Current State of Transcatheter Mitral Valve Replacement

Interventional Cardiology 2015: 30th Annual Symposium

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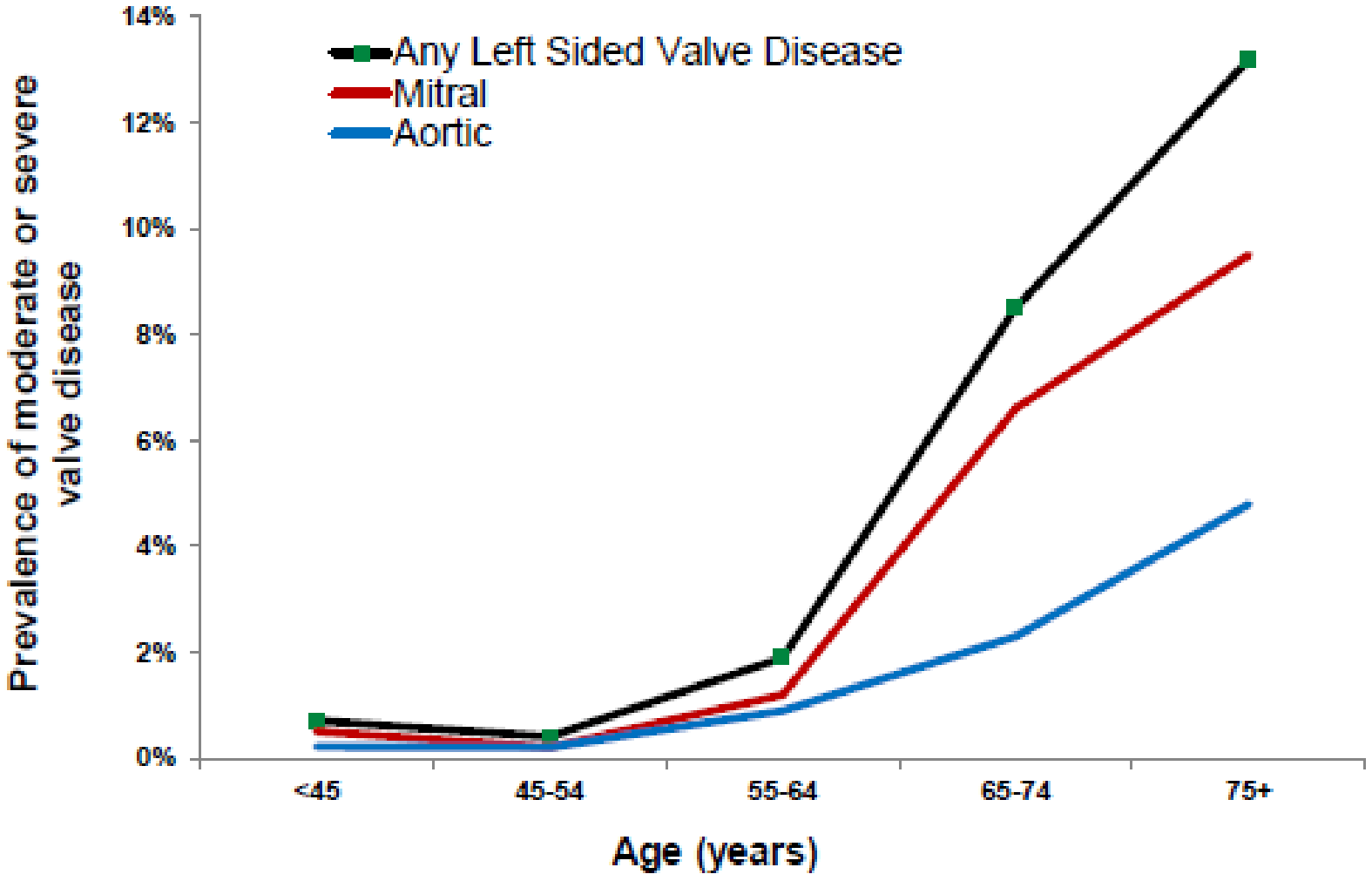
Disclosures

- I have no financial conflicts of interest (sadly)

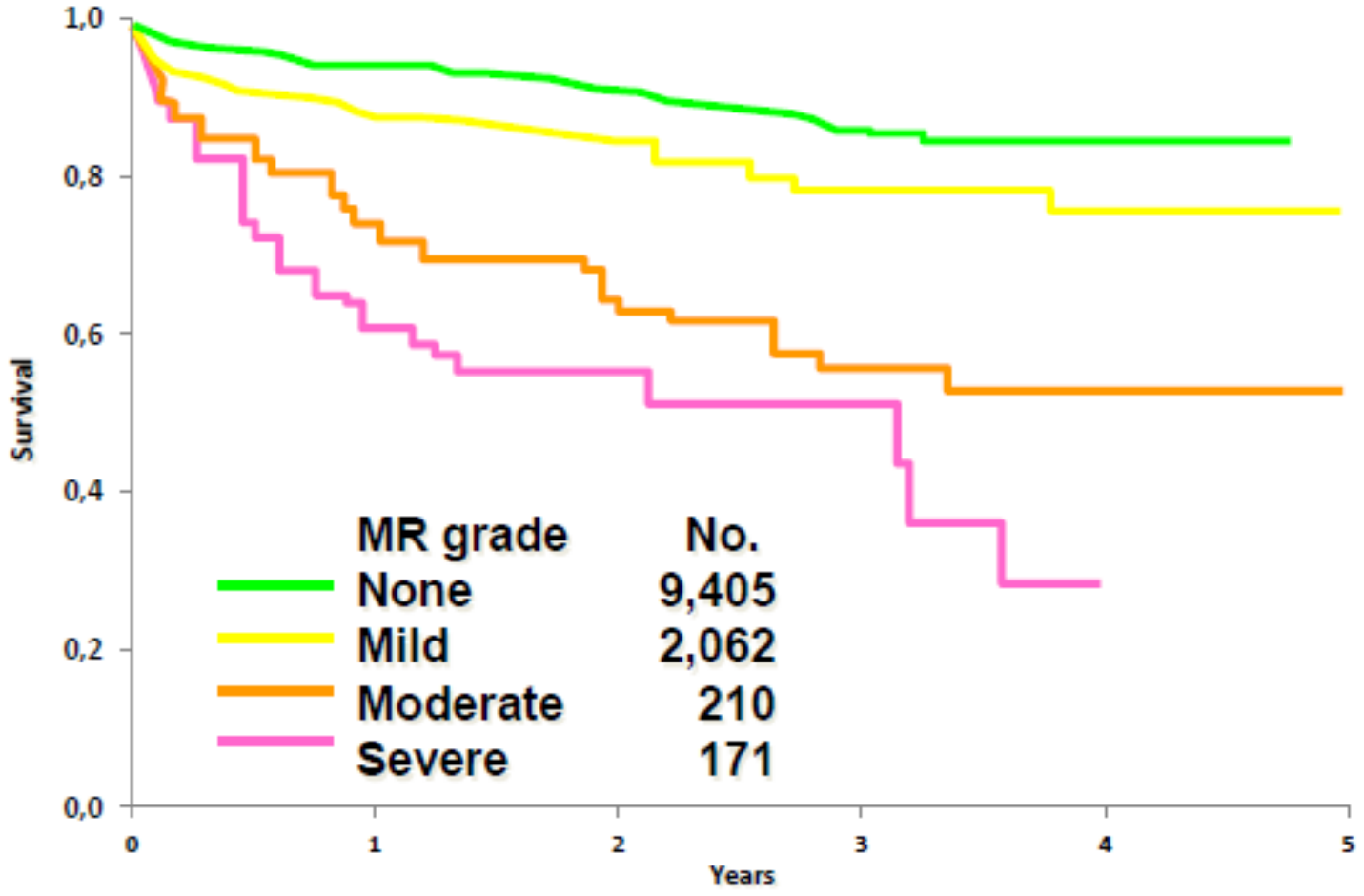
Left Sided Valvular Diseases



Graph adapted from *Burden of Valvular Heart Disease: A Population Based Study* (2006)

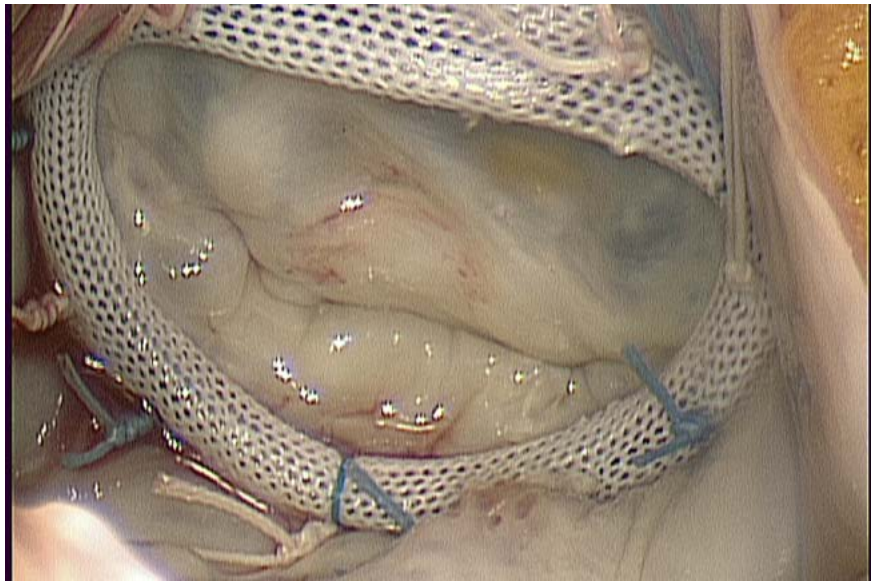
The more Severe the MR, the worse the survival

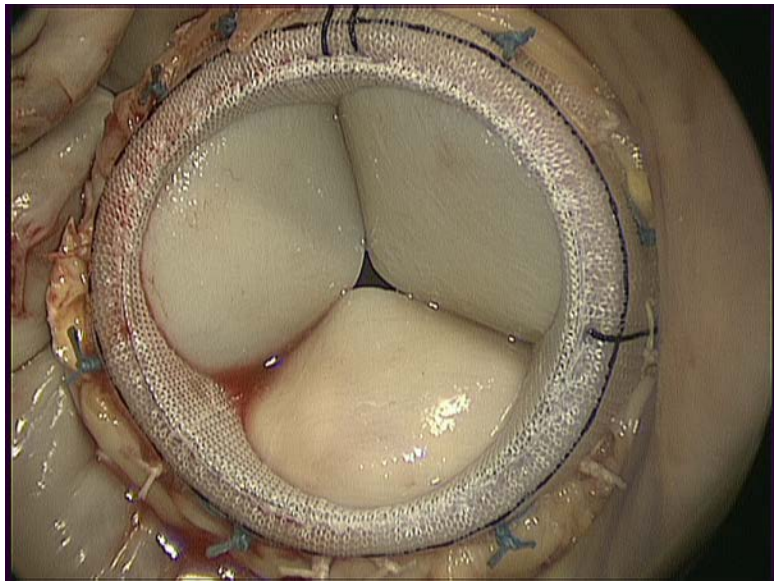
Medically managed CAD patients experienced lower survival rates with higher degrees of MR



Hickey et al: Circulation 78:1-51, 1988

Current Options to Treat MR





Potential for Future Therapies

Functional MR

Surgical treatment rate of moderate – severe patients: **16%** [1]

- Low treatment due to:
  - Previous guidelines didn't stress surgical intervention for FMR

High Risk Patients, Bad Left Ventricles

Degenerative MR

Surgical treatment rate of moderate – severe patients: **53%** [1]

- Low treatment due to:
  - Asymptomatic
  - Stable LVEF, stable chambers
  - Co-morbidities / risk

High Risk Patients, Complicated Procedure

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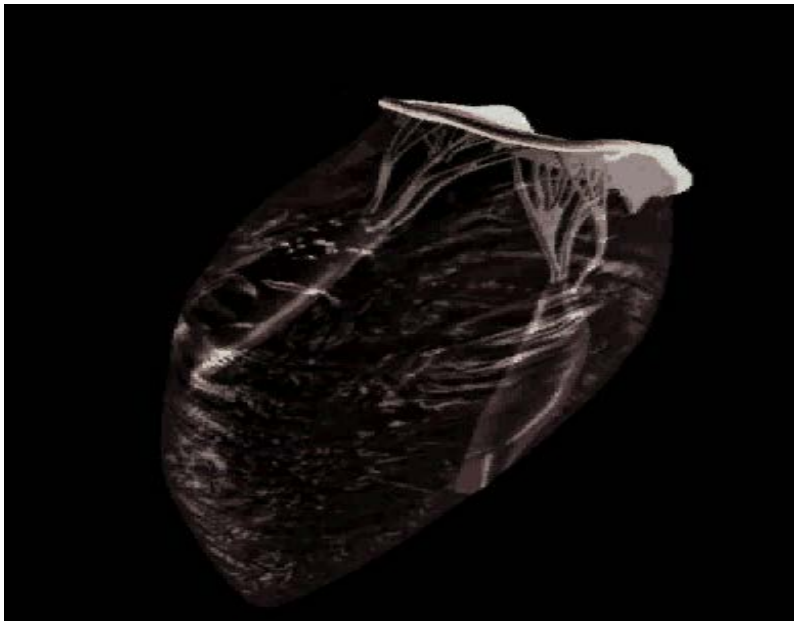
Table 3. Pooled and predicted proportions of 30-day operative mortality, operative strokes, and long-term survival.

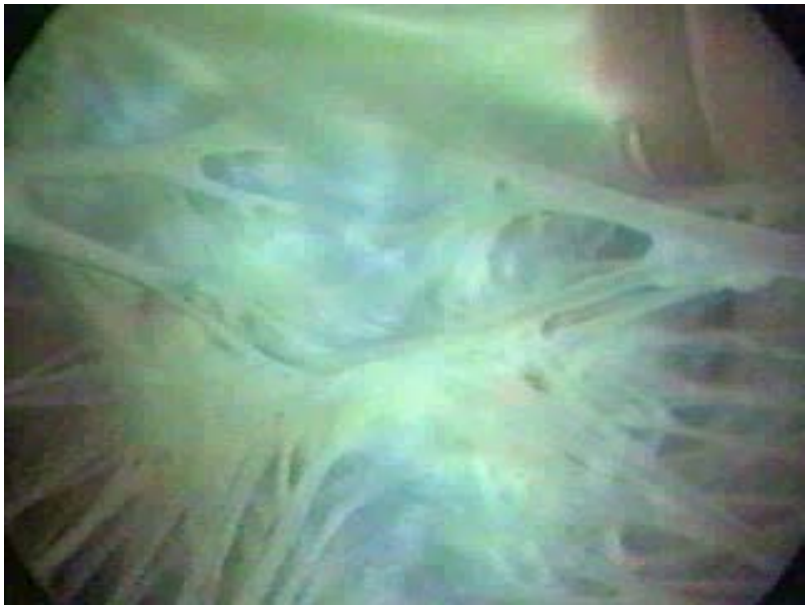
Outcome	Type of surgery		Number of studies	Number of patients	Pooled proportion Median (95% credible interval)	Predicted proportion Median (95% credible interval)	Between-study variance Median (95% credible interval)
30-day mortatlity	MVR		10	3,015	13% (9, 18)	13% (5, 30)	0.2045 (0.0794, 0.6665)
	MVRpr		6	2,642	6% (3, 12)	6% (1, 24)	0.3850 (0.1253, 1.5530)
Operative strokes	MVR		6	2,945	4% (3, 7)	4% (2, 11)	0.3632 (0.2082, 0.7769)
	MVRpr		3	348	3% (1, 8)	3% (1, 13)	0.251 (0.0840, 1.1920)
Long-term survival	MVR	1 year	4	250	67% (50, 80)	67% (33, 89)	0.2882 (0.1026, 1.1420)
		5 years			29% (16, 47)	29% (8, 66)	0.3623 (0.1206, 1.5320)
	MVRpr	1 year	3	333	69% (50, 83)	69% (34, 91)	0.2891 (0.0965, 1.3290)
		5 years			23% (12, 39)	23% (7-55)	0.2728 (0.0941, 1.2110)

MVR: mitral valve replacement; MVRpr: mitral valve repair

A systematic review and meta-analysis of surgical outcomes following mitral valve surgery in octogenarians: implications for transcatheter mitral valve interventions

The Complex Mitral Complex





The annulus, the leaflets, the chordae, the papillary muscles, the inflow and outflow of the ventricle, the aortic valve

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Table 2. CT screening and anatomical criteria measured to determine suitability for a 29 mm FORTIS valve.

Dimension	Sizing feature/potential adverse effect	Phase	Target range
LA minor diameter	Atrial flange diameter	Systole	≤52 mm
LA minor diameter		Diastole	≥38 mm
LVOT width	LVOT obstruction damage to ventricular wall	Systole	N/A
Aorta to device plane angle			≥90 degrees
Calculated LVOT clearance			>0 mm
LV diameter at papillary muscle plane	Damage to ventricular wall	Systole	>32 mm
LA height	Delivery system clearance	Diastole	>30 mm

EuroIntervention 2014;10:U120-U128
Transcatheter mitral valve implantation (TMVI) using the Edwards FORTIS device

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Table 1. Echocardiography inclusion criteria to determine suitability of the patient for a 29 mm FORTIS valve implantation.

Dimension	Sizing feature/potential adverse effect	Phase	Target range
A2 P2 distance	Valve body diameter	Systole	≥3.0 cm
A2 P2 distance		Diastole	≤4.4 cm
AML length from the hinge point	Valve body diameter	NA	<2.3 cm
PML length	Inability to capture leaflets	NA	>0.5 cm

PML: posterior mitral leaflet

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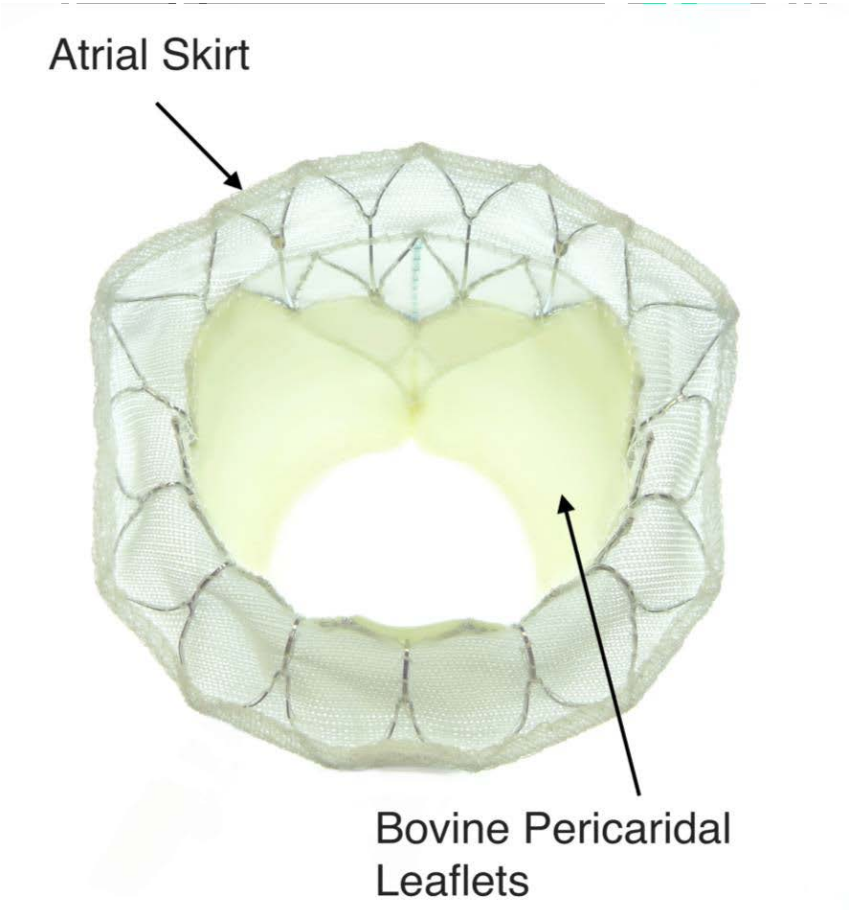
Transcatheter mitral valve implantation (TMVI) using the Edwards FORTIS device

Transcatheter Mitral Implant Devices

Company	product	access	status
Caisson	Caisson TMR	TF	preclinical
CardiaQ	TMVI-TA	TF / TAp	clinical
Edwards	Fortis	TAp / TF	clinical
Emory U	MitraCath	NA	Early develop.
HighLife	HighLife MVR	TAt	preclinical
Invalve	Invalve	NA	IP
Medtronic	TMVR	TAt / TF	preclinical
Micro Interv. Devices	Endovalve TA	NA	preclinical
MitrAssist	Mitrassist valve	NA	preclinical
Mitralix	MAESTRO	NA	Early develop.
MITRICARES	Mitricares	NA	IP
NCSI	NAVIGATE TMVR	TAt /TF	clinical
Neovasc	Tiara	TA / TF	clnical
Tendyne	Tendyne Lutter	TA	clinical
Twelve	TMVR	NA	IP
ValtechCardio	Cardiovalve	TF	preclinical

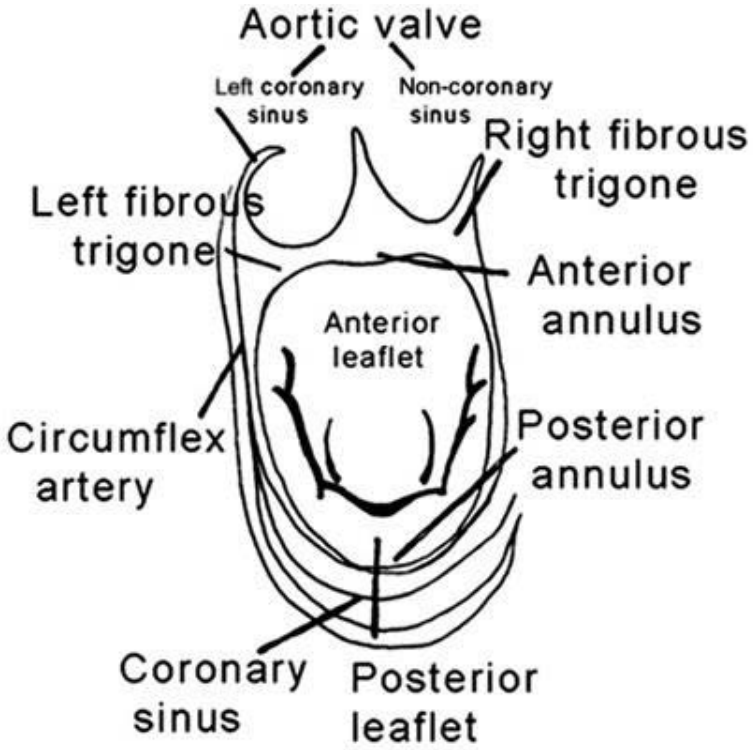
Tiara Mitral Prosthesis

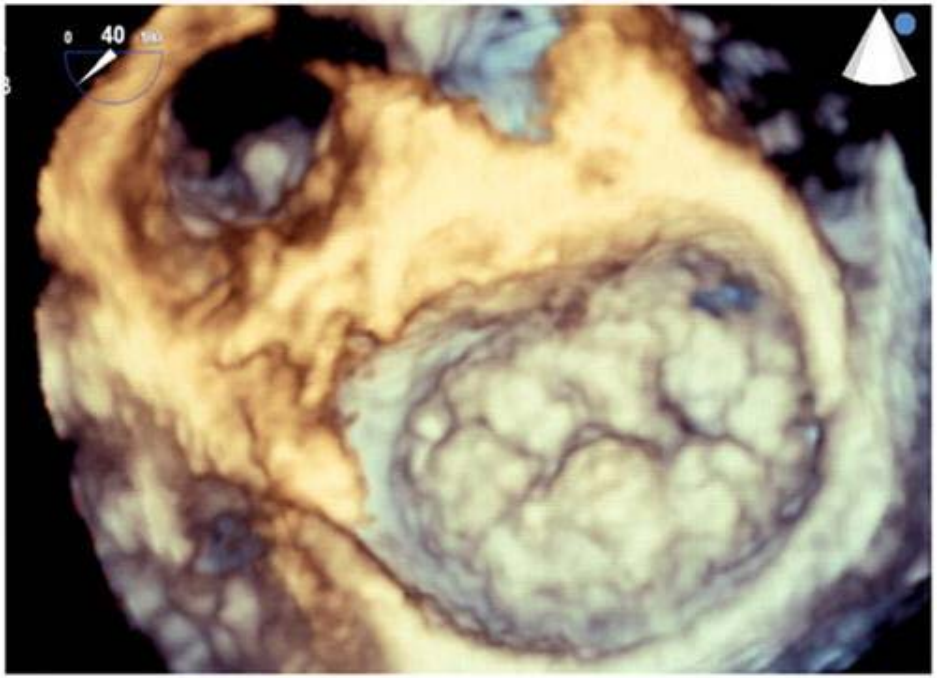
- Anatomically D-shaped
- Nitinol, self-expanding frame
- Bovine pericardium leaflets
- Atrial skirt



Tiara Mitral Prosthesis

- Ventricular anchors
- Fixation
  - fibrous trigones
  - posterior annulus
- Captures the anterior and posterior leaflets


Aortic valve
Left coronary sinus
Non-coronary sinus
Right fibrous trigone
Left fibrous trigone
Anterior annulus
Anterior leaflet
Circumflex artery
Posterior annulus
Coronary sinus
Posterior leaflet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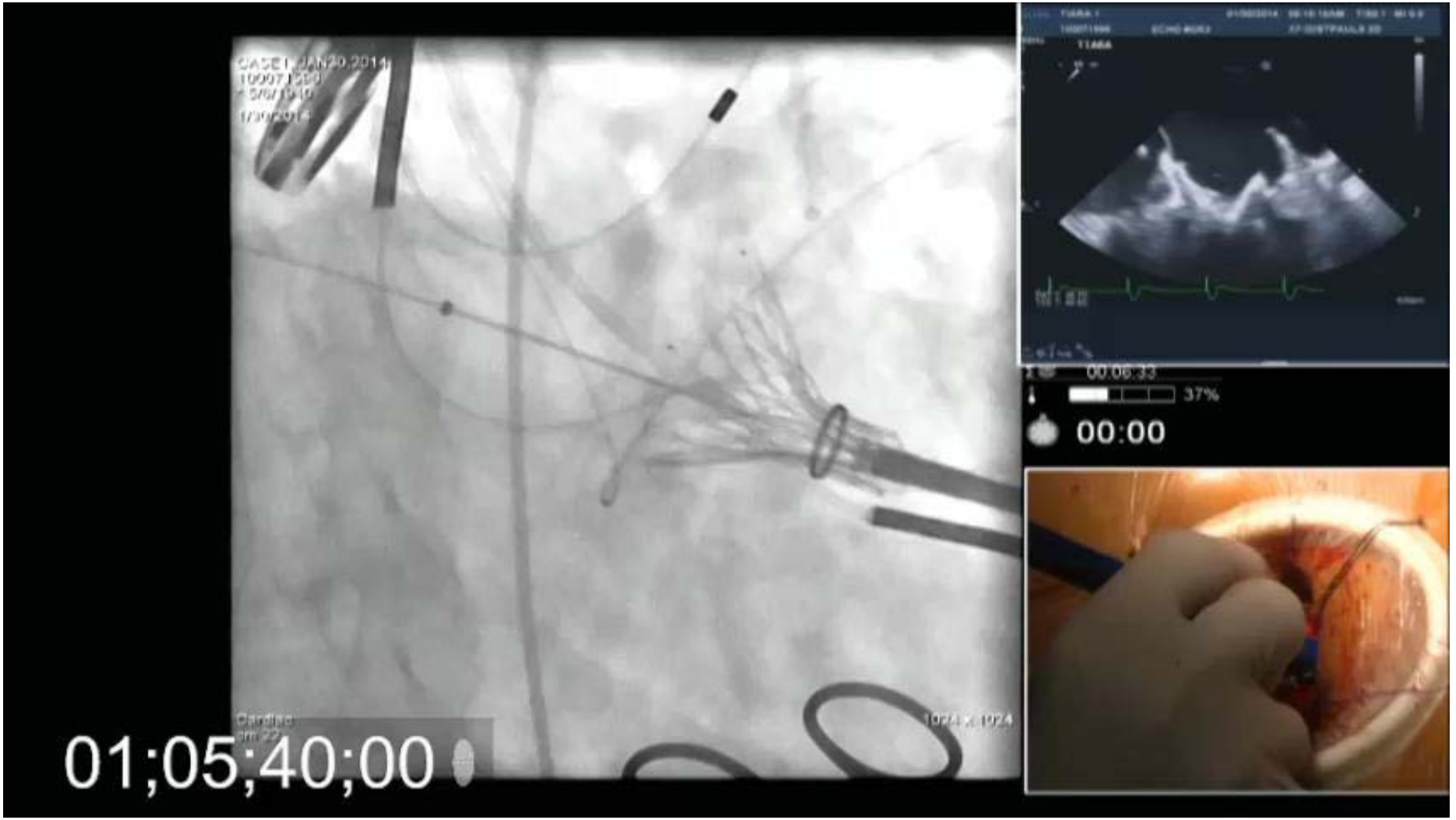
TIARA
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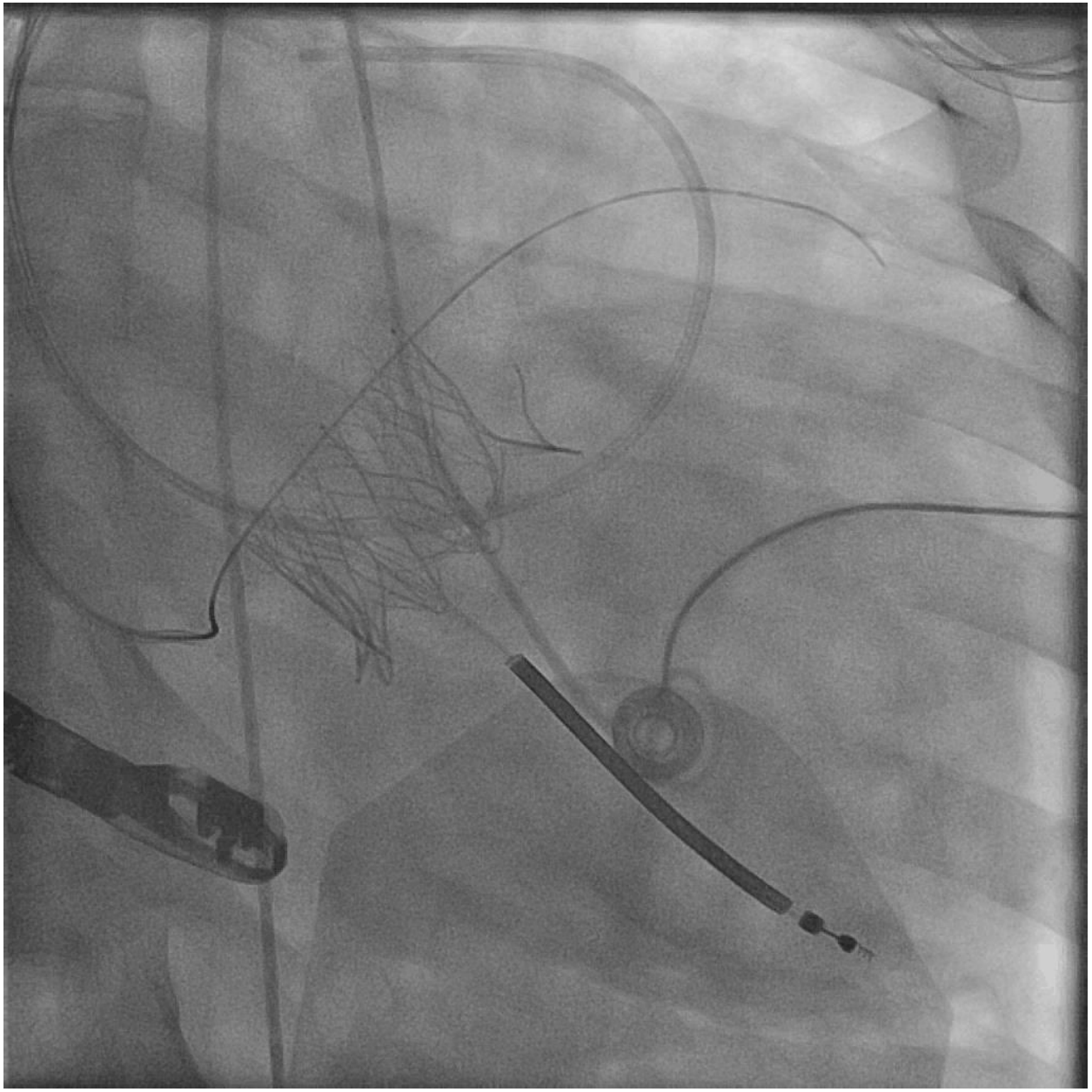


Tiara Experience

- 3 successful human implants
- No intra-operative complications, no transfusion
- All extubated in operating theatre
- Improvement in stroke volume and lowering of pulmonary pressure immediately post implant
- All patients discharged from hospital
- No mortality at 30 days

Tiara Next Steps

- **TIARA- I**
- Feasibility study
- Up to 30 patients
- Primary Endpoint: Safety
- Secondary Endpoints:
- Device and procedure success
- Clinical performance
- Canada, Belgium Germany, US

CardiAQ™ TMVR System

Multiple access routes

Transfemoral	successful FIH June 2012
Transapical	successful FIH May 2014

Controlled deployment

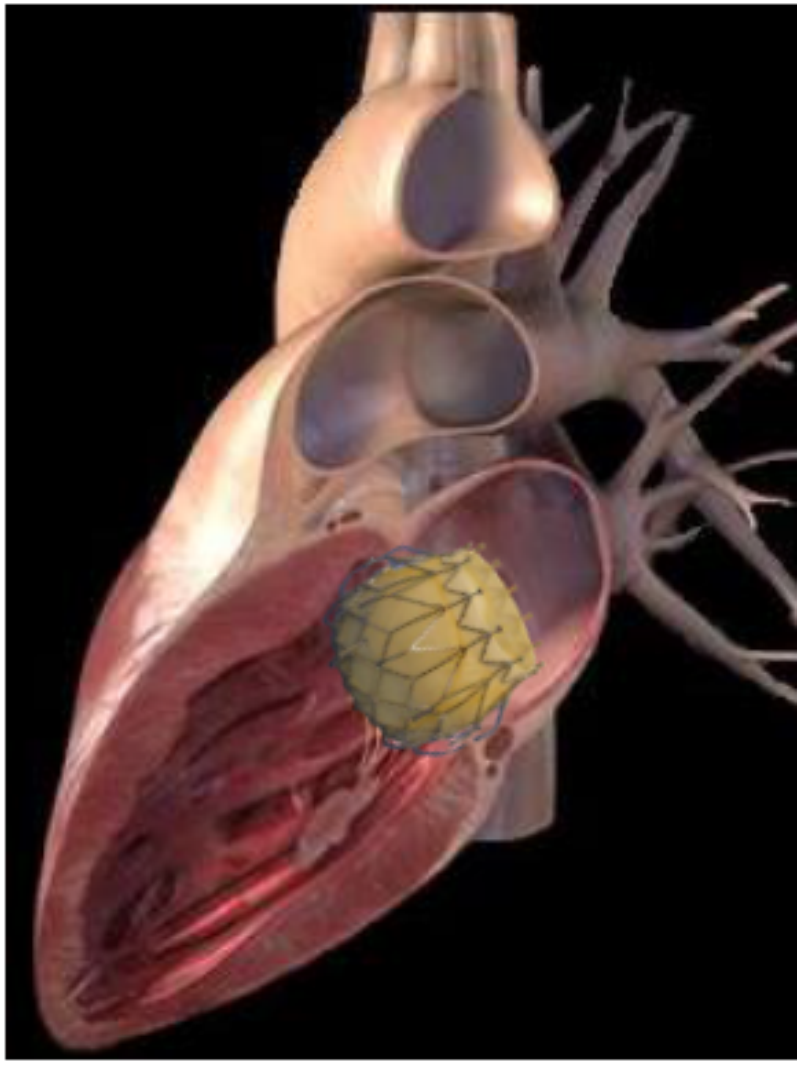
- Multi-stage deployment

Accurate positioning

- Self-positioning within native valve annulus
- Intra/supra annular placement to preserve LV contractility and maximize LVOT area

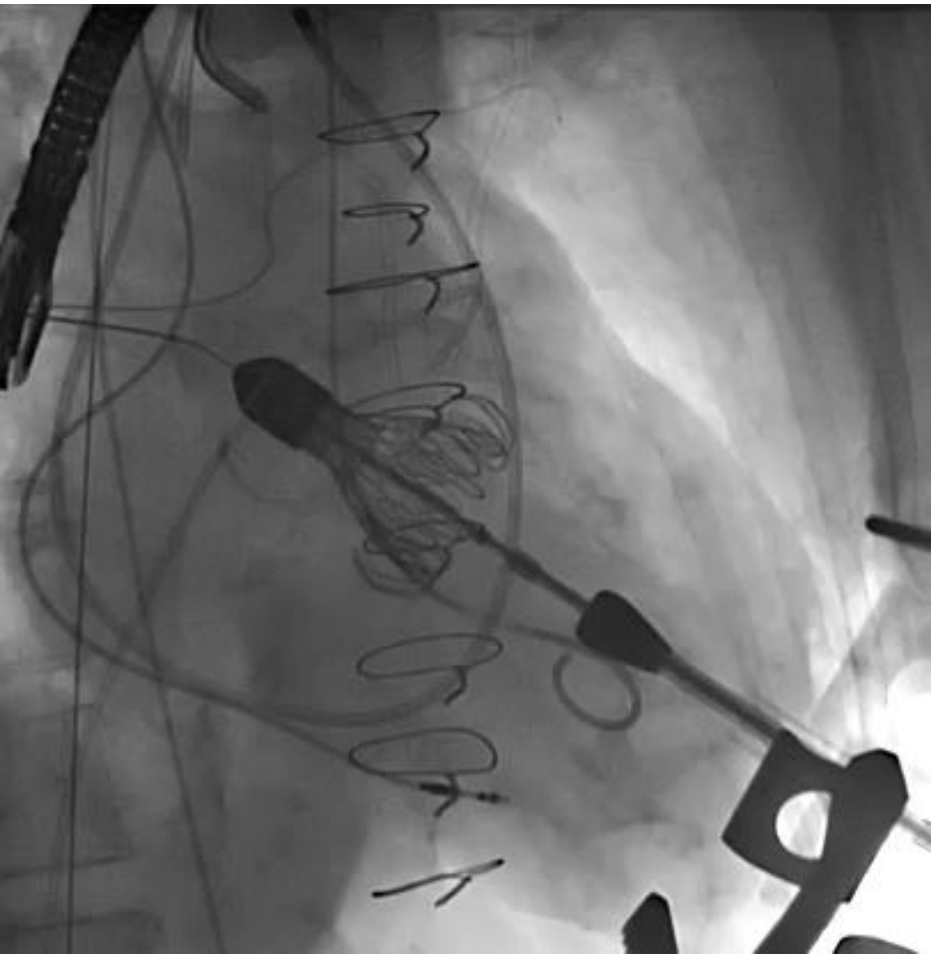
Secure anchoring

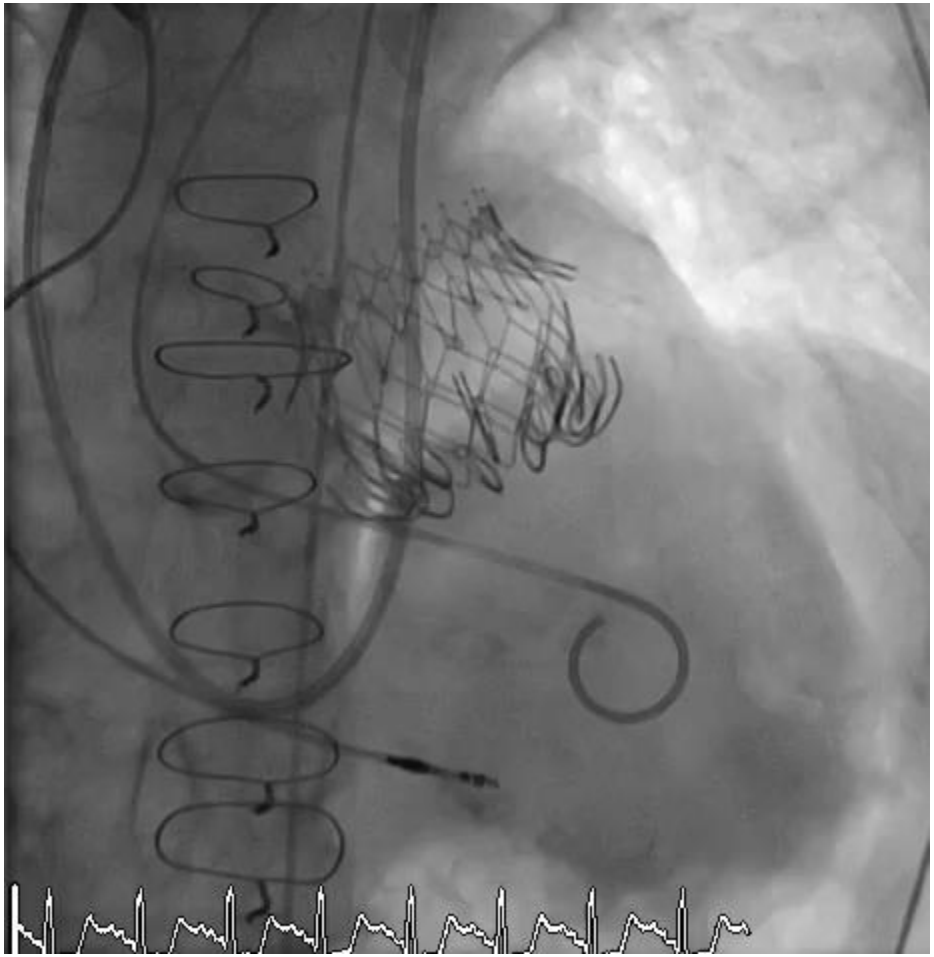
- Preserves native chordae and leaflets
- Anchoring without radial force



Release Ventricular Anchors and Capture of Both Leaflets

Deployment, Atrial Anchors and Final Release





Clinical results

4 patients treated in Copenhagen:

- All turned down for surgery and technically not candidates for MitraClip
- TMVR on compassionate ground approved by DMA

No	*Date*	*Gen*	*Time*	*Status*		
TF-1	2012/6	1	60 min	Died day	3	(SIRS)
TA-1	2014/5	2	20 min	Alive day	139	
TA-2	2014/7	2	13 min	Alive day	83	
TA-3	2014/7	2	13 min	Died day	9	(pneumonia)

CardiAQ Next Steps

- Gain more experience on both TF and TA TMVR procedure during compassionate cases
- CE mark trial anticipated to start by early 2015
- 100 patients at 10 sites

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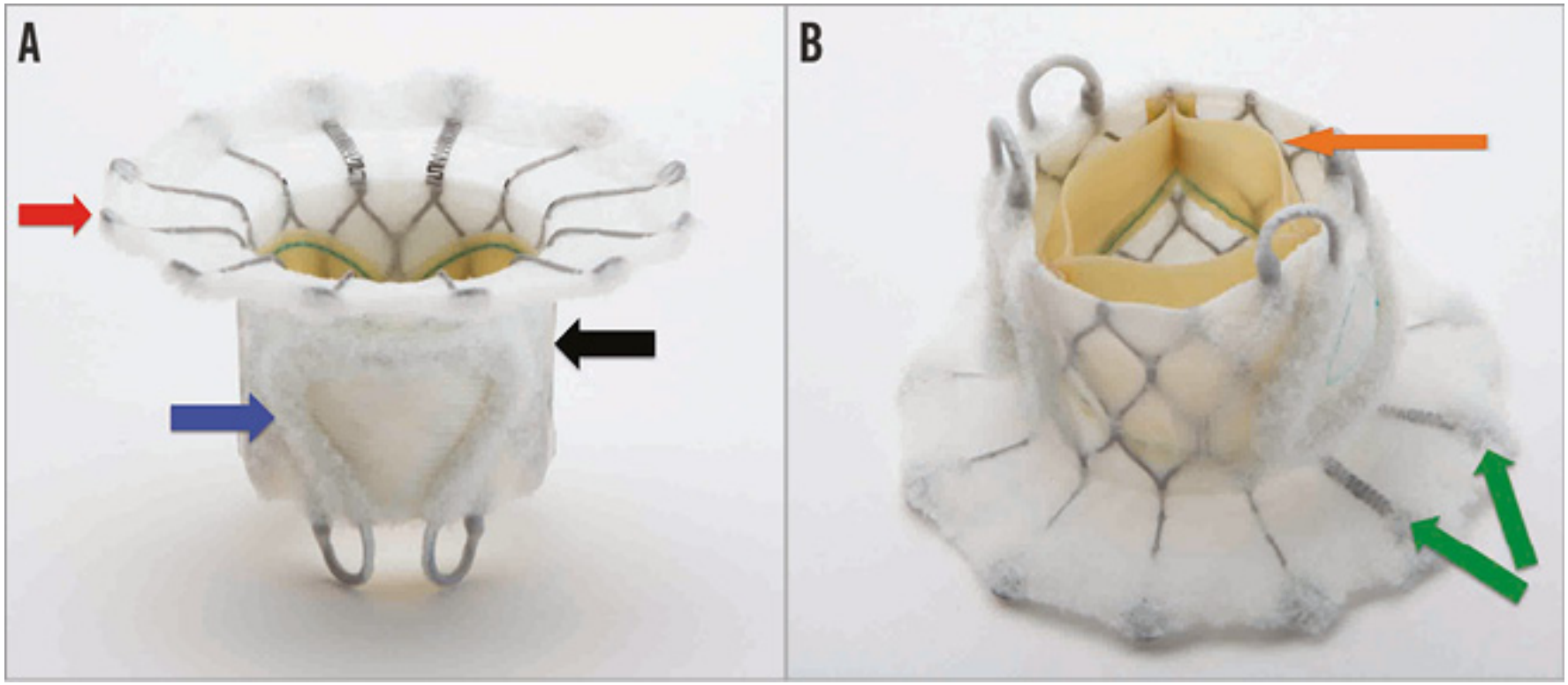
Edwards Fortis



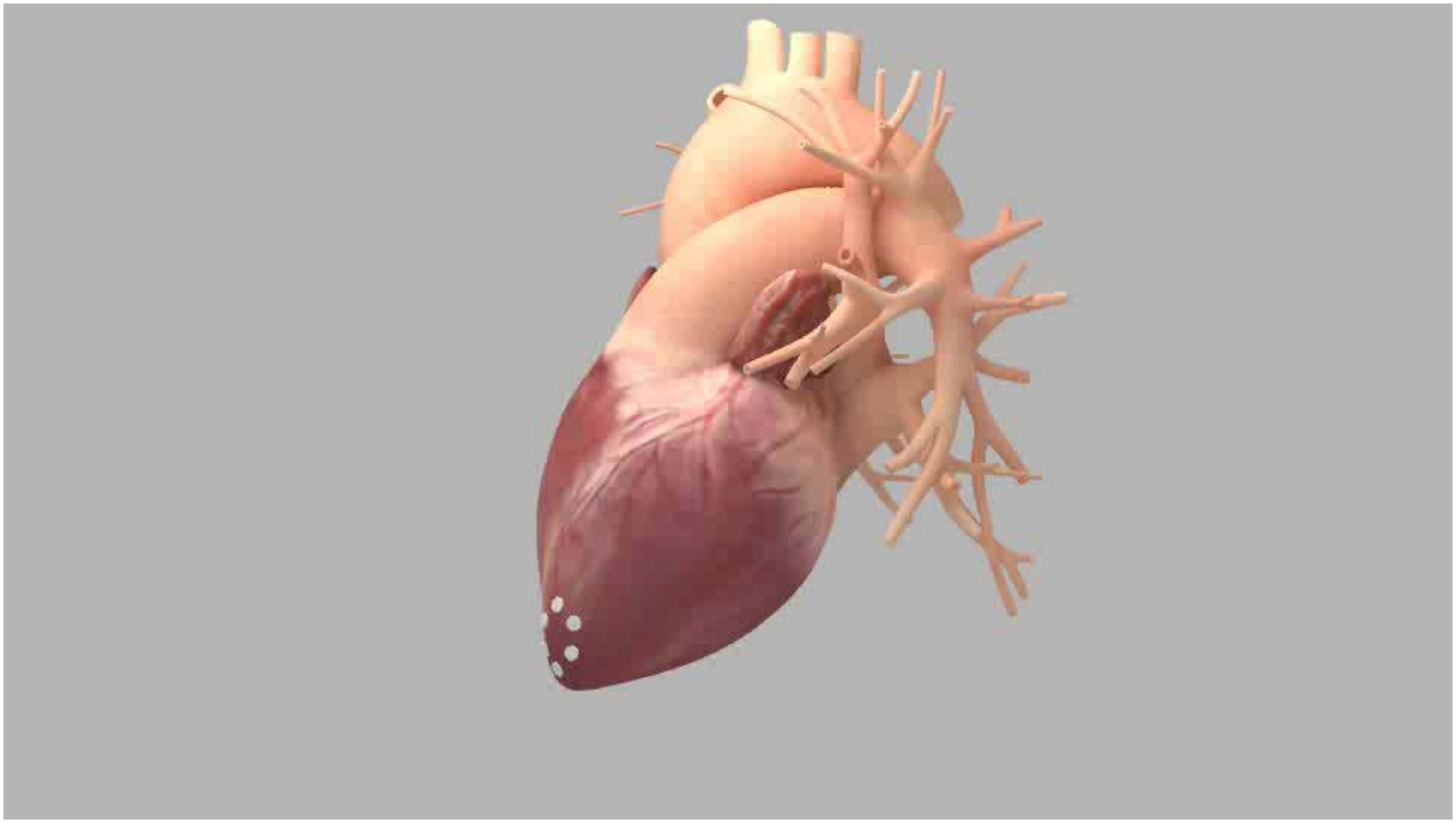
EuroIntervention 2014;10:U120-U128

Transcatheter mitral valve implantation (TMVI) using the Edwards FORTIS device

Delivery system

- Transapical delivery
- Multiple levels of control
- Repositionable

Fortis Valve Animation

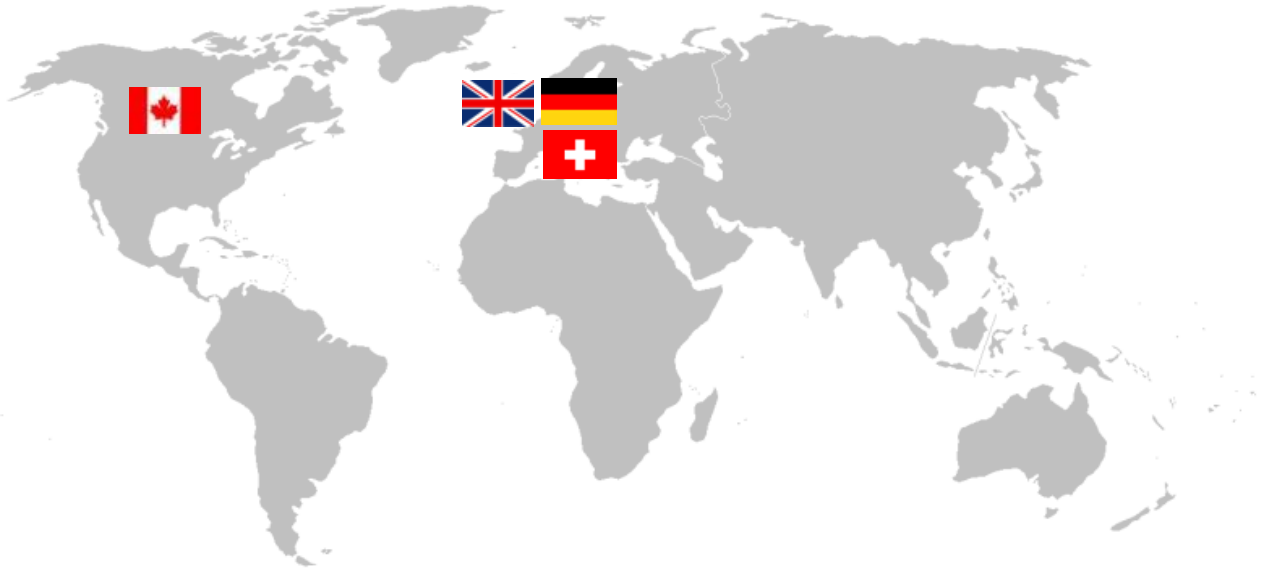


Fortis Compassionate Use Summary

Patient	1	2	3	4	5	6	7	8
Full Release of Valve	84 min	69 min	36 min	31 min	37 min	67 min	25 min	Converted to surgery – inadequate imaging
MR Grade	1+	1+	1+	Trace	0	0	0	
Acute Recovery	Slow	N/A	Better	Better until 12d	Better	Better	Better	
Death	Day 76	Day 4	-	Day 15	-	-	-	Day 7
Cause of Death	CHF	Renal failure & system failure	-	Thrombosis?	-	-	-	Septic shock

Fortis Next Steps

- Continue compassionate use
- Limited clinical feasibility study underway: multi-center, protocol driven, prospective study
  - Enrollment started August 2014



Challenges

- Focus on TF approach delayed and complicated the device development
  - TA approach simplifies delivery and size issues
- Orifice saddle shaped and larger size more complex
  - 3D CT imaging of mitral should help
- LVOT obstruction
  - “Capture” of anterior leaflet and atrial positioning will help
- Cannot rely solely radial force- no calcium; elasticity
  - Requires more complex anchoring system
  - Need to minimize PV leak
- Impingement/distortion of adjacent structures
  - LVOT, coronary sinus, circumflex coronary artery, aortic valve

Conclusions

- Transcatheter mitral valve replacement (TMVR) is HERE

- We still require
  - Better patient selection
  - Improved Technology
  - Improved procedural steps
  - Discover the optimal post operative anti-coagulation
  - Improved patient outcomes