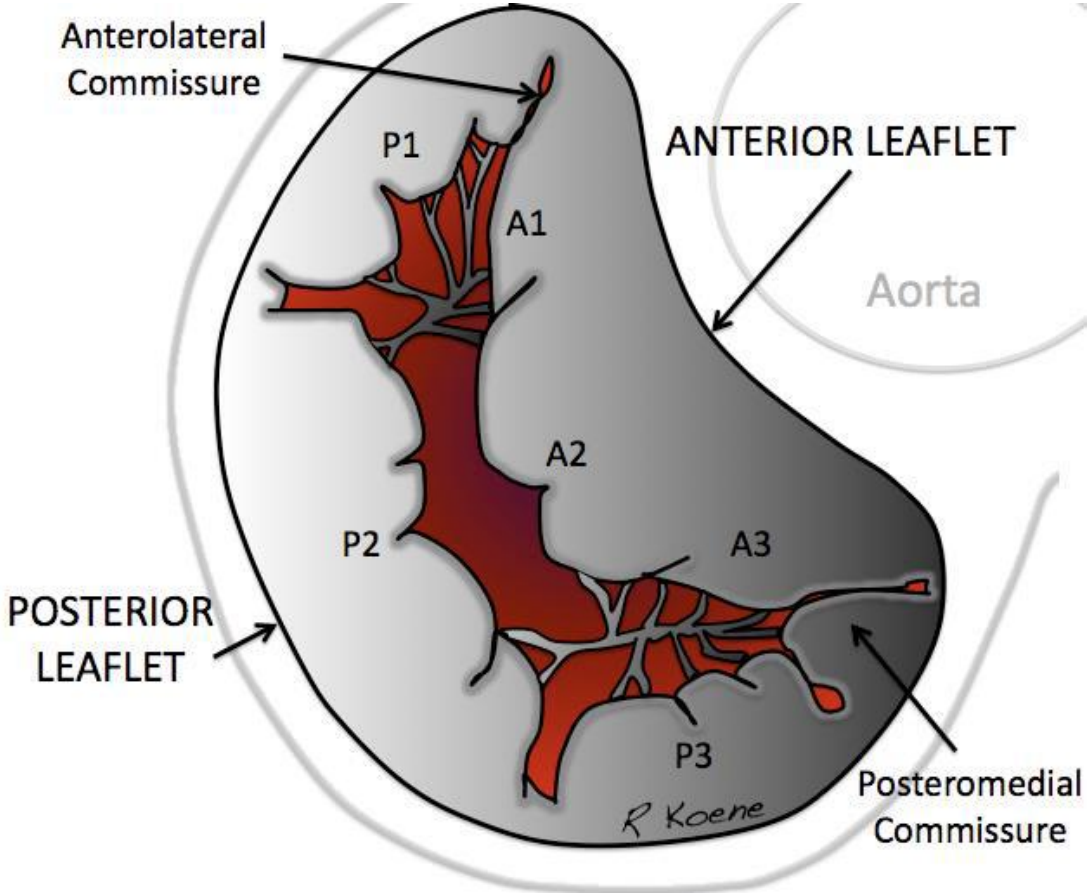
Case Examples

Future Technologies

# The Mitral Valve Anatomy

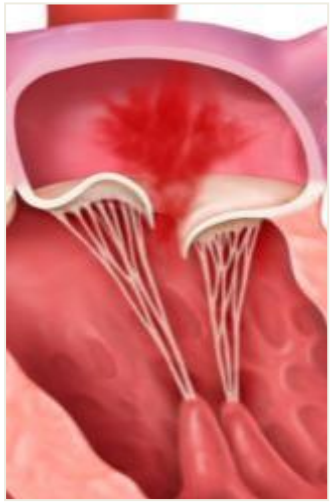


# The Leaflets



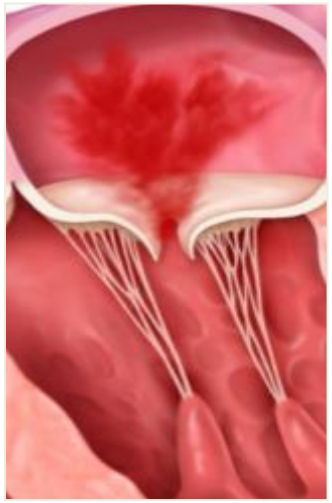
# Mitral Regurgitation Etiologies

Normal
Mitral Valve



Degenerative
MR: Prolapse

Degenerative
MR: Flail



Functional MR

- **Degenerative MR is due to an anatomic abnormality of the mitral valve itself, including the leaflets, and/or the subvalvular apparatus.**
- **2 Million or 30%**

- **Functional MR is the result of left ventricular dilation leading to annular dilation and incomplete coaptation of the mitral valve leaflets.**
- **5 Million or 70%**

# Signs and Symptoms of MR

- Acute – usually associated with CAD and AMI
  - Dyspnea
  - Fatigue
  - Orthopnea
  - Pulmonary Edema

- Chronic – May remain asymptomatic for years
  - Systolic LV dysfunction
  - Atrial fibrillation as a consequence of atrial dilatation
  - Eventually progress to symptomatic CHF with pulmonary congestion and edema

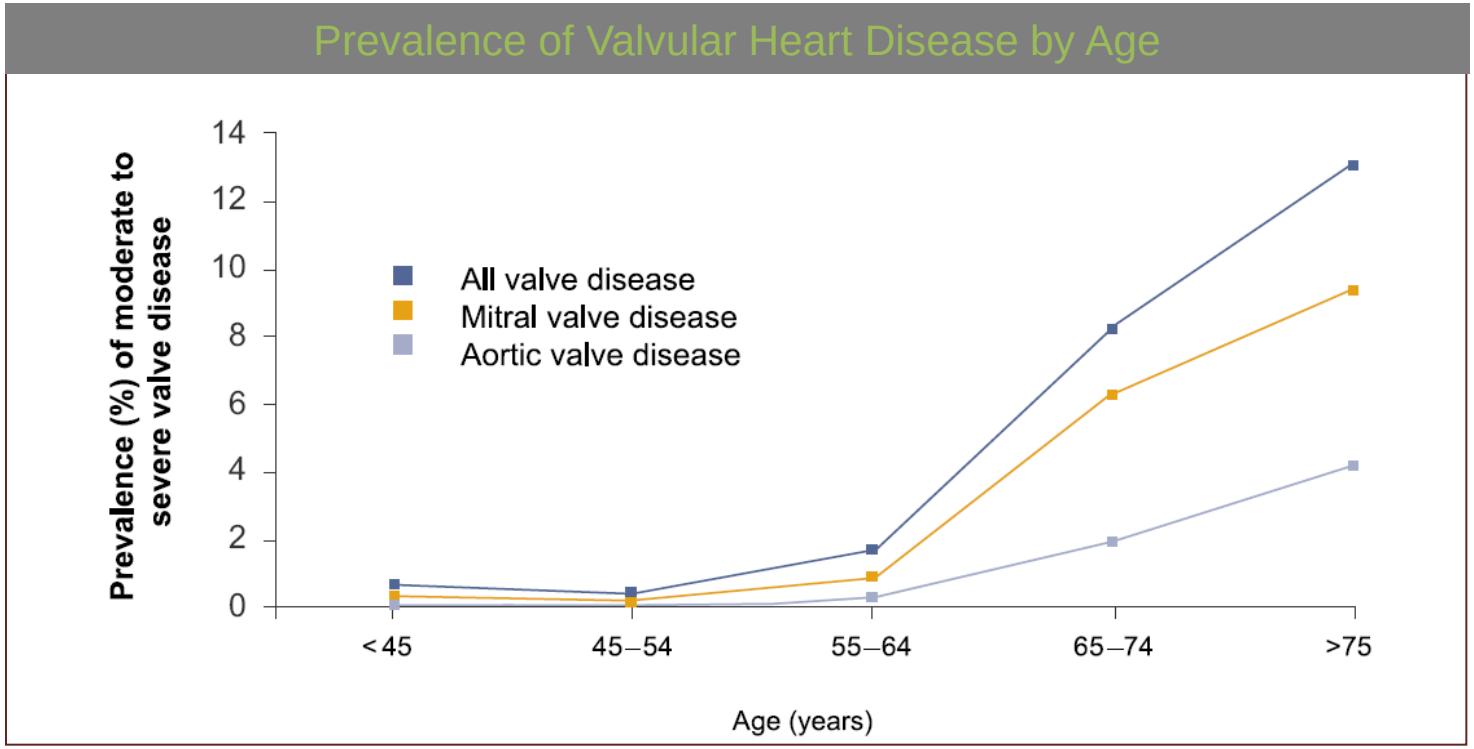
# Severe MR Echo “Hall Marks”

- LA Dilated >34ml/m2
- LV Dilated >5.7cm or 117ml Women or >6.3cm 178ml Men
- EF Elevated > 65% (initially in response to increased volume)
- Pulmonary vein flow reversal
- RV and RA are usually Dilated
- MV inflow >1.2-1.5m/sec
- **Jet area (% of LA area) > 40%**
- **Vena contracta > 0.7cm**
- **EROA > 0.4cm2**
- **Reg Fraction > 50%**
- **Reg Volume > 60 ml/beat**

# Moderate or Severe Valvular Disease Is Common and Increases With Age

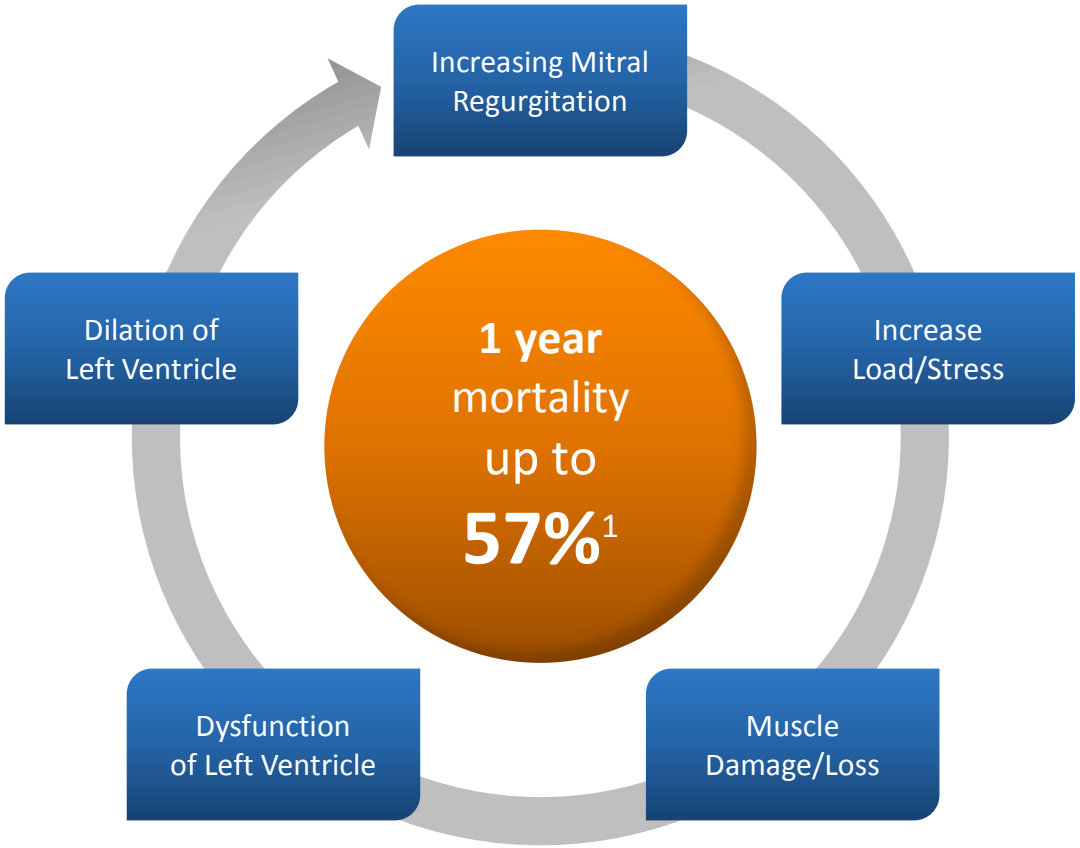
**Mitral regurgitation is the most common type of heart valve insufficiency in the US[1,2]**

Prevalence increases with increasing age, from 0.5% for 18-44 yr olds rising to 9.3% for ≥75 year olds (p<.0001)




1. Heart Disease and Stroke Statistics 2010 Update: A Report From the American Heart Association. *Circulation.* 2010;121:e46-e215.
2. Nkomo et al. Burden of Valvular Heart Diseases: A Population-based Study, Lancet, 2006; 368: 1005-11.

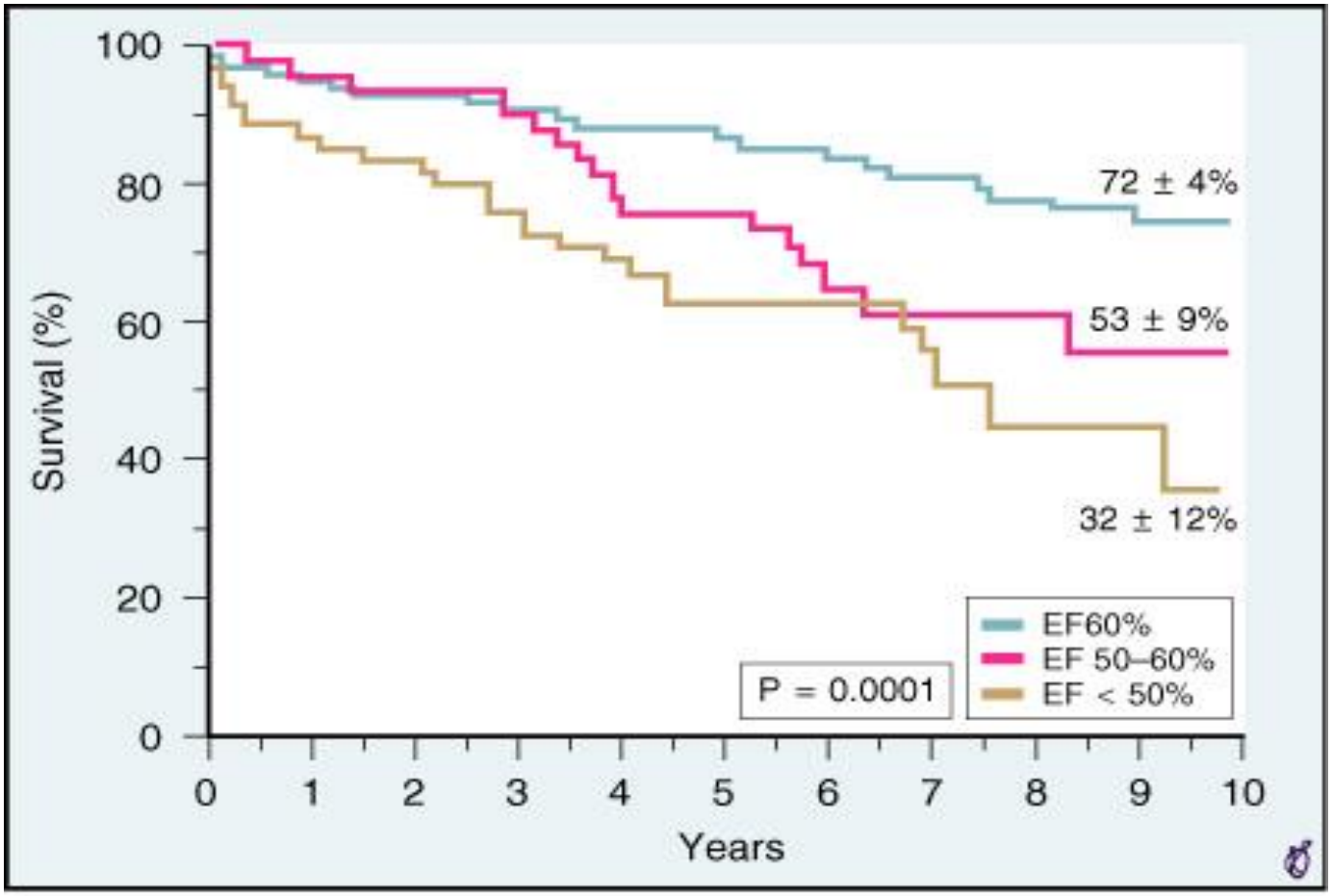
# MR Progresses to Heart Failure




MR initiates a cascade of events progressing to heart failure, then death, if untreated[2,3]

[1] Cioffi G, et al. Functional mitral regurgitation predicts 1-year mortality in elderly patients with systolic chronic heart failure. European Journal of Heart Failure 2005 Dec;7(7):1112-7
[2] Grigioni F, et al. Outcomes in mitral regurgitation due to flail leaflets a multicenter European study. JACC Cardiovasc Imaging. 2008 Mar;1(2):133-41
[3] Enriquez-Sarano M, et al. Quantitative determinants of the outcome of asymptomatic mitral regurgitation. N Engl J Med. 2005 Mar 3;352(9):875-83

# Severe MR Survival : Impact of EF



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Anatomy and Mitral Regurgitation

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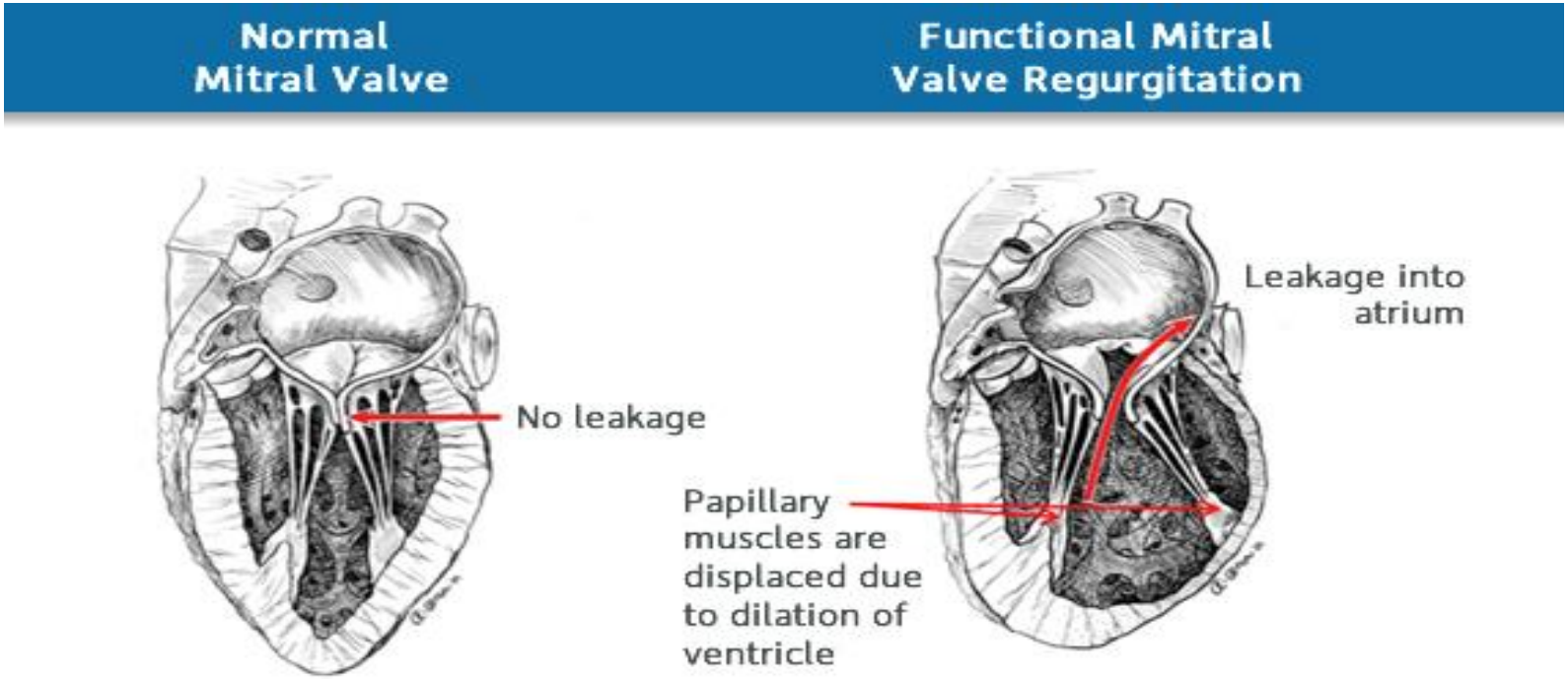
# Mitral Regurgitation: Functional (Secondary)

- LEFT VENTRICULAR PATHOLOGY/LV DILATATION
- RESTICTED LEAFLET MOBILITY/POOR COAPTATION LEAFLETS



# Functional (Secondary) MR: Treatment

- OPTIMIZE MEDICAL THERAPY:
  - Afterload reduction with nitrates and antihypertensives
  - ACE, BB, K Sparing diuretics, ARB-Neprilysin inhibitors
- RE-VASCULARIZATION-CABG, PCI
- BiV PACING

# Degenerative (Primary) MR Treatment

**SURGICAL**

Mitral Valve replacement – Bio or Metallic prosthesis

- Operative mortality – 8-10%

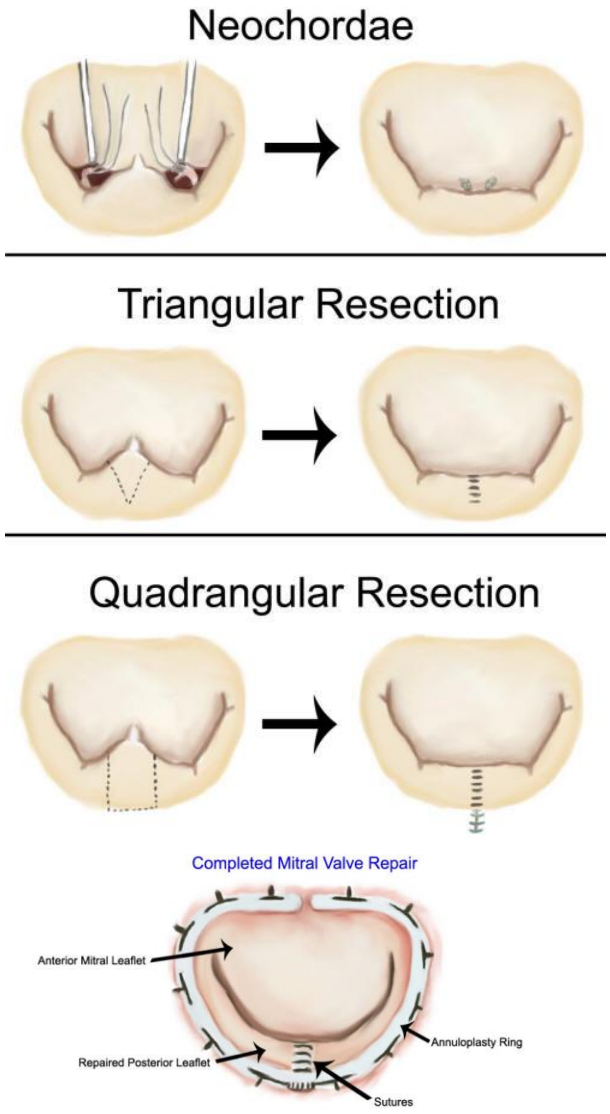
Mitral Valve repair

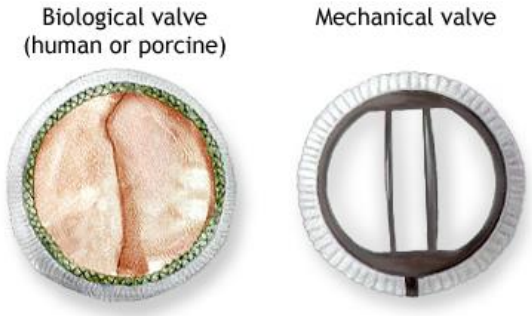
- Leaflet, Chordae repair and annuloplasty ring
- Operative mortality – 2-4 %
- Alfieri Stitch

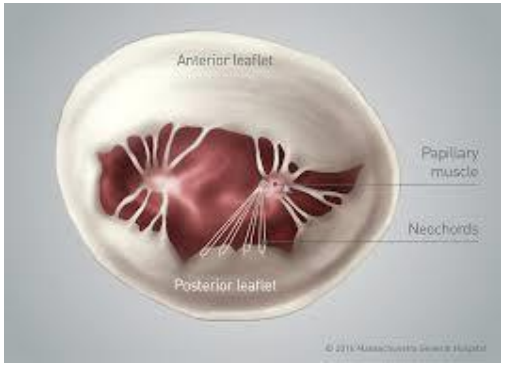
Transcatheter therapies

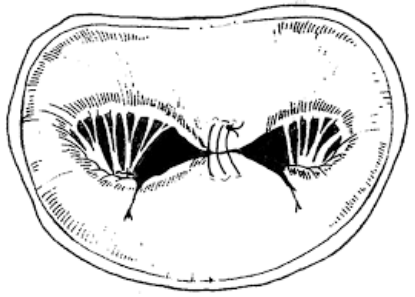
- Mitraclip
- Tendyne

# Mitral Surgery: Replacement, Repair, Stitch

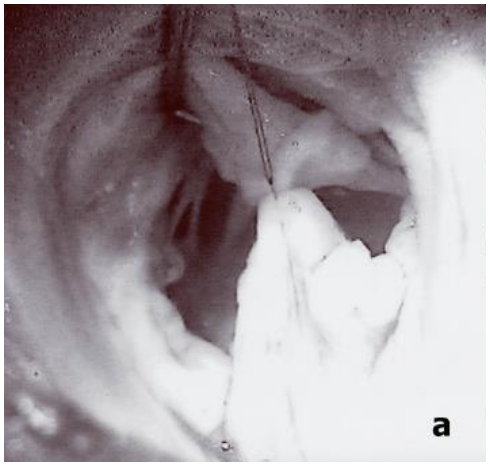


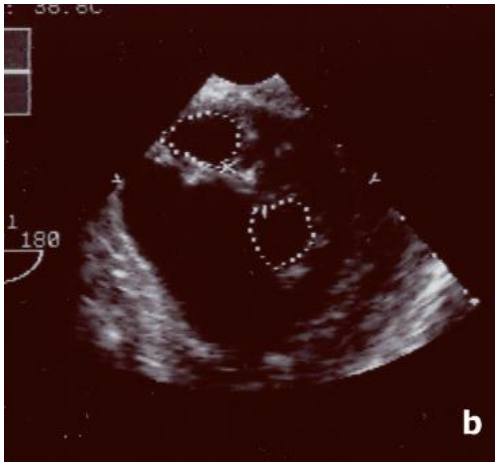



# The Alfieri Technique

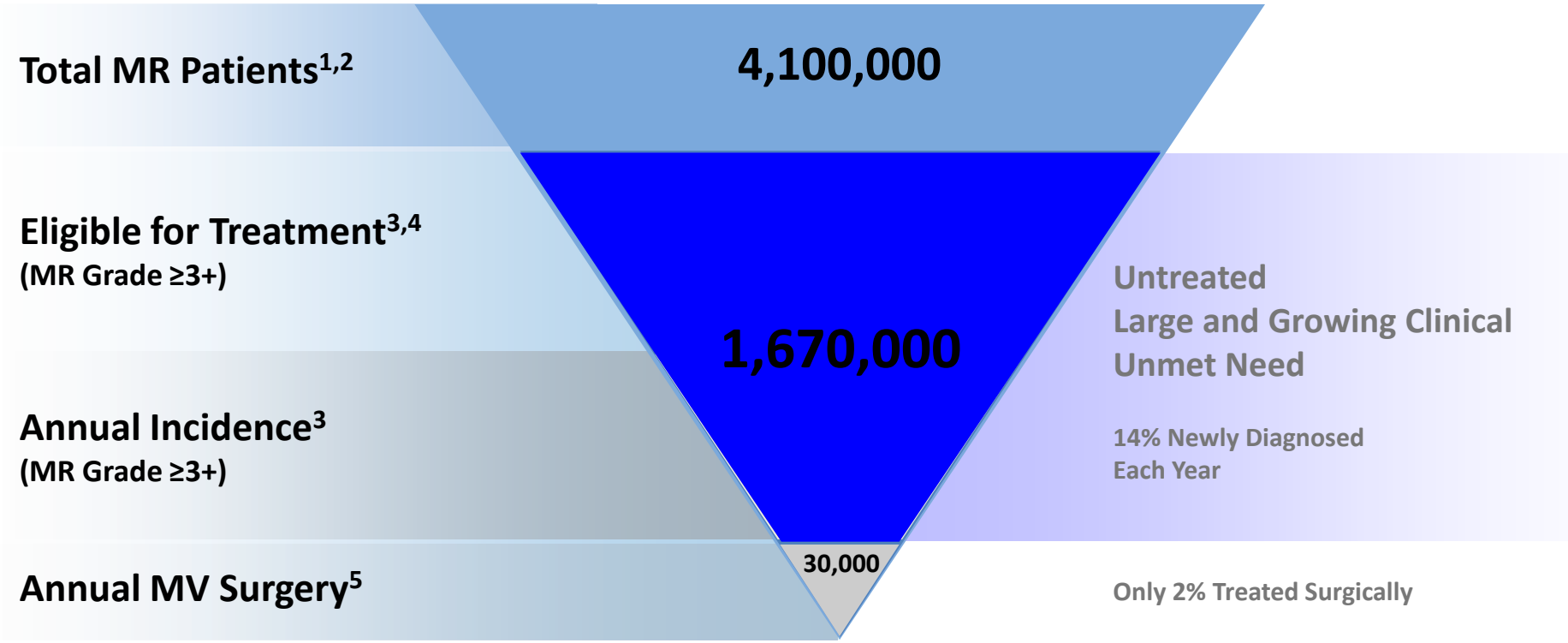



- The surgical “edge-to-edge” technique was first described in early 1990`s (Alfieri). Heals to create a tissue bridge.
- Single large orifice is converted to two smaller orifices.
- Over 1,500 pts reported in the literature
  - Safe, effective, durable AND no occurrence of mitral stenosis

# 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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Anatomy and Mitral regurgitation

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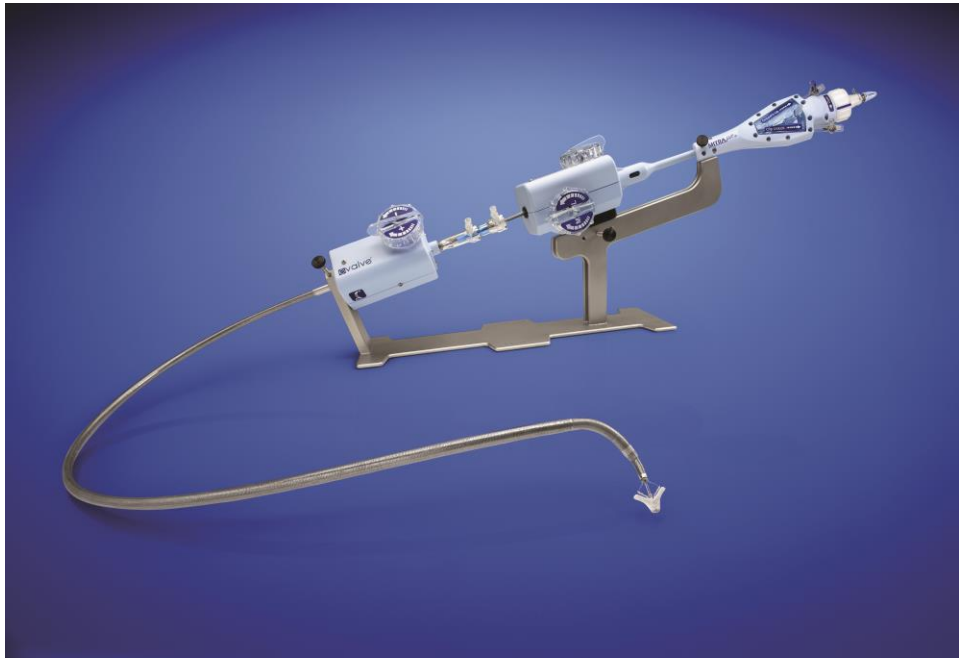
# MitraClip® procedure overview

# Procedural Animation

https://www.youtube.com/watch?v=ihEM97ApCqE

# MitraClip® System

## First-in-class, Leading Technology



1. MitraClip Clip Delivery System Summary of Safety and Effectiveness Data (SSED).
2. MitraClip Clip Delivery System Instructions for Use.

See Important Safety Information referenced within

**Class IIB Indication**
**2014 and 2017 Updated Valvular Heart Guidelines:**

***Transcatheter mitral valve repair*** **may be considered for:**

- ***Severely symptomatic*** **patients (NYHA class III to IV) with**
- **Chronic severe primary MR (stage D) who have favorable anatomy for the repair procedure and**
- **Reasonable life expectancy**
- ***Prohibitive surgical risk*** **because of severe comorbidities**
- ***Remain severely symptomatic despite optimal GDMT for HF***

- The clip was found to be SAFE, BUT LESS EFFECTIVE than surgical repair because residual MR was more prevalent.

- **Clip did reduce severity of MR, improved symptoms, and led to reverse LV remodeling.**

**Percutaneous mitral valve repair should only be considered for patients with chronic primary MR who remain severely symptomatic with NYHA class III to IV HF symptoms despite optimal GDMT for HF and who are considered inoperable.**

# Mitraclip Indications

Significant symptomatic pre treatment MR >3+.

Reduction to MR<2+ is reasonably expected

Due to primary abnormality of the mitral apparatus – Degenerative MR

Prohibitive risk for MV Surgery

No severe co morbidities that would negate procedural benefits

Data is not available on LVEF<20% or LVESD>60mm

# Mitraclip Contraindications

Patients who cannot tolerate post procedural antiplatelets or anticoagulants.

Active endocarditis of mitral valve

Rheumatic mitral valve disease

Evidence of intracardiac, IVC or femoral venous thrombus

# Mitraclip Prohibitive Risk

30 day predicted operative mortality risk score of

> 8% for MV replacement

> 6% for MV repair

Porcelain or highly calcified ascending aorta

Frailty

Hostile chest

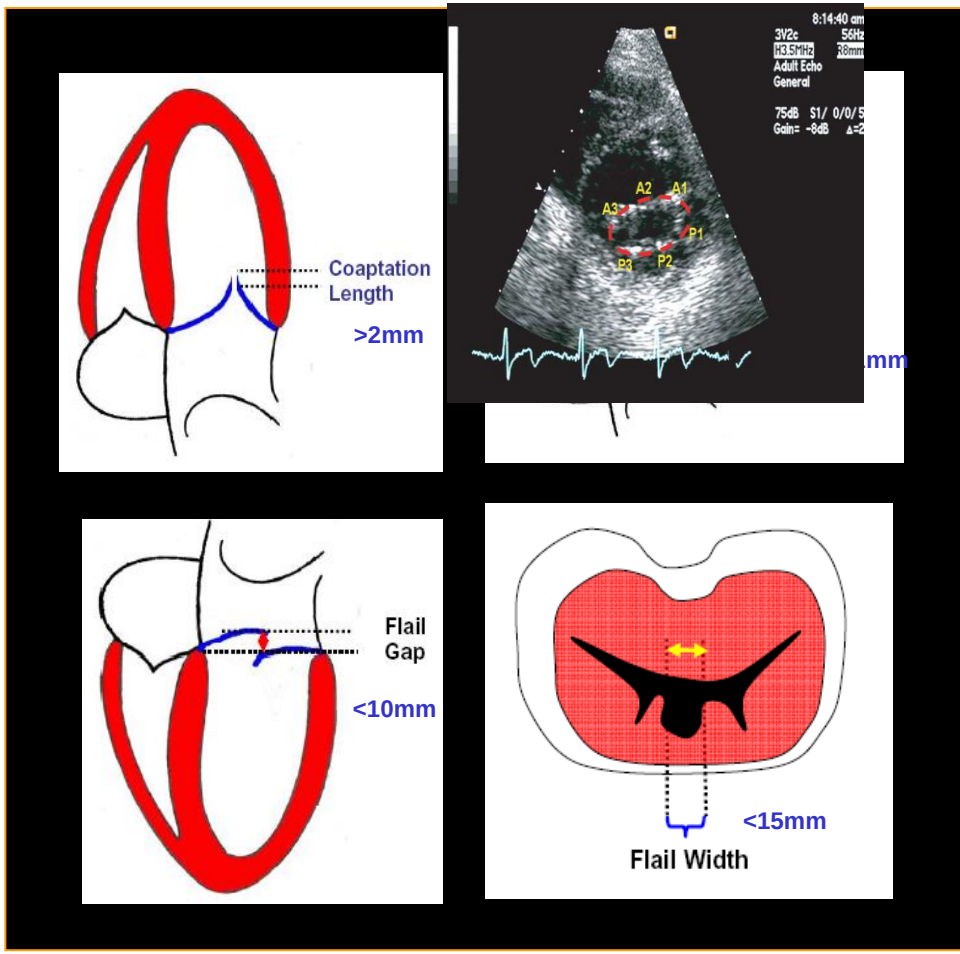
Severe liver disease MELD Score >12

Severe pulm HTN – PASP > 2/3 of SAP

Malignancy, HIV, Immobility, Severe dementia, Severe RV dysfunction …

# Anatomic Suitability
# Leaflet mal-coaptation resulting in MR

- Sufficient leaflet tissue for mechanical coaptation
- Non-rheumatic/endocarditic valve morphology
- Anatomic considerations
  - Flail gap <10mm
  - Flail width <15mm
  - Mitral Area ≥ 4.0 cm2
  - Coaptation length > 2mm
  - Minimal calcification in grasping area
  - No cleft leaflet in grasping area



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# Mitraclip Clinical Trials Worldwide

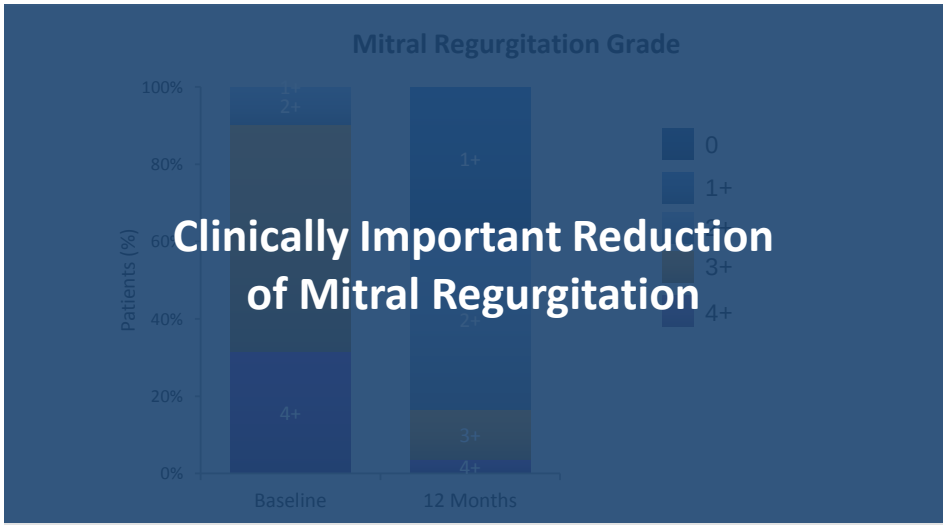
| Study | Population | N** |
|---|---|---|
| EVEREST I (Feasibility)* | Feasibility patients | 55 |
| EVEREST II (Pivotal)* | Pre-randomized patients | 60 |
| EVEREST II (Pivotal)* | Non-randomized patients<br>(High Risk Study) | 78 |
| EVEREST II (Pivotal)* | Randomized patients<br>(2:1 Clip to Surgery) | 279<br>184 Clip<br>95 Surgery |
| REALISM (Continued Access)* | Non-randomized patients | 899 |
| 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 | 9,761 |
| **Total** | | **11,956**<br>**+95 surgery** |

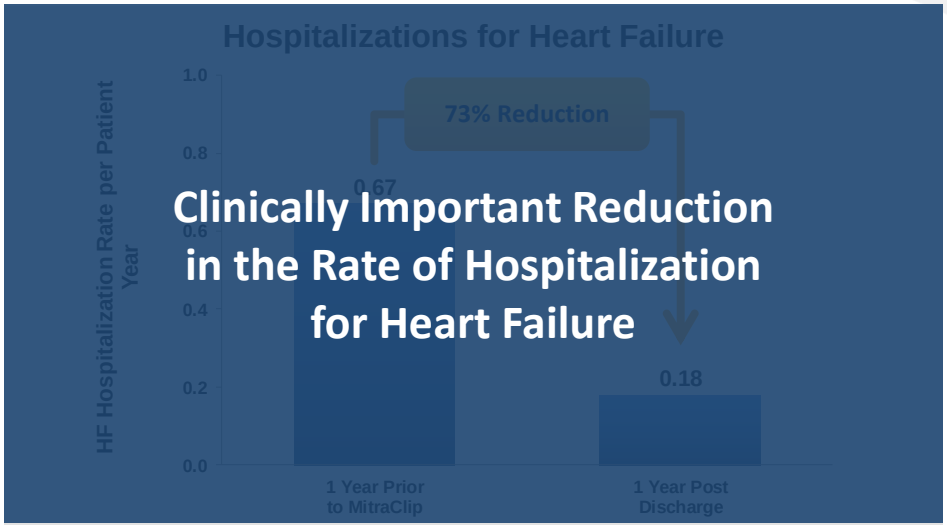
Disclaimer: Worldwide data includes experience with FMR patients. The US FDA approved indication is for DMR patients only. OUS experience with FMR represents an indication broader than the US FDA approved indication

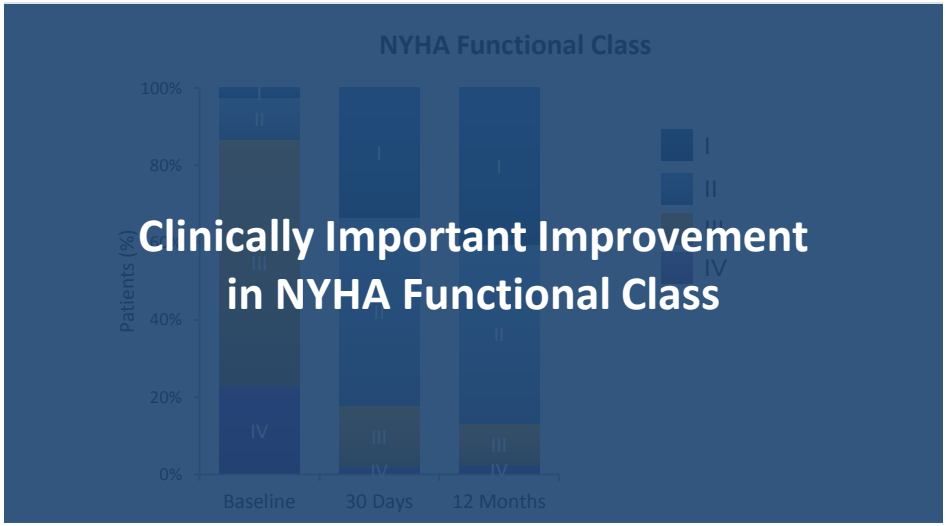
*EVEREST I, EVEREST II, REALISM, ACCESS Europe Phase I, ACCESS Europe Phase II are Abbott Vascular sponsored clinical trials

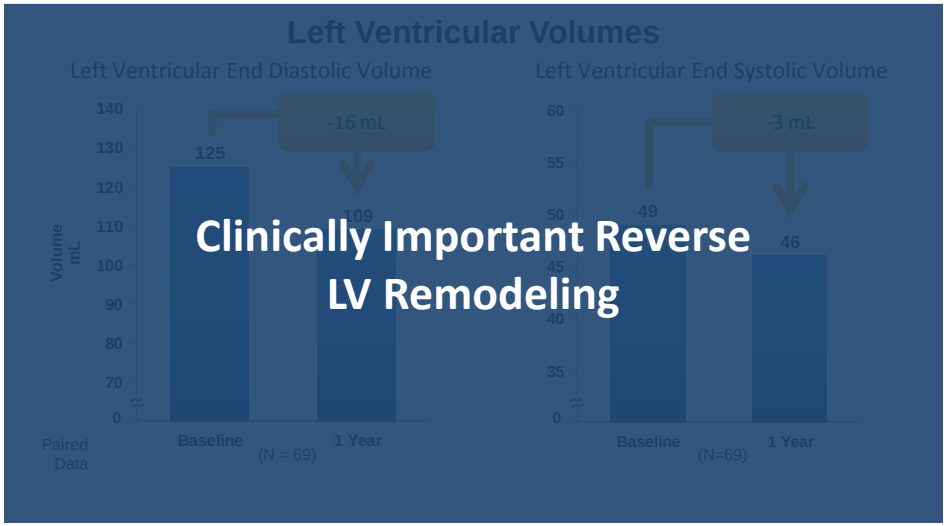
**Data as of 12/31/2013. Source: Abbott Vascular

# Prohibitive Surgical Risk DMR Cohort (n=127)



# Updated MitraClip Outcomes From the STS TVT Registry

**On behalf of the TVT Registry**

**October 11, 2015**

# Methods

- All commercial TMVR cases with MitraClip performed in U.S. from Nov 2013- March 2015 identified (n=1601)
- Patients with baseline MR data, hospital mortality, conversion to surgery included (n=1583, median per site =21, IQR= 13, 38)
- Outcomes for procedure success, MACE, device-related events, and in-hospital and 30-day mortality

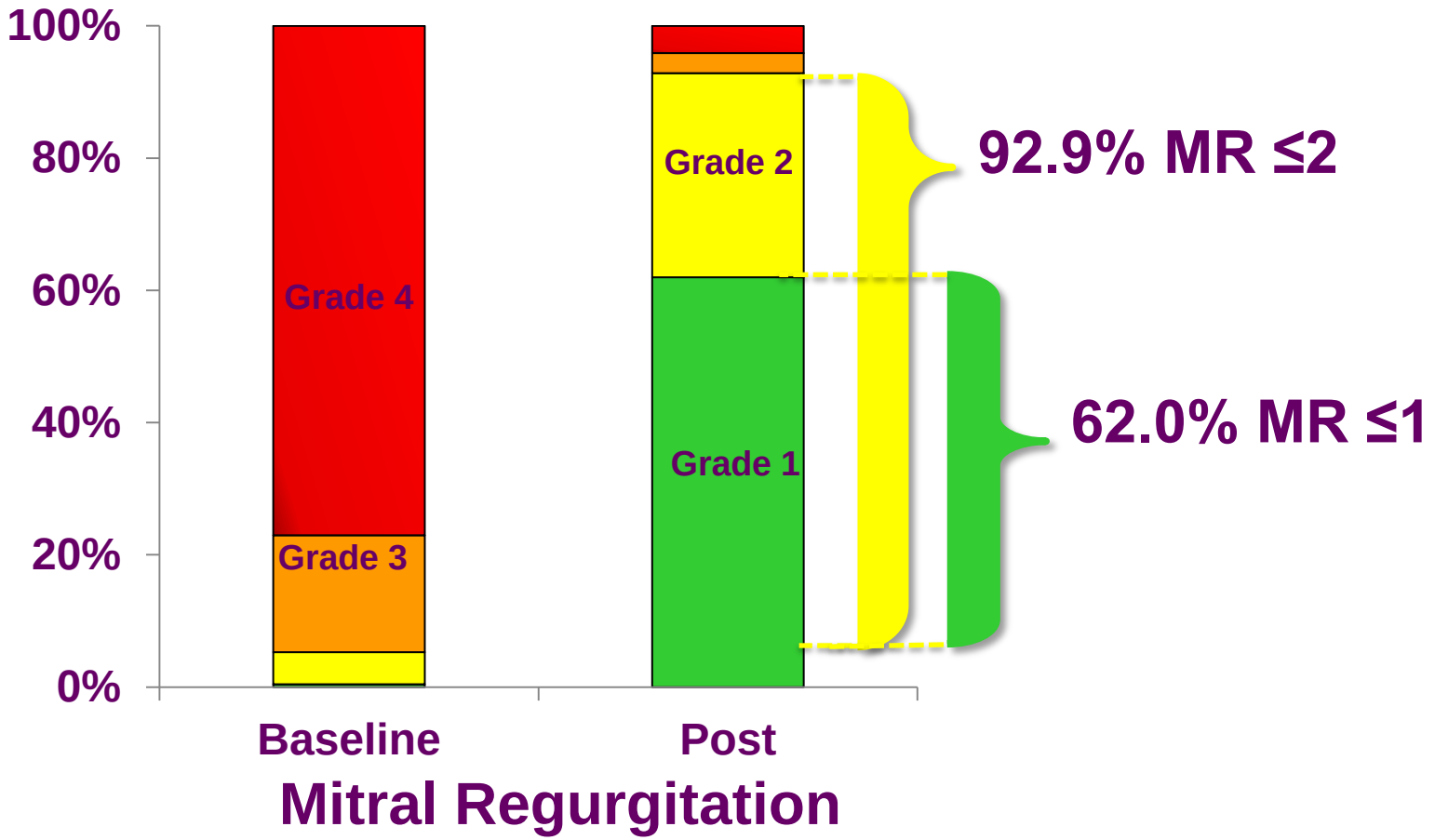
# Procedural Adverse Events

| | |
|---|---|
| Single leaflet device attachment…….. | 1.3% |
| Device embolization…….. | 0.2% |
| Other…… | 0.6% |
| Major bleeding……... | 3.7% |
| Cardiac perforation…….…… | 0.9% |
| Stroke…….. | 0.6% |
| Cardiac surgery……..…….. | 0.06% |
| ASD Closure…… | 1.6% |

# Site Reported MR Reduction

**1 Clip= 54%, 2 Clips= 40%, ≥ 3 Clips= 5%**

**Clip implanted = 97.7%**



# Outcomes at Discharge

| | |
|---|---|
| MR moderate (2+) or less | 92.9% |
| MR mild (1+) or less | 62.0% |
| MV mean Gradient (mm Hg) | 4.00 mmHg (IQR: 3-6) |
| Median LOS | 3 days (IQR: 1-6) |
| Discharge location=home | 84% |

# Mortality

In-hospital Mortality ..... 2.6%

- MR>2 / Need for Surgery (7.5%). 8.4%
- MR≤ 2 / No Surgery ..... 2.1%

30 day mortality ..... 5.5%

- MR>2 / Need for Surgery..... 14.6%
- MR≤ 2 / No Surgery..... 4.9%

1 year mortality .....20.6%

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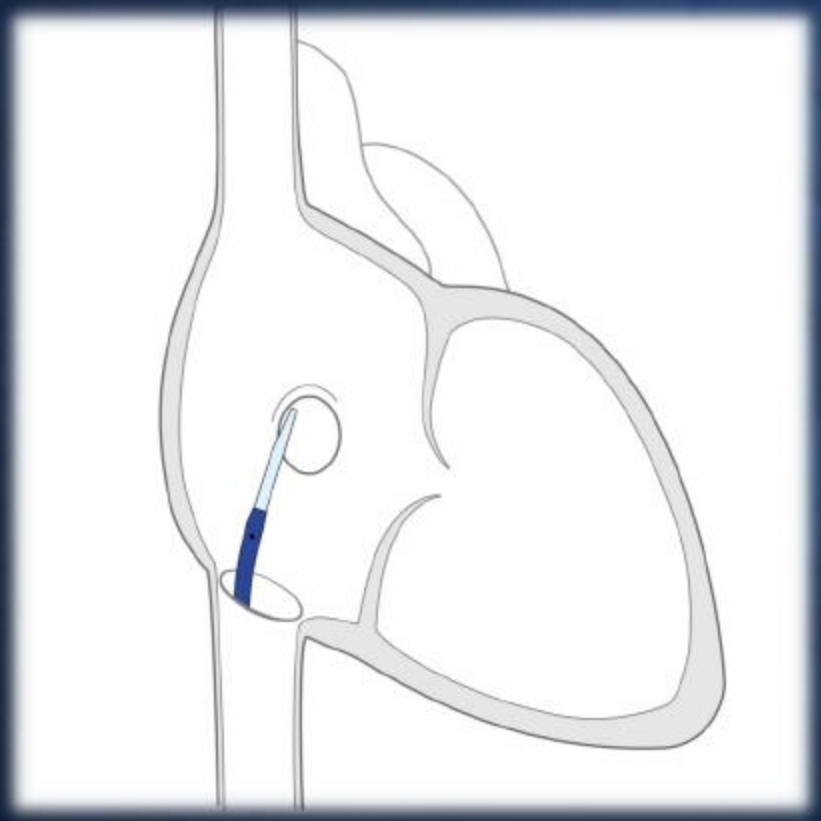
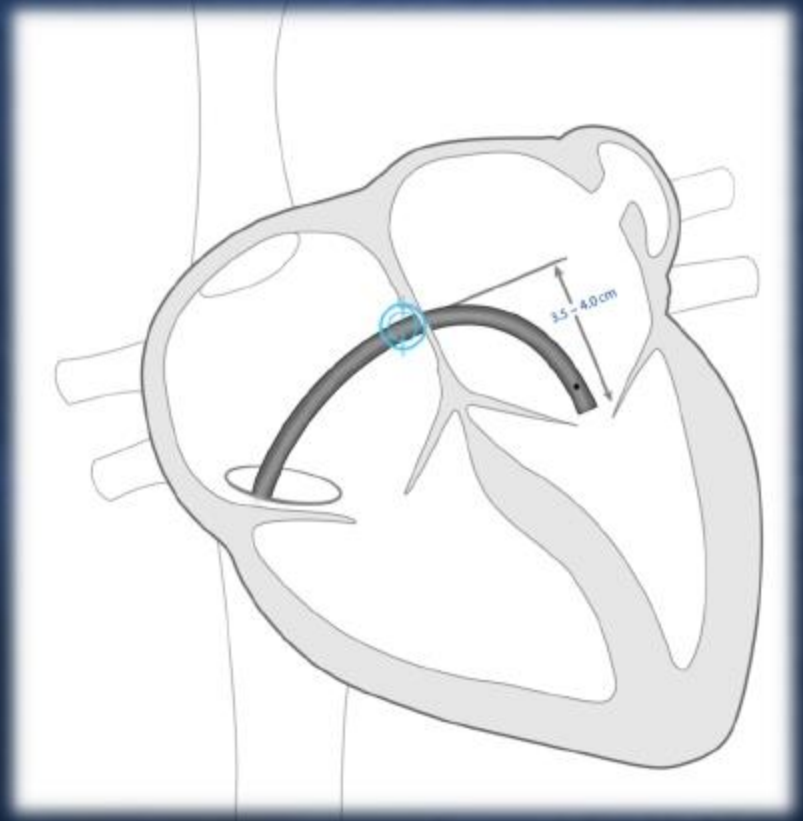
# Post-Superior Transseptal

## It Matters Greatly



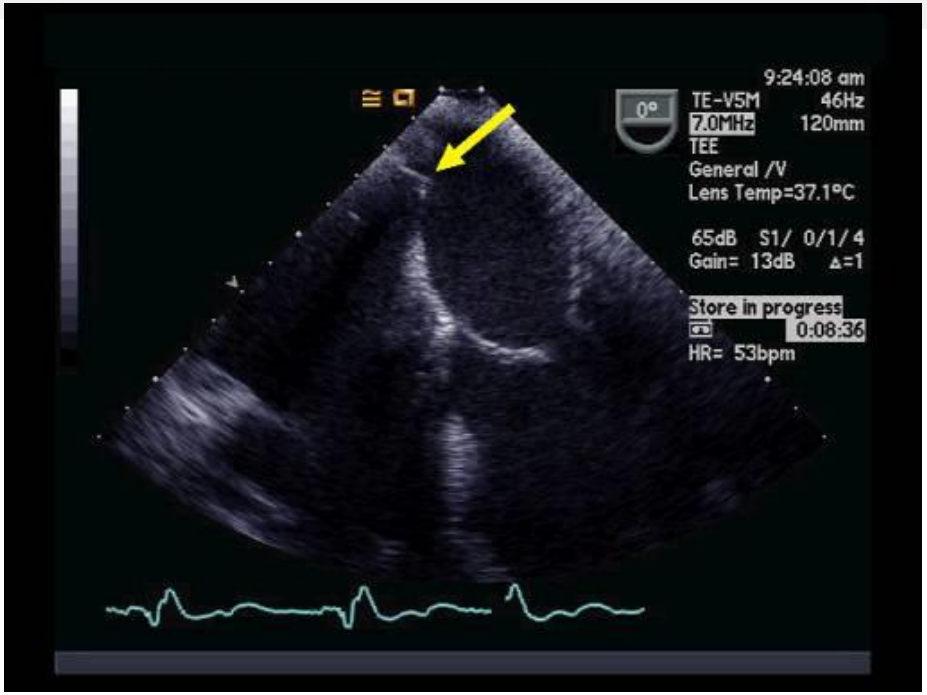


# Post-Superior Transseptal



AvoidingASD

***Avoid PFO – Usually Anterior***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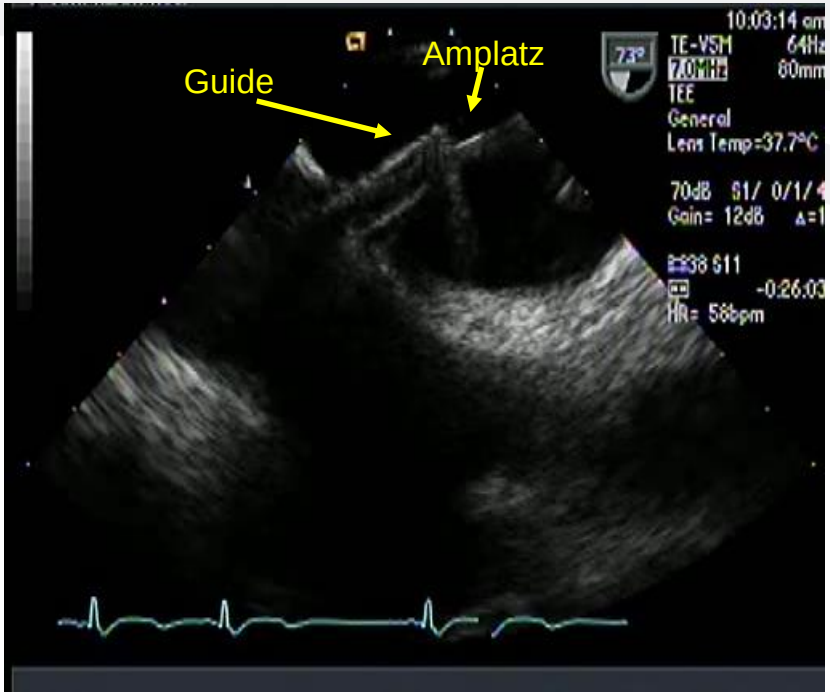
HR= 53bpm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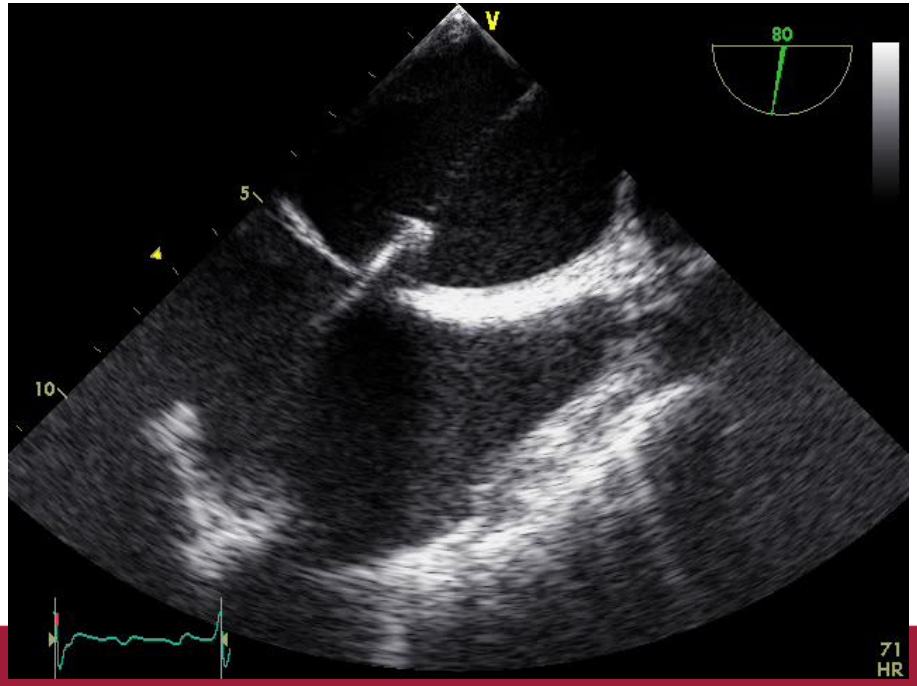
TEE
General
Lens Temp=37.7°C
HR= 58bpm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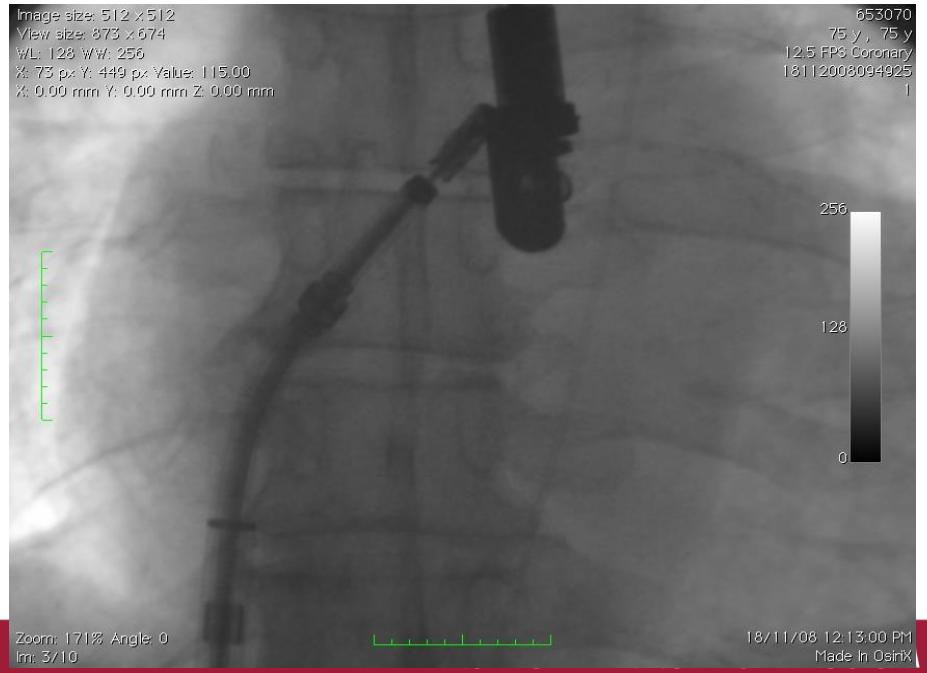
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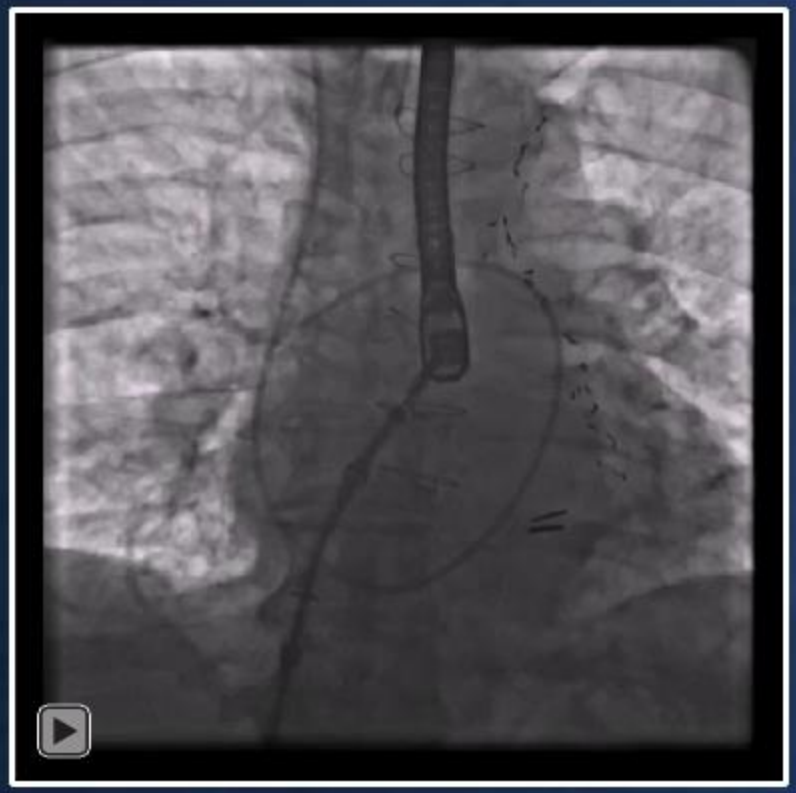
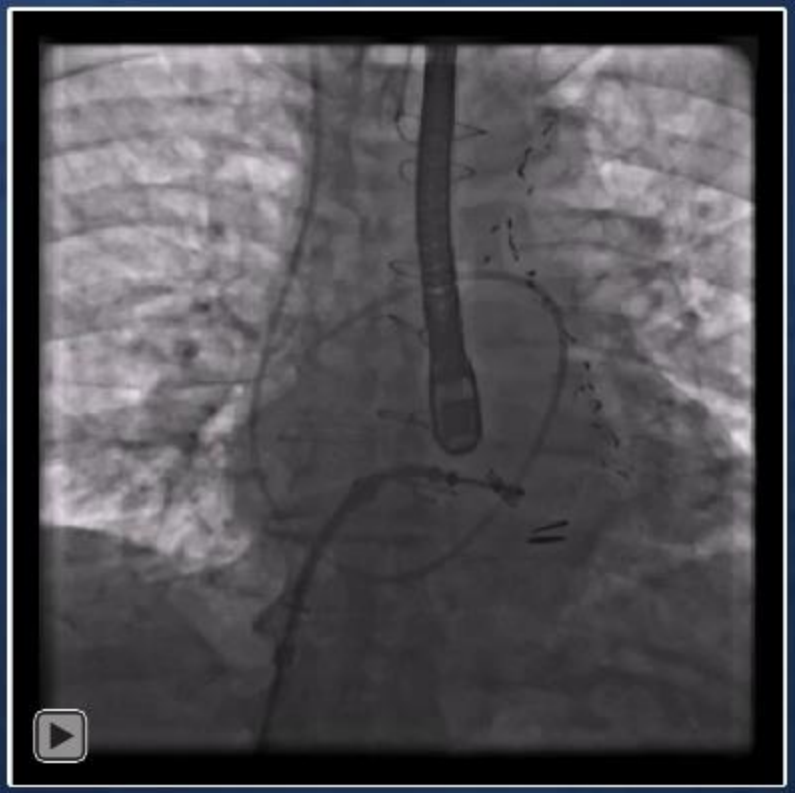
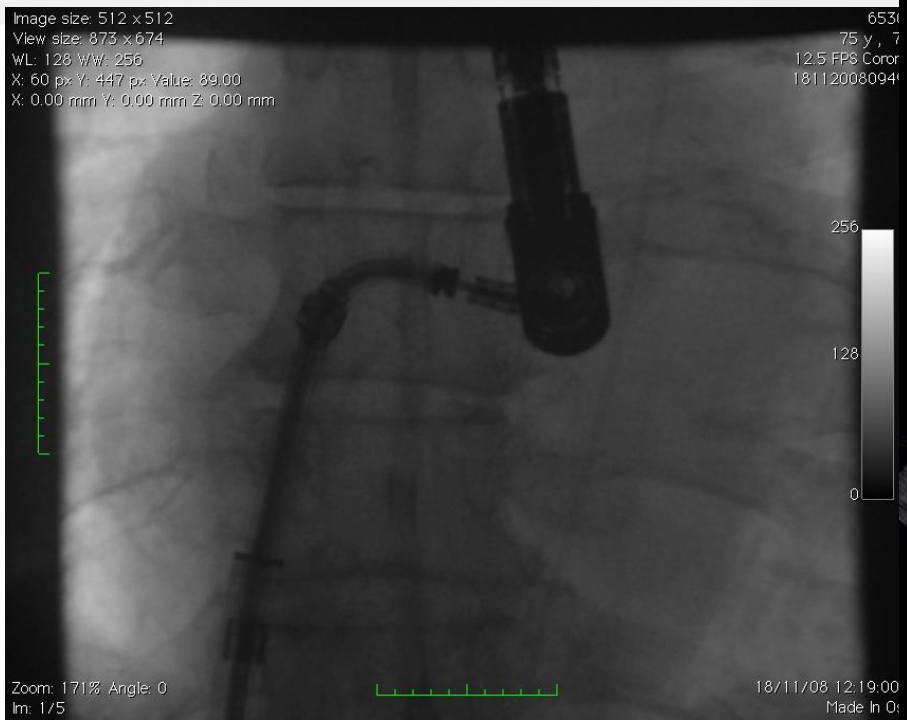






See Important Safety Information Referenced Within.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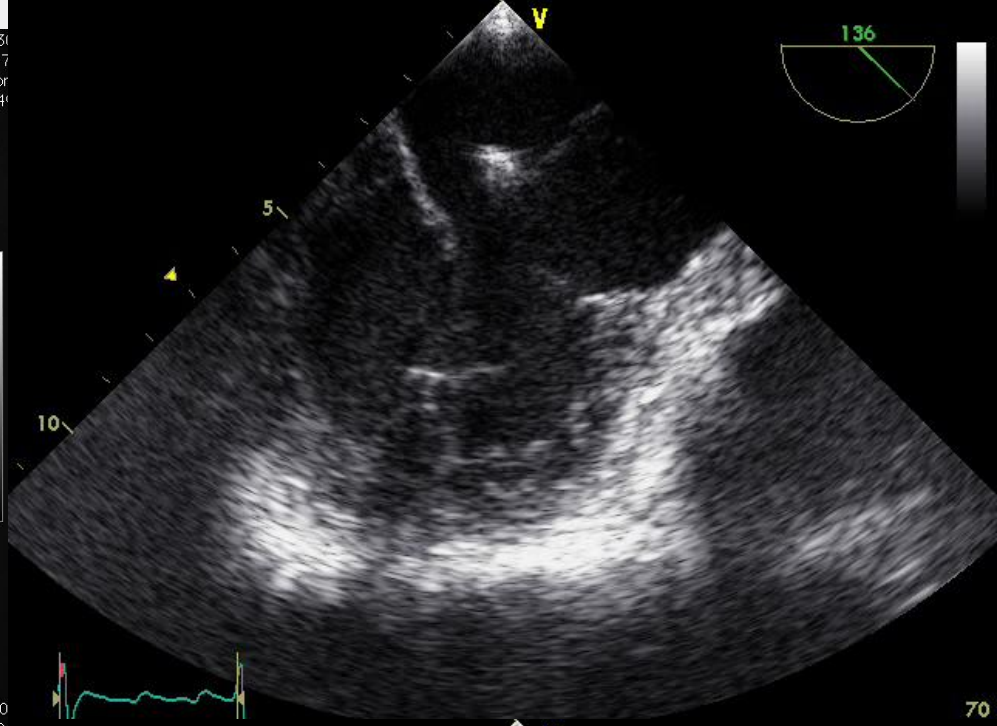
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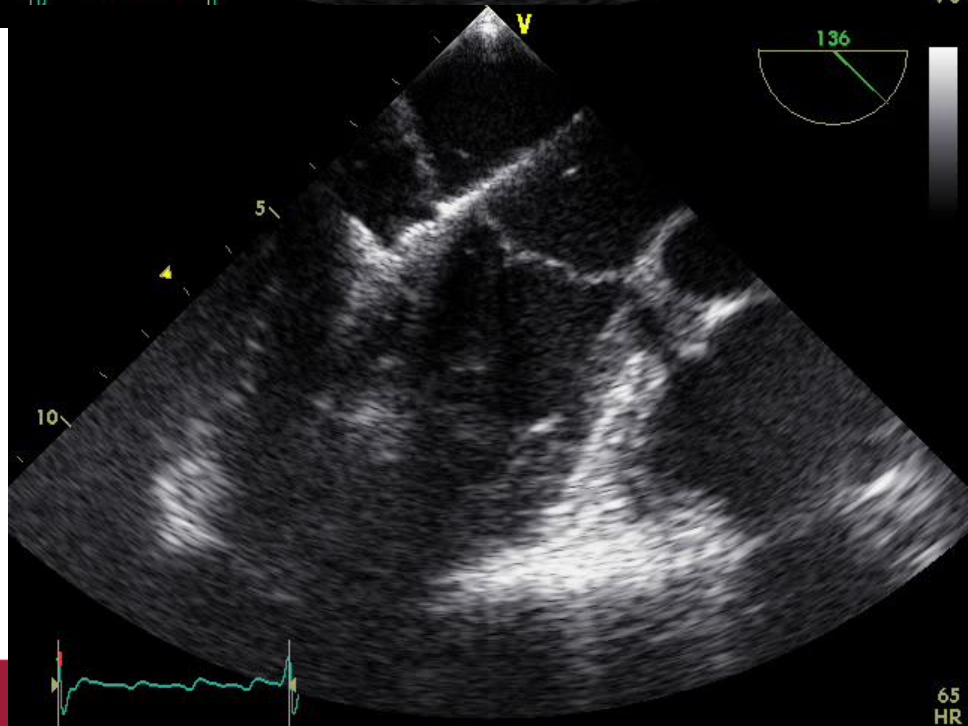
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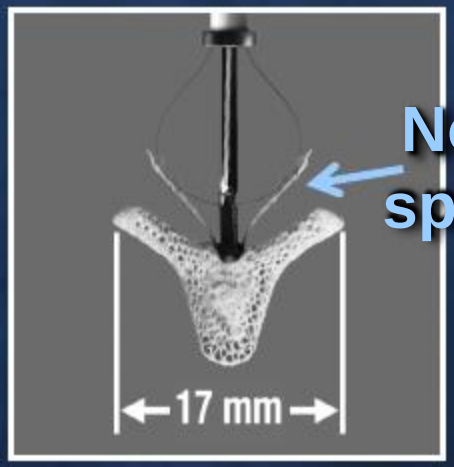
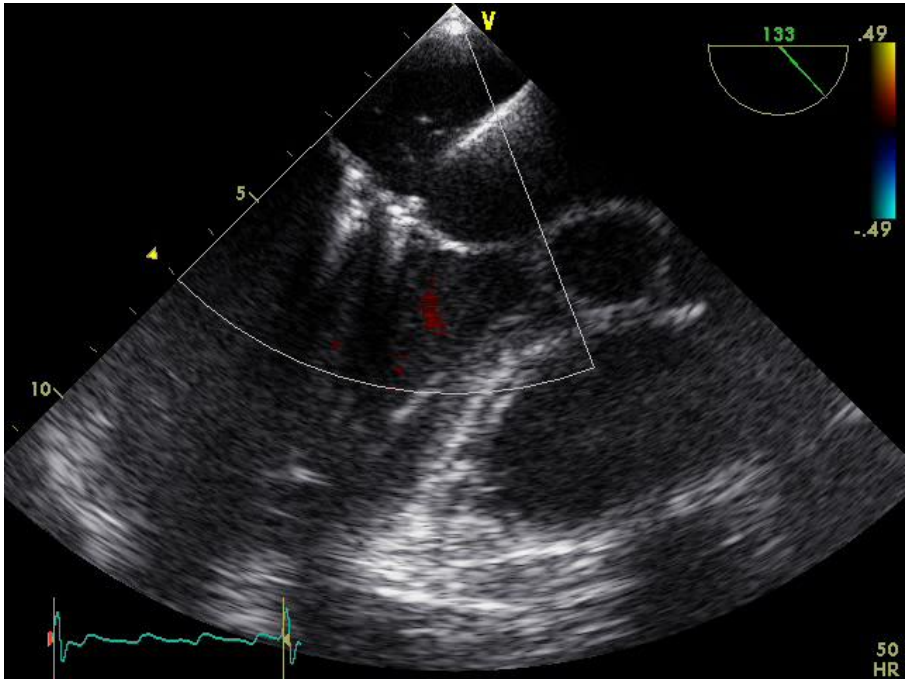
# Clip And Grippers

## Grippers Up

## Grippers Down




## Closed to 60˚


V
133
.49
-.49
5
10
50
HR

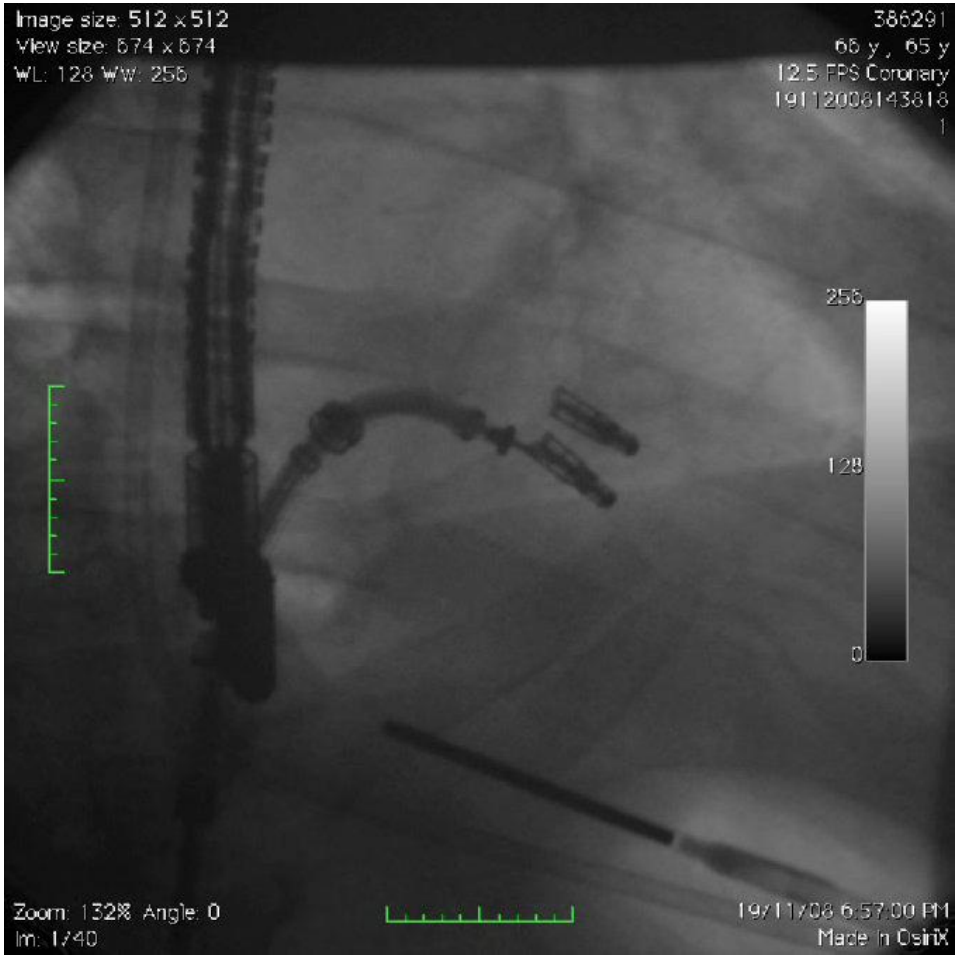


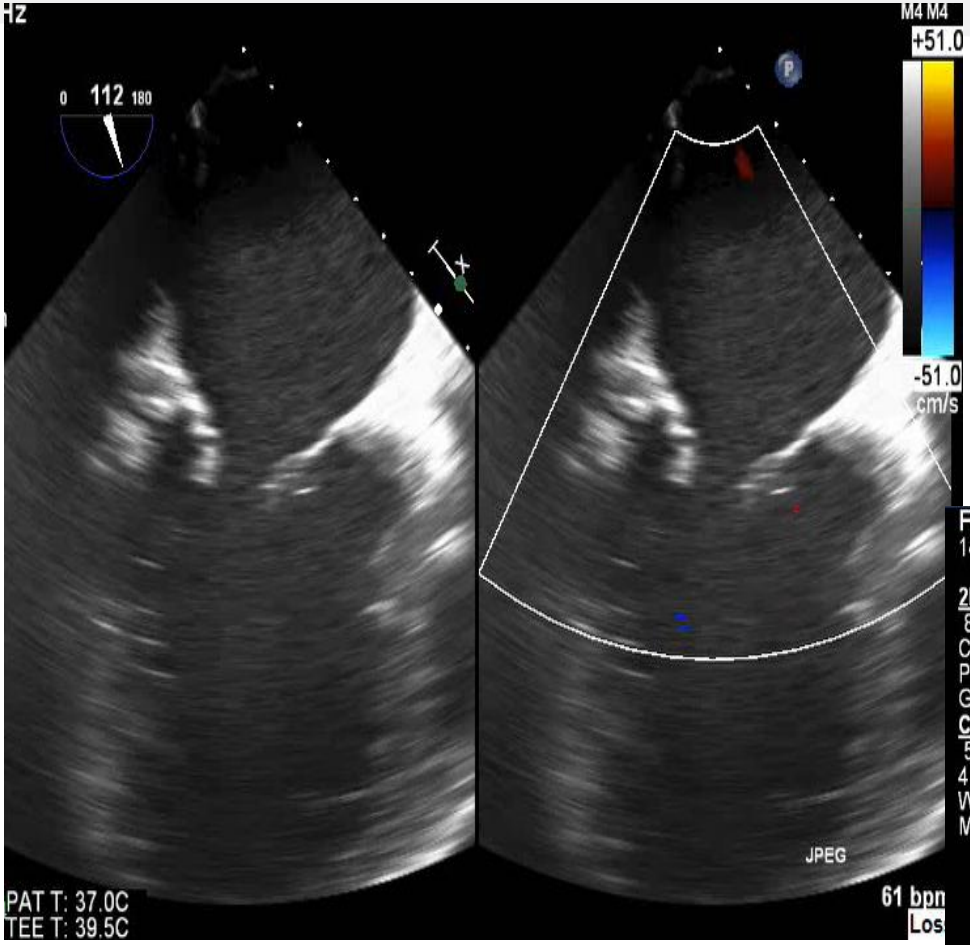
Image size: 512 x 512
View size: 674 x 674
WL: 128 WW: 256
386291
66 y , 65 y
12.5 FPS Coronary
19112008143818
1
256
128
0
Zoom: 132% Angle: 0
Im: 1/40
19/11/08 6:57:00 PM
Made in OsiriX

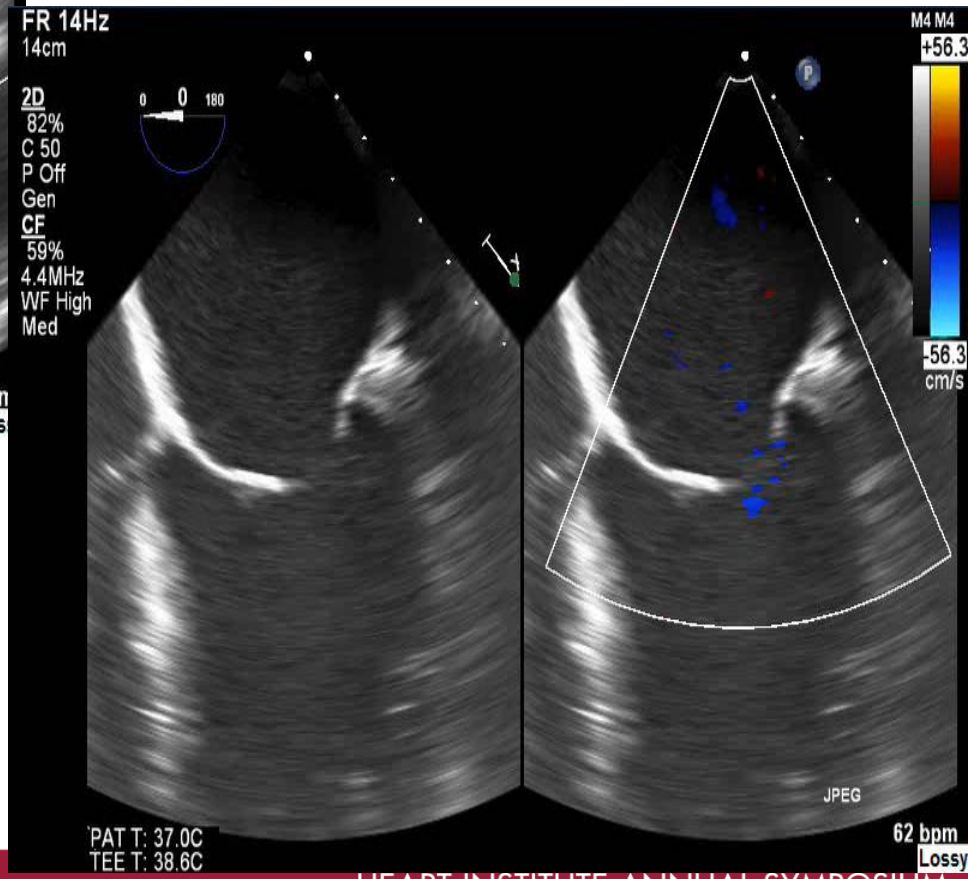
# Mitraclip at ORMC

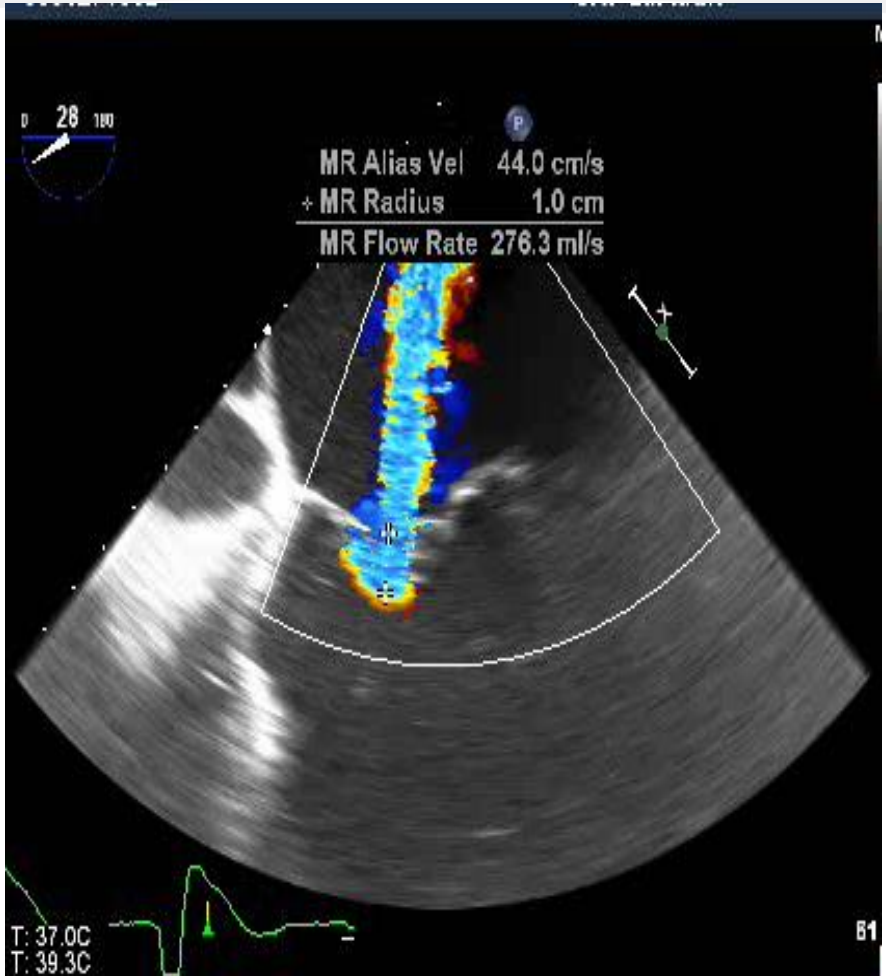
- LN – 83 YO Male
- Echo shows severe MR, moderate TR, EF 20-25%
- Acute on Chronic CHF with recurrent admissions
- CABG with Patent LIMA to LAD and SVG to R-PDA. Other SVGs occluded
- Paroxysmal A. Fib on Coumadin
- LE - PAD and moderate Carotid stenosis
- HTN, DL, Hypothyroidism, CKD, Anemia, Thrombocytopenia

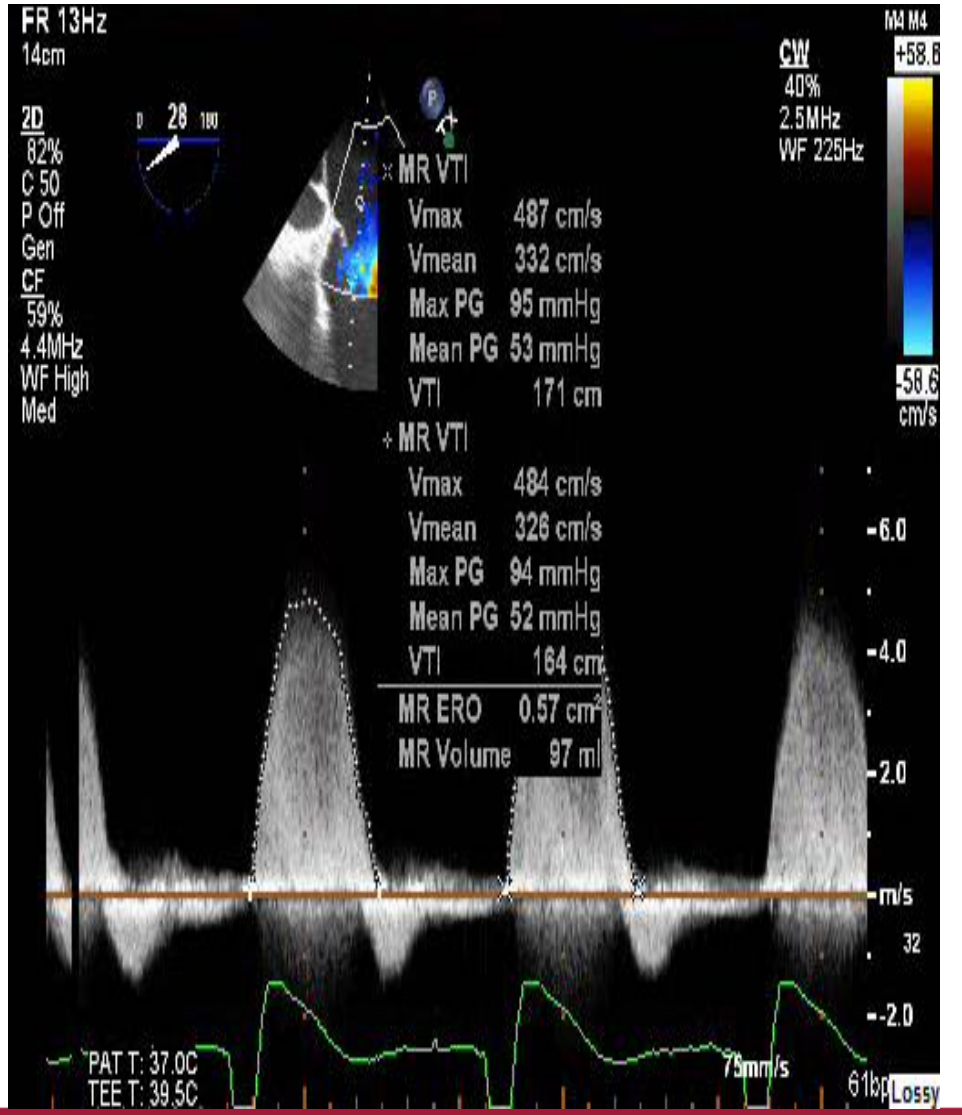
# Pre clip tee assessment

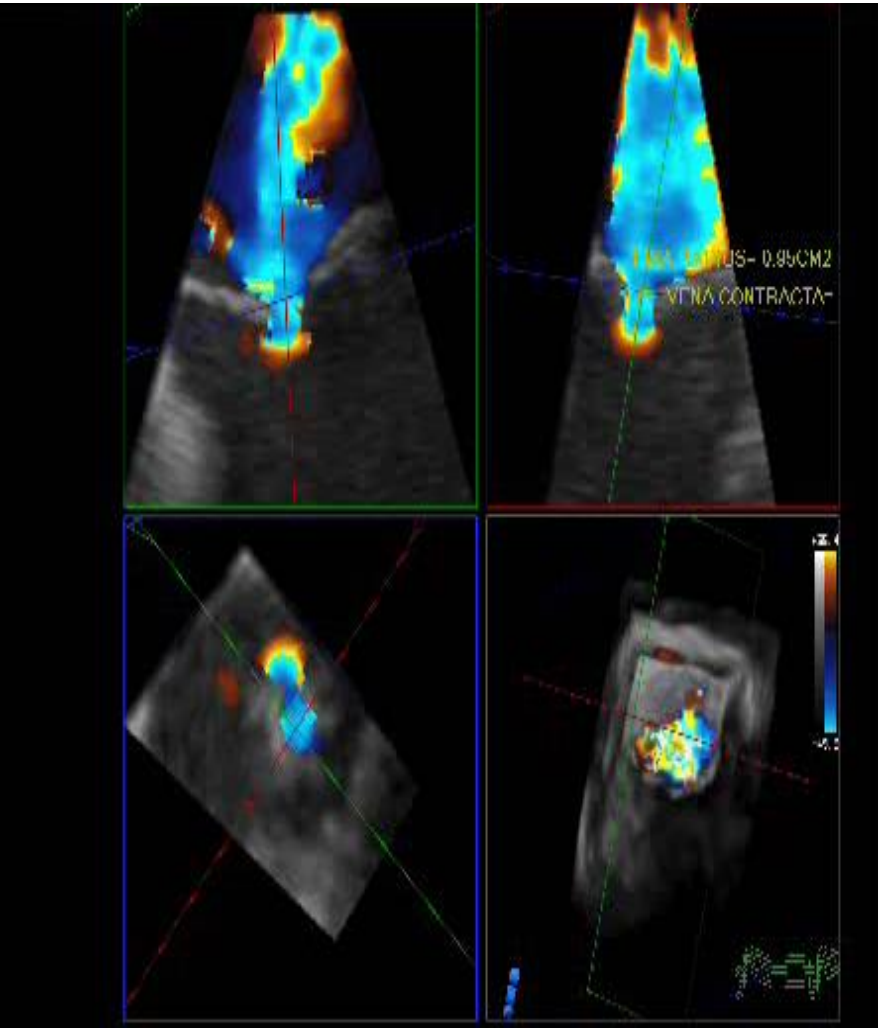

FR 7Hz
11cm
3D Beats 1
M4
3D
3D 0%
3D 40dB
0 0 180
JPEG
PAT T: 37.0C
TEE T: 38.1C
73 bpm
Lossy

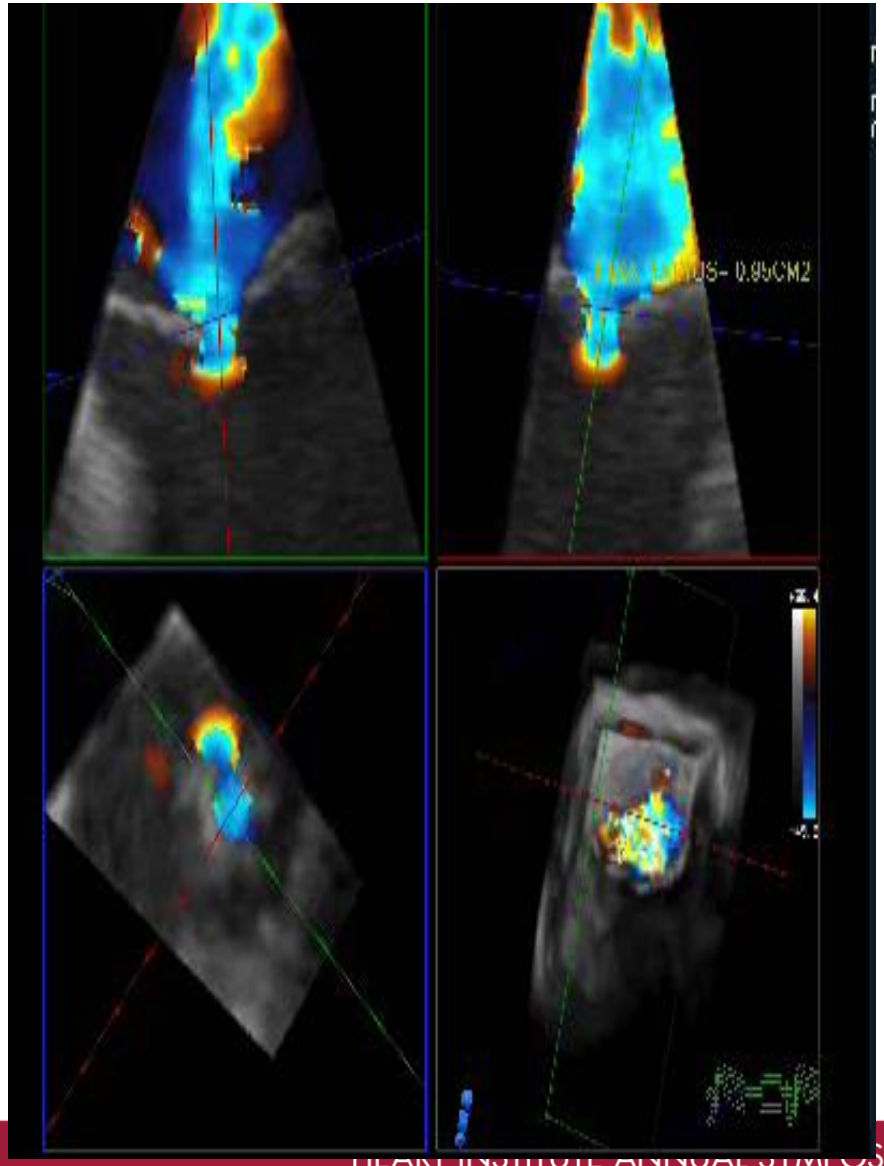

M4 M4
+51.0
0 112 180
-51.0
cm/s
JPEG
PAT T: 37.0C
TEE T: 39.5C
61 bpm
Los


FR 14Hz
14cm
2D
82%
C 50
P Off
Gen
CF
59%
4.4MHz
WF High
Med
M4 M4
+56.3
0 0 180
-56.3
cm/s
JPEG
PAT T: 37.0C
TEE T: 38.6C
62 bpm
Lossy


MR Alias Vel 44.0 cm/s
MR Radius 1.0 cm
MR Flow Rate 276.3 ml/s
T: 37.0C
T: 39.3C


FR 13Hz
14cm
2D
82%
C 50
P Off
Gen
CF
59%
4.4MHz
WF High
Med
CW
40%
2.5MHz
WF 225Hz
MR VTI
Vmax 487 cm/s
Vmean 332 cm/s
Max PG 95 mmHg
Mean PG 53 mmHg
VTI 171 cm
MR VTI
Vmax 484 cm/s
Vmean 326 cm/s
Max PG 94 mmHg
Mean PG 52 mmHg
VTI 164 cm
MR ERO 0.57 cm²
MR Volume 97 ml
-6.0
-4.0
-2.0
m/s
32
-2.0
PAT T: 37.0C
TEE T: 39.5C
75mm/s
Lossy



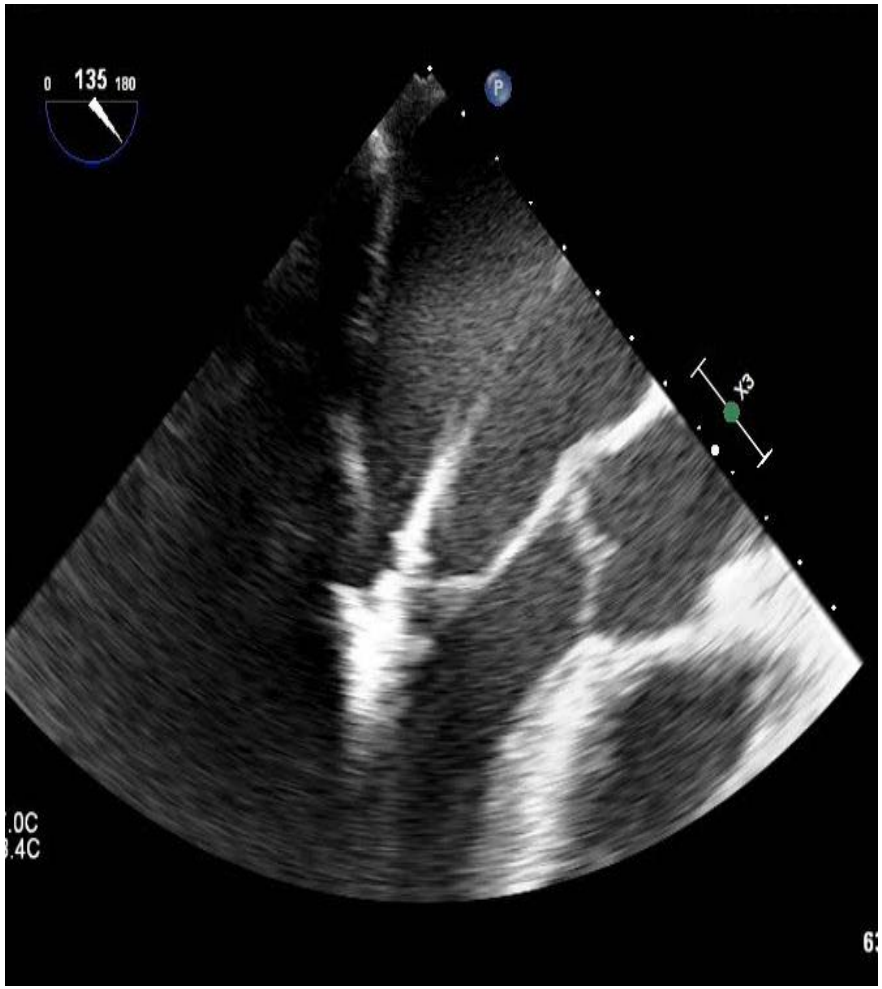
3d cropping data

Vena contracta= 0.8cm
Pisa radius= 0.95

# Intra op tee

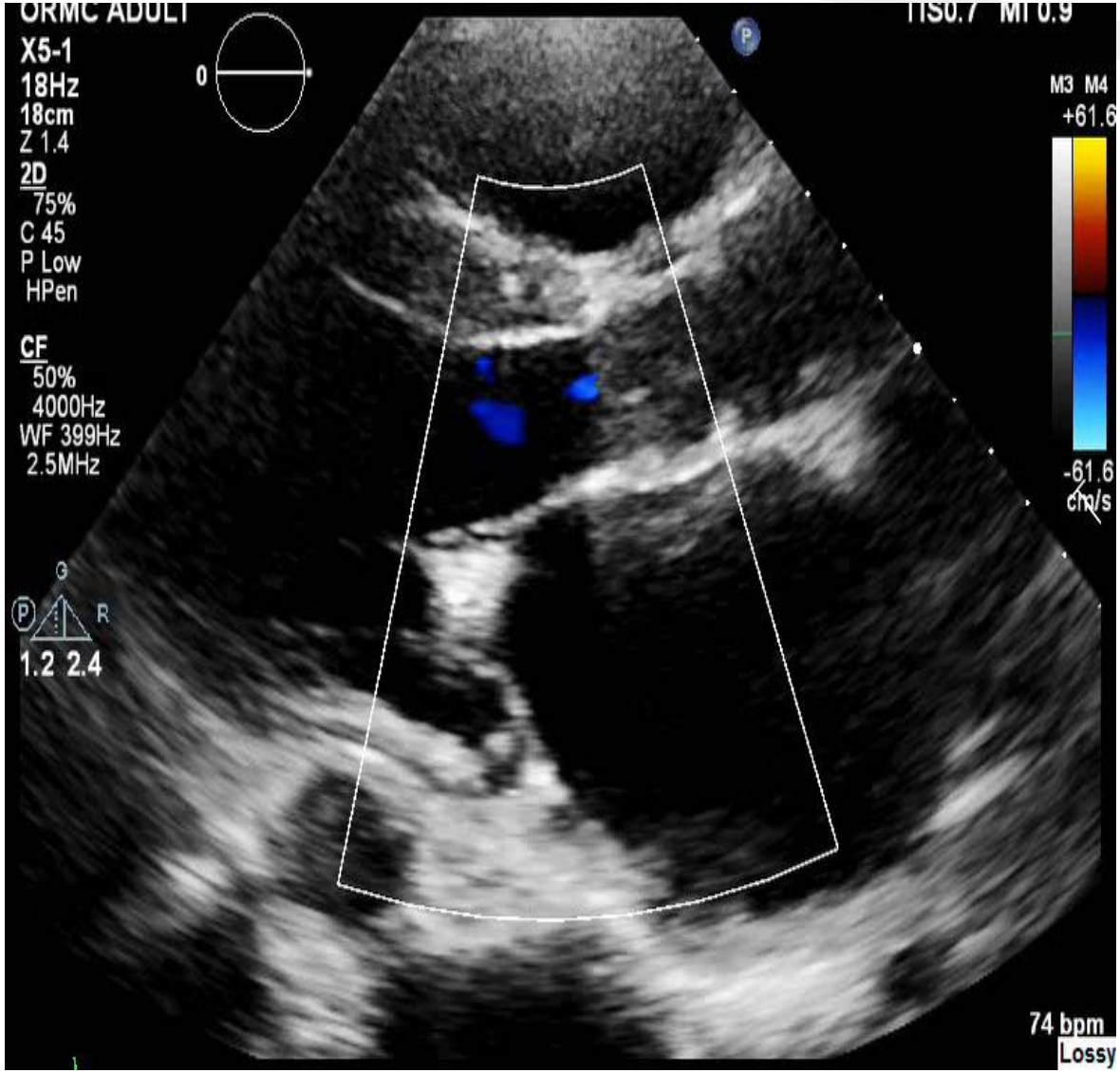

3D Beats 1
M4
62 bpm
Lossy

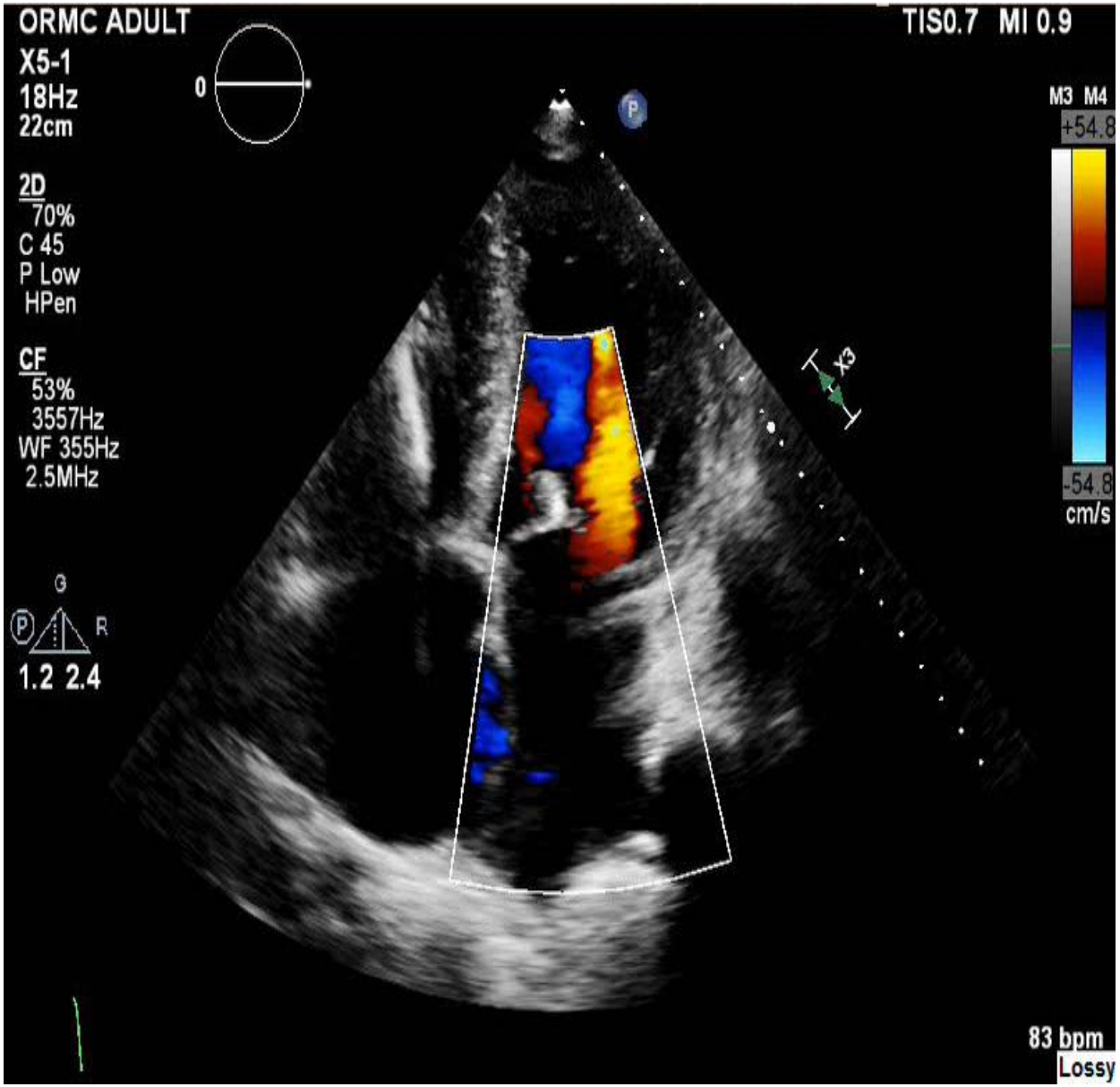

X7-2t
8Hz
13cm
3D Beats 1
0
135
180
Live 3D
2D / 3D
% 55 / 44
C 51 / 30
Gen
PAT T: 37.0C
TEE T: 38.5C


0 135 180
P
x3

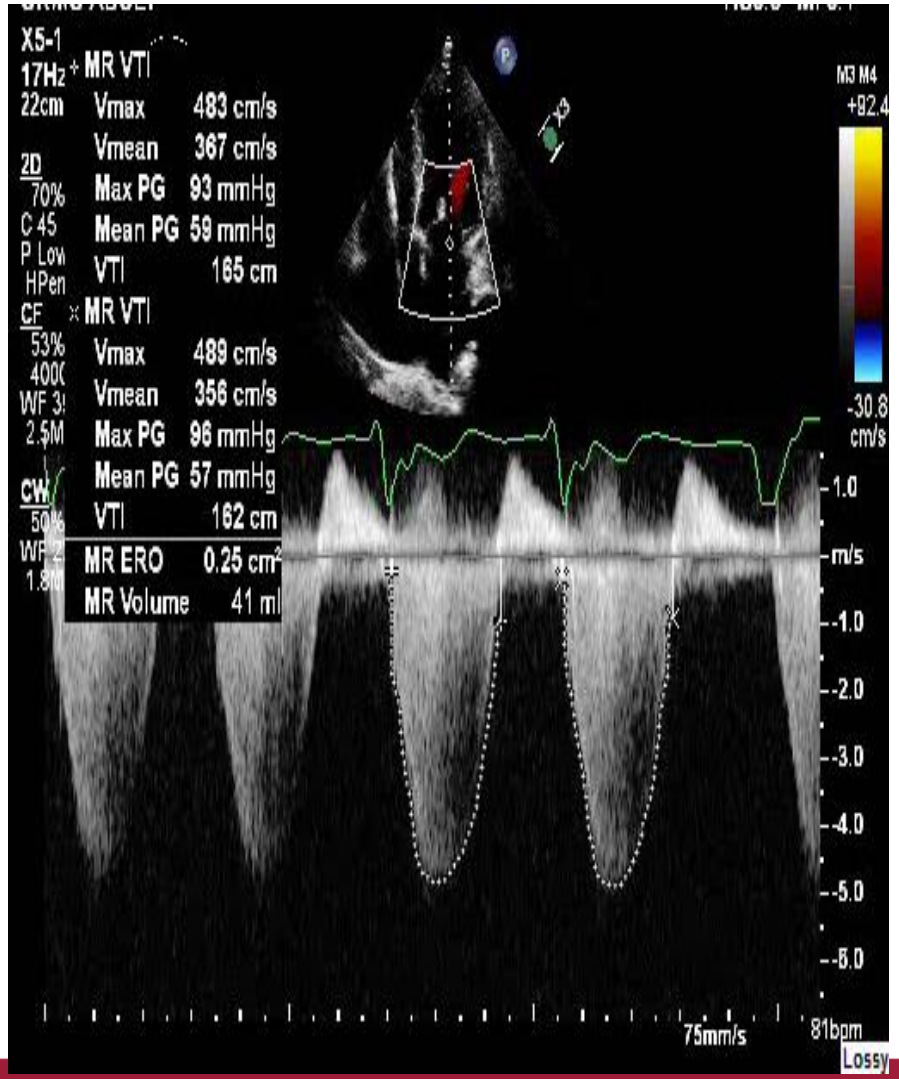

3D Beats 1
0 125 180

# Post clip tte


ORMC ADULT
X5-1
18Hz
18cm
Z 1.4
2D
75%
C 45
P Low
HPen
CF
50%
4000Hz
WF 399Hz
2.5MHz
1.2 2.4
M3 M4
+61.6
-61.6
cm/s
74 bpm
Lossy


ORMC ADULT
X5-1
18Hz
22cm
2D
70%
C 45
P Low
HPen
CF
53%
3557Hz
WF 355Hz
2.5MHz
1.2 2.4
TIS0.7 MI 0.9
M3 M4
+54.8
-54.8
cm/s
83 bpm
Lossy


X5-1
17Hz
22cm
Z 2.0
2D
70%
C 45
P Low
HPen
CF
53%
4000Hz
WF 399Hz
2.5MHz
M3 M4
+82.4
-30.8
cm/s
MR Radius 0.8 cm
MR Alias Vel 30.8 cm/s
MR Flow Rate 123.8 ml/s
77bpm
Lossy


X5-1
17Hz
22cm
2D
70%
C 45
P Low
HPen
CF
53%
WF 399Hz
2.5MHz
CW
50%
MR VTI
Vmax 483 cm/s
Vmean 367 cm/s
Max PG 93 mmHg
Mean PG 59 mmHg
VTI 165 cm
MR VTI
Vmax 489 cm/s
Vmean 356 cm/s
Max PG 96 mmHg
Mean PG 57 mmHg
VTI 162 cm
MR ERO 0.25 cm²
MR Volume 41 ml
M3 M4
+82.4
-30.8
cm/s
1.0
m/s
-1.0
-2.0
-3.0
-4.0
-5.0
-6.0
75mm/s
81bpm
Lossy

# Procedure Results

| | Pre clip | Post Clip | Severe MR |
|---|---|---|---|
| ERO | 0.57 cm2 | 0.25 cm2 | >0.35 cm2 |
| MRV | 97 ml | 41 ml | >60 ml |
| Vena Contracta | 0.8 cm | 0.58 cm | 0.7 cm |

# Mitral Valve Disease and Mitra Clip

Anatomy and Mitral Regurgitation

Treatment Options

Mitra Clip technology

Clinical Trials

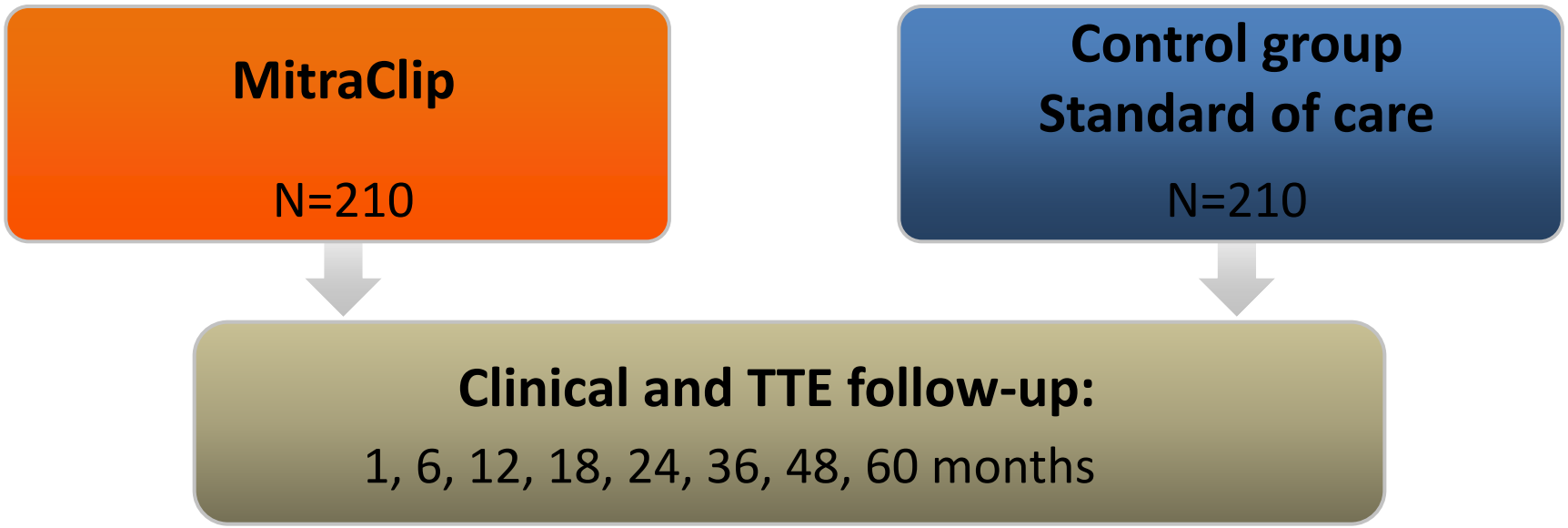
Case Examples

**Future Technologies**

# COAPT : Trial design

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

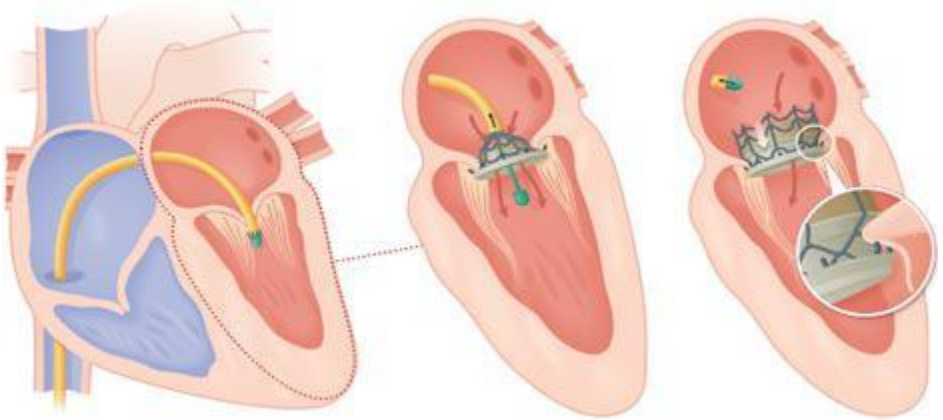
Randomize 1:1




Protocol conditionally approved by FDA July 26, 2012

# Future Technologies

Trans septal – CardiAQ with atrial and ventricular flanges



Trans apical – Tendyne with ventricular anchor

# THANK YOU