Percutaneous mitral valve leaflet repair for mitral regurgitation

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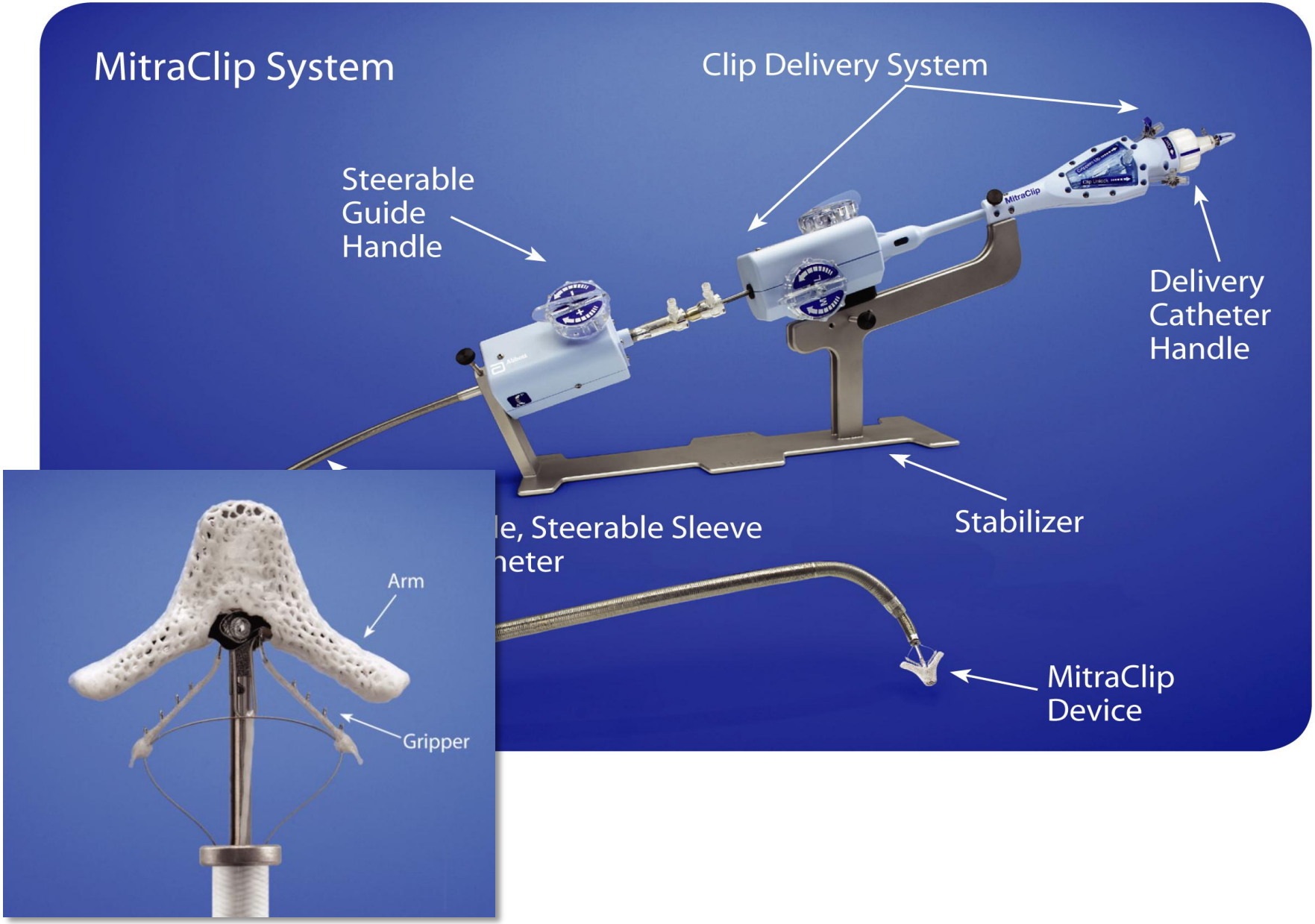
Percutaneous mitral leaflet repair: MitraClip and Beyond

- Mitraclip
  - How does it work
  - What is the evidence
  - Who is the ideal candidate
- What is beyond Mitraclip


MitraClip System
Clip Delivery System
Steerable
Guide
Handle
Delivery
Catheter
Handle
Stabilizer
MitraClip
Device
Arm
Gripper

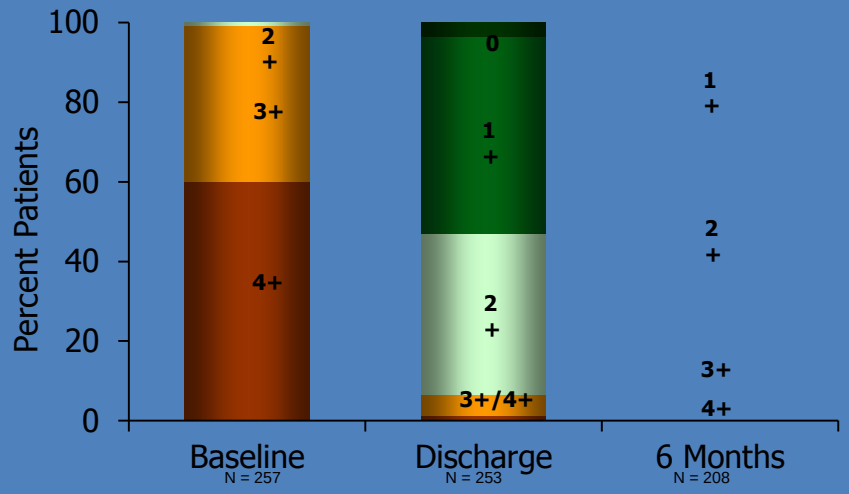
Worldwide Clinical Experience

Study	Population	N*
EVEREST I (Feasibility)	Feasibility patients	55
EVEREST II (Pivotal)	Pre-randomized patients	60
EVEREST II (Pivotal)	Non-randomized patients (High Risk Study)	78
EVEREST II (Pivotal)	Randomized patients (2:1 Clip to Surgery)	279 184 Clip 95 Surgery
REALISM (Continued Access)	Non-randomized patients	571
ACCESS Europe	Non-randomized patients	529
Commercial Use	Commercial patients	1,658
Total		**3,135 +95 surgery**

*Data as of 4/20/2011. Source: Abbott Vascular

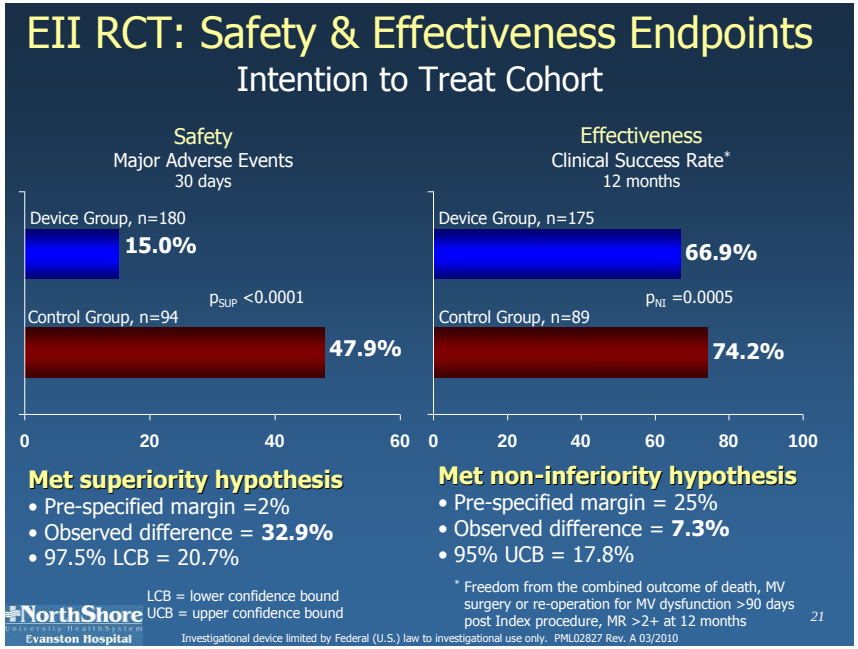
Available evidence on Mitraclip

- EVEREST
  - In selected patients (mainly with DMR), Mitraclip is safer than surgery, but less efficacious
- ACCESS-EU
  - The procedure remains safe also in high risk patients, with efficacy both in DMR and FMR
- HRR and REALISM registry



EVEREST Trial: MitraClip is less invasive than surgery with efficacy in selected patients

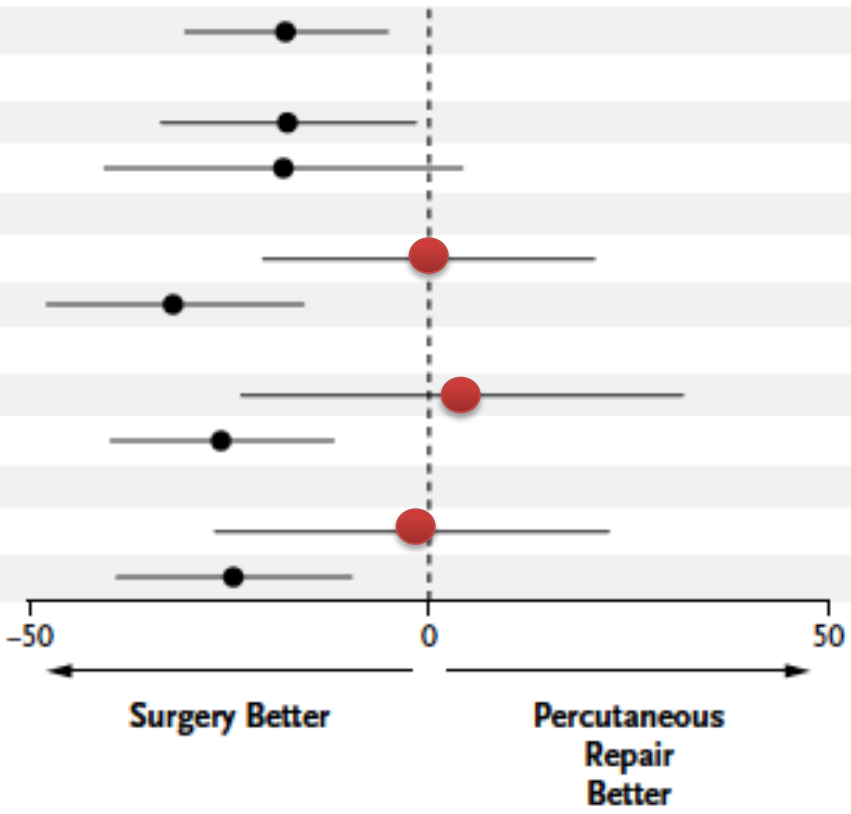
- Enrolled only surgical candidates
- Effect of learning curve
- Few FMR patients



Feldman et al. NEJM 2011

Everest surgery vs mitraclip

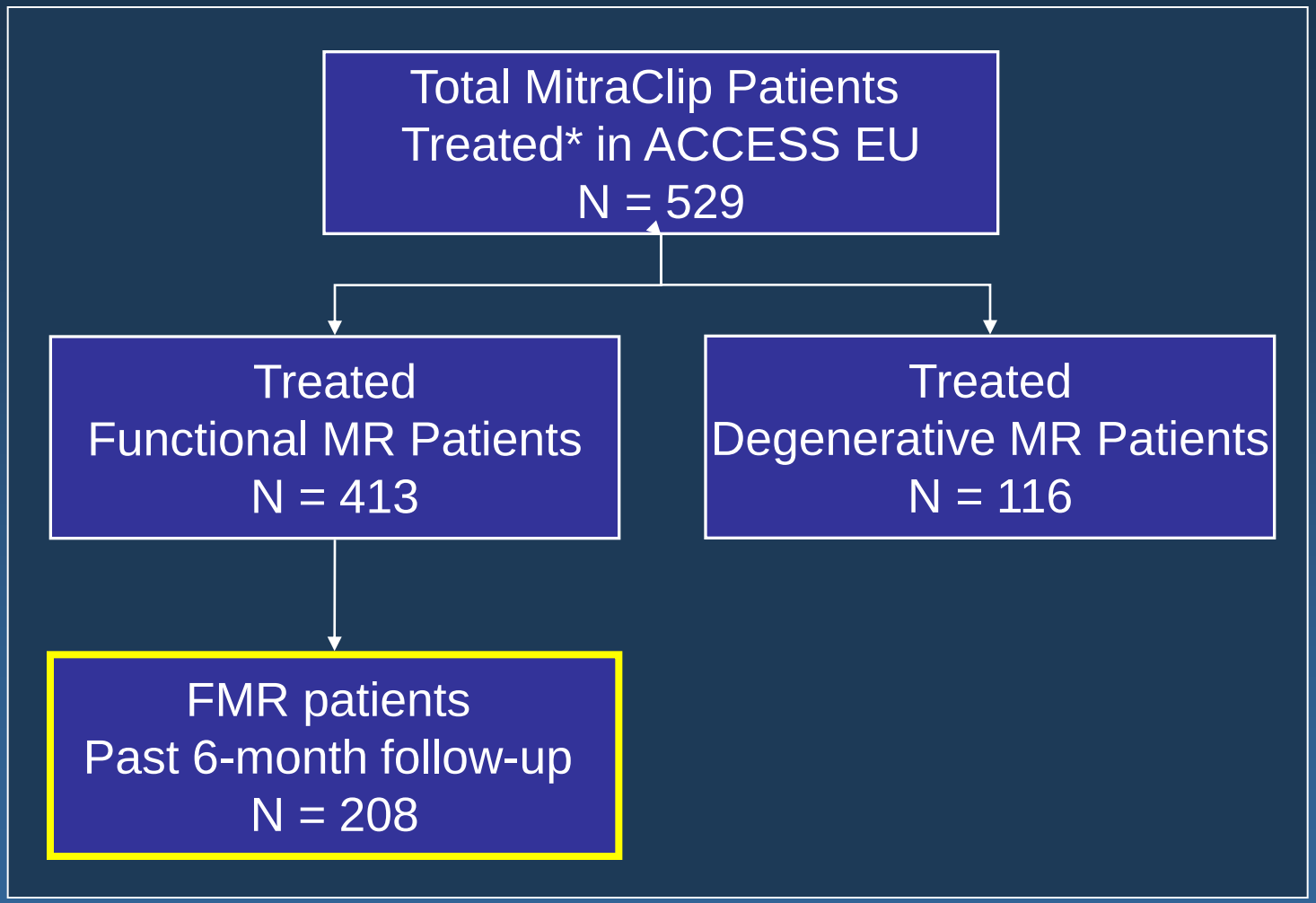
Subgroup	Percutaneous Repair	Surgery	P Value for Interaction
	no. of events/total no. (%)		
All patients	100/181 (55)	65/89 (73)	
Sex			0.97
Male	63/114 (55)	43/59 (73)	
Female	37/67 (55)	22/30 (73)	
Age			0.009
≥70 yr	52/86 (60)	23/38 (61)	
<70 yr	48/95 (51)	42/51 (82)	
MR			
Functional	26/48 (54)	12/24 (50)	0.02
Degenerative	74/133 (56)	53/65 (82)	
LVEF			0.06
<60%	35/68 (51)	15/28 (54)	
≥60%	64/111 (58)	50/61 (82)	



Feldman et al NEJM 2011

Analysis Cohort

Functional MR Analysis Cohort



* Treated as April 12, 2011

Baseline Demographics and Co-Morbidities

ACCESS-EU and Functional MR Analysis Cohort

Demographics and Co-morbidities	ACCESS EU All MitraClip Patients N=529	Functional MR Analysis Cohort N=208
Age (Mean ± stdev)	74 ±10	71 ± 9
Logistic EuroSCORE, %		
Mean ± SD	21 ±16	23 ±17
EuroSCORE ≥ 20%	32%	32%
Male Gender, %	65%	71%
Coronary Artery Disease, %	65%	66%
Previous Cardiovascular Surgery, %	38%	40%
Myocardial Infarction, %	32%	35%
Cerebro-vascular Disease, %	13%	13%
Previous stroke, %	6%	4%
Atrial Fibrillation, %	68%	64%

Baseline Demographics and Co-Morbidities

ACCESS-EU and Functional MR Analysis Cohort

Demographics and Co-morbidities	ACCESS EU All MitraClip Patients N=529	Functional MR Analysis Cohort N=208
Mitral Regurgitation Grade ≥ 3+, (%)	98%	99%
NYHA Functional Class III or IV, (%)	85%	85%
Ejection Fraction < 40%, (%)	54%	68%
Functional MR, (%)	78%	100%
Ischemic	33%	49%
Non-ischemic	45%	51%
Degenerative MR, (%)	22%	0%

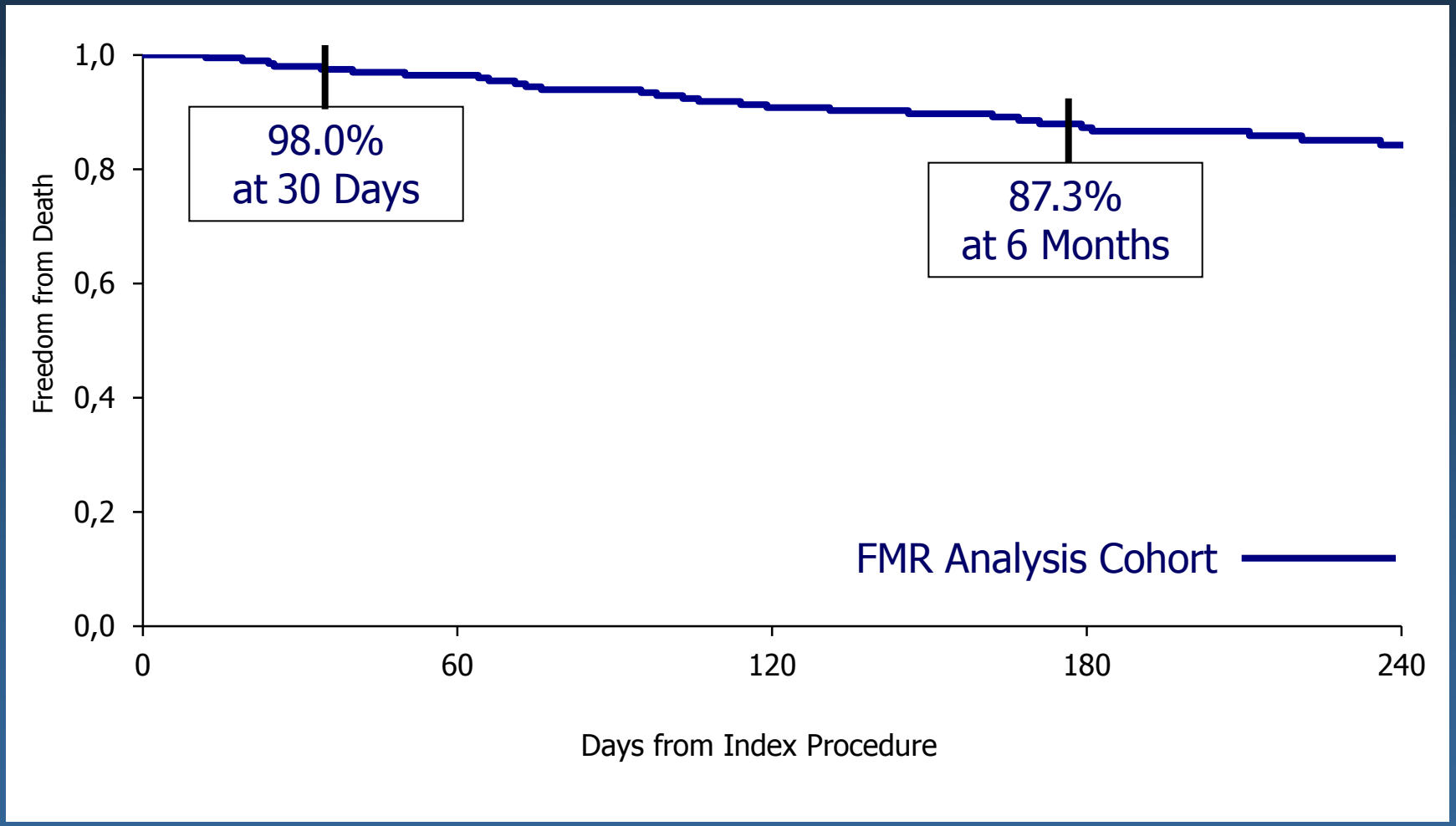
Procedure, Post-Procedure and Discharge Results

Functional MR Analysis Cohort

Post-procedure and Discharge data	Functional MR Analysis Cohort N=208
Procedural data, (mean ± stdev)	
Procedure time, (min)	110 ±70
Contrast volume, (ml)	21 ±40
Fluoroscopy duration, (min)	45 ±119
Post-procedural data, (mean ± stdev)	
ICU/CCU duration, (days)	2.4 ±4.3
Length of hospital stay, (days)	7.5 ±6.7
Discharge to, (%)	
Home	79%
Skilled nursing home/nursing home	19%
Died prior to discharge	2%

Kaplan-Meier Freedom from Death

Functional MR Analysis Cohort

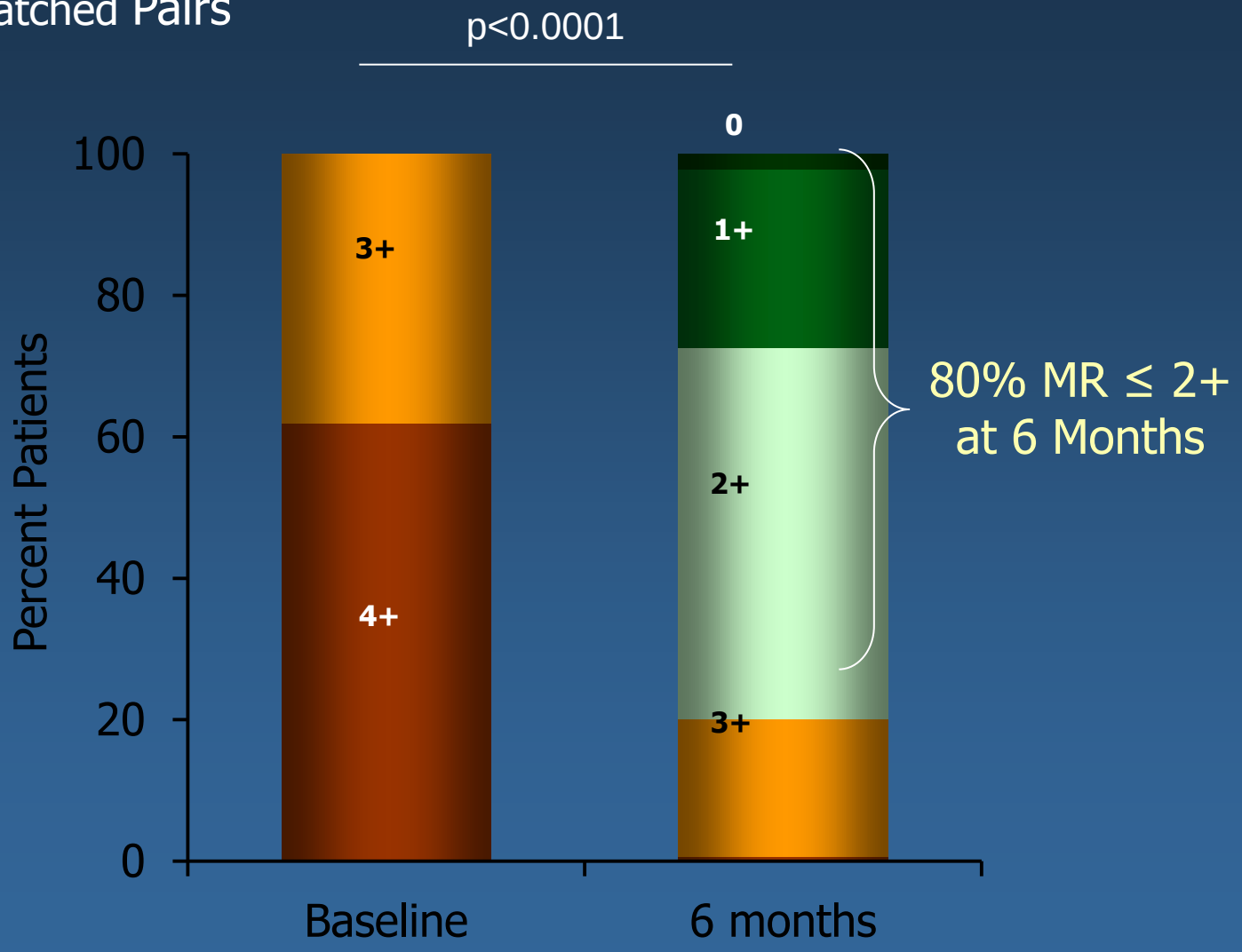


At Risk:	0 Days	30 Days	6 months
Device N	208	195	137

Mitral Regurgitation Grade

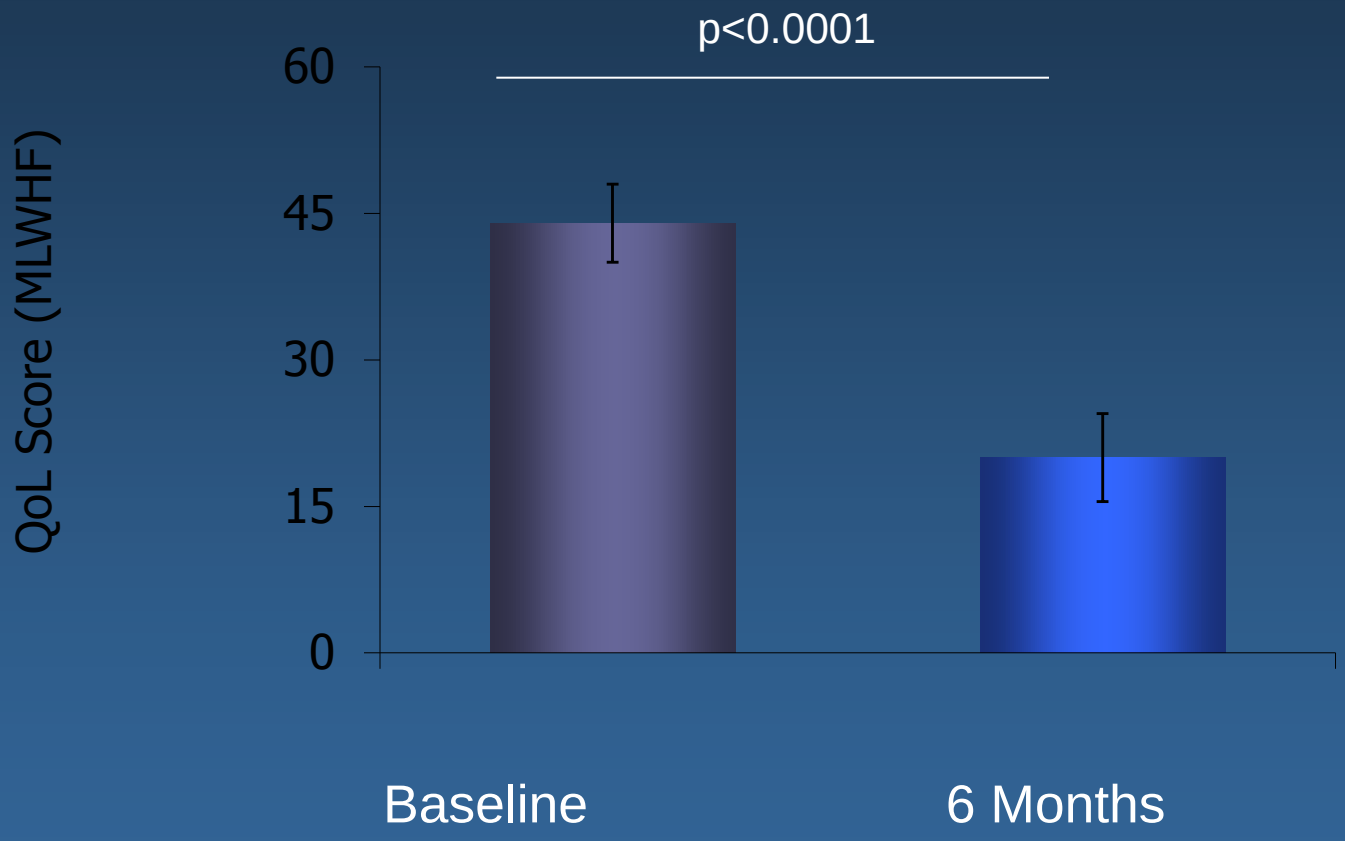
Functional MR Analysis Cohort (matched data)

N = 139 Matched Pairs



Quality of Life Score (MLWHF)

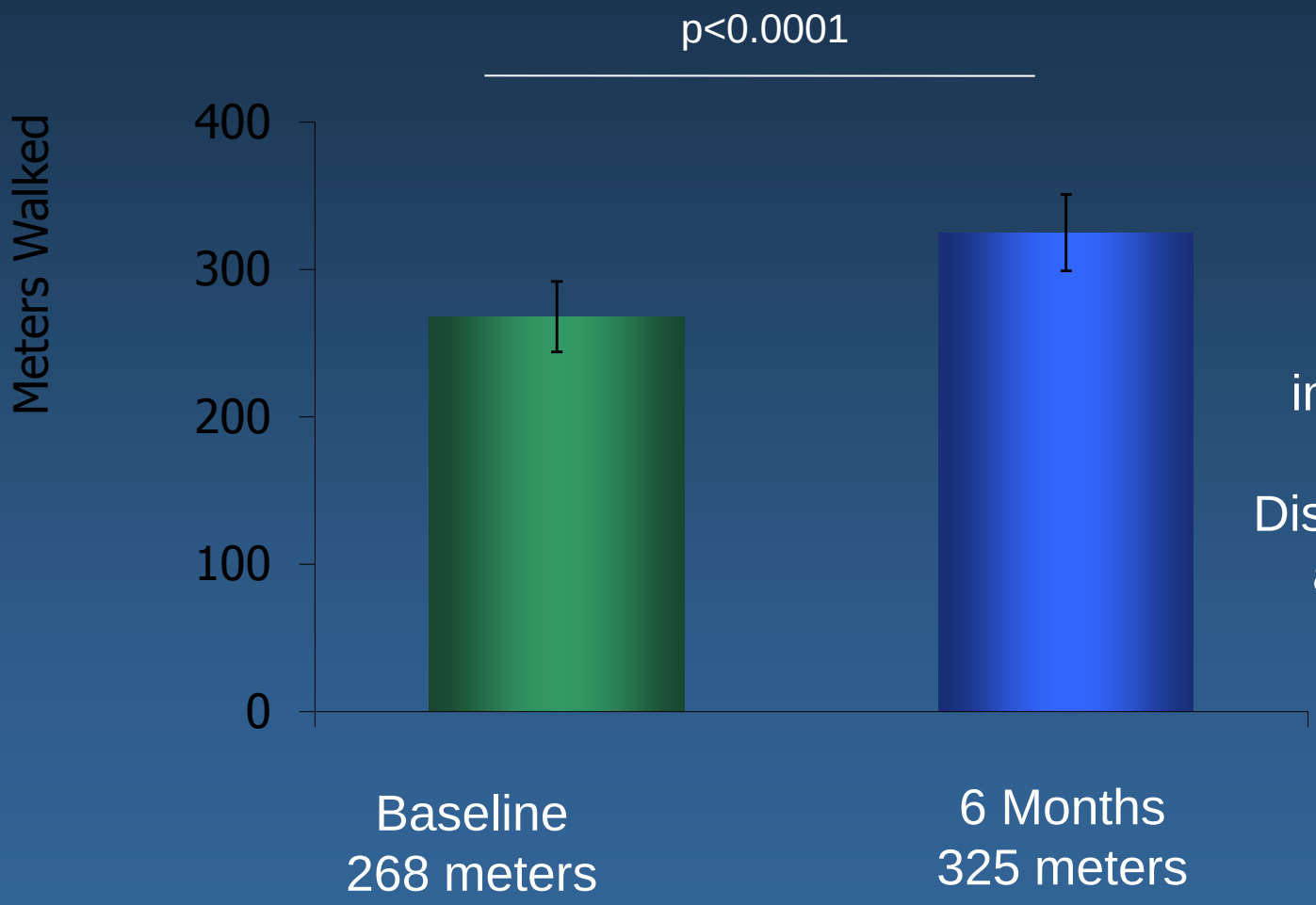
Functional MR Analysis Cohort (matched data)



N = 98 Matched Pairs

Data presented as mean ± 95% confidence interval

6 Minute Walk Test (6MWT)
Functional MR Analysis Cohort (matched data)



57 meter improvement in 6MWT Distance walked at 6 months

N = 93 Matched Pairs

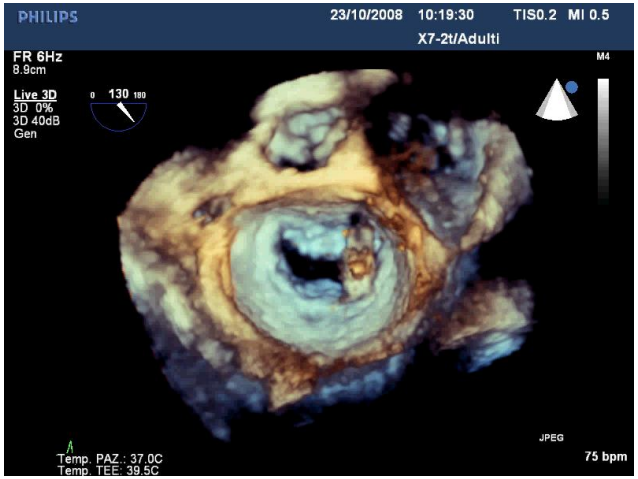
Data presented as mean ± 95% confidence intervals

Patient selection – a teamwork effort

- Confirm severity of MR + evaluate symptoms
- Analize risk of surgery and evaluate life-expectancy and quality of life
- Assess feasibility of Mitraclip.
- DMR vs FMR

Mitraclip for DMR

- In experienced centers, DMR is treated with surgical repair at low risk, long term durability of repair is achieved in the majority of patients
  - 50% of Euro Heart Survey patients were not referred to surgery (Mirabel EHJ 2007)
  - Age and comorbidity increase the risk of surgery (STS database, 2010)
  - Surgery is not associated with improved QoL in most elderly patients (Maisano et al EJCTS 2009)



Mitraclip for FMR

- Surgical treatment of FMR is associated with
  - High hospital mortality
  - High recurrence rate
  - Long hospital stay
  - Unproven survival benefit
- Mitraclip for FMR
  - Procedure more simple than for DMR
  - Improvement of symptoms at low risk
  - HRR suggests survival benefit
  - Failure does not modify the surgical option

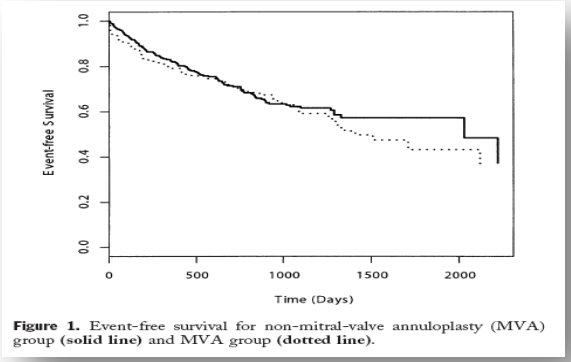
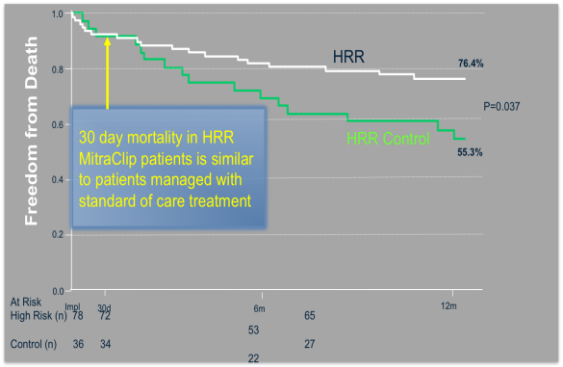


Figure 1. Event-free survival for non-mitral-valve annuloplasty (MVA) group **(solid line)** and MVA group **(dotted line)**.



Retrospective analysis of 143 symtomatic pts with severe FMR

-Clinical evaluation
-TEE +/- dobutamine
- Coronary Angiogram
-Multimodality screening process

From 2000 to 2011

Surgery

91 pts (63.6%)

- **49% ischemic**
- **51% Idiopathic**

All surgical pts received undersized annuloplasty with a complete ring, rigid or semirigid;

EVEREST criteria and beyond (central MR with a basal area >4 cm^2, coaptation length of at least 2 mm, coaptation depth <11 mm)

From 2008 to 2011

MitraClip

52 pts (36.4%)

- **71% ischemic**
- **29% Idiopathic**

Associated procedures:
CABG 35%
Tricuspid Repair 25%
AF ablation 26%

Results: baseline characteristics

	Surgery	MitraClip	p-value
Age (years)	64.9±9.8	68.4±9.2	0.04
Female gender	23.1%	17.3%	0.4
Previous AMI	37.4%	59.6%	0.01
Log EuroScore (%)	10.2±7.4	21.9±14.8	<0.0001
Previous cardiac surgery	9.9%	23.1%	0.03
Coronary Artery Disease	48.3%	71.2%	0.03
Atrial Fibrillation	32%	17.3%	0.01
Chronic Renal Failure	17.6%	57.7%	<0.0001
COPD	3.3%	21.2%	0.0005
Cerebrovascular disease	6.6%	9.6%	0.5
Diabetes	26.9%	9.9%	0.007
NYHA functional class			
I	4.4%	0%	0.1
II	28.6%	15.4%	0.3
III	51.6%	63.3%	0.2
IV	15.4%	17.3%	0.2

Baseline echocardiography

	Surgery	MitraClip	p-value
LV Ejection fraction (%)	32.1±8.6%	27.6±10.0	0.006
LVEDD (mm)	66.4±8.5	70.2±7.7	0.01
LVESD (mm)	52.1±7.9	55.5±8.6	0.05
sPAP (mmHg)	43.9±12.4	46.9±15.4	0.2
TR 3-4+	17.1%	23.6%	0.009
Tented Area (cm^2)	2.8±1.2	2.9±1.0	0.5
Coaptation Depth (cm)	1.2±0.6	1.3±0.3	0.2
Septolateral mitral diameter (mm)	31.7±13.6	37.2±4.7	0.02
Intercommissural mitral diameter (mm)	32.4±15.3	41.1±6.0	0.001

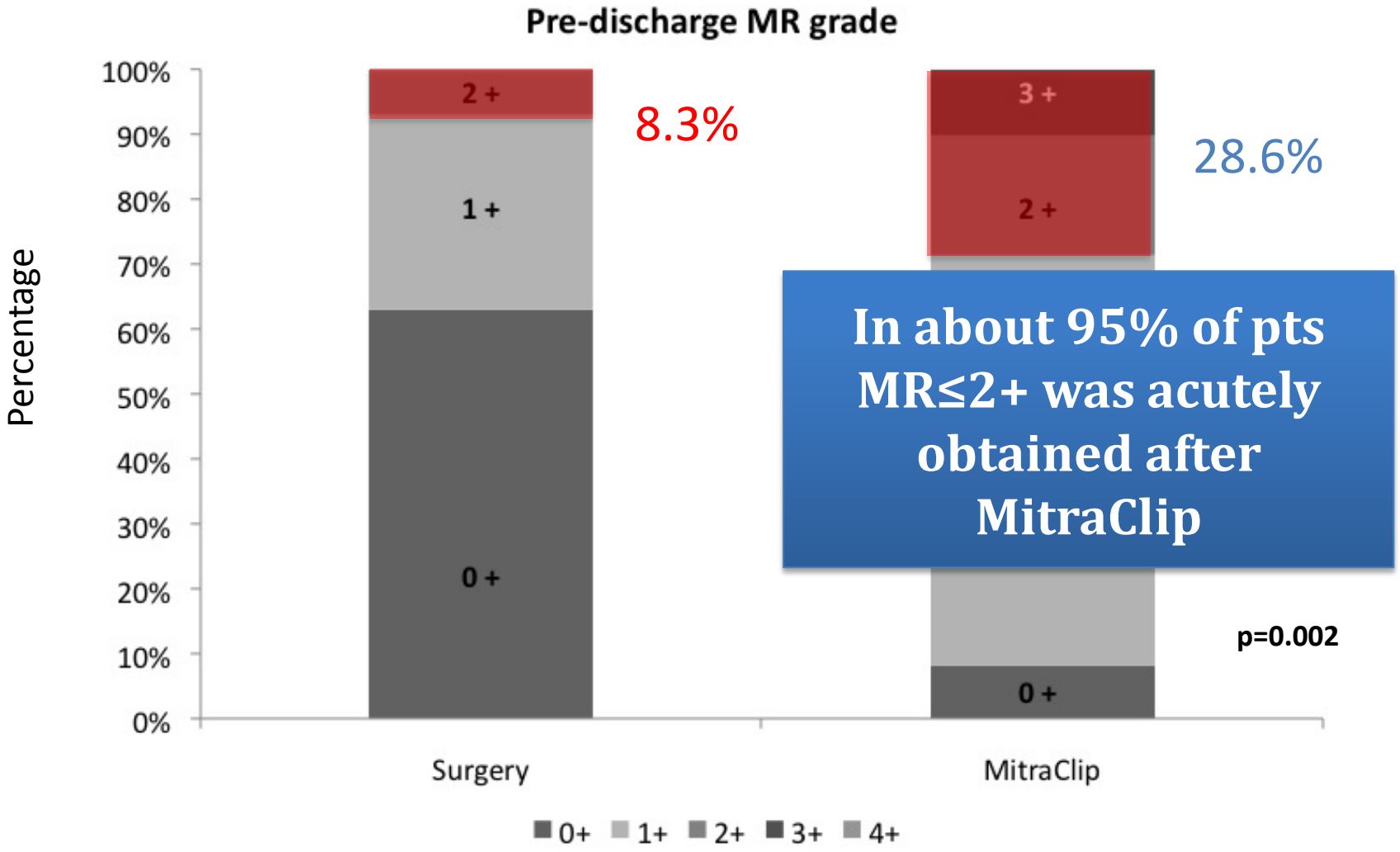
Perioperative outcomes

	Surgery	MitraClip	p-value
In-hospital mortality	6.6%	0%	0.01
Acute Kidney Injury	30.7%	30.7%	1
Need for CVVH	2.2%	5.8%	0.2
Perioperative IABP	65.9%	13.5%	<0.0001
LCOS	3.3%	7.7%	0.2
Major Infection/Sepsis	16.5%	3.8%	0.02
Stroke	2.2%	0%	0.2
AMI	0%	0%	na
Length of stay (days)	15.8±15.1	9.6±16.3	0.02
Discharged home	0%	61.2%	<0.0001

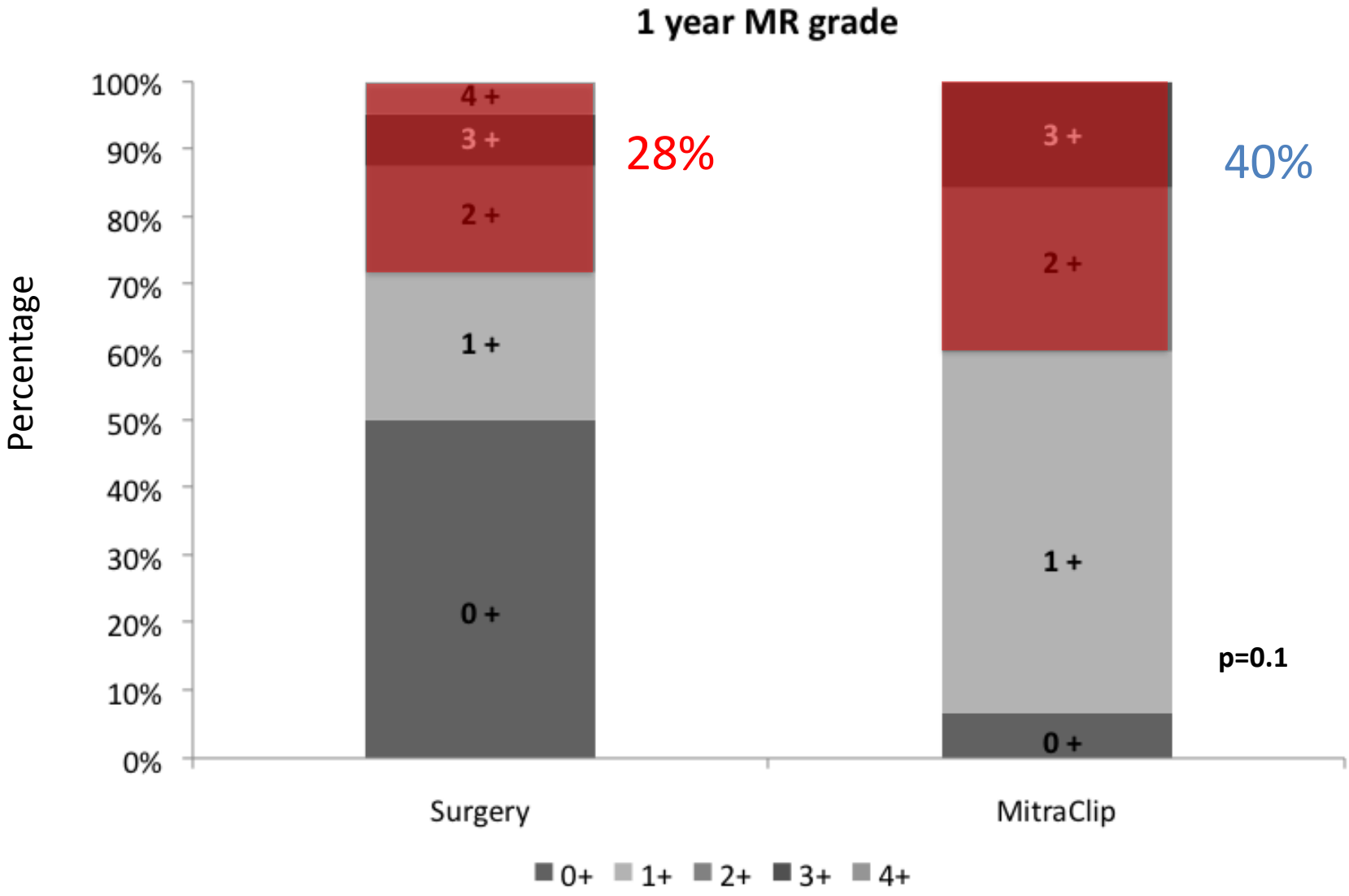
1/52 MitraClip pt was converted to surgery

1 clip in 11 pts (21.2%), 2 clips in 38 pts (73.1%) , 3 clips in 3 pts (5.7%)

Residual MR≥2+ at discharge



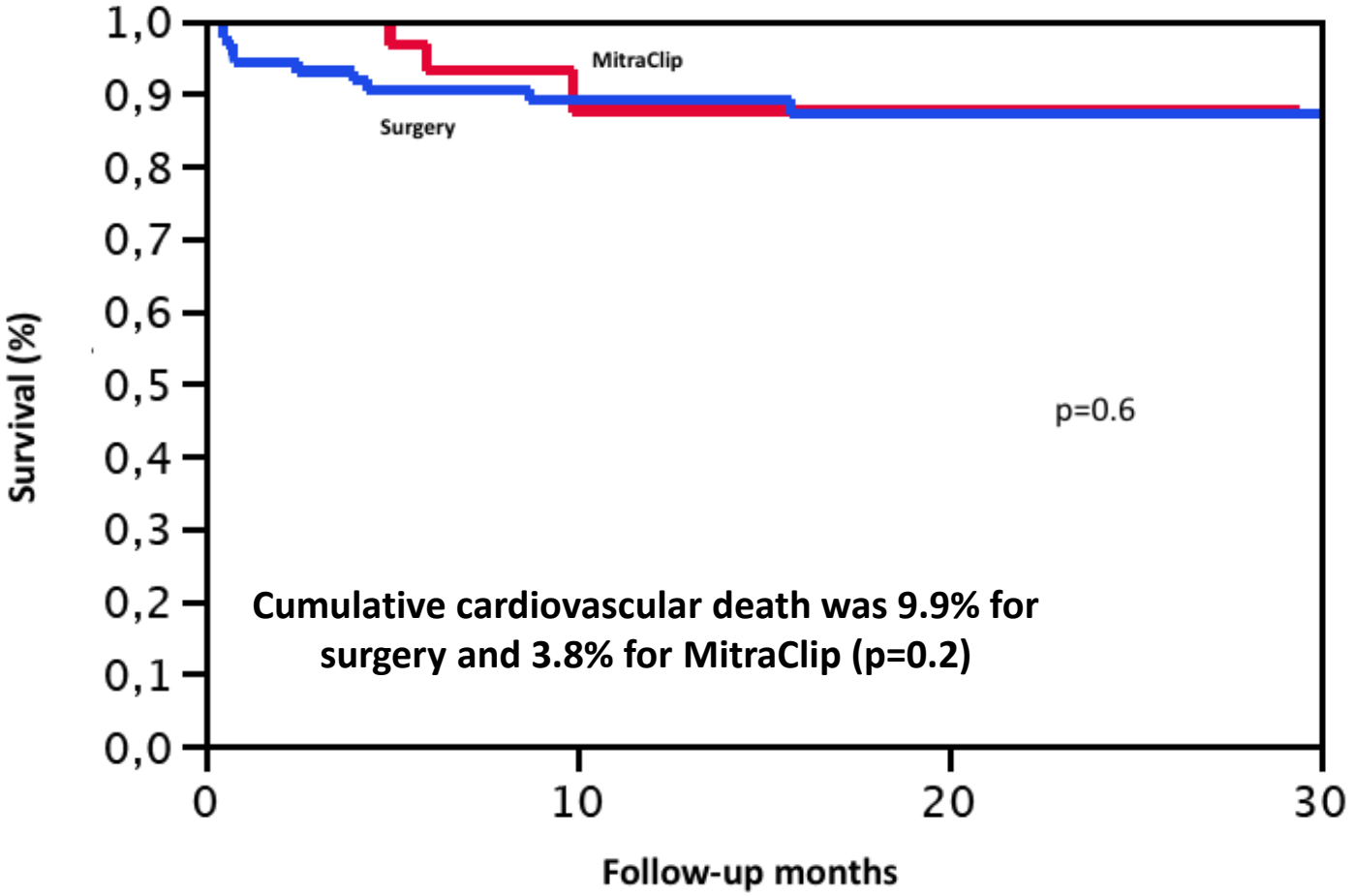
Residual MR≥2+ at 1 year



Follow-up

29.7±28 months for surgery

9.6±7.7 months for MitraClip



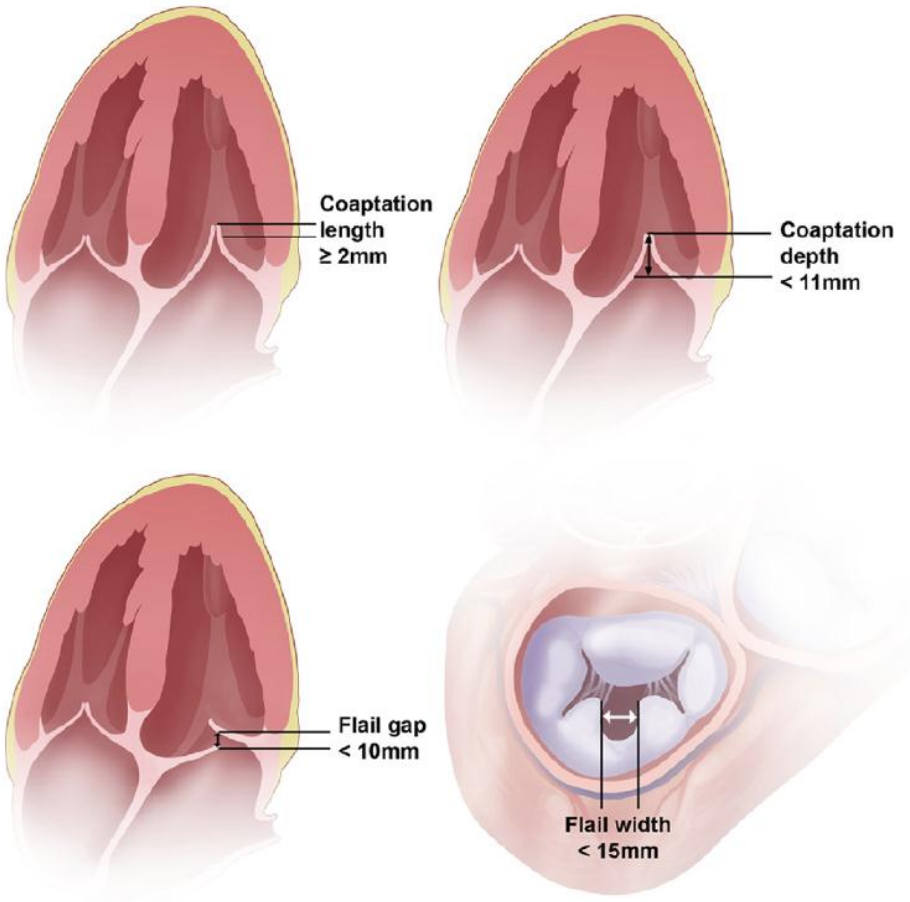
Actuarial survival at 1 year:

Surgery	**88.9±3,5%**
MitraClip	**87.5±7%**

MitraClip anatomical patient selection considerations

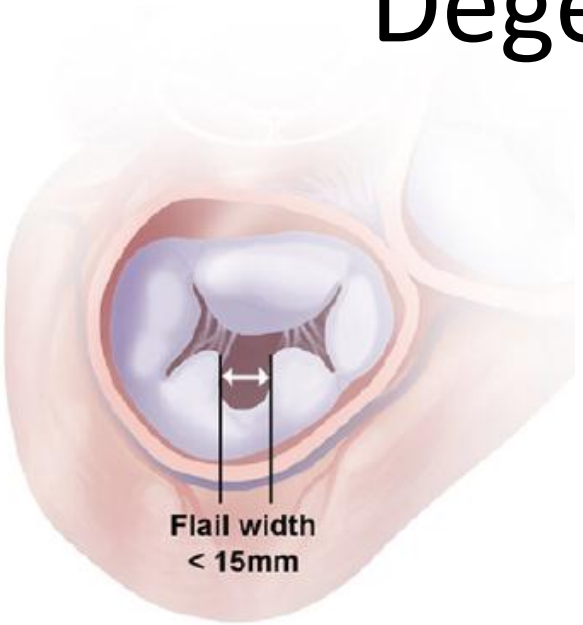
Recommended criteria[1]

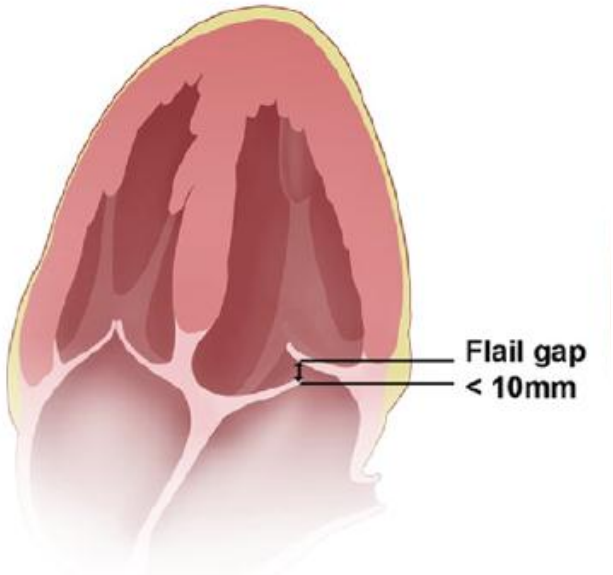
- Moderate to severe MR (Grade 3 or more out of 4 grades)
- Pathology in A2-P2 area
- Coaptation length > 2 mm (depending on leaflet mobility)
- Coaptation depth < 11 mm
- Flail gap < 10 mm
- Flail width < 15 mm
- Mitral valve orifice area > 4cm^2 (depending on leaflet mobility)
- Mobile leaflet length > 1 cm

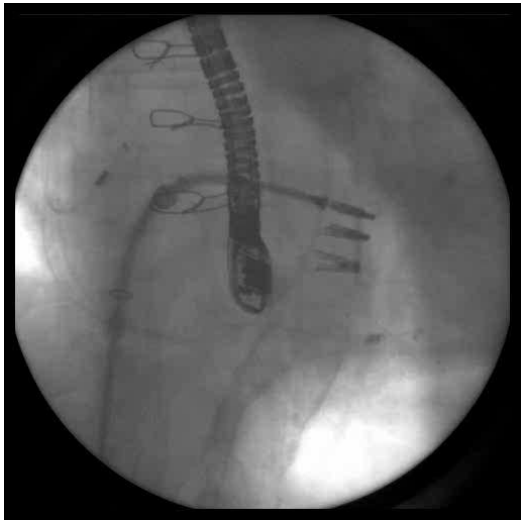


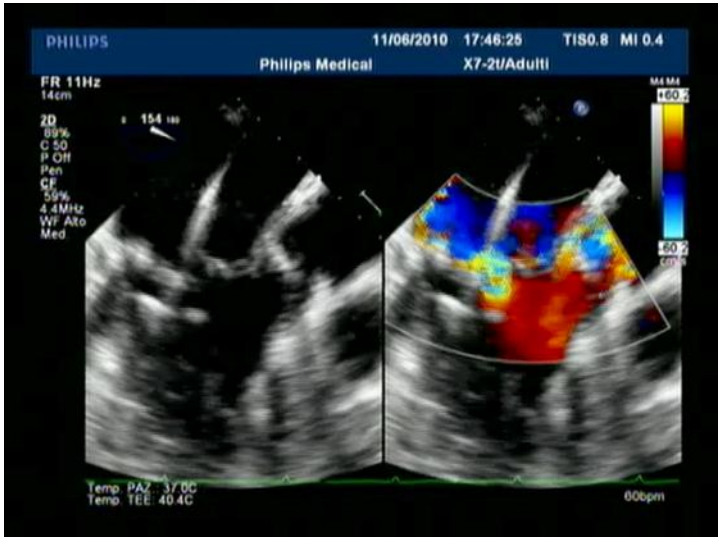
1. The current patient considerations are based on EVEREST II and commercial European experience to date. The MitraClip Patient Selection Coniderations document has been endorsed by Expert Opinion (Crossroads institute).

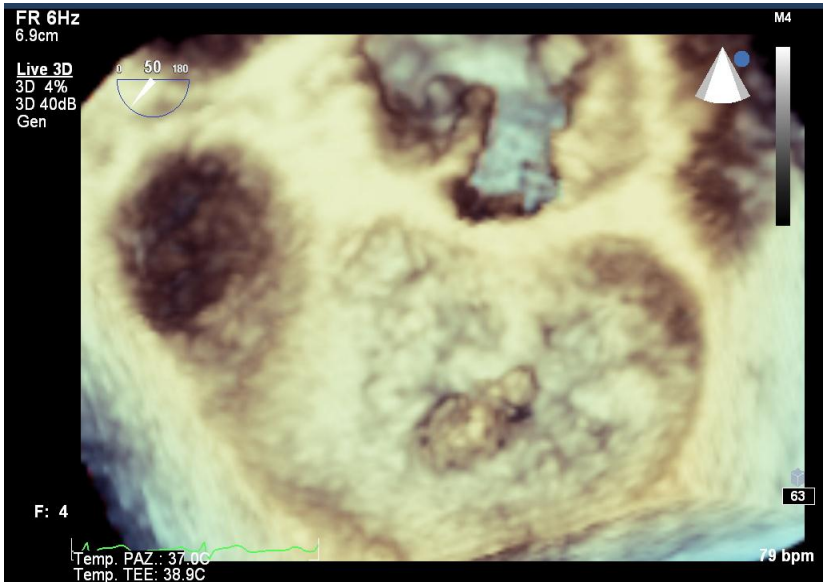
Degenerative MR

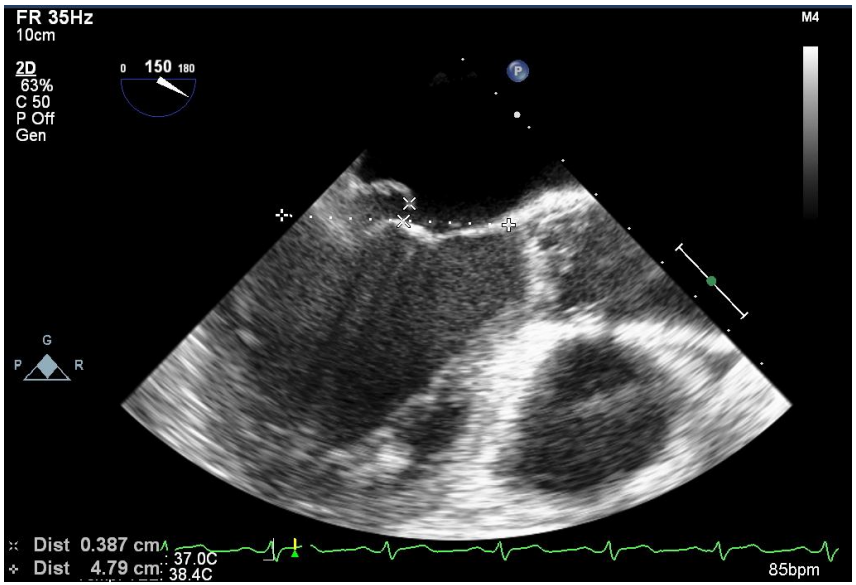


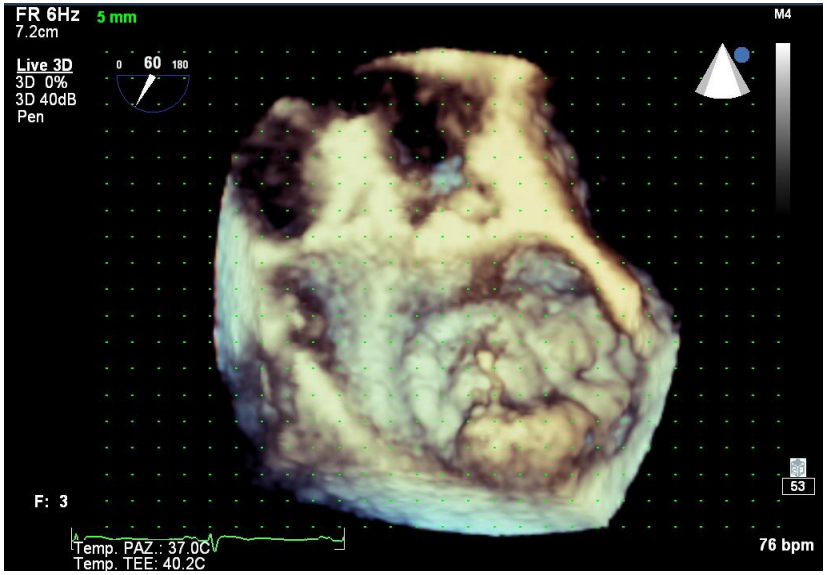


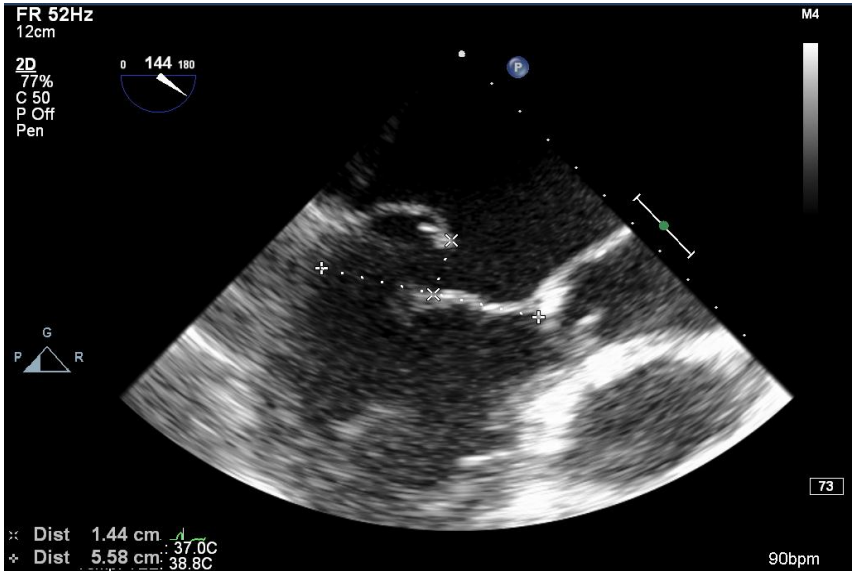




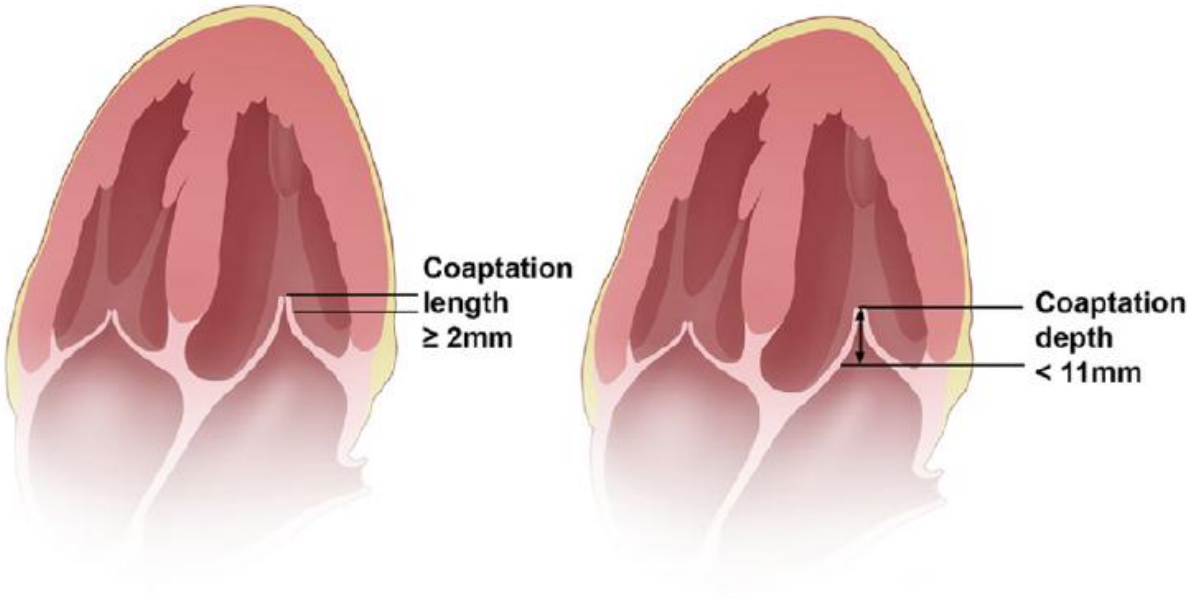

FR 6Hz
6.9cm
M4
Live 3D
3D 4%
3D 40dB
Gen
0 50 180
F: 4
63
Temp. PAZ.: 37.0C
Temp. TEE: 38.9C
79 bpm

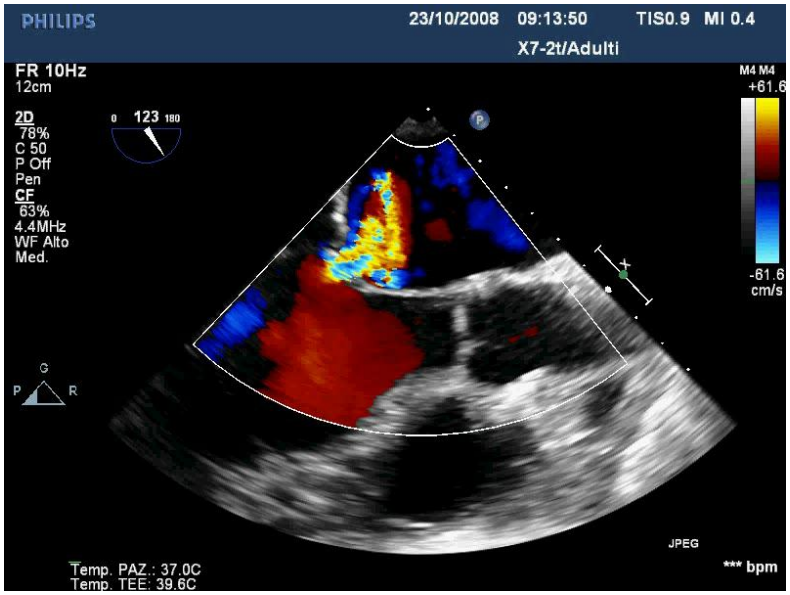

FR 35Hz
10cm
M4
2D
63%
C 50
P Off
Gen
0 150 180
G
P
R
Dist 0.387 cm
Dist 4.79 cm
37.0C
38.4C
85bpm

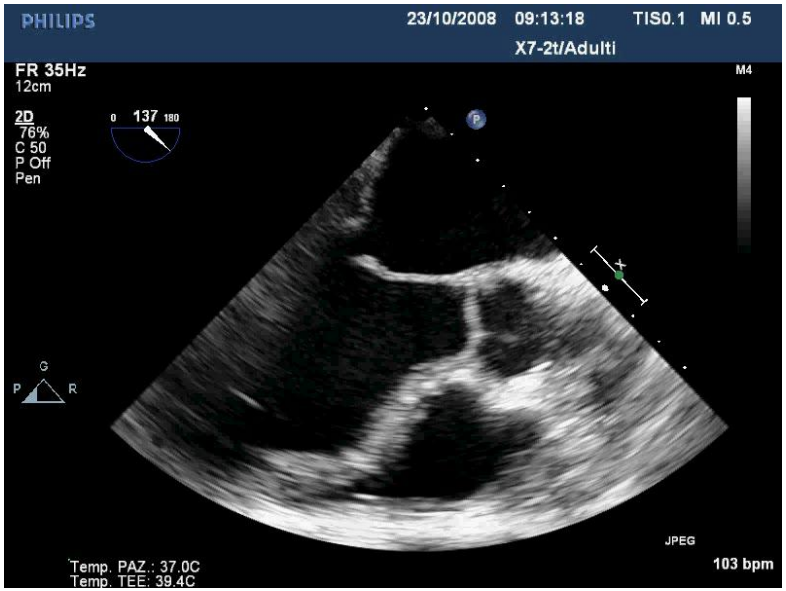

FR 6Hz
5 mm
7.2cm
M4
Live 3D
3D 0%
3D 40dB
Pen
0 60 180
F: 3
53
Temp. PAZ.: 37.0C
Temp. TEE: 40.2C
76 bpm


FR 52Hz
12cm
M4
2D
77%
C 50
P Off
Pen
0 144 180
G
P
R
73
Dist 1.44 cm
Dist 5.58 cm
37.0C
38.8C
90bpm

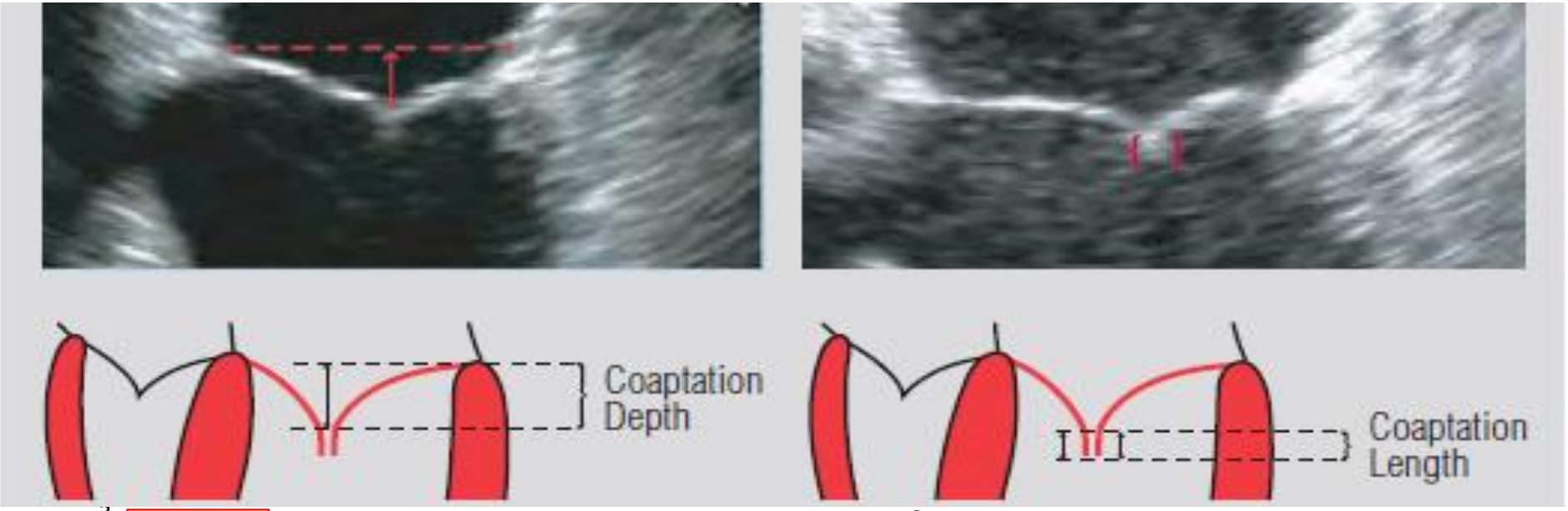
Functional MR

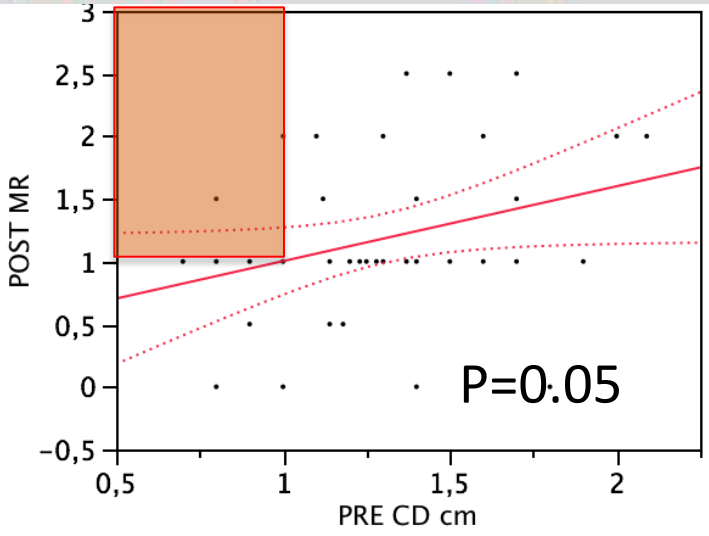


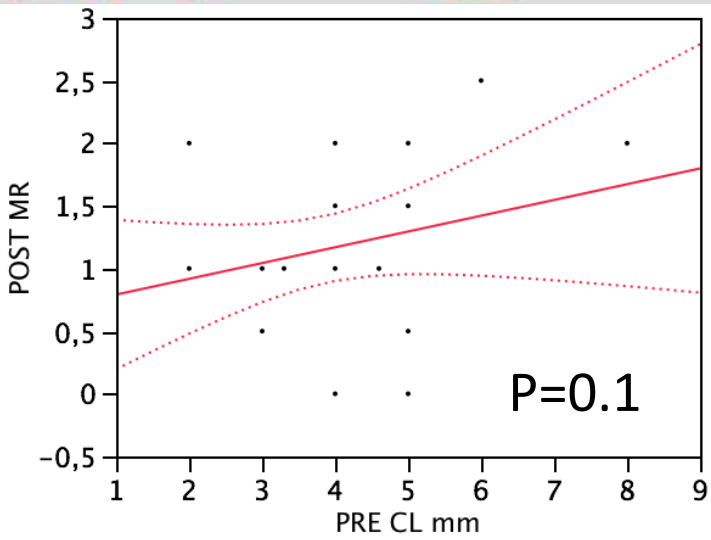




Anatomic Measurements

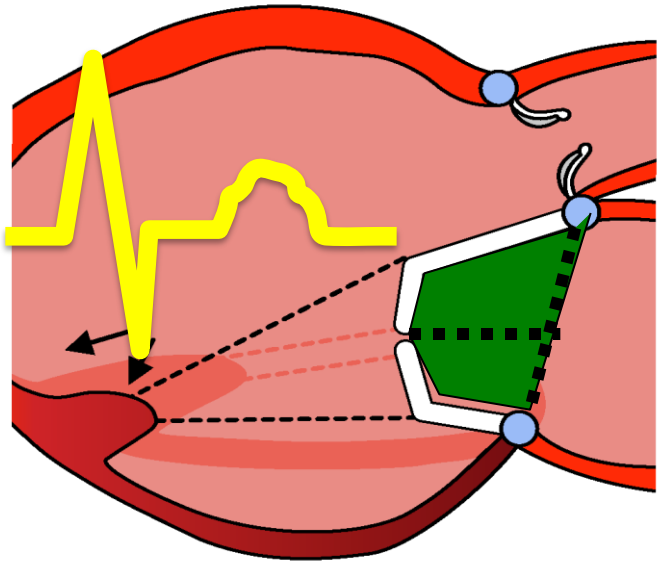


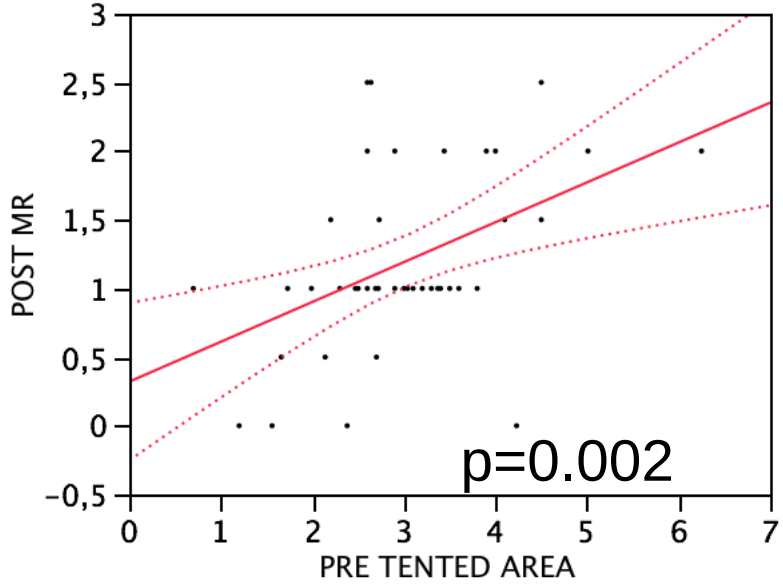


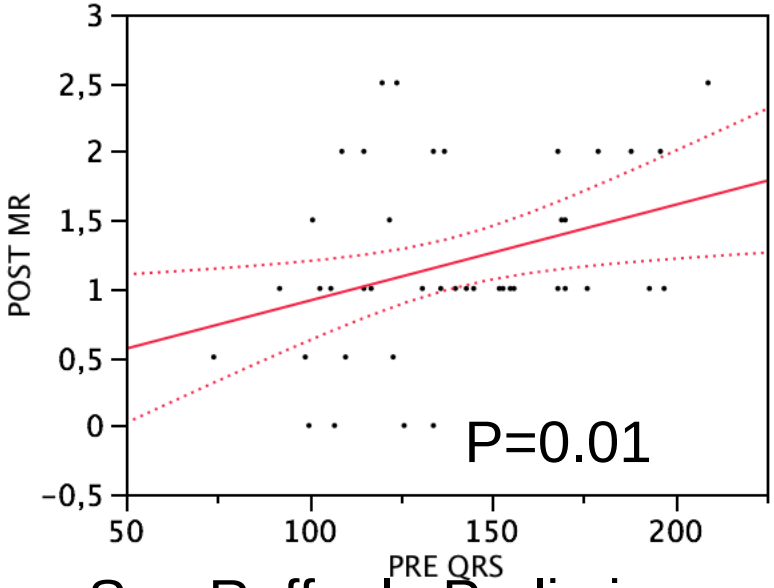


San Raffaele Preliminary data, 85pts

Tenting area and QRS duration



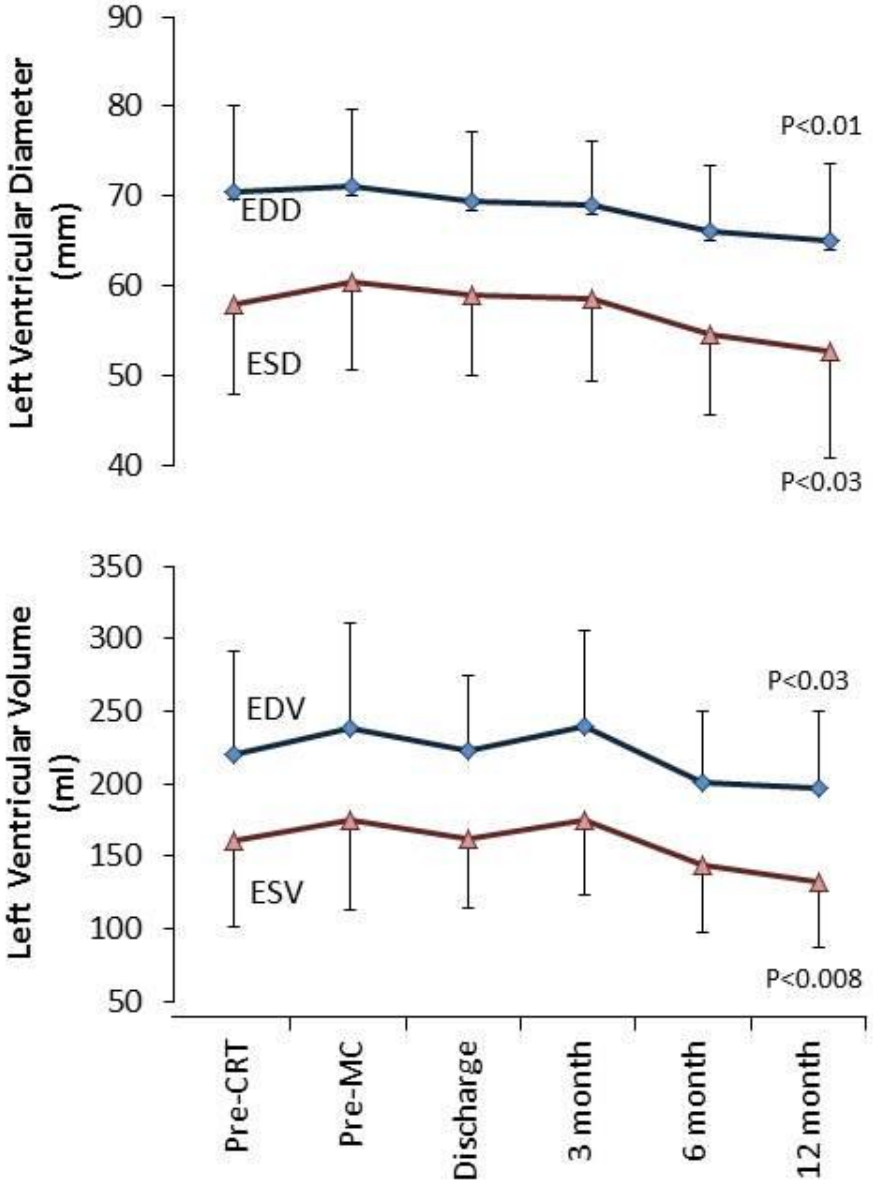


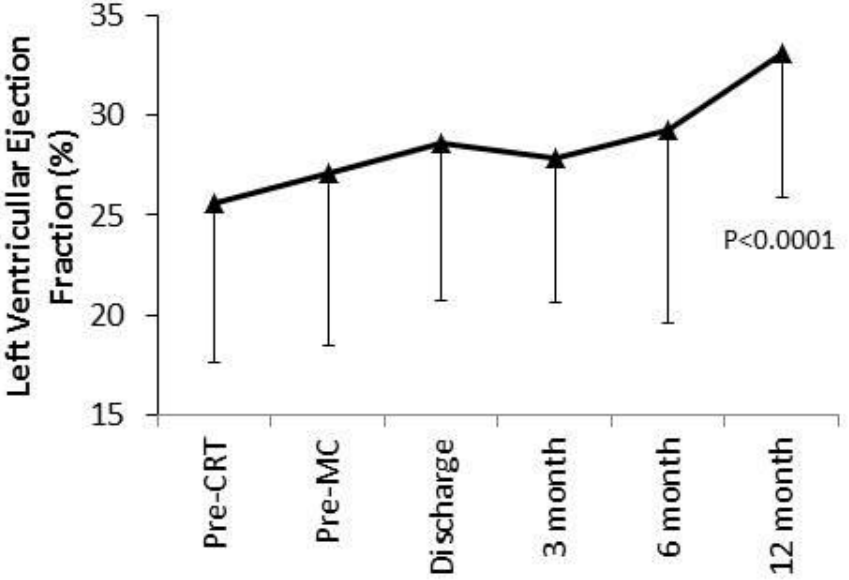


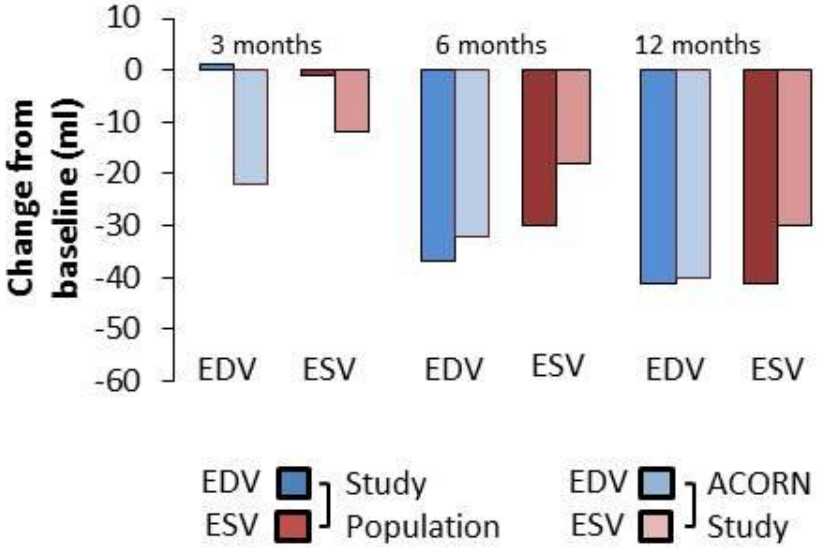
San Raffaele Preliminary data

Concomitant conditions

- Coronary artery disease
  - STAGED PCI, VS COMBINED CABG AND MVR/REPAIR
- Atrial fibrillation
  - CONSIDER ABLATION, APPENDAGE CLOSURE
- Tricuspid disease
  - STAGED APPROACH, MITRACLIP FIRST
- Aortic stenosis
  - STAGED APPROACH, TAVI FIRST
- Dissinchrony
  - CRT FIRST





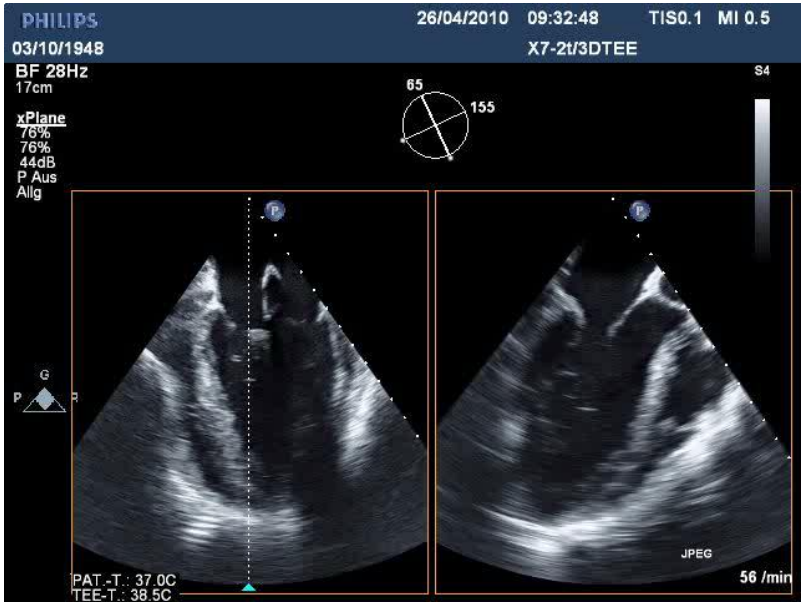


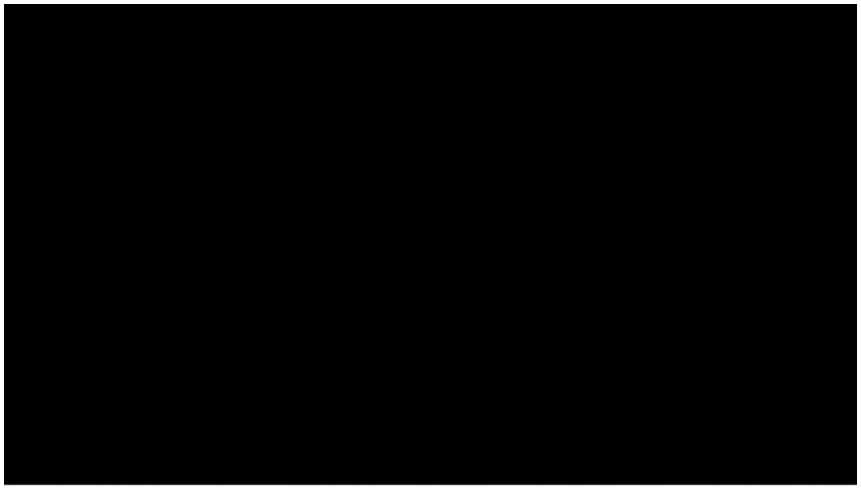
Auricchi et al. PERMIT CARE, JACC in press

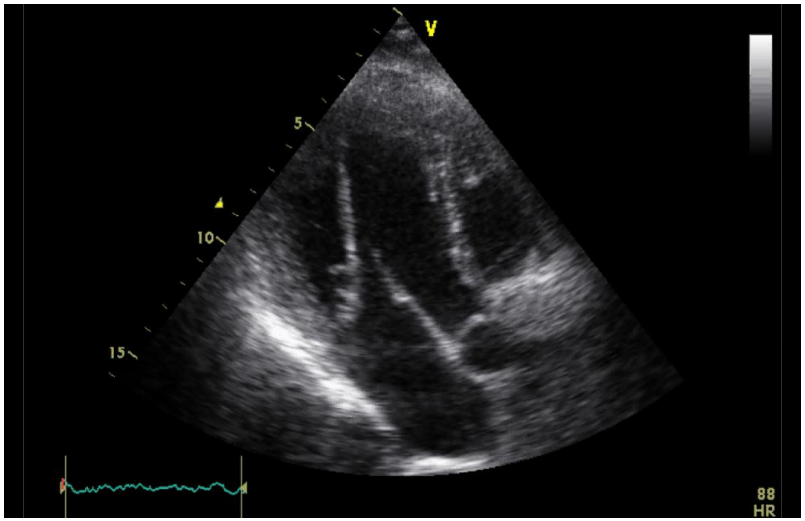
Current transcatheter technologies to treat MR at the leaflet level

technique	device	status
Edge-to-edge	MitraClip	CE mark
	Mobius	Early clinical
	Mitraflex	preclinical
neochordae	Neochord	Early clinical
	Babic	preclinical
	Mobius	preclinical
	Valtech - vchordal	preclinical
Tissue reduction	Thermocool	preclinical
Spacer	Percupro	Early clinical

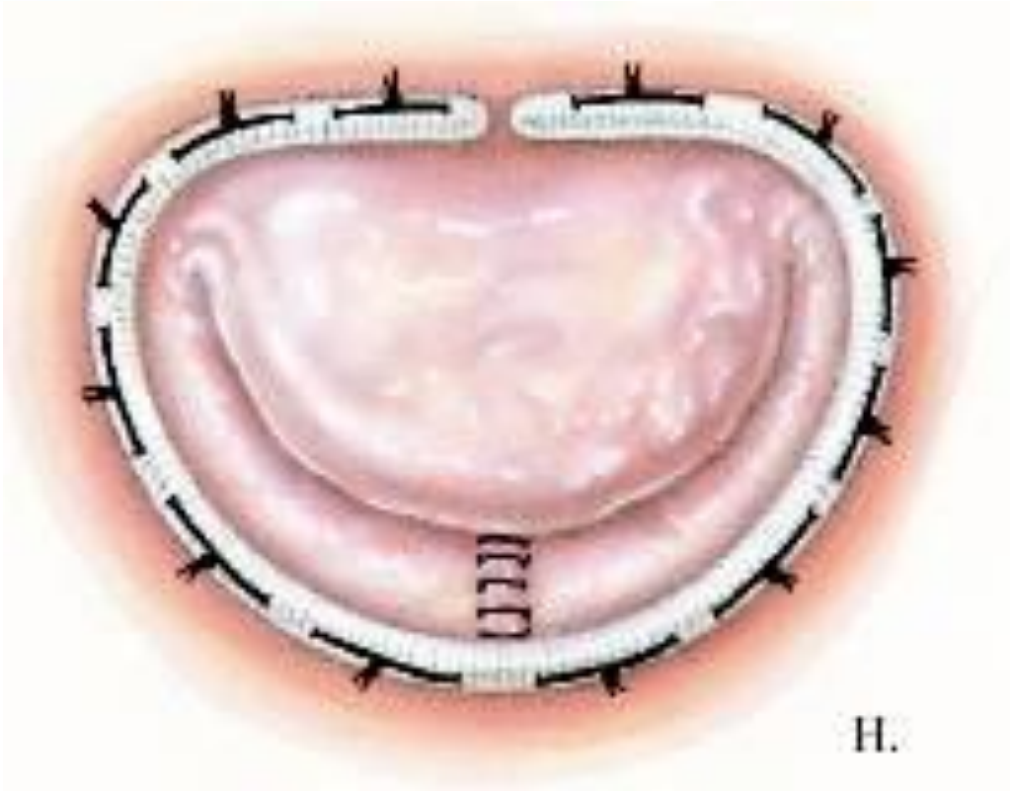
Neochord Inc.

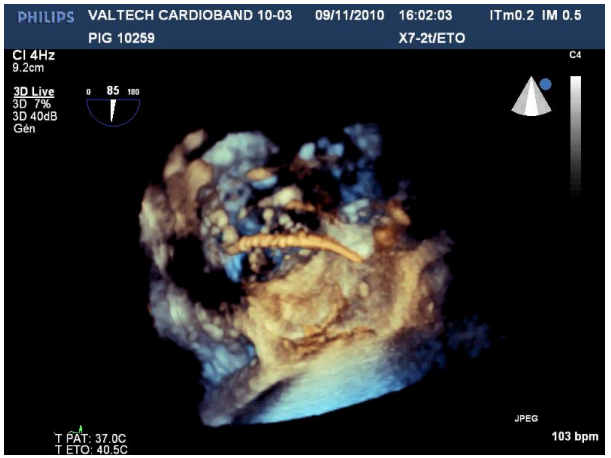


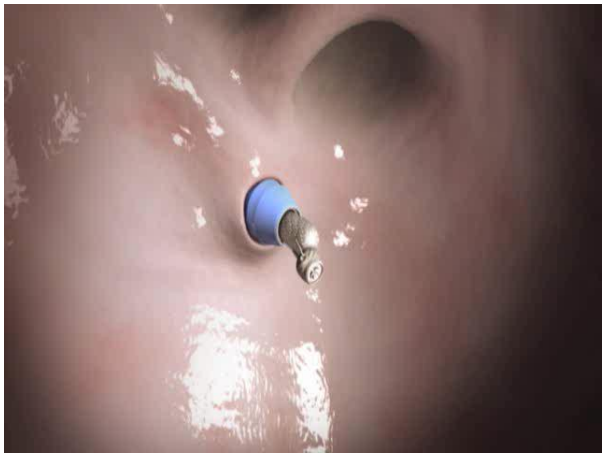




Beyond MitraClip: Annuloplasty







Individualize the therapy waiting for more actual randomized trials

- Anatomy and function
- Comorbidities, Life expectancy
- Compare risk and probability of success
- Preservation of surgical option
- Patient informed consent for therapy
- collaboration