EuroValve
January 26-27, 2017

Centre Hospitalier Régional Universitaire de Lille

Transcatheter Mitral Valve Implantation: Techniques and Early Clinical Outcomes

Dr. T. Modine MD, PhD, MBA

Heart team

CHRU de Lille

EuroValve

January 26 -27, 2017

Speaker's name: Thomas Modine

☑ I have the following potential conflicts of interest to report:

Affiliation/Financial Relationship	Company
Grant/Research Support	• Edwards
Consulting Fees / Honoraria	• Abbott, Boston Scientific, Medtronic, Edwards, Cephea, Microport, GE
Major Stock Shareholder/Equity	• Nanosurg
Royalty Income	• Microport
Ownership/Founder	• Valmy ltd
Intellectual Property Rights	• Yes
Other Financial Benefit	• Nil

Prevalence of Valvular Heart Disease

Nkomo V et al. *Lancet* 2006;368:1005-11

Prevalence

Population-based study of 11,911 adults

18-44 years old	0.7%
>75 years old	13.2%

Diagnosis

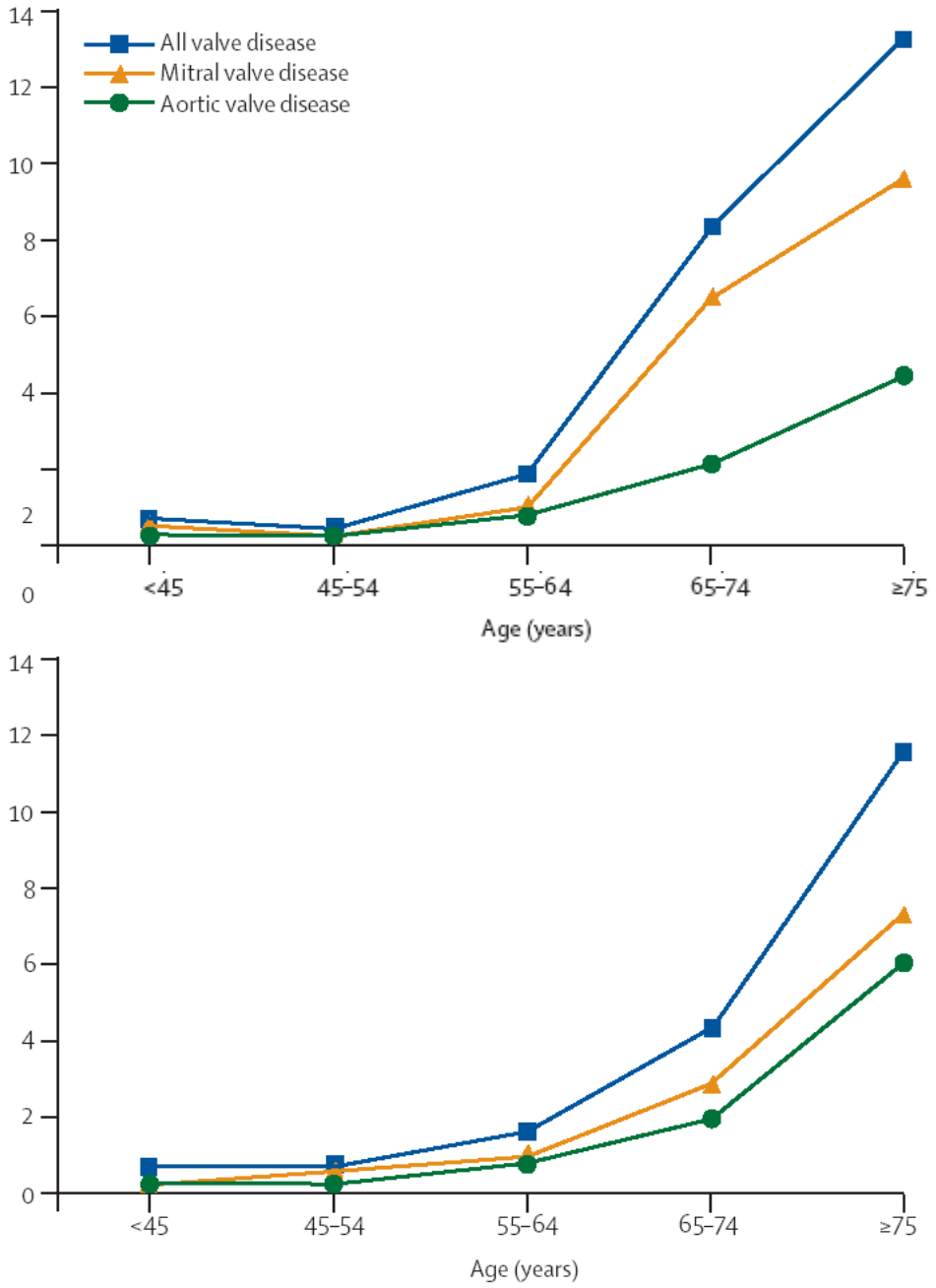
Community-based study of 16,501 adults

18-44 years old	0.3%
>75 years old	11.7%

US Population

15 million adults ≥ 75 years of age

600,000 patients with aortic stenosis



Prevalence

- In the United States, patients are often undertreated for both mitral and aortic valve disease.
  - Only 1 in 40 patients with moderate or severe mitral regurgitation are surgically treated.[1-3]
  - "Only 59% of the patients who should have had aortic valve replacement according to the practice guidelines were actually offered surgical treatment..." [4]
- Patients are often not being referred or are opting out of surgery for a variety of reasons that may include[5]:
  - Co-morbid disease, risk factors and age
  - Perceived fear of traumatic nature of conventional surgery
  - Patients concerns of body image/cosmesis, pain, time out of work, etc.

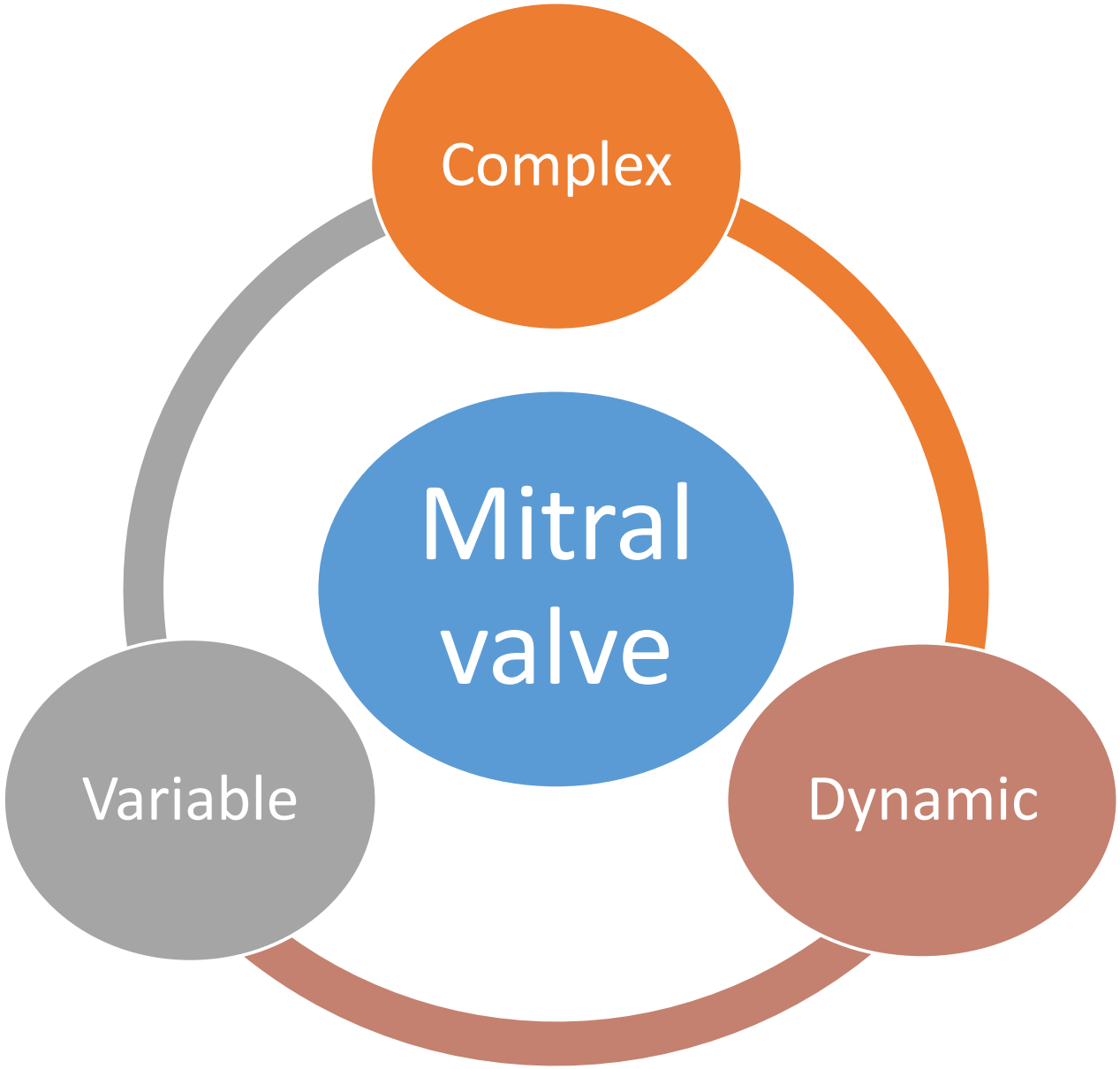
1. U.S. Census Bureau, Population Estimates and Projections, 2008. Projected Population by Single Year of Age, Sex, Race, and Hispanic Origin for the United States: July 1, 2000 to July 1, 2050. http://www.census.gov/population/www/projections/downloadablefiles.html
2. Nkomo, VT et al. Burden of valvular heart diseases: a population-based study. *Lancet*, 2006;368:1005-11.
3. Health Research International. U.S. Opportunities in Surgical Heart Valve Technologies. July 2009.
4. B J Bouma et al. To operate or not on elderly patients with aortic stenosis: the decision and its consequences. Heart. 1999;82:143-148.
5 Helium Market Research, Coady 051109; pages 25-34.

Education

Mitral Regurgitation is not Properly Diagnosed

- 66% (6/9) of asymptomatic patients and 47% (8/17) of patients cited with stable LV size had at least 1 indication for surgery
- Of 53 unoperated patients, 43 (81%) were followed up by cardiologist; only 5 (9%) were referred to cardiothoracic surgeon for evaluation

11. Bach, David S., Mazen Awals, Hitinder S. Gurm, and Sarah Kohnstamm. Failure of Guideline Adherence for Intervention in Patients with Severe Mitral Regurgitation. Journal of the American College of Cardiology. 2009;54: 860-65.


Complex
Mitral valve
Variable
Dynamic

It’s complex . . .

Pulmonary veins	Left atrium	Left atrial appendage
Mitral annulus	Leaflets	Chords
Papillary muscles	Left ventricle	Left ventricular outflow tract
Aortic valve	Atrial septum	LV apex

It’s dynamic . . .

Absence of calcium

Submitral apparatus

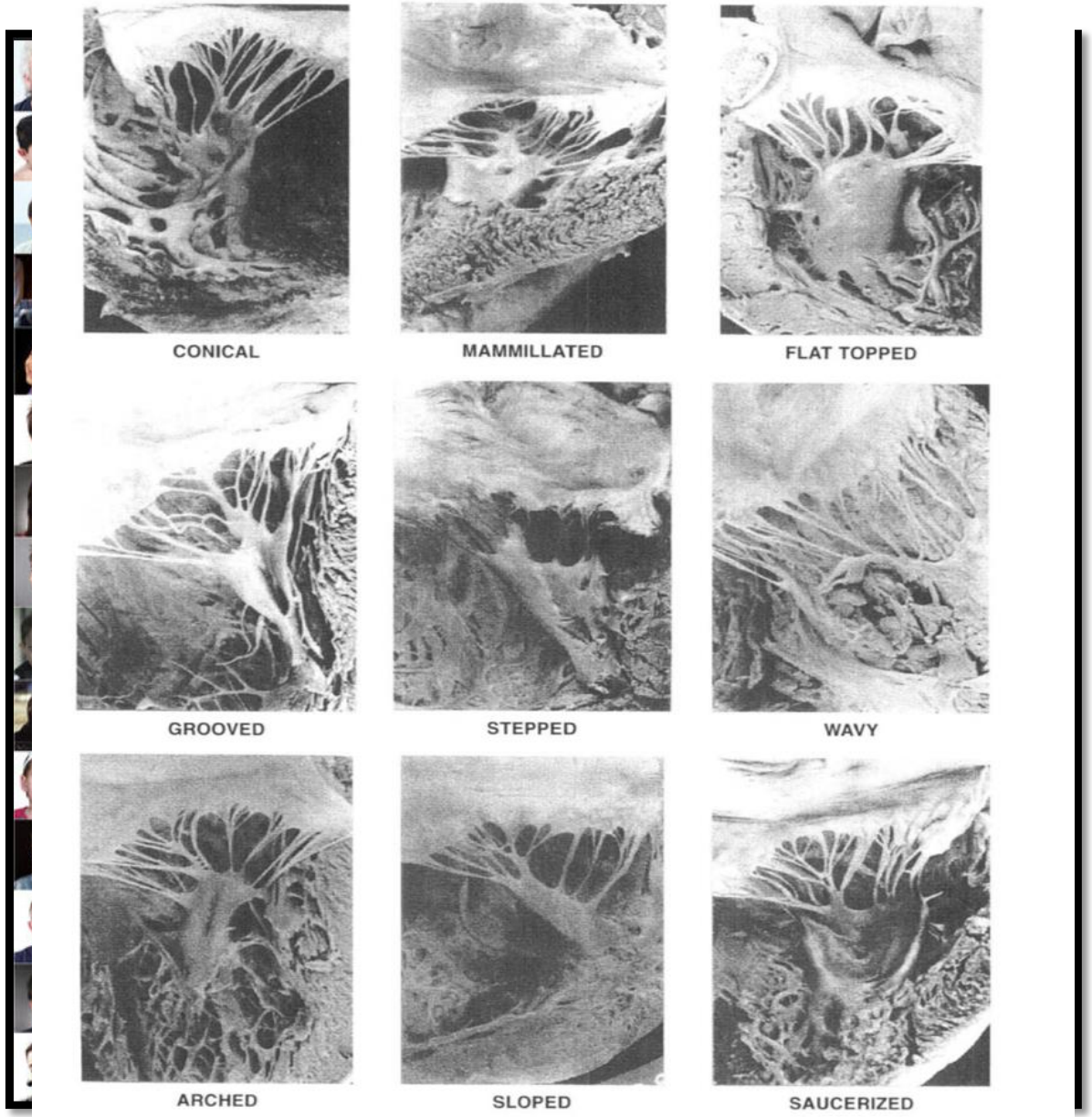
Delivery catheter profile

Higher dislodgement forces

High transvalvular gradients

Large effective orifice area

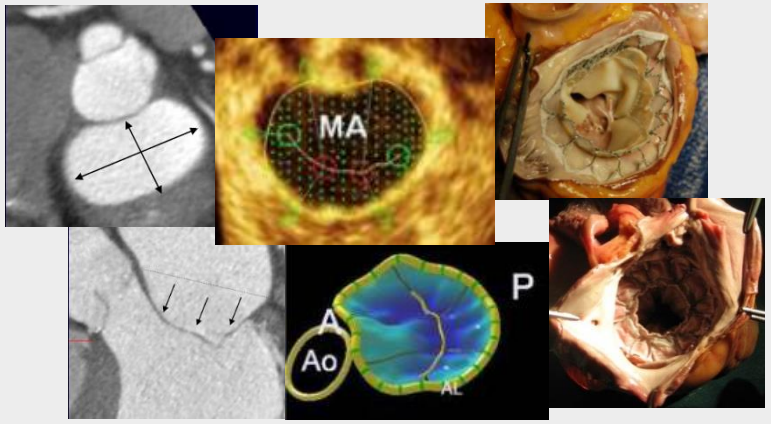
It’s variable . . .



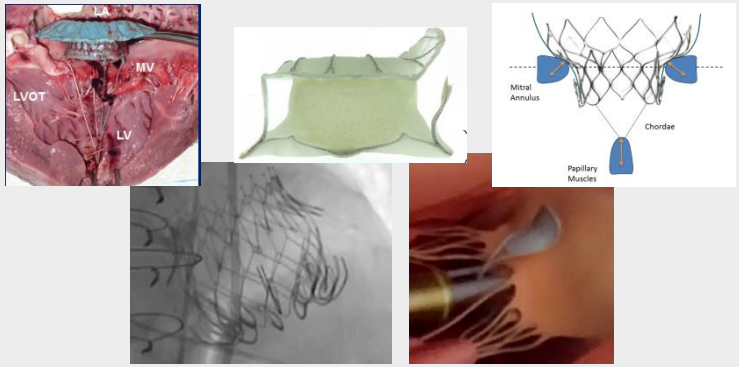
TMVI journey

Technical Challenges

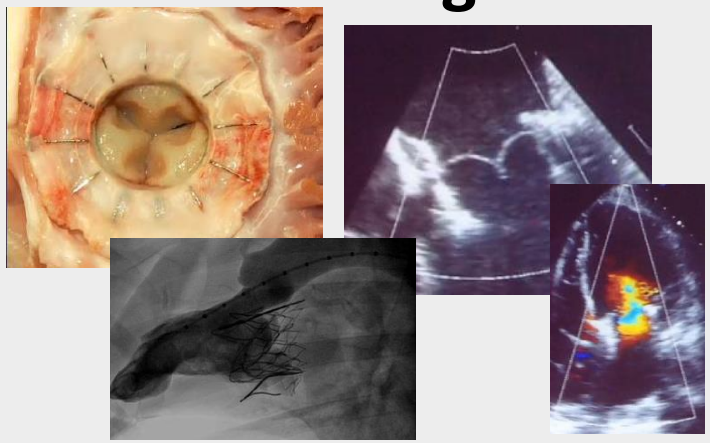
Sizing



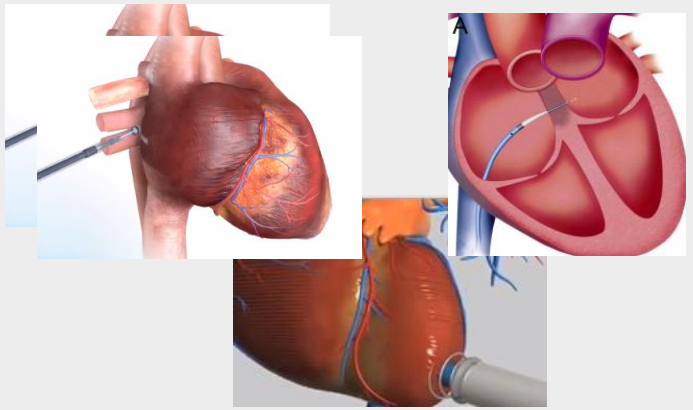
Fixation

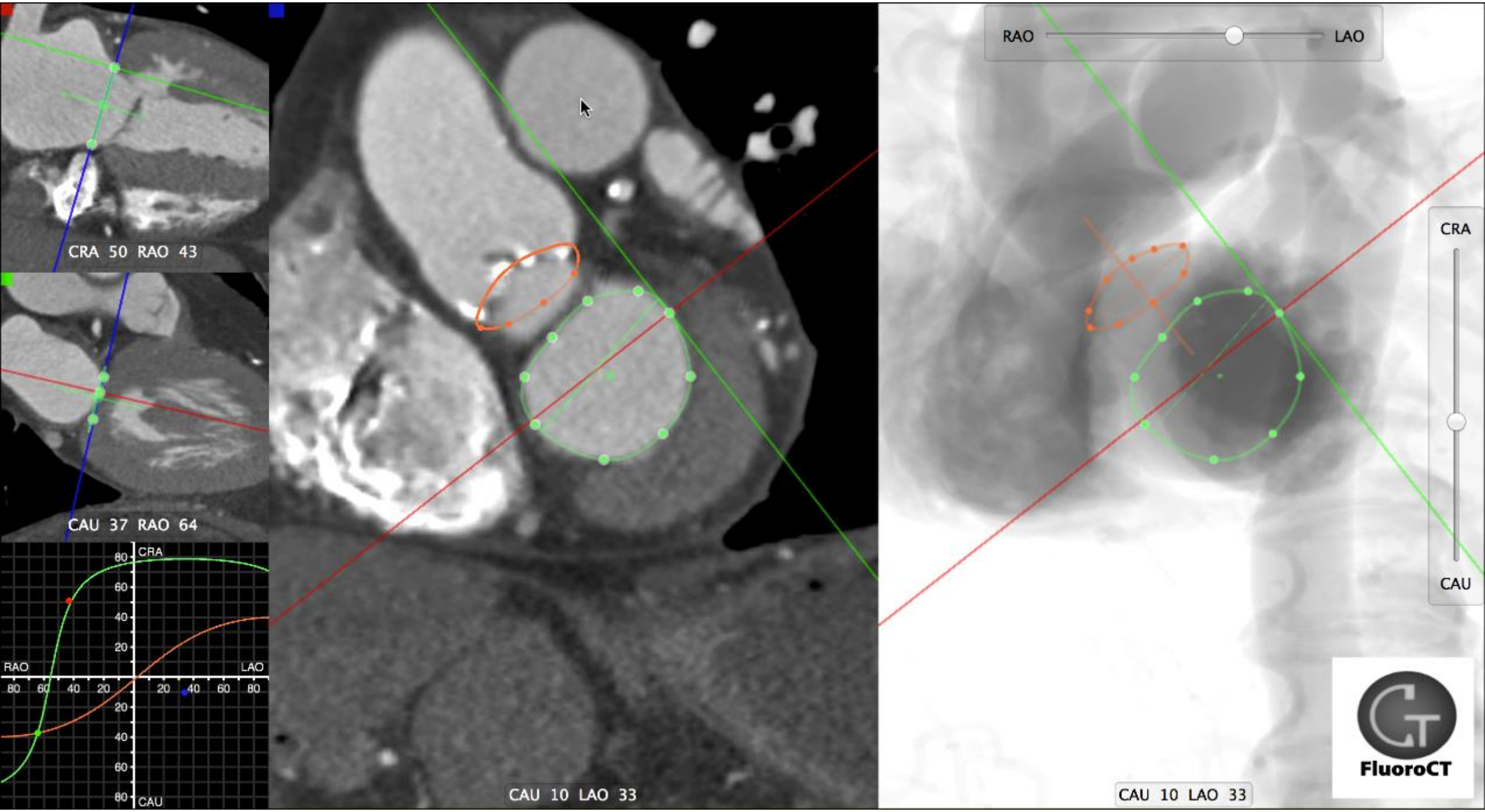


Sealing



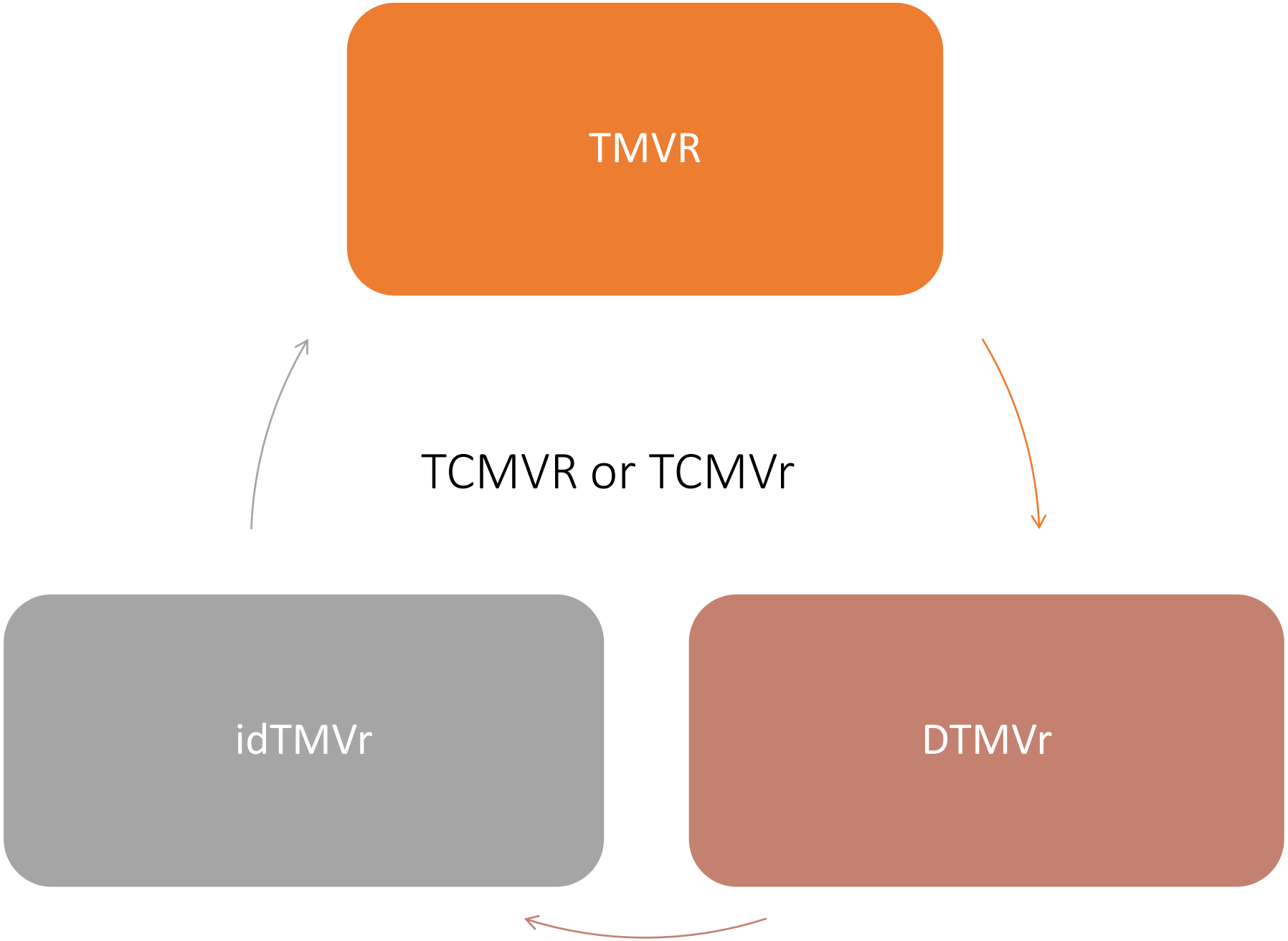
Delivery




CRA 50 RAO 43
CAU 37 RAO 64
CRA
RAO
LAO
CAU
CAU 10 LAO 33
RAO
LAO
CRA
CAU
CAU 10 LAO 33
FluoroCT

“If it is not awfully simple then it is simply awful”

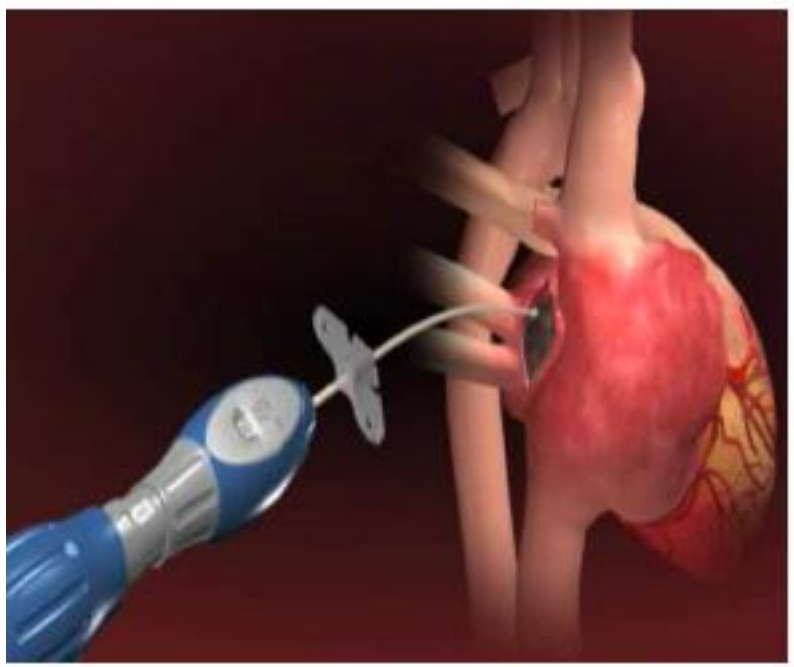
Matt Paneth


TMVR
TCMVR or TCMVr
idTMVr
DTMVr

MIS / Interventional Cardiology

Valtech Cardio – CARDIOBAND

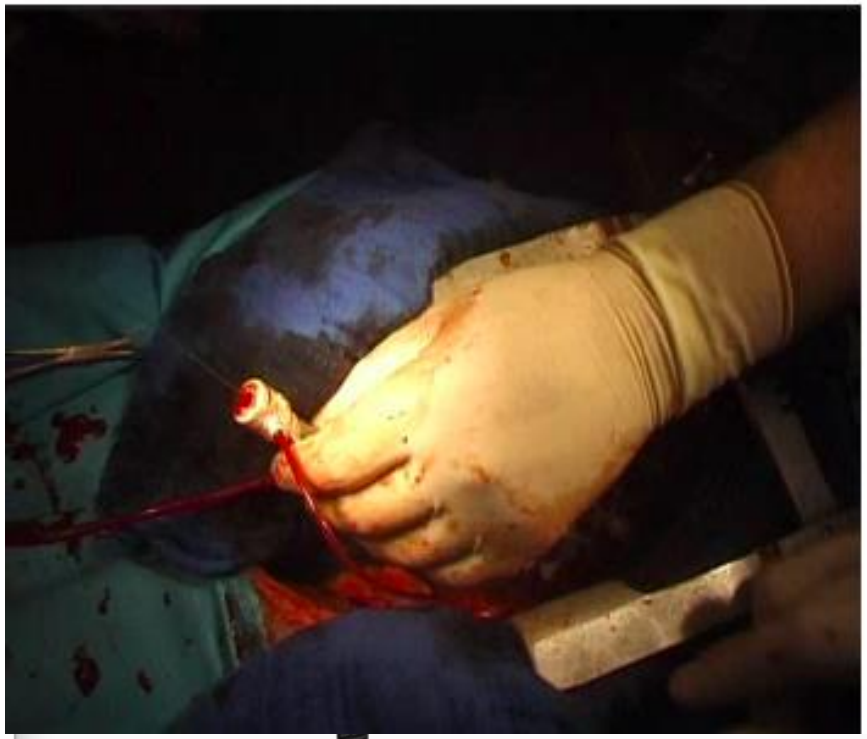
Beating Heart assessment

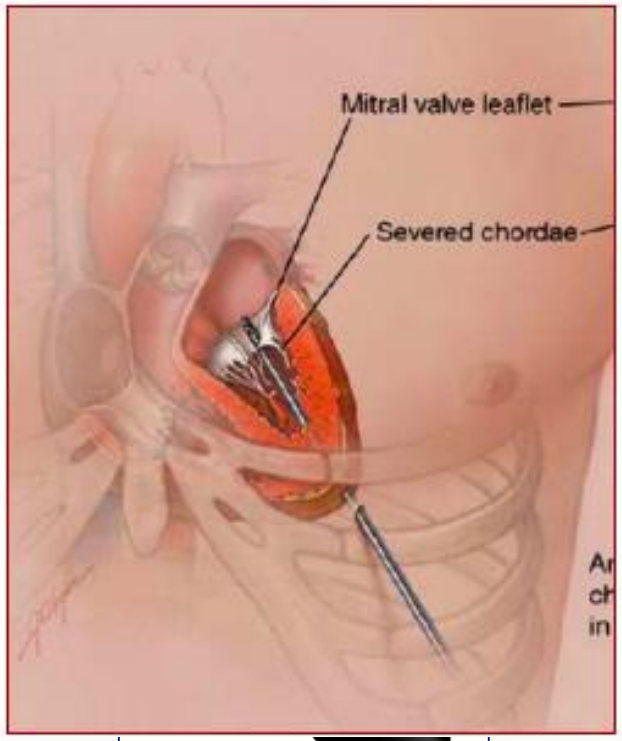


Neochord Delivery System 1000

Trans-apical NeoChordae implantation

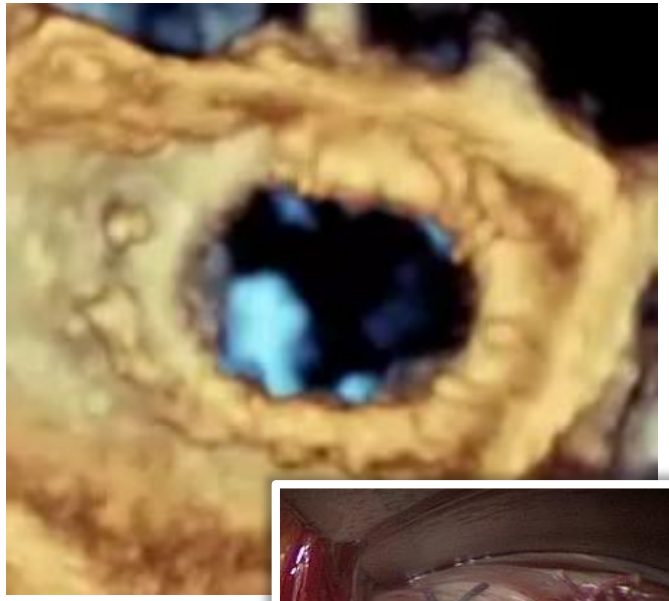
NeoChord DS 1000 Device



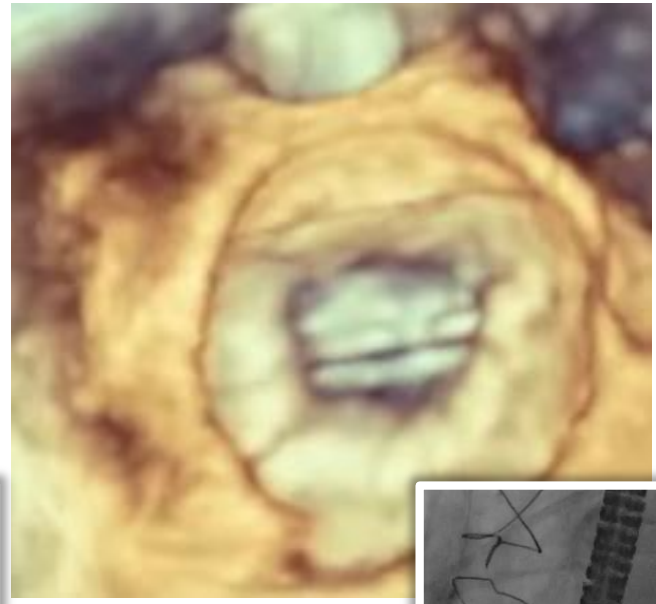


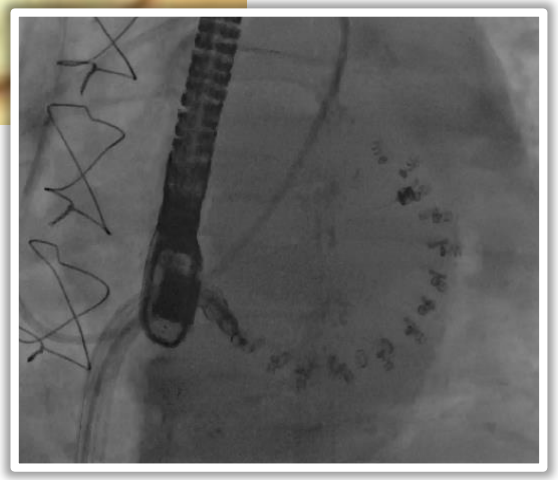
Cardioband – Surgical Like Annuloplasty

Which is Cardioband?



Surgery

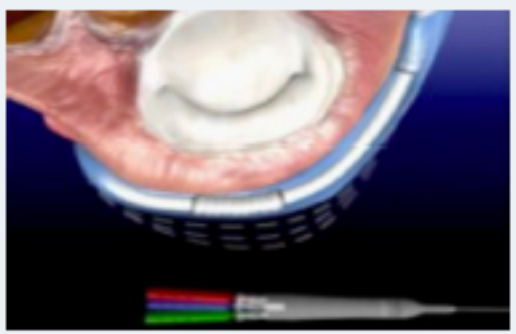




Cardioband

Courtesy F. Maisano

Coronary Sinus Annuloplasty

	MONARC (Edwards Lifesciences LLC)	Two-anchor design with chronic reshaping (6weeks) by a foreshortening bridge	EVOLUTION trial (72 pts 82% success)
	CARILLON (Cardiac Dimensions Inc)	Acute reshaping device acting in P2P3, repositionable, retrievable	AMADEUS trial (113 pts 58 % success)
	PTMA (Viacor Inc)	Tri-lumen catheter, reshapable, possibility of multiple long term adjustment	PTOLEMY (31 pts 29 % success)

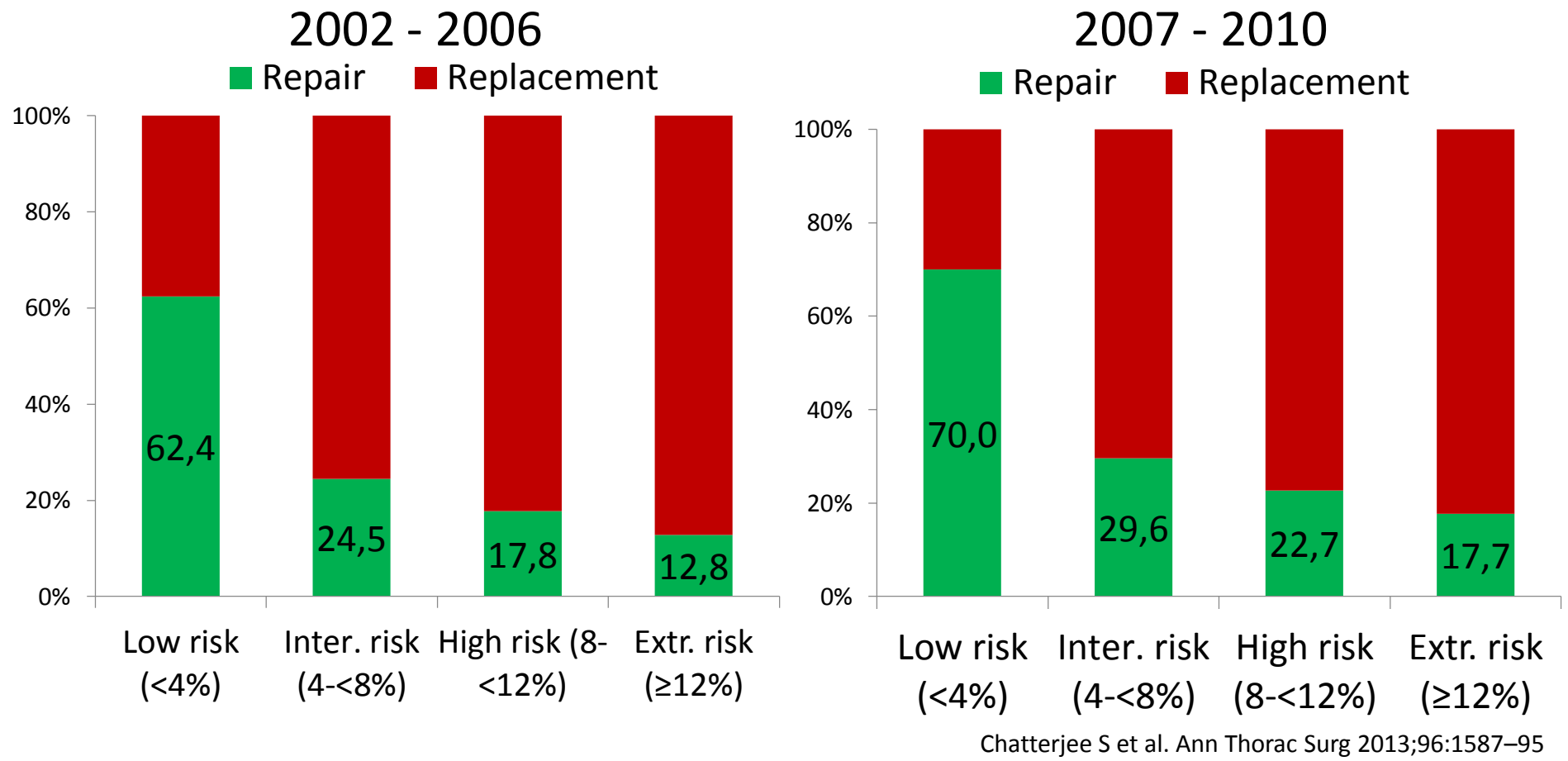
TMVR Device Landscape

TMVI technologies with active clinical programs under protocol	4	**Abbott Tendyne** · **Edwards CardiAQ** · **Medtronic Twelve** · **Neovasc** · **Highlife**
TMVI technologies FIH studies <24 months	5	Cephea · M-Valve · Caisson · Valtech · **Microport MX**
TMVI technologies with valves in development	11+	Braile · Navigate · Venus · HT Consultant · MitralHeal · Direct Flow · Verso · Micro Interventional · SinoMed · TransMural Systems · MitrAssist

MV Surgery Trends: STS database 2002-2010

N = 77,836 cases (58.4% repair vs.41.6% replacement)

Proportion treated with MV repair vs. replacement according to predicted risk



Chatterjee S et al. Ann Thorac Surg 2013;96:1587–95

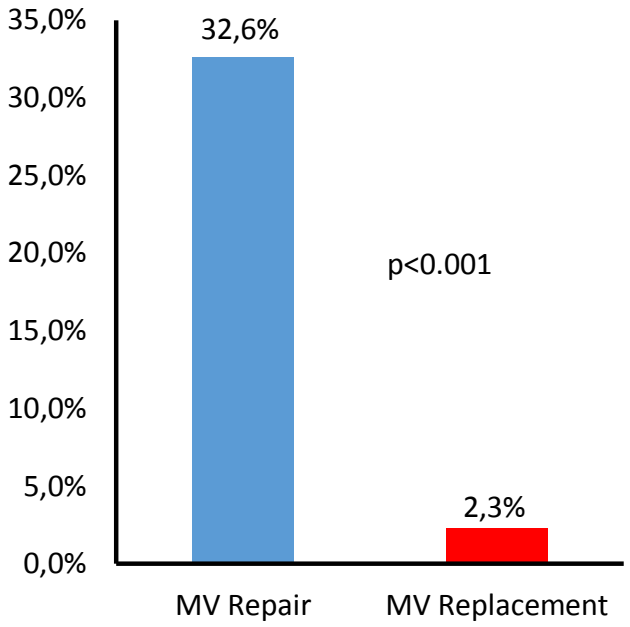
The NEW ENGLAND JOURNAL of MEDICINE

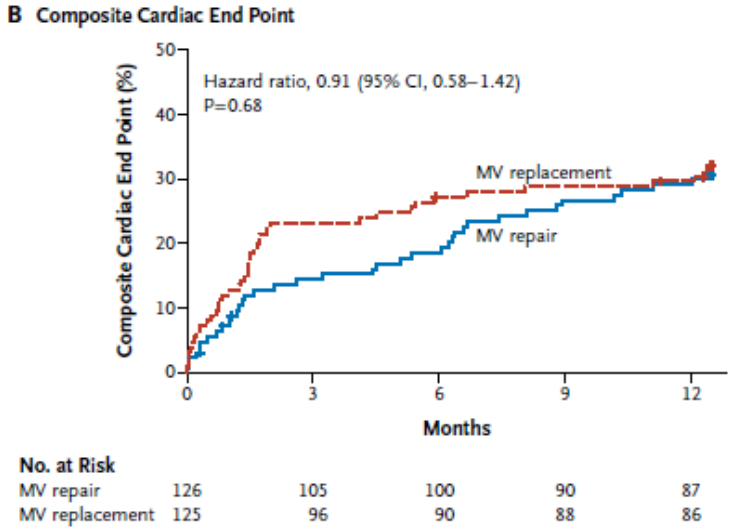
ORIGINAL ARTICLE

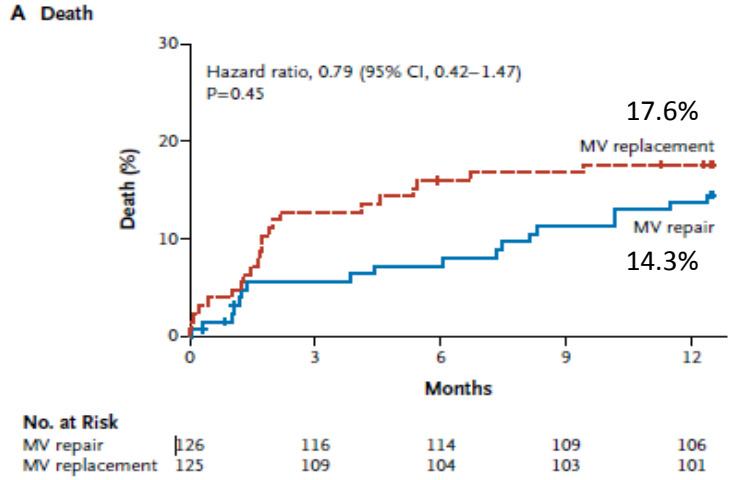
Mitral-Valve Repair versus Replacement for Severe Ischemic Mitral Regurgitation

- 251 patients (126 repair vs. 125 replacement)
- Primary end-point: LVESVI at 12 months
- LVEF ~40% in both groups

Recurrence of moderate or severe mitral regurgitation at 12 months







Acker M. et al. N Engl J Med 2014;370:23-32

Percutaneous Mitral Valve Repair for Mitral Regurgitation in High-Risk Patients

Results of the EVEREST II Study

- EVEREST II High risk registry and REALISM continued access study high-risk arm
- STS >12%, 70% FMR

	Degenerative MR (n = 105)	Functional MR (n = 246)
Age, years	81.8 ± 8.9 (105)	73.2 ± 10 (246)
LV ejection fraction, %	61.0 ± 10.1 (95)	**41.7 ± 11.5 (223)**
NYHA class III to IV HF	81.9 (86/105)	86.2 (212/246)
Previous CAD	74.8 (77/105)	85.4 (210/246)
Previous MI	29.5 (31/105)	59.8 (146/244)
History of AF	71.6 (73/102)	67.0 (144/215)
Previous CV surgery	50.5 (53/105)	63.8 (157/246)
Previous PCI	35.2 (37/105)	56.1 (138/246)
Prior stroke	9.5 (10/105)	14.2 (35/246)
Hypertension	89.5 (94/105)	89.4 (220/246)
COPD	28.5 (30/105)	29.0 (71/245)
Diabetes	29.5 (31/105)	43.7 (107/245)

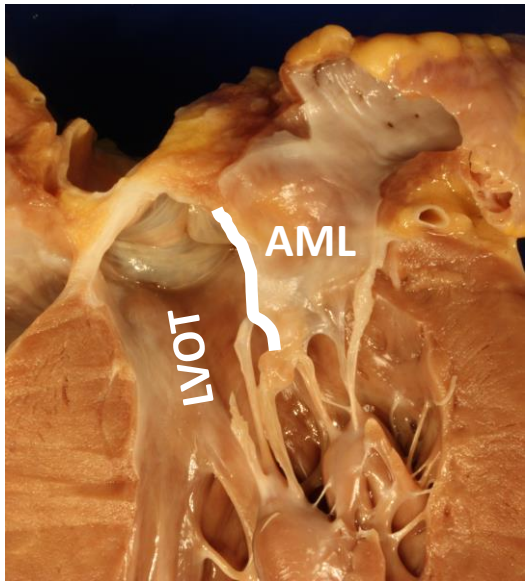
	Degenerative MR (n = 105)	Functional MR (n = 246)
30-day mortality	6.7 (7/105)	**4.1 (10/246)**
30-day MACE	18.1 (19/105)	**19.1 (47/246)**
30-day MACE (excl transfusions)	8.6 (9/105)	9.3 (23/246)
30-day major bleeding	11.4 (12/105)	8.9 (22/246)
12-month mortality	23.8 (25/105)	**22.4 (55/246)**
12-month MACE	36.2 (38/105)	**38.2 (94/246)**
12-month MACE (excl transfusions)	26.7 (28/105)	28.5 (70/246)
Implant success: MR grade	95 (100/105)	96 (236/246)
• **≤1+ at discharge**	48.5 (48/99)	45.1 (102/226)
• **≤2+ at discharge**	80.8 (80/99)	**88.1 (199/226)**
• **≤1+ at 12 months**	30.9 (21/68)	39.4 (62/157)
• **≤2+ at 12 months**	85.3 (58/68)	**82.8 (130/157)**
LVEDV ↑ at 12 months, ml	18.6 ± 22.3 (58)	17.6 ± 35.0 (145)
LVESV ↑ at 12 months, ml	4.3 ± 14.7 (58)	9.6 ± 25.7 (144)

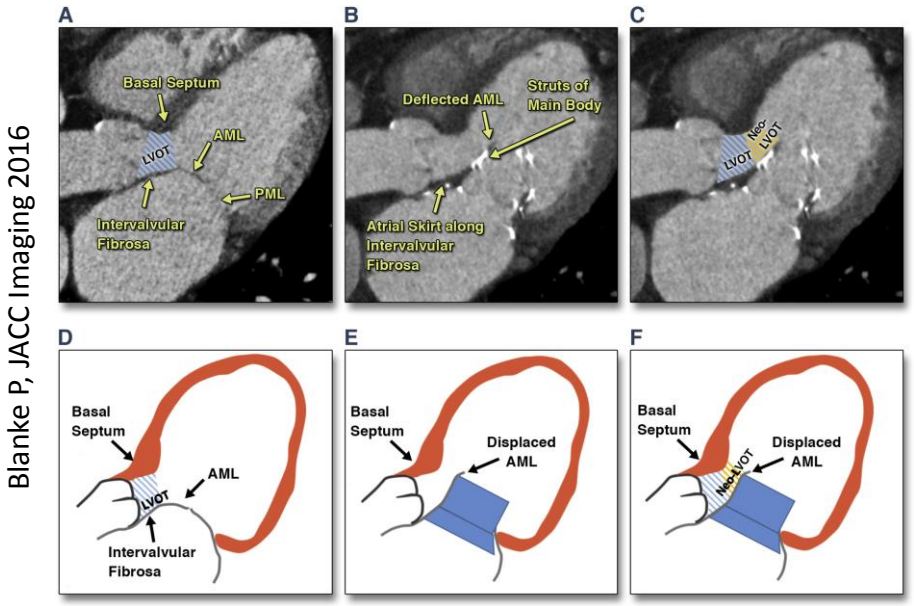
Glower D. et al. J Am Coll Cardiol. 2014 Jul 15;64(2):172-81

Early Clinical Experience

	Abbott Tendyne	Edwards CardiAQ	Edwards Fortis	Medtronic Twelve	Neovasc	Highlife
						
Implant Shape	D-Shaped	Circular	Circular w paddles	Circular	D-Shaped
Construction	Self-expanding frame, tri-leaflet valve	Self-expanding frame, tri-leaflet valve	Self-expanding frame, tri-leaflet valve	Self-expanding frame, tri-leaflet valve	Self-expanding frame, tri-leaflet valve
Leaflet Material	Porcine Pericardium	Bovine Pericardium	Bovine Pericardium	Bovine Pericardium	Bovine Pericardium
Catheter Size OD	*32 Fr*	*33 Fr*	*42Fr*	*35 Fr*	*32Fr* for 30mm valve, OD increases w valve size
Access Site	T-Apical	T-Apical , T-Femoral/Septal	T-Apical	T-Apical	T-Apical
Recapture	Fully recapturable system	No recapture	No recapture	Retrievable system expected shortly	No recapture

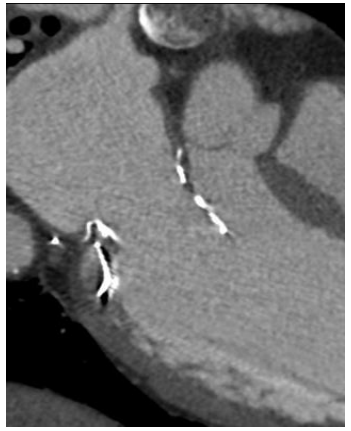
Potential for LVOT Obstruction: Prediction Algorithms

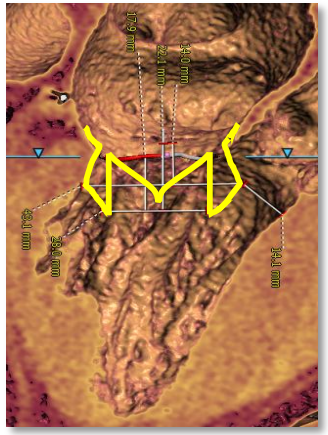




Blanke P, JACC Imaging 2016

Prediction algorithms highly dependent on specific design features





Impact of Transapical Aortic Valve Replacement on Apical Wall Motion

Israel M. Barbash, MD, Danny Dvir, MD, Itsik Ben-Dor, MD, Paul J. Corso, MD, Steven A. Goldstein, MD, Zuyue Wang, MD, Elizabeth Bond, BS, Petros G. Okubagzi, MD, Lowell F. Satler, MD, Augusto D. Pichard, MD, and Ron Waksman, MD, *Washington, District of Columbia*

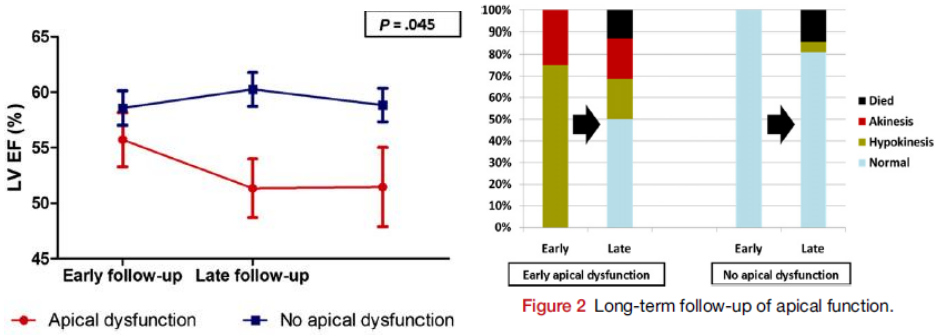


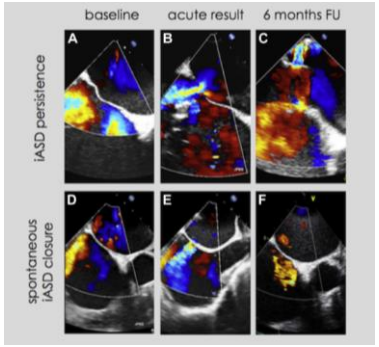
Figure 2 Long-term follow-up of apical function.

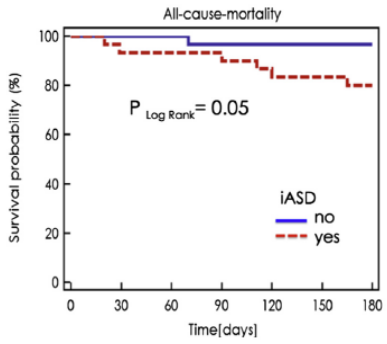
Barbash IM, J Am Soc Echocardiogr. 2013 Mar;26(3):255-60

Transition to trans-septal delivery will not be smooth…

Persistence of Iatrogenic Atrial Septal Defect After Interventional Mitral Valve Repair With the MitraClip System

A Note of Caution





Schueler R. et al. JACC Cardiovasc Interv. 2015 Mar;8(3):450-9

Current trans-apical TMVR systems are ~32 to 45 french. The transition to trans-septal delivery of clinically available TMVR devices will require important engineering modifications in size, possibly valve design and delivery methods

Early Clinical Experience

Abbott Tendyne

CE approval study

Edwards CardiAQ

Edwards Fortis

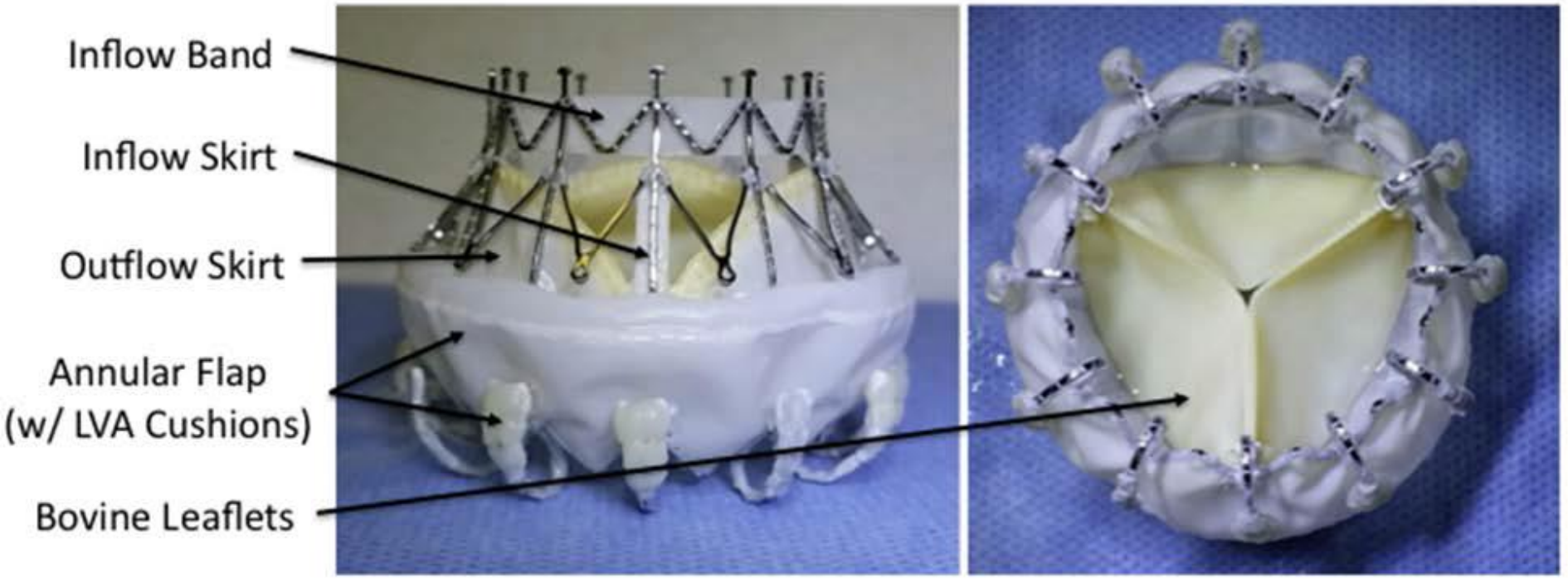
Medtronic Twelve

CE approval study

Neovasc

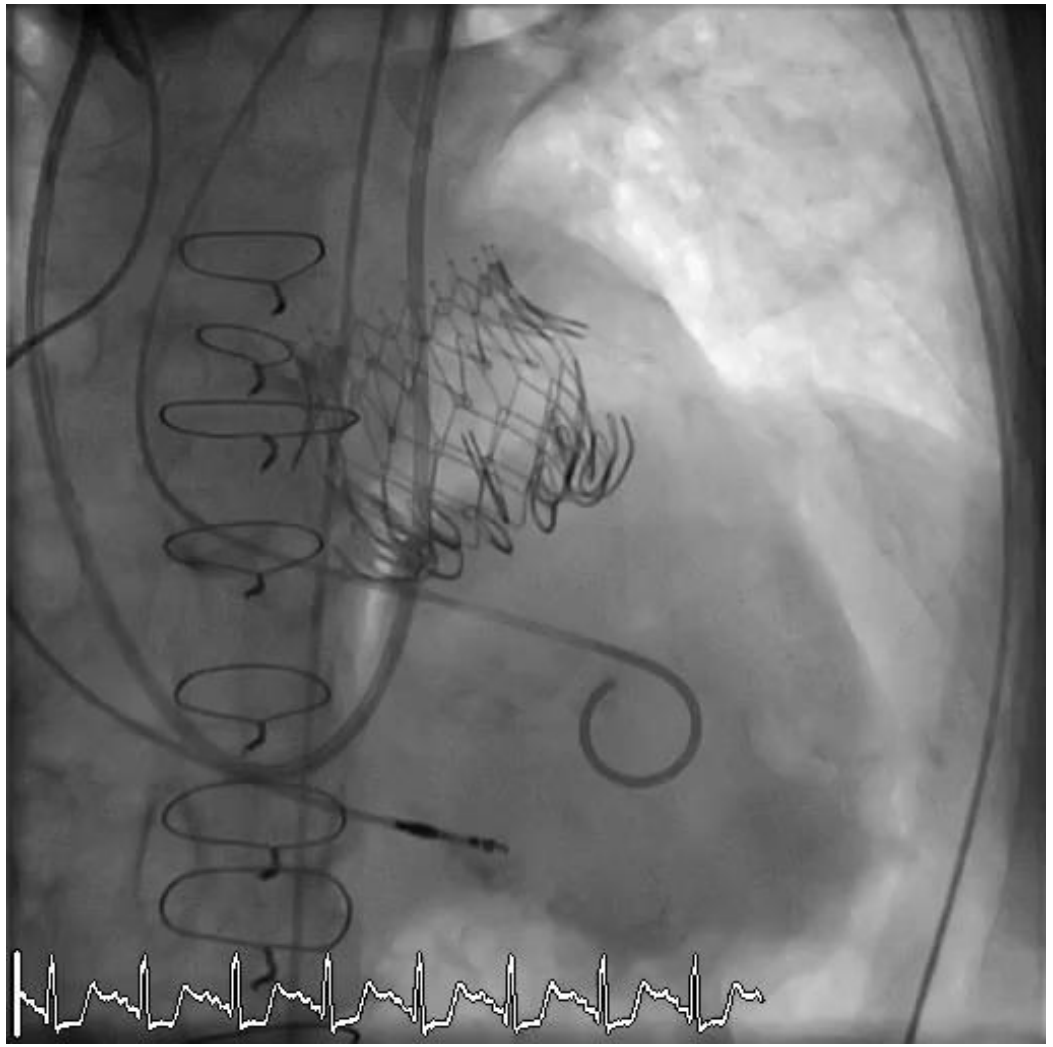
Human Experience	52 cases	12 cases	23 cases	38 cases	20 cases
First Implant	October-2013	June-2012	February-2014	September-2014	January-2014
Longest Patient F/U	2 year+	1 year+	2 years+	2 year+	2 years+
Patient Population	Clinically significant severe MR and high risk surgical candidates, NYHA II-IV				
FMR Etiology	86% (n=22)	64% (n=11)	100% (n=13)	73% (n=15)	54% (n=11)
Successful Deployment	21 / 23	9 / 11	10 / 13	14 / 15	9 / 11
30-Day Mortality	1 / 23	5 / 11	5 / 13	2 / 15	3 / 11
30-Day Rehosp	3 / 23	Data not available	Data not available	1 / 14	Data not available
MR Grade 0 at F/U	19 / 19	Data not available	8 / 9	13 / 14	Data not available

CARDIAQ


Inflow Band
Inflow Skirt
Outflow Skirt
Annular Flap
(w/ LVA Cushions)
Bovine Leaflets

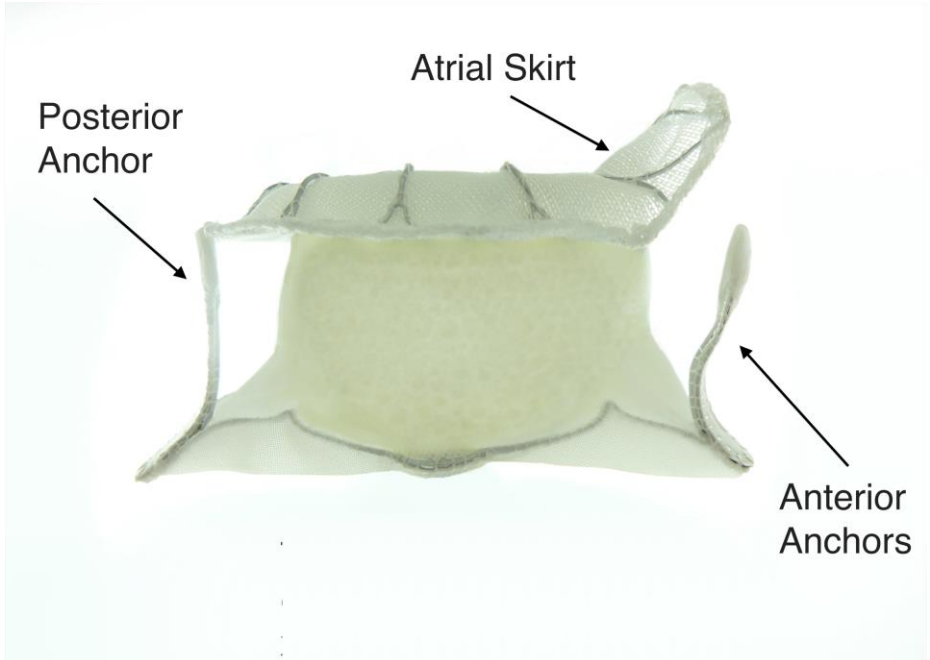

LASSO CONTROL
NOSECONE RETRIEVAL
NOSECONE
LASSO RELEASE
CAPSULE

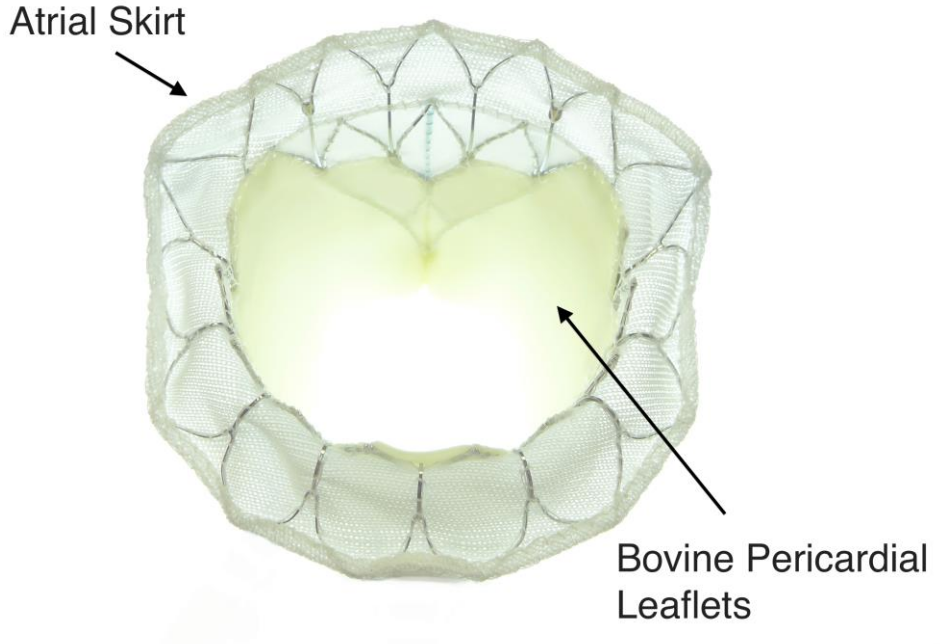
CardiaQ



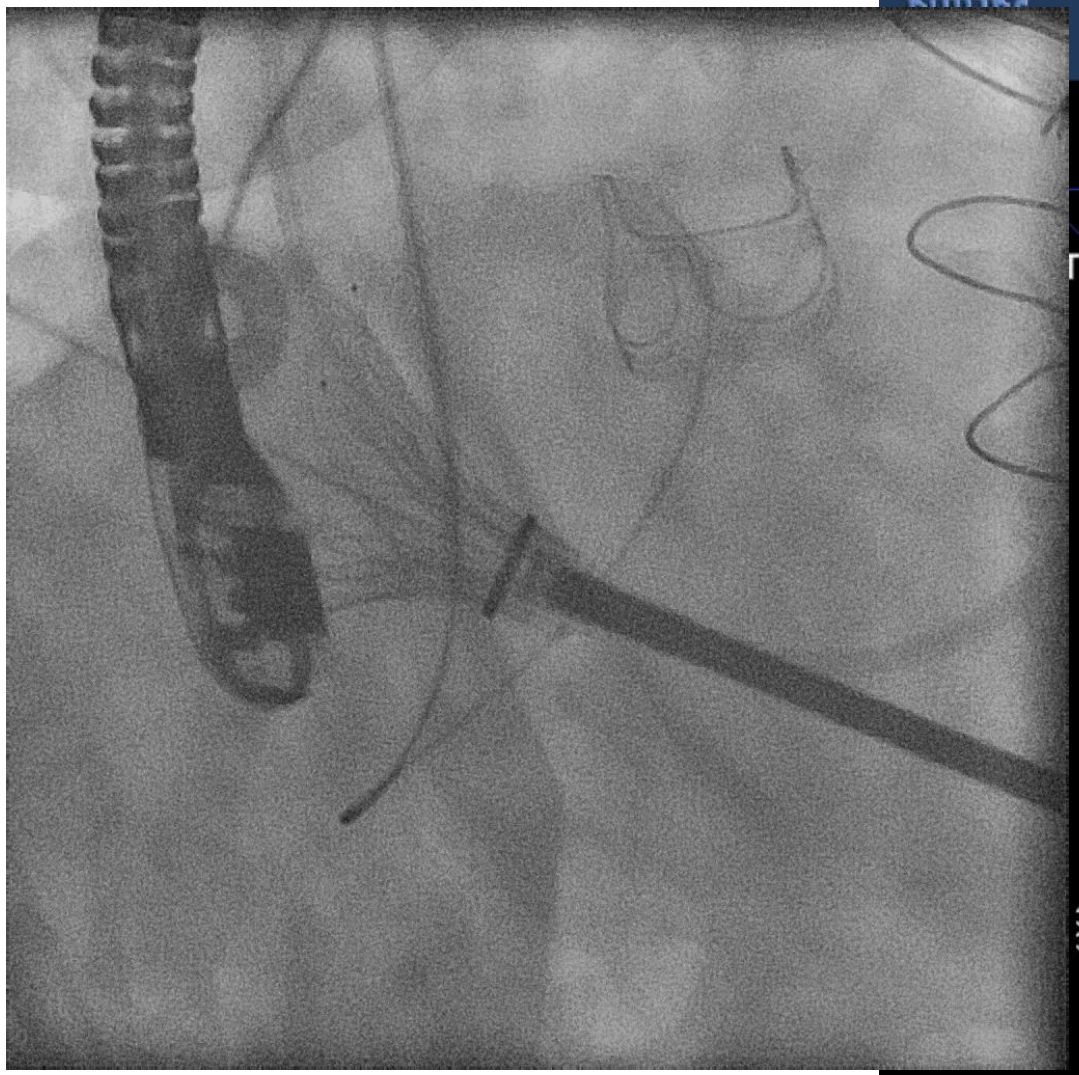
Neovasc Tiara Transcatheter Mitral Valve

- Anatomically shaped (D-shaped)
- Nitinol based, self-expanding frame
- Ventricular anchors to fix the valve onto fibrous trigone and posterior annulus
- Captures the anterior and posterior leaflets

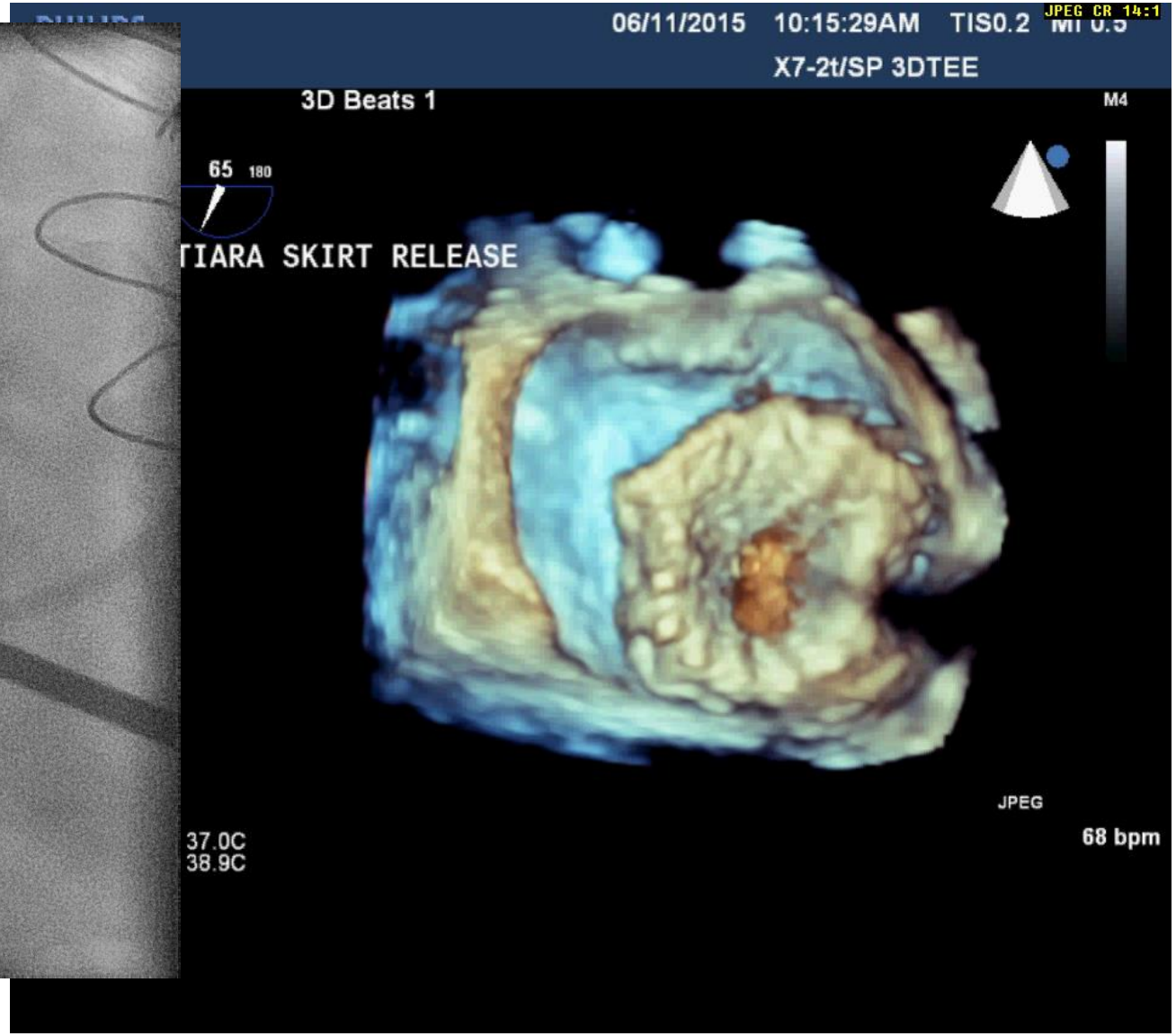




Unsheathing of atrial skirt

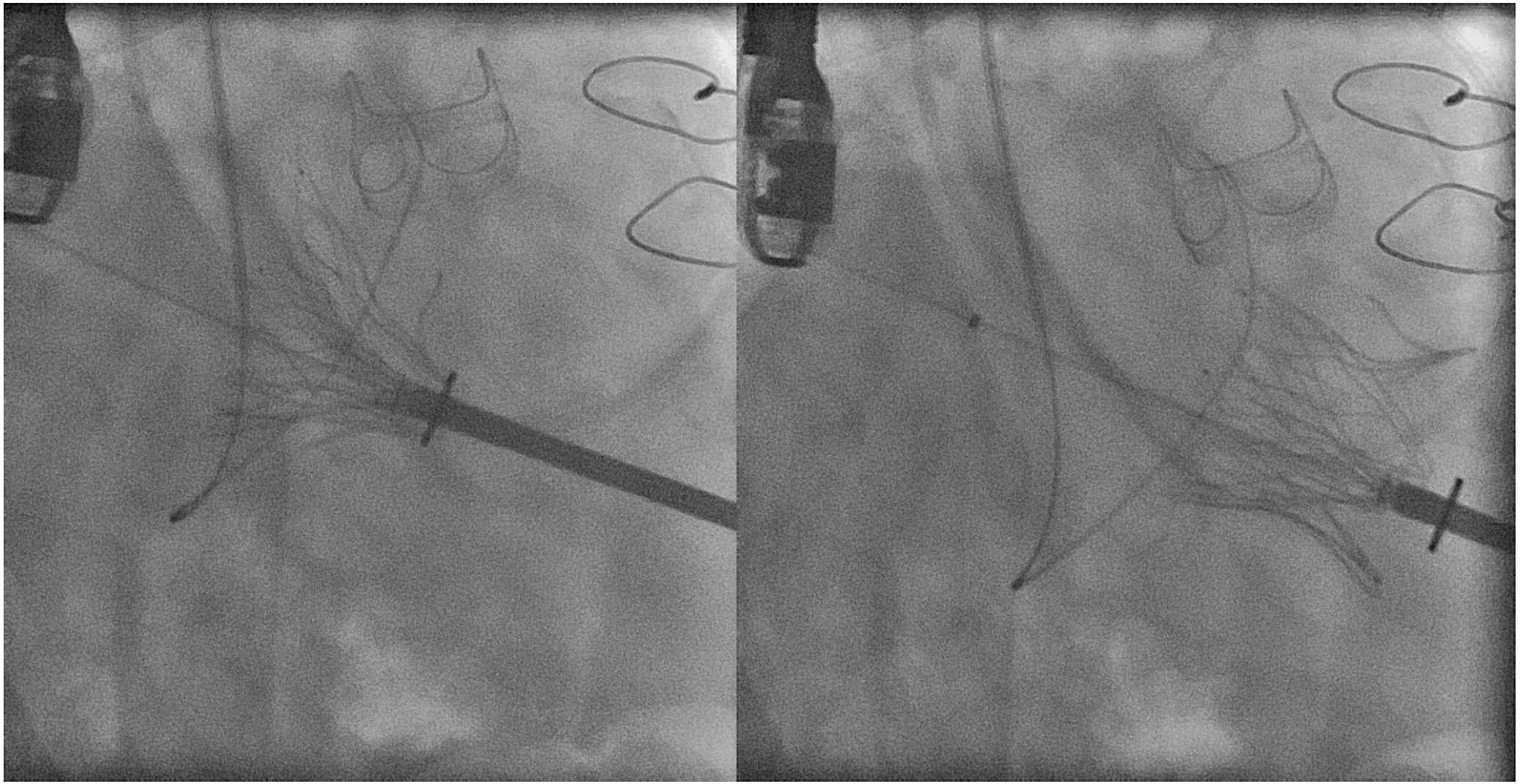


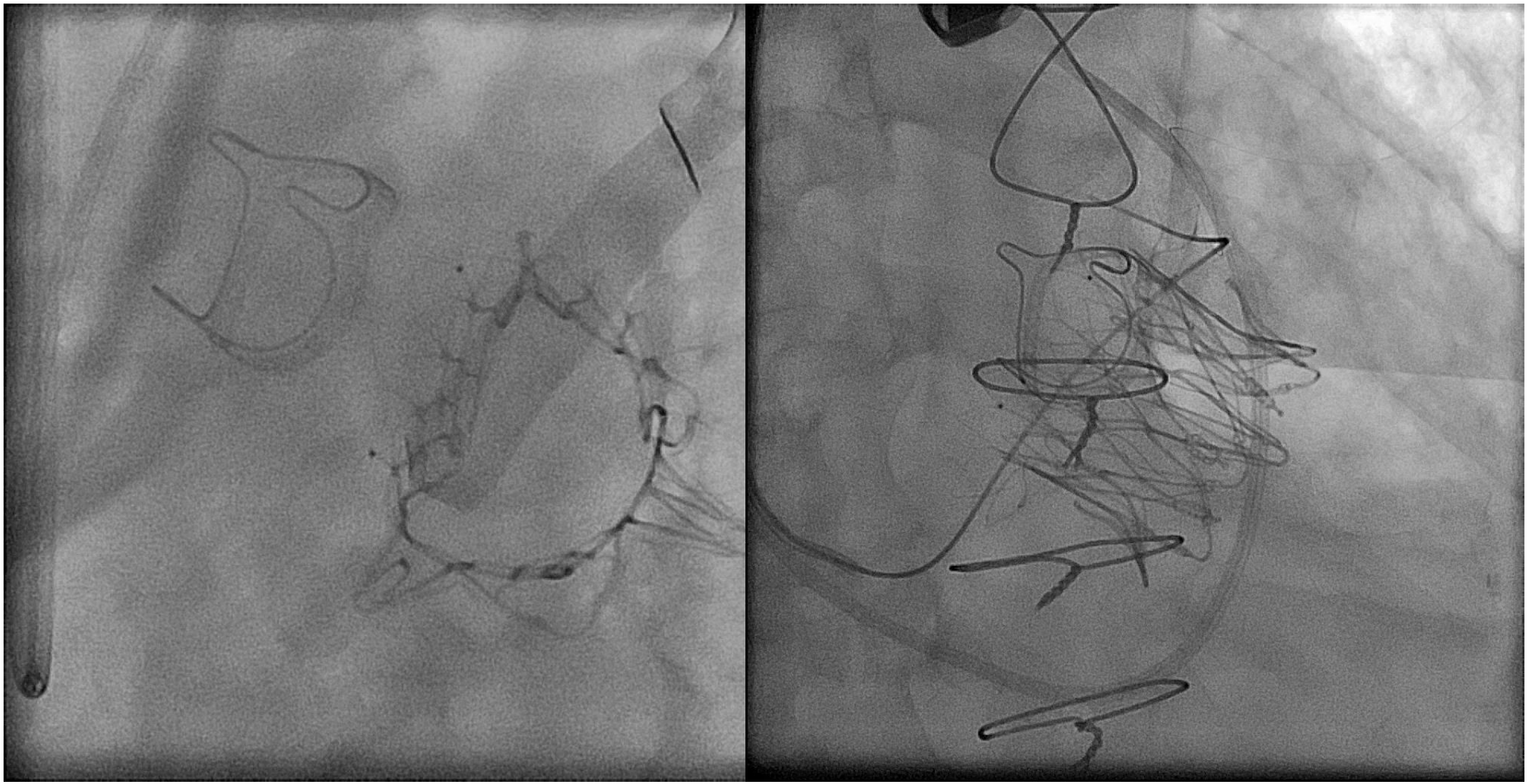
Orientation of the “D”



Release of Ventricular Tabs and Skirt

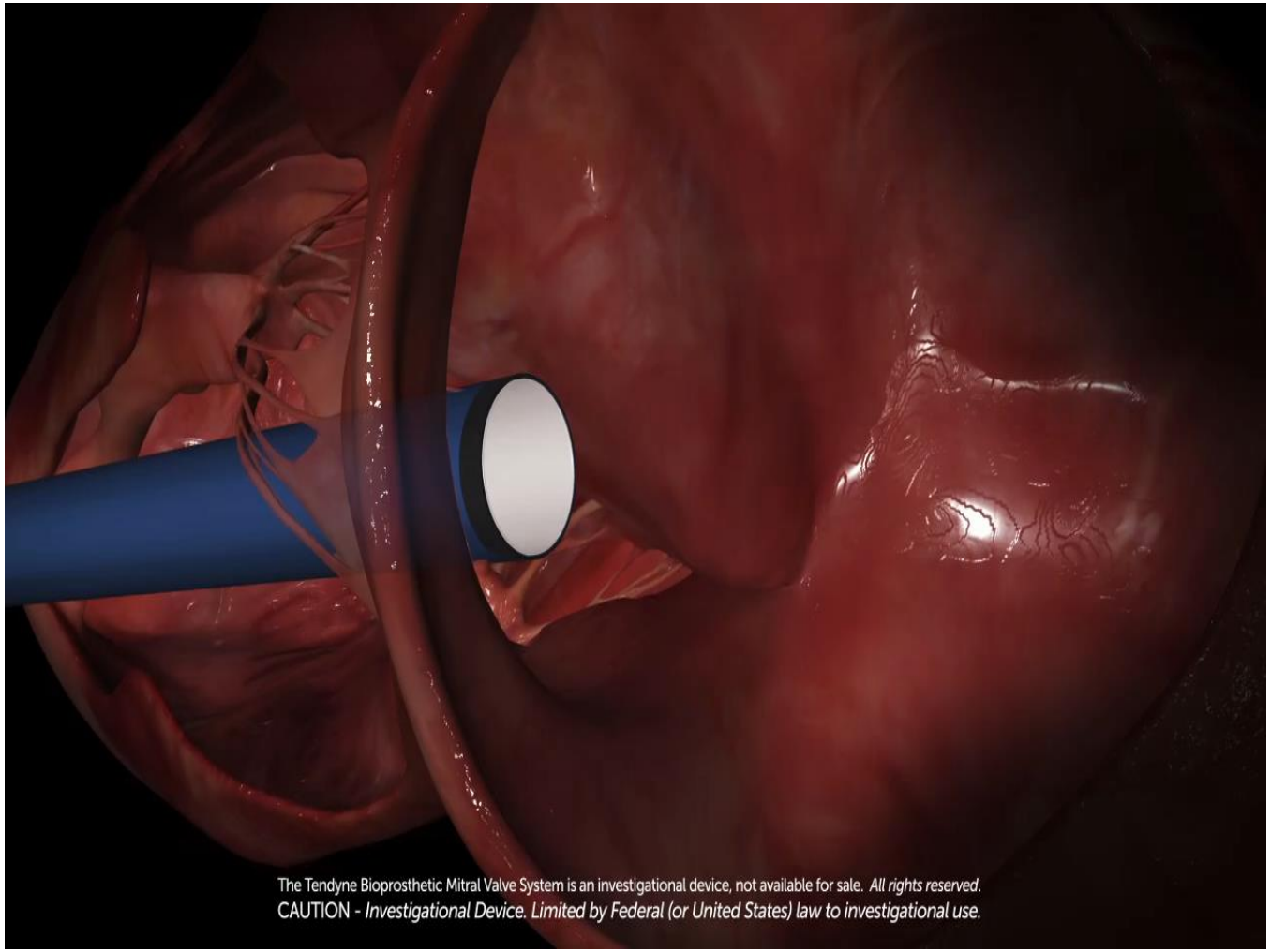
Valve release





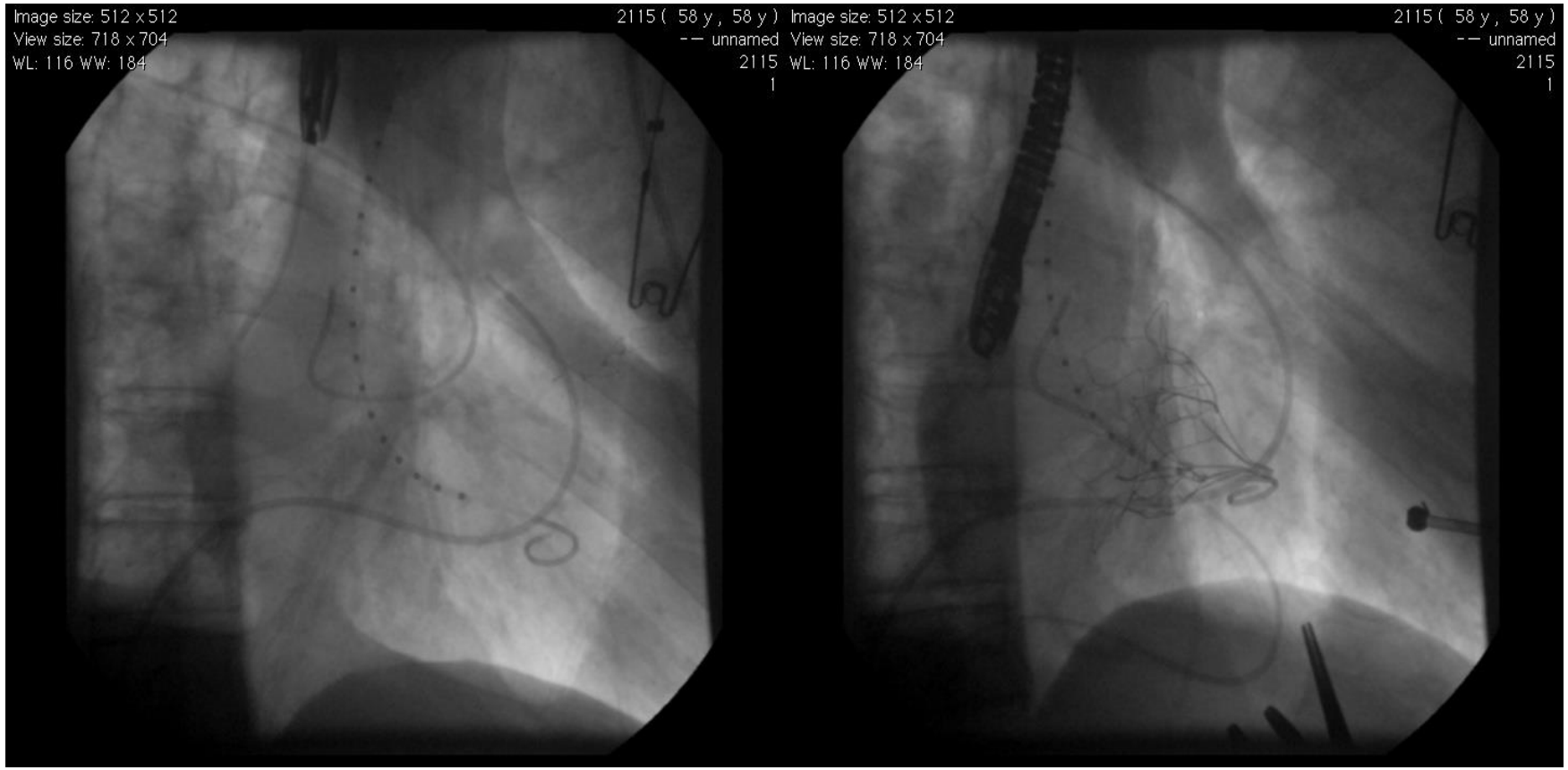
Courtesy F. Maisano

Tendyne Transcatheter Mitral Valve



Tendyne product is currently in development at Abbott. Neither approved or available for sale.

Acute Human Use, February 2013



Intra-operative Baseline
Severe MR

Intra-operative Post-Valve
No MR

Tendyne product is currently in development at Abbott. Neither approved or available for sale.

Tendyne GFS: Patient Overview (n=30)

Baseline Mitral Valve pathology	
Primary MR	3 (10%)
Secondary MR	23 (76.7%)
Mixed pathology	4 (13.3%)
Baseline LV function	**N=29**
LVEF <30%	3 (10.3%)
LVEF 30-50%	14 (48.3%)
LVEF>50%	12 (41.4%)

D. Muller, TCT 2016

GFS: Acute Outcomes

Outcome	N=30
Death (all cause)	0 (0%)
CVA	0 (0%)
Major bleeding	
Transfusion	3 (10%)
Device-related	
Device embolization	0 (0%)
Cardiac perforation	0 (0%)
Paravalvular leak	1 (3.3%)
Device Retrieval	
LVOT obstruction	1 (3.3%)
Did not properly seat - access issue	1 (3.3%)

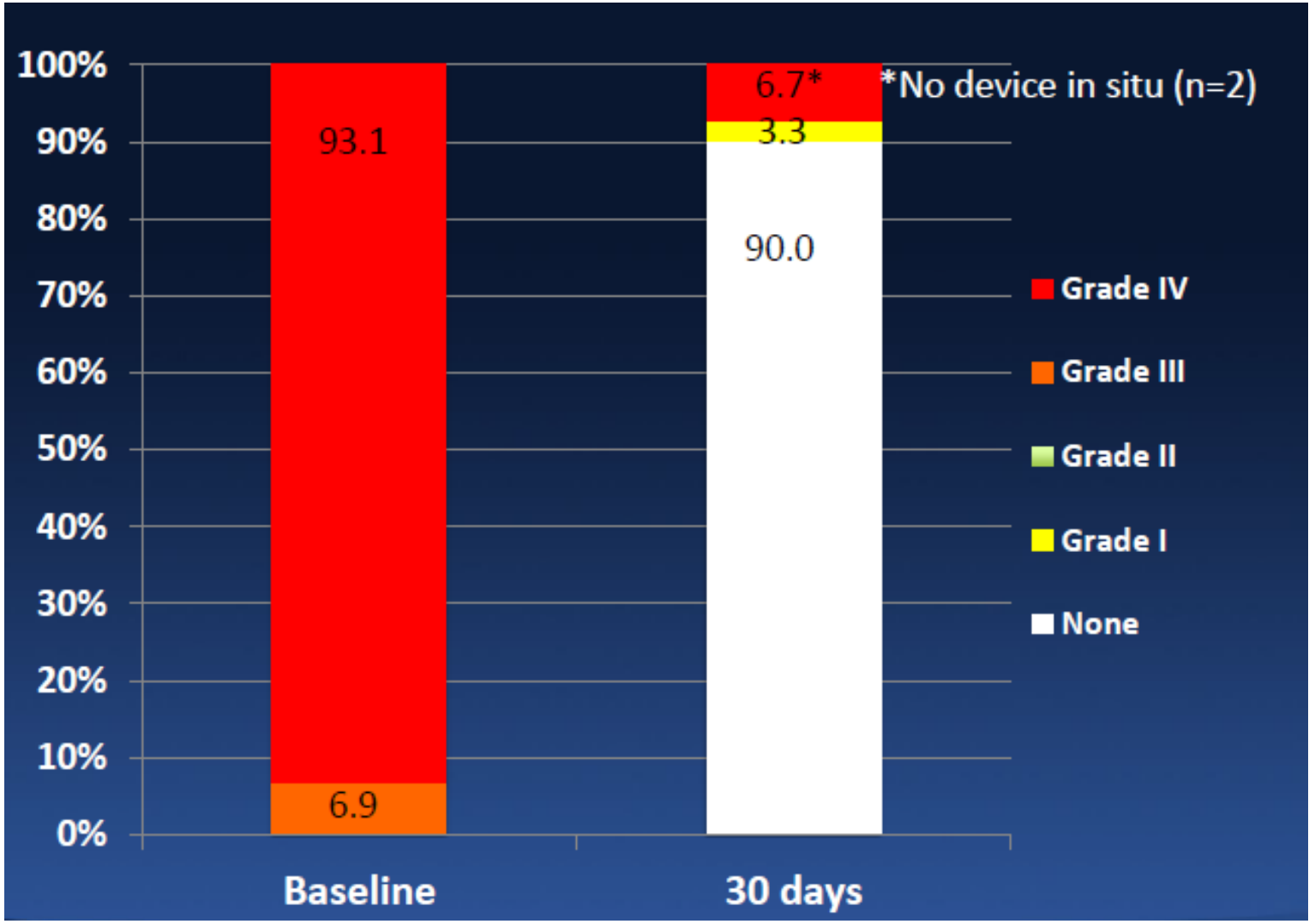
D. Muller, TCT 2016

Tendyne TMVI: D30 Outcomes

Outcome	N=30
Death (all cause)	1 (3.3%)
Cardiac	0 (0%)
Non-cardiac	1 (3.3%)
CVA	0 (0%)
MV surgery	0 (0%)
Re-hospitalisation	
Heart failure	4 (13.8%)
LVAD/transplant	0 (0%)
Other (ileus)	1 (3.3%)
Device-related	
Hemolysis, transfusion	1 (3.3%)
Leaflet thrombosis	1 (3.3%)

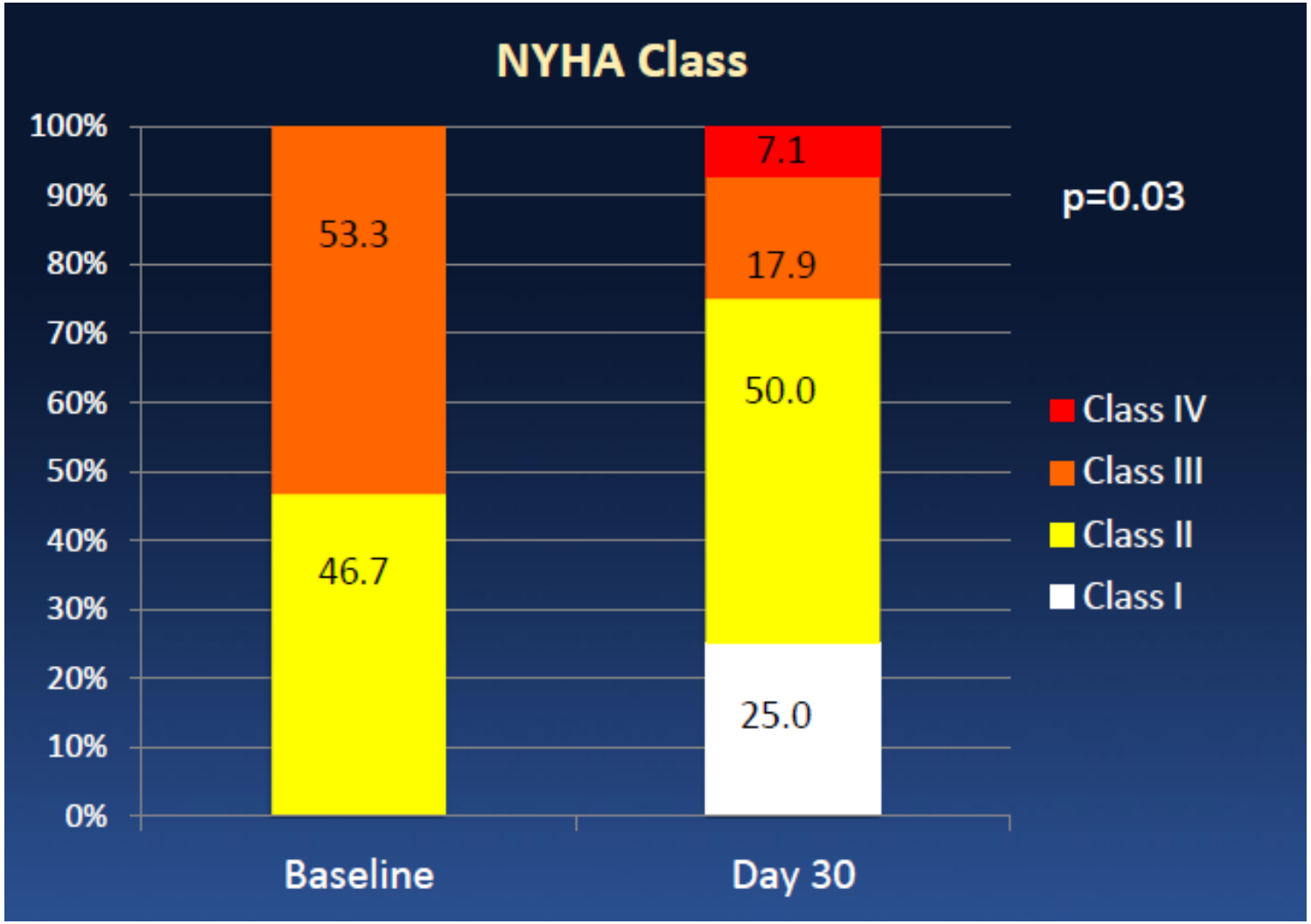
D. Muller, TCT 2016

MR severity post-TMVI (n=30)



D. Muller, TCT 2016

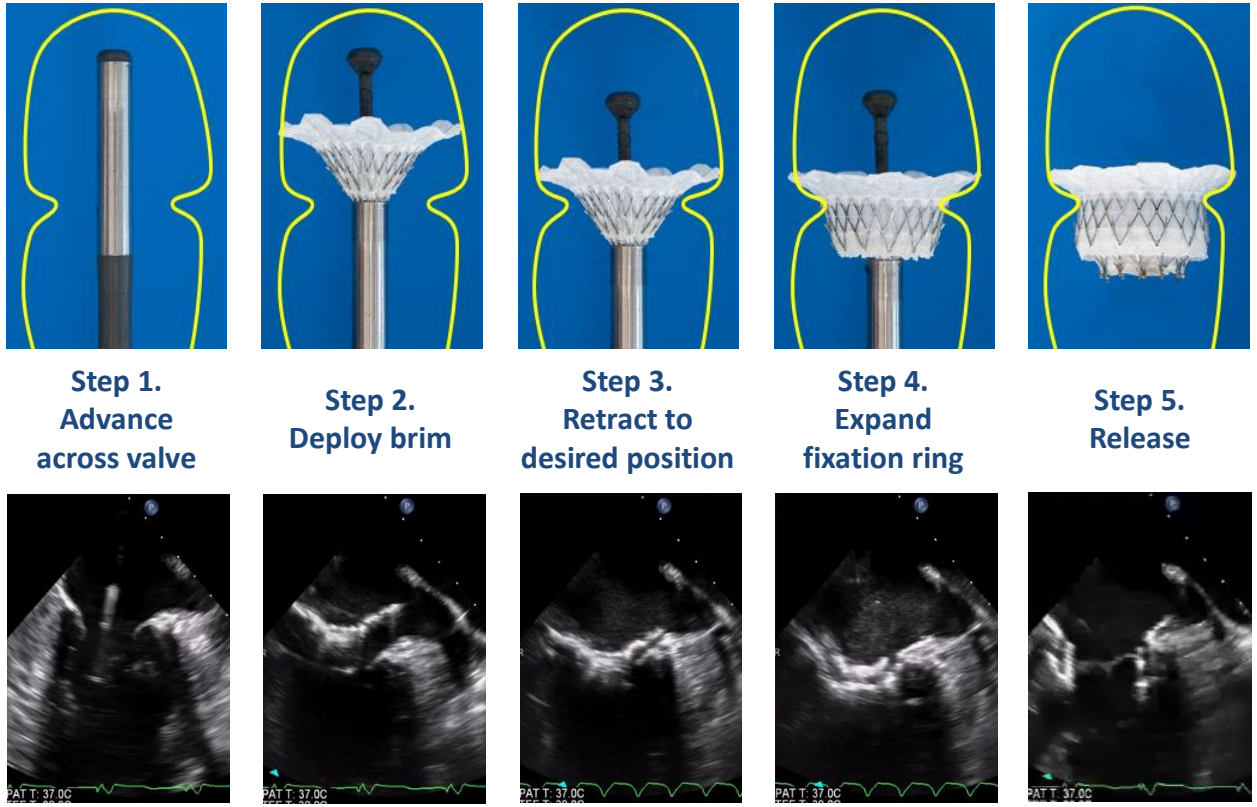
Functional capacity post-TMVI (n=30)



D. Muller, TCT 2016

Medtronic Twelve TMVR

Hydraulic Deployment of Self-expanding Stent

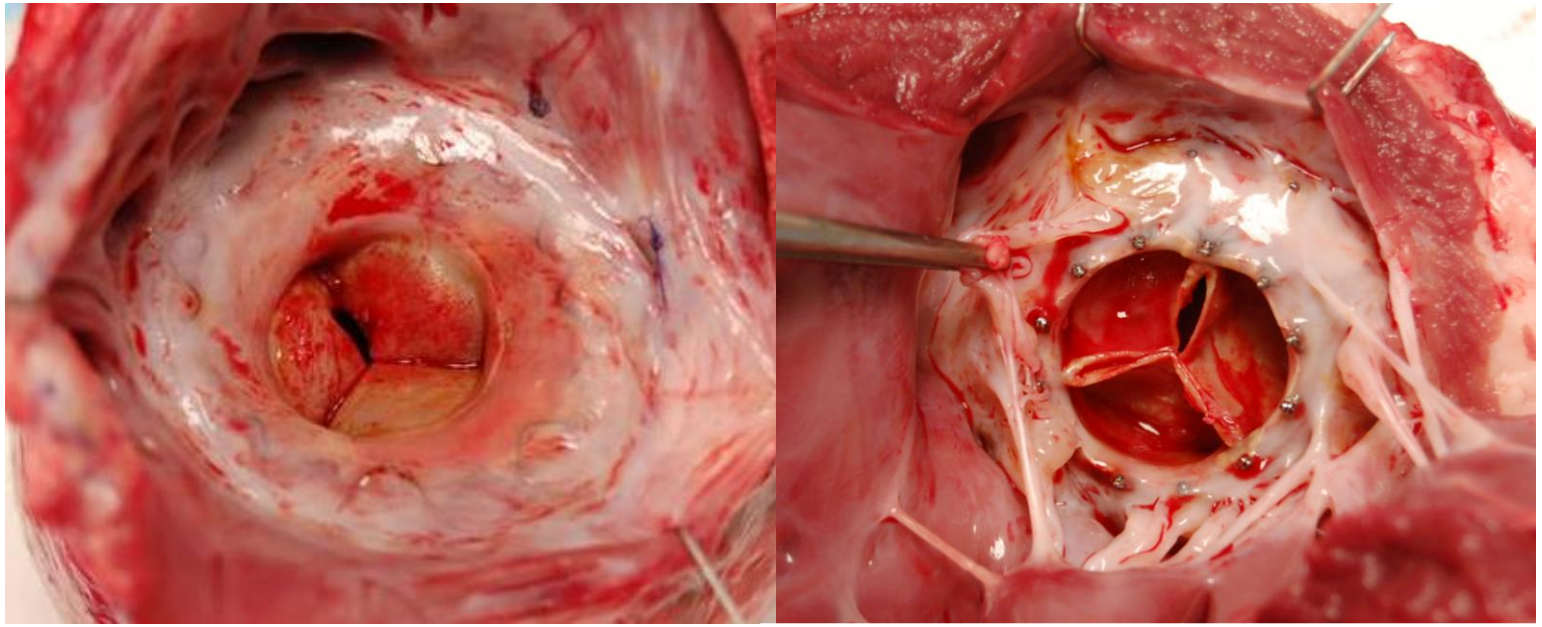


No need for rotational alignment - No need to search for leaflets

Accommodates tilt & lateral misalignment

Medtronic Twelve TMVR

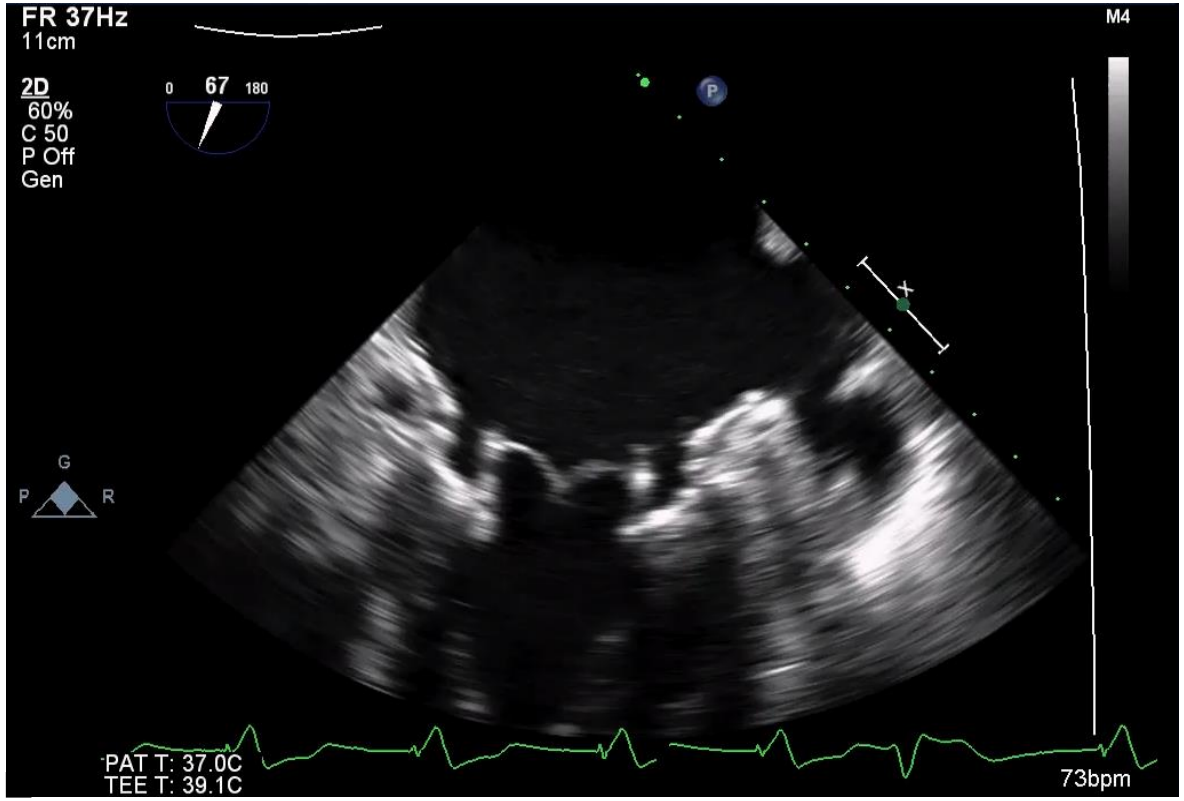
Dual Stent Design



Excellent healing response in longer term porcine and ovine studies.

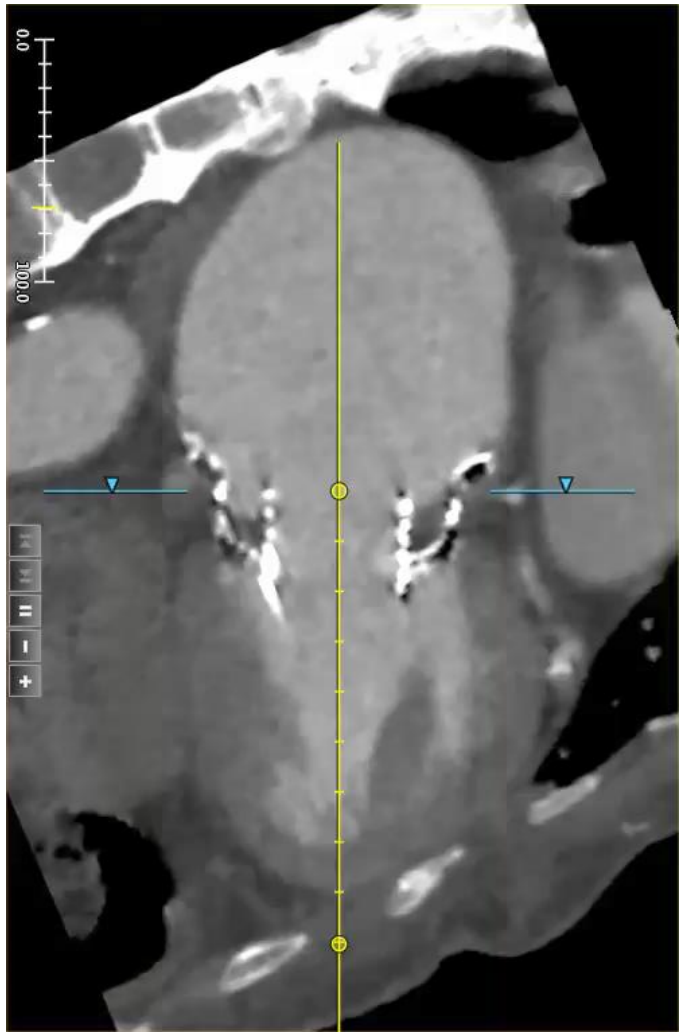
Gross and histological evaluation reveals the implants are well integrated with the native tissue, with neo-endocardial coverage

Results



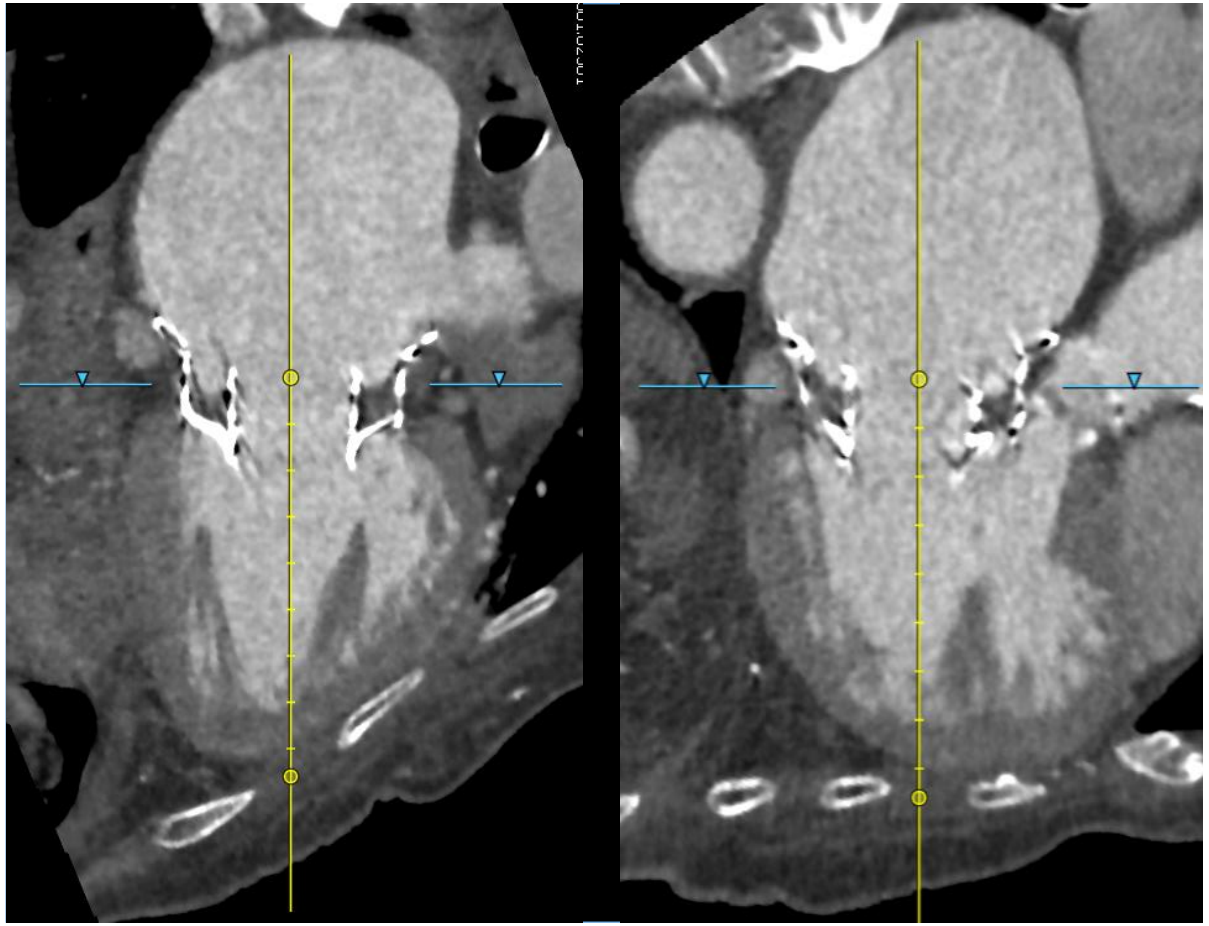
Post Procedure: Good Valve Function - No PVL or TVL

Results



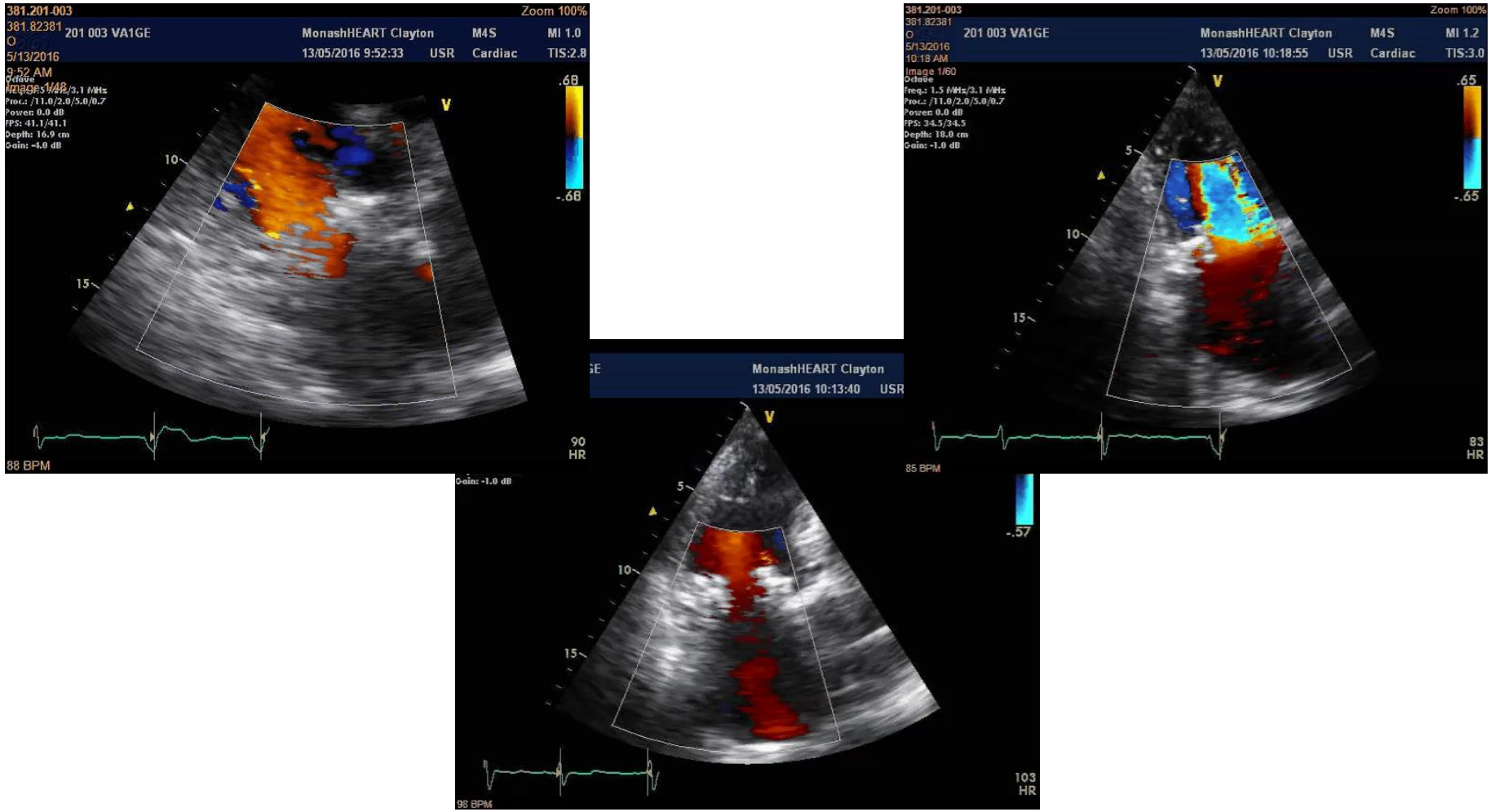
12-Month Follow-up: Stable position & excellent ingrowth

Results



12-Month Follow-up: Stable position & excellent ingrowth

Results



12-Month TTE Follow-up: Good Valve Function

No PVL or TVL with Patent LVOT (4 mmHg)

PILOT CLINICAL STUDY

Design	Multi-Center, prospective, non-randomized, single-arm
Leadership	Principal Investigator: Ian Meredith, Monash Heart, AU Principal Investigator: Vinnie Bapat, St. Thomas' Hospital, UK
Sites	15 sites in AU, EU & US
Population	Patients with severe, symptomatic MR who are at high risk for conventional mitral valve surgery
Objectives	Primary Objective: To evaluate the nature, severity & frequency of any complications with the delivery &/or implantation of the device Secondary Objectives: • To evaluate the ability to accurately deliver & place the implant • To evaluate the fit of the implant within the native anatomy, including fixation, sealing & compatibility with native structures • To evaluate the degree of improvement of MR grade & symptoms

PATIENT DEMOGRAPHICS

Reardon, M STS 2017

Baseline Characteristics (n=38)

Age (years)	73	(range: 48-90)
Sex (female)	12	
NYHA Functional Class		
II	4	
III	27	
IV	7	
Prior MI / Coronary Artery Disease	28	
Previous Cardiac Surgery	17	
Atrial Fibrillation	25	
Pacemaker/BiV/ICD	14	
STS Mortality score mean (%)	6.5	(range: 1-31)

PATIENT DEMOGRAPHICS

Reardon, M STS 2017

Baseline Echocardiogram (n=38)

	FMR	DMR
MR Etiology	30	8
LVEF mean (%)	38	53
< 30	4	0
30 – 50	22	3
> 50	4	5
MR grade ≥ 3+ (%)	100	

RESULTS

Reardon, M STS 2017

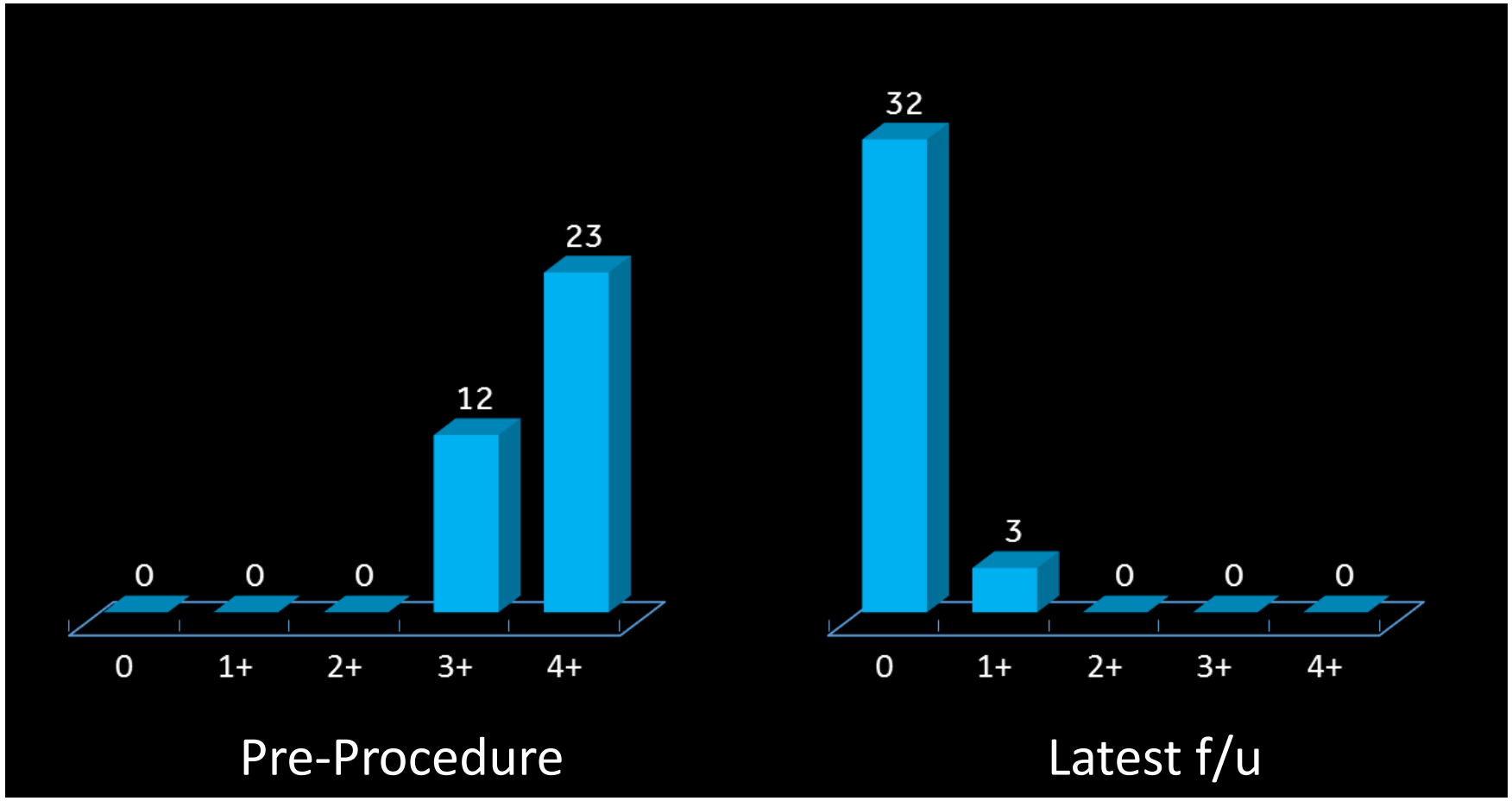
Procedural Outcomes (n=38)

Successful Deployment	35/37[1]	
Apical Access Time (min)	30	(range: 17-53)
Deployment Time (min)	15	(range: 4-29)
Mean LVOT Gradient[2] (mmHg)	2	(range: 0-4)
Mean MV Gradient[2] (mmHg)	4	(range: 0-7)

1 - in one patient deployment was not attempted
2 - latest follow-up

RESULTS

MR Grade

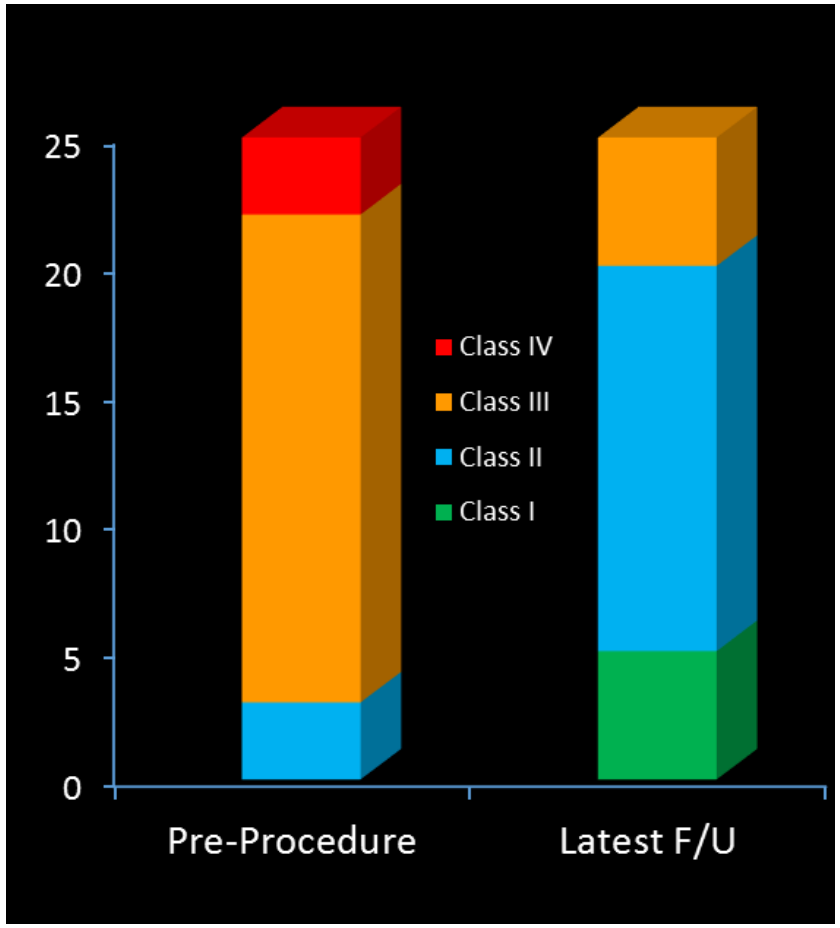


Reardon, M STS 2017

RESULTS

Reardon, M STS 2017

NYHA Class

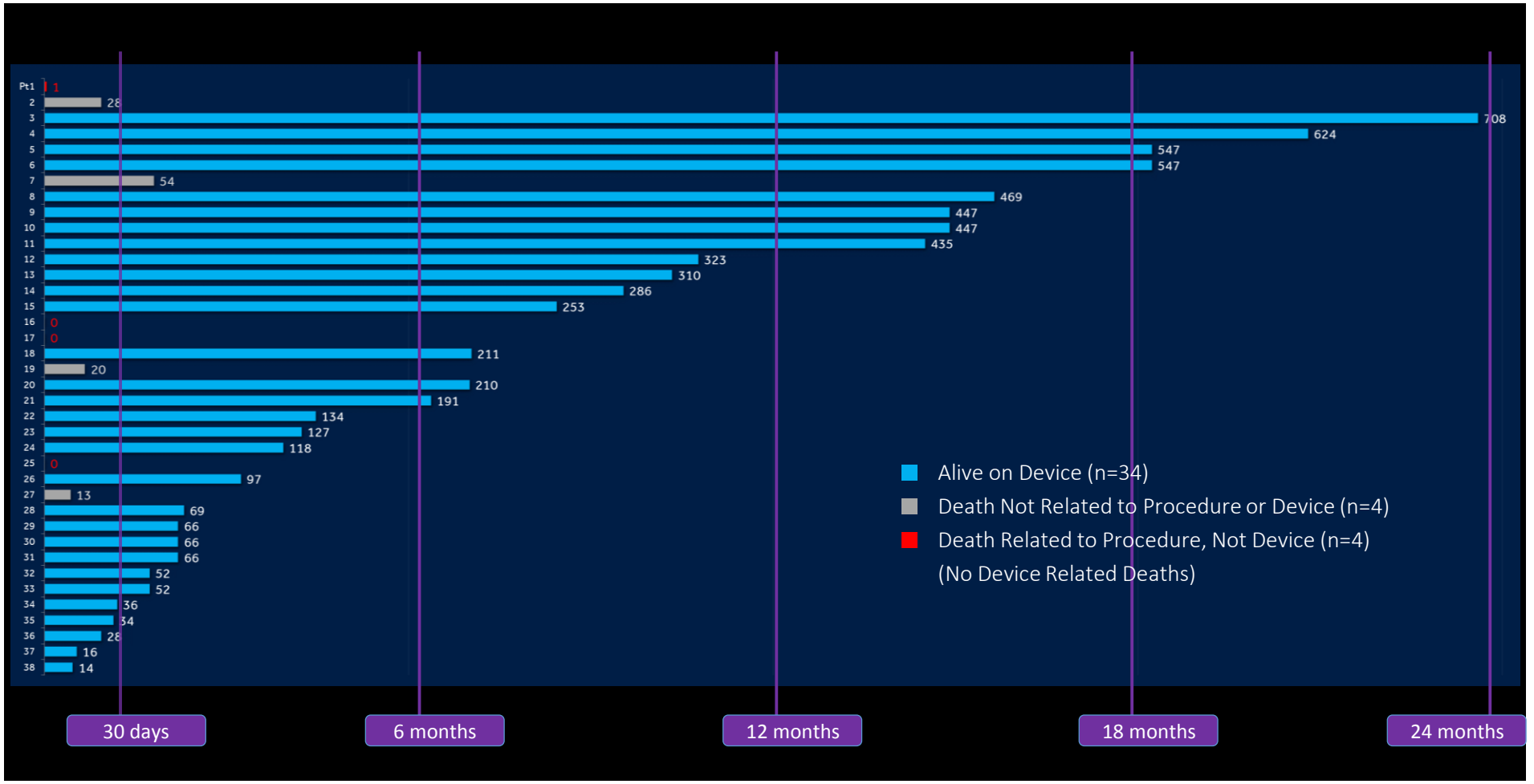


21/25
with ≥ one grade improvement

RESULTS

Reardon, M STS 2017

Survival



Conclusions

- TMVR programs in 2017 are demonstrating promising early efficacy and safety results
- The outcomes are underpinned by extensive pre-procedural planning guided by MSCT and TEE and supported by dedicated heart teams
- Development of alternative access mechanisms and devices is critical – trans-septal and trans-atrial
- Larger numbers of patients followed for longer periods will be required to determine the clinical impact of this emerging technology

Conclusion

Nothing is impossible
Need to make it possible

Fear change, and it will destroy you,
embrace change and it will enlarge you

Elizabeth moon, the darkness of speed