

Pathology of TAVR and Mitral devices

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Consultant: 480 Biomedical, Abbott Vascular, Medtronic, and W.L. Gore.

Employment in industry: No

Honorarium: 480 Biomedical, Abbott Vascular, Boston Scientific, Cook medical, Lutonix, Medtronic, Terumo Corporation, and W.L. Gore.

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Owner of a healthcare company: No

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Pathology of TAVR

Surgically Implanted Bioprosthetic Valve: Summary

Disadvantages: Limited durability beyond 10 years especially in younger patients: cusp degeneration or tears, Ca^{++} , pannus formation and endocarditis (1–4% of patients during the 1st year, and in approximately 1% per year thereafter.)

Tears



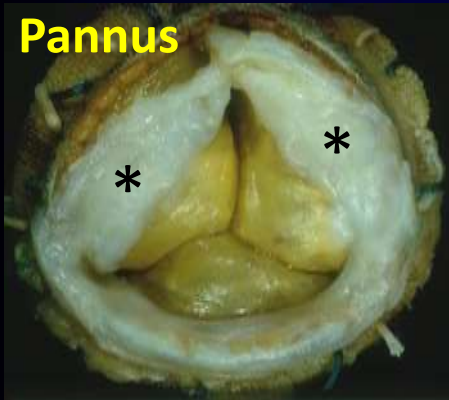
Calcification



Infective endocarditis



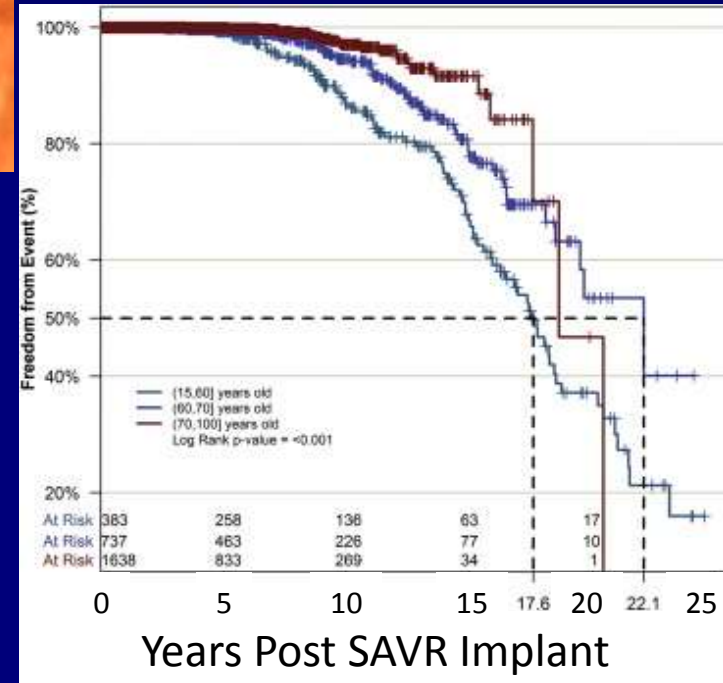
Pannus



Thrombus

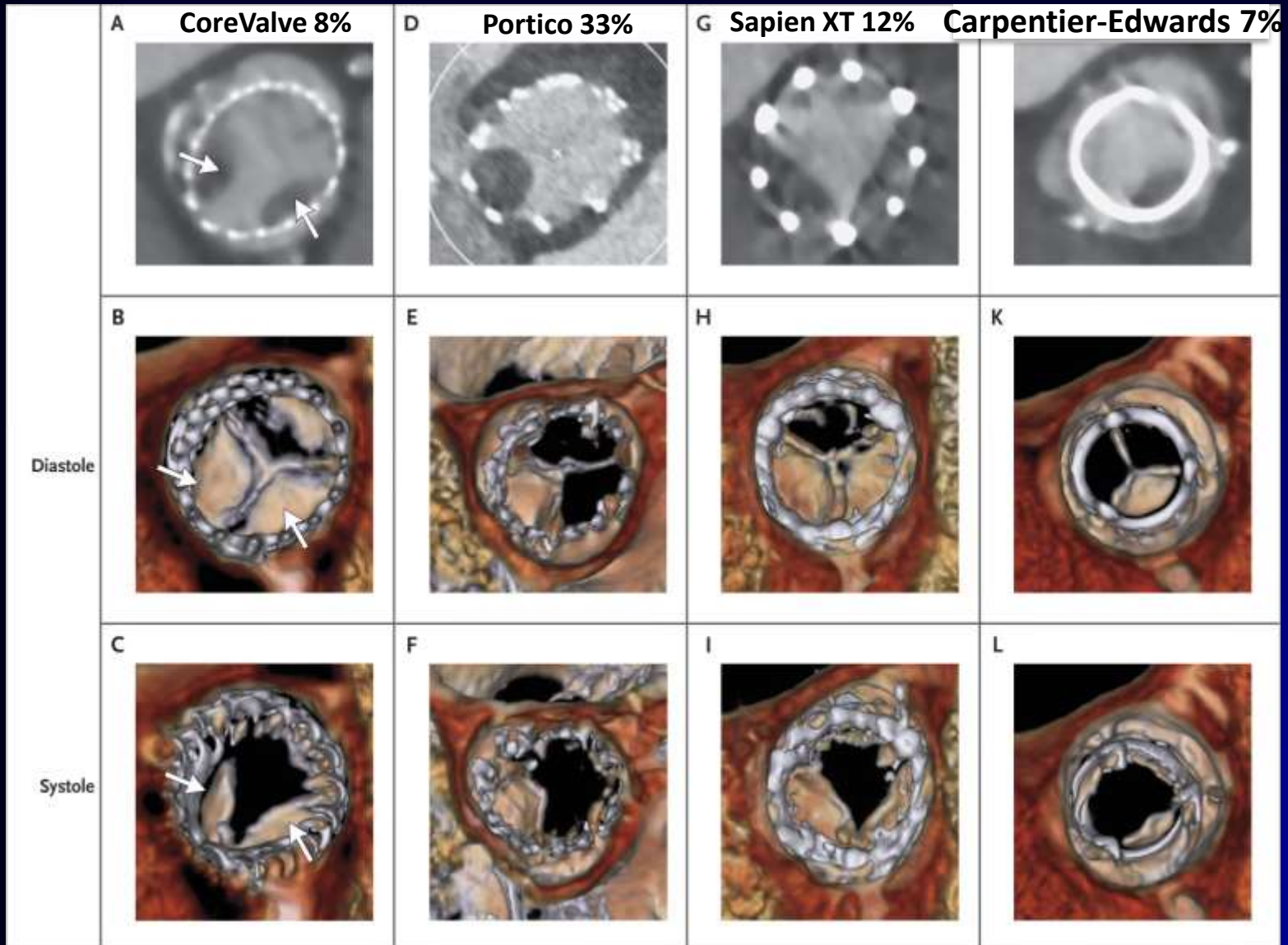


**Freedom from Event
(Severe AS/AR or Redo)**



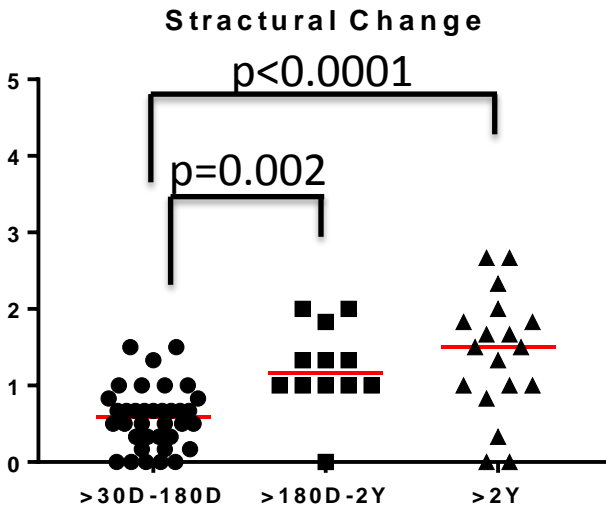
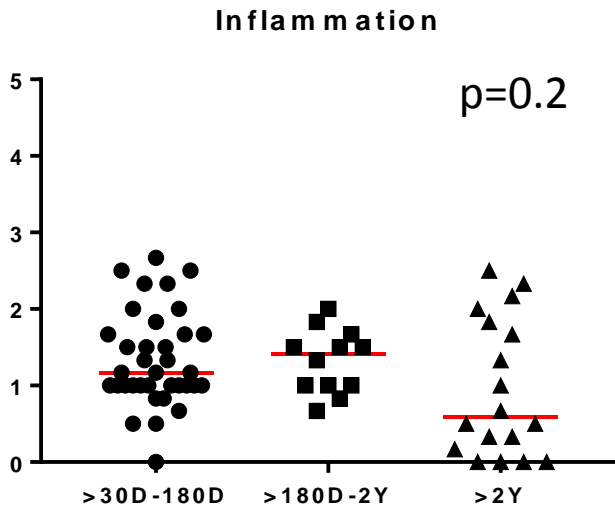
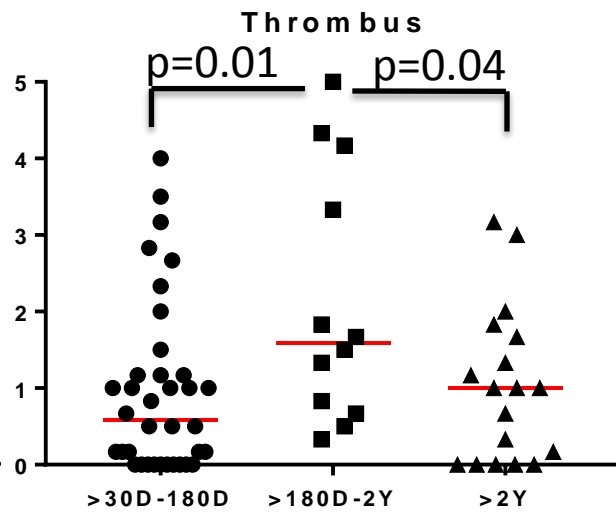
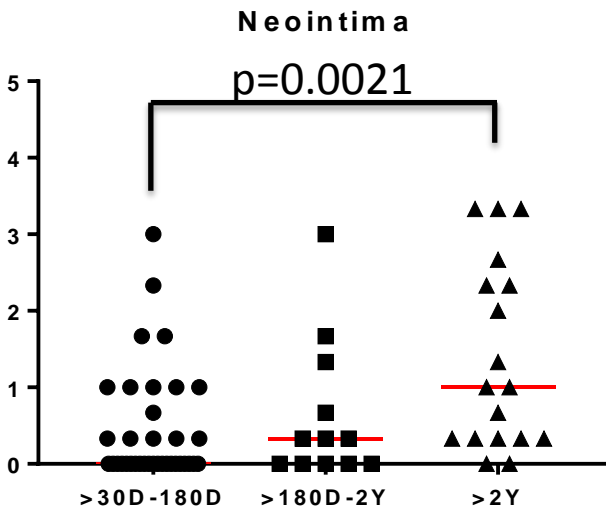
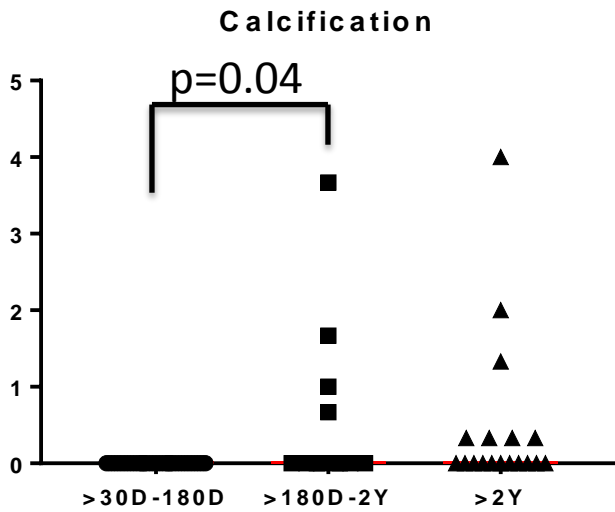
Bourguignon T et al.
Ann Thorac Surg.
2015;99(3):831-7.

Evidence of Reduced Leaflet Motion in Multiple Prosthesis Types.



Histologic changes of leaflets from TAVR valves by duration of implant

Medtronic and Edwards TAVR valve		≥30 days, n=78
Age, years (Median [IQR; range])		81 (76-88)
Male sex		65%
Following TAVR, days (Median [IQR; range])		252 (67-850 [30-1825])
Medtronic / Edwards		61 (73%) / 22 (27%)
CoreValve / Evolut R / Sapien / Sapien XT / Sapien 3		60 / 1 / 13 / 6 / 3
IE, % (n) *excluded from the analysis		15% (12)



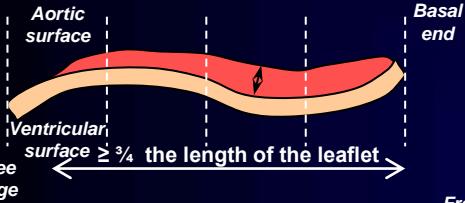
≥30D-180D n=36
 >180D-2Y n=12
 >2Y n=18

Assessment of Valve Thrombus on Pathology

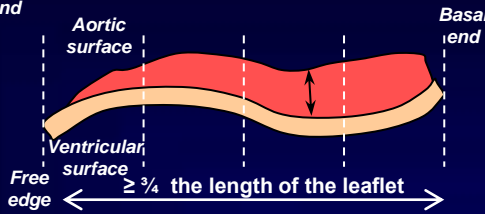
Moderate thrombus (Score 4)

Severe thrombus (Score 5)

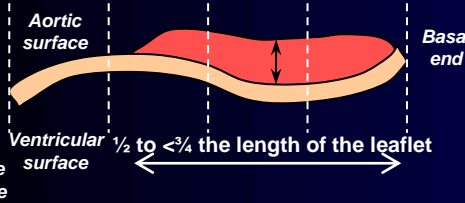
Greater than leaflet thickness, but less than 2x the thickness



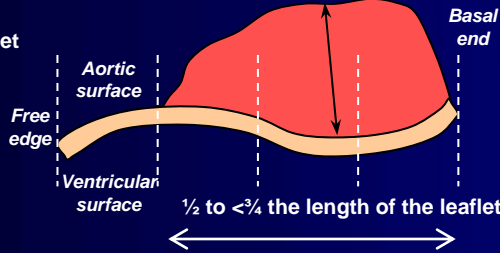
Greater than 2x leaflet thickness, but less than 4x the thickness



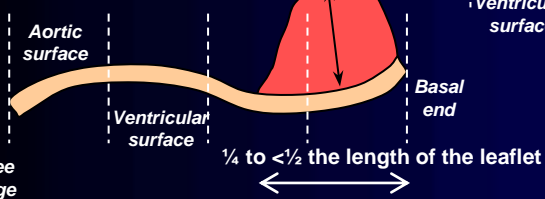
Greater than 2x leaflet thickness, but less than 4x the thickness



Greater than 4x leaflet thickness



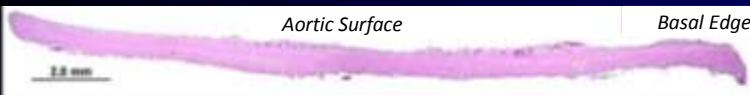
Greater than 4x leaflet thickness



● Thrombus
● Leaflet

	< 1/4 the length of the leaflet	1/4 to <1/2 the length of the leaflet	1/2 to <3/4 the length of the leaflet	≥3/4 the length of the leaflet
Absent	0	0	0	0
Less than leaflet thickness	0	1	2	3
Greater than leaflet thickness, but less than 2x the thickness	1	2	3	4
Greater than 2x leaflet thickness, but less than 4x the thickness	2	3	4	5
Greater than 4x the thickness	3	4	5	5

Score 0



≤30 days

Score 4



≥3 years

Score 5

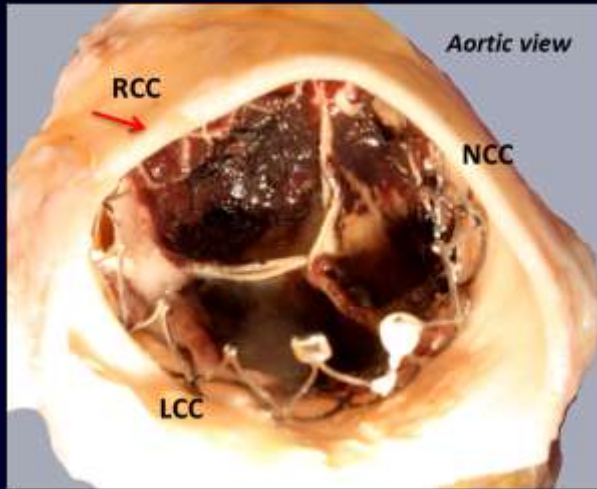


31 days – 1 year

Transcatheter aortic valve failure: Severe Thrombosis (5%)

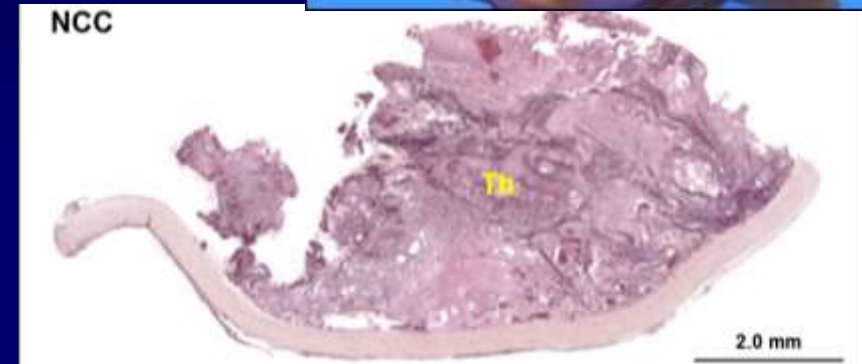
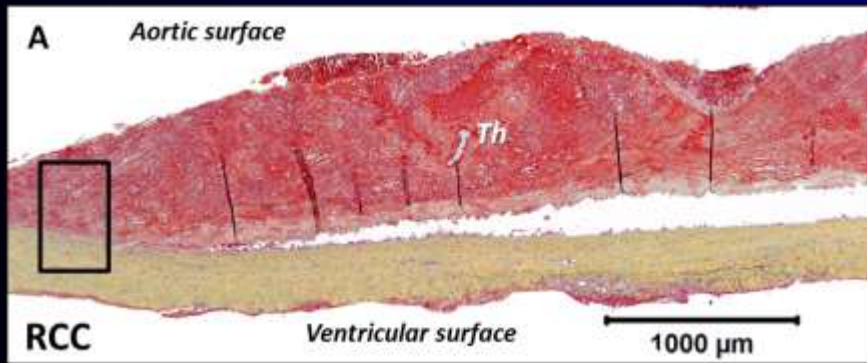
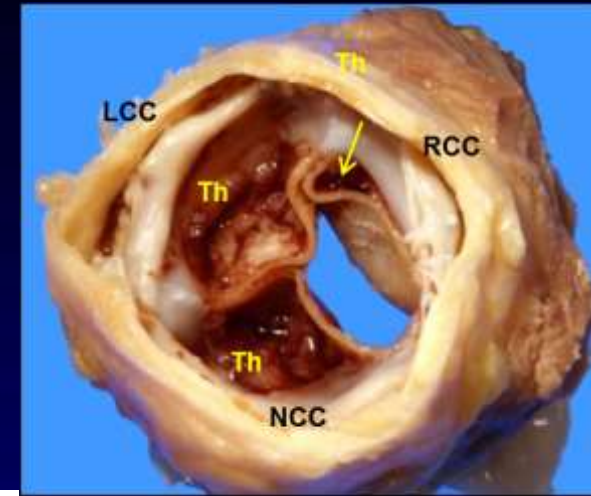
**CoreValve:
15 days**

De Marchena E,
R Virmani, et al.
JACC Cardiovasc Interv.
2015 Apr 27;8(5):728-39.



**SAPIEN:
495 days**

Yahagi K, et al.
Catheter Cardiovasc
Interv. 2017
15;90(6):1048-1057.

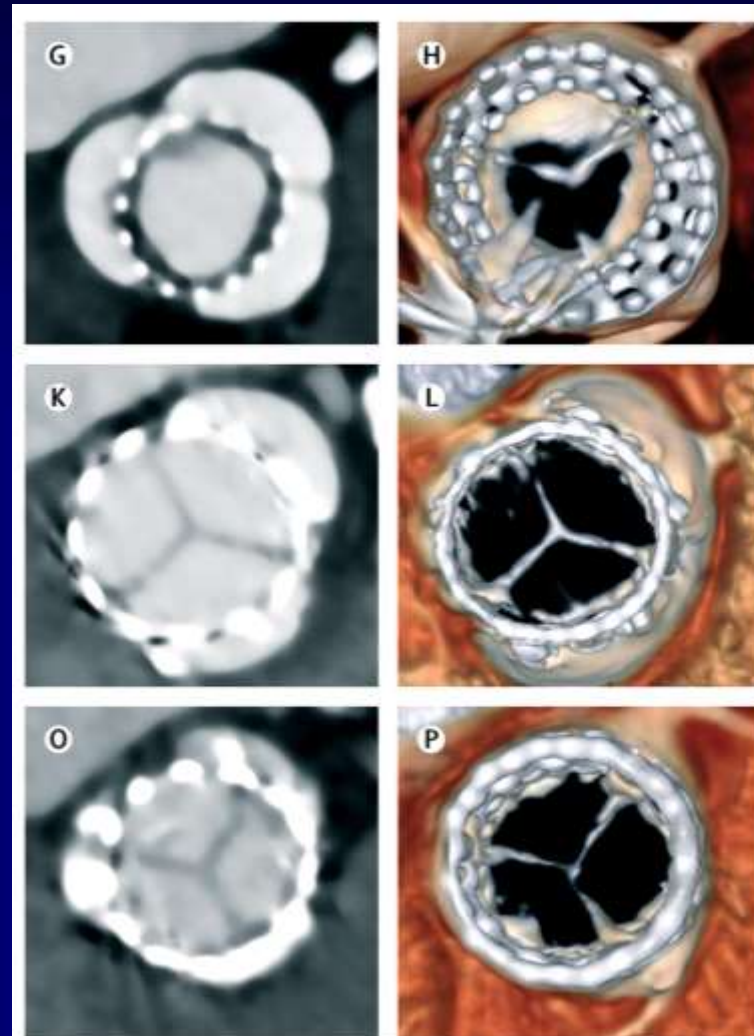
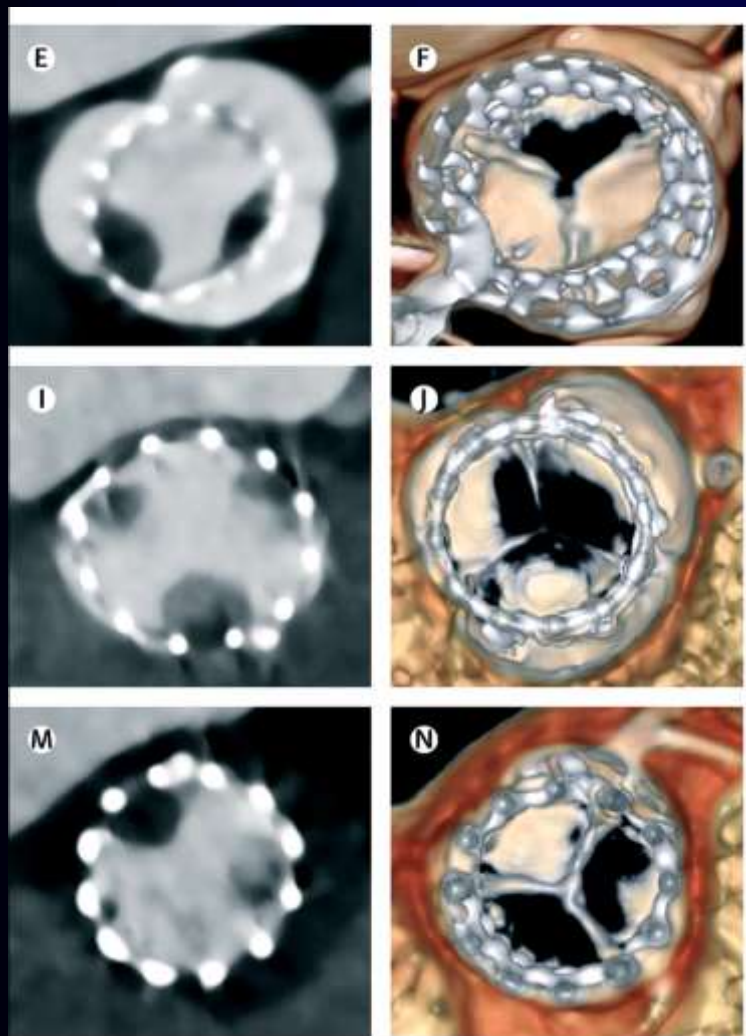


	Overall N=66	Cases with Severe thrombus N=12 (18%)	Cases without Severe thrombus N=54 (82%)	P value
Age	81 (76-88)	85 (76-89)	81 (76-88)	0.7
Sex (male), %	65%	50%	67%	0.3
Duration, days	252 (67-850)	257 (86-857)	104 (54-776)	0.3

Oral anticoagulation therapy (OAC), but not DAPT, was effective in prevention or treatment of subclinical leaflet thrombosis.

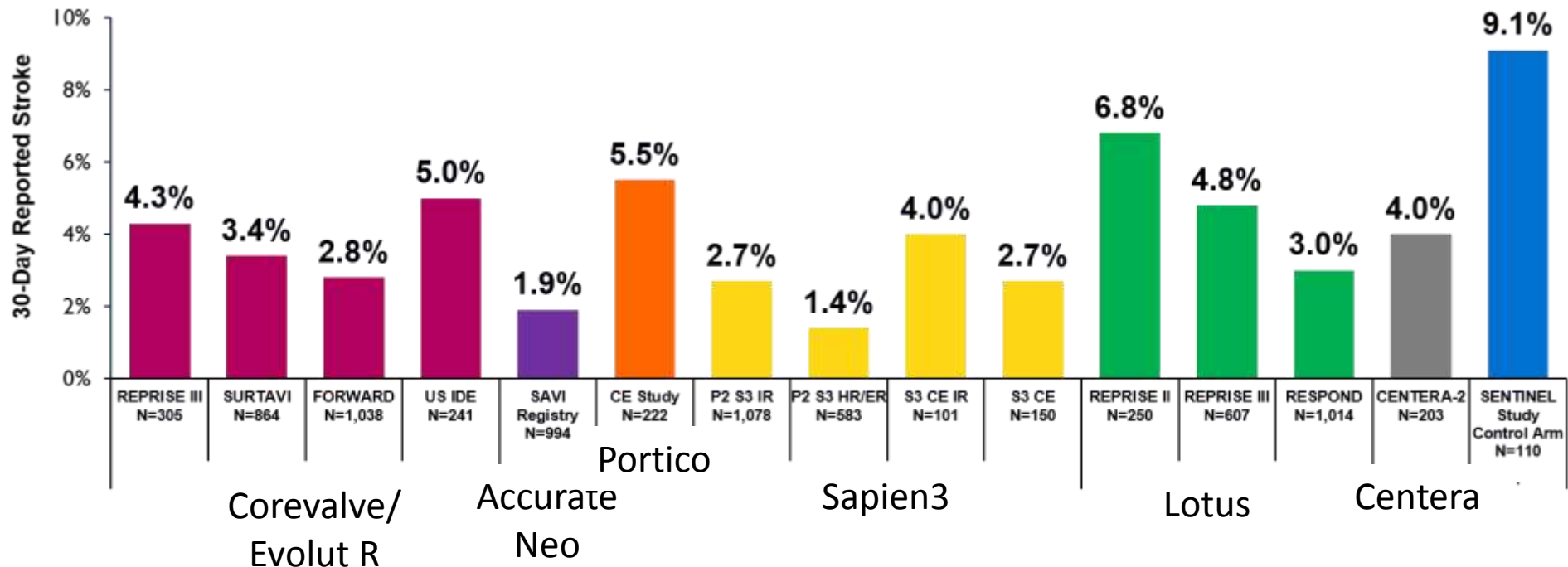
Reduced leaflet motion in a patient receiving **DAPT** after TAVR

Resolution of reduced leaflet motion following 3 months of **OAC**



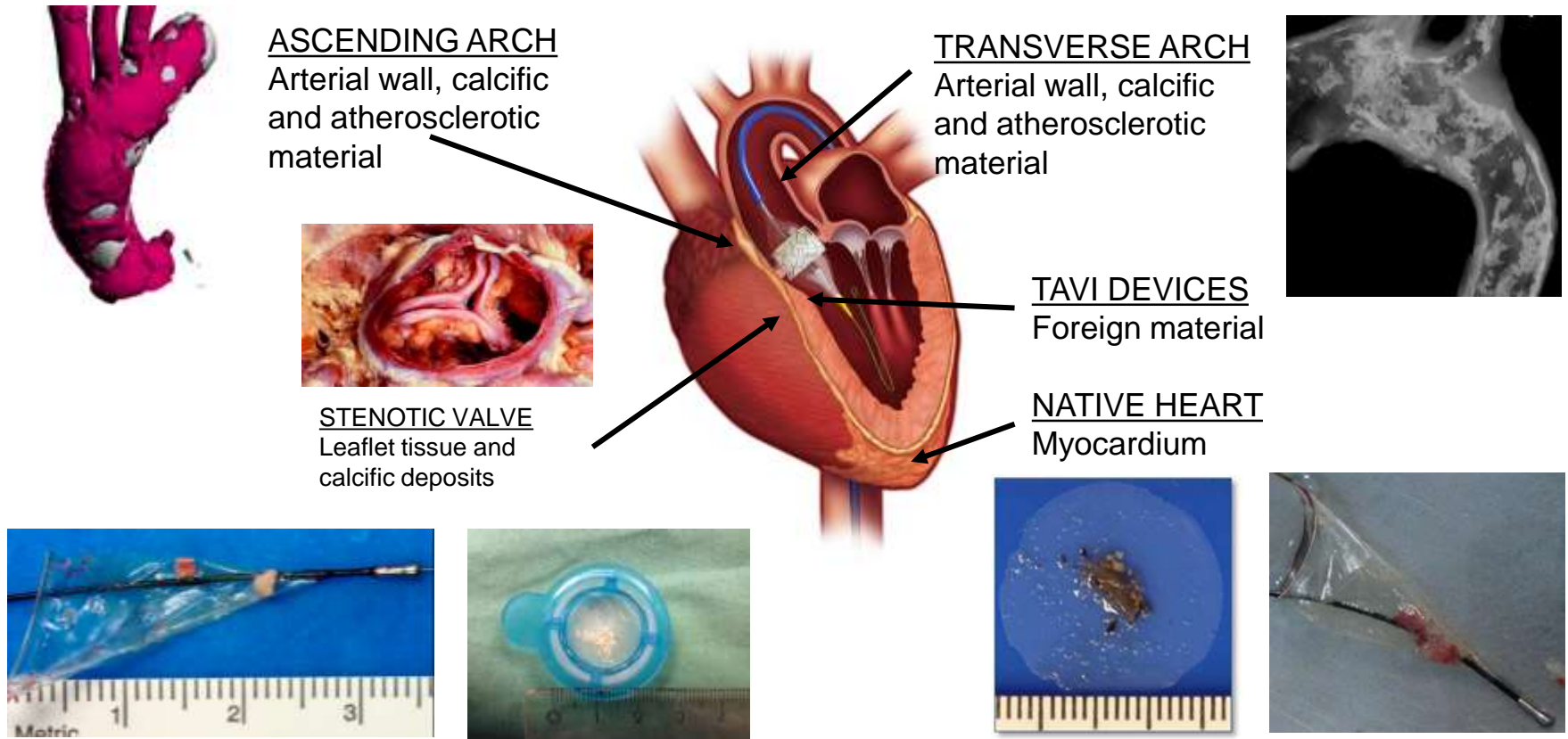
TAVR Stroke Rates with Contemporary Devices

- Stroke remains an issue (~4.4% average rate) in contemporary TAVR studies.
- TAVR device trials tend to emphasize only the major/disabling stroke rates.

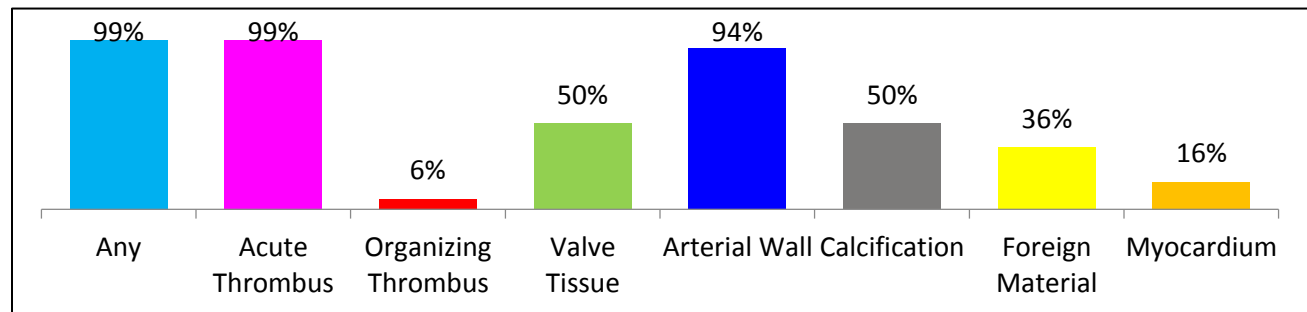


¹ Feldman, et al., EuroPCR 2017; ²Manoharan, et al., *J Am Coll Cardiol Intv* 2015; 8: 1359-67; ³Moellman, et al., PCR London Valves 2015; ⁴Grube, et al., EuroPCR 2017; ⁵Kodali, et al., *Eur Heart J* 2016; ⁶Vahanian, et al., EuroPCR 2015; ⁷Webb, et. al. *J Am Coll Cardiol Intv* 2015; 8: 1797-806; ⁸DeMarco, et al, TCT 2015; ⁹Meredith, et al., PCR London Valves 2015; ¹⁰Falk, et al. *Eur Heart J* 2017; ¹¹Kodali, TCT 2016; ¹²Reardon, M *NEJM* 2017; ¹³Reichenspurner H, et al., *JACC* 2017; ¹⁴Popma et al, *JACC:CVInt* 2017;10(3):268-75

Sources of Debris During TAVR

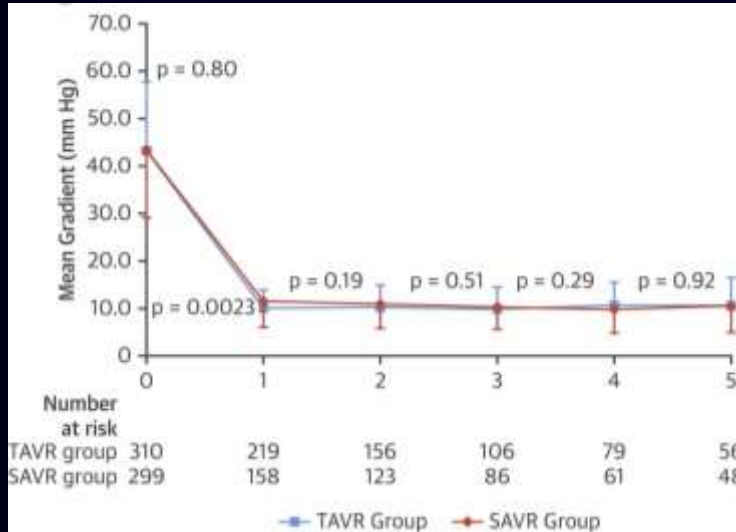


Patients with captured debris



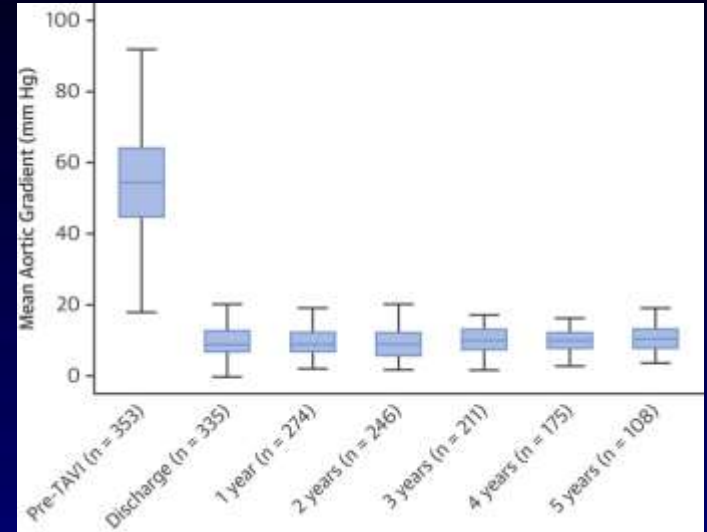
Transcatheter Valve Durability

PARTNER 5-year Echocardiographic performance (SAPIEN)

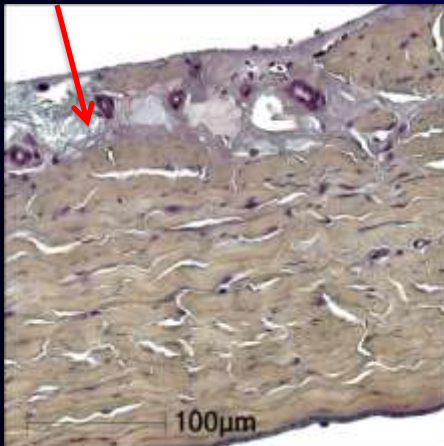


Mack MJ, et al. Lancet. 2015;20:385(9986):2477-84.

CoreValve 5-year Follow-up (registry)



Rodriguez-Gabella, T. et al. J Am Coll Cardiol. 2017;70(8):1013-28.



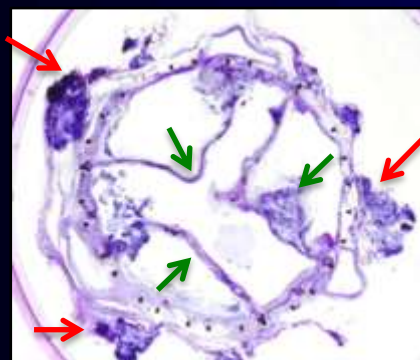
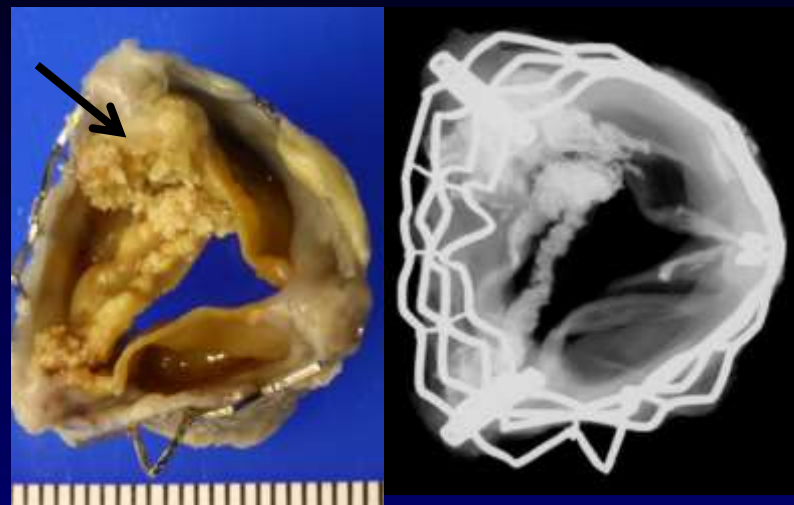
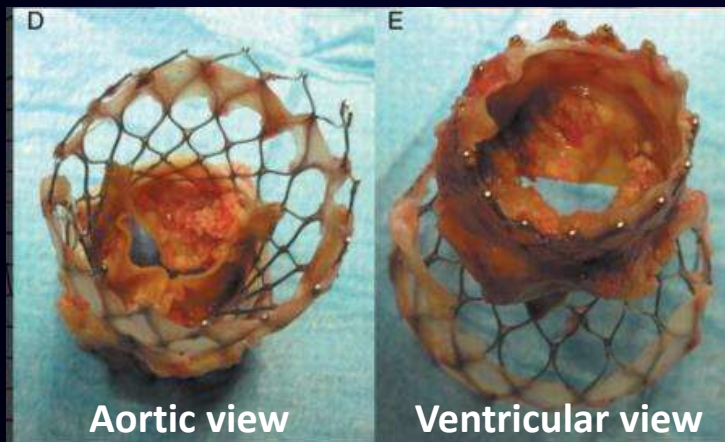
A case with mild structural changes

89 y.o. female, with a history of AS, DM, HLP, HTN, and CHF
 Died due to congestive heart failure, **1477**days (**4** years)
 after TAVR implantation

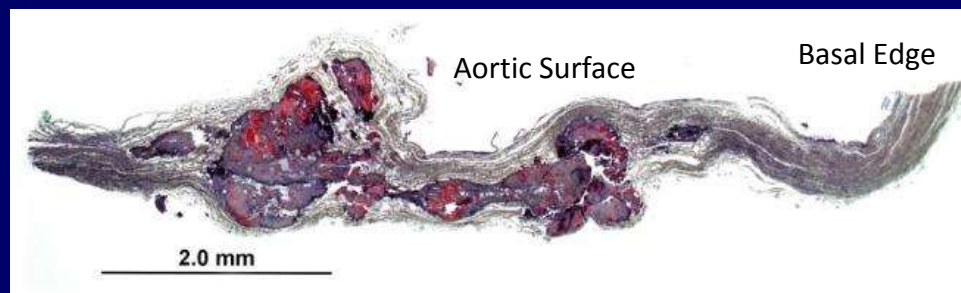
Transcatheter aortic valve failure: Calcification

CoreValve: 5 years

Edwards SAPIEN: 5 years

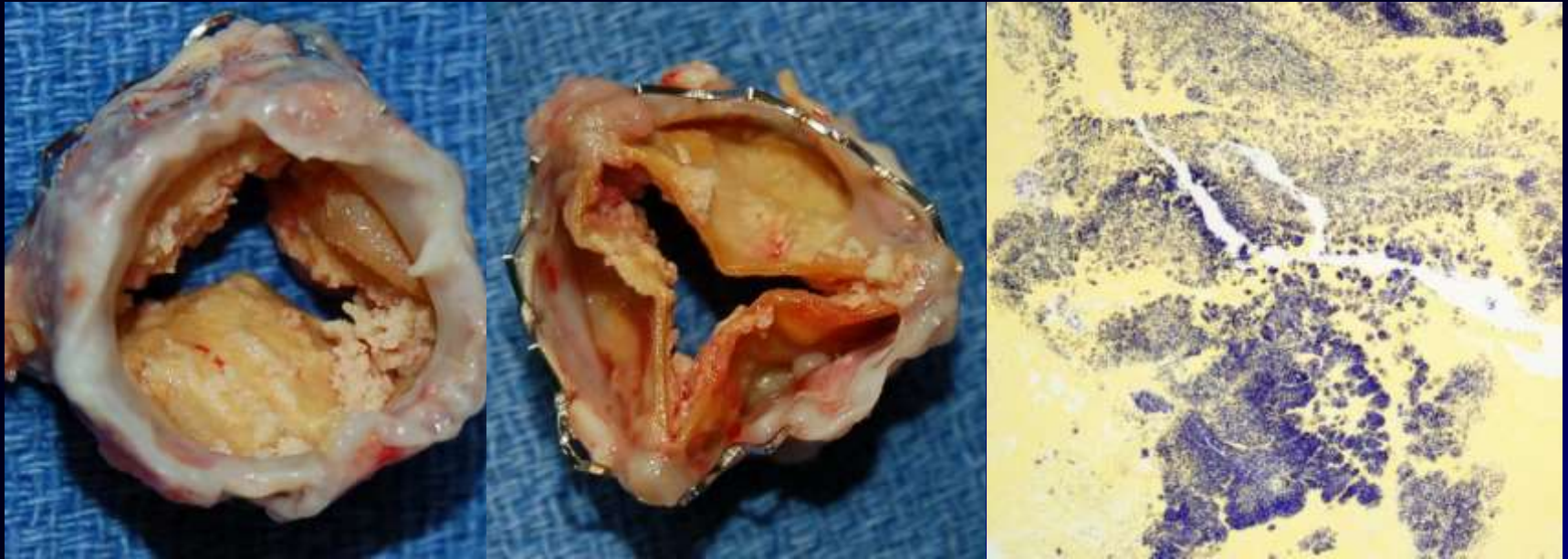


Eur Heart J 2012;33(5):586



	Overall N=66	Cases with Leaflet calcification N=11 (17%)	Cases without Leaflet calcification N=55 (83%)	P value
Age	81 (76-88)	84 (77-89)	81 (74-88)	0.4
Sex (male), %	65%	54%	65%	0.5
Duration, days	252 (67-850)	877 (517-1470)	93 (49-499)	0.0002

Bioprosthetic valve failure: Endocarditis



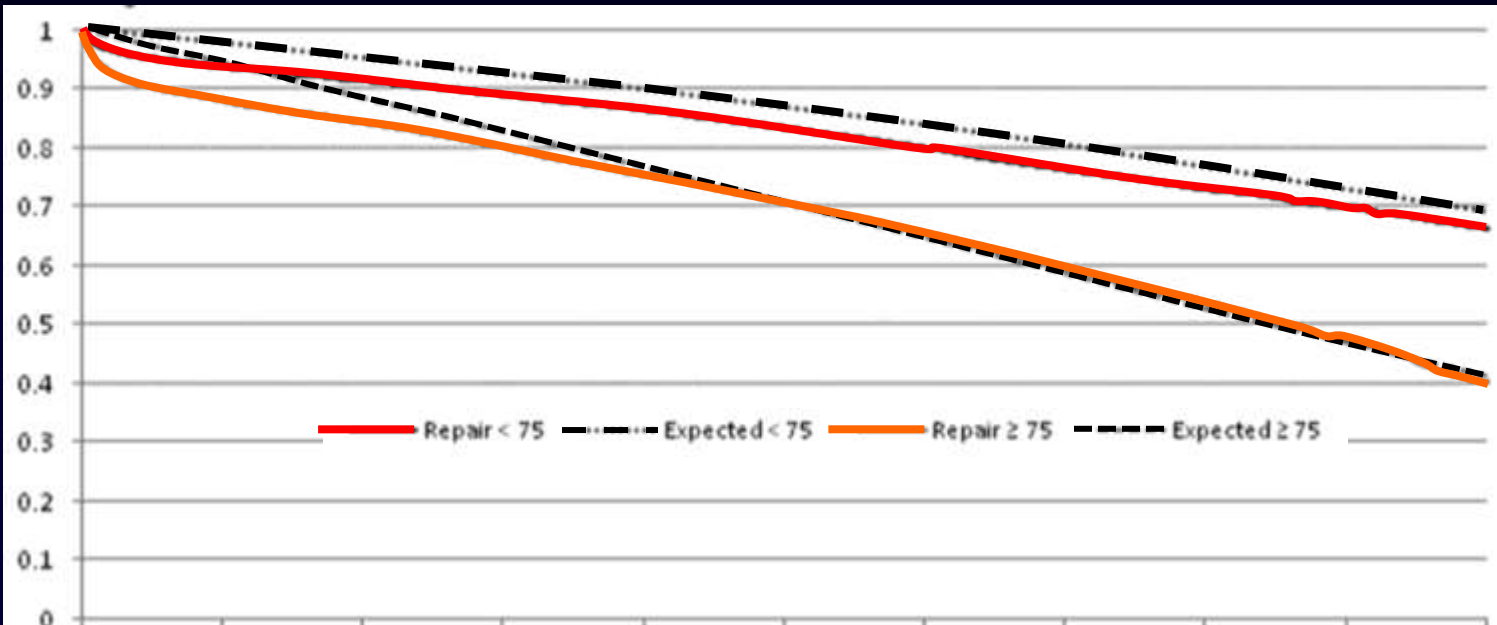
Endocarditis: CVPath Registry

	Cases with Endocarditis N=12 (15%)
Age	80 (74-87)
Sex (male), %	67%
Duration, days	340 (111-962)

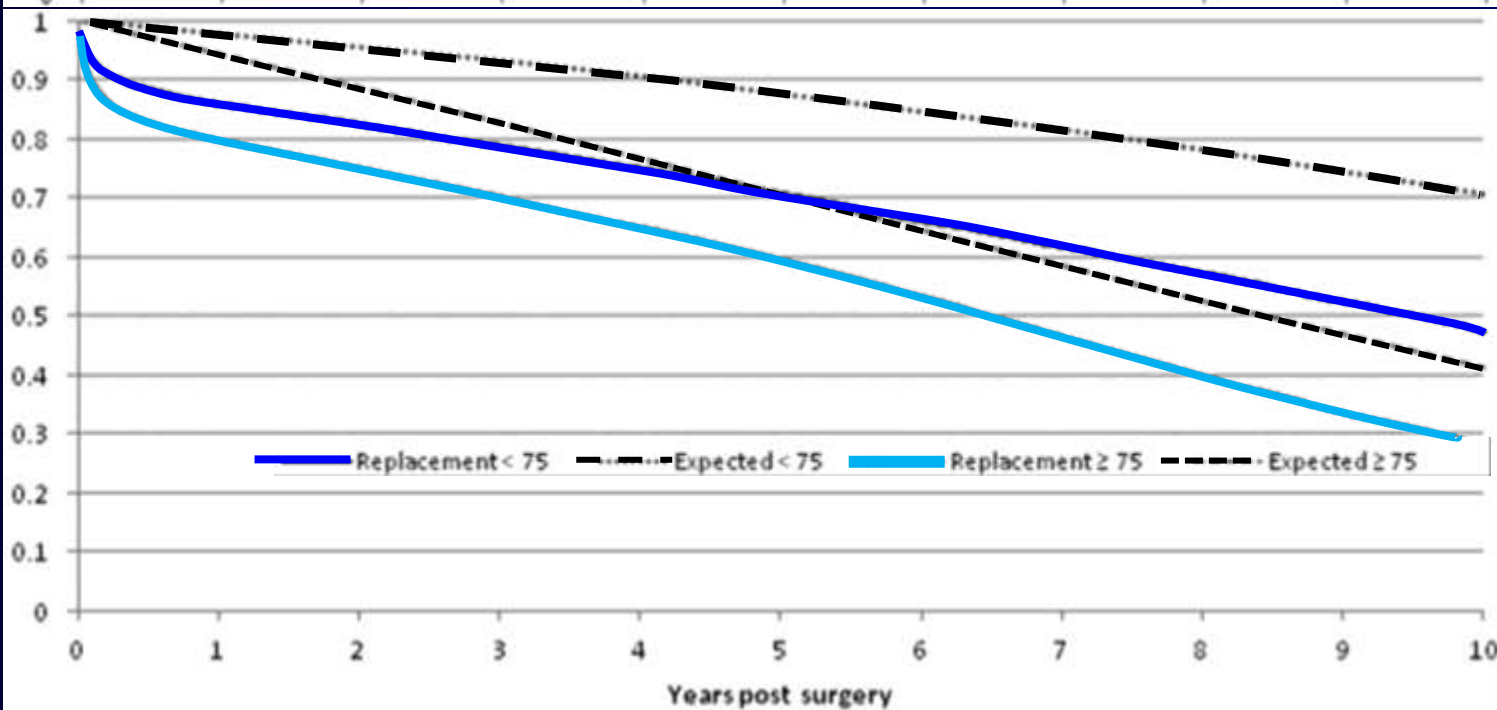
Pathology of mitral devices

Mitral Valve repair vs. Replacement

Cumulative proportion surviving



Survival following
Mitral Valve
Repair by age








Survival following
Mitral Valve
Replacement by
age

*Christina M.
Vassileva et al.
Circulation.
2013;127:1870-1876*







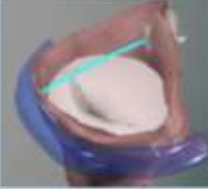
CE-marked Transcatheter Mitral Valve Repair Technologies

Table 1. CE-marked transcatheter mitral repair technologies.

Company	Abbott	NeoChord	Cardiac Dimensions	Valtech Cardio	Mitralign
Name	MitraClip	DS1000	Carillon*	Cardioband	Bident
					
Description	Edge-to-edge technique	Implantation through TA access	Coronary sinus cinching	Transcatheter surgical-like annuloplasty	Plication device
Strengths	Versatility (DMR and FMR)	Solid surgical background	Simplicity	Solid surgical background	Simpler than other direct annuloplasty
Weaknesses	Lack of annuloplasty	TA access	Limited efficacy, unpredictable results	Complexity, advanced imaging	Limited efficacy
MR aetiology	DMR and FMR	DMR	FMR	FMR	FMR
Status	About 40,000 patients worldwide	About 300 patients	About 500 patients	About 100 patients	About 100 patients

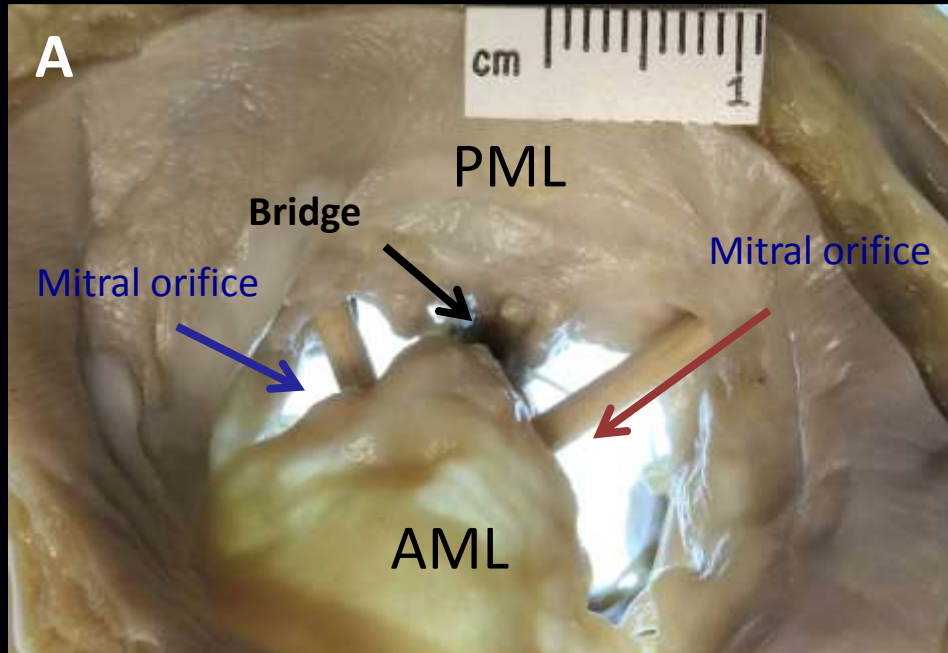
DMR: degenerative mitral regurgitation; FMR: functional mitral regurgitation. * Carillon® Mitral Contour System®; Cardiac Dimensions Inc., Kirkland, WA, USA

Latest Transcatheter Mitral Valve Annuloplasty Devices

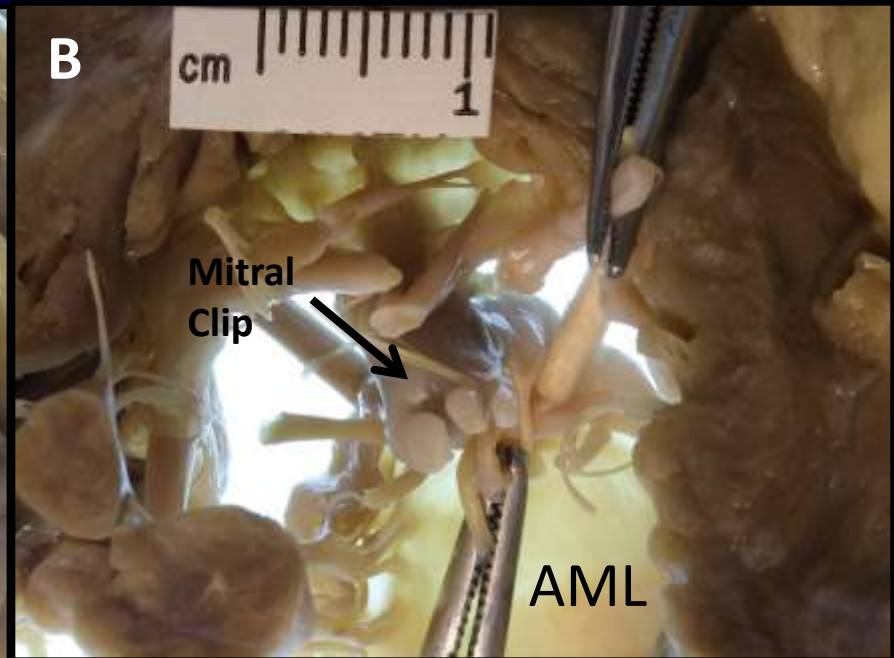
	Indirect annuloplasty	Direct annuloplasty					
Company	Cardiac dimensions, Kirkland, WA	Edwards Lifesciences, Irvine, CA	Mitralign Inc., Tewksbury, MA	Millipede Inc, Santa Rosa, CA	Guided Delivery Systems, Santa Clara, CA	Valcare Medical, Israel	MVRx, Inc., Belmont, CA
Valve Name	Carillon Mitral Countour System	Cardioband	Mitralign	Millipede	Accucinch	AMEND	ARTO
Device Image							
Description	Indirect coronary sinus annuloplasty	Adjustable cinching device	Leaflet plication using pledgets	Complete semi rigid ring	endovascular technique to reduce the sub-mitral LV dimensions	Complete D-shaped semi rigid ring	Direct A-P Diameter Shortening
Access	Transjugular	TF/transseptal	TF/transaortic	TF/transseptal	TF/transaortic	TA	Endovascular venous delivery

Mitral Clip implanted for Functional MR

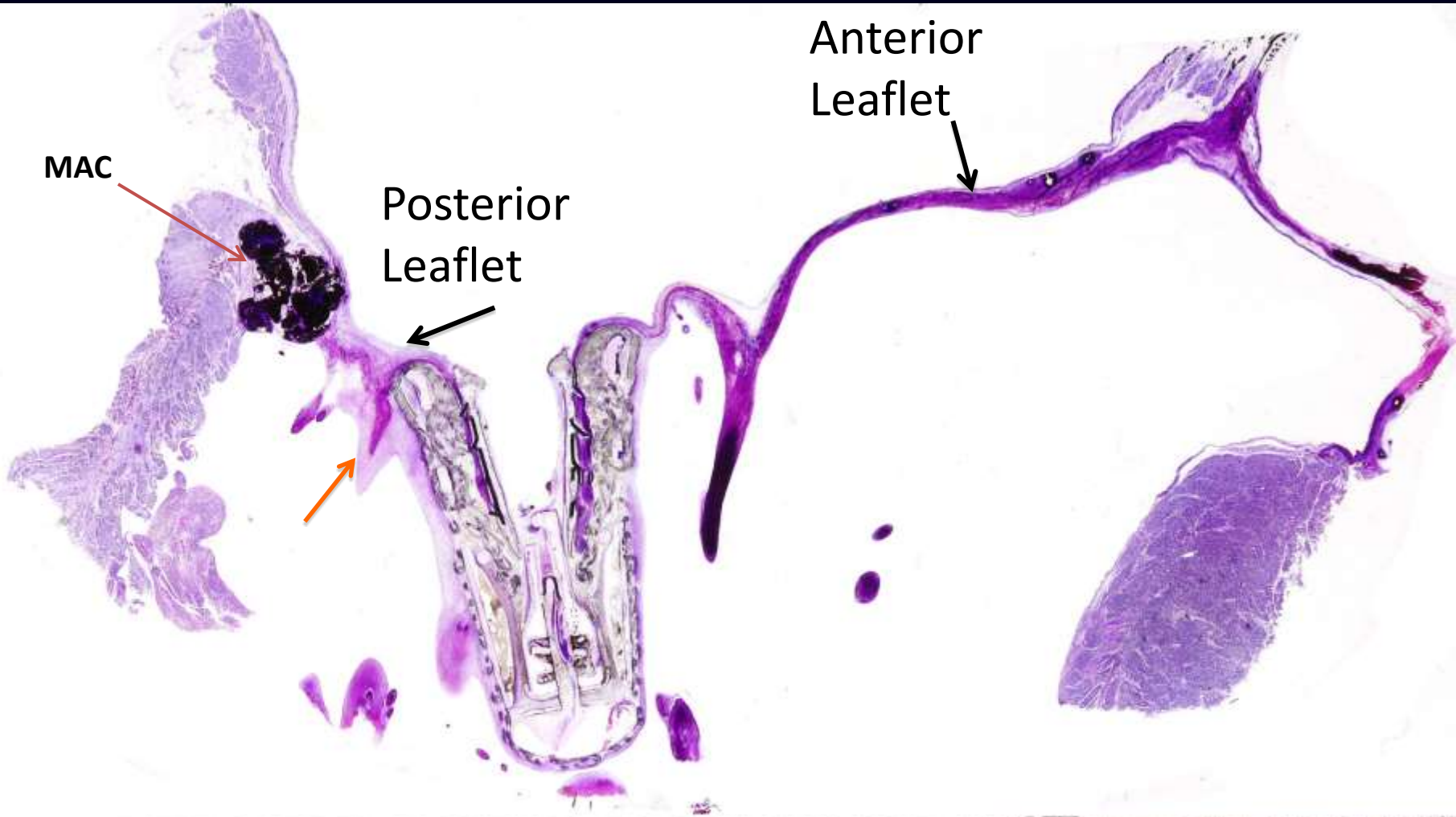
Atrial View



Ventricular view



Implant duration 356 days



MAC

Posterior
Leaflet

Anterior
Leaflet

cm





1

2

3

4

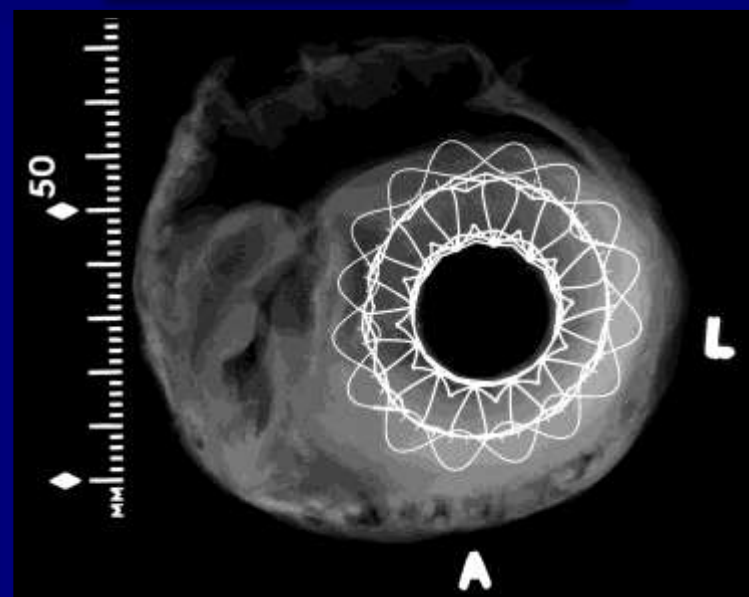
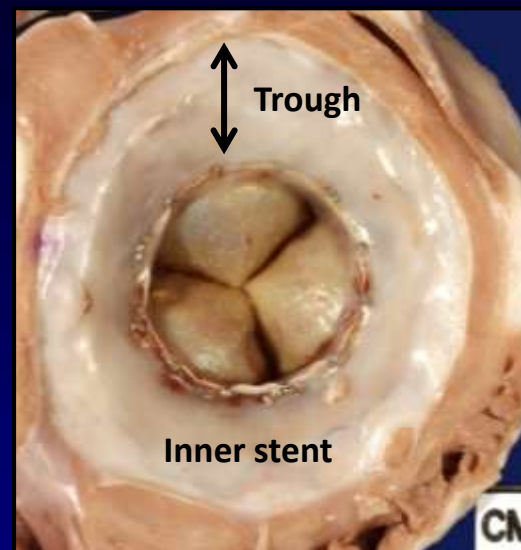
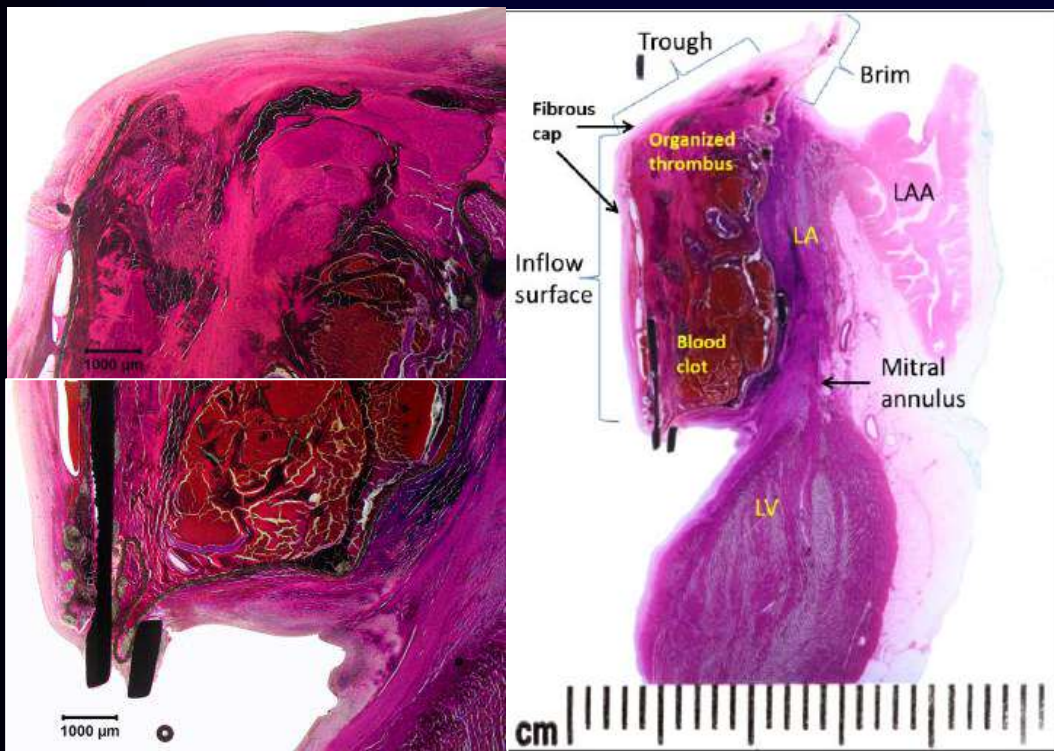
Transcatheter mitral valve replacement technologies: early clinical experiences.

Company	Abbott	Edwards	Medtronic	Neovasc
Name	Tendyne	CardiAQ	Intrepid	Tiara
				
Patients treated	31	12	15	15
First implant	October 2014	June 2012	September 2014	January 2014
Functional aetiology	86%	64%	73%	54%
Successful deployment	21/23 (91%)	9/11 (82%)	14/15 (93%)	9/11 (82%)
30-day mortality	1/23 (4%)	5/11 (45%)	2/15 (13%)	3/11 (27%)
MR grade 0 at follow-up	19/19 (100%)	na	13/14 (93%)	na
MR: mitral regurgitation; na: not available (adapted from Meredith I. Transcatheter Mitral Valve Replacement: Early Clinical Outcomes. EuroPCR 2016).				

Several TMVR devices are currently under clinical evaluation and the early experience has demonstrated the feasibility of TMVR

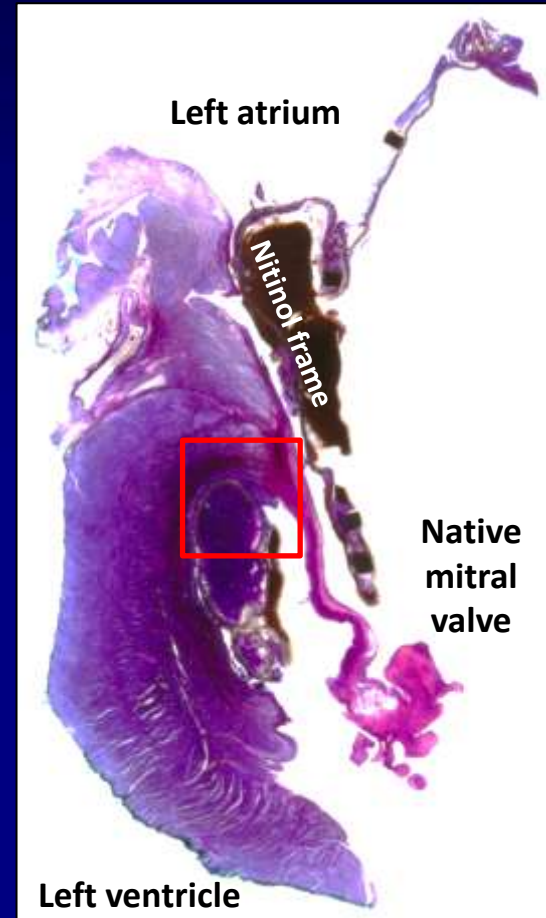
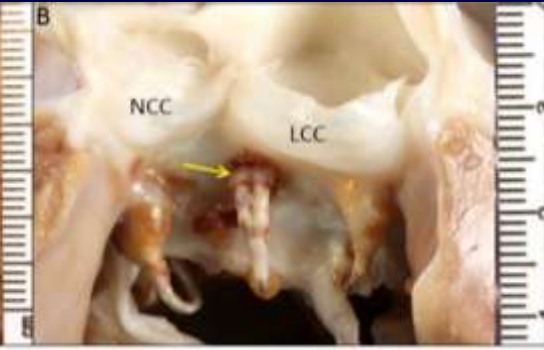
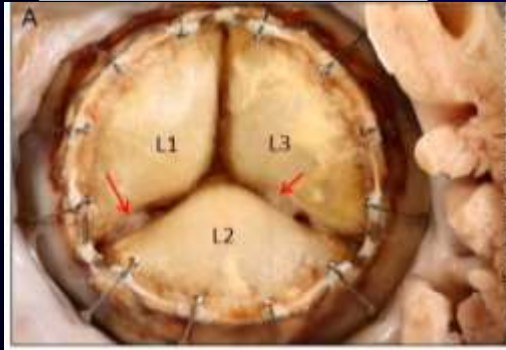
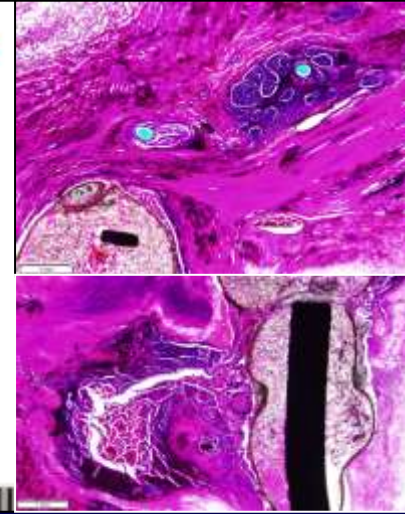
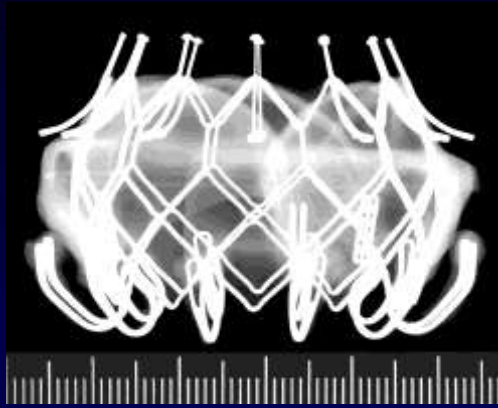
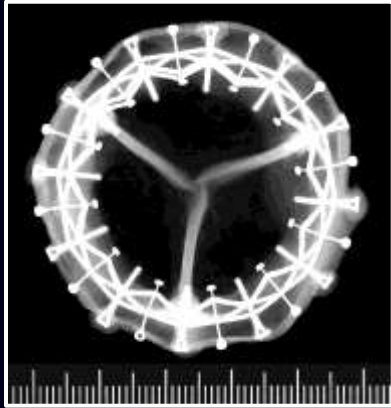
Intrepid TMVR: Medtronic

APOLLO Trial - pivotal trial designed to evaluate the Intrepid(TM) TMVR system



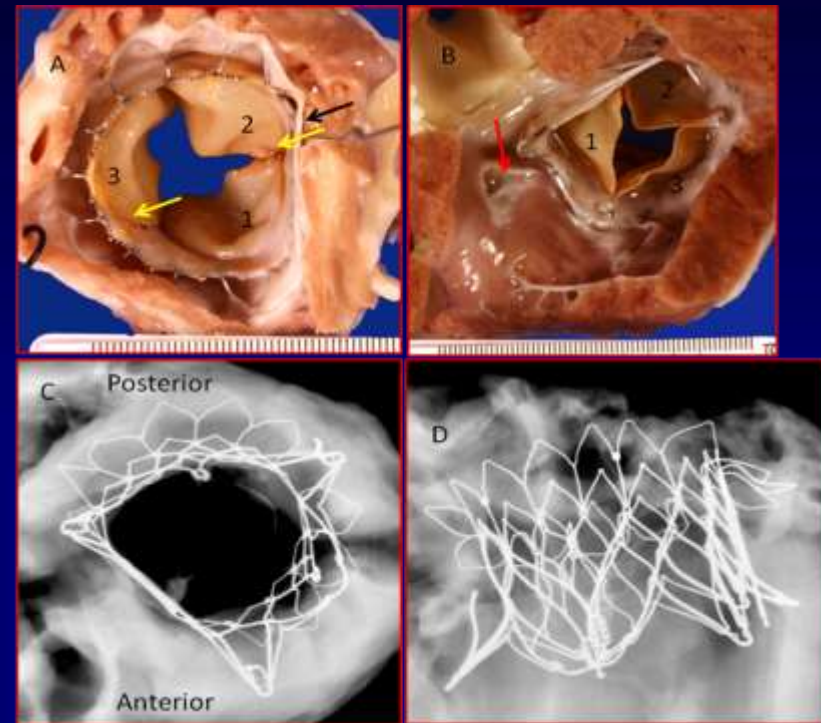
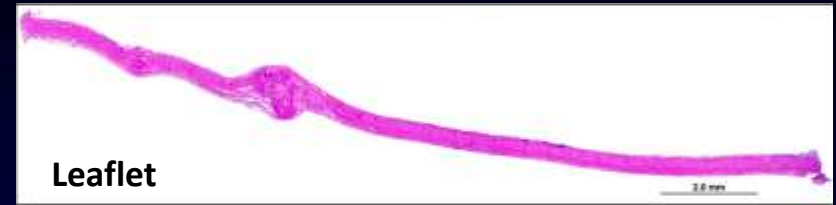
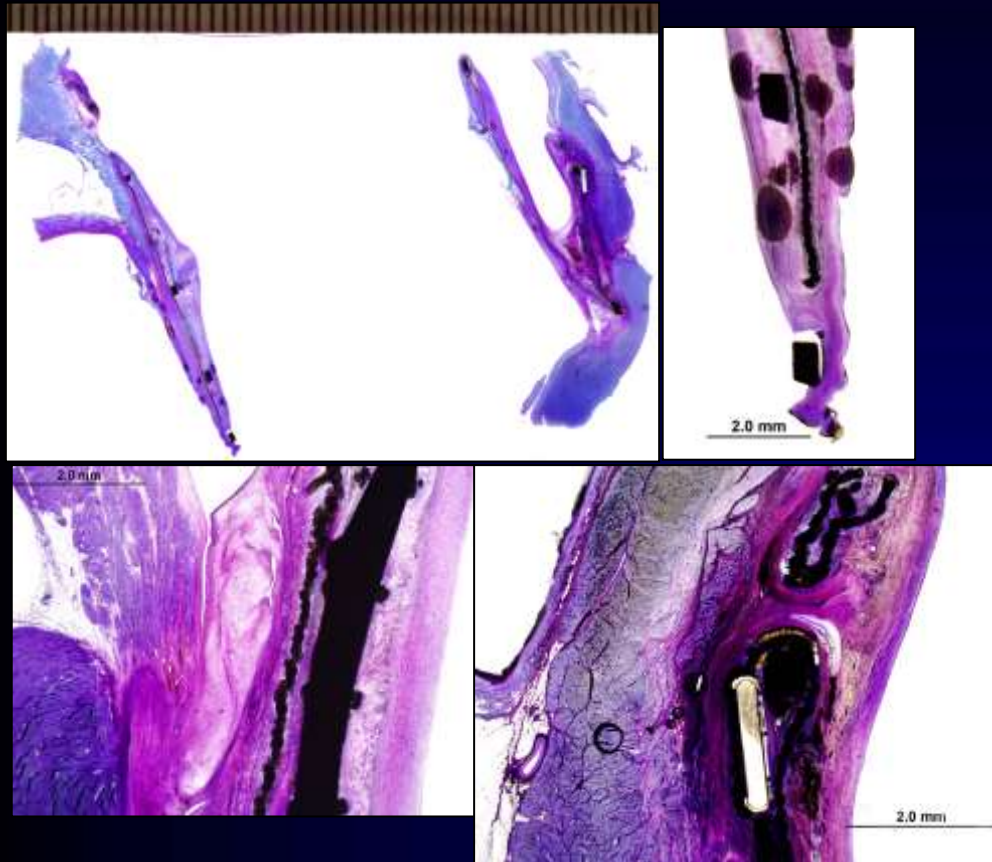
- Intra-annular, trileaflet bovine pericardial valve contained in a self-expanding nitinol frame.
- The inner stent houses the valve and the outer fixation ring accommodates the variability of the Mitral valve.
- Notice the trough completely covered by organized neoendocardial tissue.

CardiAQ (Edwards)



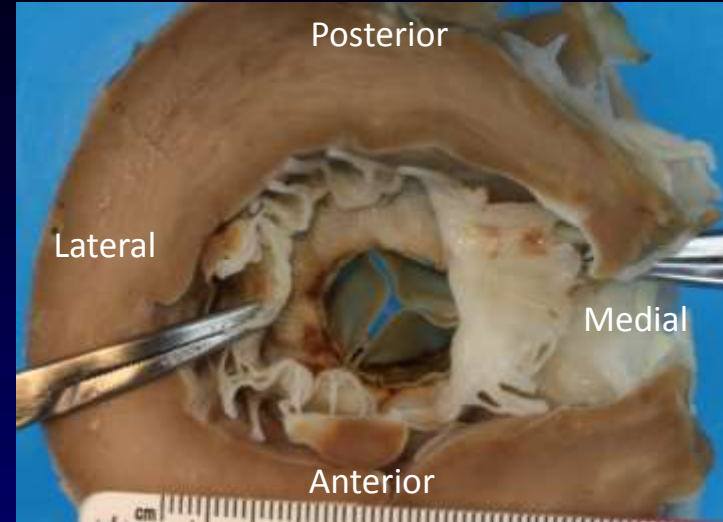
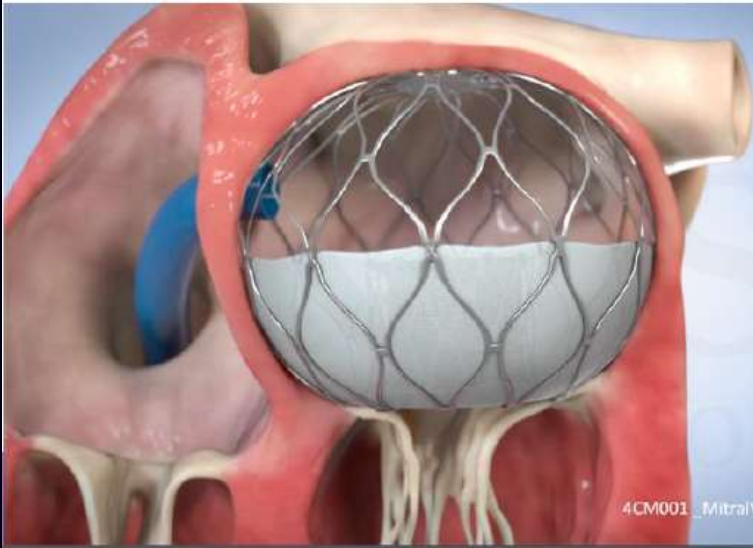
- Self-expanding supra-annular trialeaflet valve composed of bovine pericardial tissue.
- The nitinol frame has 2 sets of opposing anchors which secure the device to the mitral apparatus.
- The ventricular anchors rest behind the mitral leaflets and subvalvular apparatus preserving the chords and using native leaflets as support.
- Currently, Cardi-Q is undergoing design evaluation so we can expect to see this device soon in a clinical trial .

Tiara CE marked

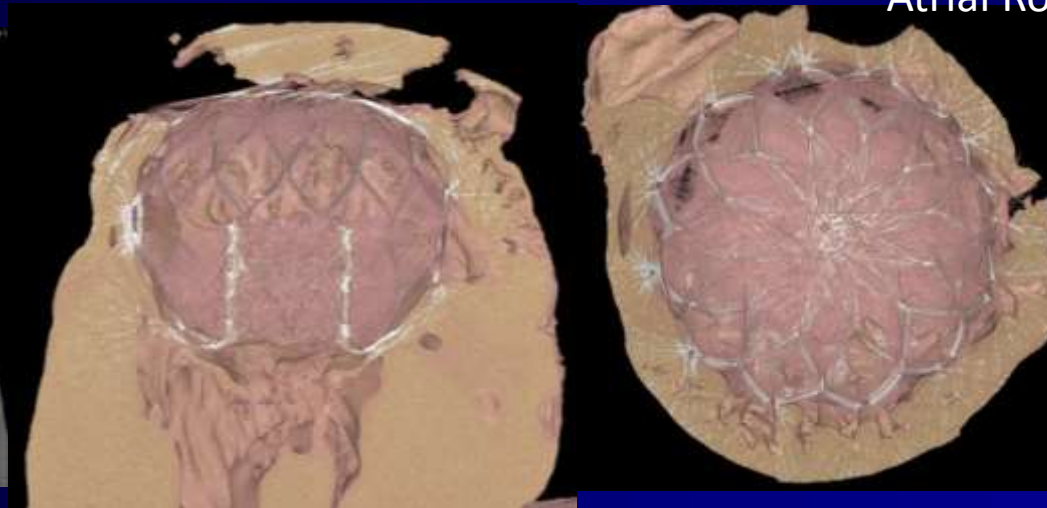
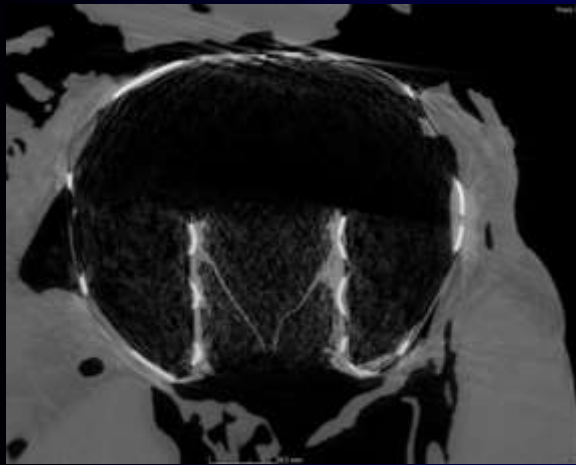


- Neovasc Tiara TMVR it is the only valve with a D-shape design.
- It is a self-expanding trialeaflet valve made of bovine pericardium and a nitinol frame.

4C Medical



MicroCT



Atrial Roof



- The first transcatheter MR treatment that preserves the native mitral valve and left ventricle using a supra-annular, atrial-only fixation technology.
- The device is placed and anchored entirely in the left atrium.

Summary

TAVR

- ✓ Pathological severe thrombosis, that may cause reduced leaflet motion; was seen in 12% in CVPath TAVR registry.
- ✓ Oral anticoagulation therapy, but not DAPT, is effective in prevention or treatment of subclinical leaflet thrombosis.
- ✓ Structural changes of the leaflet are likely the main causation of late (>5 year) bioprosthetic valve failure.

Mitral devices

- ✓ Transcatheter valve repair in patients with high operative surgical risk are an extremely relevant clinical group for percutaneous repair than replacement.
- ✓ It is likely that combinations of percutaneous repair or valve replacement will be needed to achieve optimal results.
- ✓ Percutaneous repair may be the preferred alternative.

Acknowledgments

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Jinky Beyer

Lila Adams, HT

Frank D Kolodgie, PhD

Aloke V Finn, MD



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