

Valvular Heart Disease and TAVR

Grand Rounds, Cedar Sinai

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Renu Virmani, MD
CVPath Institute Inc.
Gaithersburg, MD

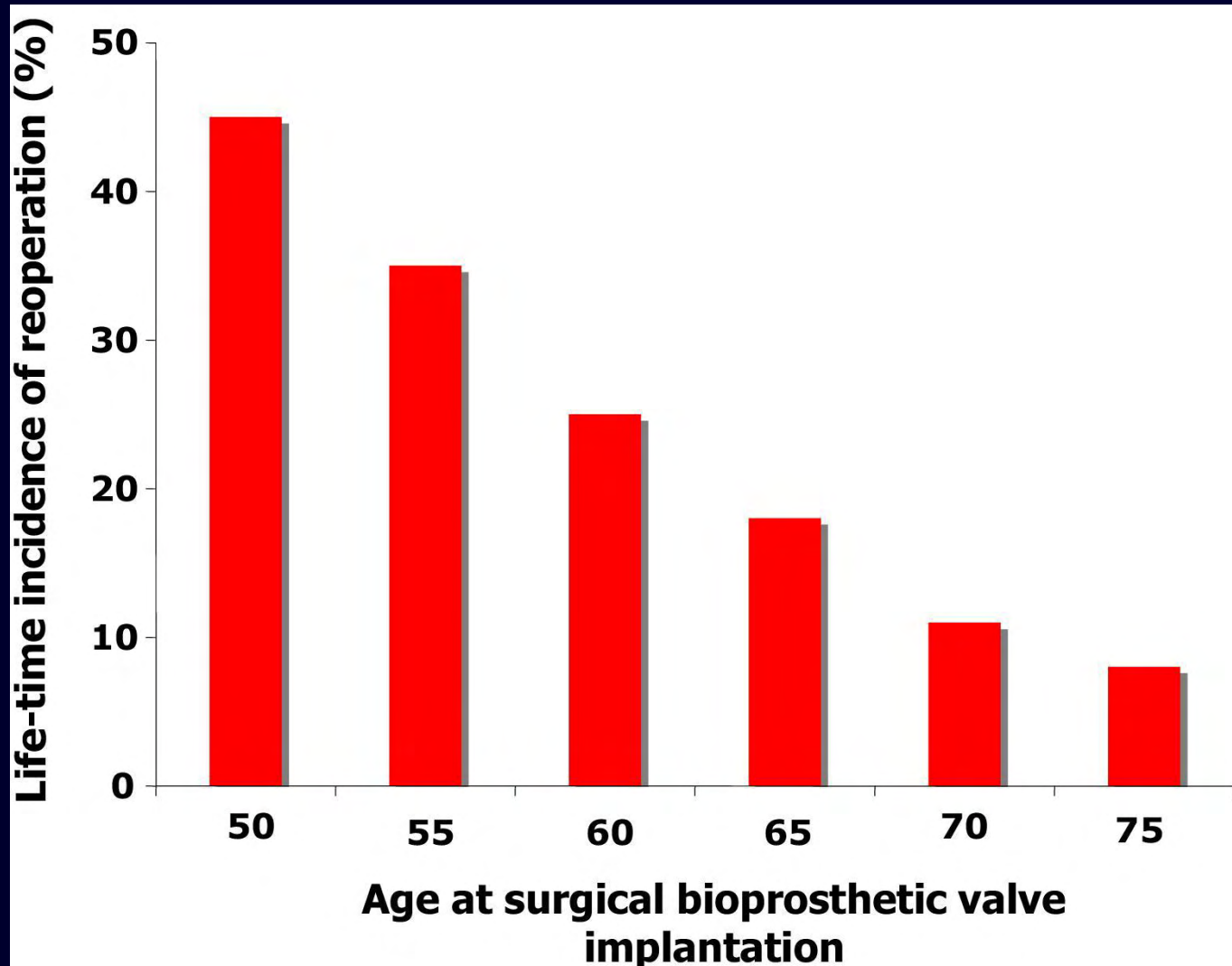
Background TAVR

- First aortic valve replacement 1960 (Harken DE et al J. Thorac. Cardiovasc surg 1960; 40 744)
- Balloon aortic valvuloplasty (BAV) was first developed by Alain Cribier over 30 years ago for the management of aortic stenosis. (Lancet 1986; 1:63–67.)
- 1992 first balloon expandable stent valve implanted in pig (Andersen HR et al. Eur Heart J. 1992;13:704)
- 2002 first human stented valve implant in a 57-year-old man with calcific AS (Cribier A et al. Circ. 2002;106:3006)

General Mode of Failure

- Mechanism of Surgically Implanted Bioprosthetic Heart Valves failure is slow, gradual and progressive, as well as time dependent
- Currently <1% of porcine aortic valves implanted <5 years in adults suffer structural dysfunction
- 20 to 30% become dysfunctional within 10 years
- >50% fail due to tissue degeneration within 12 to 15 years post implantation

Life-time Risk of Reoperation as a Function of Age at Surgical Aortic Valve Replacement



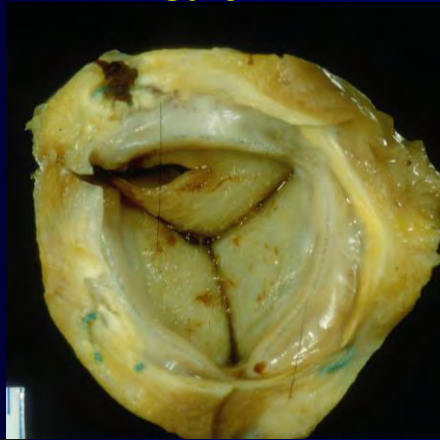
Surgically Implanted Bioprosthetic Valve: Summary

Disadvantages: Limited durability beyond 10 years in younger patients: Cusp degeneration (tears) leading to regurgitation or Ca^{++} leading to stenosis
Pannus formation common to mechanical and bioprosthetic valves in latter can extend into the leaflet and lead to regurgitation and rarely stenosis
Endocarditis, although rare seen mostly in drug abusers

Normal



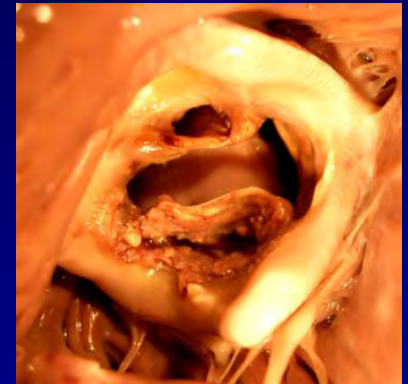
Tears



Calcification



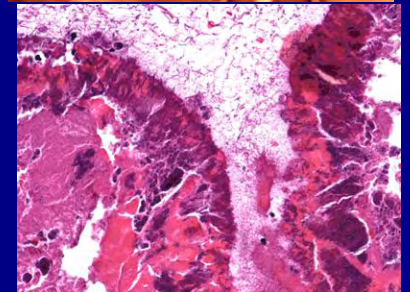
Infective endocarditis



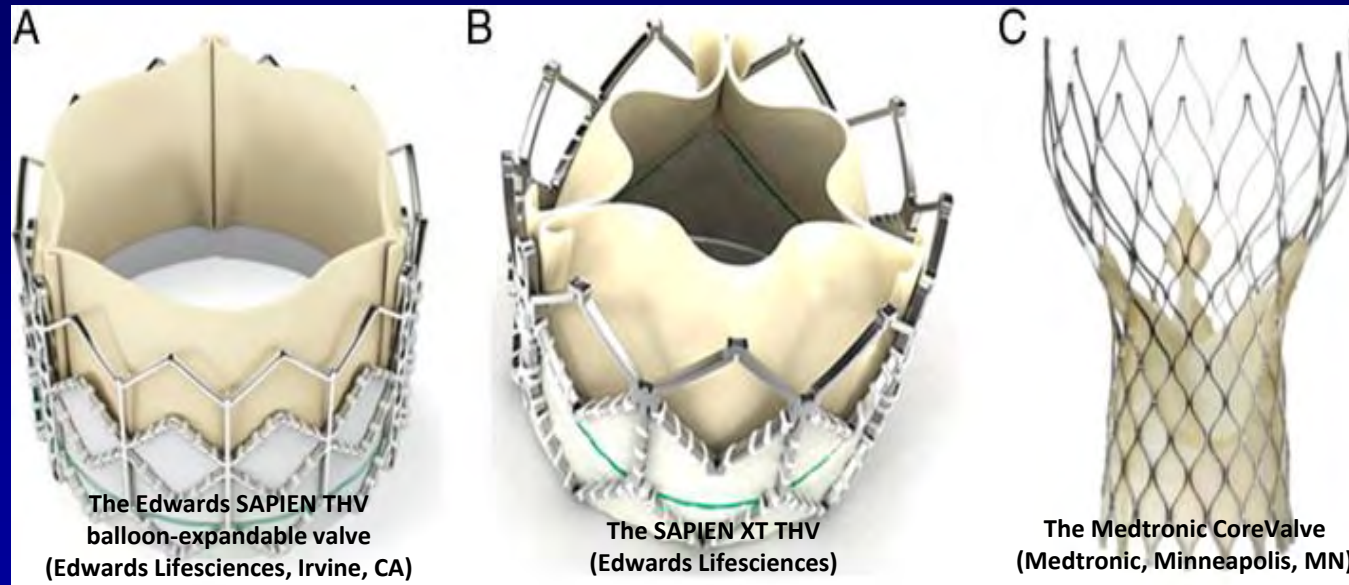
Pannus



Thrombus



Current Widely Available Transcatheter Valves

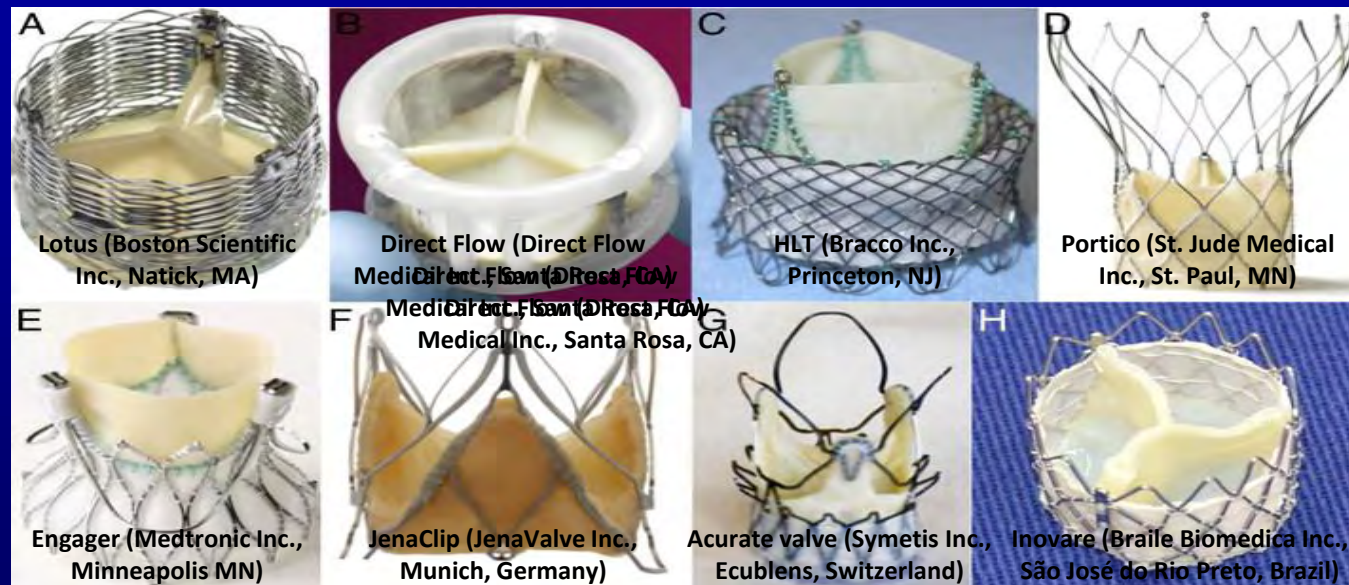


A. Stainless steel frame, bovine pericardial leaflets, and a fabric sealing cuff.

B. Cobalt chromium alloy frame, compatible with lower profile delivery catheters.

C. Self-expandable frame, porcine pericardial leaflets, and a pericardial seal.

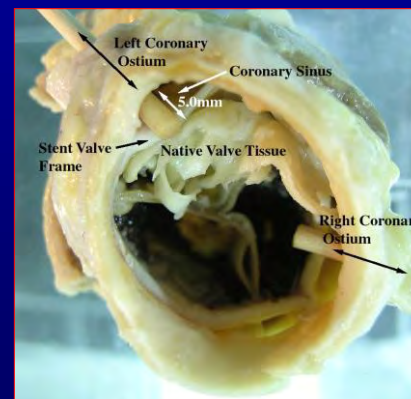
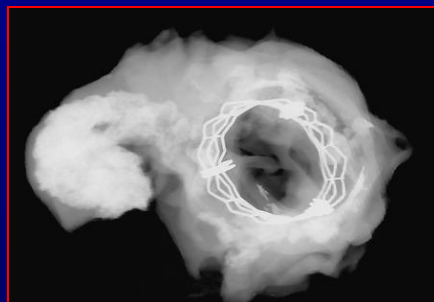
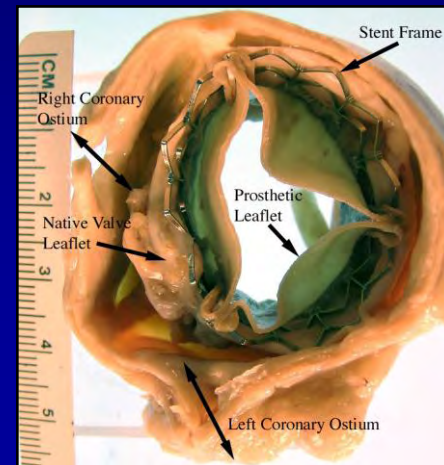
Valves Undergoing Early Evaluation



Cribier Edwards valves retrieved for histopathologic analysis

Case #	Patient Age/Sex	Valve generation	Implant duration	Autopsy –cause of death (COD)
1	87F	LC5649	1 day	COD - unknown
2	82M	LA2022	3 days	Paravalvular leak
3	unknown	PHV 23	> 2months	COD –unrelated
4	unknown	PHV 23	acute	Evulsion of native cusp
5	87M	PHV 23	5 days	COD – multiorgan failure
6	70M	PHV 26	2 days	COD- multiorgan failure

Paravalvular leak



Evulsion of native cusp obstructing LCO

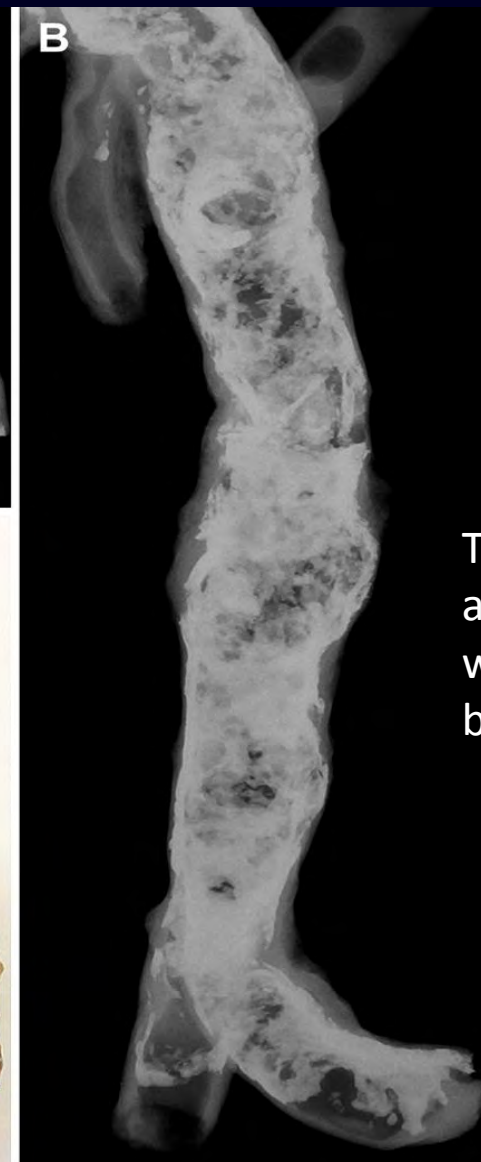
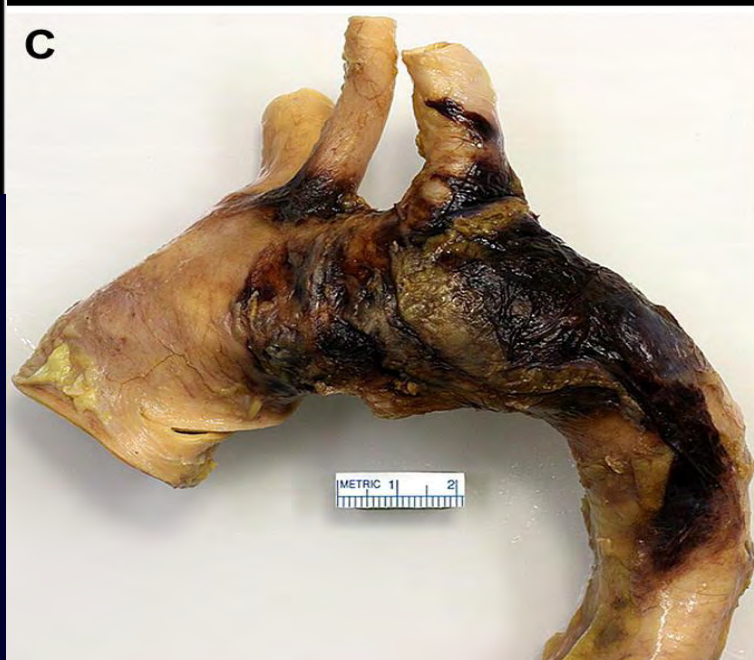
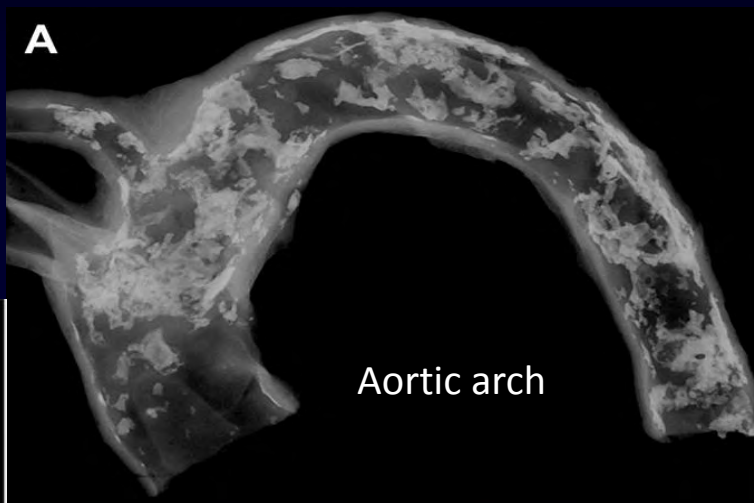
Edwards Sapien Valves retrieved for pathologic analysis

Mean age=84.5 years
M=9, F=8
Range: 1-1487 days
Mean duration= 207 days
< 30 days=10
31-90 days=4
>90 days=3

Case #	Patient Age/Sex	Implant duration (days)	Cause of death (COD)
1	87F	5	<u>Unknown</u>
2	85F	5	Perforation of apex
3	79F	23	Retroperitoneal hemorrhage
4	84M	1	Perforation of apex,
5	89M	44	Paravalvular leak, pneumonia
6	85M	27	<u>Unknown</u>
7	85M	10	Pneumonia
8	81M	1487 (4 y)	CHF
9	91M	1102 (3Y)	Aortic dissection
10	76M	586	Surgical: endocarditis (<i>Strep bovis</i>)
11	85M	20	Paravalvular leak
12	82F	7	Renal failure, ARDS
13	81F	6	Valve normal, COD unknown
14	83F	60	Endocarditis; <i>Aspergillus</i>
15	93M	30	CHF
16	88F	45	Cerebral bleed, thrombi AV
17	83M	65	Endocarditis; bacterial (gram+,

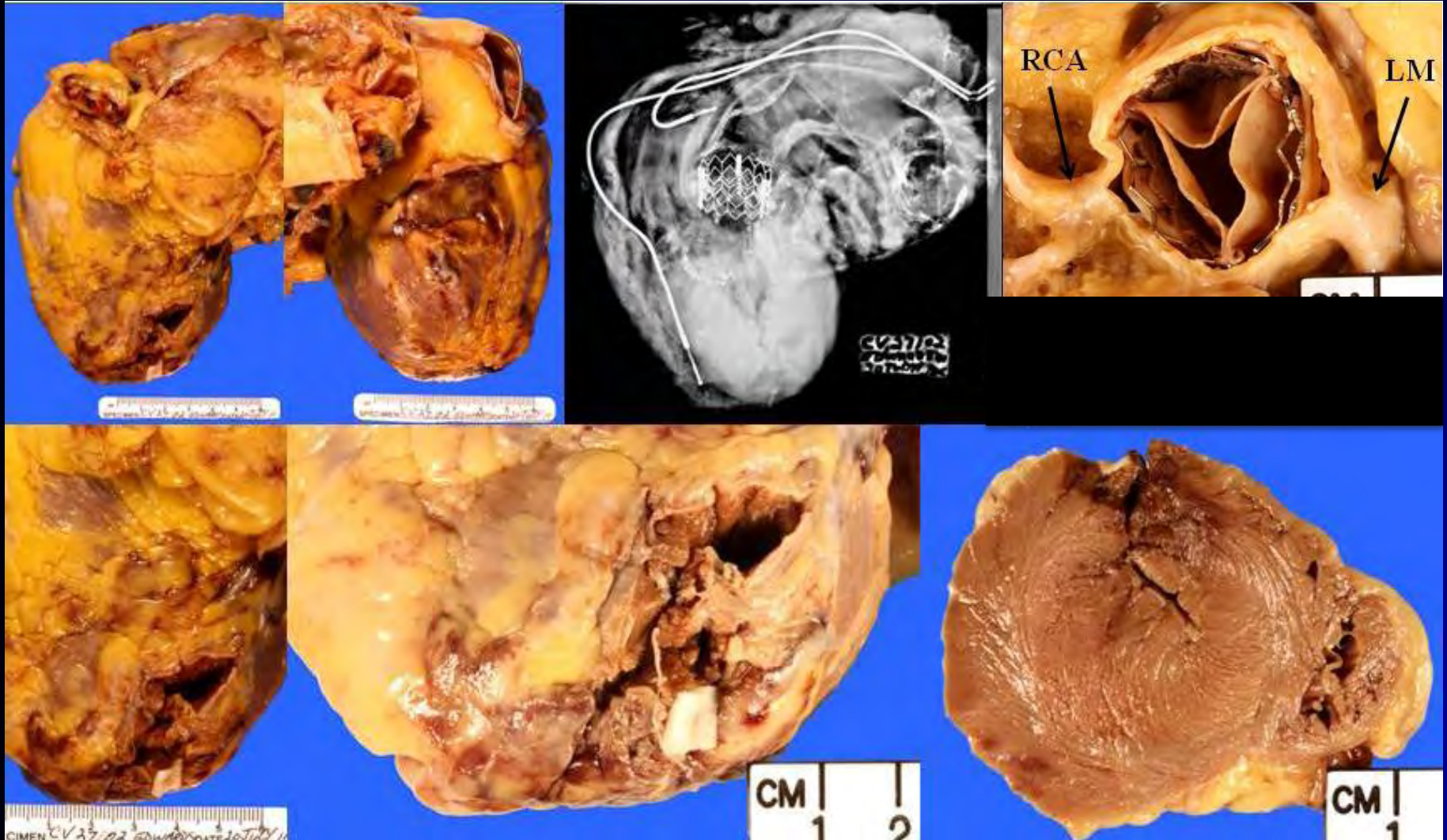
86 years old male, with severe AS (gradient 65 mm Hg, valve area 0.77 cm²) died 3 hours post Edward Sapien Valve placement.

Porcelain Aorta

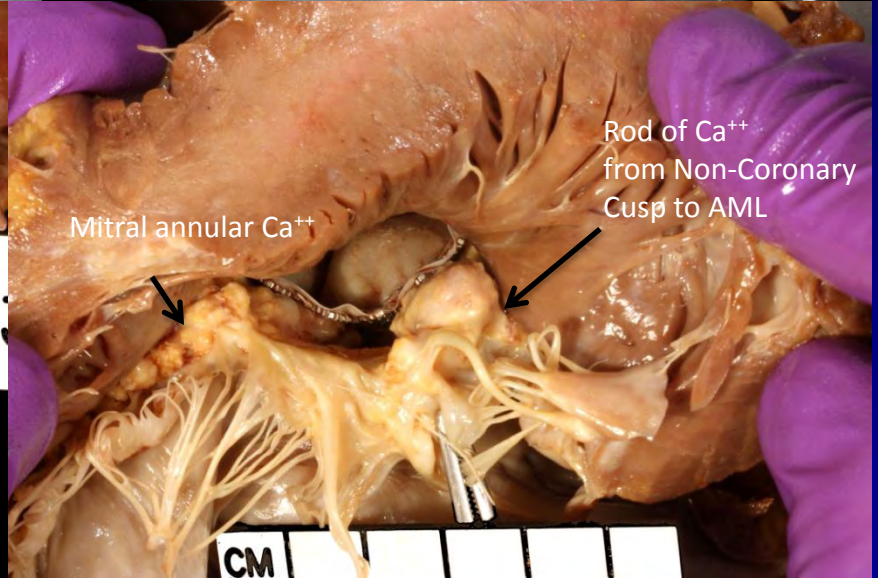
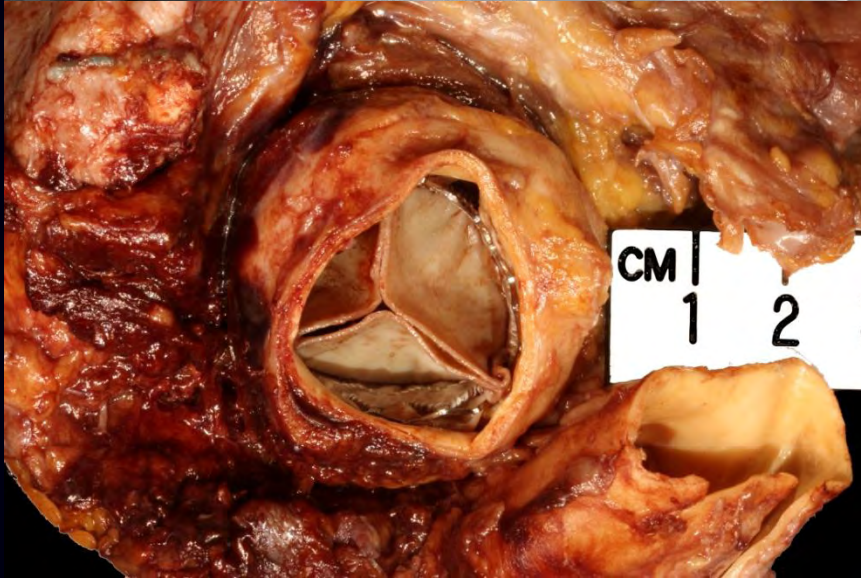
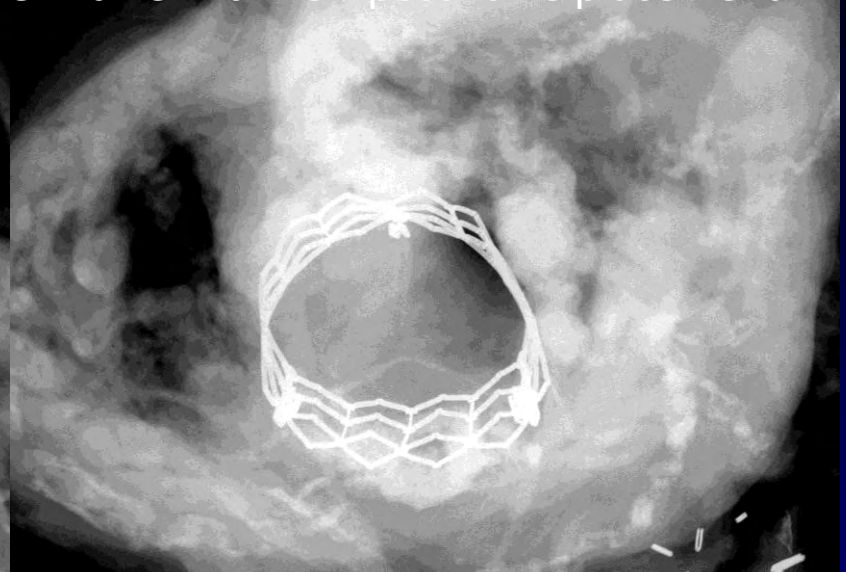
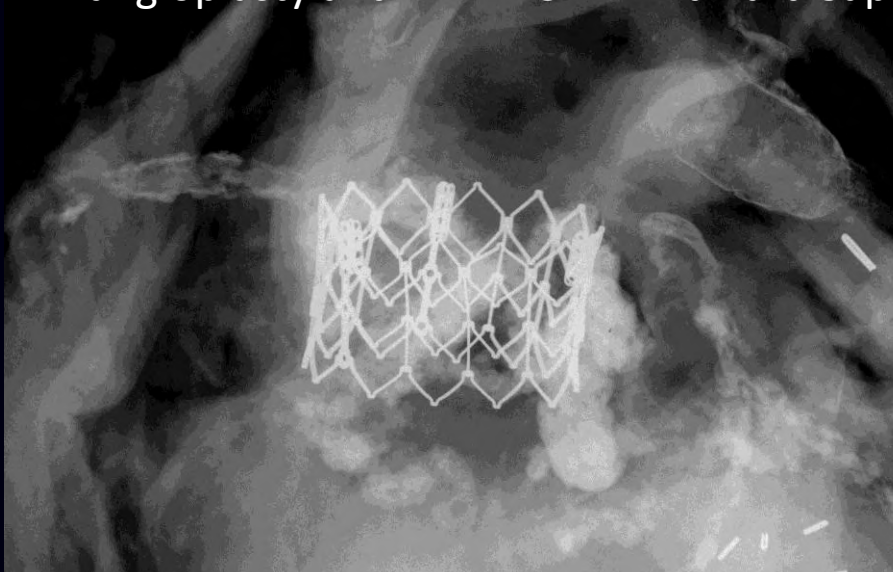


Thoracic and abdominal aorta with iliac bifurcation

84 year old male, with severe aortic valve stenosis and severe pulmonary fibrosis on chronic steroids and oxygen dependence

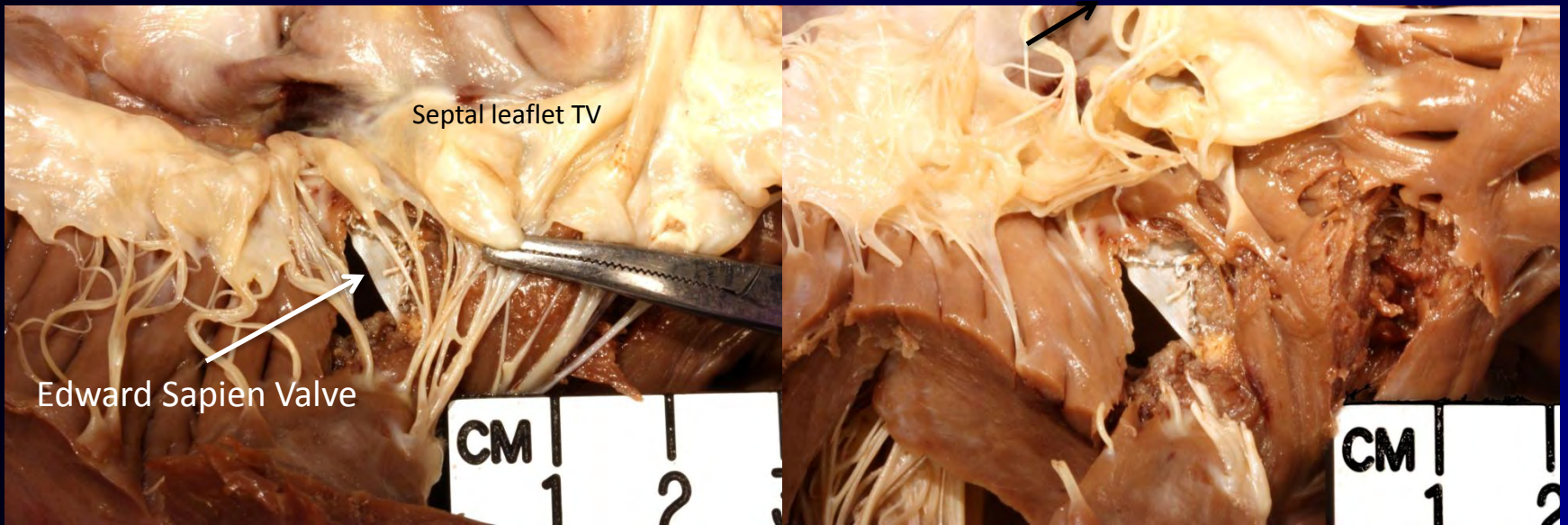


91-year old M, Hx of CAD with CABG and PCI, PAD, COPD, AS with previous balloon angioplasty and TAVR 29 mm Edward Sapien valve with VSD post valve placement



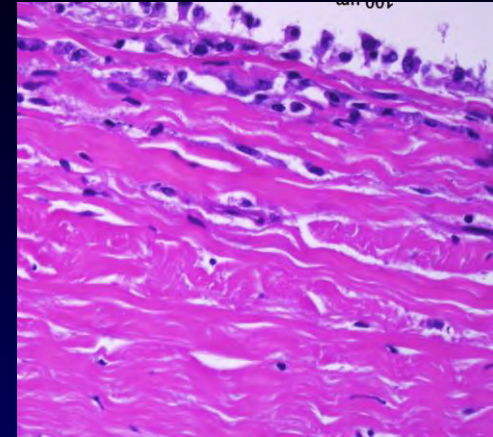
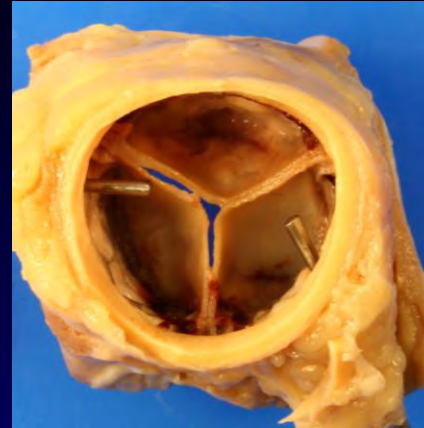
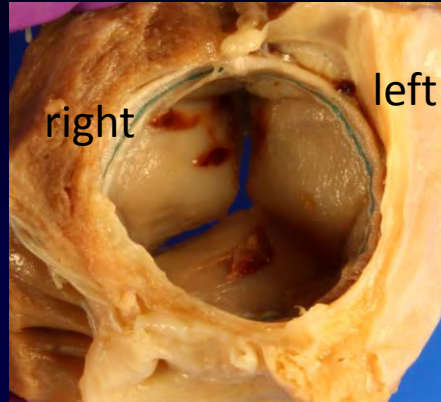
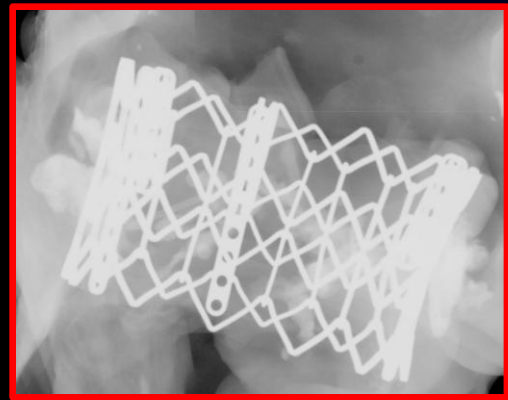
RA

Ventricular Septal Defect, Post TAVR Procedure

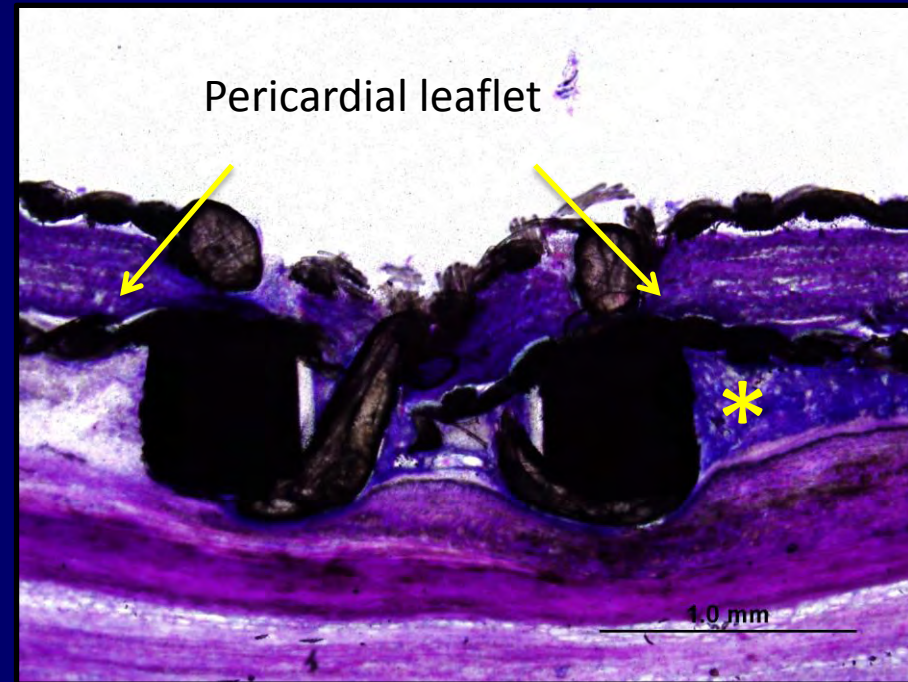
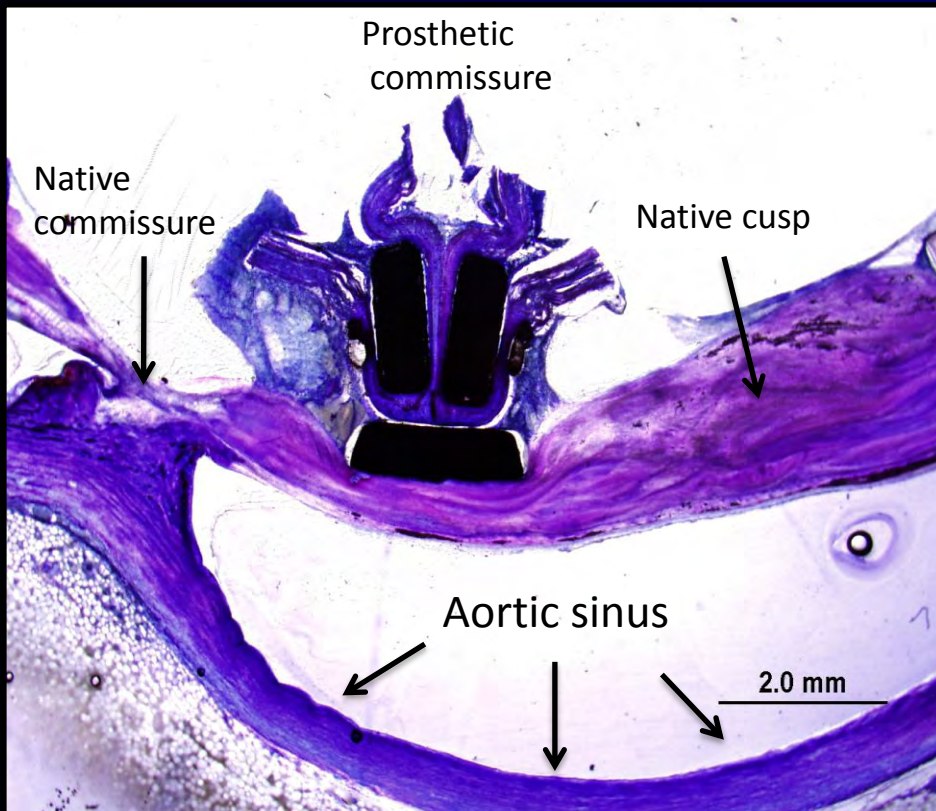


6 days post Edwards Sapien implantation (81F)

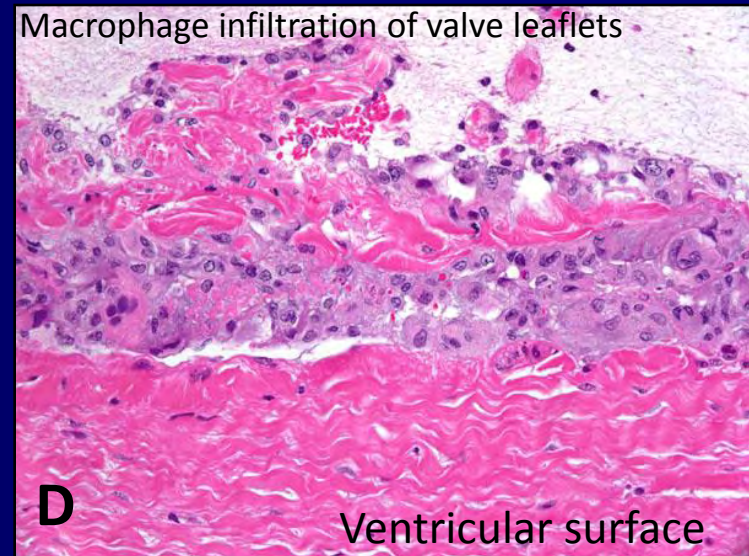
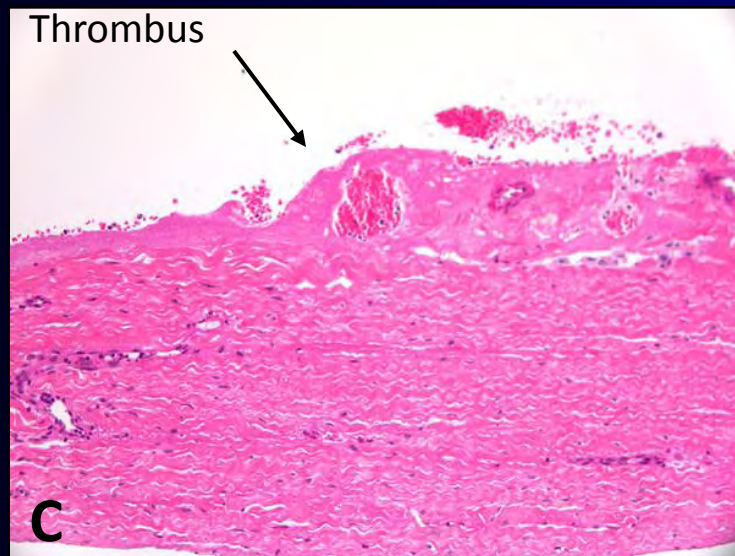
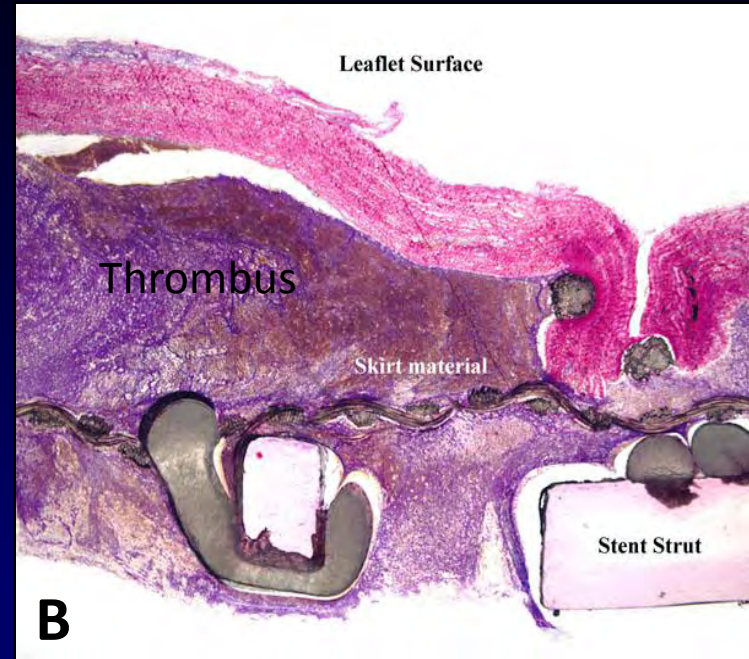
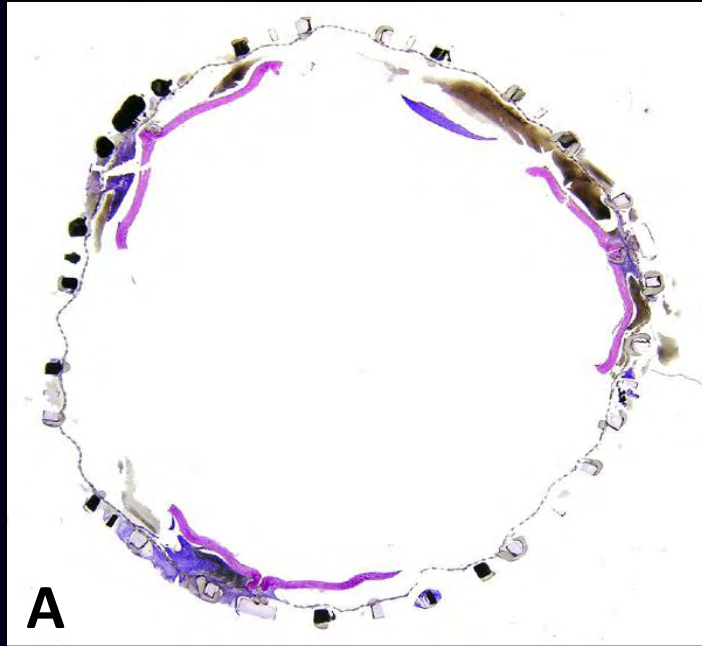
Aortic surface



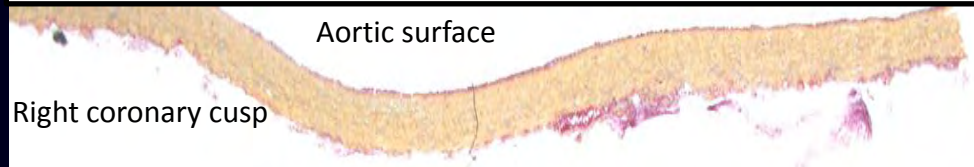
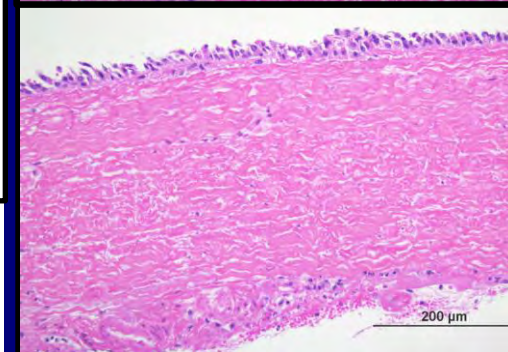
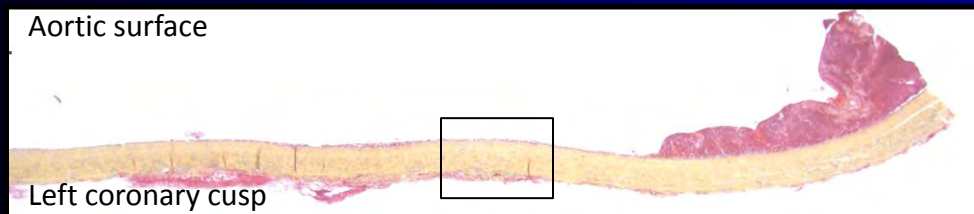
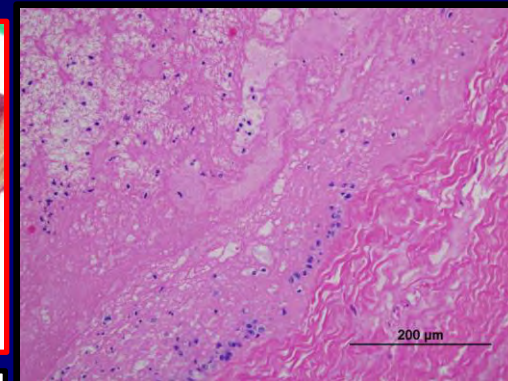
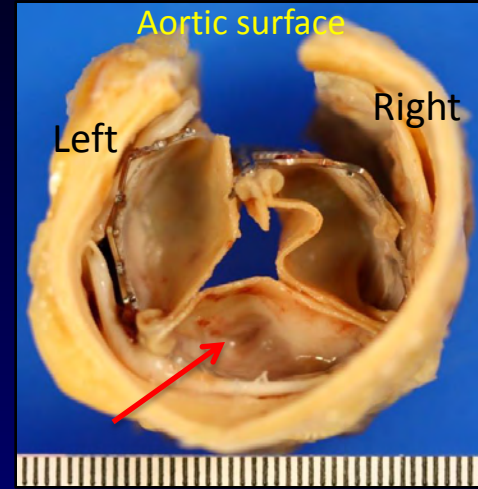
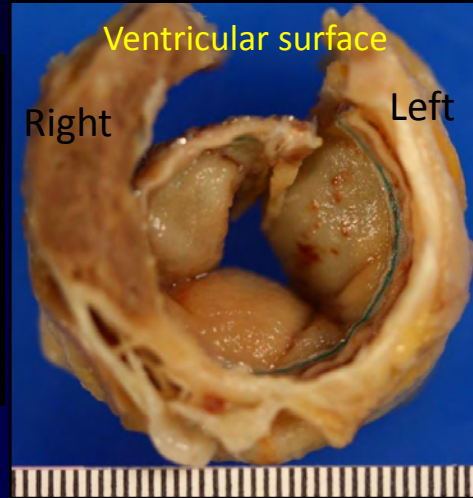
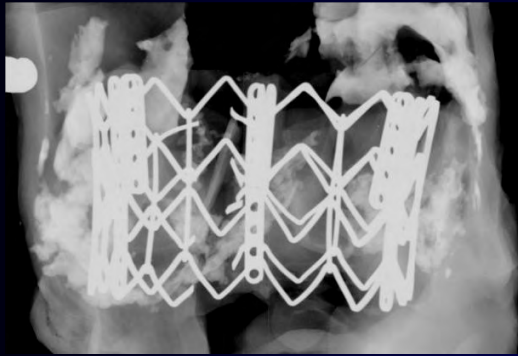
Aortic wall



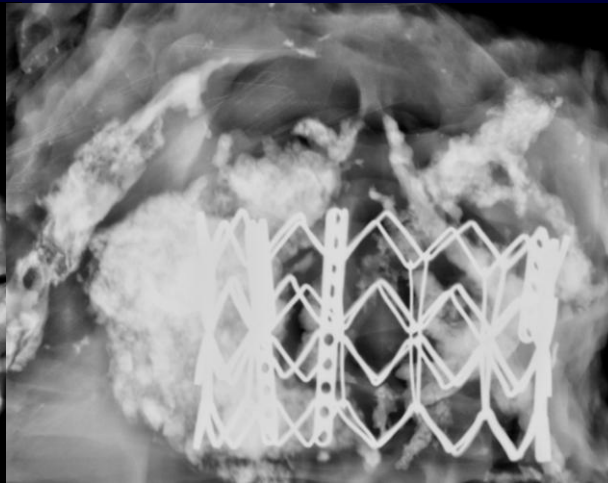
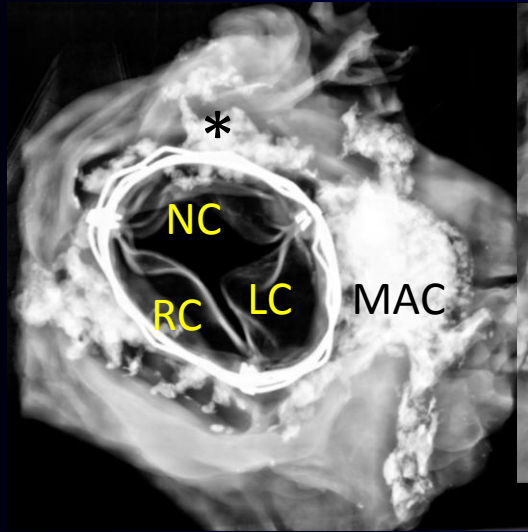
9 days post Edward SAPIEN valve implantation in a 85 years old male



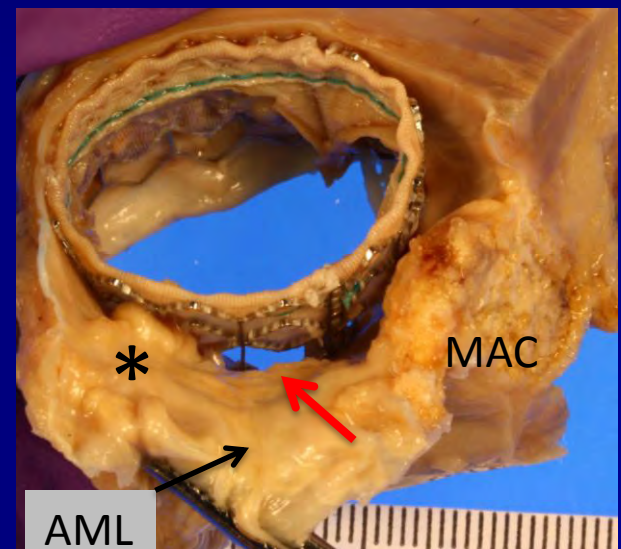
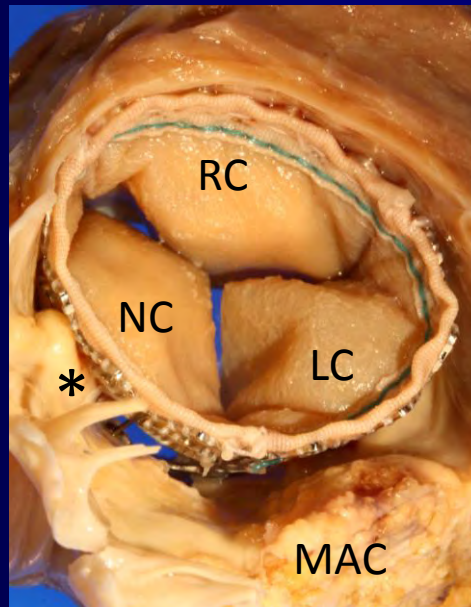
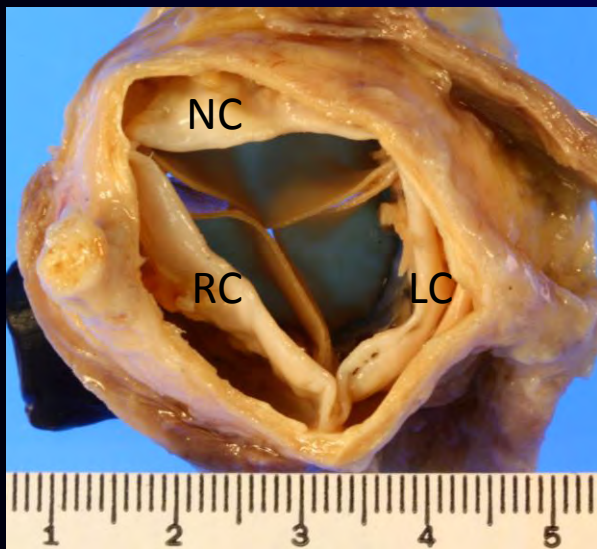
1.5 months post implantation Edwards Sapien valve (88 F)/ fell out of bed, cerebral bleed at autopsy



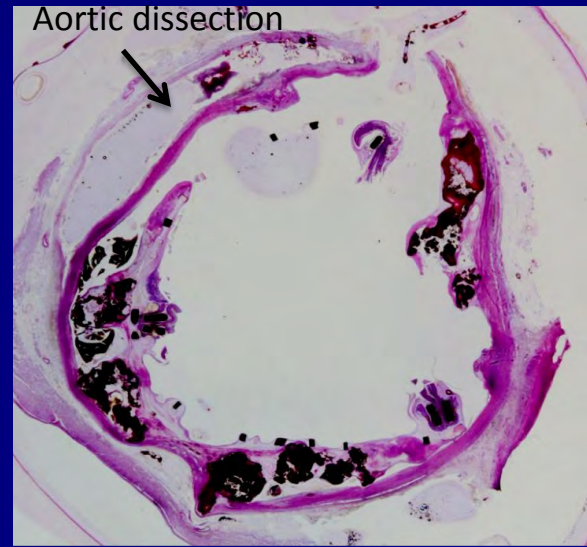
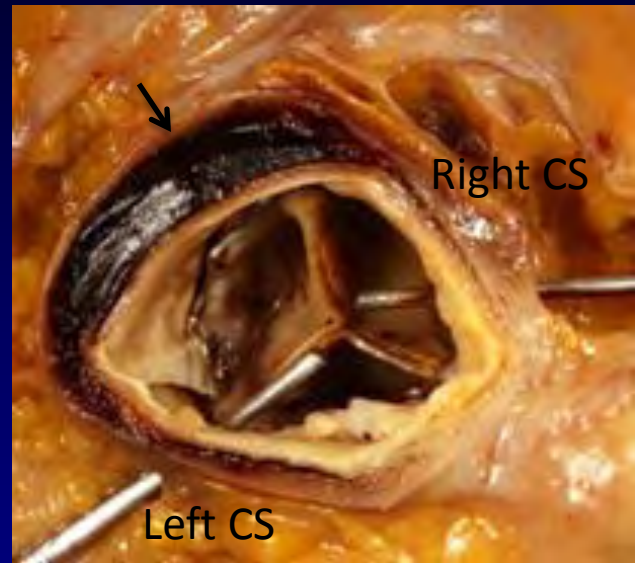
89 M status post percutaneous valve replacement (44 days) with subsequent paravalvular leak, severe and at death had pneumonia



Paravalvular gap between NCC and LCC. Linear calcification of NCC that extends into anterior mitral leaflet (*) and the mitral annular calcification extends into the medial commissure

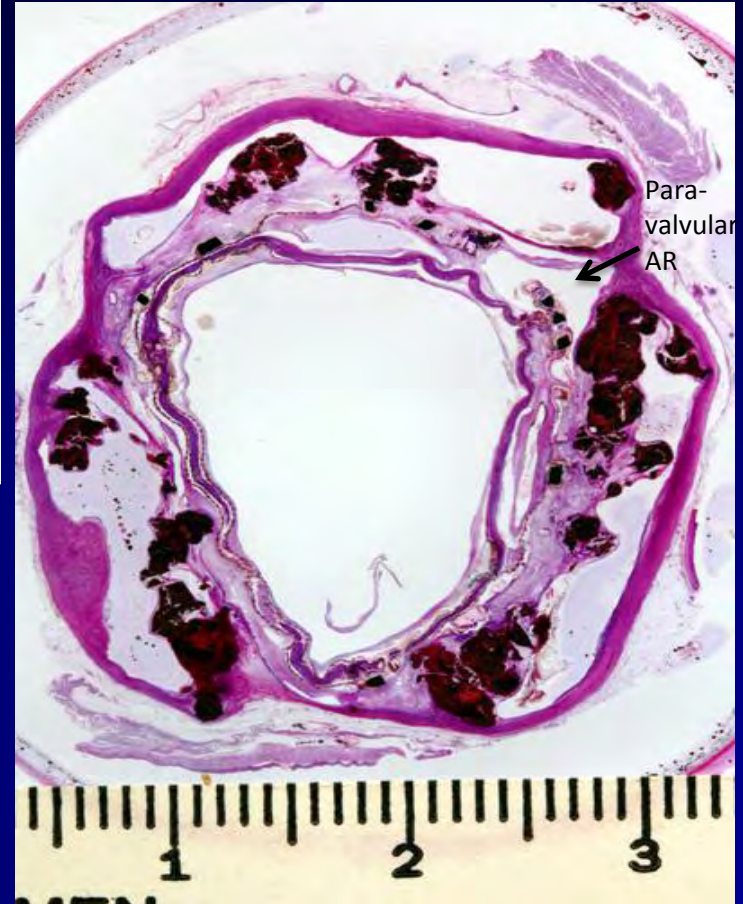
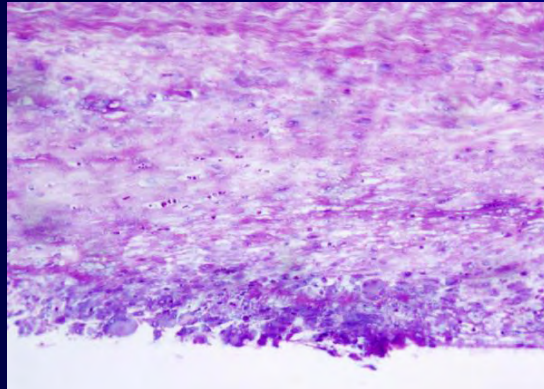
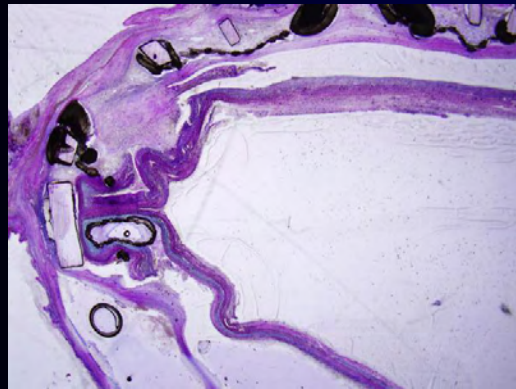
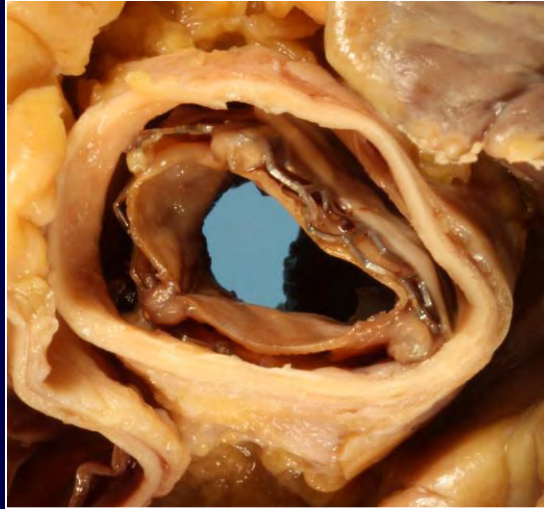
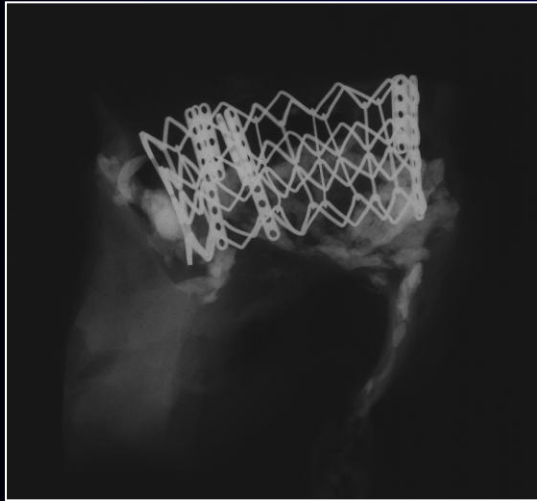


91 year old female with severe 3 vessel disease and critical aortic stenosis. Underwent TAVI with 23 Edward SAPIEN valve® (Edward Lifesciences, Irvine, CA) on 12/01/06. Patient died of Type I aortic dissection 7/27/09.



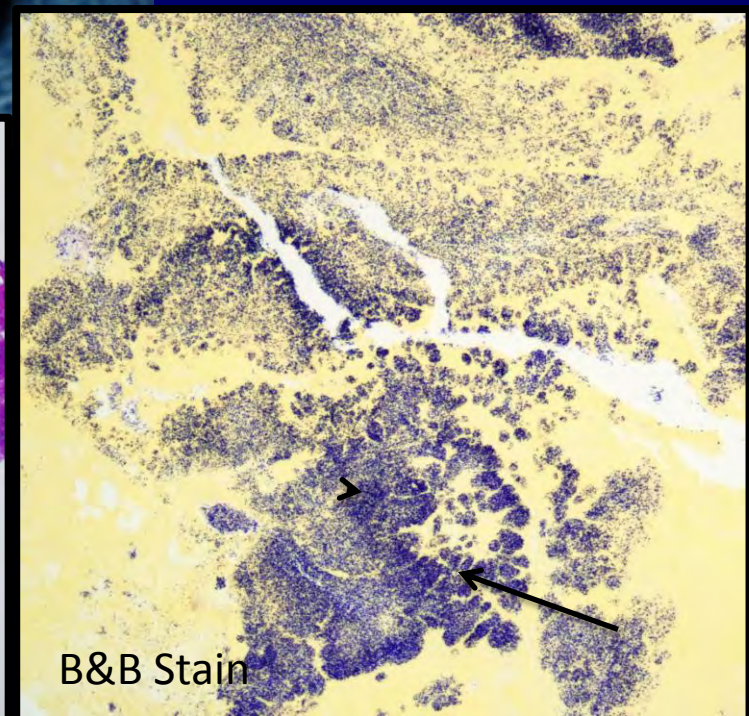
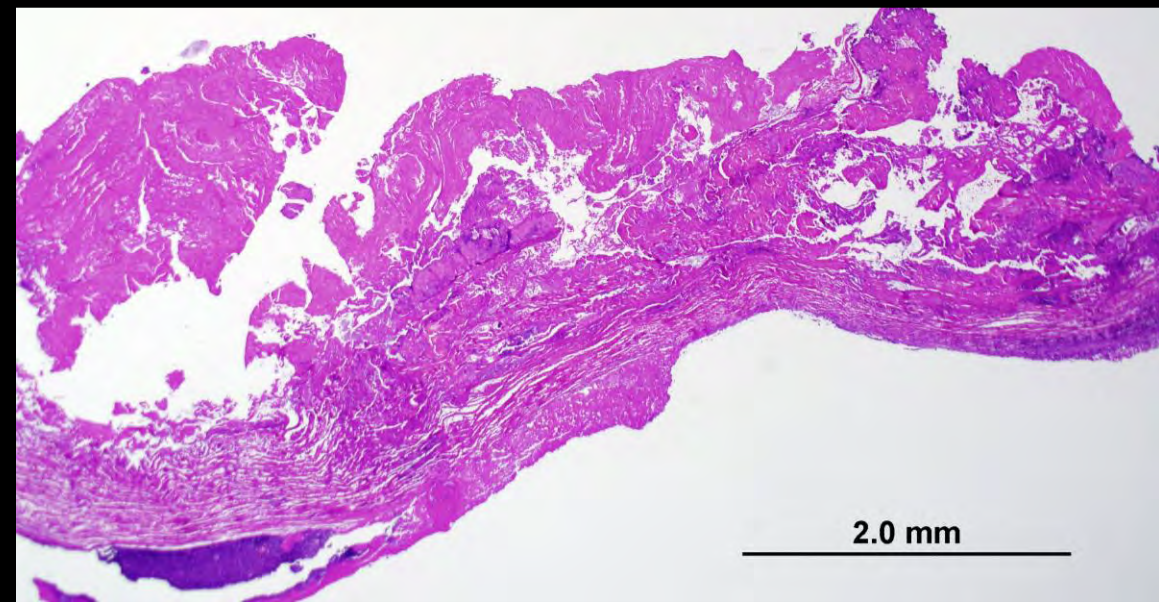
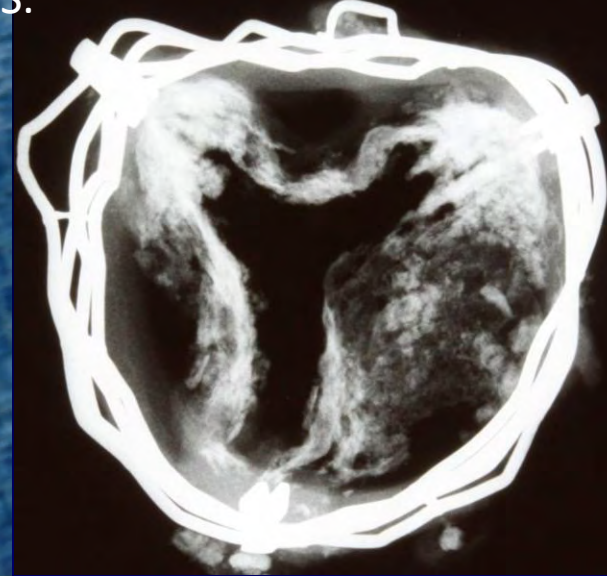
Aortic dissection, not related to superior edge of valve strut as no entry observed.

81 year old man with coronary artery disease status post stent placement, congestive heart failure, pulmonary hypertension, and severe aortic stenosis status post percutaneous heart valve replacement 4-years before death.



Normal Edward Sapien valve with complete healing of inferior margin and minimal inflammation of valve leaflet edge

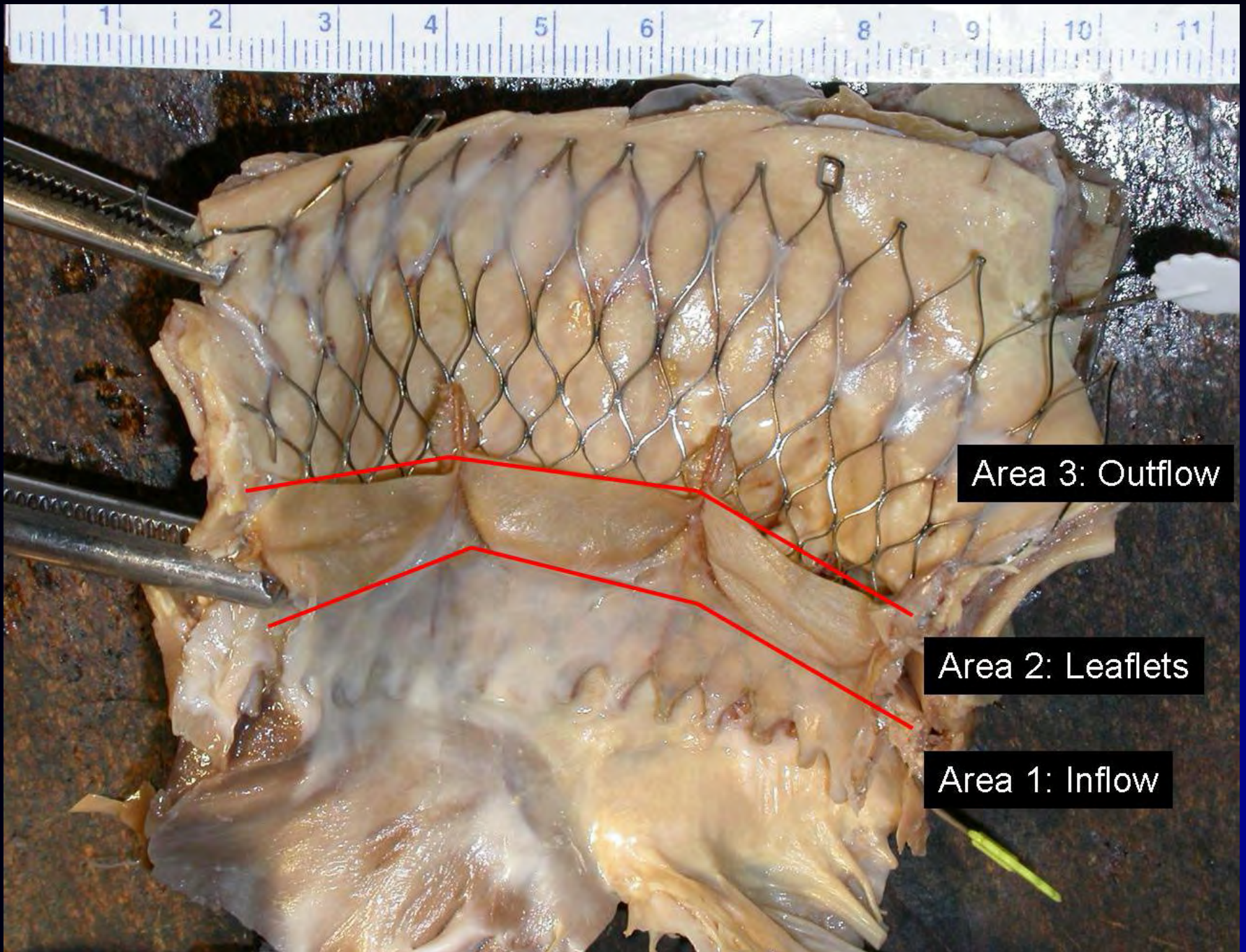
Edward Sapien valve explanted surgically 20 months after implantation. Patient had 3 episodes of bacteremia with *Strep bovis* 6 months and had positive culture 7 days prior to surgery attributed to extensive diverticulosis. He had developed severe AS.



B&B Stain

Human CoreValves retrieved for pathologic analysis

Case #	Patient Age/Gender	Implantation	Autopsy
1	85F	3 days	Aortic perforation
2	85M	4 days	Embolism (LV and CVA)
3	77M	13 days	AR- Valve in valve, cardiac failure
4	81F	104 days	Sudden death, Valve functioning normally
5	85M	350 days	Autopsy, amyloidosis
6	80F	425 days	Autopsy , suicide, valve functioning normally
7	84M	22 days	Paravalvular leak/multi-organ failure
8	89F	2 years	Metastatic adenoCA, moderate pannus in one leaflet
9	74 M	5 years	Post TAVR AS, surgically replaced
10	78M	25 days	COPD
11	72M	5 days	Bicuspid valve/ severe paravalvular AR/pneumonia

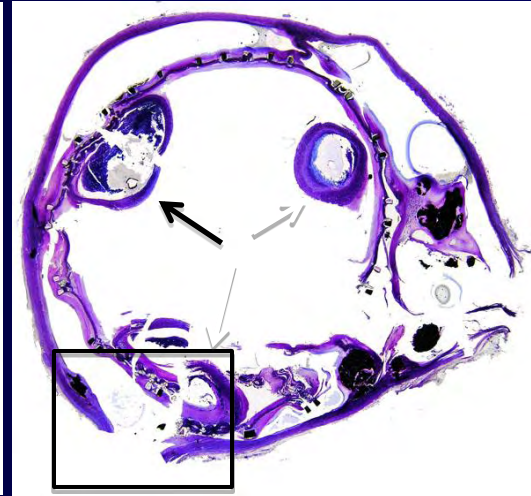
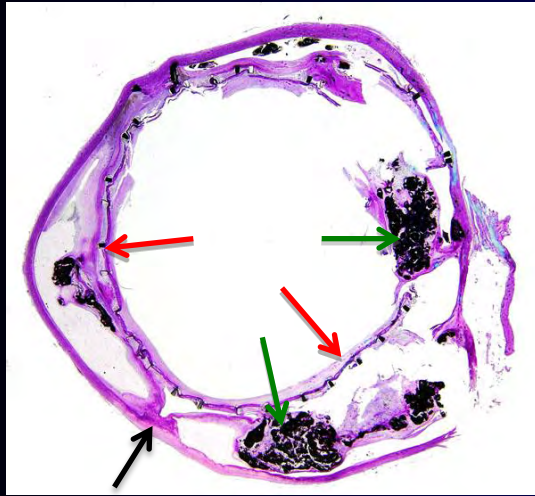
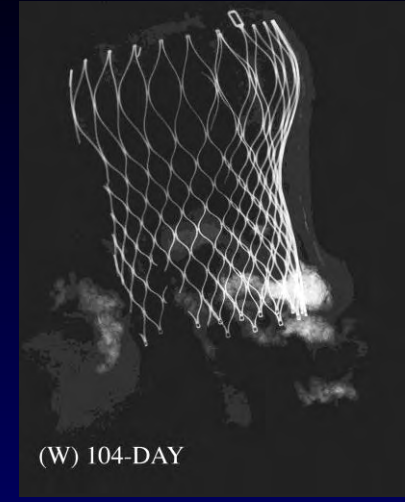
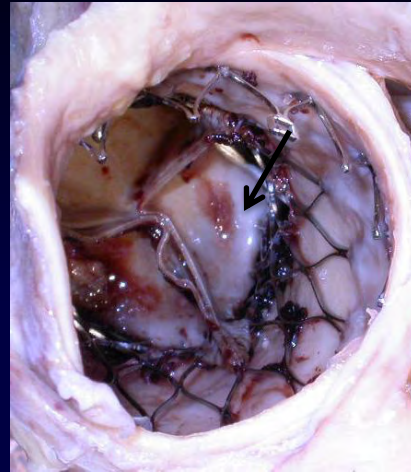
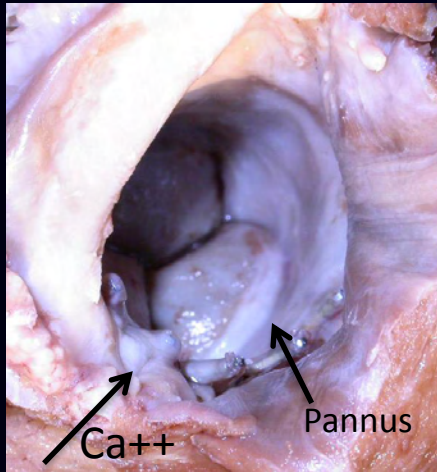


Area 3: Outflow

Area 2: Leaflets

Area 1: Inflow

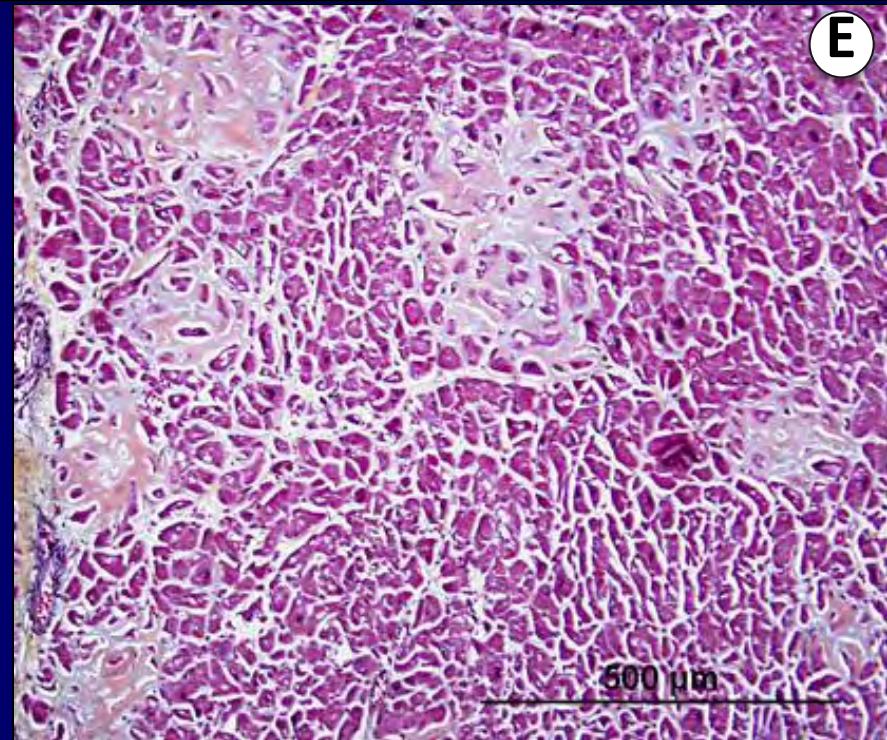
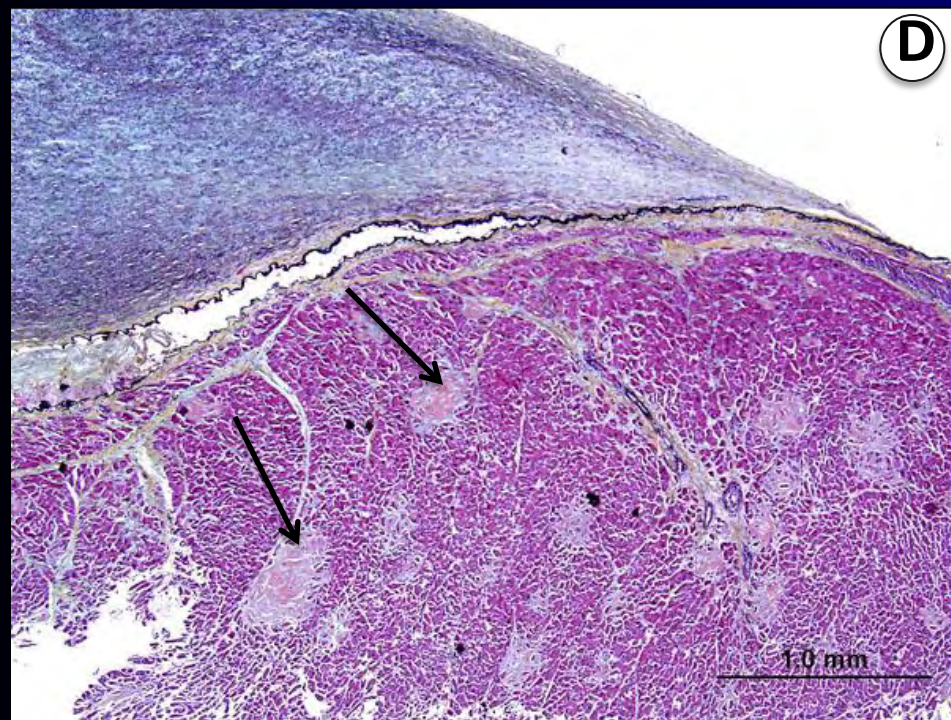
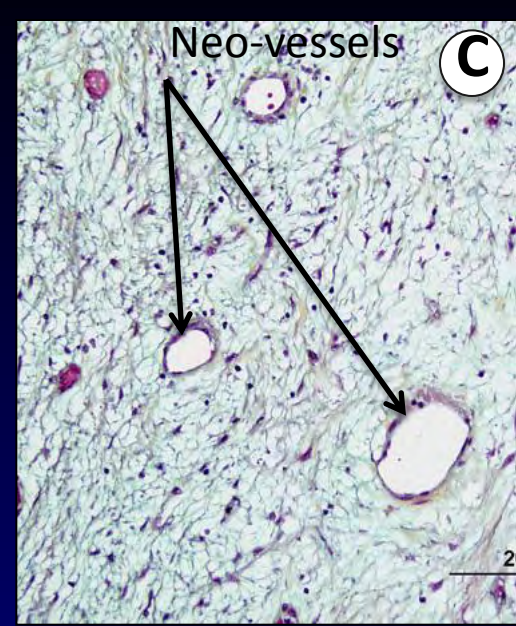
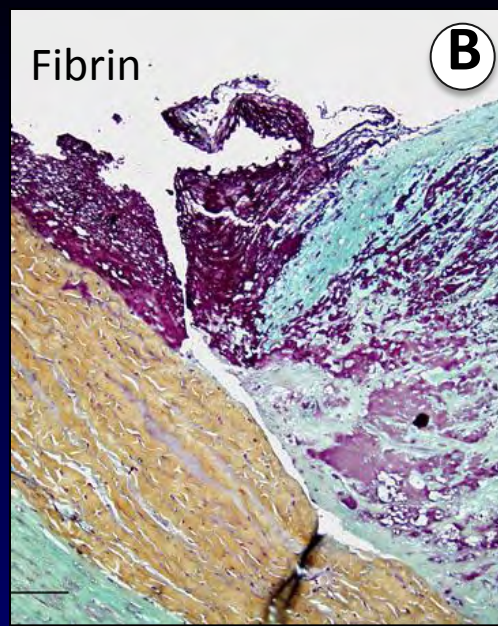
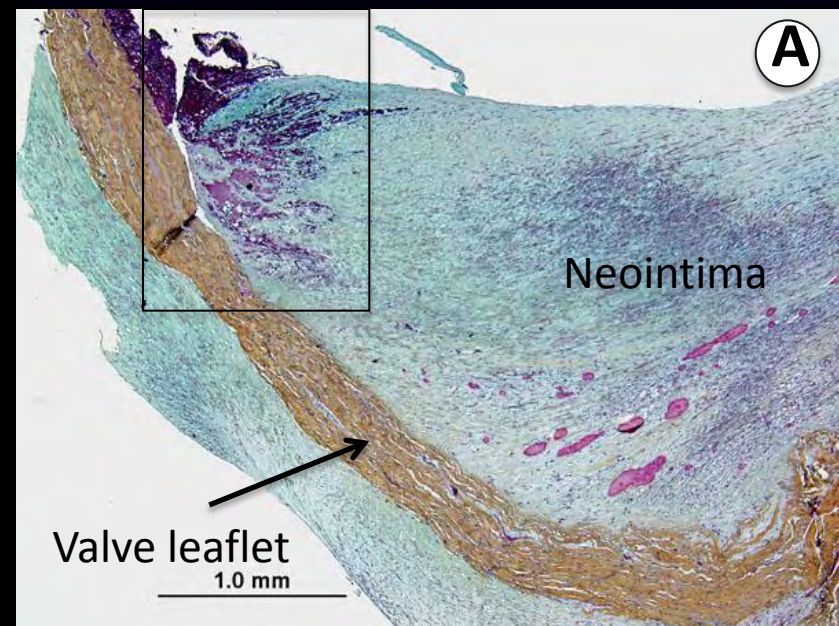
CoreValve 104 days post implantation



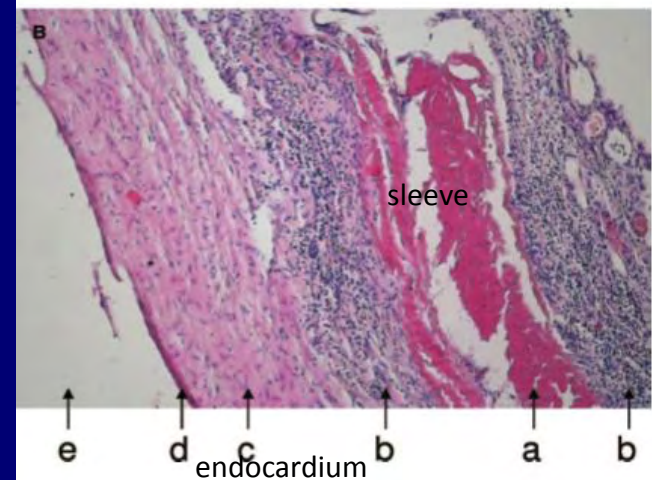
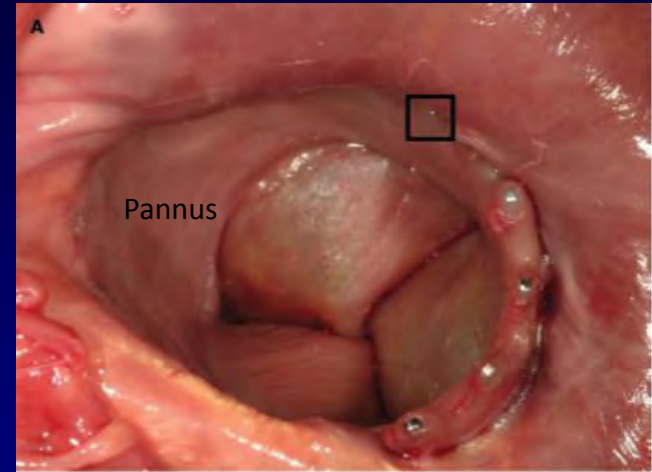
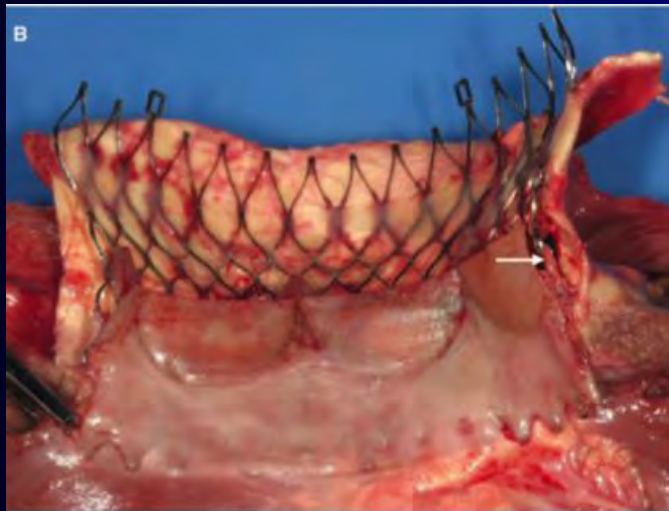
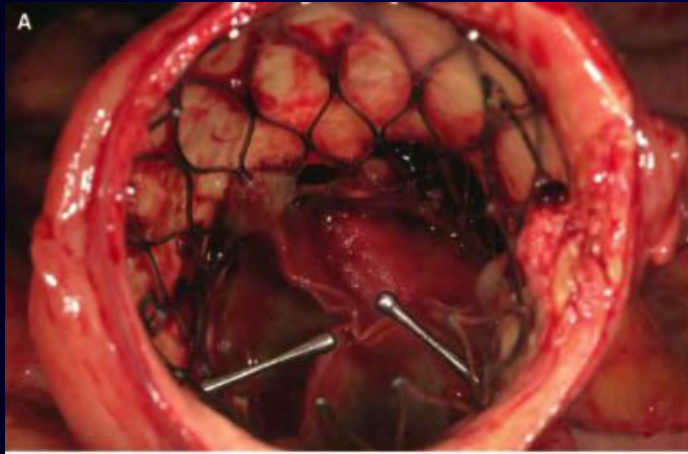
Transverse section of aorta with in-situ prosthetic device. Native leaflets are heavily calcified (arrows) and are excluded by the stent frame (arrows).

Transverse section of the aorta and valve assembly at the level of the prosthetic leaflet sinus (arrows). Inset shows coronary artery ostium.

Transverse section of the aorta and valve assembly at the level of the prosthetic leaflet and commissures (arrows).

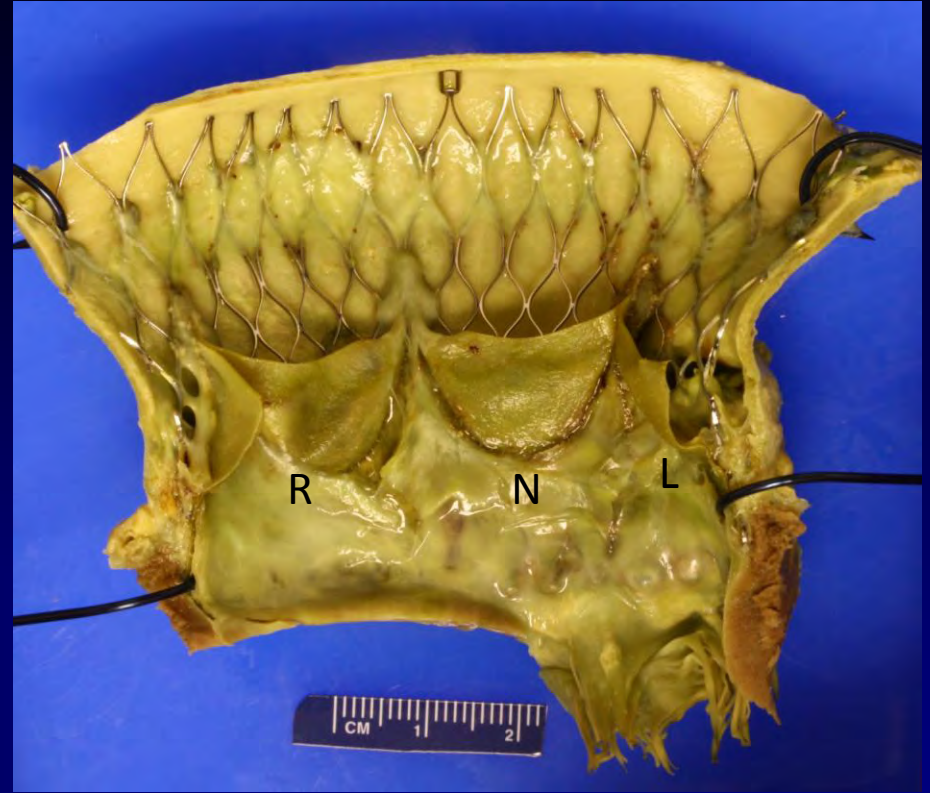
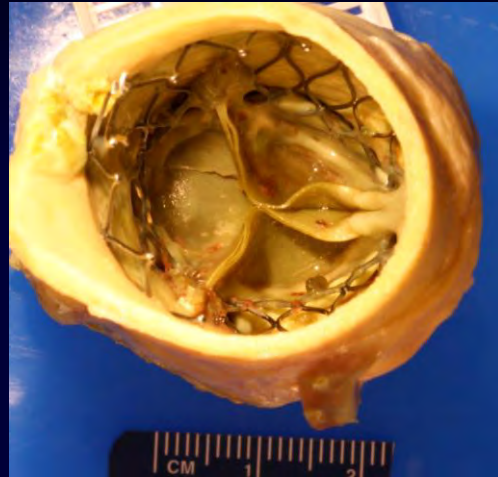
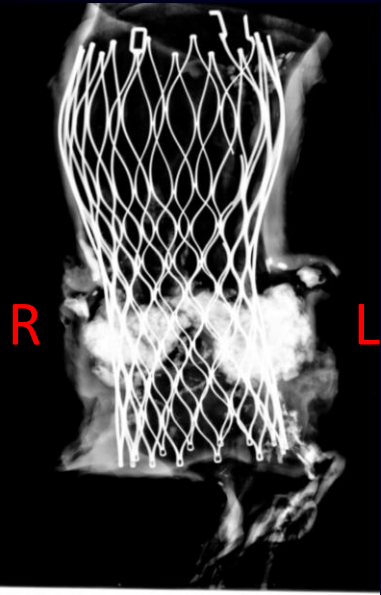


80 year old female, NY Heart Association Grade III, stable angina had stent placed and mild AS, progressed to severe stenosis in 2 years, valve area 0.5 cm² with increased symptoms had CoreValve implanted via a transfemoral approach. At 1 year gradient 3 mm Hg no AR, improvement in symptoms. At 425 days committed suicide.

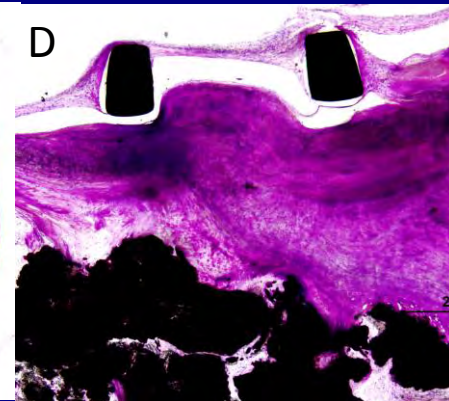
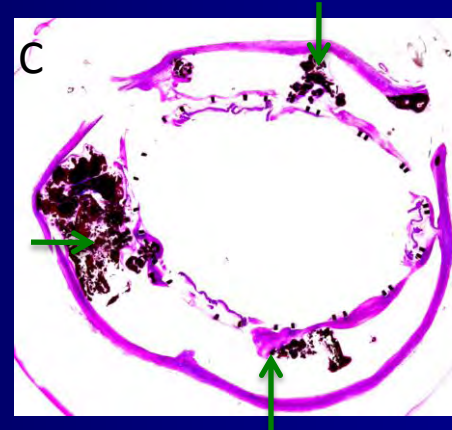
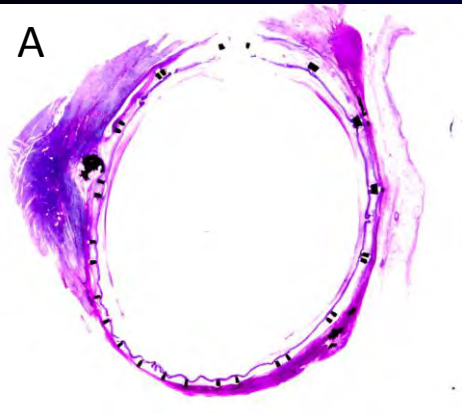


LVOT Luminal side of prosthesis inflammation

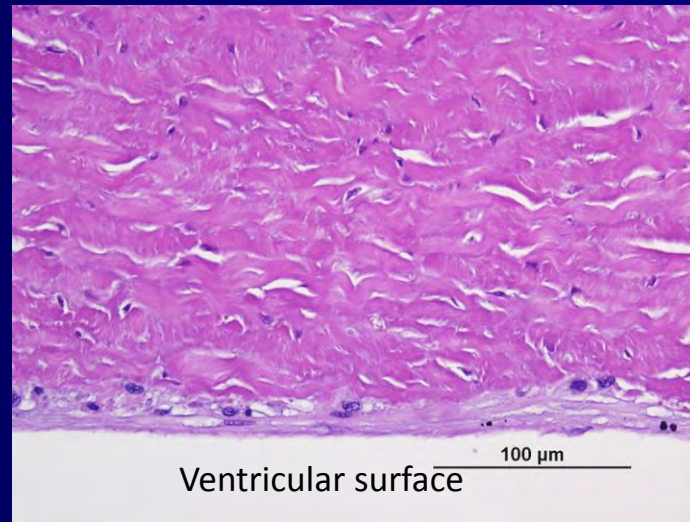
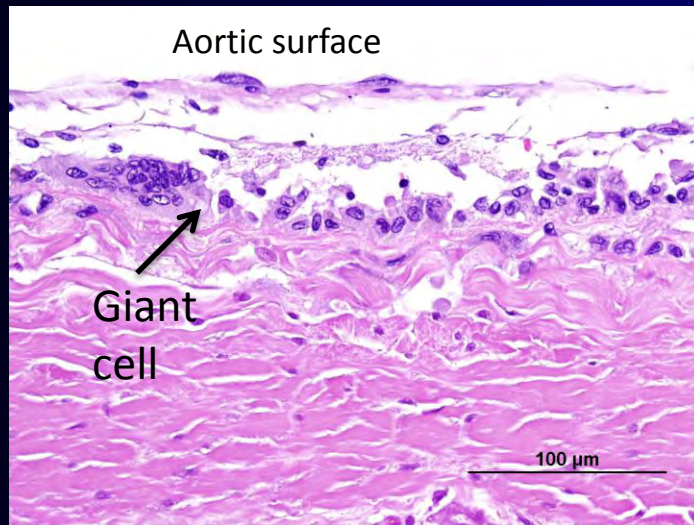
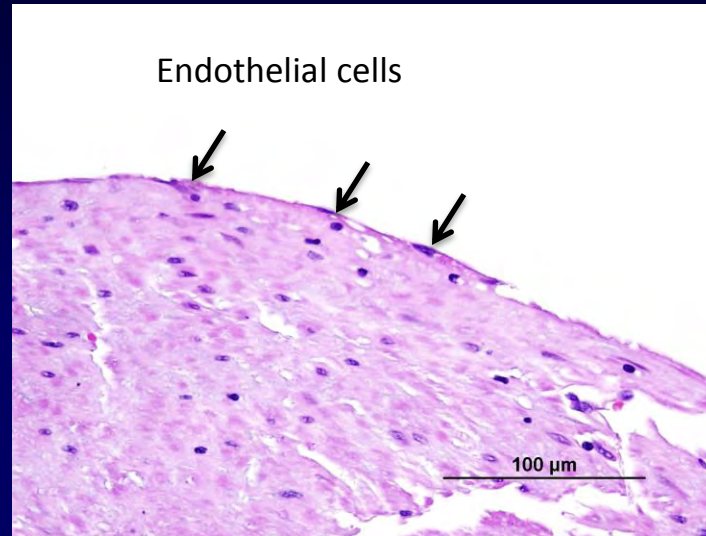
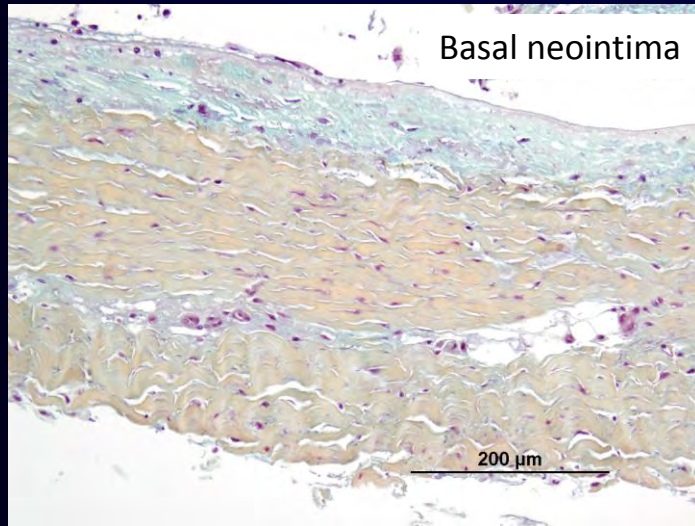
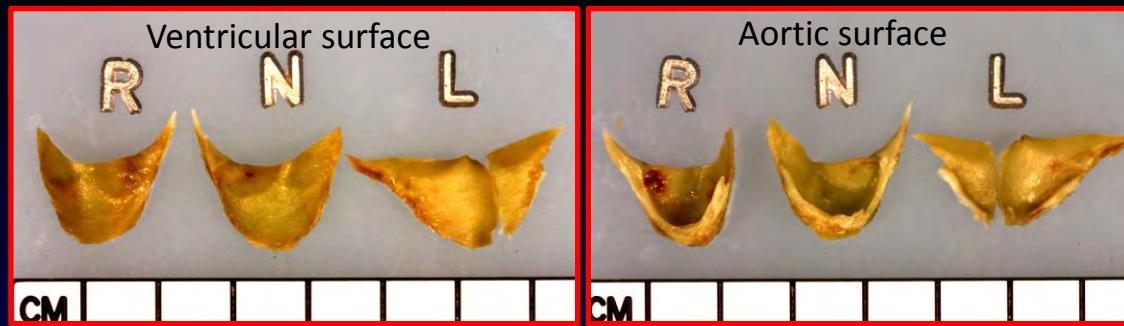
CoreValve 2 years post implantation (89F with metastatic adenoCA)



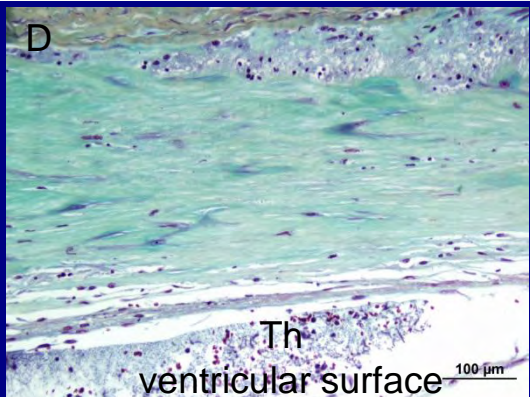
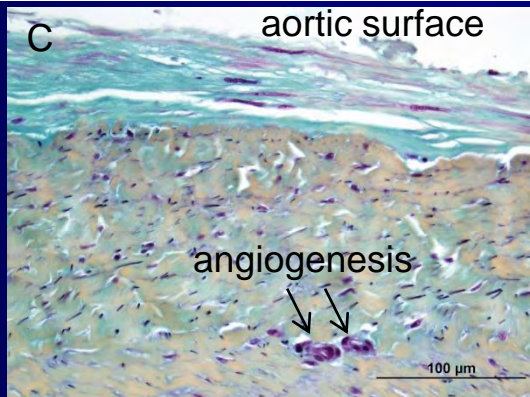
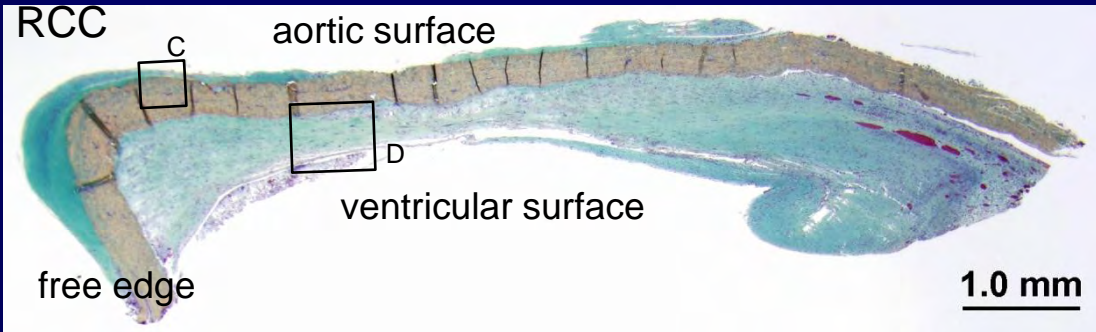
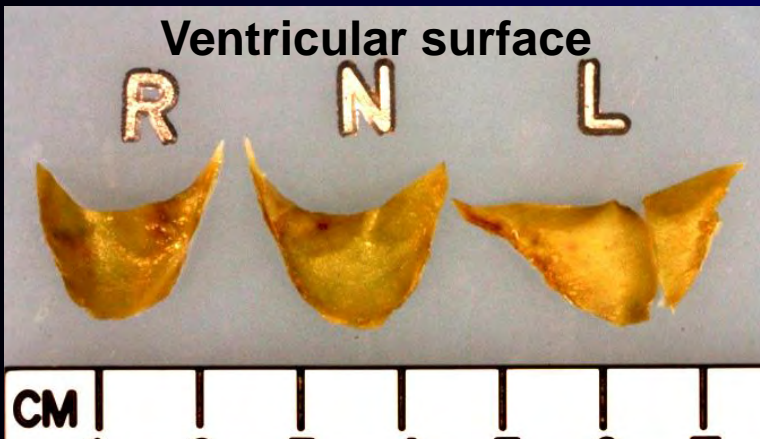
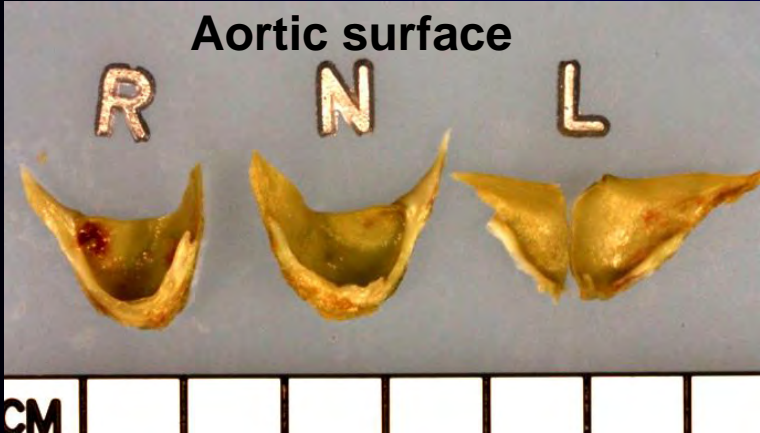
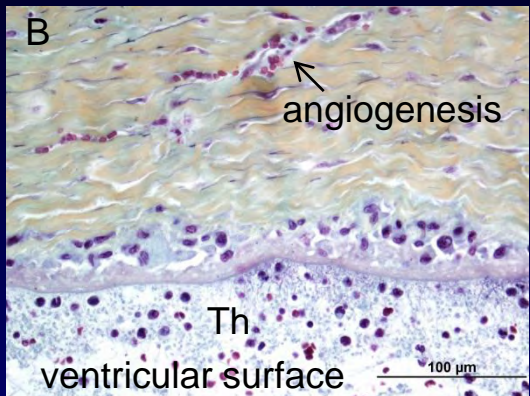
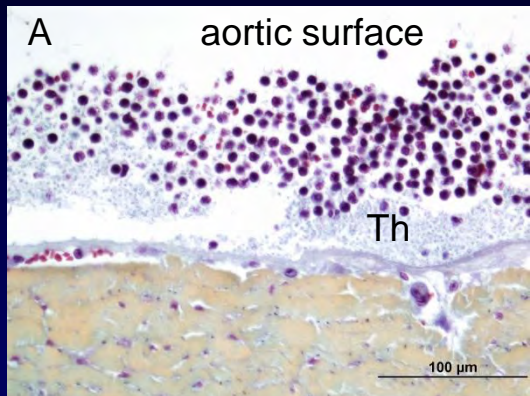
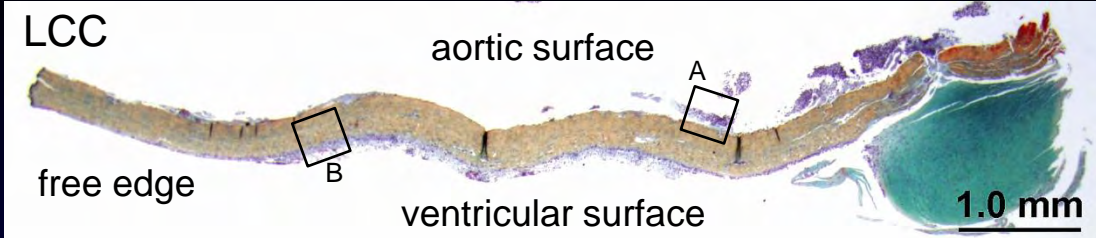
A,B) Inflow : frame incorporated by thin neointimal coverage
C,D) Mid : Native leaflets calcified (green arrow); frame excludes native leaflets; thin neointima covers frame



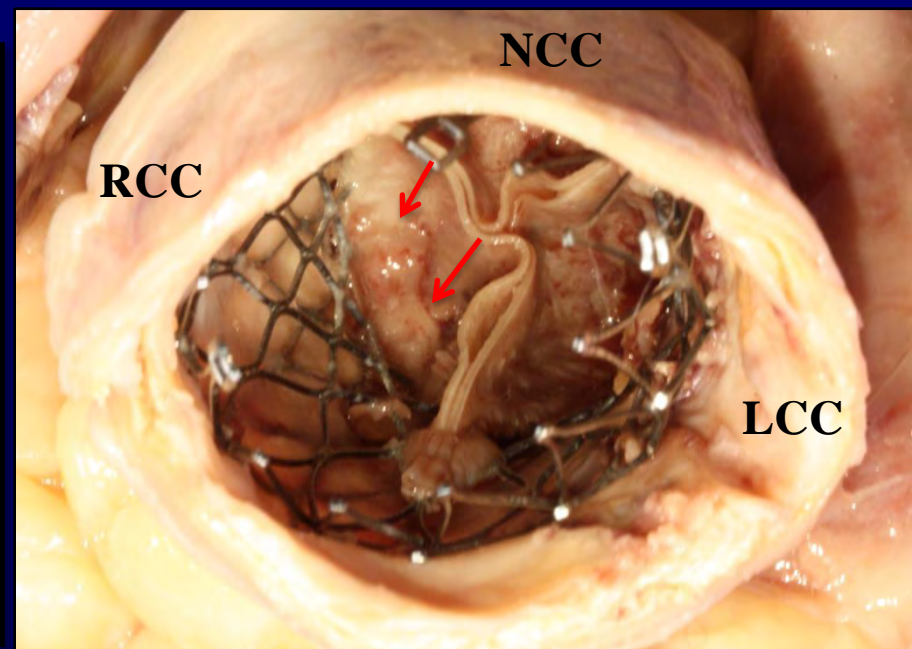
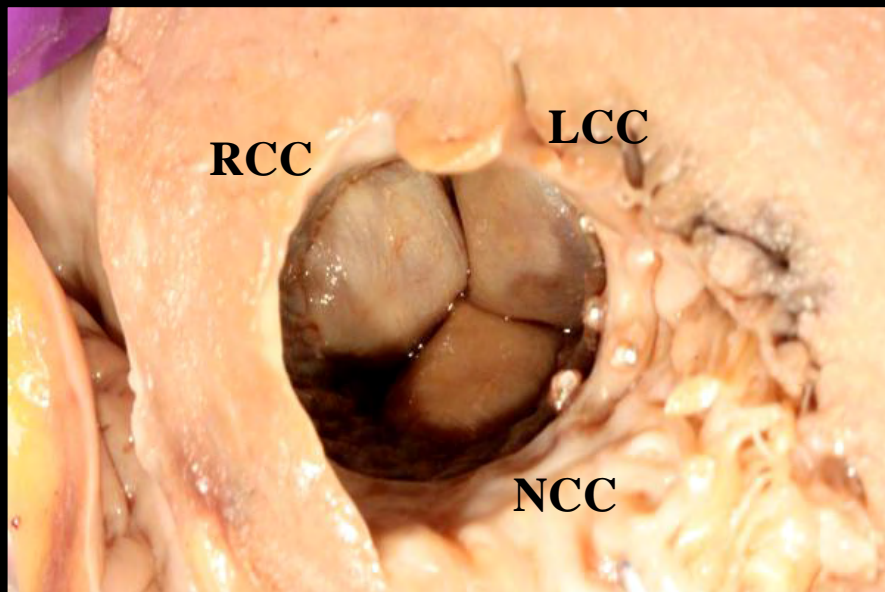
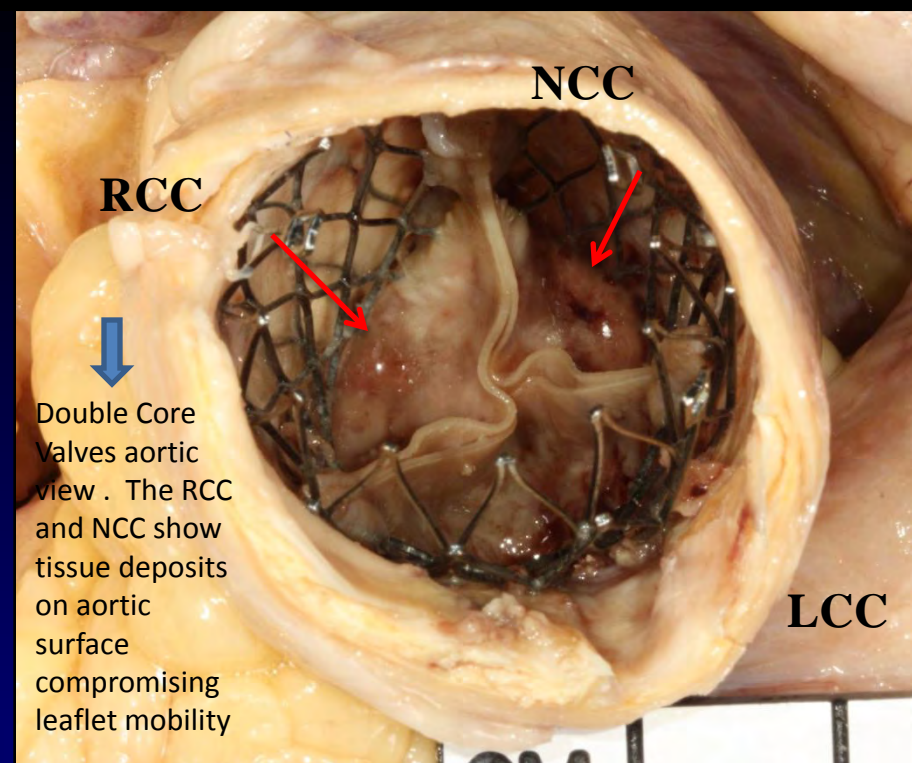
Excised bovine pericardial leaflets and histologic analysis

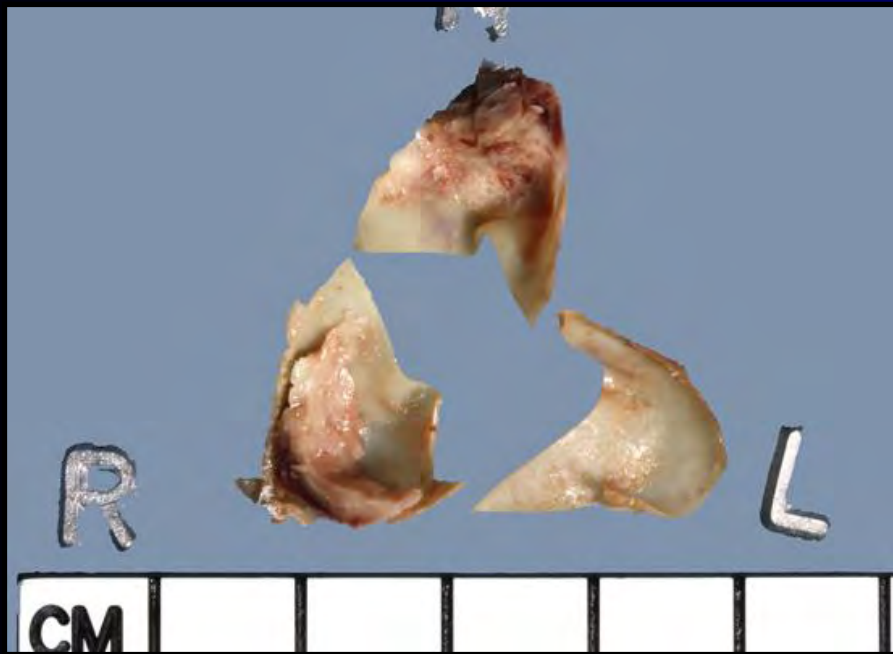
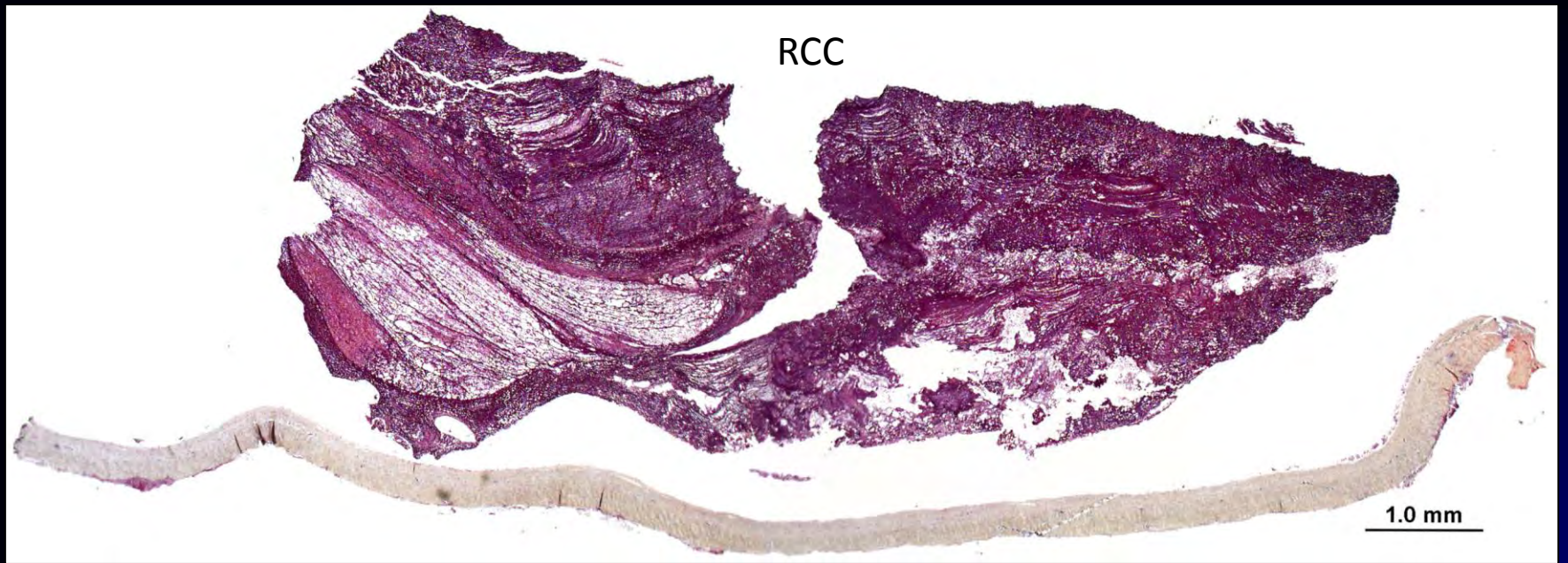


Gross and Microscopic Images of Leaflets Removed from Valve Frame



70-years WF, h/o hypertension, dyslipidemia, PVD, moderate chronic lung disease on home oxygen, anemia and NYHA functional class III; a 26 mm Core Valve was implanted on 6/6/2011, and a new LBBB and 1st degree AV block were noted at discharge on 6/11/2011; at one month there was mild paravalvular AR and NYHA functional class II; at six month there was transvalvular and paravalvular AR, NYHA functional class III, on echo panningus/aortic restenosis; a valve-in-valve procedure was performed on 1/6 /2012 without complications and died on 1/23 /2012 of AR

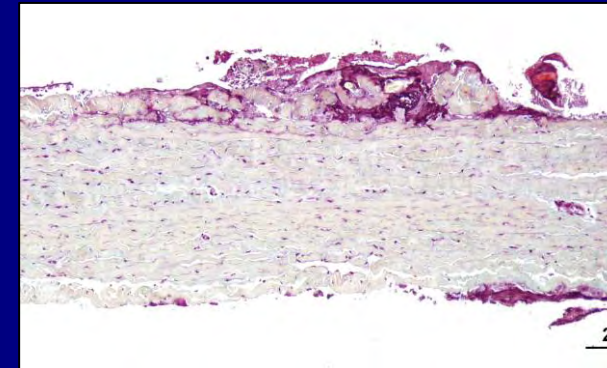
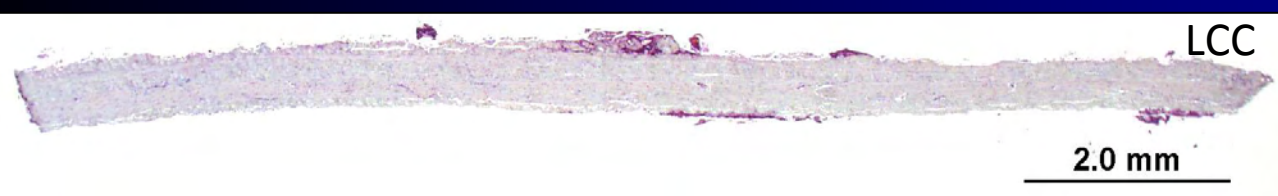
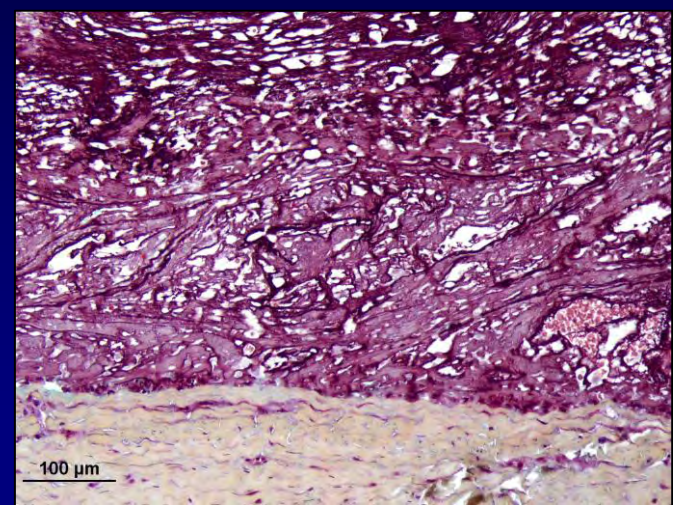
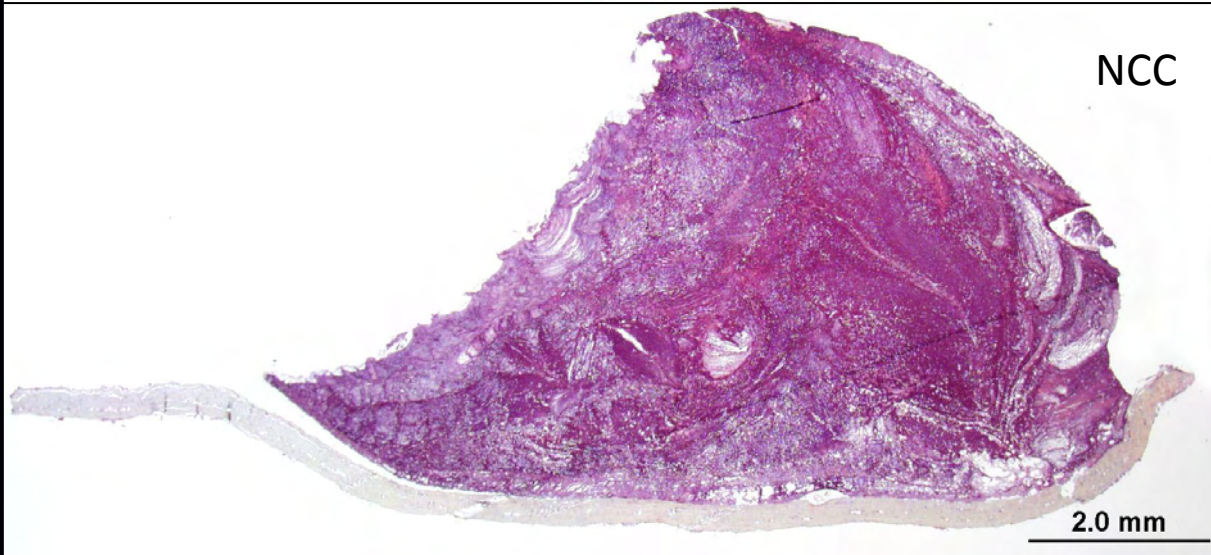
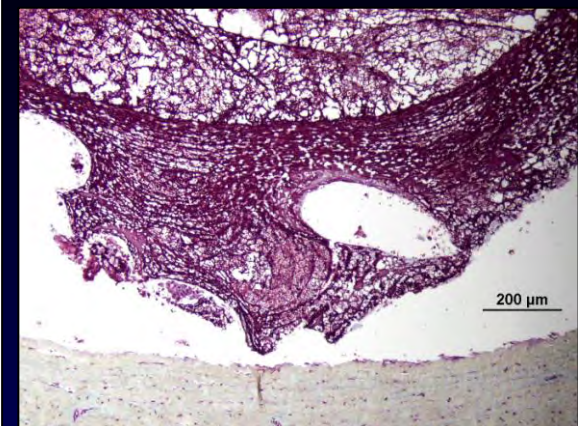


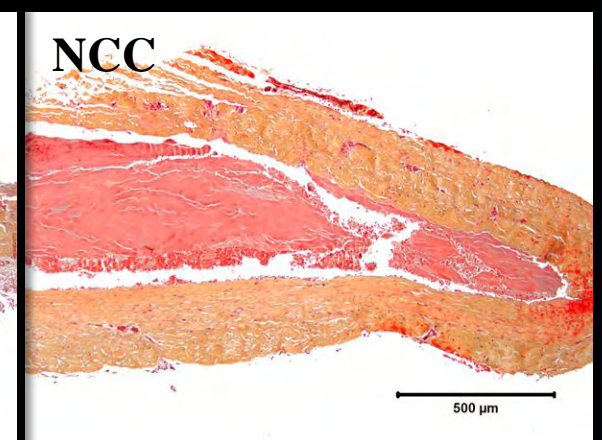
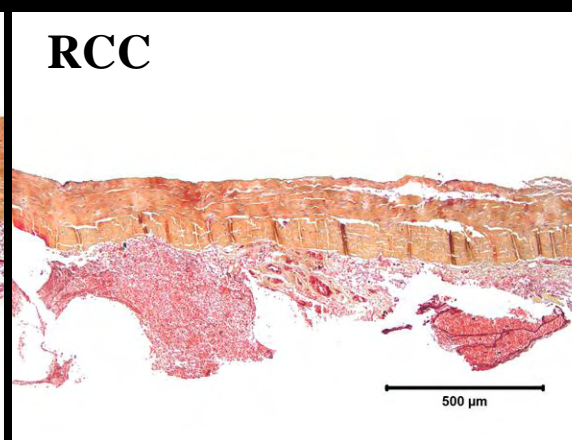
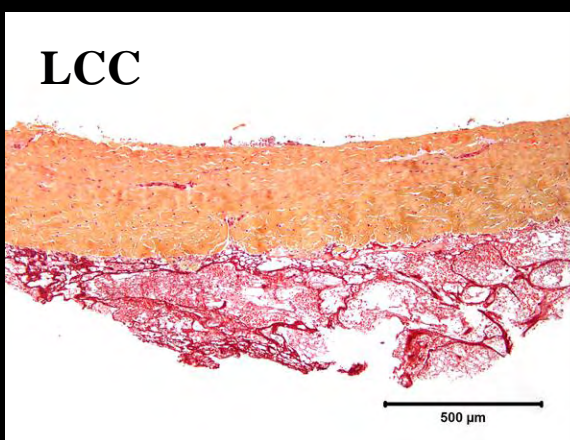
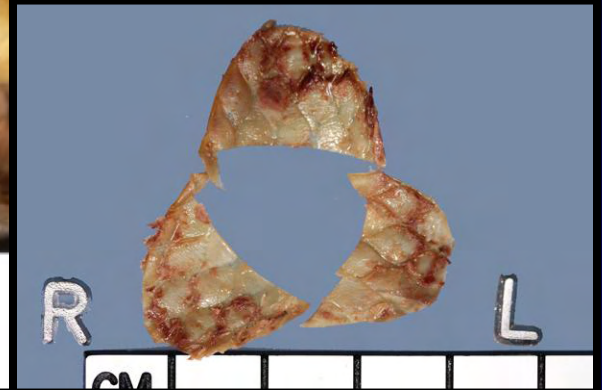
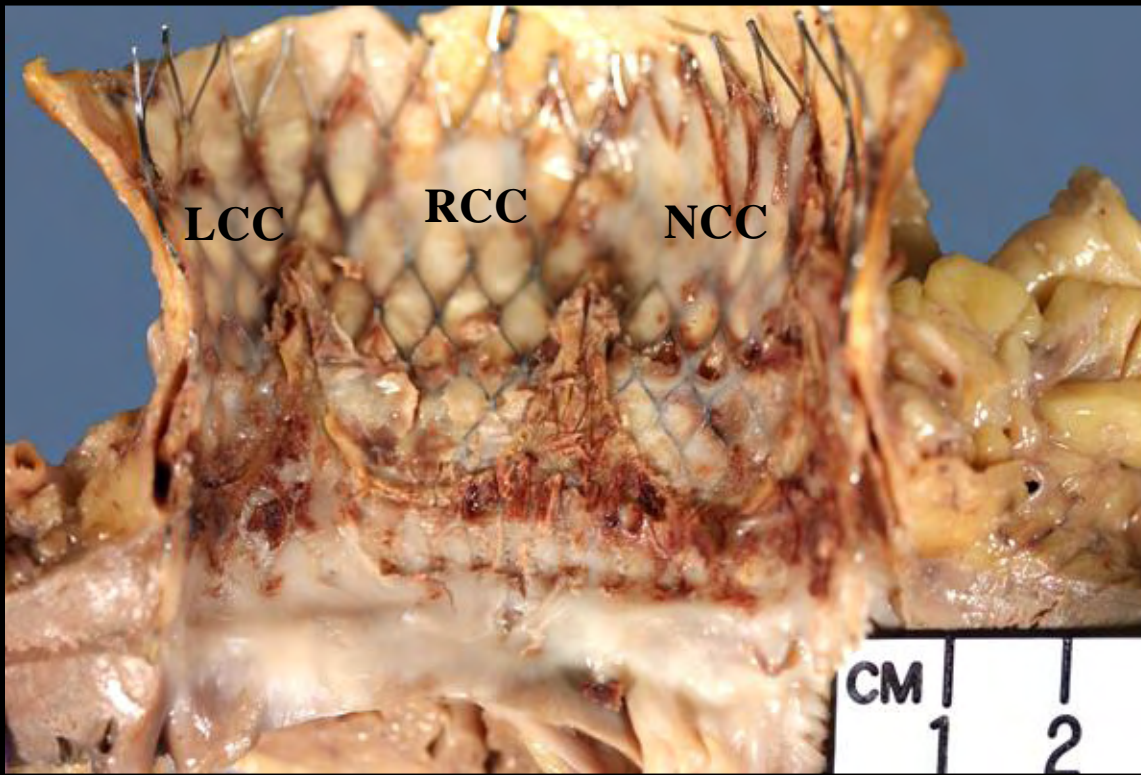


Aortic view



Ventricular view



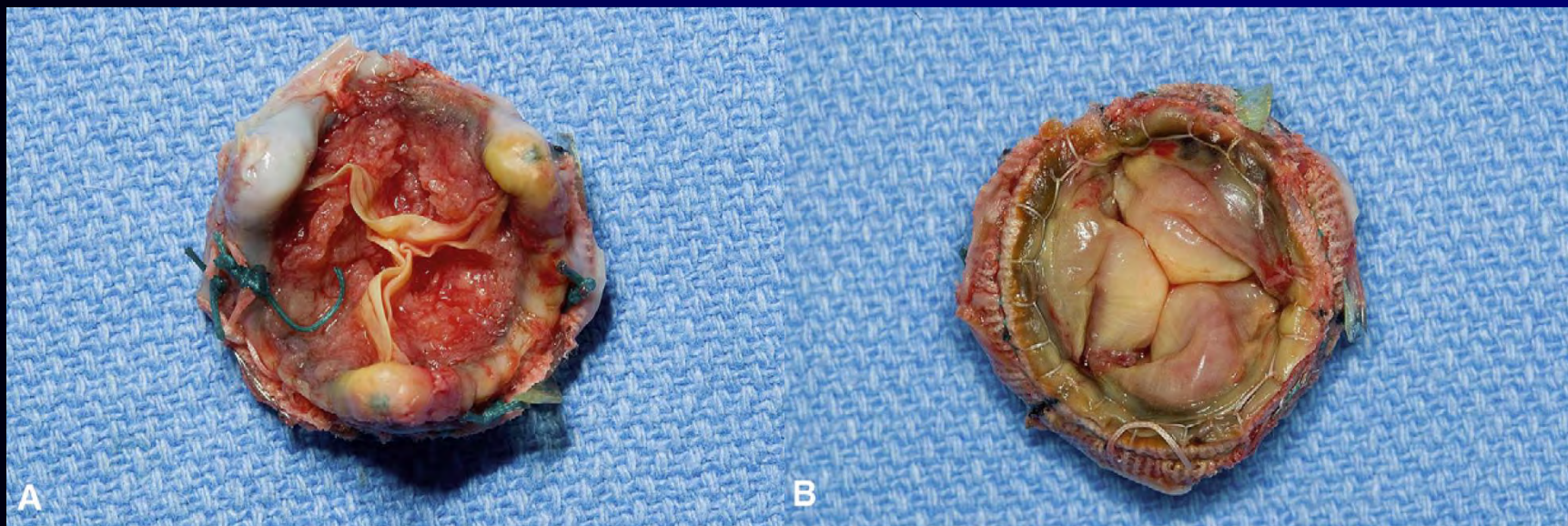


Incidence of Valve Thrombosis in Surgically Implanted Biological Valves in Aortic Position

	N	Incidence of thrombosis
Stented Porcine	1463	0.55%
St Jude Biocor (St Jude Medical)	318	1.26%
Medtronic Mosaic (Medtronic Inc)	541	0.37%
Medtronic Hancock (Medtronic Inc)	270	0.84%
Stented pericardial	3031	0%
Stentless	74	0%

Aortic side

Ventricular side



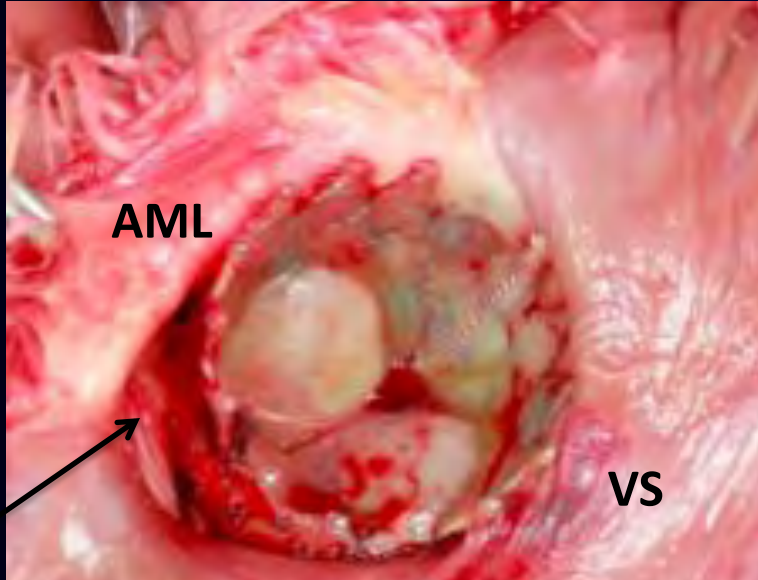
Modified from Brown ML, et al. J Thorac Cardiovasc Surg 2012;144:108-11.

Bioprostheses “Thrombosis” After TAVR

- Three case reports:
- Case 1. 80-years-old W with severe AS, underwent TAVR (23-mm Sapien XT), discharged day 5 asymptomatic on DAPT, mean pressure gradient (MPG) 10mm Hg, at 1- mo 12mm Hg, at 10-mo symptomatic with dyspnea (NYHA functional class III), MPG 54mm Hg. TEE fusion of 2 leaflets with suspicion of “thrombotic apposition”. Oral anticoagulants (OAT) prescribed, 3 months MPG 13 mm Hg, patient asymptomatic.
- Case 2. 81-years-old M severe dysfunction of AV prosthesis (25-mm Carpentier Edwards) underwent TAVR (23-mm Sapien XT), discharged day 5, MPG15mm Hg, 1- mo 14mm Hg, at 4-months dyspnea (NYHA class III), MPG 51mm Hg, TEE 2 leaflets suspicion of thrombotic apposition, OAT prescribed, at 2 months MPG mm Hg, patient asymptomatic.
- Case 3. 74-years-old W with severe AS , TAVR (26-mm Sapien XT), discharged day 4 on DAPT, MPG 7mm Hg, 1-moMPG 8mm Hg, at 2-months patient symptomatic with dyspnea (NYHA class II), MPG 3 mm Hg. TEE suspicious of thrombotic apposition blocking the movement of bioprosthetic leaflets. OAT prescribed, at 2- mo asymptomatic, TEE restored function, MPG 9mm Hg.
- Need for proper anticoagulant therapy after TAVR

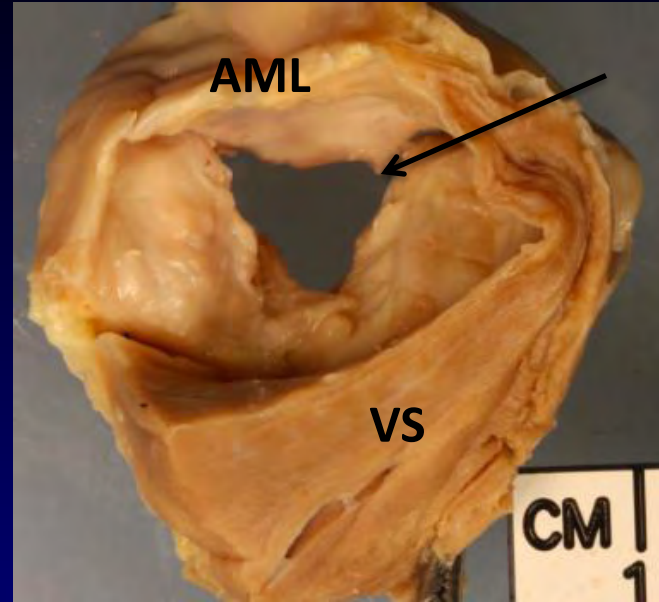
84-year old M with AS had CoreValve Implanted 22 days prior to death developed aortic regurgitation post TAVI.

Left ventricular out flow

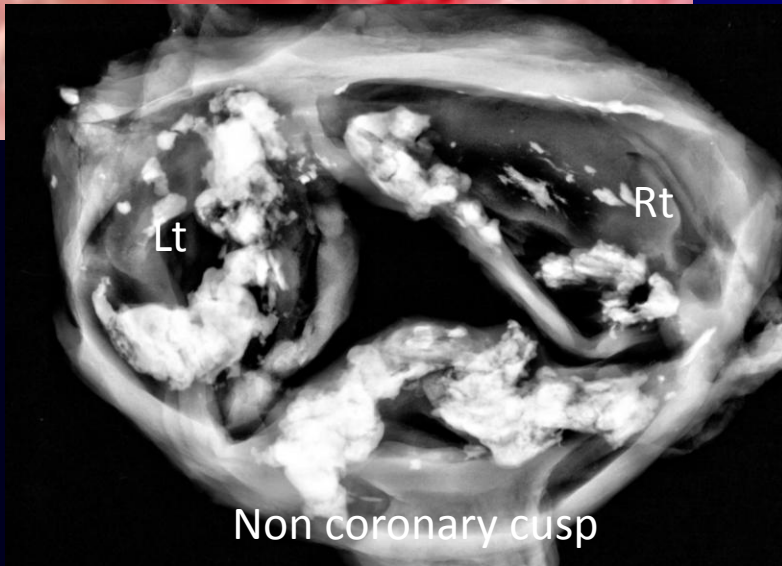
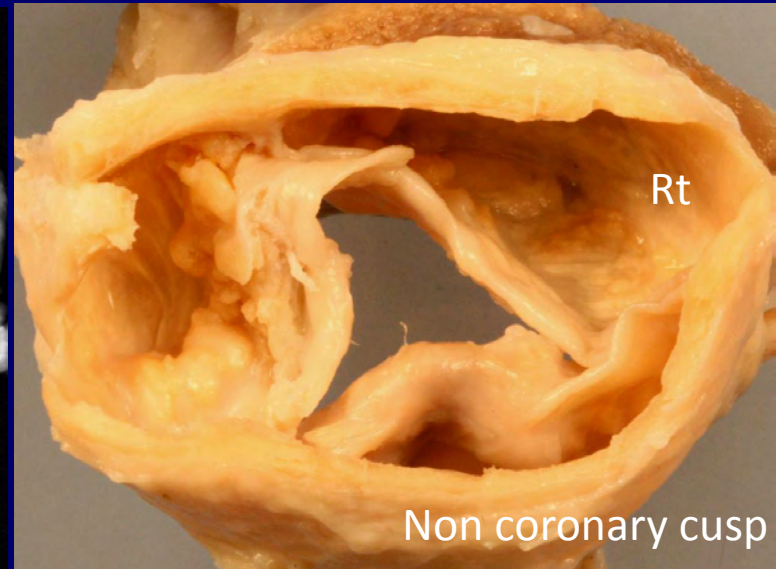


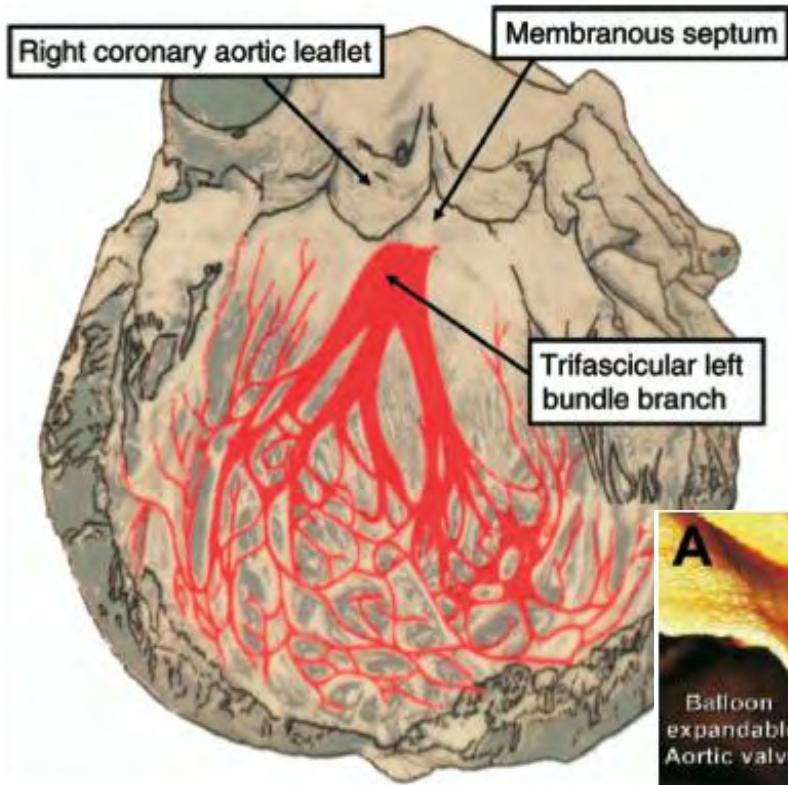
Inferior view

Non-coronary cusp

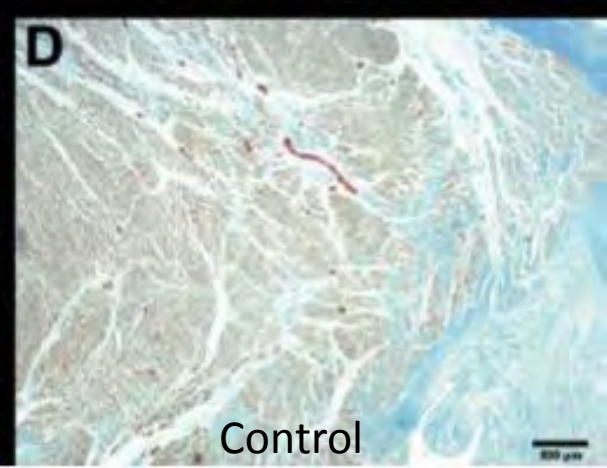
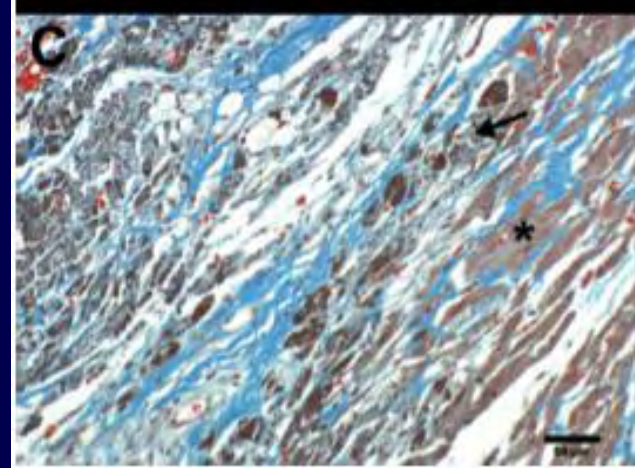
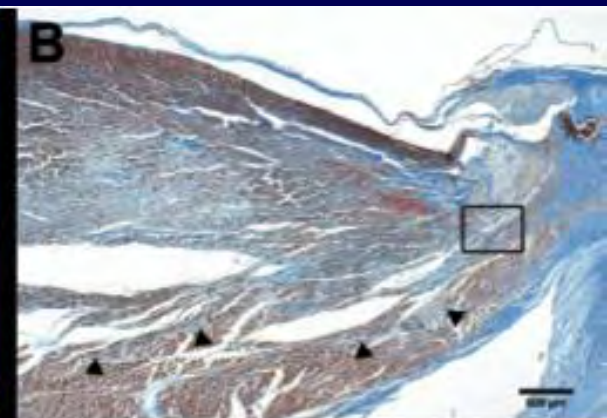
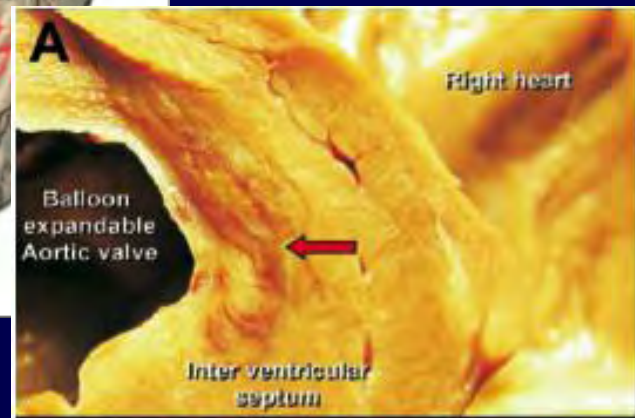
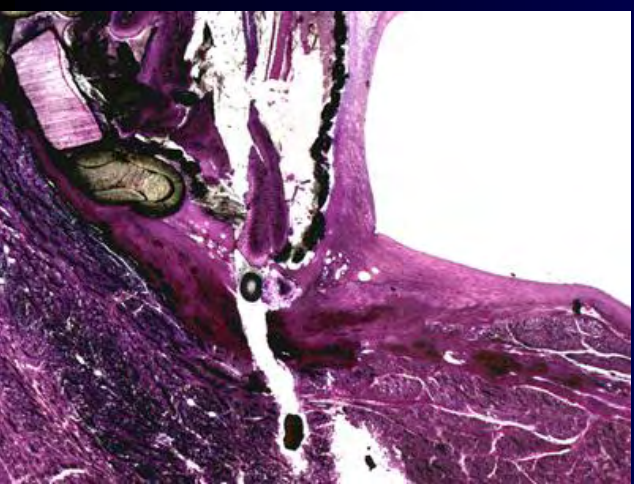


Superior View



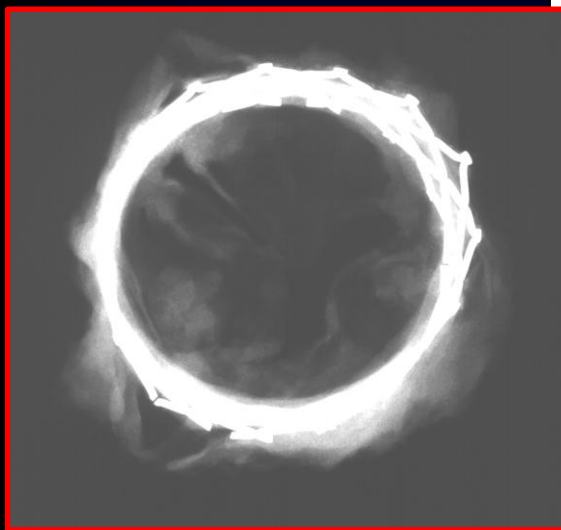


AV block after Transcatheter balloon expandable AV insertion varies from 10 to 50%, those requiring permanent pacemakers (PPM) is close to 30% occurs frequently after transfemoral TAVI with the Core valve prosthesis (31%) versus Edward Sapien valve (15.2%) . Older age, chronic atrial fibrillation, pre-operative bradycardia, and larger or significantly oversized prostheses were independent risk factors for PPM
Europace 2012;14 (12):1759-63

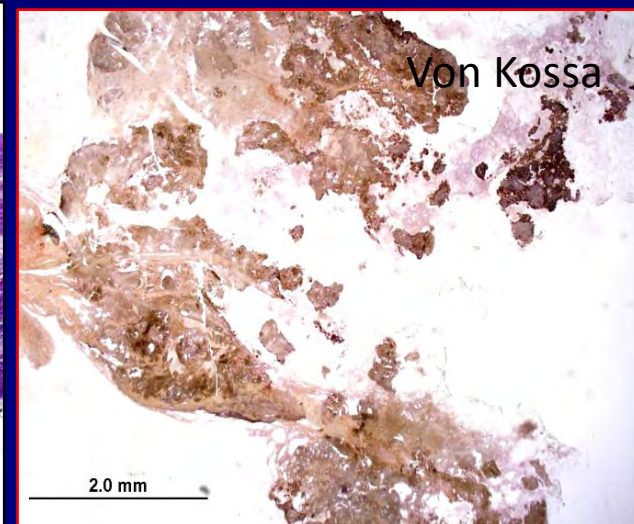
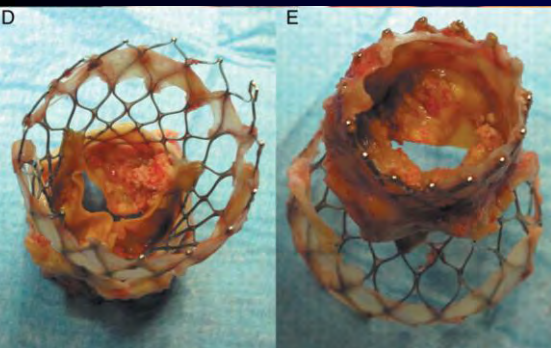
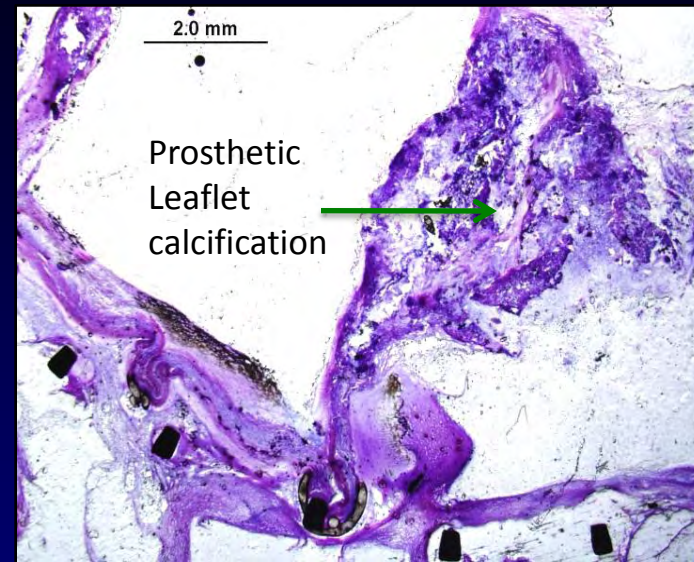
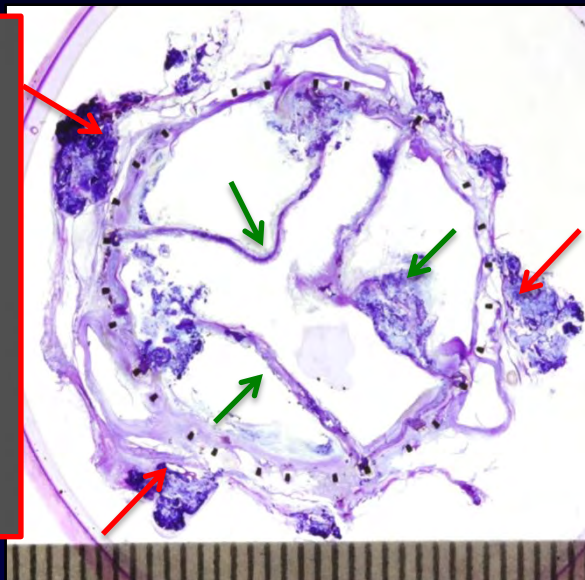


5 years post CoreValve Implantation

Structural valvular failure due to calcification, surgically removed

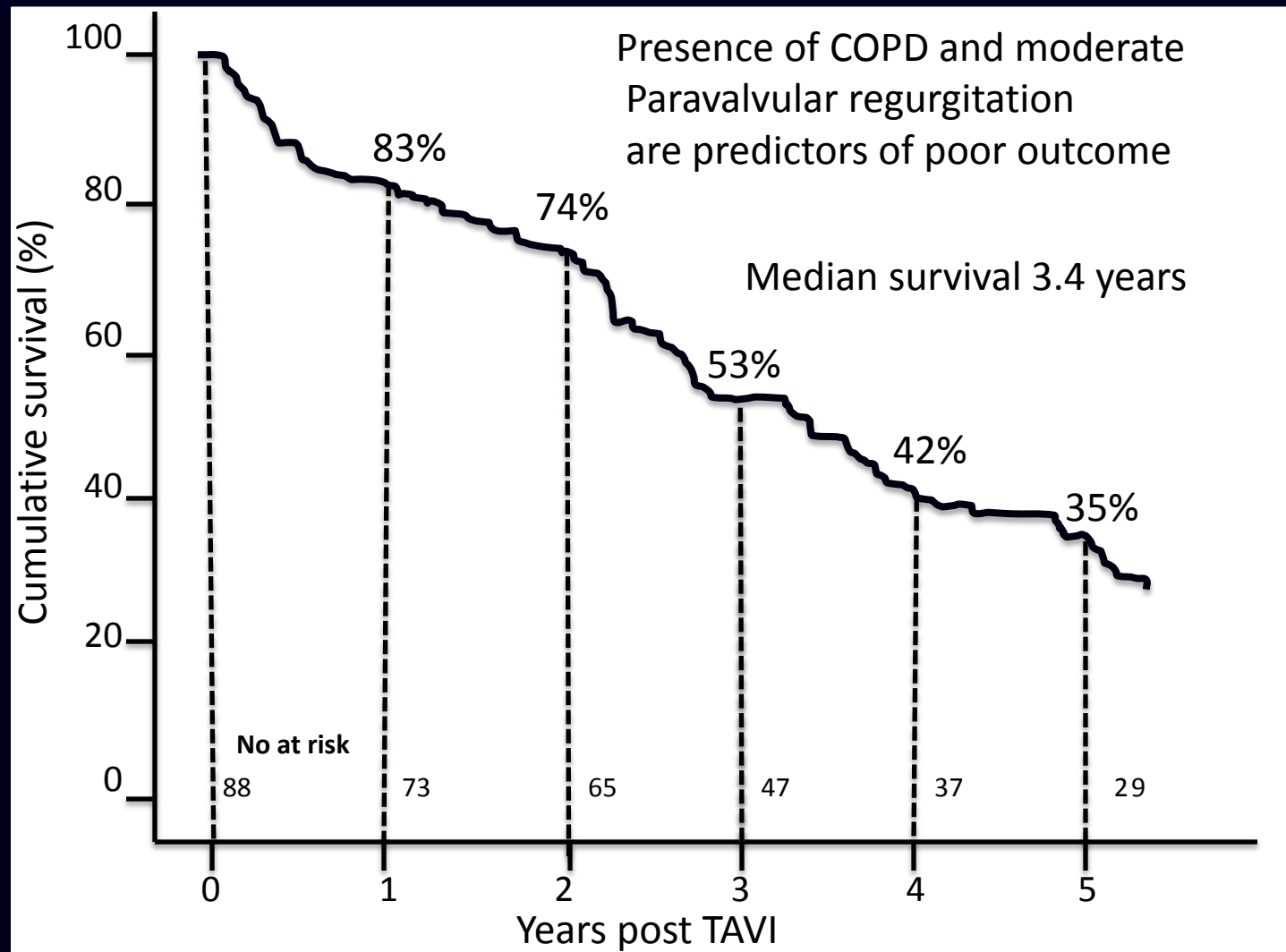


Superior view



Cumulative Survival following TAVI over a 5-year period

(88 patients (mean age 83 ± 7 years) >30 days)

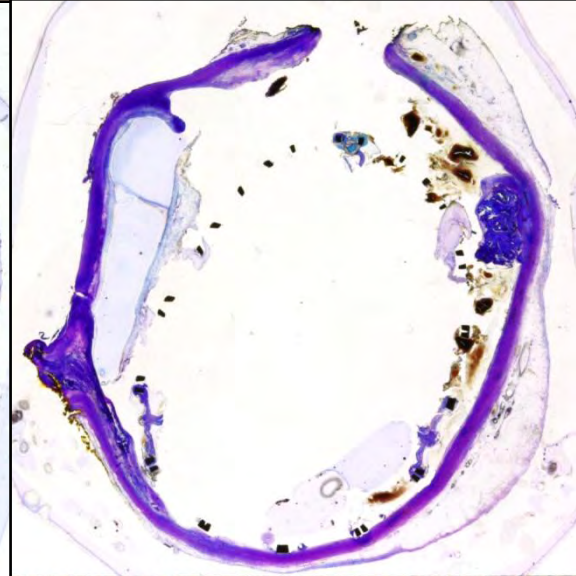
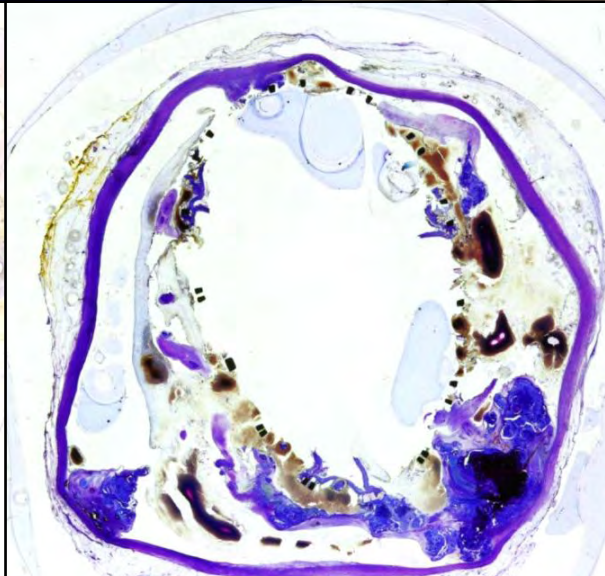
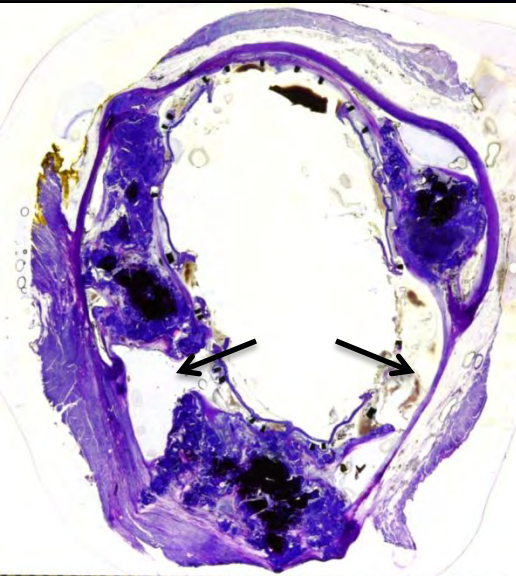
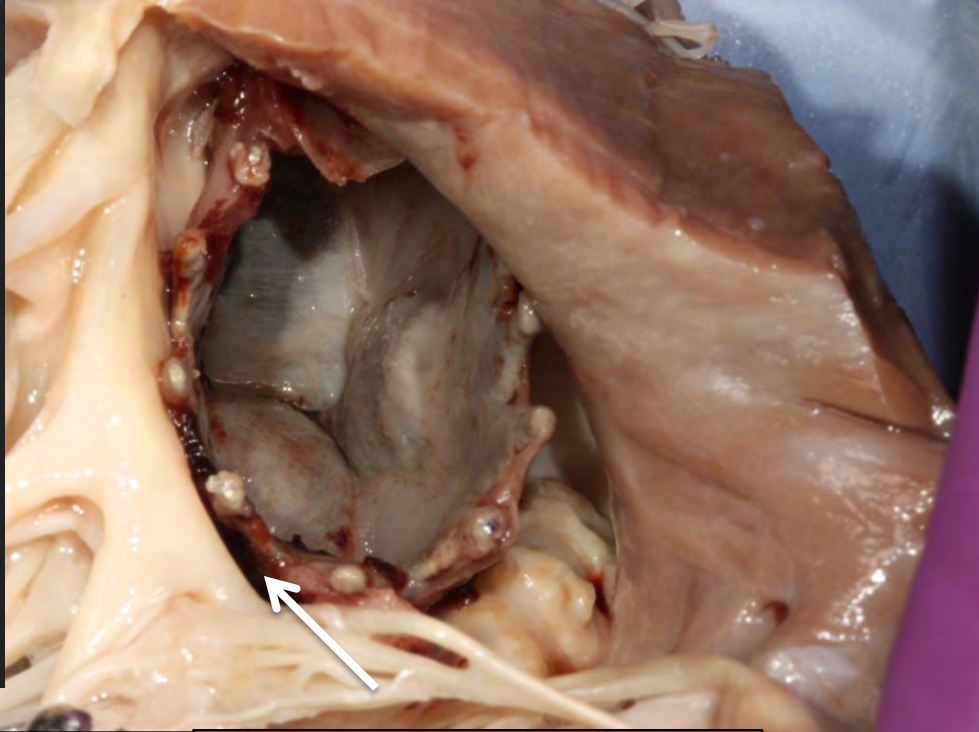
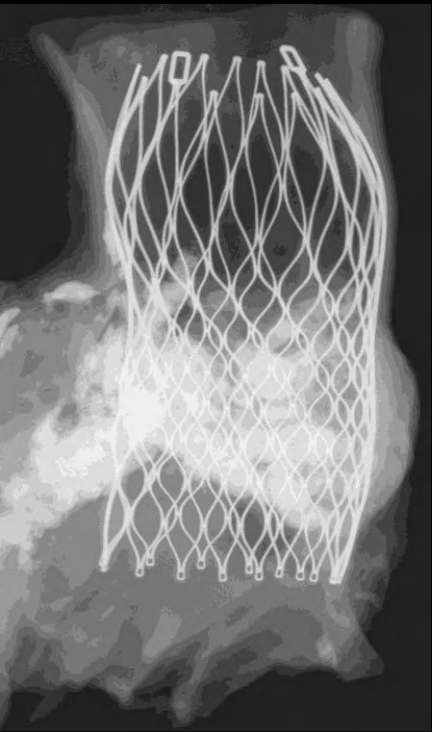


At 5 years 3 patients (3.4%) showed signs of prosthetic valve failure: 1 had moderate regurgitation and moderate stenosis (aortic valve area 1.2 mm^2 ; mean gradient 26 mm Hg); 1 had moderate regurgitation and the third had moderate stenosis (valve area 1.1 mm^2 ; gradient 23 mm Hg)

Toggweiler S, Webb JG, et al. *J Am Coll Cardiol* 2013;61(4): 413-9

Aortic valve prosthesis associated complications

Prosthesis associated complication	Surgical Valve	TAVI
Thrombosis/thromboembolism	1-4% per patient year (highest in first year)	Thrombus presence noted, failure rare but improves with coumadin
Infective endocarditis	1-6% (first several months) <i>staph epidermidis</i>	Rare
Structural valve deterioration	> 1% <5yrs 20-30% 5-10 years >50% within 15 years. Rate is lower in older patients > 65 years, 10% at 10 years	Mild Inflammation and platelet fibrin deposition of valve leaflets not uncommon, may be slightly higher than that reported in surgically implanted valves
Calcification	¾ degenerative failures caused by tears secondary to calcification: at 4 years most have some Ca++ depending on age of patient	Rarely reported in valves beyond 5 years
Non structural degeneration: Pannus	rare	Not uncommon but limited mostly to basal 1/3
Paravalvular leak	rare	Common upto 70%



72-year-old man with bicuspid aortic valve, COPD, and severe symptomatic AS. Death occurred 8th day from acute colitis and ventilator pneumonia.

Procedural Complications:

- Patient-Prosthesis mismatch
 - Malapposition/ valve displacement
 - Aortic root rupture/ dissection/ VSD
 - Cardiac perforation/ tamponade
 - Coronary occlusion
 - Paravalvular leak/ Aortic regurgitation
 - AV block – more accurate placement
 - Stroke
 - **Late complications** - thrombosis and calcification
- Perhaps we need to be more selective in those who under go TAVI procedure if we want to reduce the incidence of paravalvular leak, especially if one leaflet is heavily calcified and in patient with heavy mitral annular calcification
 - Distal capture during procedure
 - Improve anticoagulant therapy to reduce incidence of stroke – especially those older than 70-years
- All cause mortality must be monitored and when ever possible autopsy should be performed to monitor cause of death as well as valve deterioration

Acknowledgments

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Laura Abu

Paul Yates

Youhui Liang, MD

Abebe Atiso, HT

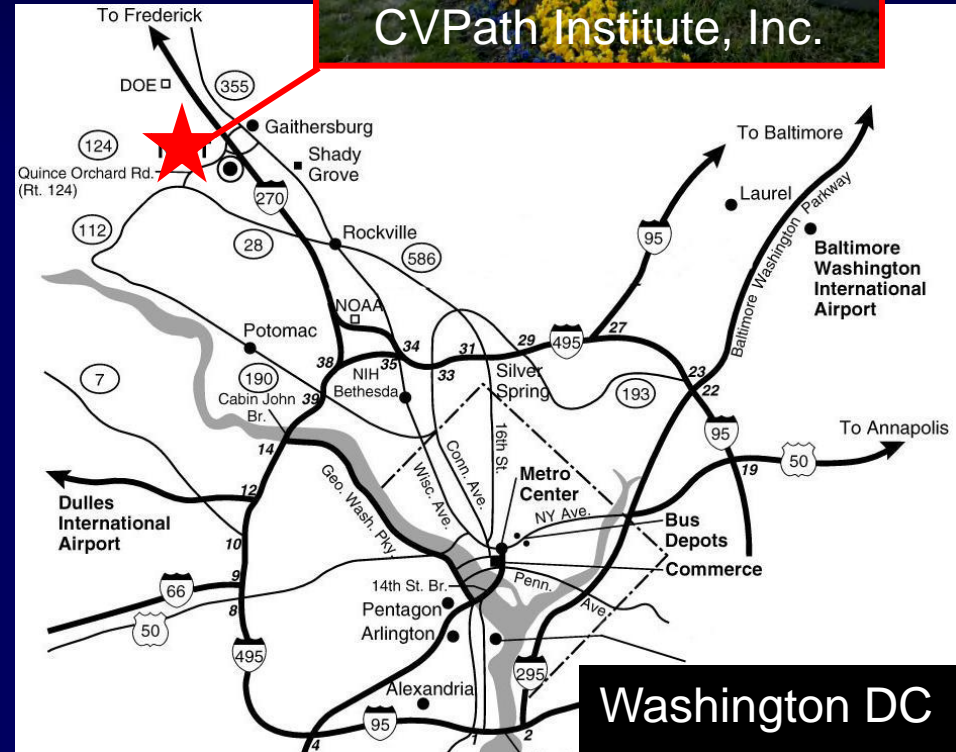
Jinky Beyer

Giselle Magsalin

Hedwig Avallone, HT

Lila Adams, HT

Hengying Ouyang, MD



Complications of PAVR

- 1). Acute structural valve failure
 - Valve remaining immobile in the open position
- 2). Non-structural valve failure
 - Paravalvular aortic regurgitation
 - Valvular AS/AR - thrombosis
 - Malapposition including valve migration
 - Acute coronary occlusion
 - Cardiac tamponade
 - Aortic annular tear
 - Vascular injury (including access site injury)
 - Acute heart block
 - Stroke
- 3). Procedure related

Factors Other than Prosthetic Heart Valve (PHV) that Determines Outcome After PHV

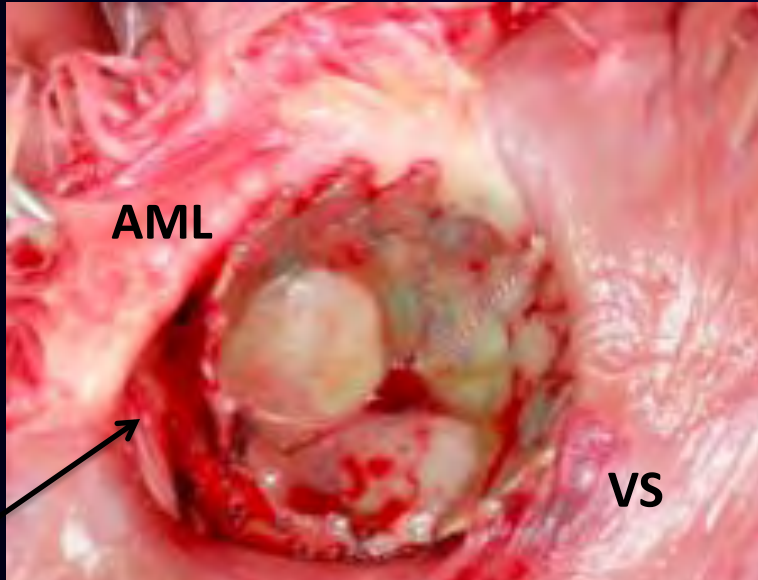
- Decade of Age
- Other valve disease
- Complications of prosthetic heart valve
- Co-morbid conditions
- Cardiac
 - LV dysfunction (systolic and diastolic), heart failure, NYHA functional class III and IV, CAD, myocardial infarction, CABG, arrhythmias (e.g., atrial fibrillation), pulmonary hypertension, infective endocarditis
- Non-cardiac
 - Impaired renal function (creatinine clearance), renal dialysis, diabetes, hypertension, dyslipidemia, metabolic syndrome, smoking, liver disease, lung disease (e.g., COPD)

Pathology of Transcatheter (6 Cribier-Edwards and 11 Edwards Sapien) Valve Therapy

Group	Number of Cases	Type of death Cardiac vs. non-cardiac	Cause of cardiac death
Immediate-early (<7 days)	9	Cardiac causes 5; Cerebrovascular accident 1; major bleeding 2; sepsis in 1.	Cardiac causes 5: heart failure , major arrhythmia, rupture of adjacent structures, left main occlusion
Intermediate (7-29days)	4	Cardiac causes 3, and 1 sepsis	Cardiac causes 3 (details not given)
Late (\geq 30 days)	4	Cardiac and renal failure 3, 1 intracerebral bleed	Progressive heart failure and renal failure 3
Surgically excised valves: 108 to 336 days	3	Embolization at time of procedure, requiring surgery (108d); low implant –aortic regurgitation(109d); endocarditis (336d)	3 Post surgical

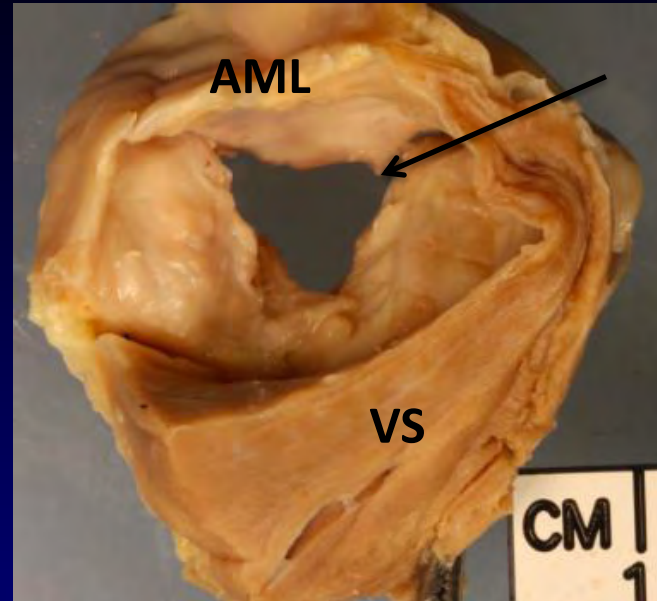
84-year old M with AS had CoreValve Implanted 22 days prior to death developed aortic regurgitation post TAVI.

Left ventricular out flow



Inferior view

Non-coronary cusp



Superior View

