Transcatheter Therapies for Mitral and Tricuspid Regurgitation
Evolving Approaches Under Investigation

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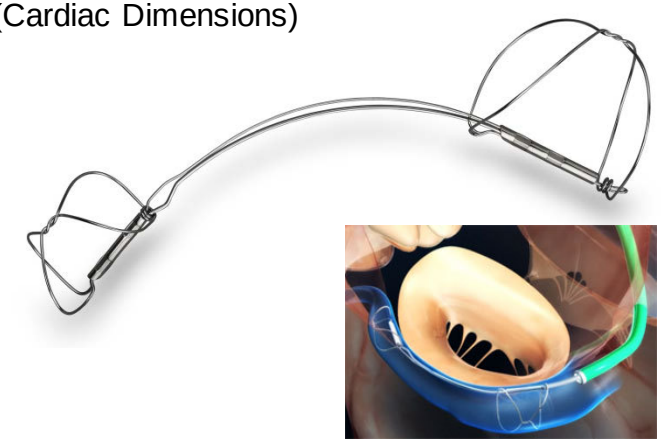
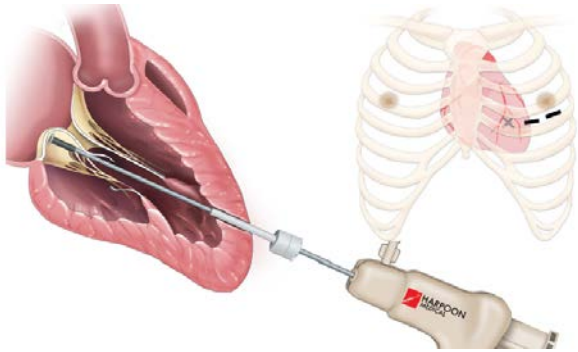
AMERICAN COLLEGE of CARDIOLOGY

Transcatheter Mitral Repair

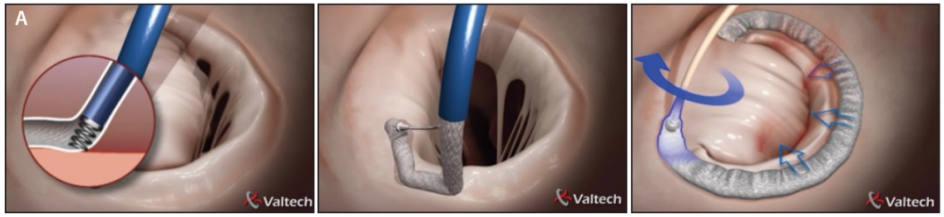
CARILLON Mitral Contour System
(Cardiac Dimensions)



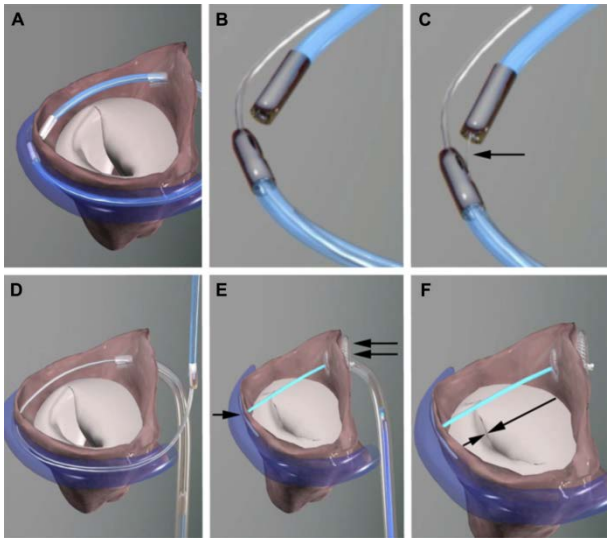
HARPOON System
(Harpoon Medical)



CARDIOBAND System
(Edwards Lifesciences)

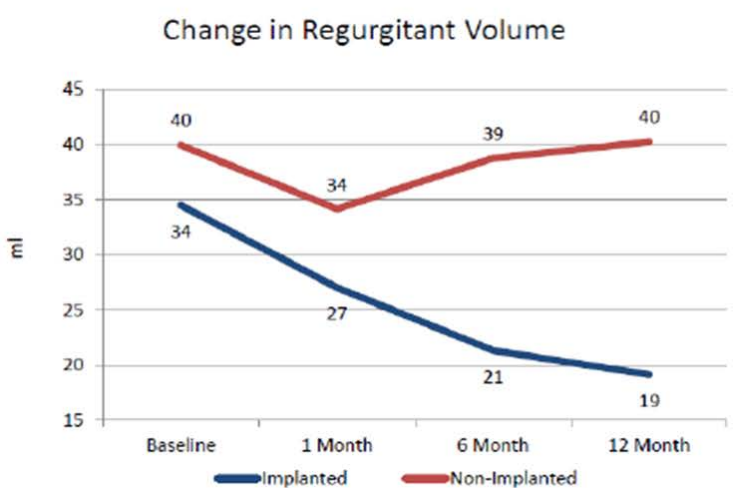


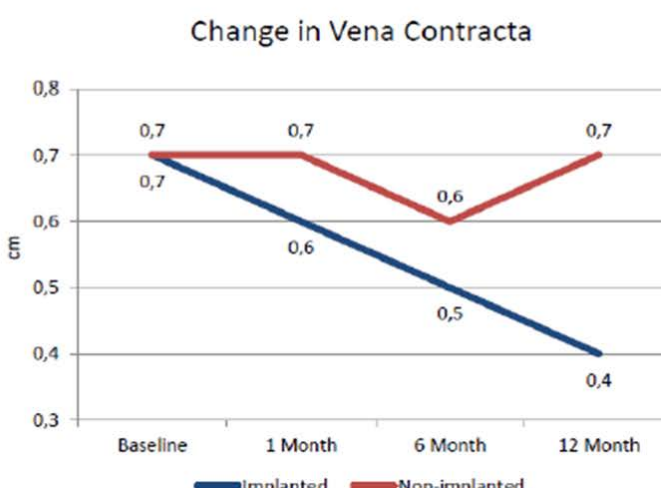
ARTO System
(MVRx)

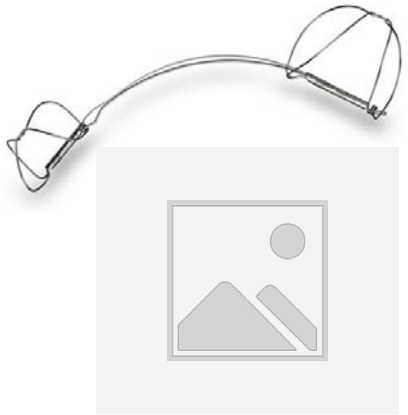


CARRILLON System (TITAN Trials)

	TITAN[1]		TITAN II[2]	
	30-day Rate	Device Related	30-day Rate	Device Related
Death	1.9%	0.0%	2.8%	0.0%
MI	0.0%	0.0%	0.0%	0.0%
Cardiac Perforation	0.0%	0.0%	0.0%	0.0%
Device Embolism	0.0%	0.0%	0.0%	0.0%
Surgery or PCI related to the device	0.0%	0.0%	0.0%	0.0%
MAE Rate	1.9%	0.0%	2.8%	0.0%



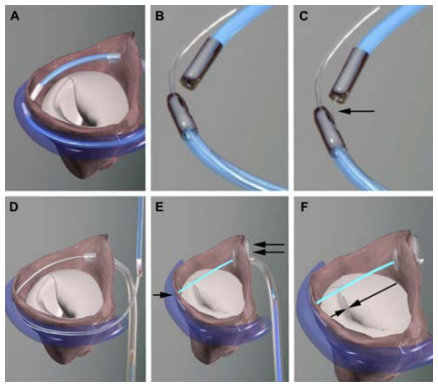


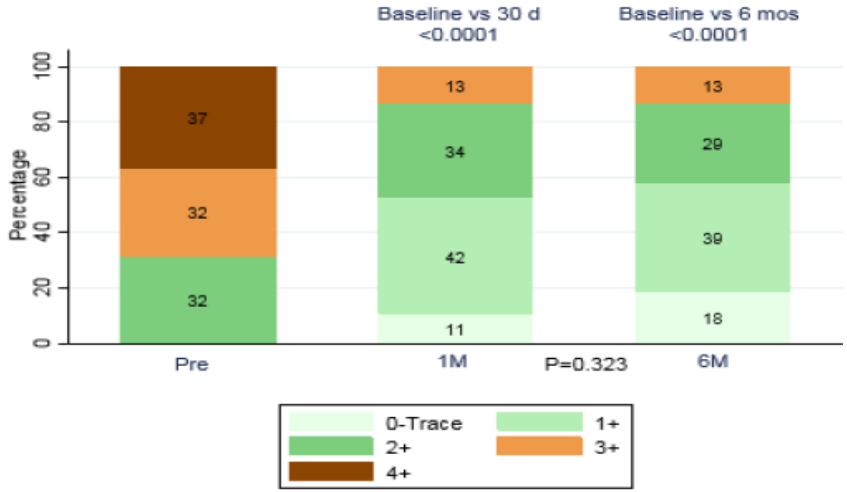


Houde
London Valve 2016

ARTO System (MAVERICK Trial)

CEC Adjudicated Event	30 days N=45 N(%)	6 months N=42 N(%)
Safety Composite Endpoint at 6 months*	2(4.4)	7(16.0)
Death	0	3(7.2)
Cardiovasc	0	3(7.2)
Non-cardiovasc	0	0
Stroke	0	1(2.3)
Myocardial Infarction	0	0
Mitral Operation/Intervention	0	1(2.3)
Cardiac Tamponade	1(2.2)	1(2.2)
Renal Failure	1(2.2)	3(6.9)

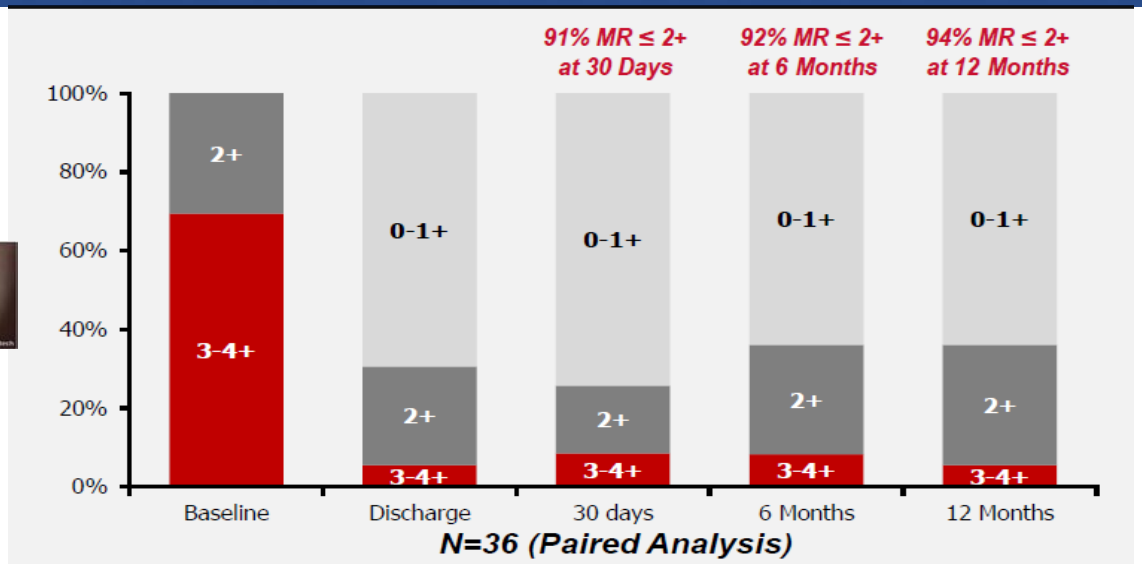




Worthley et al.
TCT 2017

CARDIOBAND SYSTEM (CE-MARK TRIAL)

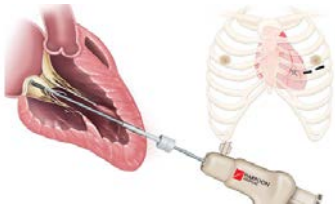
30 Day Events*	Patients Experiencing Event, # (%) Full Analysis Set N=61
Death	2 (3.3%)
Hemorrhagic Stroke**	1 (1.6%)
Need for elective MV Operation**	1 (1.6%)
Myocardial Infarction	1 (1.6%)
Major Bleeding Complications	2 (3.3%)
Renal Failure	4 (6.6%)
Respiratory Failure	0 (0.0%)
Cardiac Tamponade	1 (1.6%)



Thourani V
TCT 2017

HARPOON System (TRACER Trial)

Outcome	N (%)
Mortality	0
Stroke	0
Renal Failure	0
Blood Transfusion	1 (3 %) (intraoperative conversion)
Permanent Pacemaker	0
Intraoperative Inotrope	0
Myocardial Infarction	0
New Postoperative AF	2/21 (10 %)



Technical success rate: 93 % (28/30)

4.1 (1-5) ePTFE cordal pairs inserted

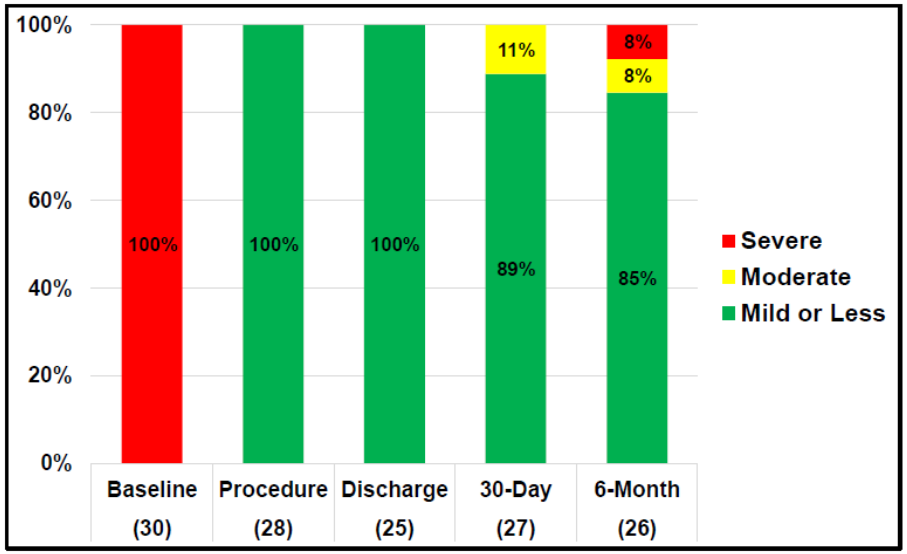
Procedural Time = 125 ± 43 min

Two intraoperative conversions to conventional surgery

-Patient #1 Imaging equipment dysfunction, insufficient MR reduction

-Patient #10 Imaging equipment dysfunction, access site bleeding

Both received MV repair with ePTFE cords, No MR at D/C



Gammie et al
JACC 2017

Transcatheter Mitral Valve Replacement Challenges of the Mitral Valve Anatomy

-Assymetrical saddle-shaped mitral annulus, irregular mitral leaflets

-Complex structure (including chordae, papillary muscles)

-No calcified structure in most cases

-Interaction with the LVOT

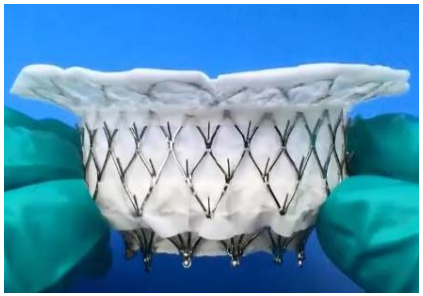
-Valve position and dimension

TMVR Devices Under Clinical Evaluation

CardiAQ
Edwards Lifesciences

MValve
MValve Technologies
Boston Scientific

Tendyne
Abbott Vascular



Intrepid
Medtronic

Fortis
Edwards Lifesciences

Caisson
Caisson Interventional

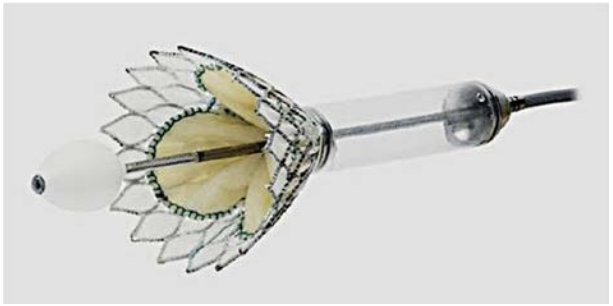
HighLife
HighLife SAS

Tiara
Neovasc Inc.

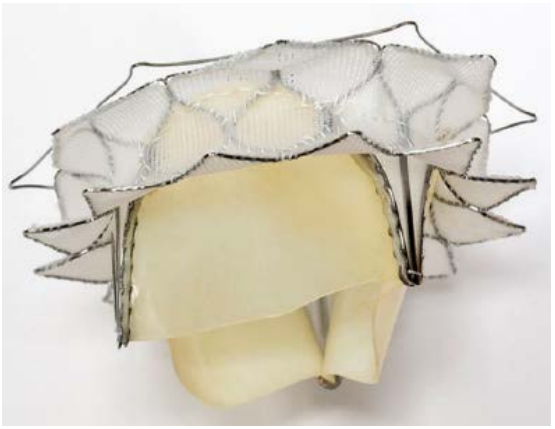
NCSI NaviGate
NaviGate Cardiac
Structures Inc.

TMVR Devices Under Pre-Clinical Evaluation

AccuFit
Sino Medical Science Technology Inc.

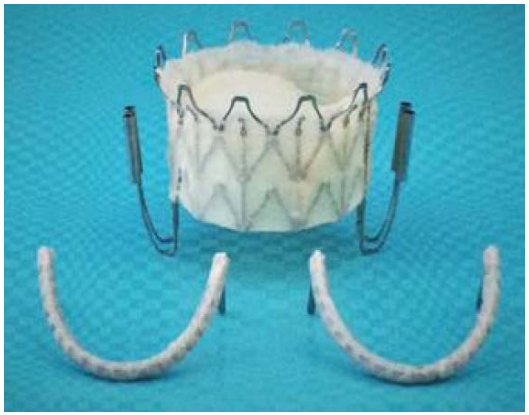


Cardiovalve
Valtech HQ



Cephea
Cephea Valve Technologies

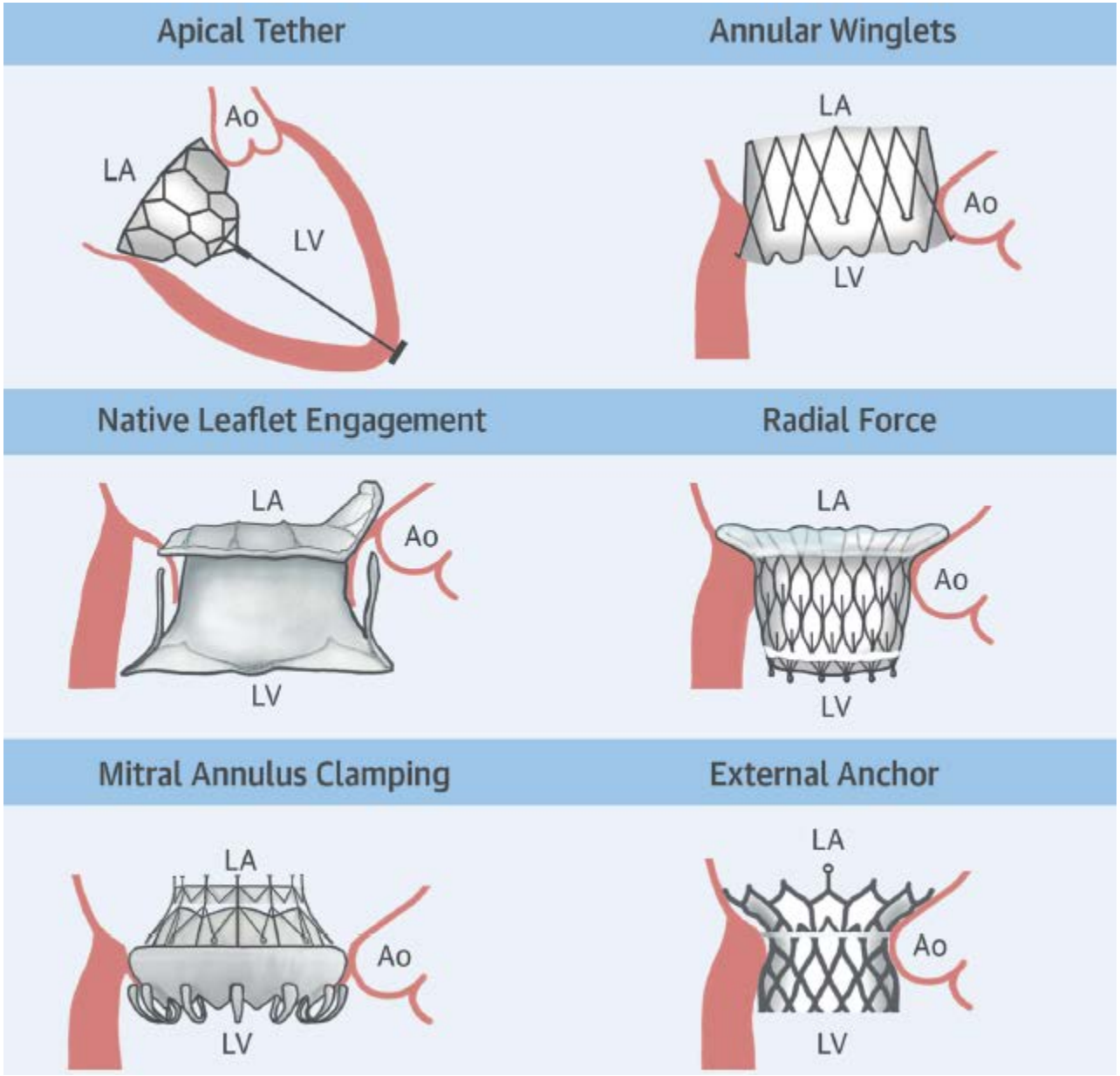
Direct Flow Medical
Direct Flow Medical Inc.



Saturn
HT Consultant

TMVR Technologies Under Clinical Evaluation

Valve type	Valve shape	Frame	Anchoring mechanism	Leaflets	Valve position
CardiAQ-Edwards	Circular	Nitinol Self-expandable	Mitral annulus capture with native leaflet engagement	Tri-leaflet Bovine pericardium	Supra-annular
Neovasc Tiara	D-Shaped	Nitinol Self-expandable	Fibrous trigone capture with native leaflet engagement	Tri-leaflet Bovine pericardium	Intra-annular
Tendyne	D-Shaped (Outer stent) Circular (Inner frame)	Nitinol, double frame, Self-expandable	Apical tether	Tri-leaflet Porcine pericardium	Intra-annular
Intrepid TMVR	Circular	Nitinol, double stent, self-expandable	Radial force and subannular cleats	Tri-leaflet Bovine pericardium	Intra-annular
Fortis[a]	Circular	Nitinol Self-expandable	Native leaflet engagement	Tri-leaflet Bovine pericardium	Intra-annular
Caisson	D-shaped	Two components (anchor and valve) Nitinol, self-expandable	External anchor Mitral annulus capture with engagement at sub-annular fibrous groove	Tri-leaflet Porcine pericardium	Supra-annular
HighLife TMVR	Circular	Two components (ring and valve) Nitinol, self-expandable	External anchor Valve-in-subannular mitral ring	Tri-leaflet Bovine pericardium	-
MValve system	-	Dock system to be used with commercially available valves	External anchor Mitral annulus capture	-	-
NCSI NaviGate Mitral	Circular	Nitinol, self-expandable, xenogeneic pericardium	Annular winglets	Tri-leaflet	-

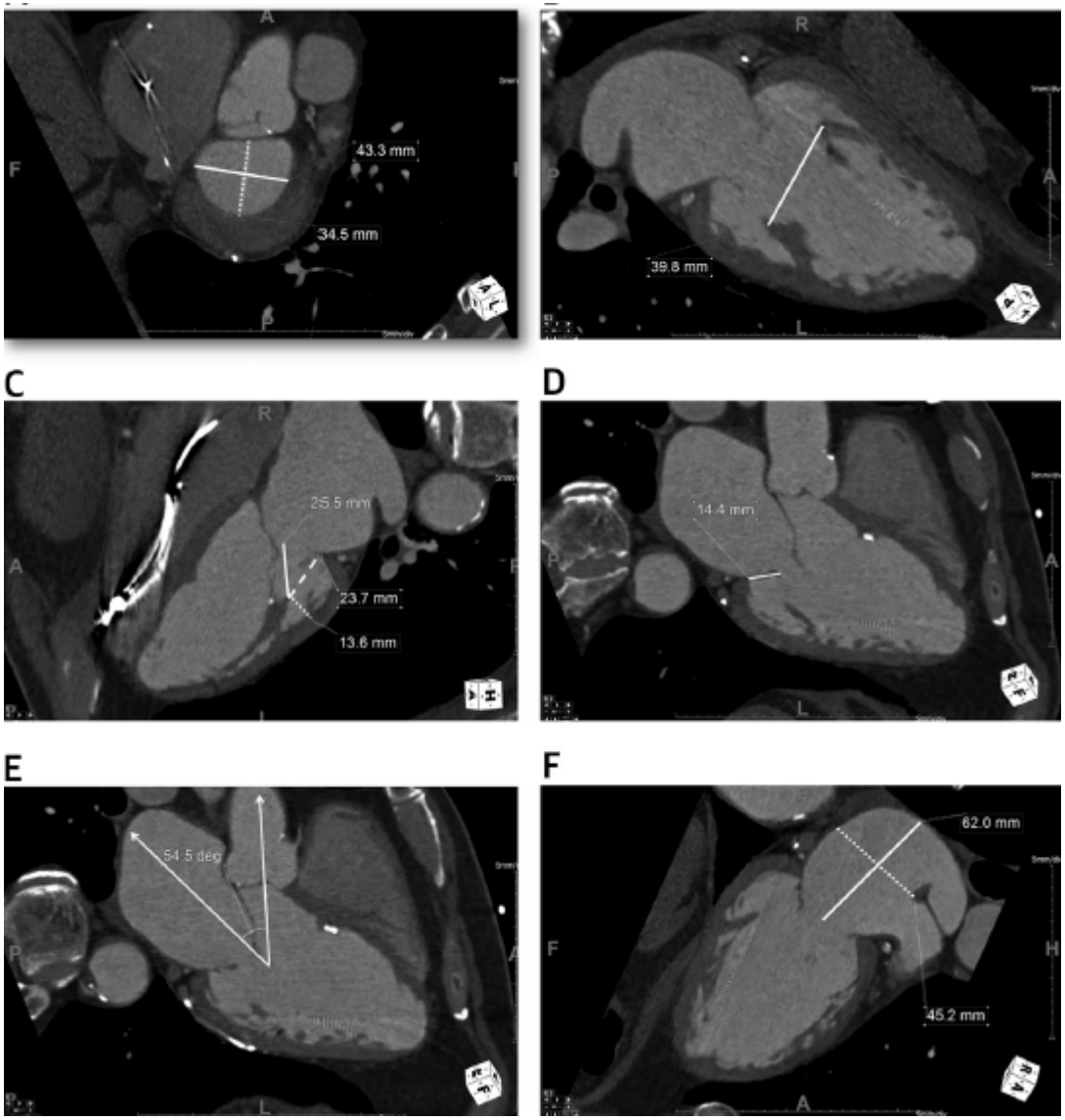


Regueiro A, Granada, J, Dagenais F, Rodés-Cabau J. JACC 2017

TMVR Technologies Under Clinical Evaluation

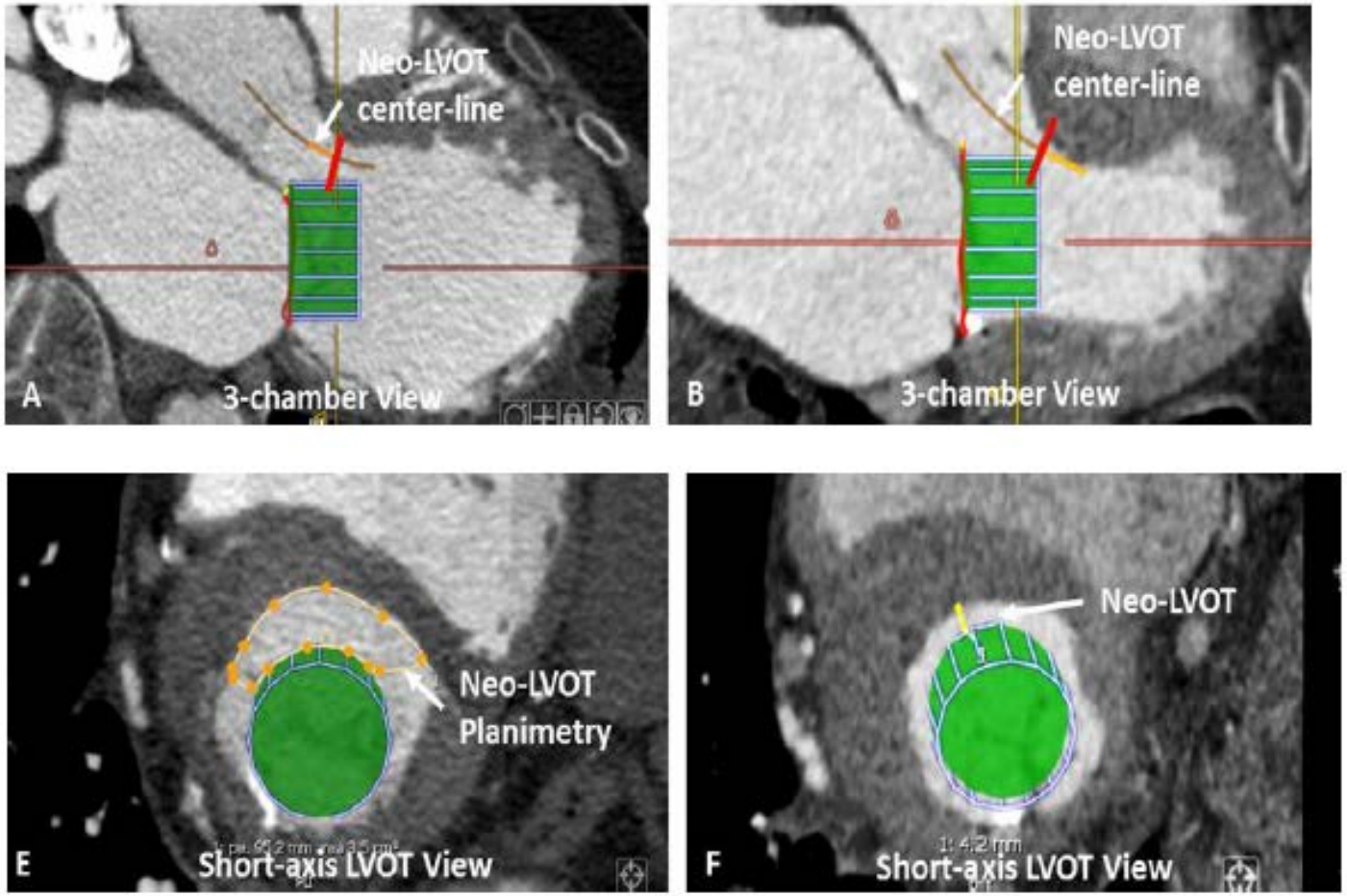
Valve type	Access	Delivery system size	Recapture	Valve size(s)	Additional features
CardiAQ-Edwards	Transapical Transeptal	33 Fr	No	30 mm	Supra-annular position Intra-annular sealing skirt Tappered Outflow
Neovasc Tiara	Transapical	32 Fr	No	35mm and 40 mm	Two anterior and one posterior anchoring structures
Tendyne	Transapical	32 Fr	Fully recapturable system after complete deployment	NA (Multiple configurations)	Single inner valve size Multiple outer frame sizes
Intrepid TMVR	Transapical	35 Fr	No	27 mm with 3 outer stent sizes (43, 46, and 50 mm)	Dual stent design Outer provide fixation and isolates the inner stent
Fortis[a]	Transapical	42 Fr	No	29 mm	-
Caisson	Transeptal	31 Fr	Fully recapturable and retrievable	35mm – 40 mm	SAM Management feature One delivery catheter for each system (anchor and valve)
HighLife TMVR	Transapical (Transfemoral artery for loop placement)	NA	No	31 mm	NA
MValve system	Transapical	32 Fr	Fully retrievable	NA	Universal dock system
NCSI NaviGate Mitral	Transapical, transatrial or transfemoral	30 Fr	NA	30/36; 30/40; 33/44	NA

TMVR
Preprocedural CT



Regueiro et al.
JACC 2017

Modeling the risk of LVOT Obstruction-



Need dynamic data to more deeply understand individual risk

Leipsic J. TCT 2017

3D Printed Modeling of the Mitral Valve for Catheter-Based Structural Interventions

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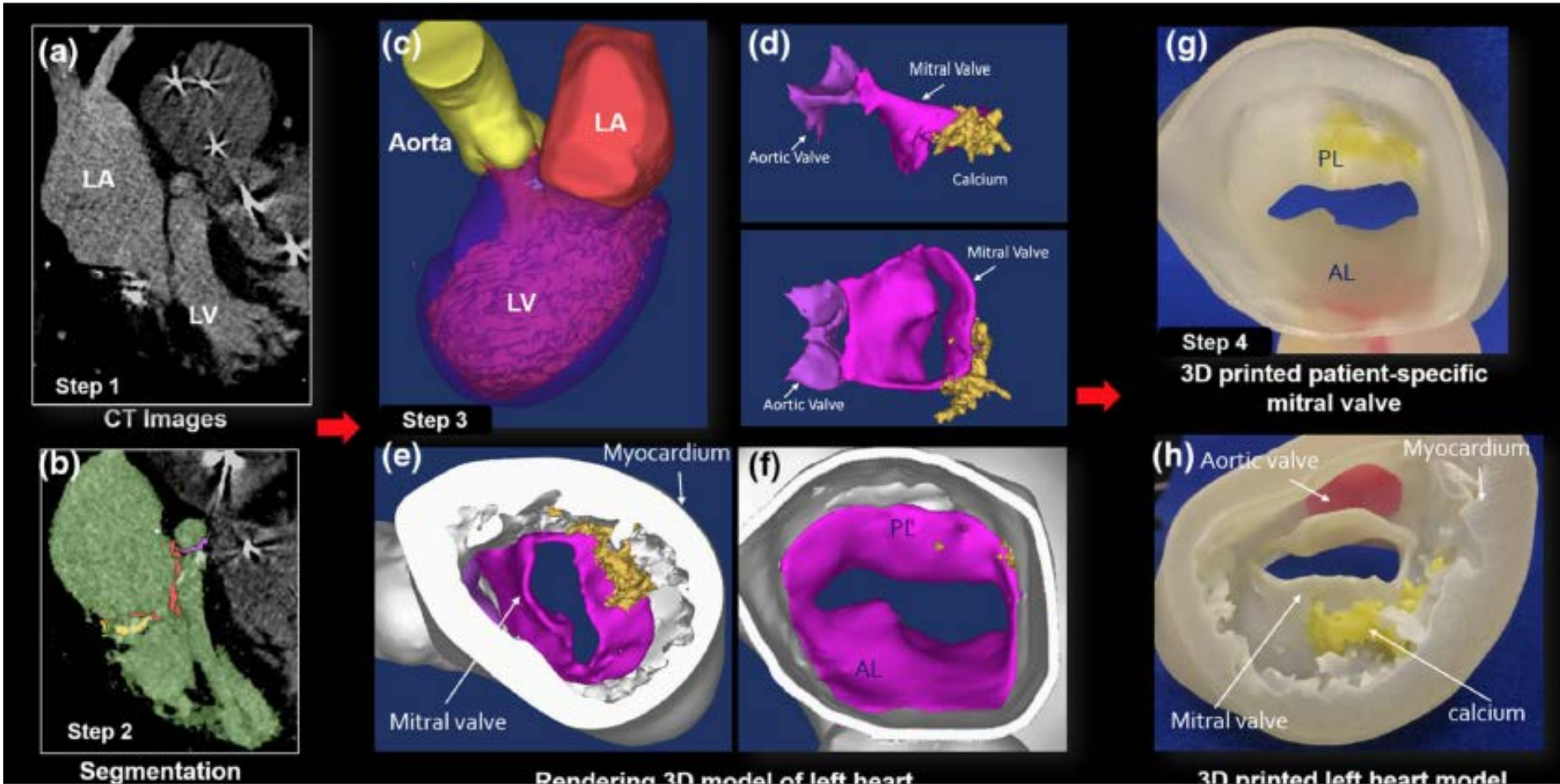
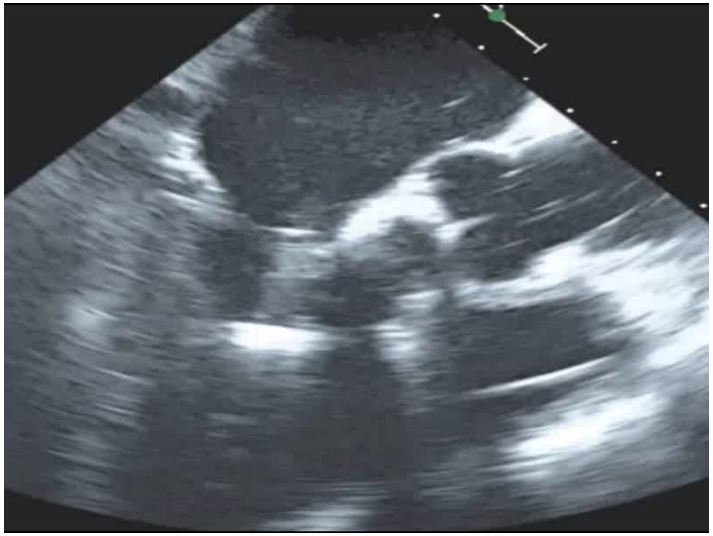
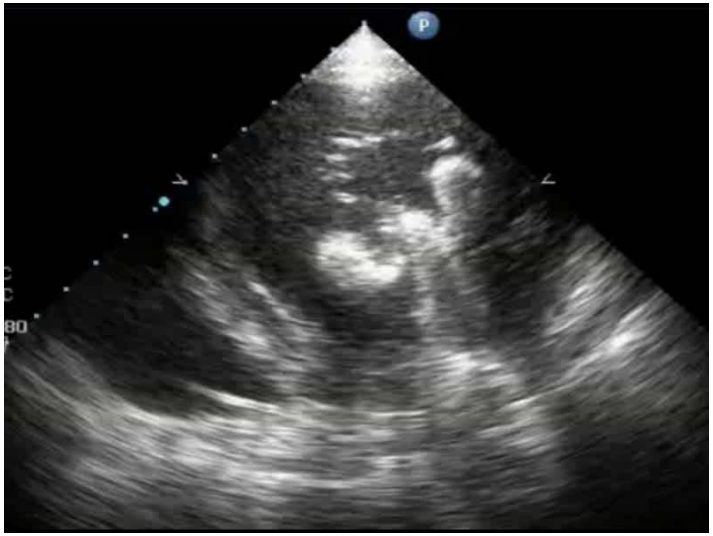
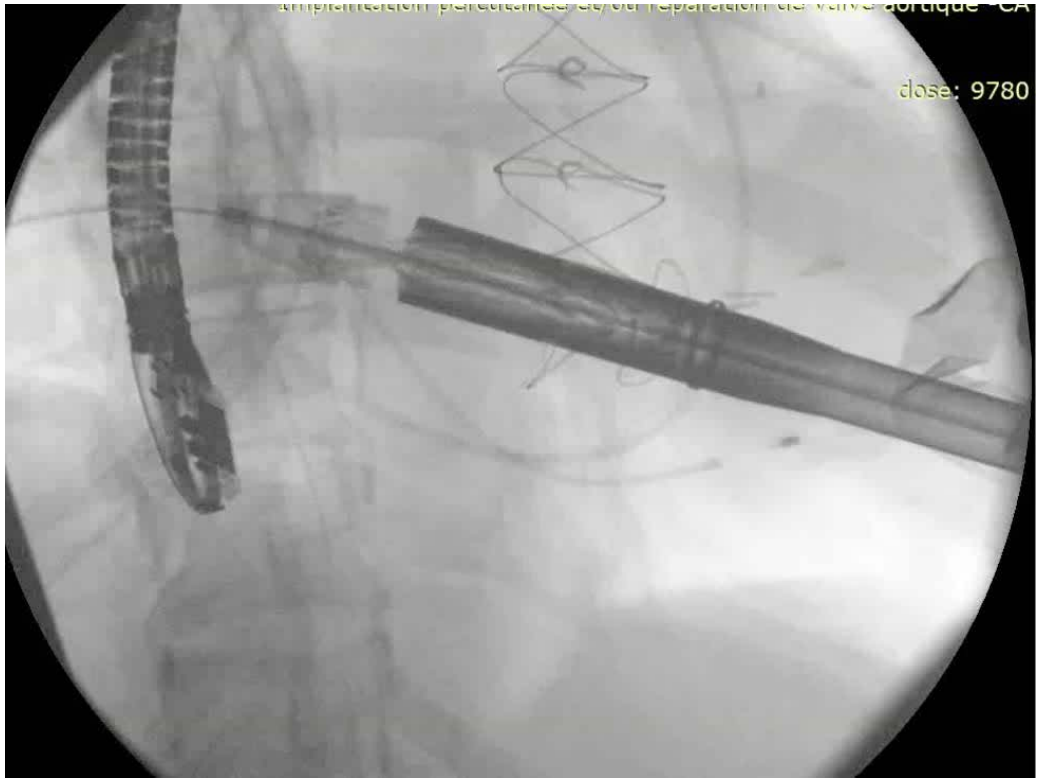


Procedure I – Leaflet Capture







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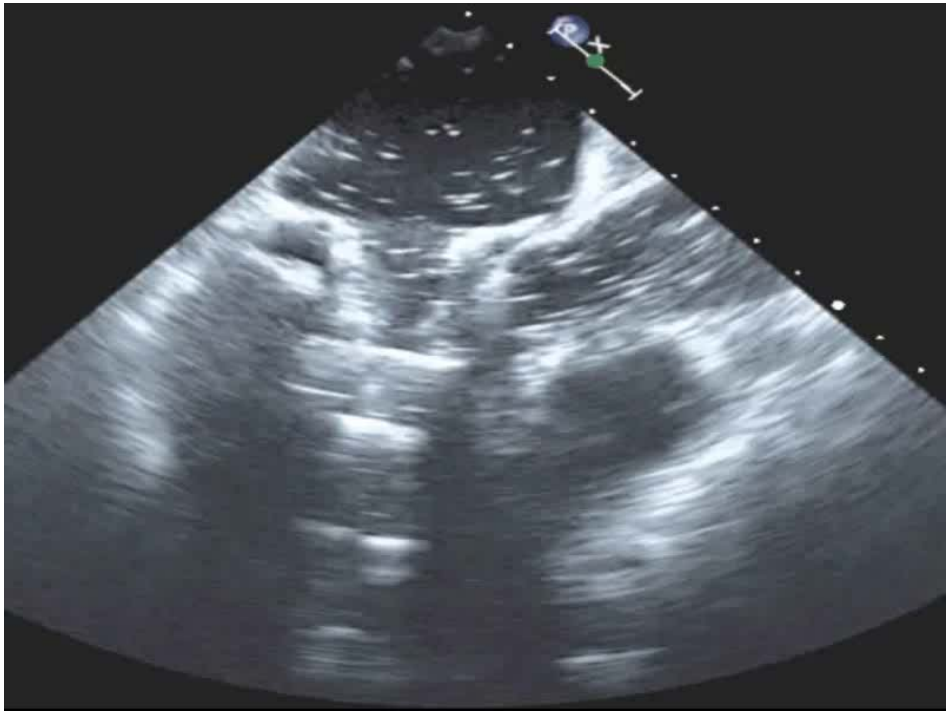
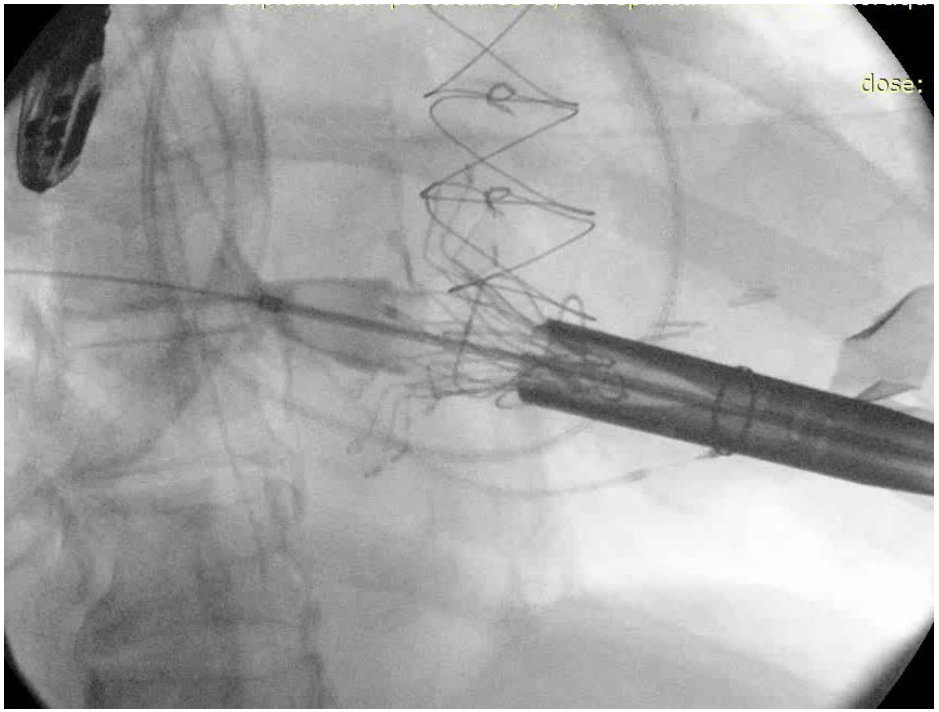
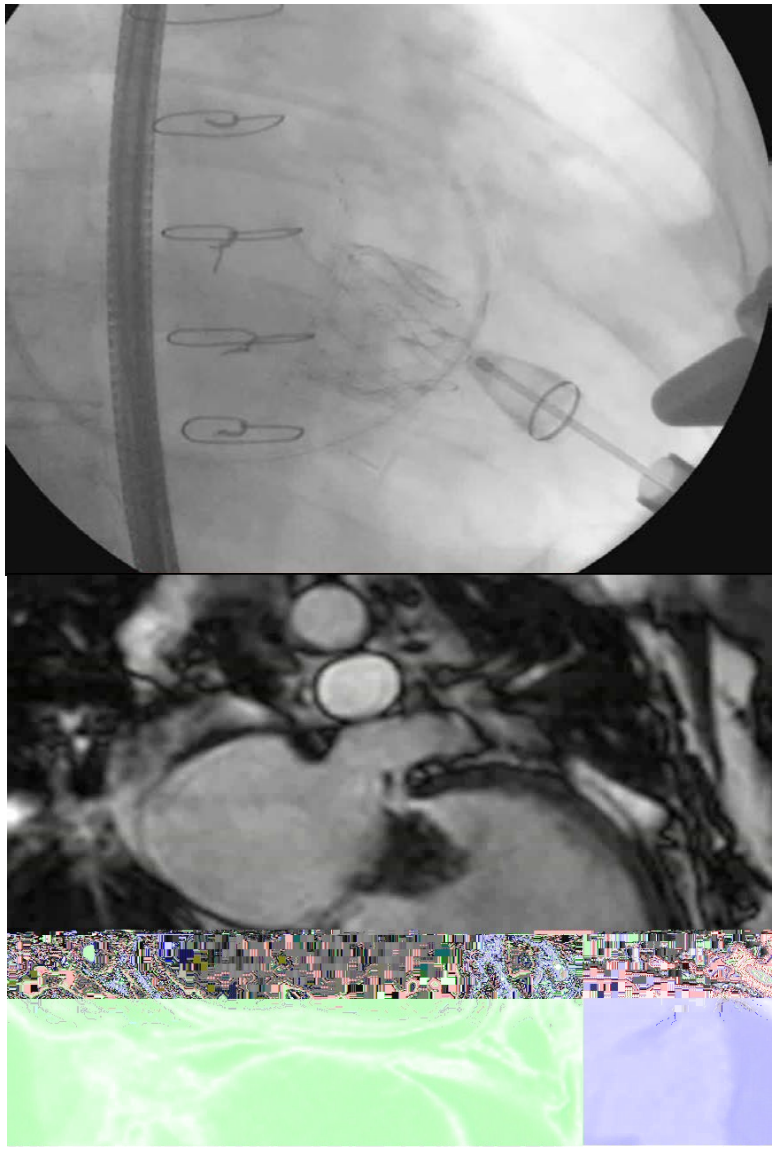
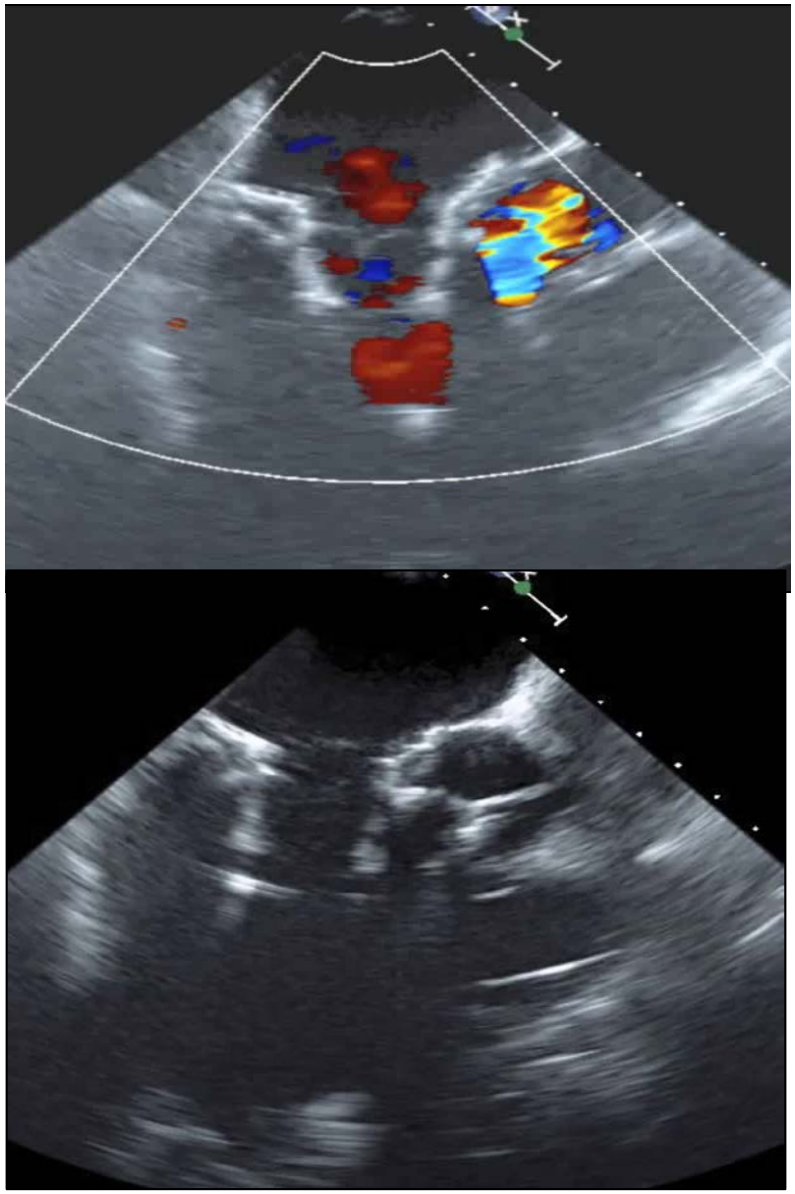
Procedure III – Valve Release



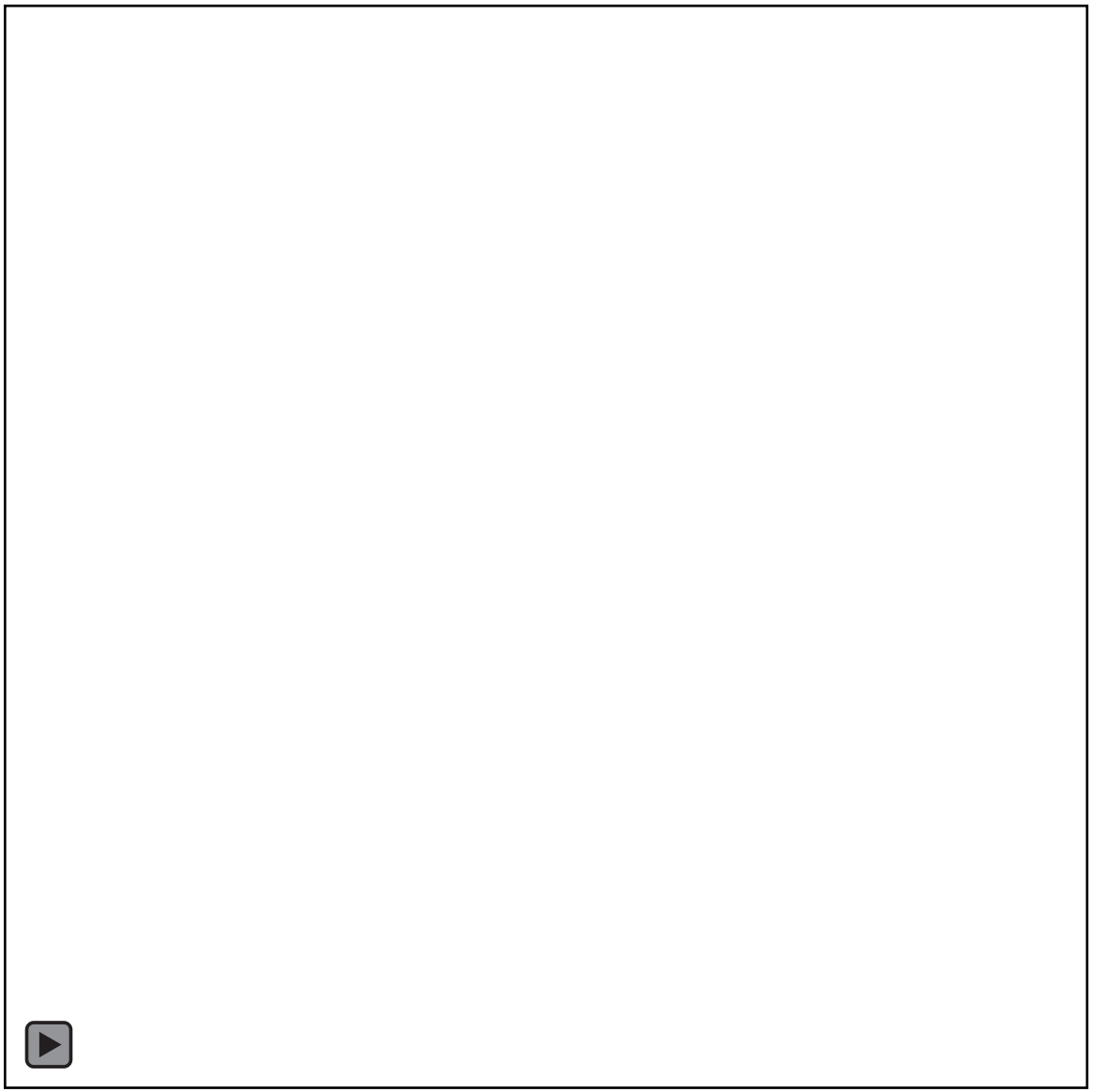


Procedural Result





CardiAQ – TF
Quebec Heart & Lung Institute



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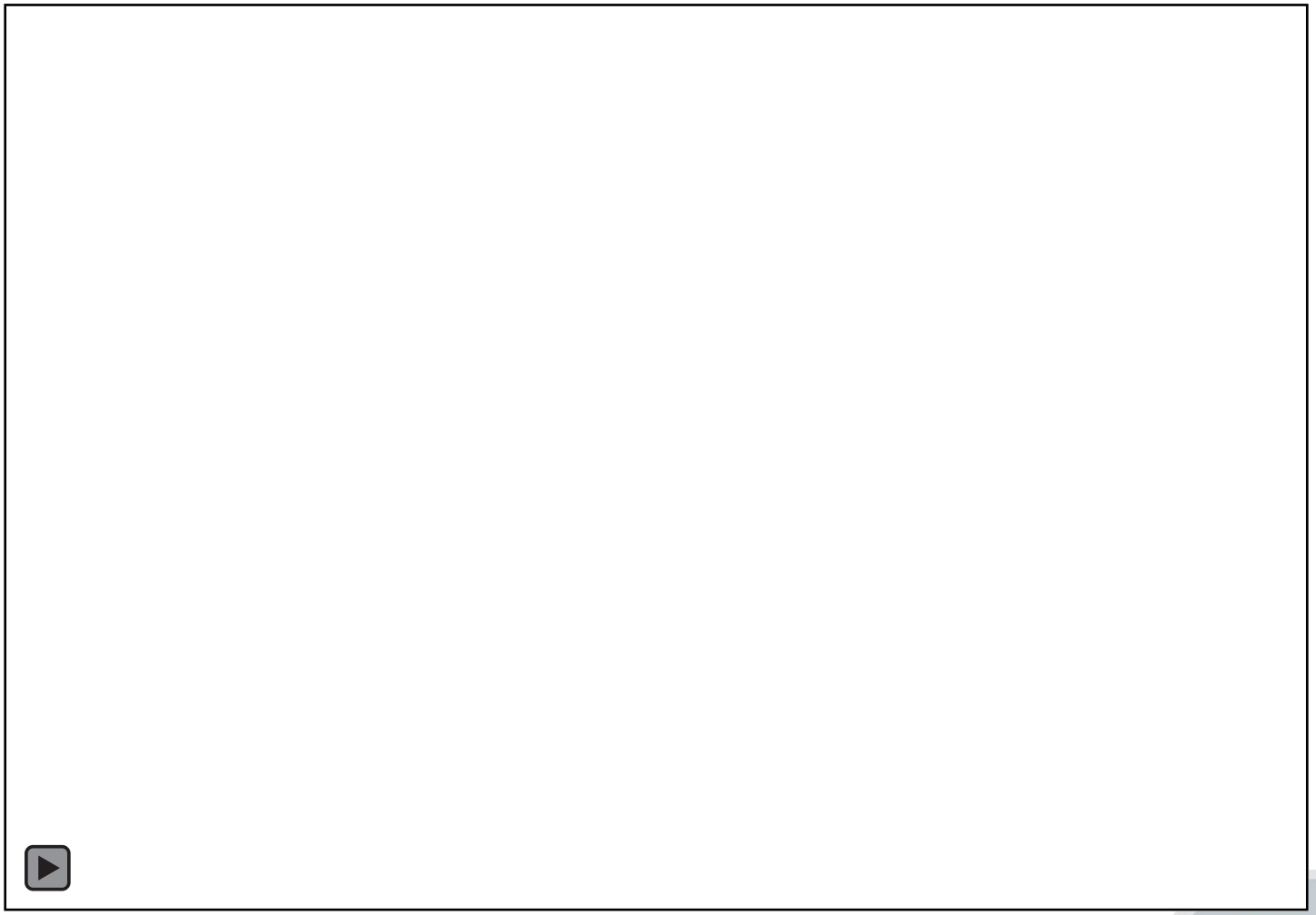
Quebec Heart & Lung Institute



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Quebec Heart & Lung Institute

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TMVR – Initial Global Clinical Experience

	n=115
Patient characteristics	
Age (range)	73.8 (39-91)
Female sex	30/115 (26.1)
STS score	7.5 (1.0-47.7)
NYHA ≥ III	83/101 (82.2)
Ischemic/Functional MR	85/114 (74.6)
LVEF <50%	65/86 (75.6)
Patient characteristics	
Devices	
Tendyne	30/115 (26.1)
Intrepid	27/115 (23.5)
Neovasc Tiara	19/115 (16.2)
CardiAQ-Edwards	13/115 (11.3)
Fortis	13/115 (11.3)
HighLife	6/115 (5.2)
Caisson	5/115 (4.3)
Mvalve	1/115 (1.0)
NCS NaviGate	1/115 (1.0)
Transfemoral approach	7/115 (6.1)
Procedural and 30-day outcomes	
Technical success	100/113 (88.4)
Procedural mortality	10/114 (8.8)
LVOT obstruction	1/96 (1.0)
Post procedural ≥ moderate MR	1/77 (1.3)
30-day mortality	26/112 (23.2)

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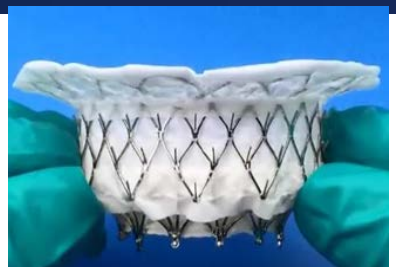
INTREPID Valve (Pilot Study)

- Device implant success in 48/49 (98%)
- 30-day mortality = 14%
  - 3 from apical bleeding, 3 from CHF, 1 from malposition
- One-year survival = 77%
  - 3 SCDs in patients with low EF and no ICDs
  - No death after 180 days
- No device malfunction, hemolysis, or thrombosis
- No or mild MR in all survivors
- 79% of patients in NYHA class I or II in follow-up



Bapat V
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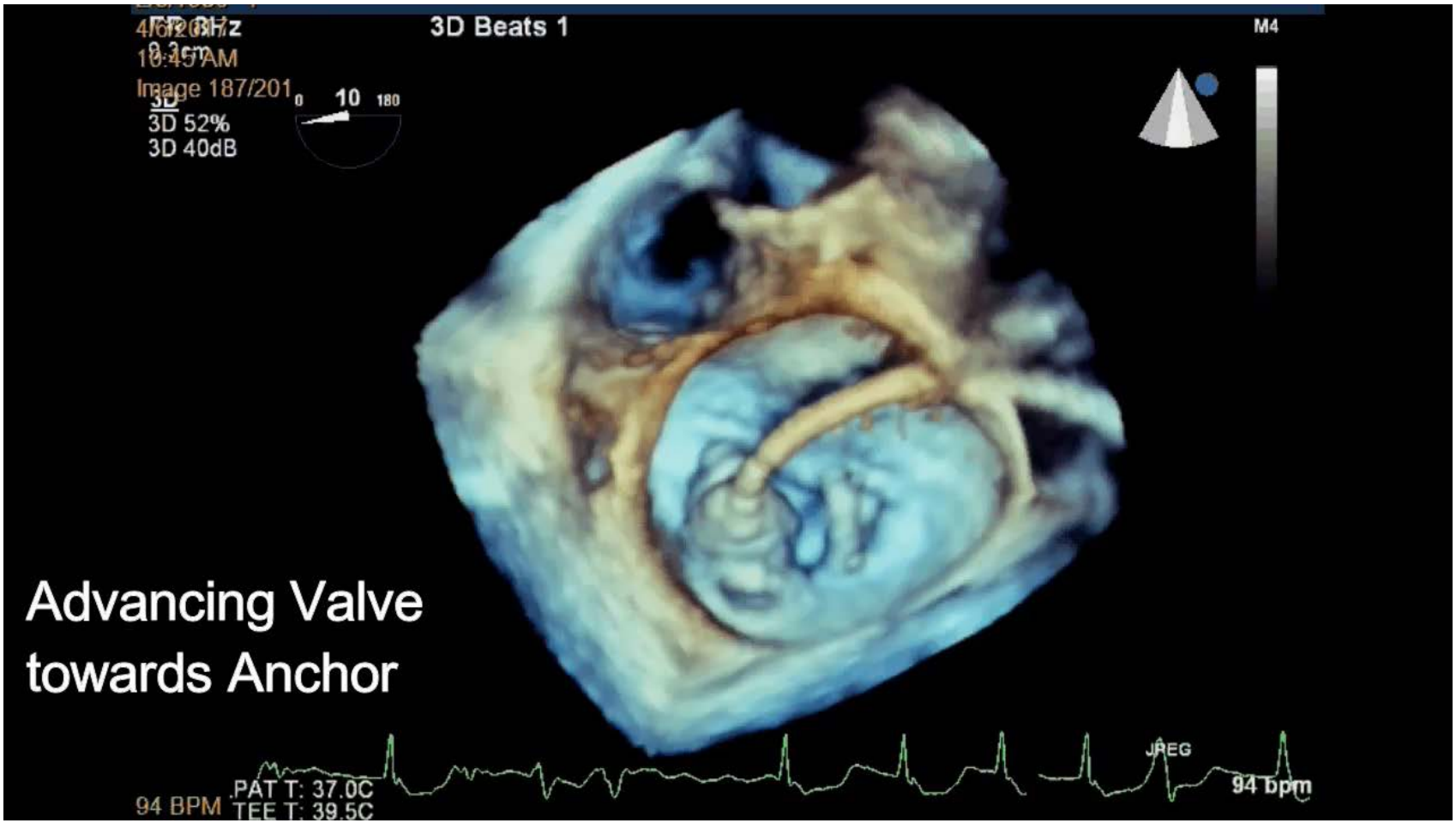
Caisson Valve – Initial Experience



Courtesy of Drs. Kipperman and Brown III
Morristown Medical Center

CAISSON Valve (Early Clinical Experience)

15 patients enrolled with 12 successful implants

Subject	Days Since Implant	MR Grade			Ejection Fraction %		NYHA	
		Baseline	Post Procedure(2)	Last Follow-up(2)	Baseline	Last Follow-up	Baseline	Last Follow-up
01 (1)	28	4+	Trace	1+	32.6	N/A	III	N/A
02	480	3+	0	0	57.3	60.2	III	I
03 (SAP)	460	4+	0	0	28.0	N/A	III	N/A
04	453	4+	0	0	57.9	61.6	II	I
05	349	4+	Trace	0	58.9	46.7	III	I
06	327	4+	Trace	0	47.6	26.8	IV	I
07 (3)	20	3+	1+	N/A	56.0	56.6	III	N/A
08	207	3+	1+	0	29.4	30.0	IV	I
09 (4)	3	4+	Trace	N/A	36.4	N/A	III	N/A
10	102	4+	Trace	0	46.0	40.0	II(5)	II
11	89	3+	0	0	47.5	41.0	III	III
12	47	4+	0	0	29.7	19.9	III	I

In Follow-up
Converted to SMVR
Deceased

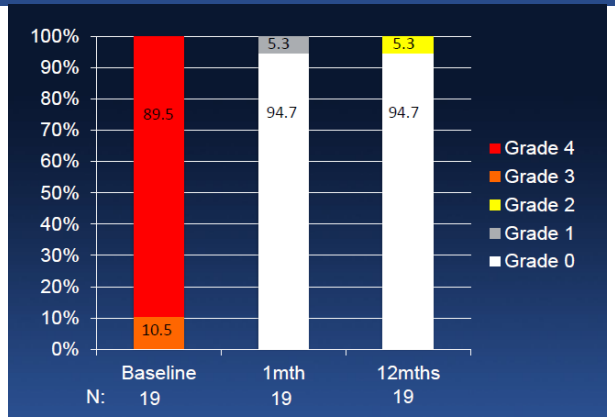
1: Early Death (Day 28) due to Sepsis
2: Grade inclusive of PVL
3: Conversion to SMVR due to excess PVL
4: Early Death (Day 3) following hypotension and PVL
5: Following medical management, NYHA III-IV at Screening

NYU Langone MEDICAL CENTER

Williams M
TCT 2017

TENDYNE Valve (Feasibility Trial)
1 Year Results

Outcome	N=30
Death (all cause)	5 (16.7%)
Cardiac	4 (13.3%)
Non-cardiac	1 (3.3%)
CVA/TIA	0 (0%)
Re-hospitalisation	
Heart failure	3 (10.0%)
MV surgery	0 (0%)
Valve performance (n=28)	
Malposition/PVL/hemolysis	1 (3.6%)
Leaflet thrombosis	1 (3.6%)



Muller D
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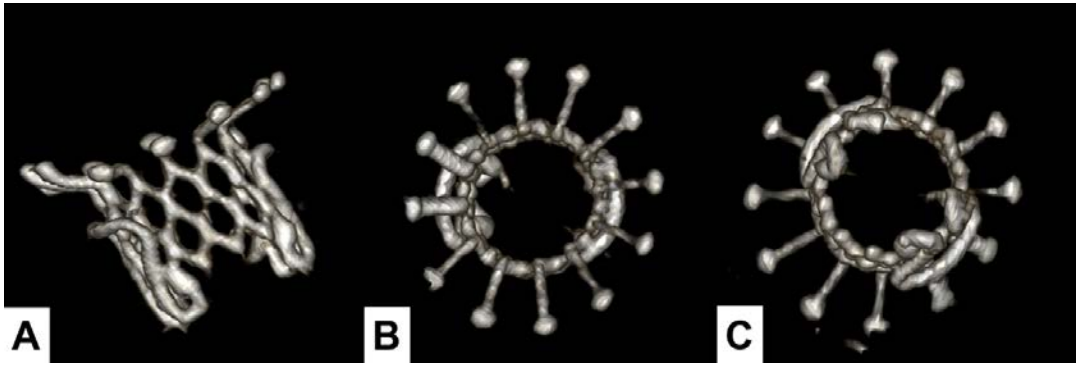
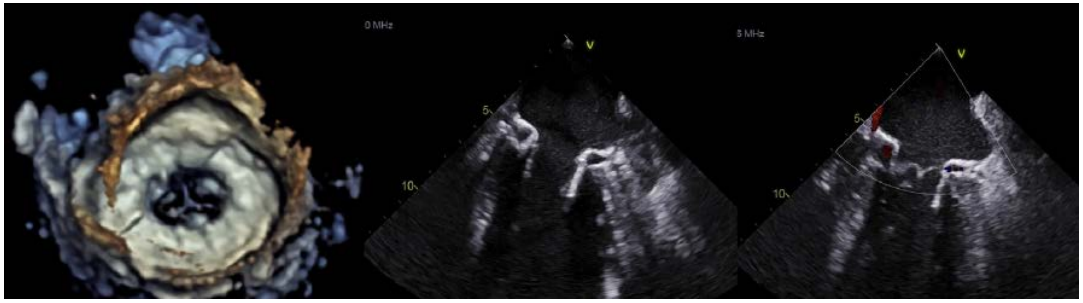
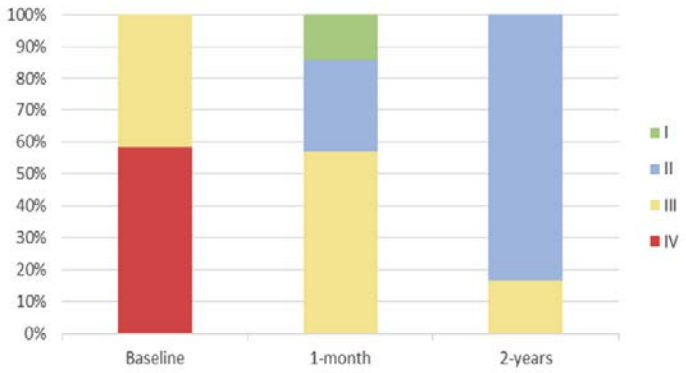
Late (2-Year) Outcomes Post-TMVR





FORTIS valve
N=13
Mortality: 54%
No late thrombosis
No late valve dysfunction



Regueiro A et al. JACC Intv 2017

TMVR – Clinical Perspective

- ***Patient selection***
  - **Secondary MR with low LVEF**
  - **High rate of screen failure (anatomical issues, limited valve size availability)**

- ***Procedural outcomes***
  - **High (close to 90%) device success rate, low rate of LVOT obstruction**
  - **High peri-procedural / 30-day mortality (transapical approach, very low LVEF, high co-morbidity burden)**

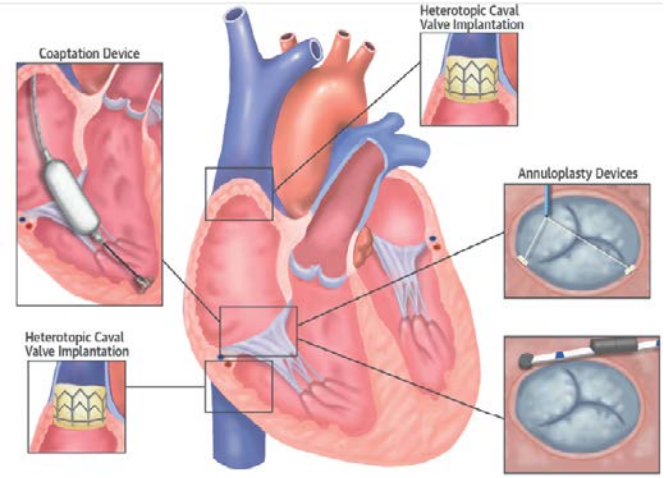
- ***Valve performance***
  - **High rate of optimal valve performance (very few cases of moderate-severe MR, low transvalvular gradient)**
  - **Valve thrombosis**

- ***Late outcomes***
  - **Promising (preliminary) hemodynamic and valve performance data at 6- to 24-month follow-up**

Transcatheter Mitral Replacement vs. Repair

	Screen failures	Successful procedure	No residual leaks	Periprocedural safety
TMVR	+++	++	+++	-
Mitral repair	+	++	-	++

Transcatheter Therapies for Tricuspid Regurgitation



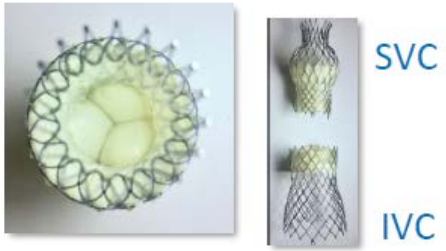
Challenges of Transcatheter Tricuspid Valve Therapies
Large tricuspid annulus size
Non-planar and elliptical annulus shape
Fragility of tricuspid anular tissue and narrower annular shelf in comparison to mitral annulus
Non calcified annulus in secondary tricuspid regurgitation
Angulation in relation to superior and inferior vena cava
Trabeculated right ventricle, muscular bands and chordae tendinae
Thin right ventricular free wall
Proximity of AV-node and right His bundle branch
Proximity of the right coronary artery to annulus and risk of coronary injury
Risk of occlusion of coronary sinus, vena cava or outflow tract
Slow-flow in right ventricle
Patients with pacemaker or defibrillator leads

Rodés-Cabau et al. JACC 2016

Caval Valve Implantation (Initial Experience)

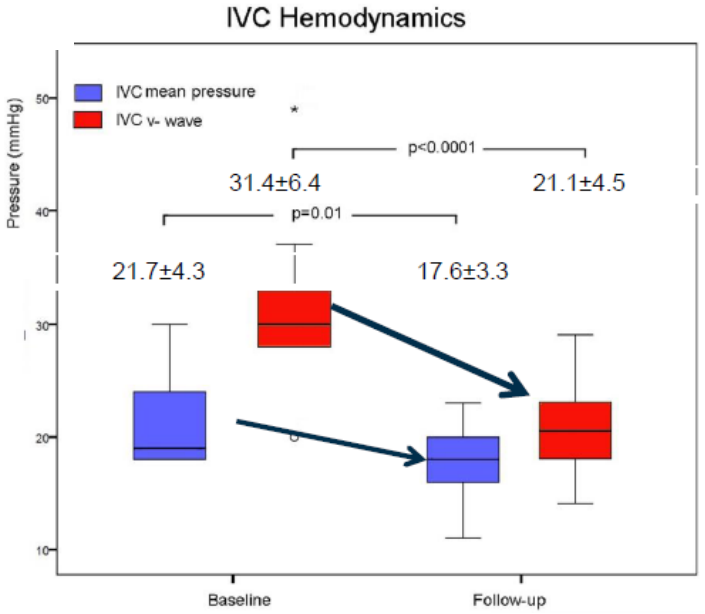
Ballon-Expandable TAVI-Valve

Self-expandable TricValve



Follow- up: *Mortality*

Procedural, Safety and in- hospital data	N (%)
30d	3/25 (12%)
In-hospital	6/25 (24%)
12 month	14/22 (63%)
Mean Long-term Follow-up (days)	316±453; (6 – 1540)



Figulla HR TCT 2017

ORIGINAL RESEARCH ARTICLE

Transcatheter Treatment of Severe Tricuspid Regurgitation With the Edge-to-Edge MitraClip Technique

Editorial, see p 1815

BACKGROUND: Current surgical and medical treatment options for severe tricuspid regurgitation (TR) are limited, and additional interventional approaches are required. In the present observational study, the safety and feasibility of transcatheter repair of chronic severe TR with the MitraClip system were evaluated. In addition, the effects on clinical symptoms were assessed.

METHODS: Patients with heart failure symptoms and severe TR on optimal medical treatment were treated with the MitraClip system. Safety, defined as periprocedural adverse events such as death, myocardial infarction, stroke, or cardiac tamponade, and feasibility, defined as successful implantation of 1 or more MitraClip devices and reduction of TR by at least 1 grade, were evaluated before discharge and after 30 days. In addition, functional outcome, defined as changes in New York Heart Assocation class and 6-minute walking distance, were assessed.

RESULTS: We included 64 consecutive patients (mean age 76.6±10 years) deemed unsuitable for surgery who underwent MitraClip treatment for chronic, severe TR for compassionate use. Functional TR was present in

Georg Nickenig, MD
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Daniel Braun, MD
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Volker Rudolph, MD
Kai Friedrichs, MD
Francesco Maisano, MD
Maurizio Taramasso, MD
Neil Fam, MD
Giovanni Bianchi, MD
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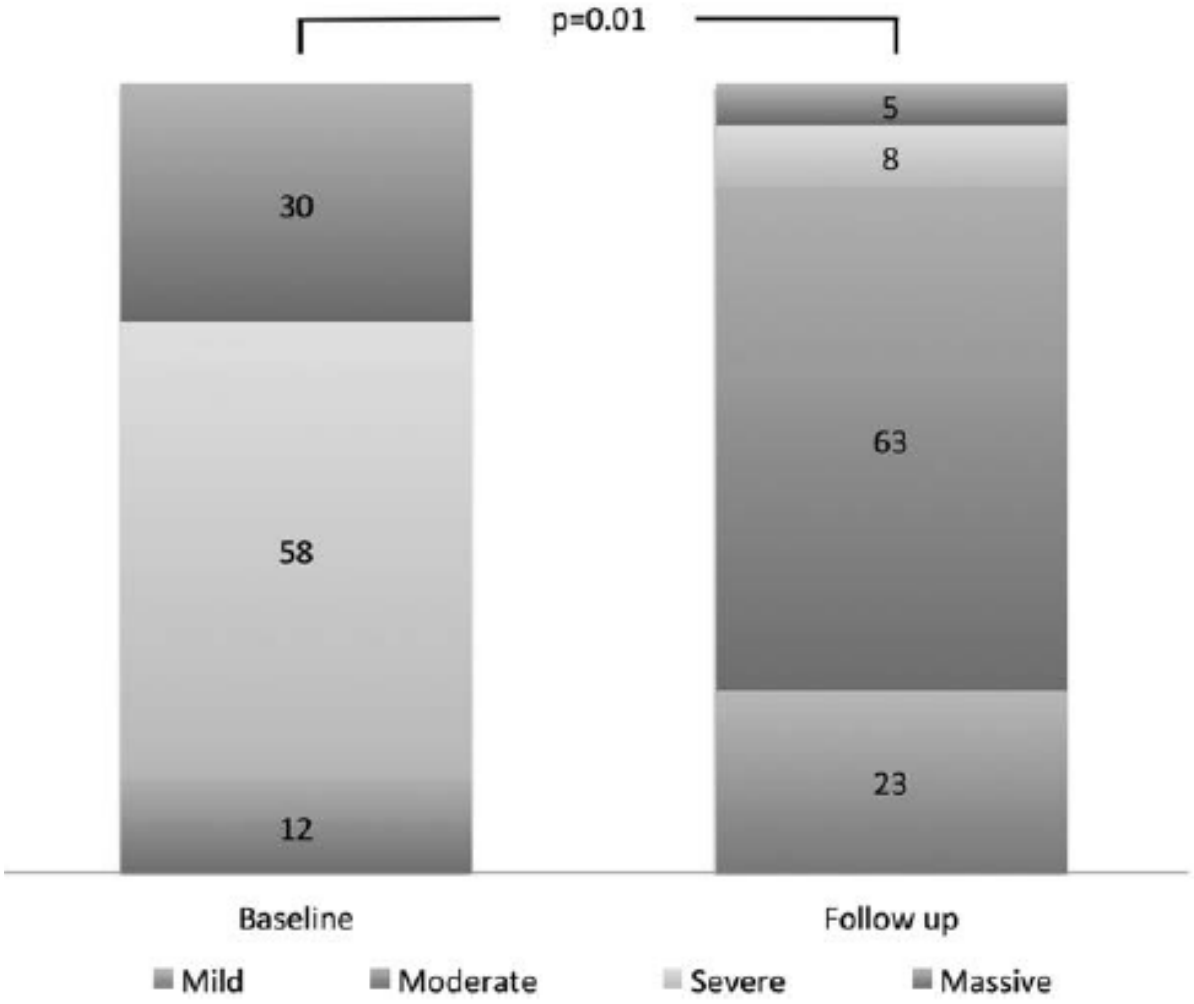
Paolo Denti, MD
Ottavio Alfieri, MD
Azeem Latib, MD
Antonio Colombo, MD
Christoph Hammerstingl, MD
Robert Schueler, MD

N=64
Successful Mitraclip implantation: 97%
Number of mitraclips ≥2: ~50%
In-hospital mortality: 5%

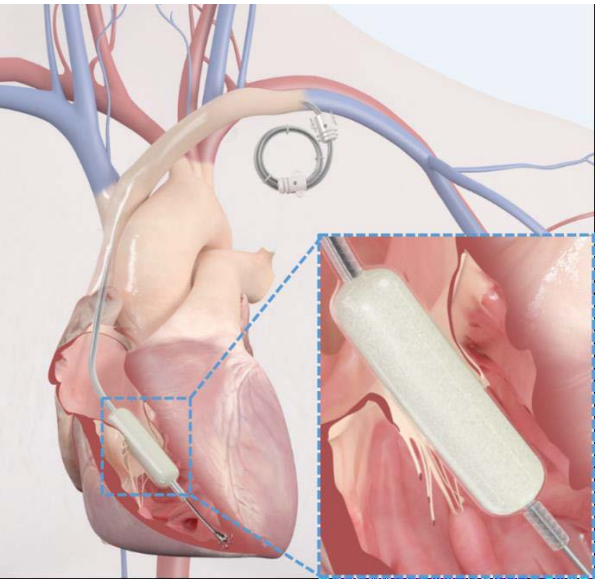
Nickening et al. Circulation 2017

MitraClip Device for TR



Nickening et al. Circulation 2017

FORMA Device (Early Feasibility)



Clinical Outcomes at 30 Days

	Patients N = 29	%
Death (All-Cause)	2	6.9
Stroke/TIA	0	0.0
Vascular Injury	1	3.4
Bleeding*		
Life Threatening or Disabling	2	6.9
Major	4	13.8
Device Related Cardiac Surgery	3	10.3
AKI ≥ Stage 2*	3	10.3

Kodali et al. TCT 2017

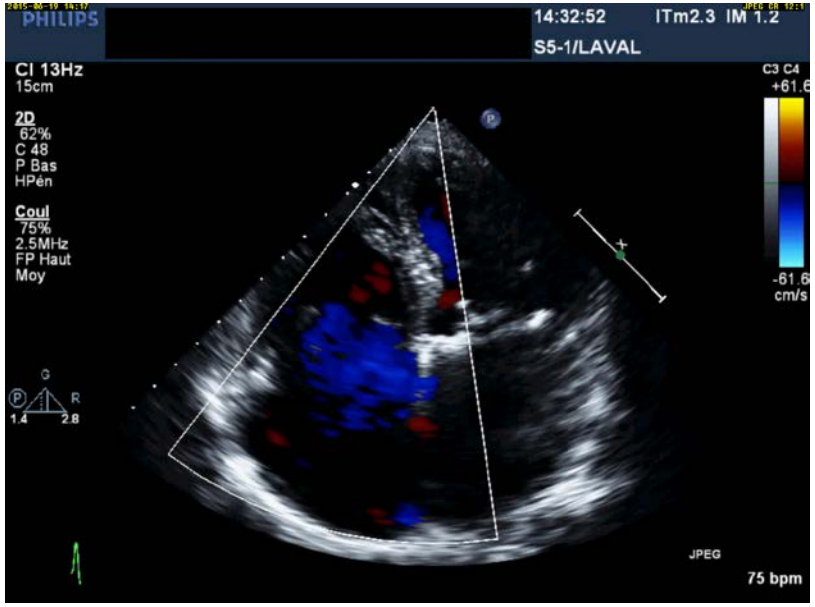
Severe TR Postcardiac Surgery

83 year-old patient, female sex

Medical history

- **Hypertension, dyslipidemia**
- **COPD**
- **Prior CABG and mitral valve surgery**
- **Atrial fibrillation**
- **LogEuroscore: 16.9**

Severe TR, NYHA class III



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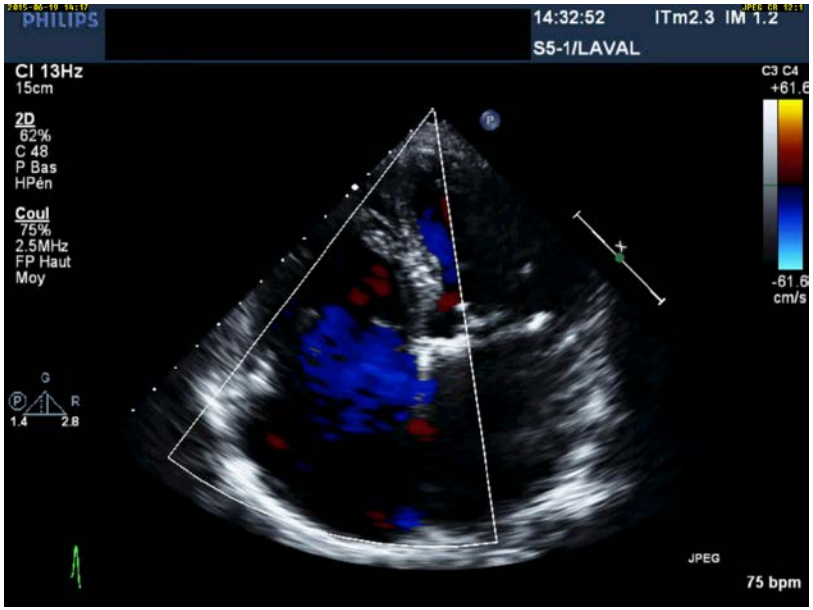
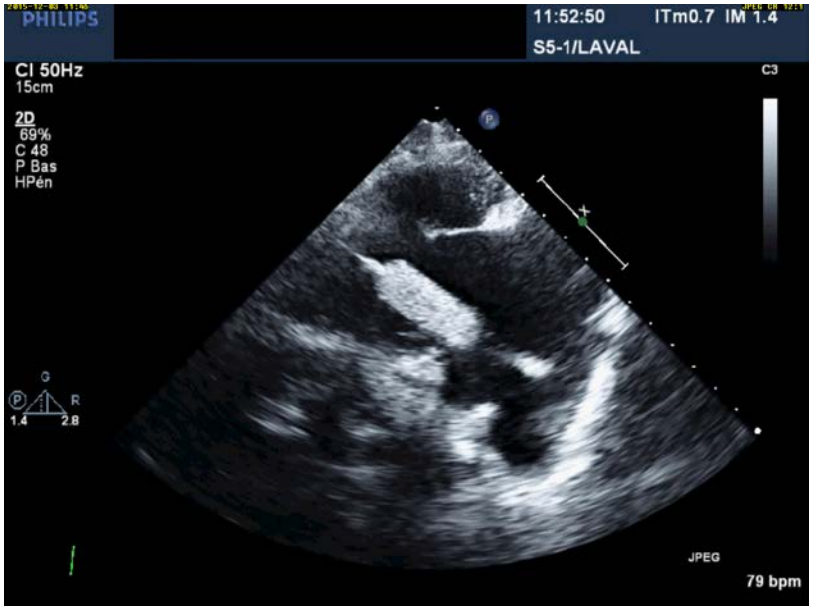
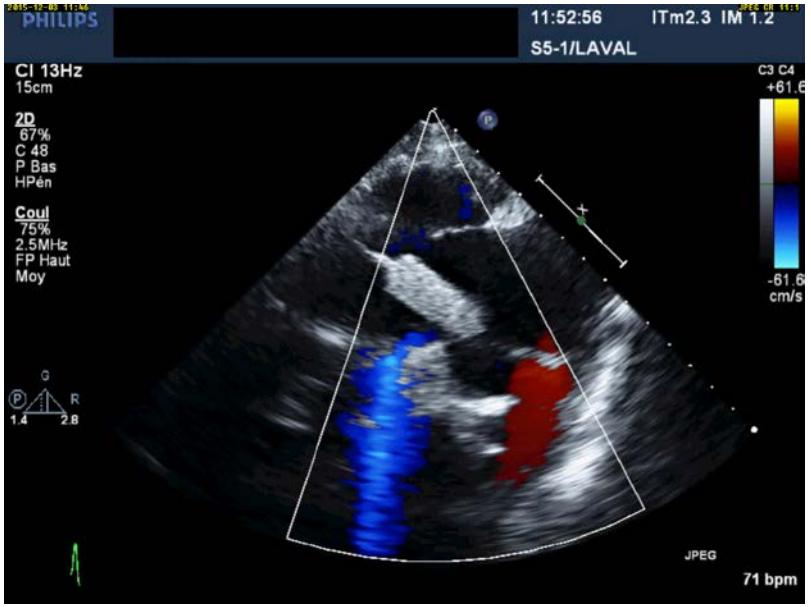
6-Month Follow-Up

Pre







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FORMA Compassionate Clinical Use

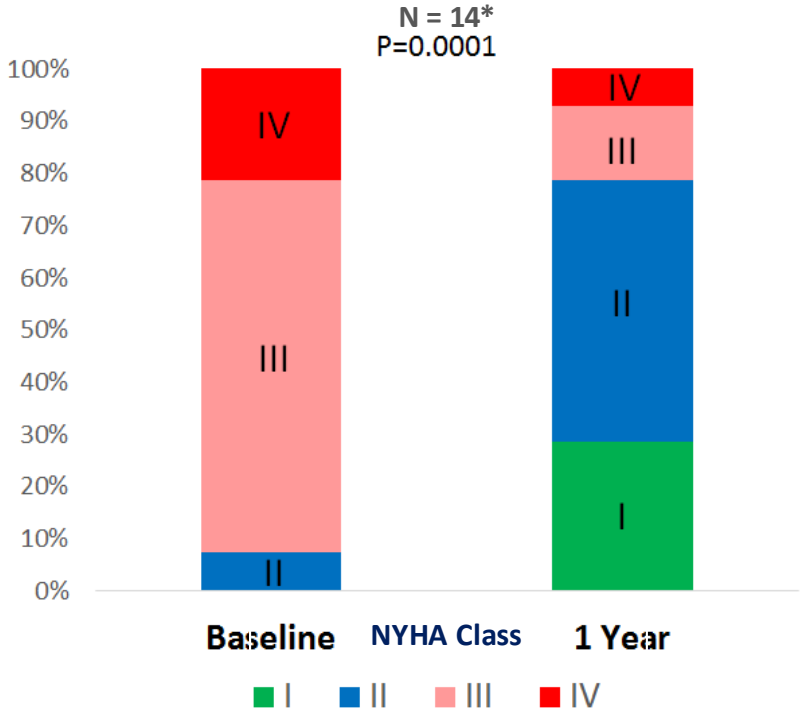
30-Day & 1-Year Follow Up

Clinical Outcomes	30 Day (n = 18)	1 Year (n=15)
Death	0 (0)	0 (0)
Rehospitalization for HF	0 (0)	1 (7)
Life threatening/Major bleeding	2 (11)	2 (13)
Major vascular complications	0 (0)	0 (0)
Acute kidney injury ≥ 2	0 (0)	1 (7)
Device thrombosis	0 (0)	1 (7)*
Pulmonary embolism	0 (0)	0 (0)
Stroke	0 (0)	0 (0)
New pacemaker	0 (0)	0 (0)

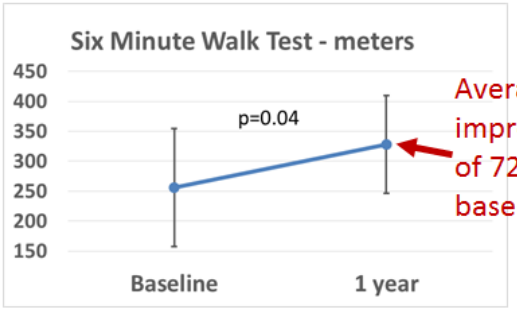
*Occurred in a patient with non-therapeutic INR levels, resolved with resumption of adequate anticoagulation

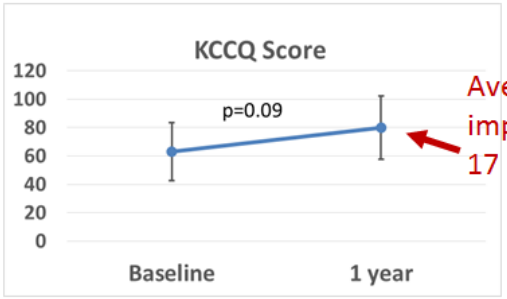
Rodés-Cabau, TVT 207

Edwards FORMA Tricuspid Repair FIH
1 Year Efficacy Outcomes

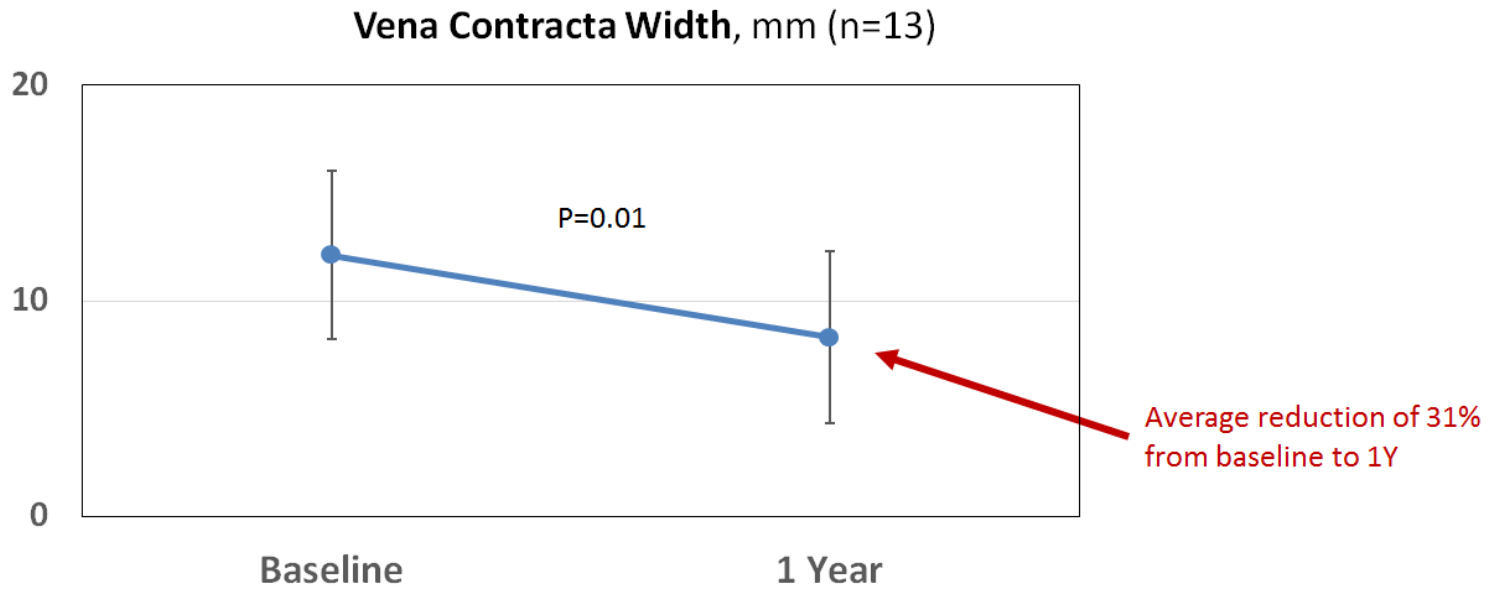


*3 patients have not reached 1Y; dislodgement patient not included





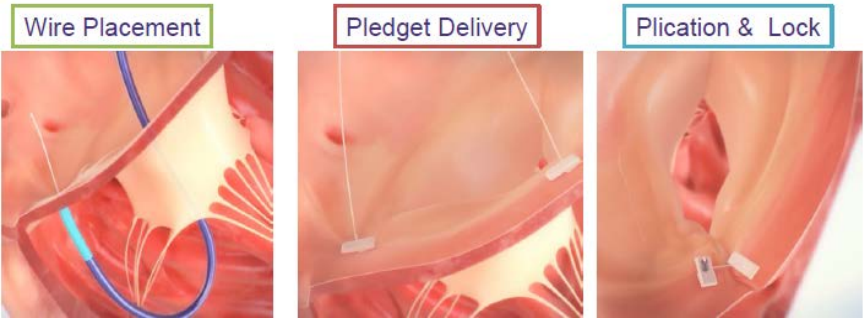
Edwards FORMA Tricuspid Repair FIH
31% Vena Contracta Reduction



- Large proportion of patients treated with “torrential” TR
- Improvements resulted in most patients achieving lower severity or moderate TR at 30 days

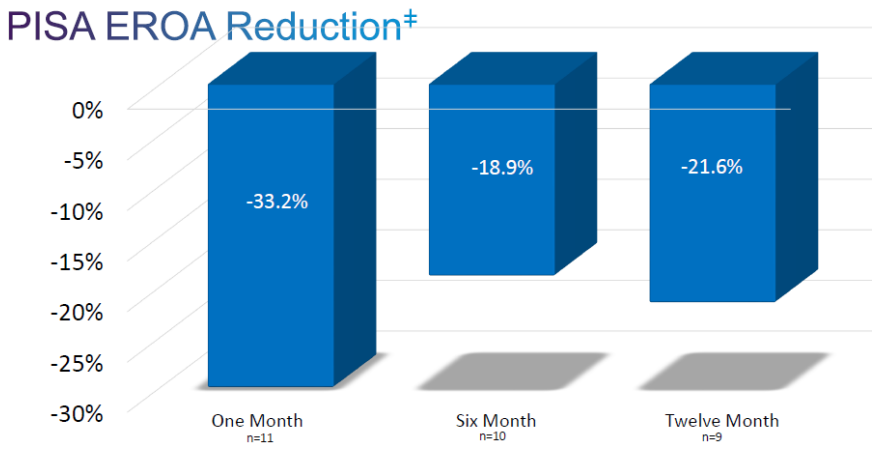
>2/3 of patients:
At least moderate TR

TRIALIGN System (SCOUT Trial)



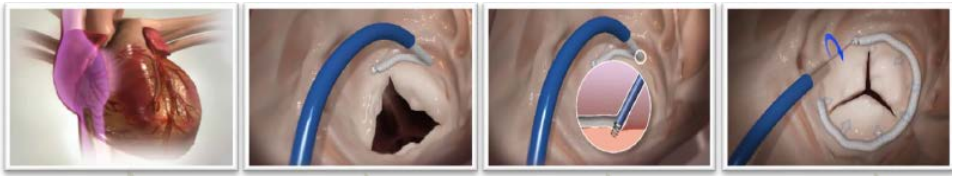
Safety profile and implant success

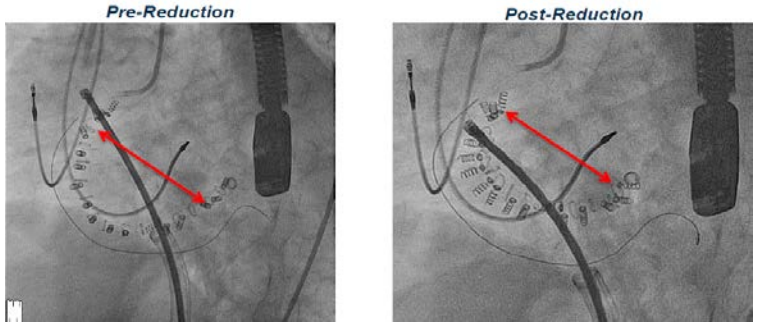
	n/N	(%)
Acute Procedure		
Implant Success	15/15	100%
Unplanned intervention	1/15	7%
Intraprocedural stenting of RCA		
30 Day Follow Up		
Freedom from death	15/15	100%
Technical Success	12/15	80%
3 single pledget dehiscence		
Major Adverse Events	0/15	0%



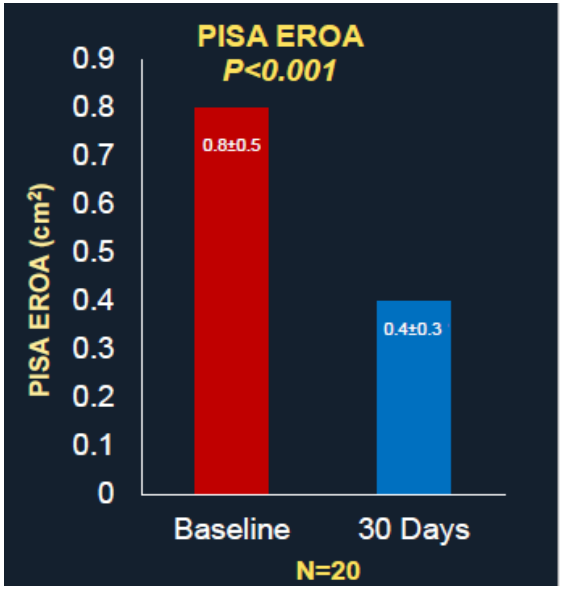
Hahn R. TCT 2017

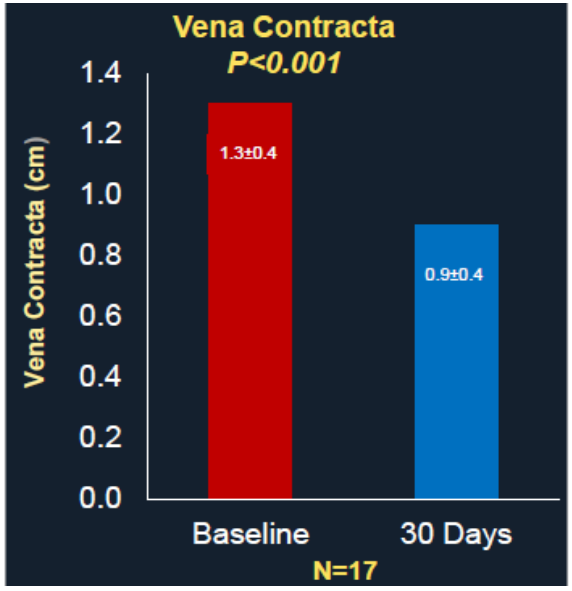
CARDIOBAND System (TRI-REPAIR Trial)

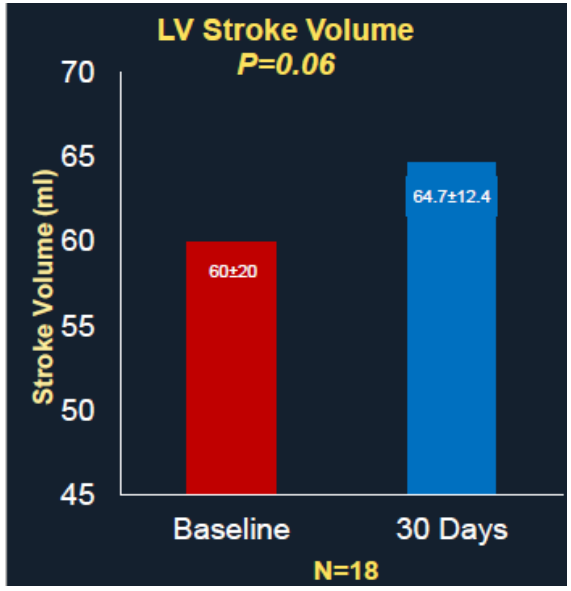




Adjudicated peri-procedural events	n
Death	2
Right ventricular failure	1
Bleeding unrelated to the device†	1
Stroke	1
Bleeding Complications*	3
Life-threatening†	2
Extensive	1
Device Related Cardiac Surgery	0
Renal Failure	0







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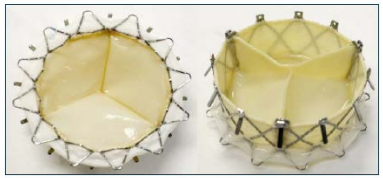
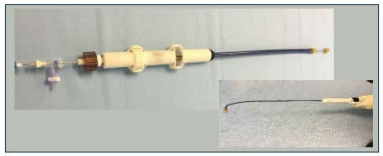
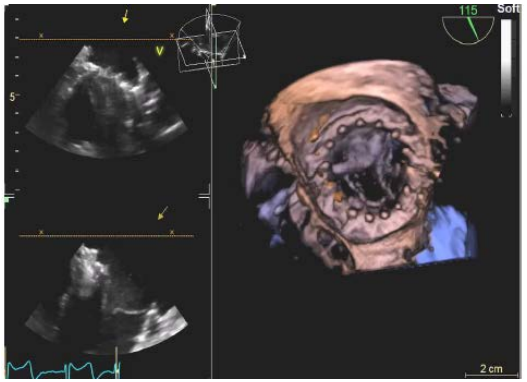
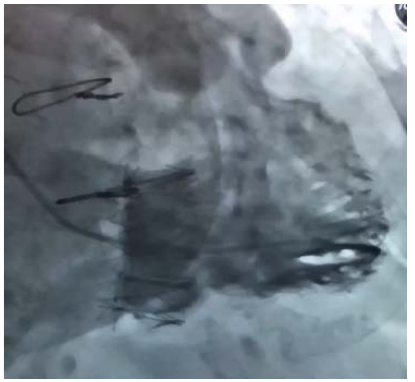
Transcatheter Tricuspid Valve Replacement. The NAVIGATE Valve





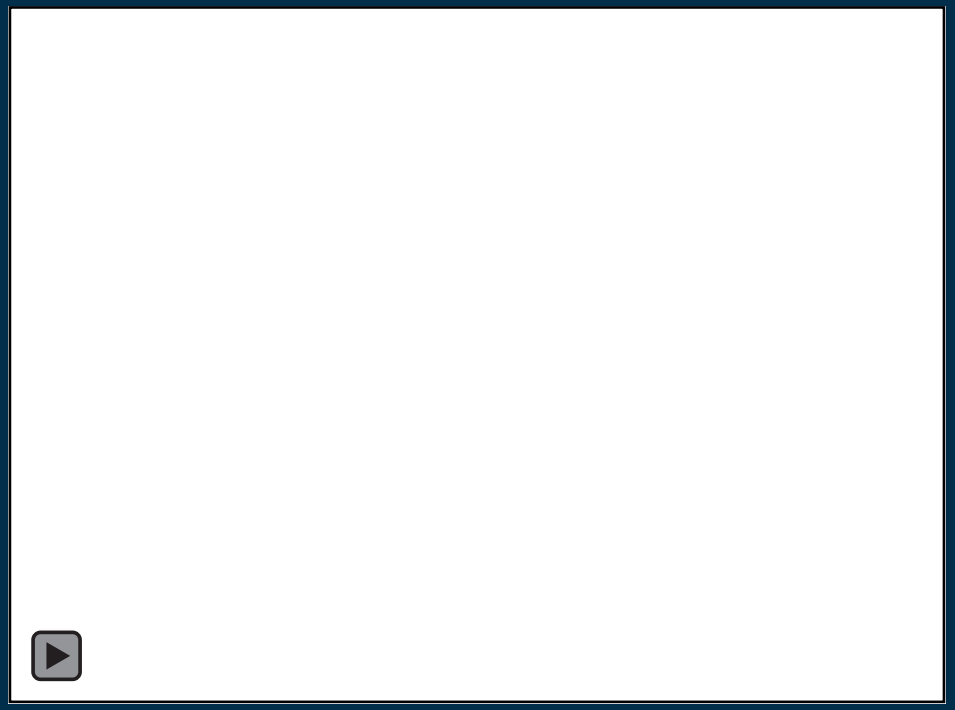




	Implant Date	Echo/CT	Gate Size	Time Implant	Peak Gradient	Mean Gradient	CVP Pre/Post	TR	TR	Clinical
		Dim(mm)	Dim(mm)	(min)	(mmHg)	(mmHg)	(mmHg)	Prep	Postop PVL	Status
1	30 Nov 2016	49.8	48	10	4.5	2.8	30/12	>4+	Trivial	Died 6 months
2	19 April 2017	34 Ring	36	12	7.0	4.0	28/6	4+	No	Alive 6 months
3	11 July 2017	50.1	52	14	4.0	2.0	27/8	>4+	No	Alive 3 months
4	18 Sep 2017	50	52	15	6.3	2.1	25/10	4+	1+	Died 1 week HF
5	12 Oct 2017	46	48	12	5.8	2.0	24/12	>4+	Trivial	Alive 2 weeks
6	12 Oct 2017	48	48	13	6.8	3.1	25/11	>4+	No	Alive 2 weeks

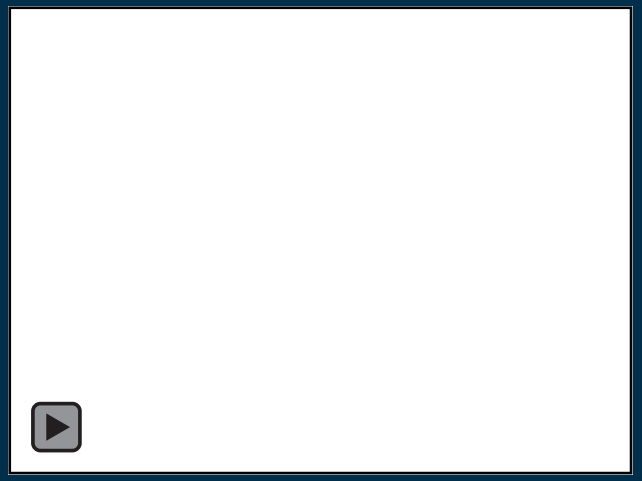
Navia J. TCT 2017

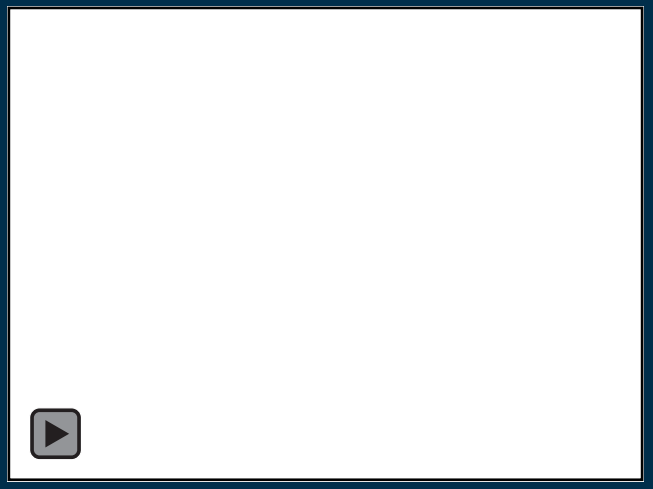
NaviagateValve Release: Complete Deployment

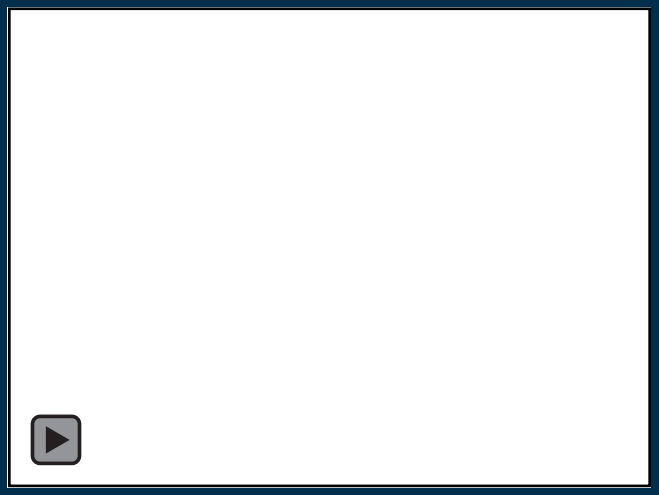


Courtesy of Drs Kodali, Hahn, Bapat
Columbia University Medical Center

Final Result







- *Trivial central and trivial paravalvular regurgitation*
- *Peak/mean transtricuspid gradient = 1.5 and 0.3 mmHg*

Courtesy of Drs Kodali, Hahn, Bapat
Columbia University Medical Center

Transcatheter Therapies for TR Feasibility/Safety

• Successful device implanation	90% (85-100%)
• 30-day mortality	~4% (0-17%)
• Major periprocedural complications	<10%
• Cardiac tamponade	3% (0-9%)

Rodés-Cabau J. TVT 2017

Transcatheter Therapies for TR
Preliminary Efficacy (30-Day Evaluation)

• TR reduction	>90%
• Moderate TR (post-intervention)	~60%
• NYHA I-II	80% (63-100%)
• 6MWT	Δ 50 meters (44-57)

Rodés-Cabau J. TVT 2017