TAVR in Bicuspid Aortic Valve

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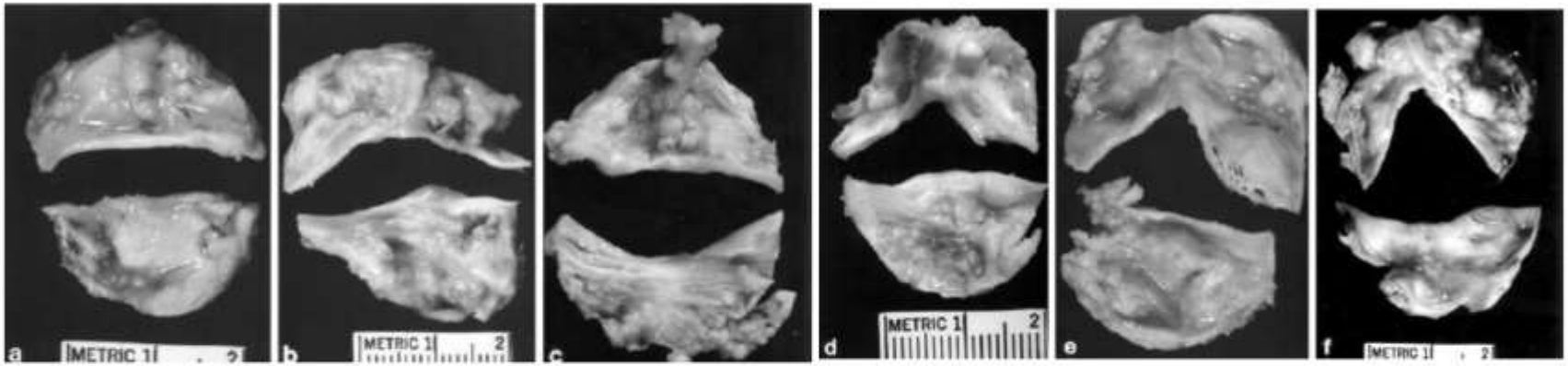
Bicuspid Aortic Valve disease and TAVR



1 to 2% incidence, 2 to 4 times more frequent in men

(Tzemos et al. JAMA 2008; 300:1317-25.)

Could be an heritable condition – mutation of gene NOTCH1

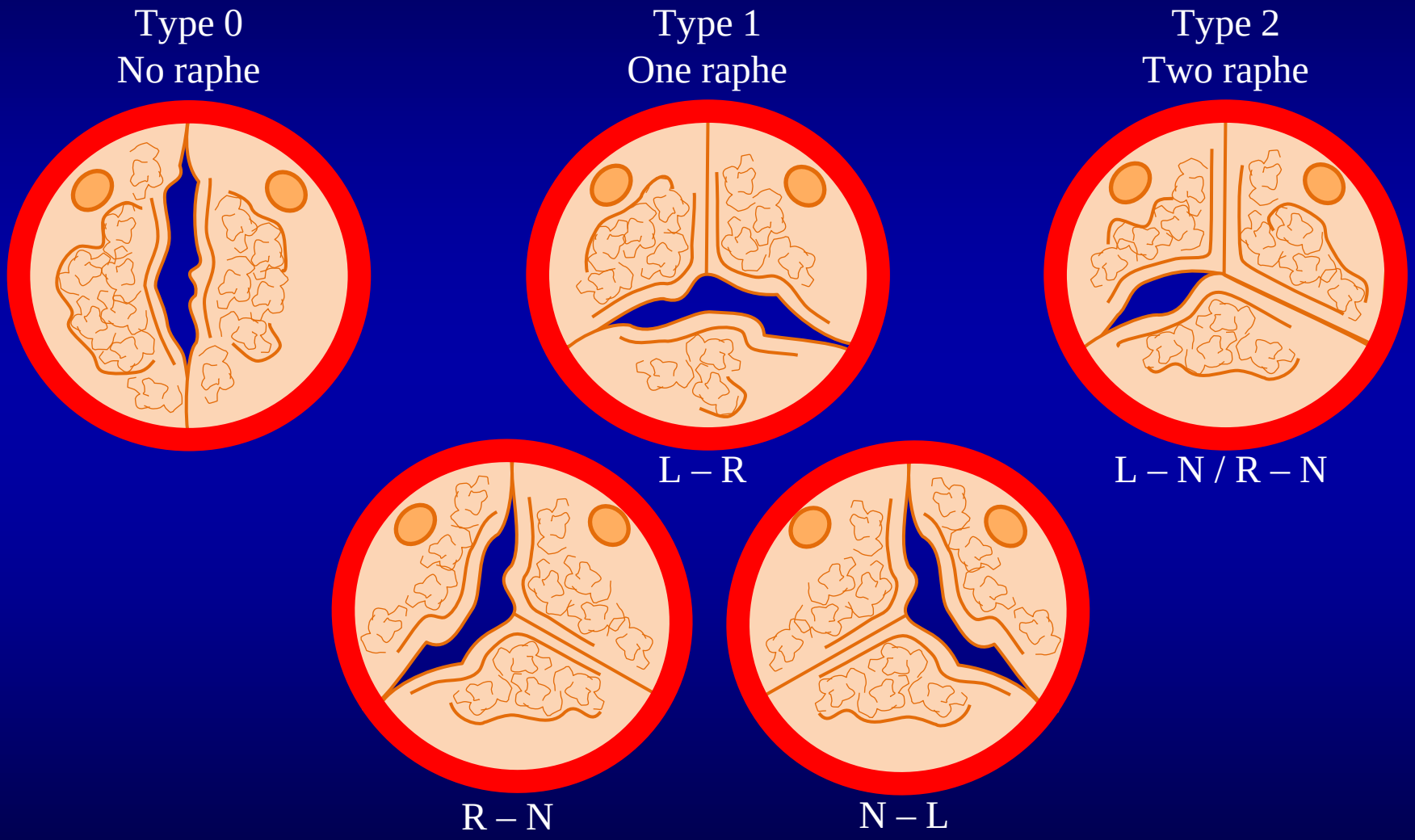
(Garg et al. Nature 2005; 437: 270-4)

High Frequency in patients having sAVR (62% < 70y / 38% > 80y

(Roberts et al. Circulation 2005; 111: 920-5)

From T. Lefevre; TVT 2015

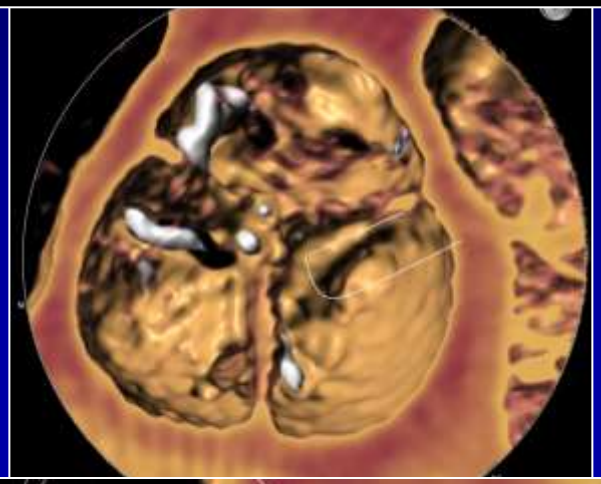
Siever's classification

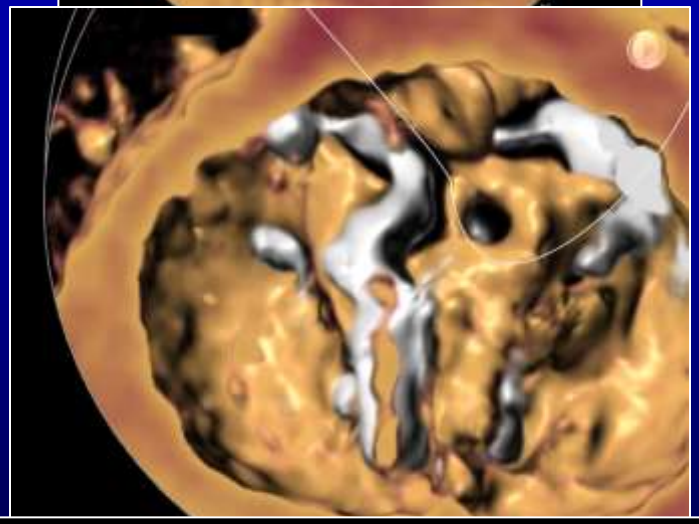


Sievers et al. J Thorac Cardiovasc Surg 2007;133:1226-33.

Heterogeneity – need for an alternative classification?

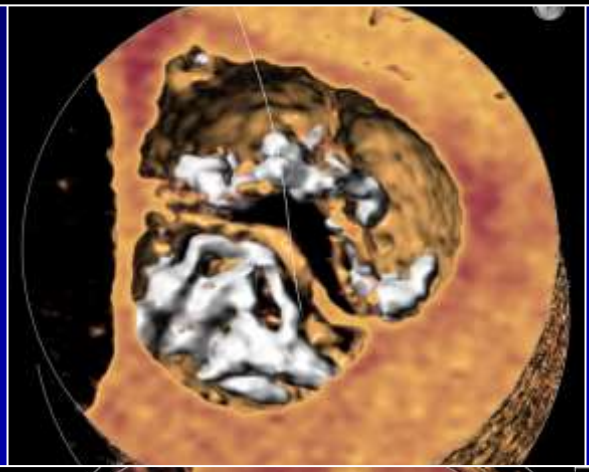
Tricuspid, tricommissural
Partial leaflet fusion (not BAV)

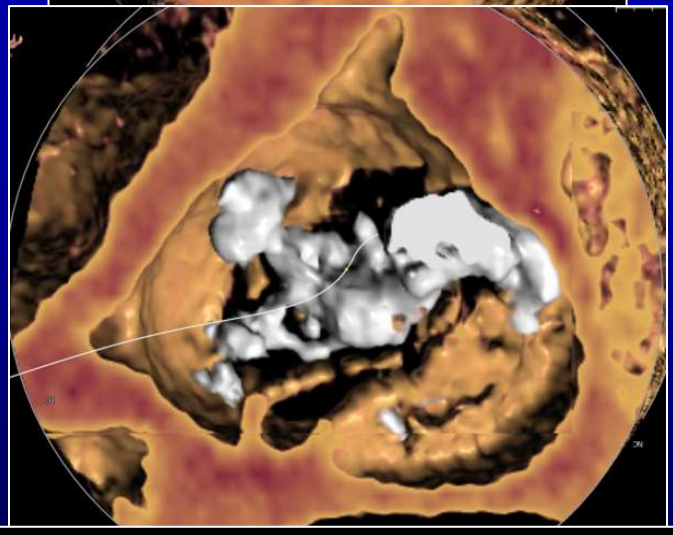




Bicuspid, bicommissural
(no raphe)

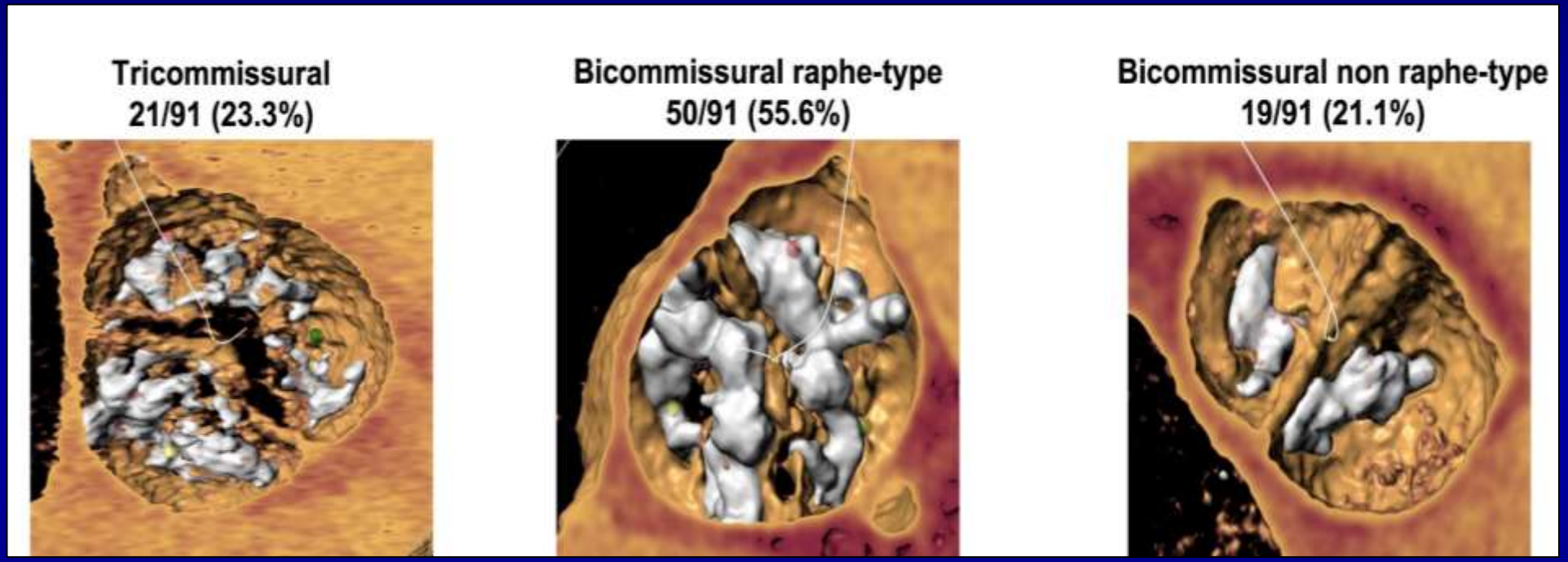
Bicuspid, tricommissural
(functional BAV)





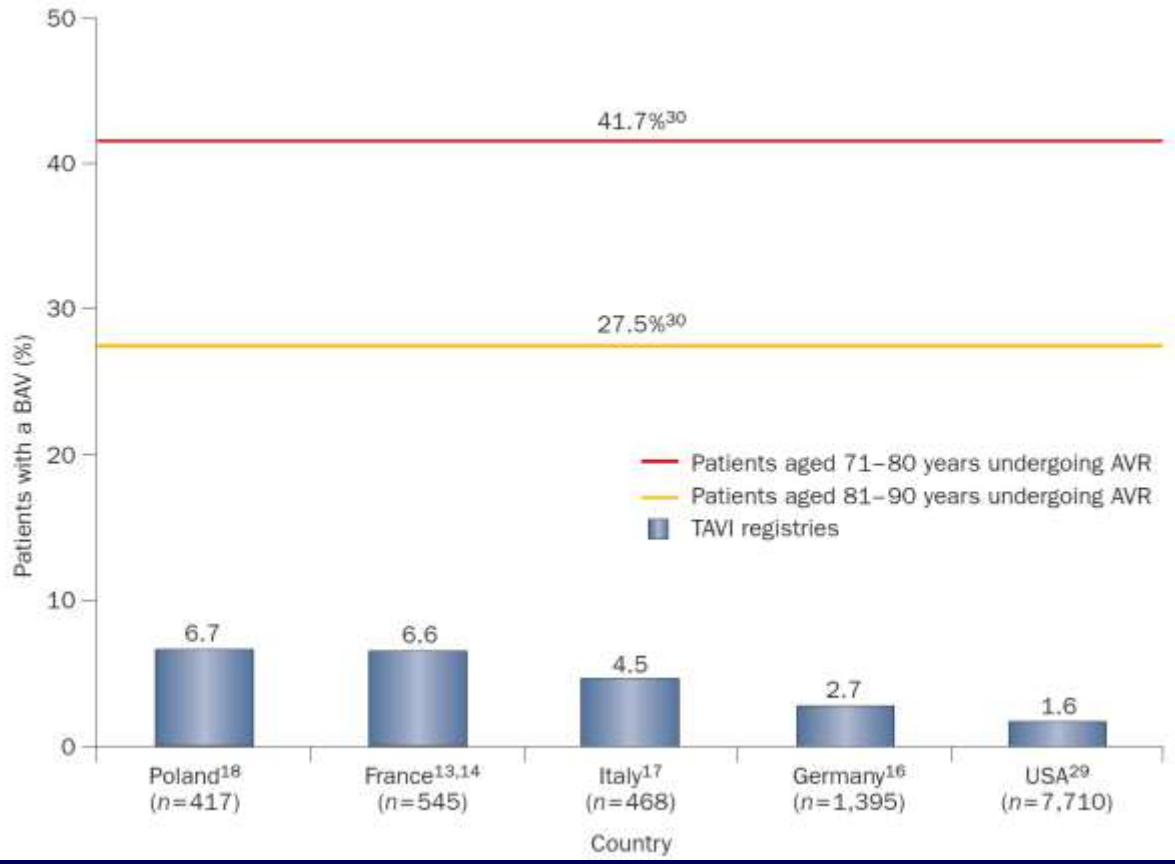
Bicuspid, bicommissural
(raphe present)

A simplified anatomical classification for TAVI (describe what you see)



Jilaihawi H. et al. JACC: Cardiovascular Imaging 2016 (in Press)

Prevalence of bicuspid aortic valve in TAVR studies is less than SAVR studies



- **Less than 7% of patients with bicuspid aortic valve in TAVR registries**
- **Septugenerians undergoing SAVR: 41.7%**
- **Octogenerians undergoing SAVR: 27.5%**

Zhao ZG. et al. Nature Reviews in Cardiology 2015

Prevalence of bicuspid valve in patients undergoing isolated AVR-almost 50%!

Operatively excised, stenotic aortic valves from 932 patients aged 26 to 91 years

Aortic Valve Structure	Cases, n (%)	Ages (y) of Patients by Decades at Time of Aortic Valve Replacement							
		21–30	31–40	41–50	51–60	61–70	71–80	81–90	91–100
Men									
Unicuspid	34 (6)	3	4	11	8	4	4	0	0
Bicuspid	309 (53)	1	4	20	54	111	94	24	1
Tricuspid	234 (40)	0	0	0	14	50	119	51	0
Uncertain	7 (1)	0	0	0	0	3	2	2	0
Subtotals, n (%)	584 (100)	4 (<1)	8 (1)	31 (5)	76 (13)	168 (29)	219 (38)	77 (13)	1 (<1)
Women									
Unicuspid	12 (3)	1	2	3	1	4	1	0	0
Bicuspid	149 (43)	1	5	10	20	44	55	14	0
Tricuspid	183 (53)	0	0	2	11	43	79	47	1
Uncertain	4 (1)	0	0	1	0	0	3	0	0
Subtotals, n (%)	348 (100)	2 (<1)	7 (2)	16 (5)	32 (9)	91 (26)	138 (46)	61 (18)	1 (<1)

Values in parentheses are percentages.

Roberts WC. et al. Circulation 2005

If almost 50% of the patients undergoing surgery are bicuspid (y), for expansion of TAVR it is imperative that these technologies work in bicuspid anatomy

Aortic Annulus and Root Characteristics in Severe Aortic Stenosis due to Bicuspid Aortic Valve and Tricuspid Aortic Valves: Implications for Transcatheter Aortic Valve Therapies

Bicuspid AV vs. tricuspid AV CT characteristics

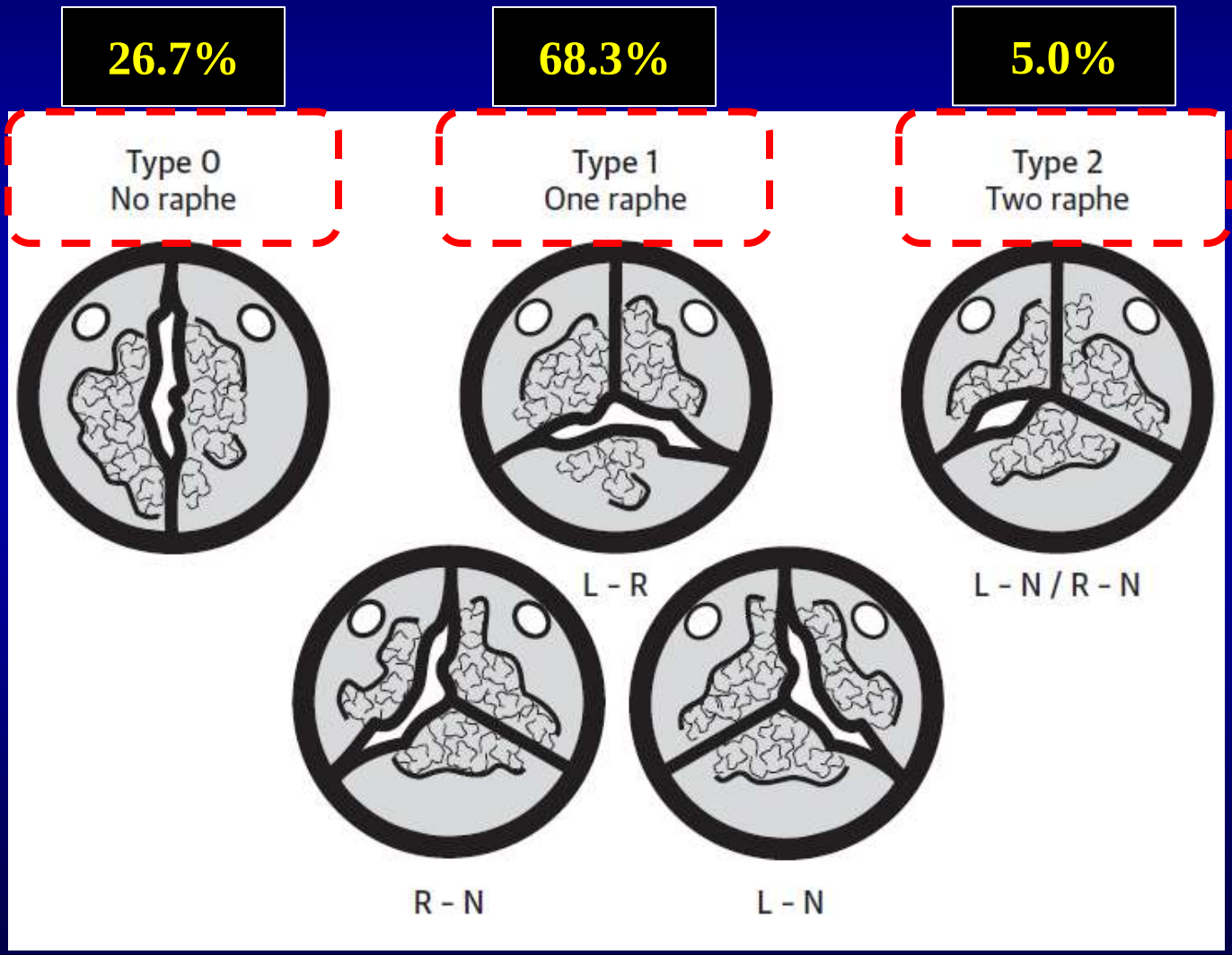
- Larger annulus
- Larger STJ
- Larger ascending aorta
- More eccentric calcium
- Less elliptical annulus

Philip F. et al. CCI 2015

Characteristics	Tricuspid aortic valve $N=200$	Bicuspid aortic valve $N=200$	P value
Annulus			
Area (mm^2)	463 (106)	521 (102)	<0.00 1
Diameter max	27 (3.4)	28.3 (3.6)	<0.001
Diameter min	21 (2.9)	23 (3.2)	<0.001
Δ Diameter	5.3 (2.8)	4.1 (5.4)	0.22
Ellipticity index	1.29 (0.1)	1.24 (0.1)	0.002
Circularity	21 (4)	78 (39)	<0.001
Eccentric calcification	64 (32)	136 (68)	<0.001
Sinus			
Perimeter	106 (15)	116(18)	<0.001
Diameter, left coronary cusp	30.8 (3.0)		
Diameter, right coronary cusp	28.6 (3.3)		
Diameter, non-coronary cusp	31.2 (3.3)		
Height, left coronary cusp	22 (3.6)	22 (5)	0.8
Height, right coronary cusp	23 (3.3)	22 (5)	0.8
Height, non-coronary cusp	21.3 (3.1)	24 (6)	<0.006
Sino-tubular Junction			
Perimeter	85.5 (12.3)	99.5 (20.3)	<0.001
Diameter	27.2 (3.9)	31.9(5.7)	<0.001
Coronary ostia			
Height, left coronary artery	14.1 ± 3.2	14.9 ± 5.7	0.14
Height, right coronary artery	16.4 ± 4.5	16.3 ± 5.3	0.14
Long axis diameter (mm)	26.9 ± 7	27.4 ± 5	0.76
Ascending aorta			
Area (mm^2)	688 (133)	740 (132)	<0.001
Diameter	29.8 (3.6)	36.9 (8)	<0.001

Transcatheter Aortic Valve Replacement in Bicuspid Aortic Valve Disease

Multicenter registry of TAVR in bicuspid aortic stenosis



139 patients undergoing TAVR

Balloon-expandable (n=48); self-expanding (n=91)

Mylotte D. et al. JACC 2014

Transcatheter Aortic Valve Replacement in Bicuspid Aortic Valve Disease

Multicenter registry of TAVR in bicuspid aortic stenosis

Characteristic	All Patients (n = 139)	Sapien (n = 48)	CoreValve (n = 91)	p Value
TAV size, mm	27.8 ± 2.2	26.3 ± 2.2	28.5 ± 1.8	0.0002
23 mm	10 (7.2)	10 (20.8)	-	-
26 mm	50 (36.0)	23 (47.9)	27 (29.7)	0.04
29 mm	59 (42.4)	15 (31.3)	44 (48.4)	0.07
31 mm	20 (14.4)	-	20 (22.0)	-
MSCT cover index, %	13.2 ± 9.1	8.9 ± 5.7	16.3 ± 9.8	<0.0001
MSCT-based TAV sizing	88 (63.3)	37 (77.1)	51 (56.0)	0.02
Vascular access				
Femoral	109 (78.5)	30 (62.5)	79 (86.8)	0.002
Subclavian	5 (3.6)	-	5 (5.5)	-
Apical	12 (8.6)	12 (25.0)	-	-
Aortic	12 (8.6)	6 (12.5)	6 (6.6)	-
Carotid	1 (0.7)	-	1 (1.1)	-
General anesthesia	85 (61.1)	33 (68.8)	52 (57.1)	0.20
Balloon predilation	137 (98.6)	51 (100.0)	89 (97.8)	0.54
Predilation balloon size, mm	22.5 ± 2.1	21.9 ± 2.2	22.9 ± 2.0	0.008
Balloon postdilation*	25 (18.1)	5 (10.6)	20 (22.2)	0.11
Postdilation balloon size, mm*	26.5 ± 2.3	24.7 ± 2.5	26.8 ± 2.1	0.07
TAV malposition*	9 (6.5)	2 (4.3)	7 (7.8)	0.72
TAV embolization*	3 (2.2)	2 (4.3)	1 (1.1)	0.27
Need for 2nd TAV*	5 (3.6)	1 (2.1)	4 (4.4)	0.66
Tamponade	5 (3.6)	0	5 (5.7)	0.16
Aortic root rupture	1 (0.7)	1 (2.1)	0	-
Conversion to SAVR	3 (2.2)	2 (4.2)	1 (1.1)	0.30
Postimplantation echocardiography				
Aortic regurgitation, grade (1-4)*	1.1 ± 0.9	1.0 ± 0.9	1.1 ± 0.9	0.53
≥Grade 2	38 (28.4)	9 (19.6)	29 (32.2)	0.11
≥Grade 3	8 (6.0)	3 (6.5)	5 (5.5)	0.99
Aortic valve gradient, mm Hg*	11.4 ± 9.9	11.7 ± 8.7	11.3 ± 10.4	0.82
Aortic valve area, cm^2*	1.7 ± 0.5	1.6 ± 0.4	1.7 ± 0.5	0.23
Contrast media, ml	174 ± 88	176 ± 118	172 ± 81.5	0.17
Fluoroscopy duration, min	20 (14-28)	14 (9-25)	20 (15-29)	0.004

139 patients undergoing TAVR
Balloon-expandable (n=48); self-expanding (n=91)

- **Procedural mortality 3.6%**
- **Valve embolization 2.2%**
- **Conversion to SAVR 2.2%**
- **≥ 2+ AR in 28%**

Mylotte D. et al. JACC 2014

Transcatheter Aortic Valve Replacement in Bicuspid Aortic Valve Disease

Multicenter registry of TAVR in bicuspid aortic stenosis

CT based sizing is an independent predictor of post-TAVR AR

139 patients undergoing TAVR
Balloon-expandable (n=48); self-expanding (n=91)

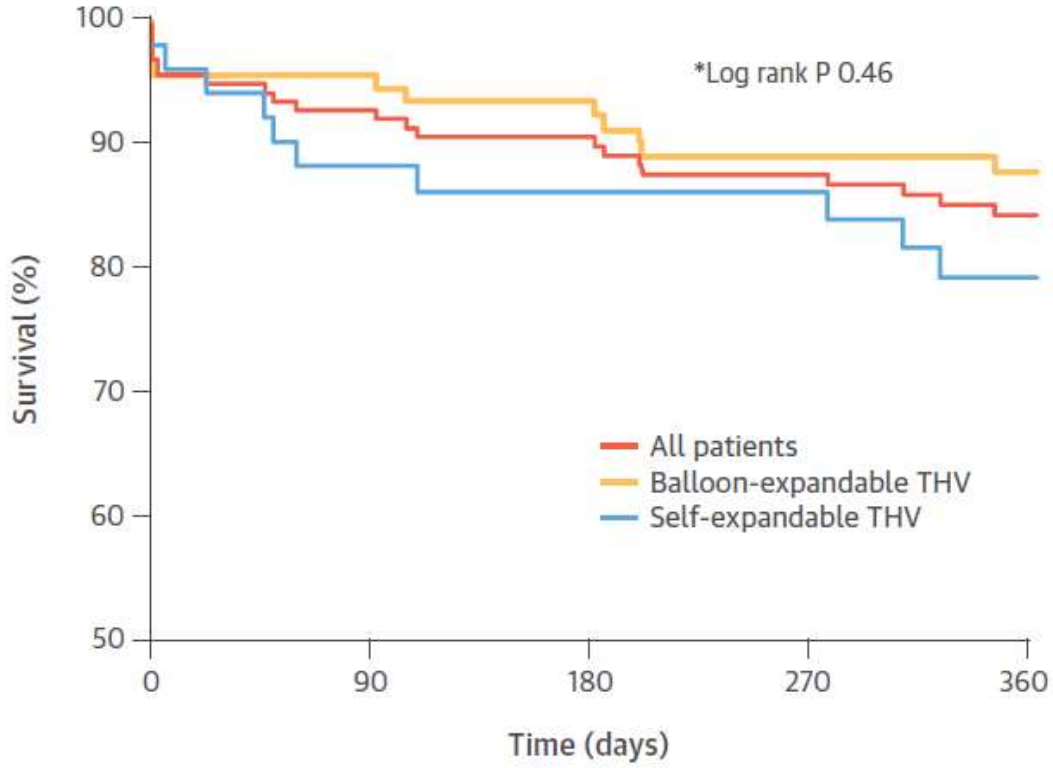
Characteristic	Univariate Analysis			Multivariate Analysis		
	Odds Ratio	95% CI	p Value	Odds Ratio	95% CI	p Value
Age	0.95	0.96-1.03	0.63			
Males	3.50	1.50-8.20	0.004	4.29	1.63-10.79	0.003
STS PROM	0.85	0.75-1.04	0.05	0.88	0.75-1.04	0.13
Mean aortic gradient	0.99	0.97-1.02	0.61			
Aortic valve area	3.20	0.34-29.86	0.31			
LV ejection fraction <40%	1.40	0.62-3.14	0.41			
Annulus size	0.93	0.82-1.04	0.20			
TAV size	1.10	0.92-1.31	0.31			
MSCT-based TAV sizing	0.23	0.10-0.51	<0.0001	0.19	0.08-0.45	<0.0001
Bicuspid type 1	2.14	0.82-5.56	0.11			
CoreValve	1.93	0.82-4.54	0.13			
Year of procedure	0.78	0.60-1.03	0.08			

Mylotte D. et al. JACC 2014

Transcatheter Aortic Valve Replacement in Bicuspid Aortic Valve Disease

Multicenter registry of TAVR in bicuspid aortic stenosis

139 patients undergoing TAVR
Balloon-expandable (n=48); self-expanding (n=91)



Patients at risk

All patients	139	130	125	114	106
Balloon-expandable THV	48	42	38	36	35
Self-expandable THV	91	88	85	78	73

1-year mortality 17.5%

Mylotte D. et al. JACC 2014

Bicuspid Aortic Valve Stenosis

Favorable Early Outcomes With a Next-Generation Transcatheter Heart Valve in a Multicenter Study

Multicenter registry of Sapien3 valve in bicuspid aortic stenosis

TABLE 4 30-Day Clinical Events (N = 51)*

Mortality	2 (3.9)
Myocardial infarction	0 (0)
Stroke, total events	1 (1.9)
Disabling stroke	0 (0)
Nondisabling stroke	1 (1.9)
Bleeding, total events	14 (27.5)
Life-threatening	2 (3.9)
Major	3 (5.9)
Minor	9 (17.6)
Vascular complications, total events	7 (13.7)
Major	2 (3.9)
Minor	5 (9.8)
Acute kidney injury ≥2	1 (1.9)
New permanent pacemaker†	12 (23.5)
Device 30-day safety endpoint	6 (11.7)

51 patients from 8 medical centers

- **30-day mortality 3.9%**
- **Pacemaker 23.5%**
- **Post-dilation 7.8%**
- **Conversion to SAVR 0%**

Perlman et al. JACC: Cardiovascular Interventions 2016

Bicuspid Aortic Valve Stenosis

Favorable Early Outcomes With a Next-Generation Transcatheter Heart Valve in a Multicenter Study

Multicenter registry of Sapien3 valve in bicuspid aortic stenosis

No cases of moderate-severe AR

51 patients from 8 medical centers

	All Patients (N = 51)	Oversizing >10% (n = 26)	Oversizing <10% (n = 25)	p Value
Aortic valve mean gradient, mm Hg	11.2 ± 4.7	11.4 ± 5.0	11.0 ± 4.5	0.76
Aortic valve peak gradient, mm Hg	22.0 ± 8.2	23.3 ± 8.3	20.8 ± 8.3	0.29
Aortic valve area, cm^2	1.68 ± 0.32	1.78 ± 0.33	1.56 ± 0.27	0.01
Aortic regurgitation				
None/trivial	32 (62.8)	19 (73.1)	13 (52.0)	0.10
Mild	19 (37.2)	7 (26.9)	12 (48.0)	0.10
Moderate	0 (0)	0 (0)	0 (0)	1.0
Severe	0 (0)	0 (0)	0 (0)	1.0
Left ventricular ejection fraction <40, %	10 (19.6)	3 (11.5)	7 (28.0)	0.17
Mitral regurgitation ≥ moderate, %	1 (1.9)	0 (0)	1 (4.0)	1.0

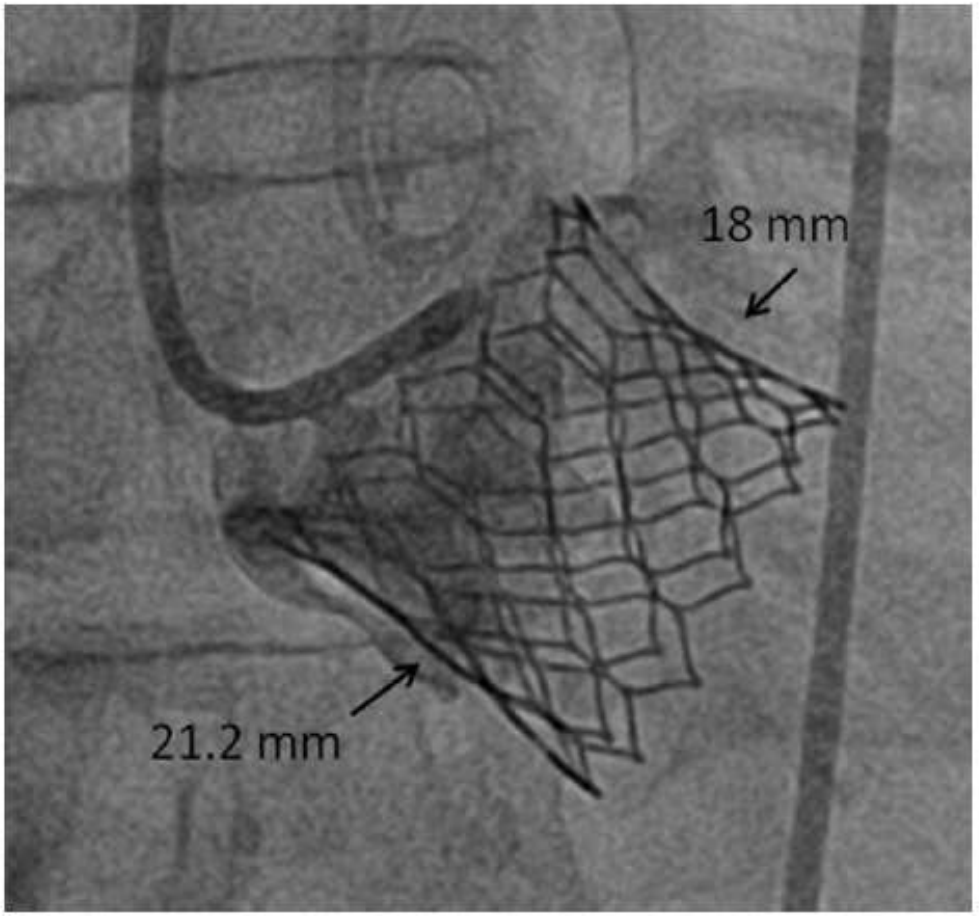
Perlman et al. JACC: Cardiovascular Interventions 2016

Bicuspid Aortic Valve Stenosis

Favorable Early Outcomes With a Next-Generation Transcatheter Heart Valve in a Multicenter Study

Multicenter registry of Sapien3 valve in bicuspid aortic stenosis

FIGURE 2 Asymmetric Valve Expansion



51 patients from 8 medical centers

Asymmetric frame expansion noted in 38% of the patients

No correlation between asymmetric expansion and pacemaker/AR rates

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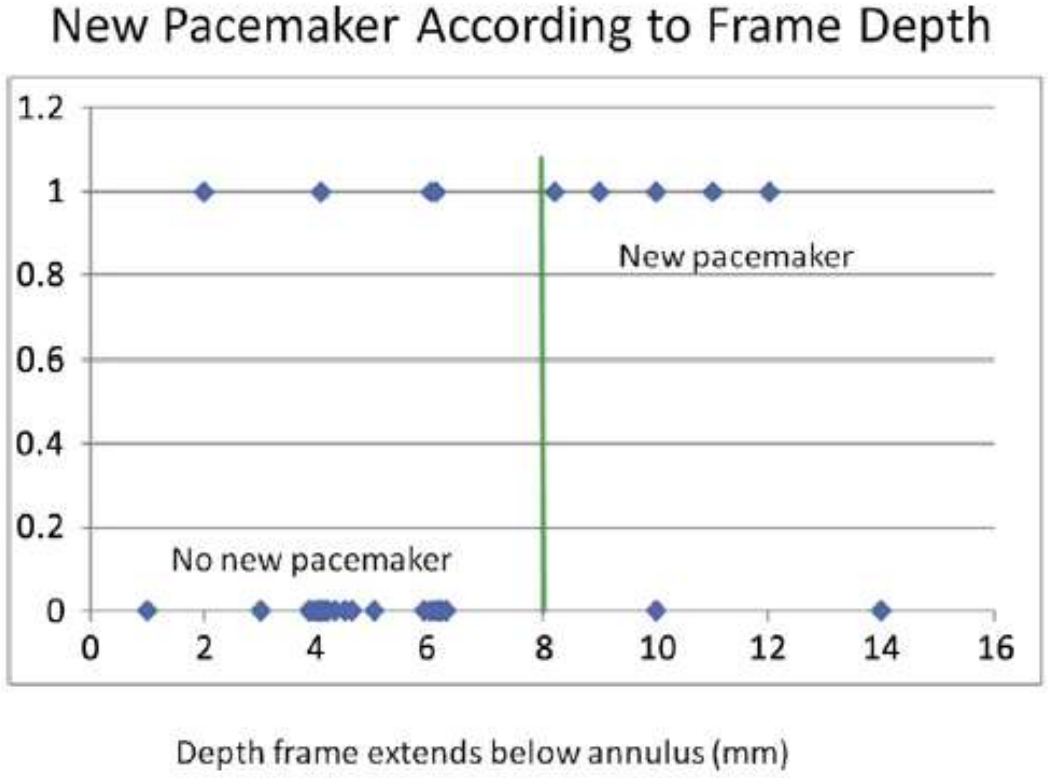
Bicuspid Aortic Valve Stenosis

Favorable Early Outcomes With a Next-Generation Transcatheter Heart Valve in a Multicenter Study

Multicenter registry of Sapien3 valve in bicuspid aortic stenosis

51 patients from 8 medical centers

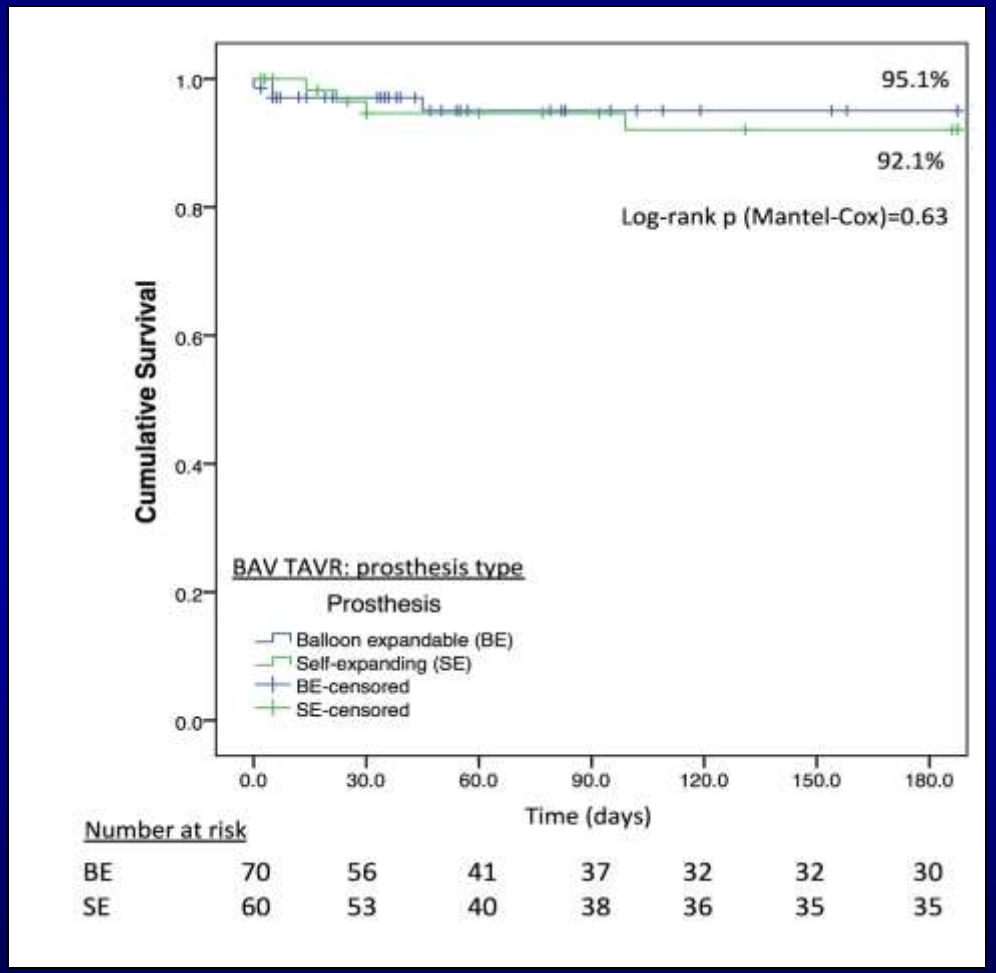
FIGURE 3 Valve Frame Implantation Depth in Relation to the Need for a New Pacemaker



Pacemaker rates high (23.5%) and related to the depth of implantation

Perlman et al. JACC: Cardiovascular Interventions 2016

Multicenter registry of TAVR in bicuspid aortic stenosis



130 patients undergoing TAVR in 14 medical centers

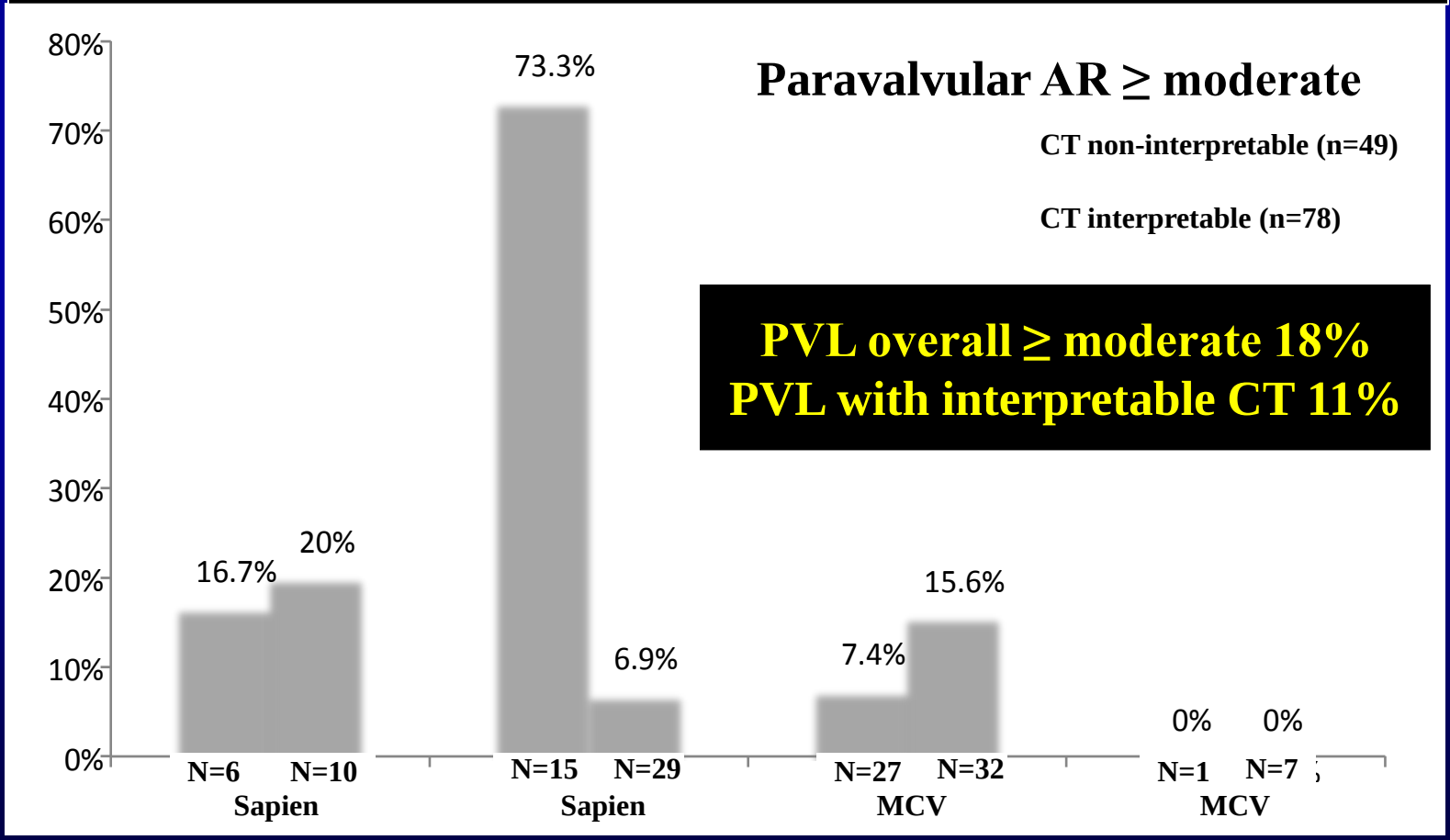
Balloon-expandable (n=70); self-expanding (n=60)

30-day mortality 3.8%

Jilaihawi H. et al. JACC: Cardiovascular Imaging 2016 (In press)

Lack of interpretable baseline CT for annular measurement predicts PVL in bicuspid aortic stenosis

130 patients undergoing TAVR in 14 medical centers
Balloon-expandable (n=70); self-expanding (n=60)



Jilaihawi H. et al. JACC: Cardiovascular Imaging 2016 (In press)

Reported series of bicuspid aortic stenosis treated with TAVR

Study/First Author (Year)	n	Multicenter	Balloon/Self-Expandable, %	30-Day Mortality, %	Device Success, %*	AR > Mild, %	New Pacemaker, %
Current (2016)	51	Yes	100/0	3.9	98	0	23.5
Mylotte et al. (2014)	139	Yes	35/65	5	89.9	28.4	23.2
Yousef et al. (2015)	108	Yes	56/44	8.3	85.2	30.8	19.4
Bauer et al. (2014)	38	Yes	32/68	11	NR	25	17
Kochman et al. (2014)	28	Yes	18/82	4	93	32	29
Hayashida et al. (2013)	21	No	52/48	4.8	100	19	14.3
Himbert et al. (2012)	15	No	0/100	7	NR	13	40
Wijesinghe et al. (2010)	11	Yes	100/0	18	NR	27	NR

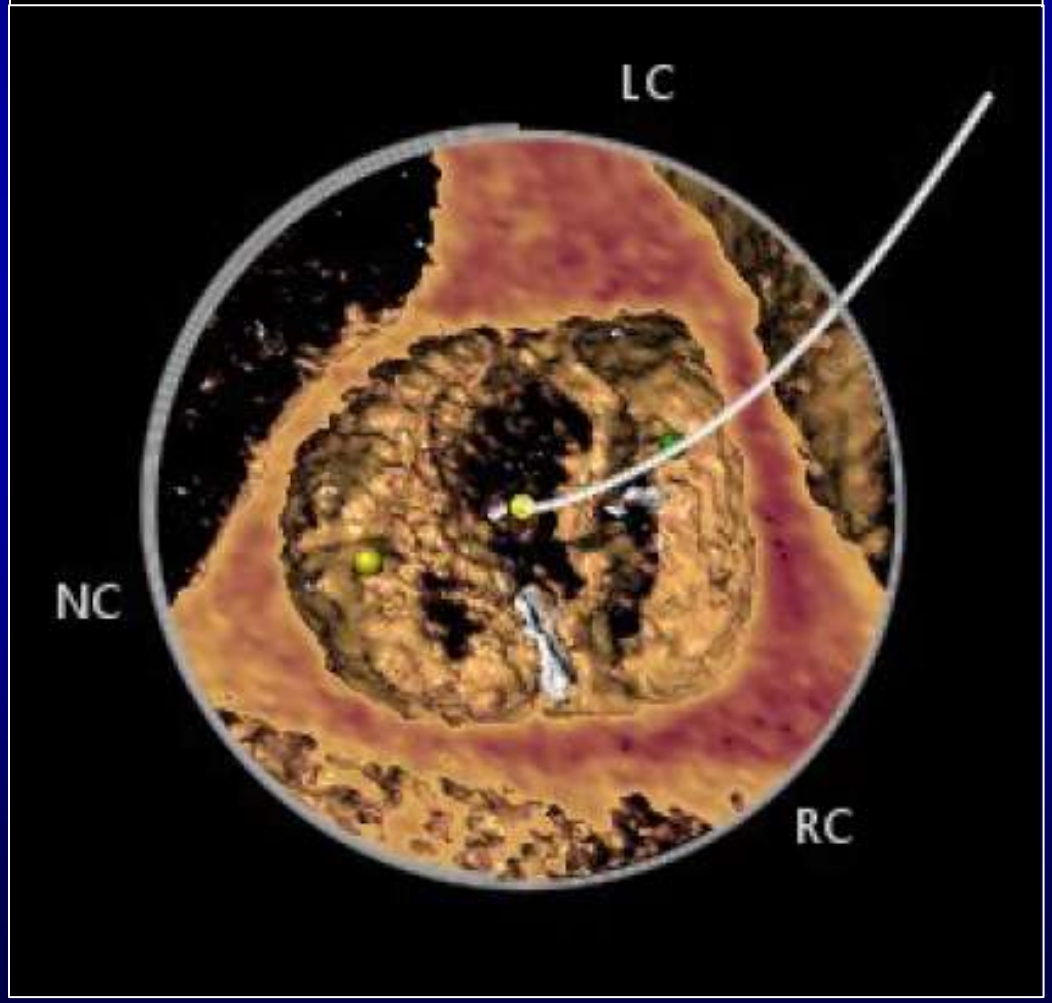
Perlman G. et al. JACC: Cardiovascular Interventions 2016

The “easy case”: Little calcium, No Raphe

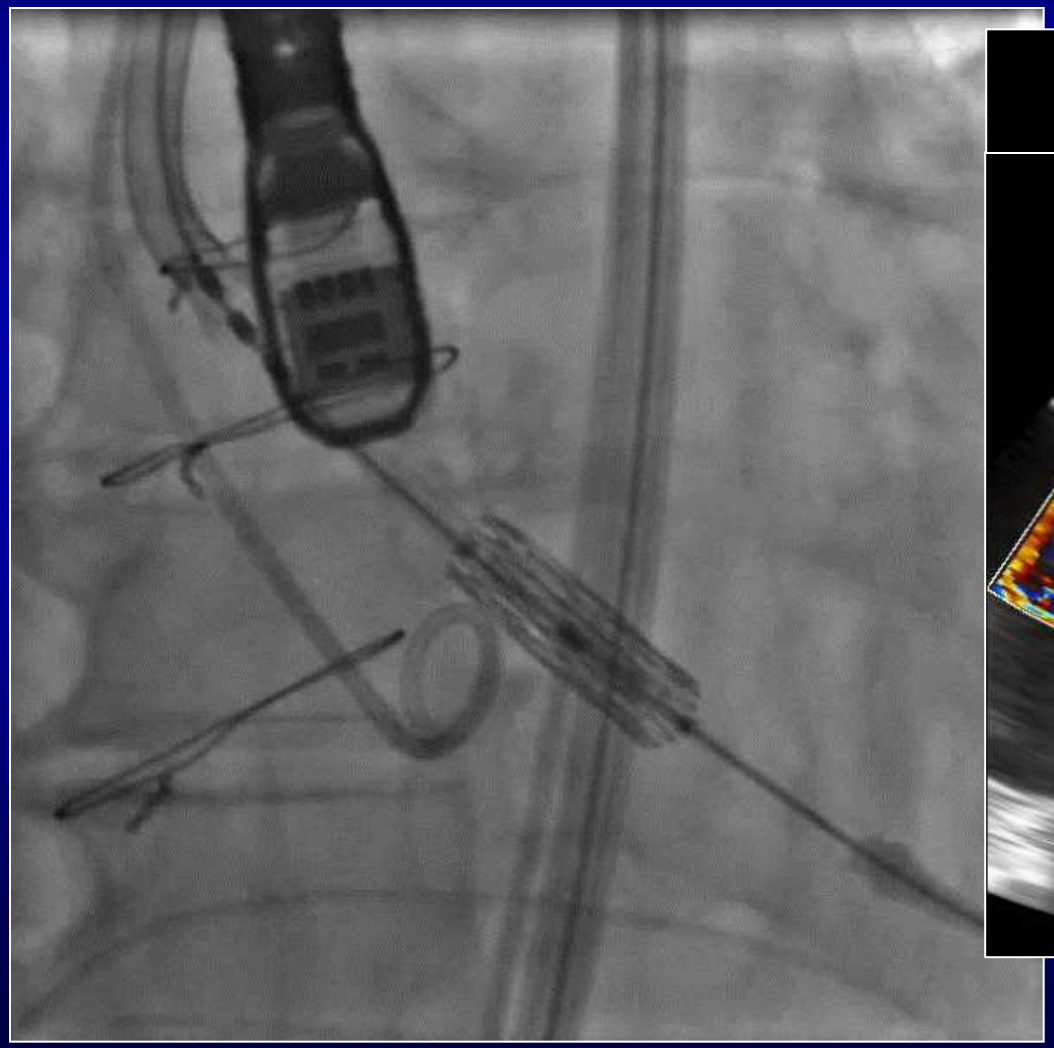
60 y/o female undergoing TAVR

Annulus Area 356.2 mm²
Dmin 18.3, Dmax 24.8 mm

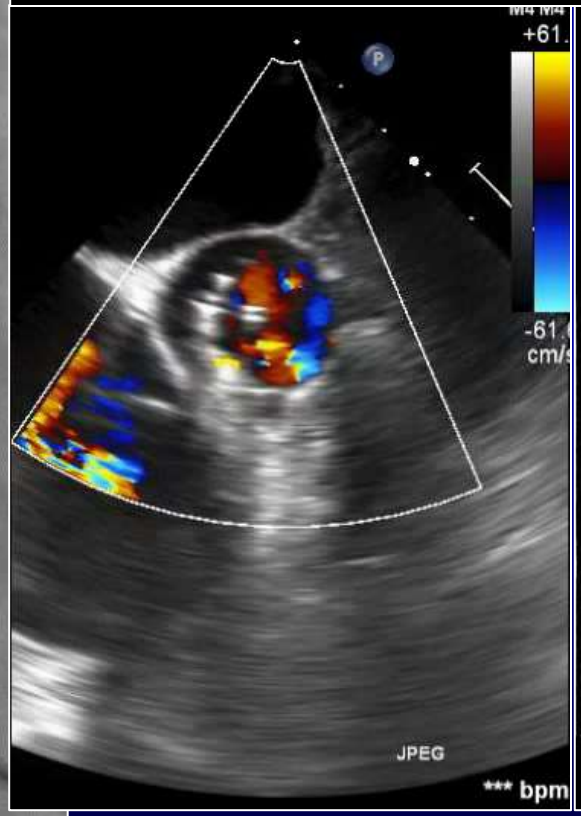
Congenital bicuspid aortic valve
Minimal calcification

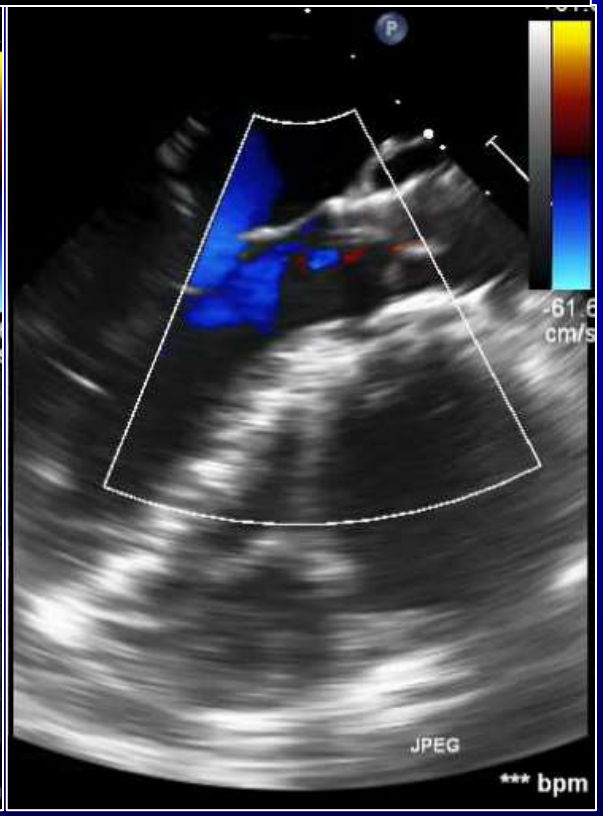


TAVR with 23mm Sapien3 performed



Trace paravalvular AR

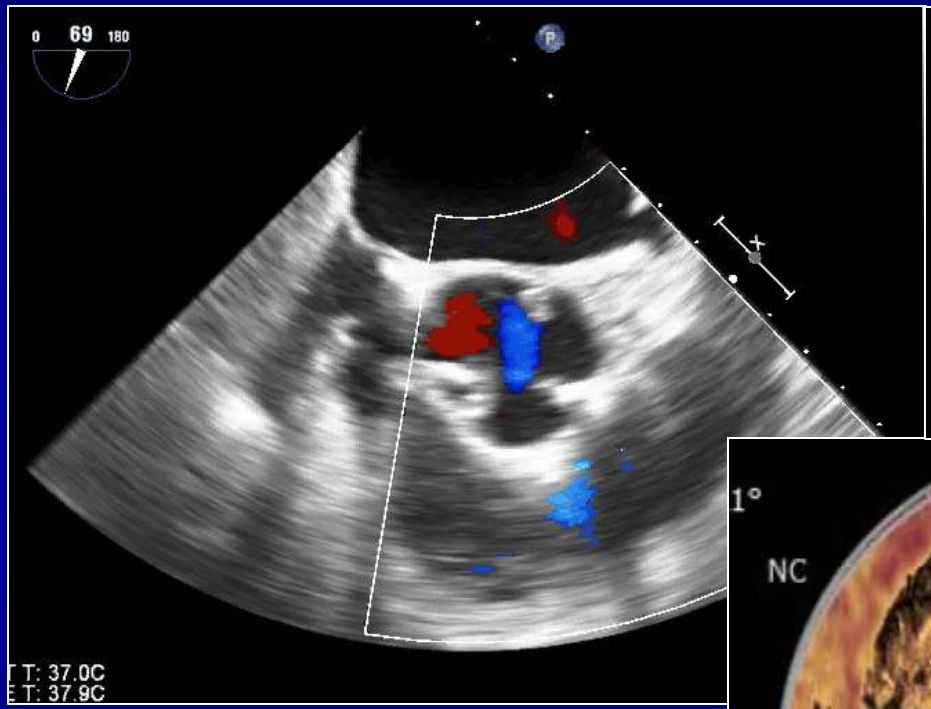




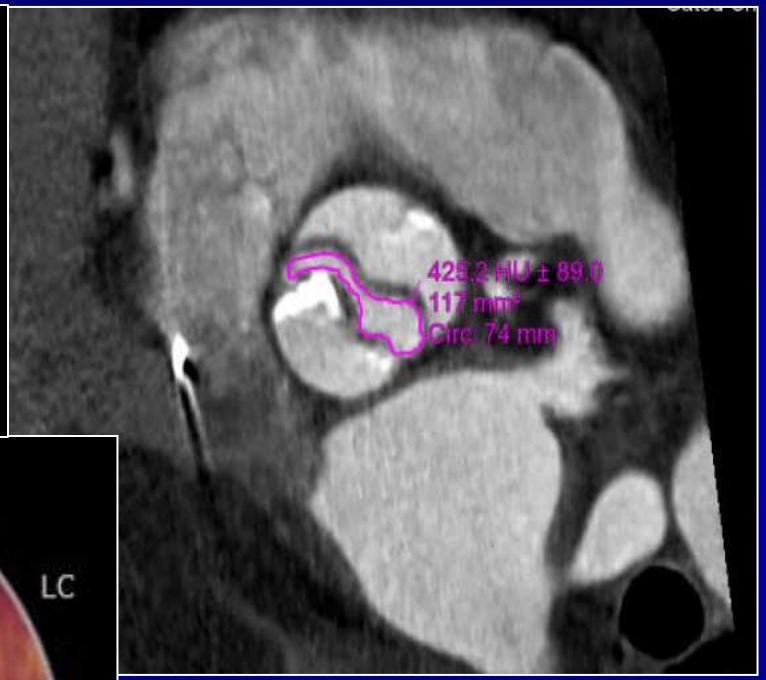
The “ok case”: Little calcium, Moderate Calcified Raphe

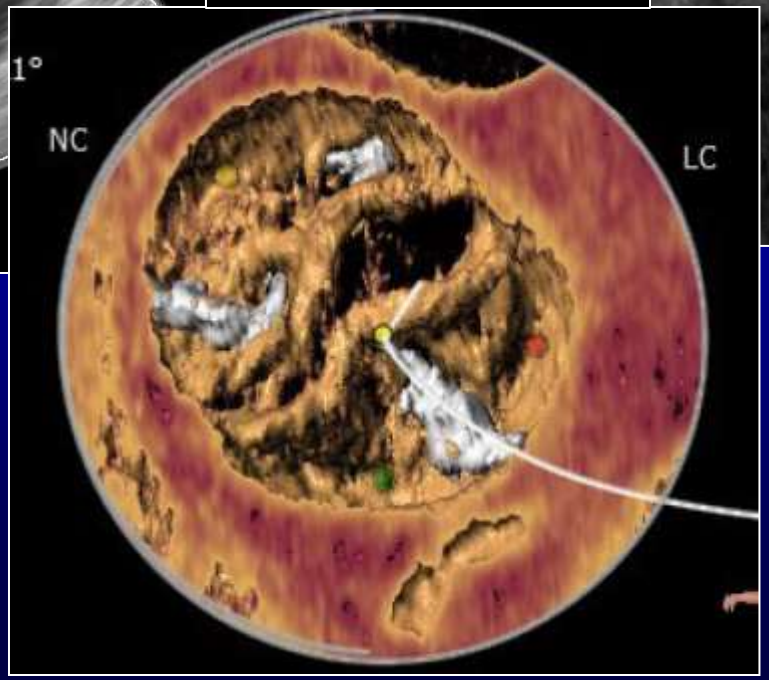
90 y/o male with severe AS referred for TAVR

Extreme risk due to age, frailty and comorbidities

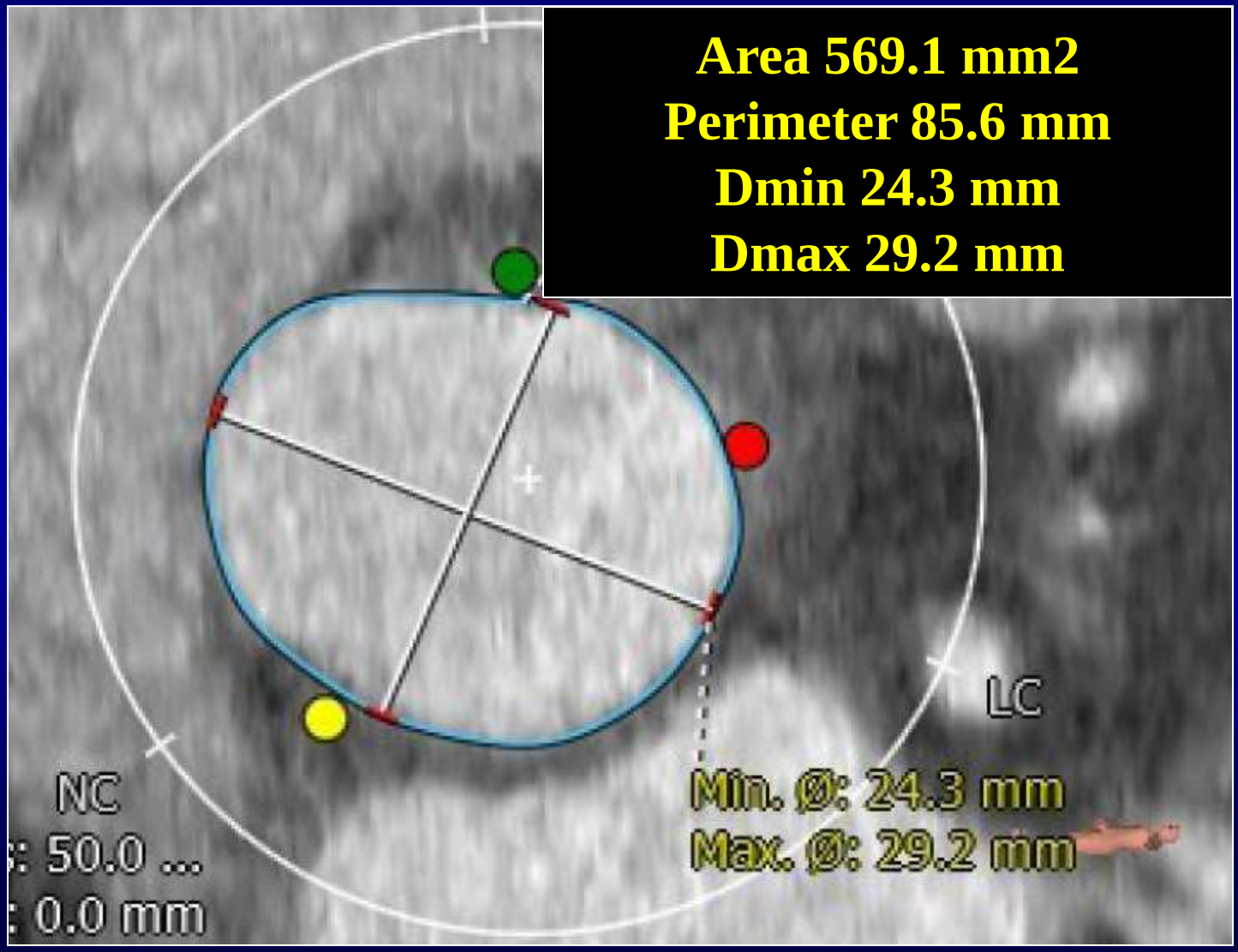


Bicuspid valve

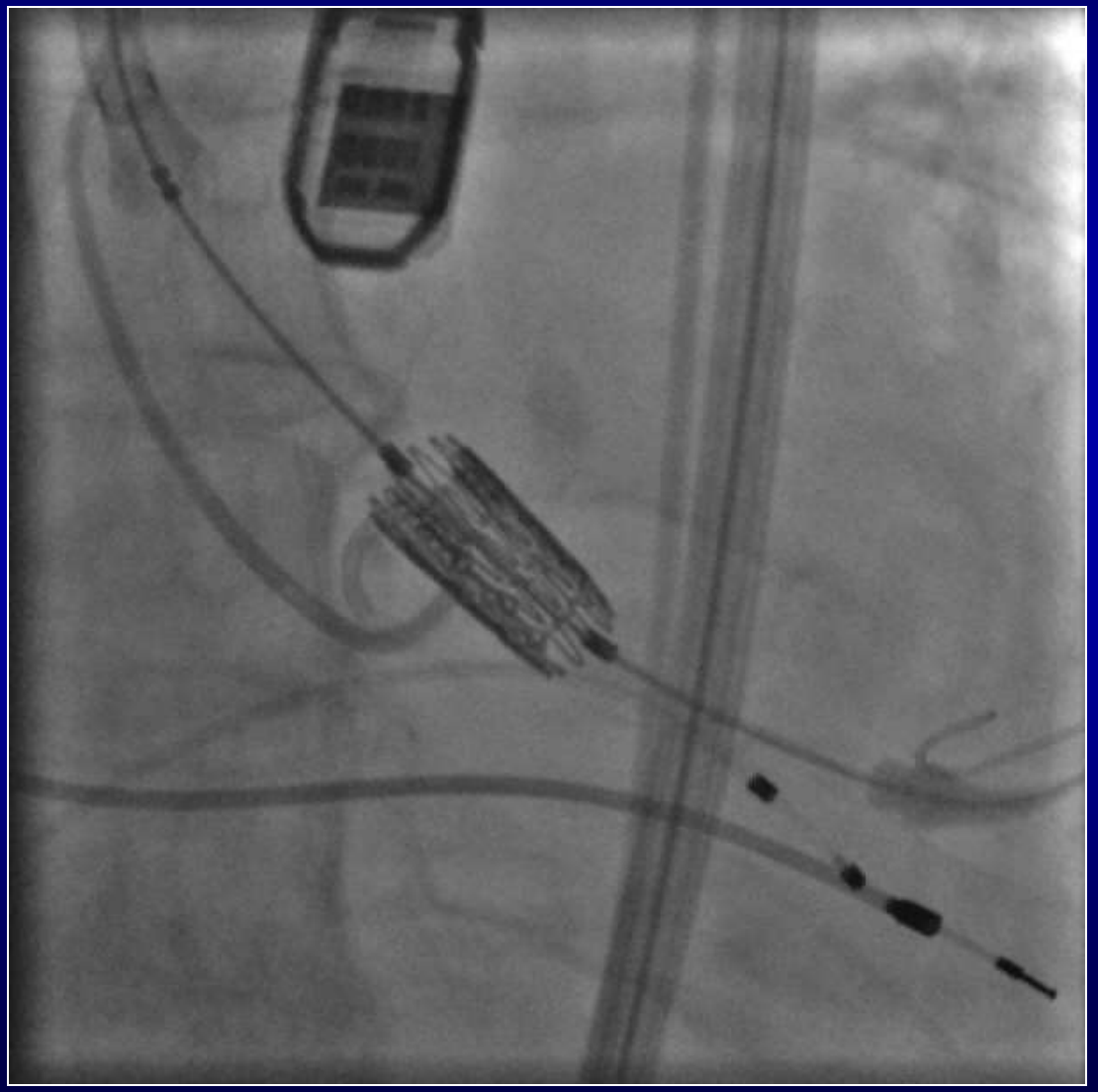




Plan for 29-mm Sapien-XT valve

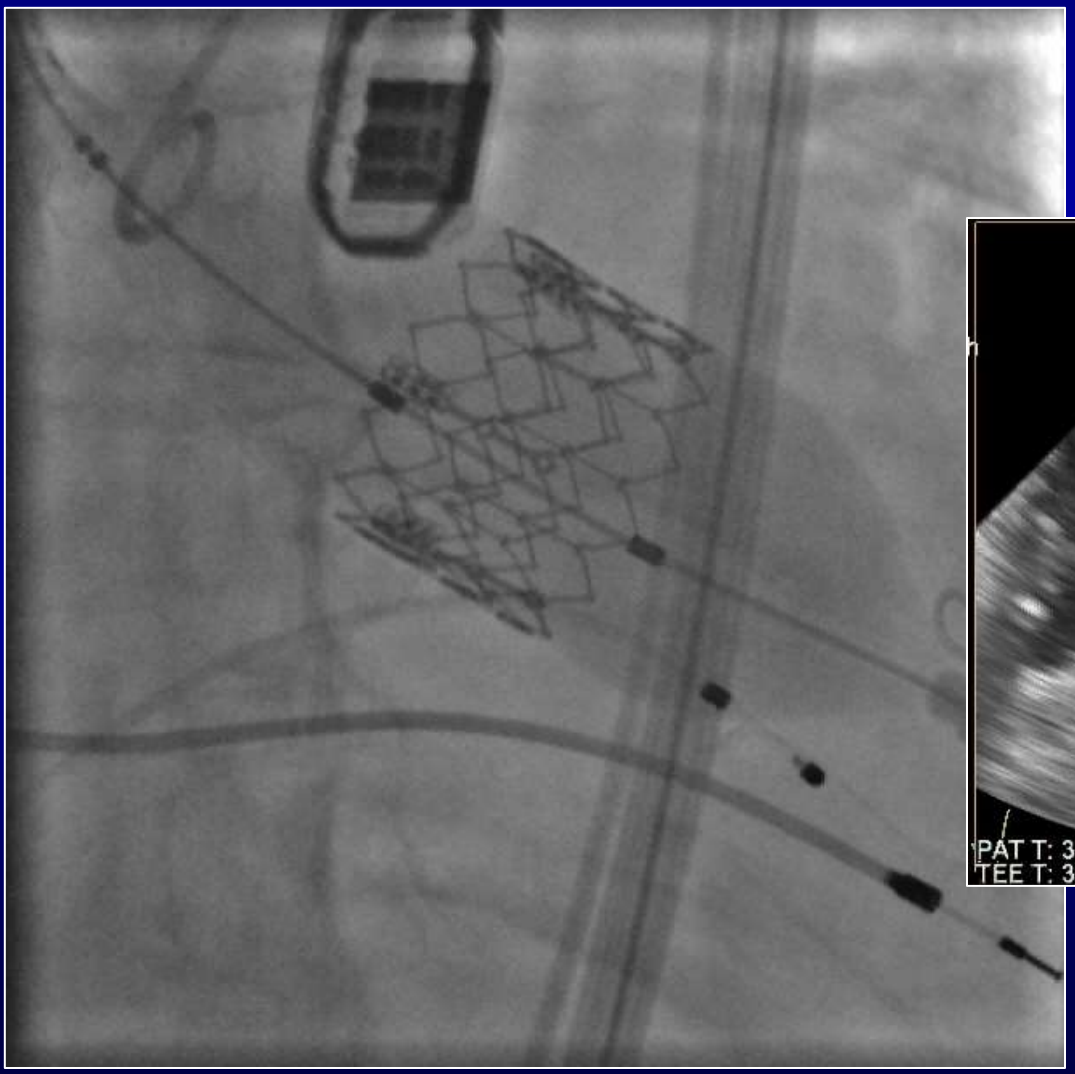


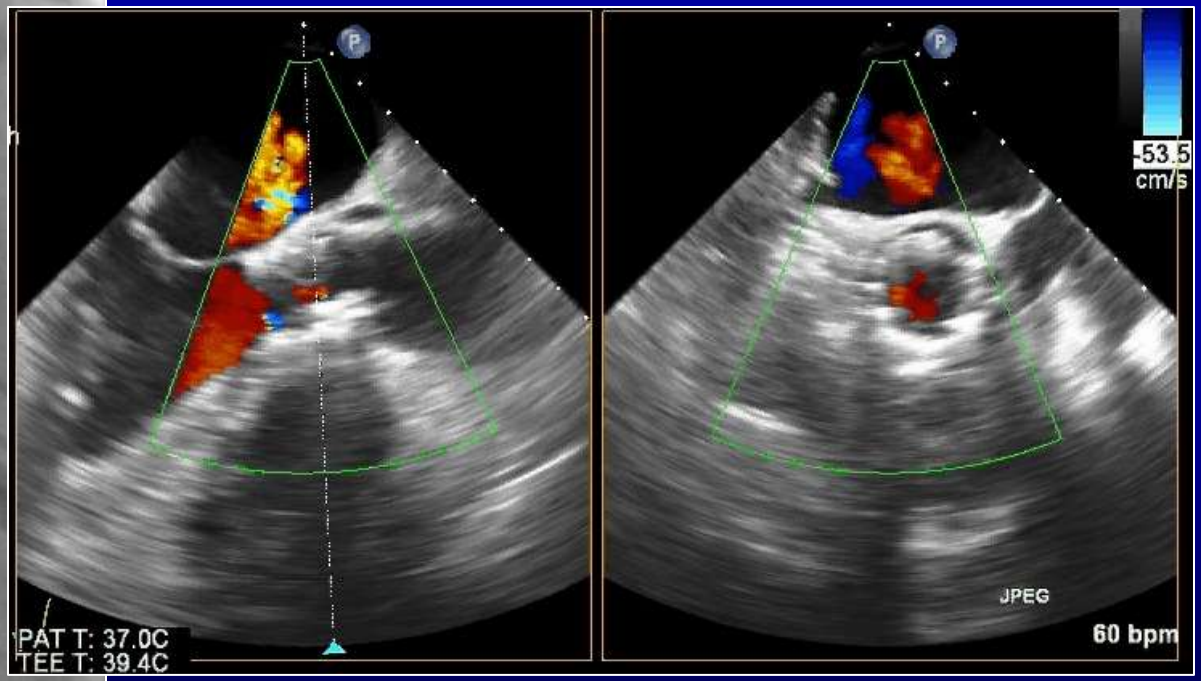
Careful coaxial valve positioning



s/p successful transfemoral TAVR with 29-mm Sapien-XT valve

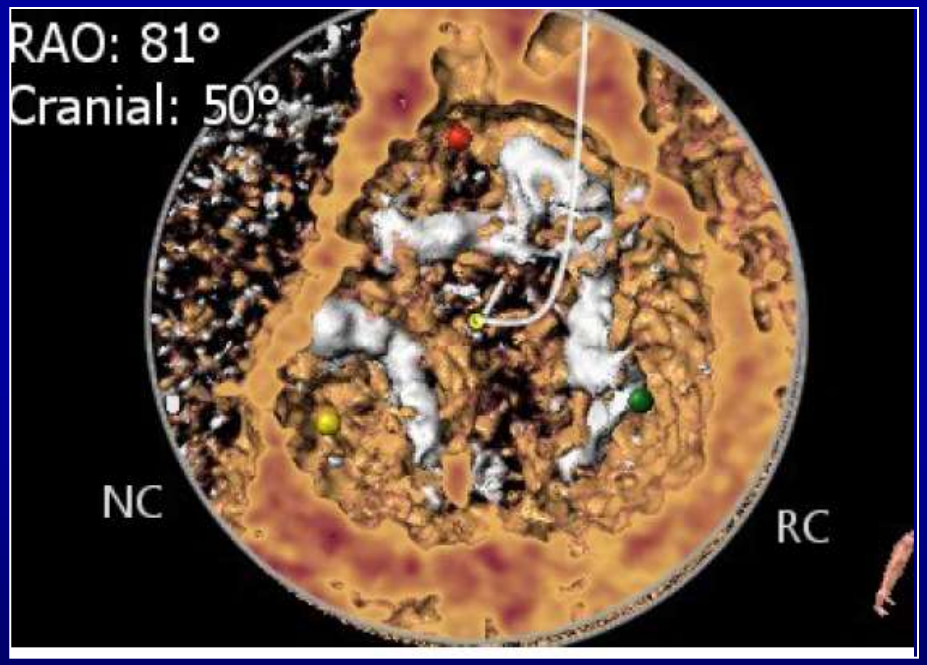
No significant paravalvular AR

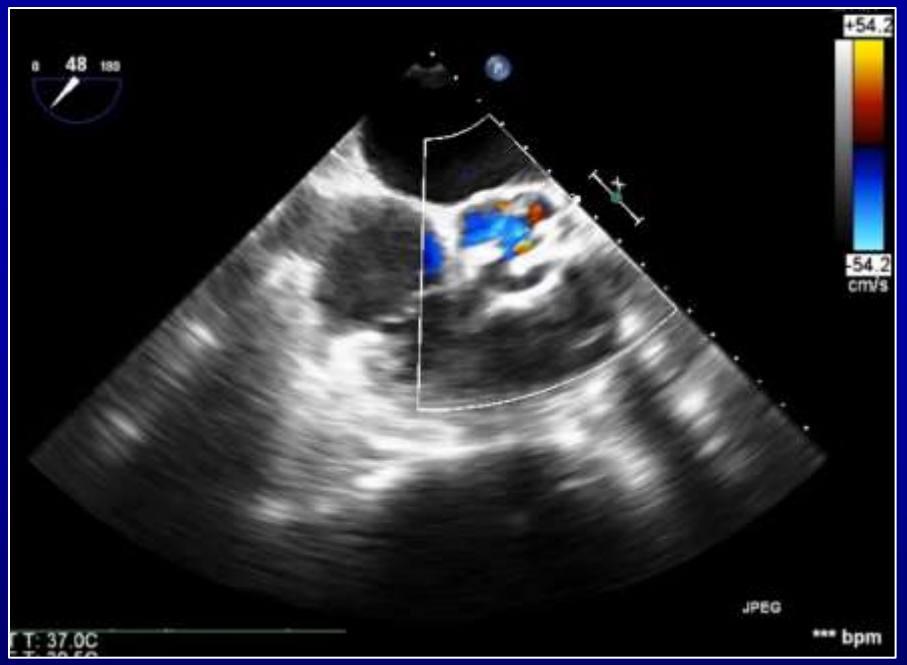




60 y/o male with bicuspid valve undergoing TAVR

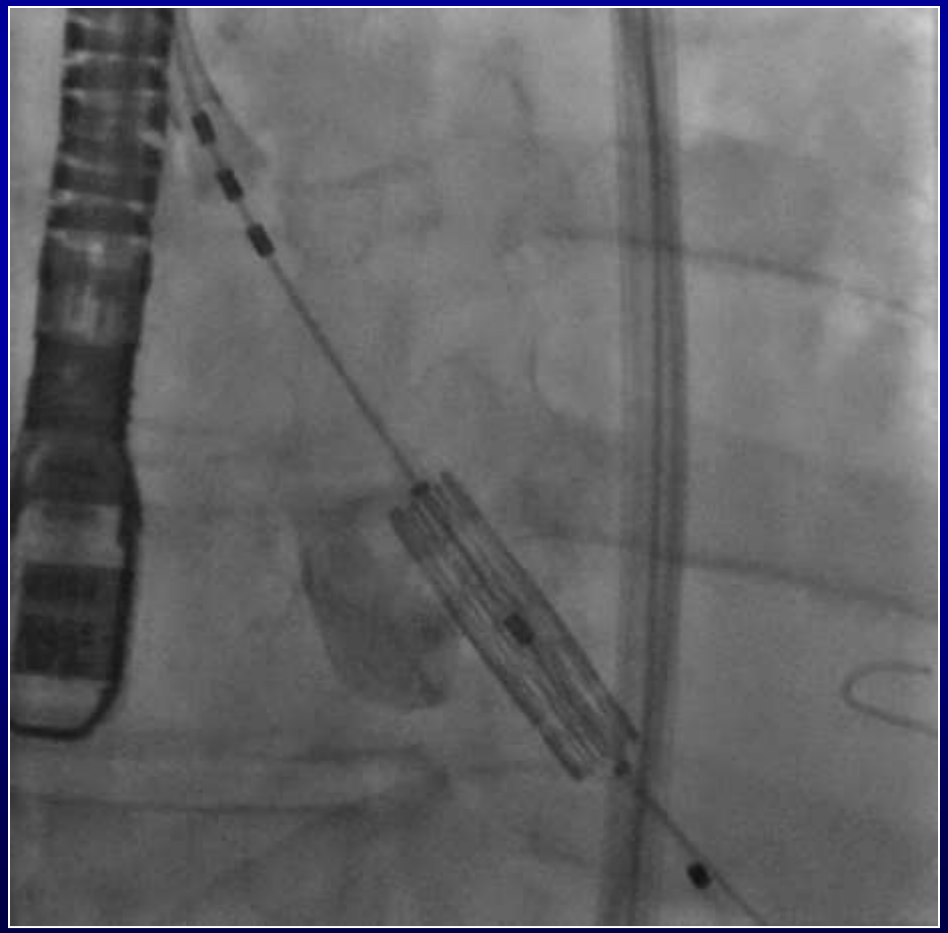
Bicuspid valve with fused left and right coronary cusps

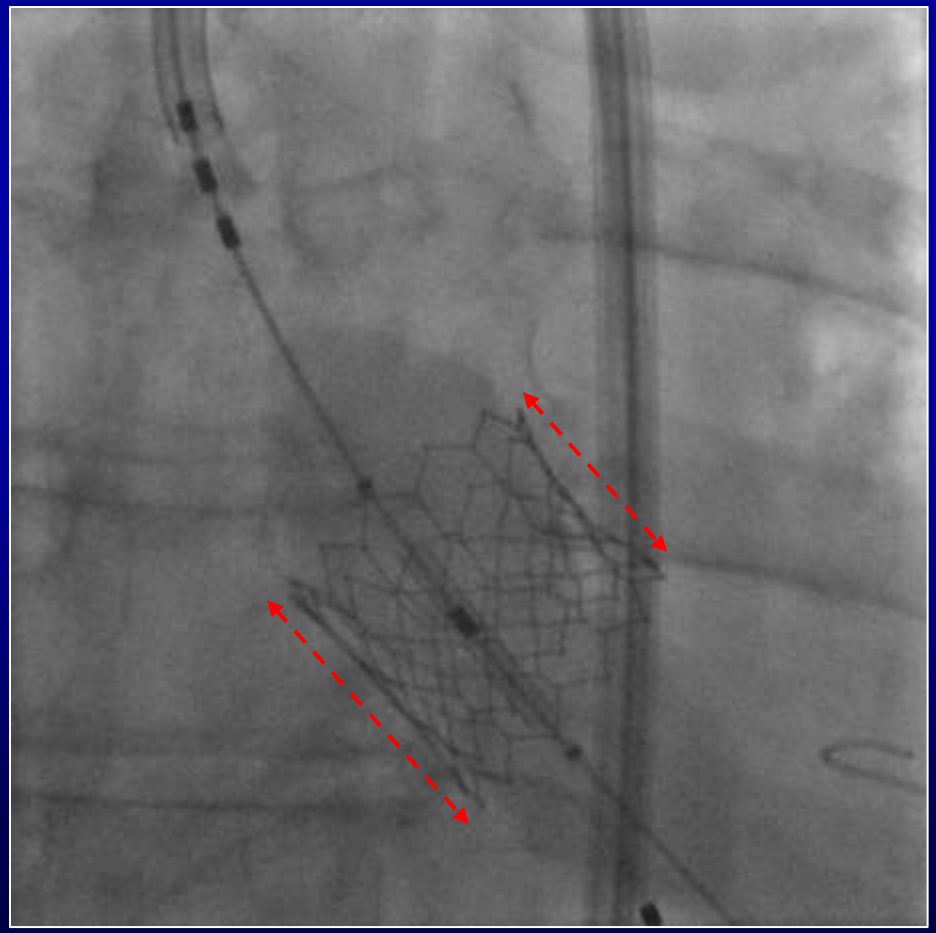




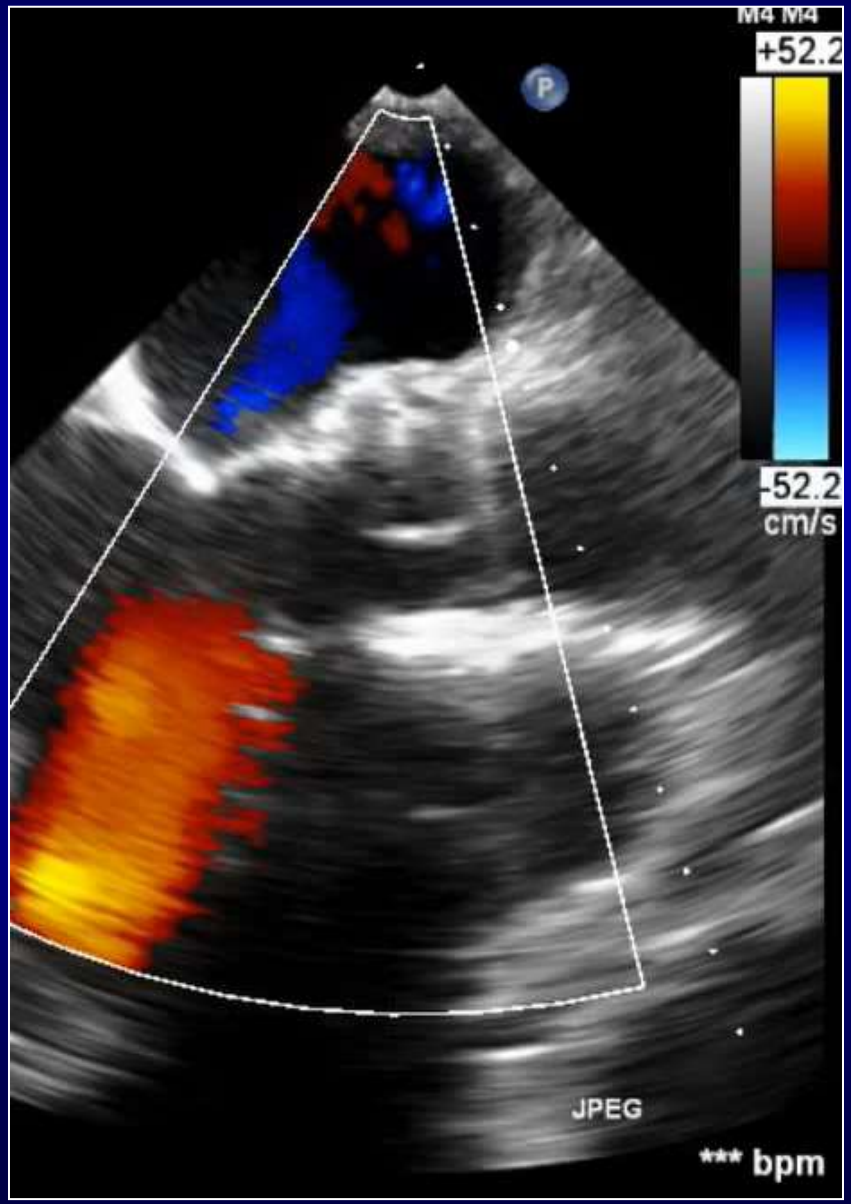
29mm Sapien3 valve deployed

Asymmetric stent expansion during TAVR





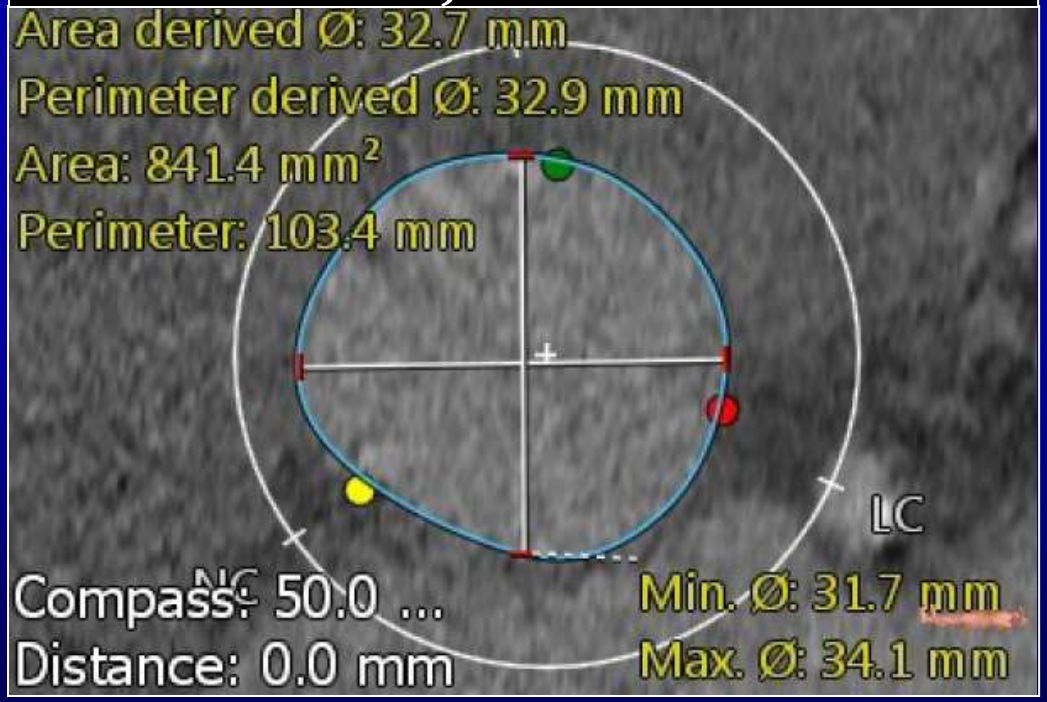
Despite asymmetric expansion, no significant PVL



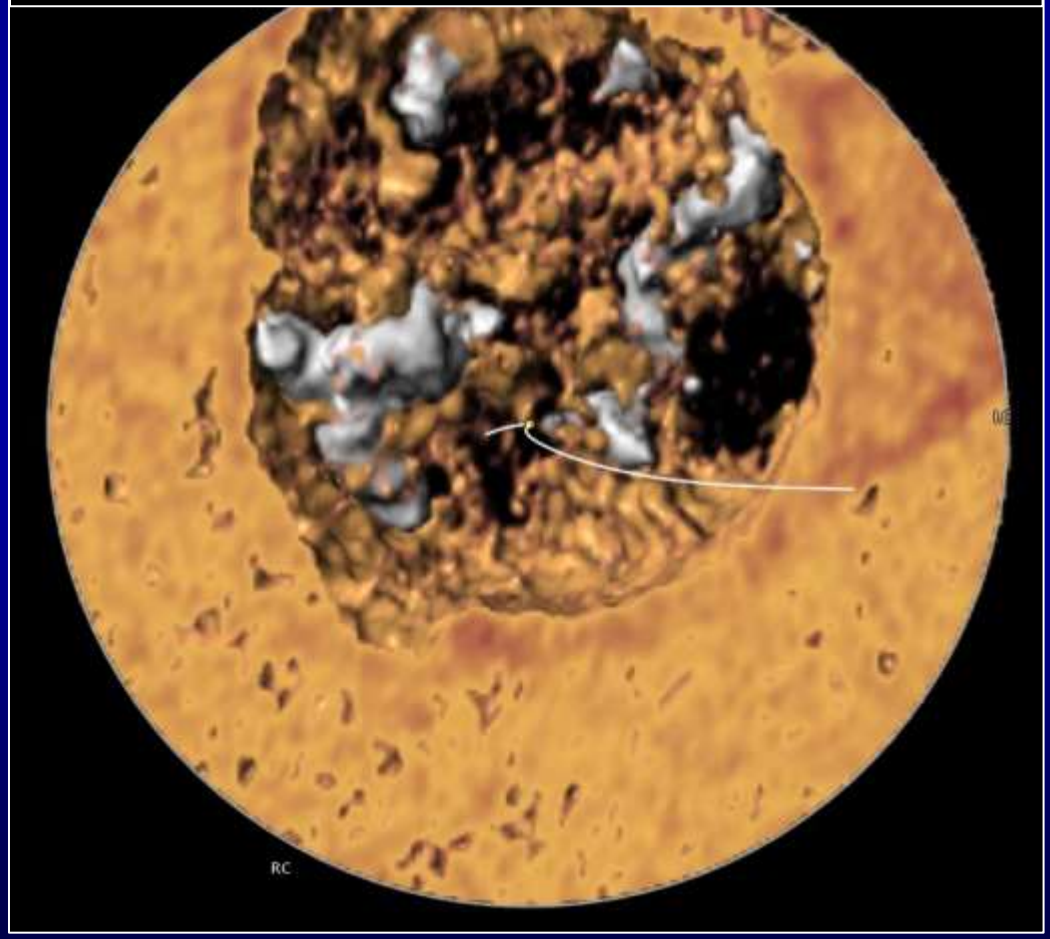
The “interesting case”: Moderate calcium, no raphe, very large annulus (840)

65 y/o male undergoing TAVR

Annulus Area 841.4 mm²
Dmin 31.7, Dmax 34.1 mm

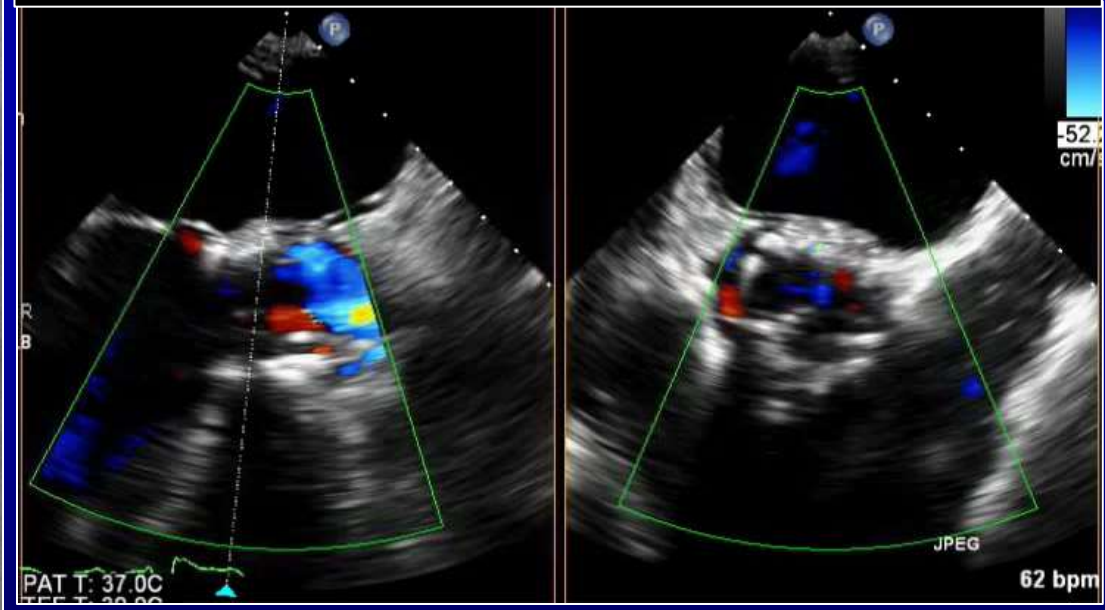


Bicuspid aortic valve
Fused left and right coronary cusps



TAVR with 29mm Sapien3 (+5cc)

Trace paravalvular AR



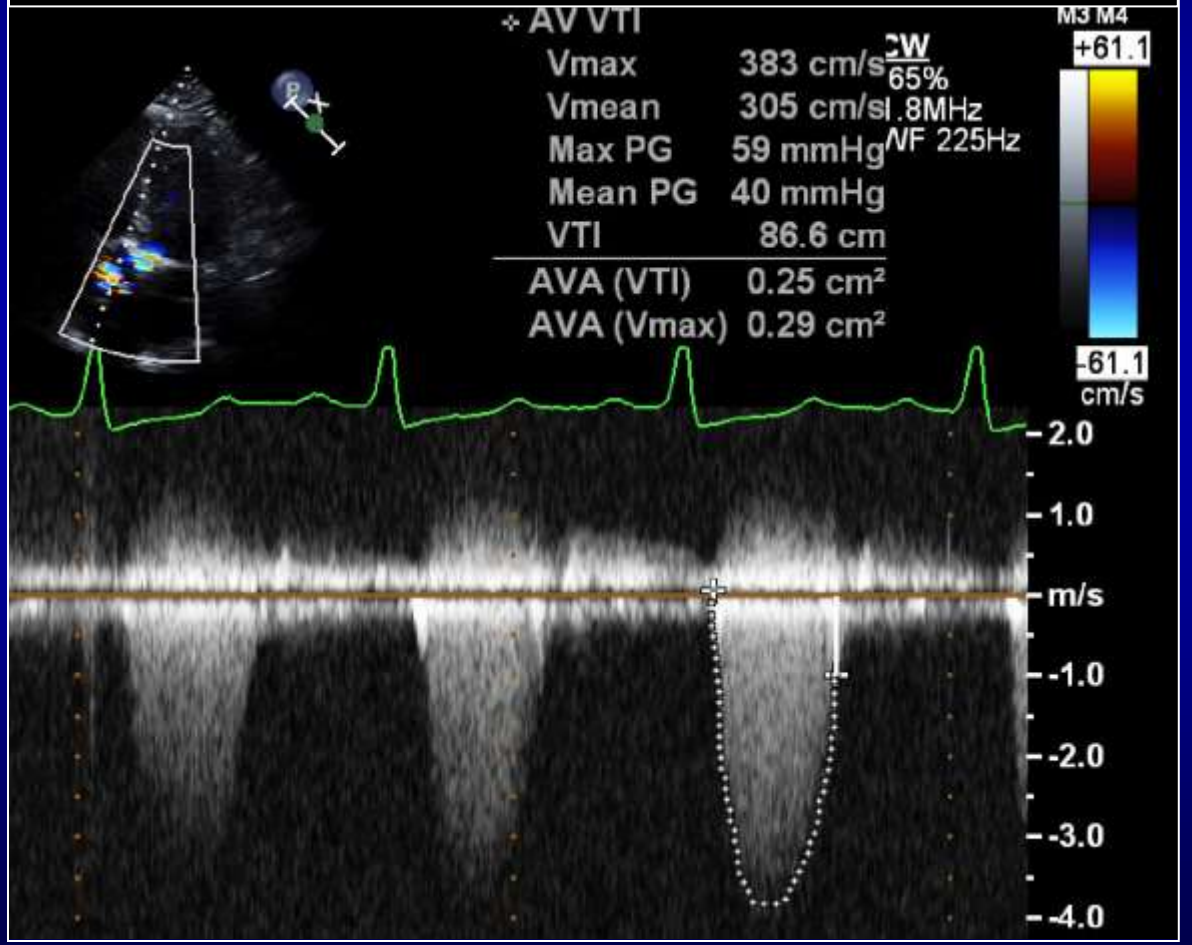
Difficult Anatomy: heavy calcium with calcified raphe

55 y/o male with severe AS, referred for TAVR

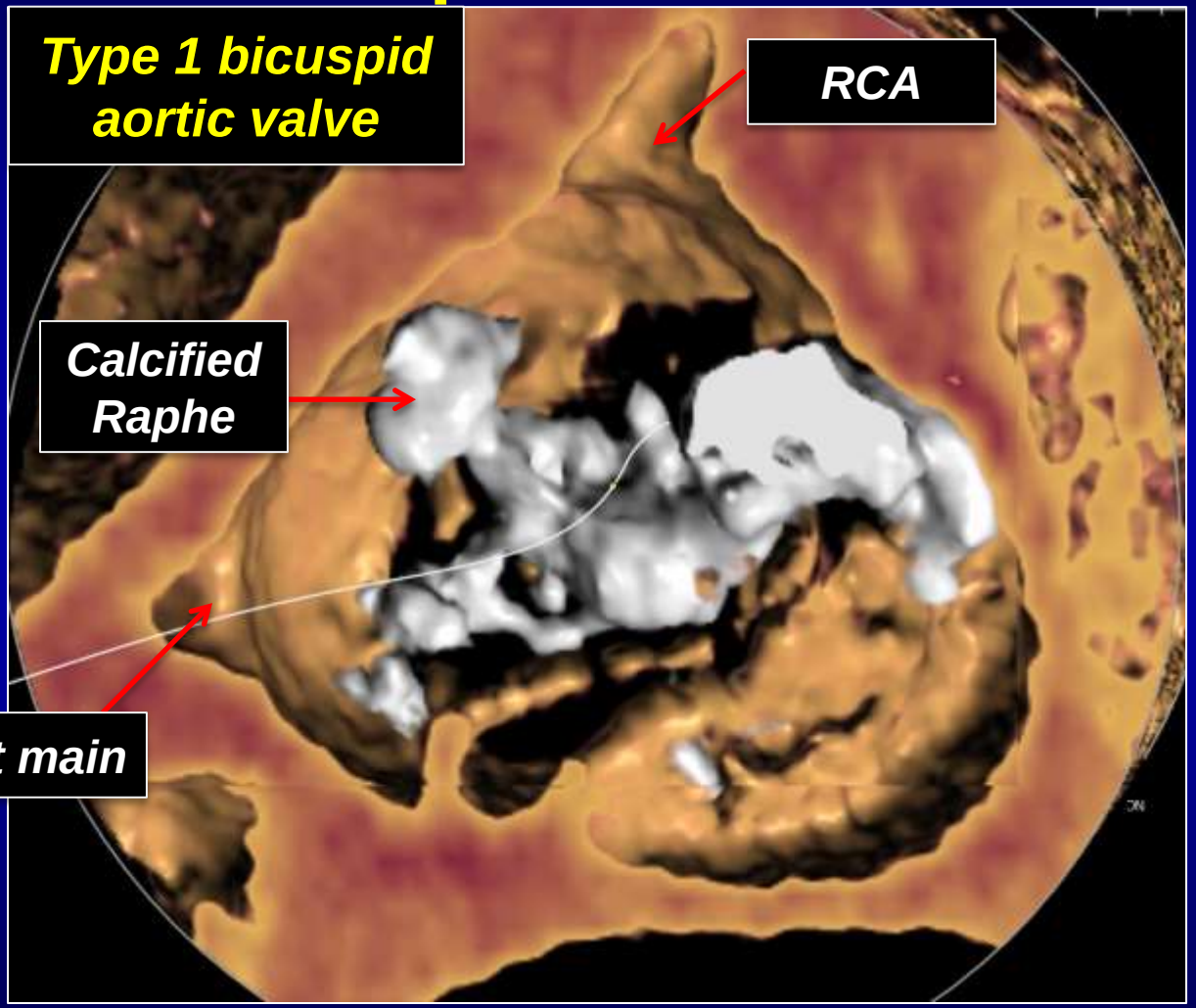
Patient turned down for OHT/VAD or SAVR/CABG

Severely depressed EF (20%)

Mean gradient = 40 mmHg



Cardiac CT for aortic valve evaluation
Bicuspid aortic valve



Left

Right

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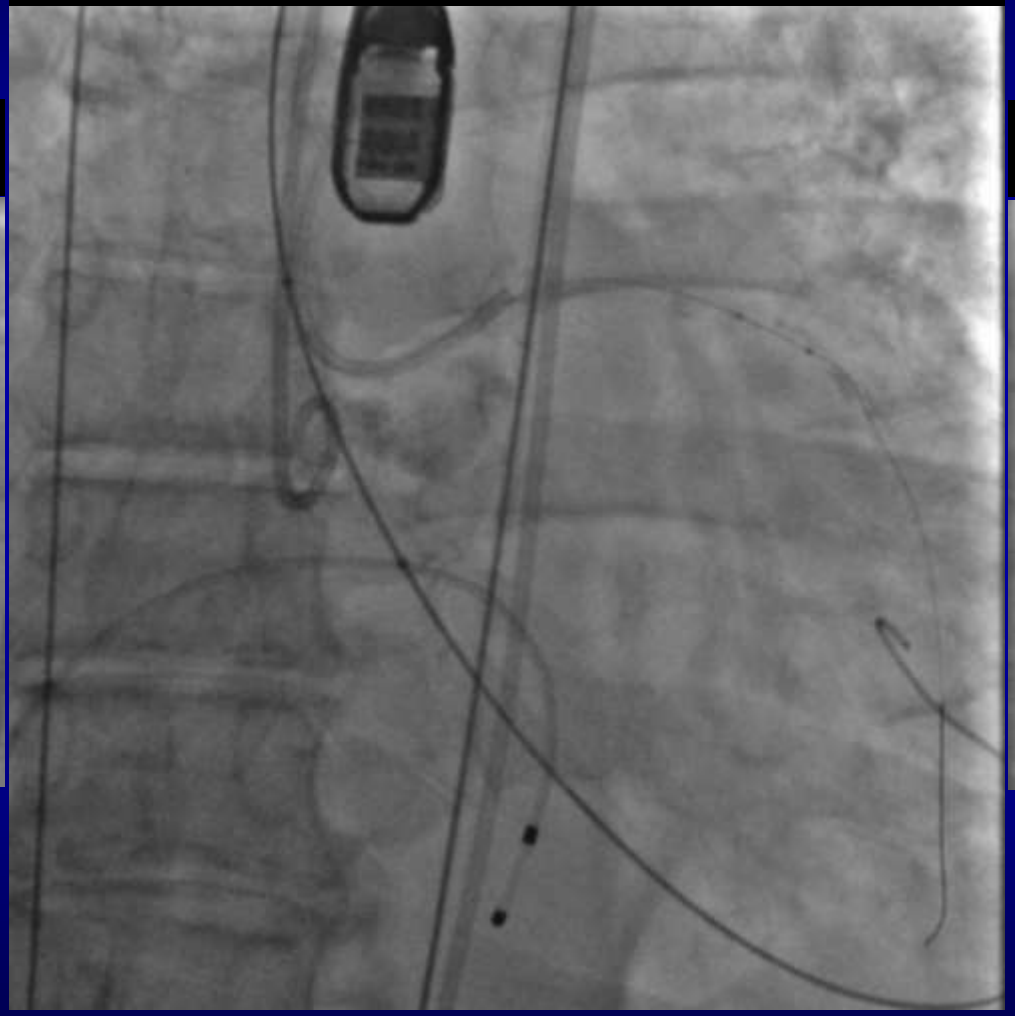
TF TAVR – Preparation and valve deployment

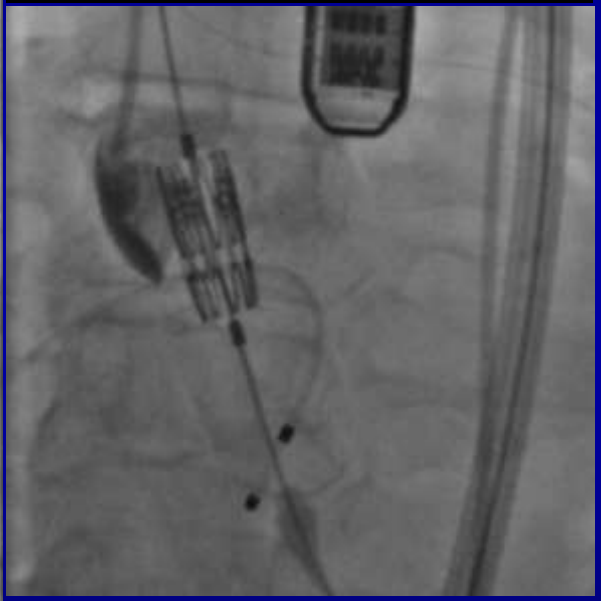
Aortogram

Valvuloplasty with Z-MED 16 mm balloon



Left main protection and secured venous access with stiff wire

Valve deployment

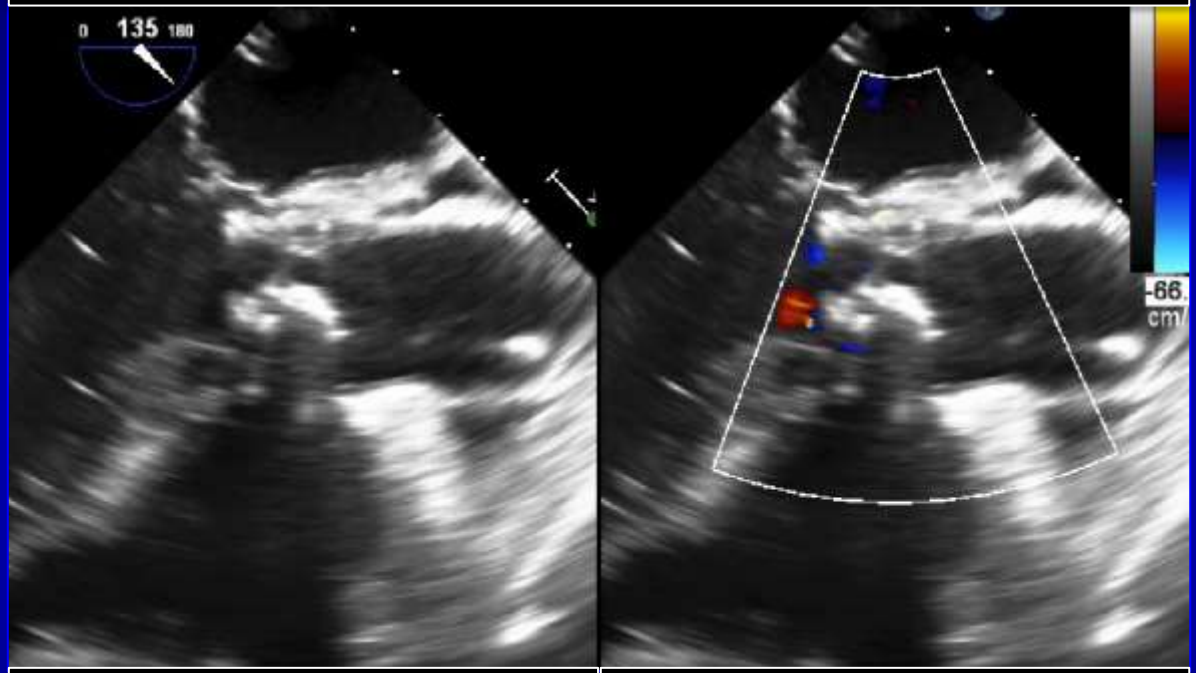


No contrast in the balloon…

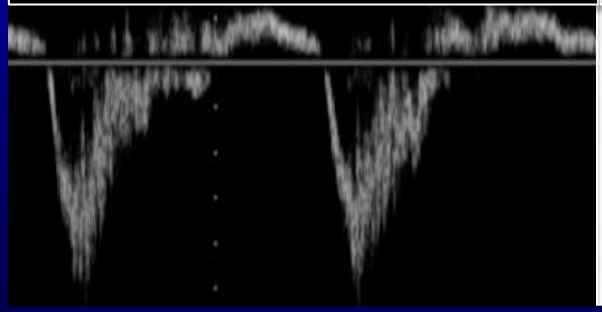
Assessment immediately post valve deployment

Patent left main

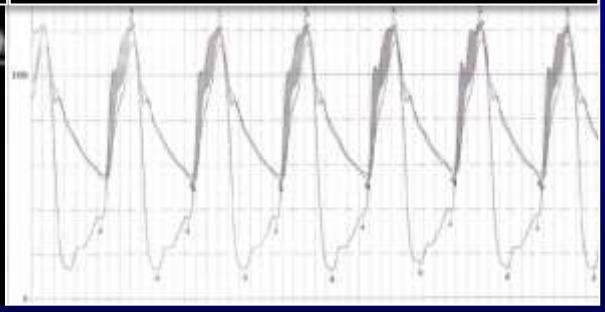
Significant PVL after Valve deployment



Diastolic flow reversal



Decreased diastolic gradient



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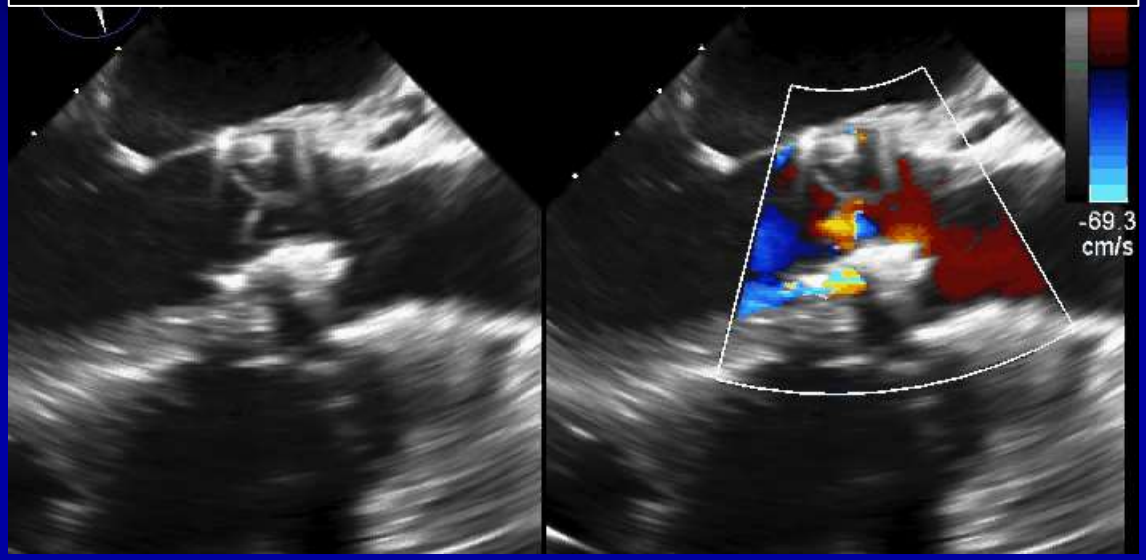
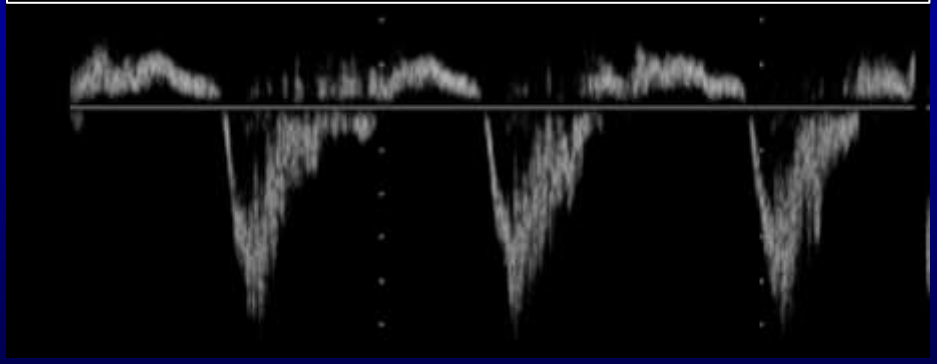
Paravalvular closure with 8 mm AVP II

AVP II positioning

Persistent PVL after AVP plug positioning



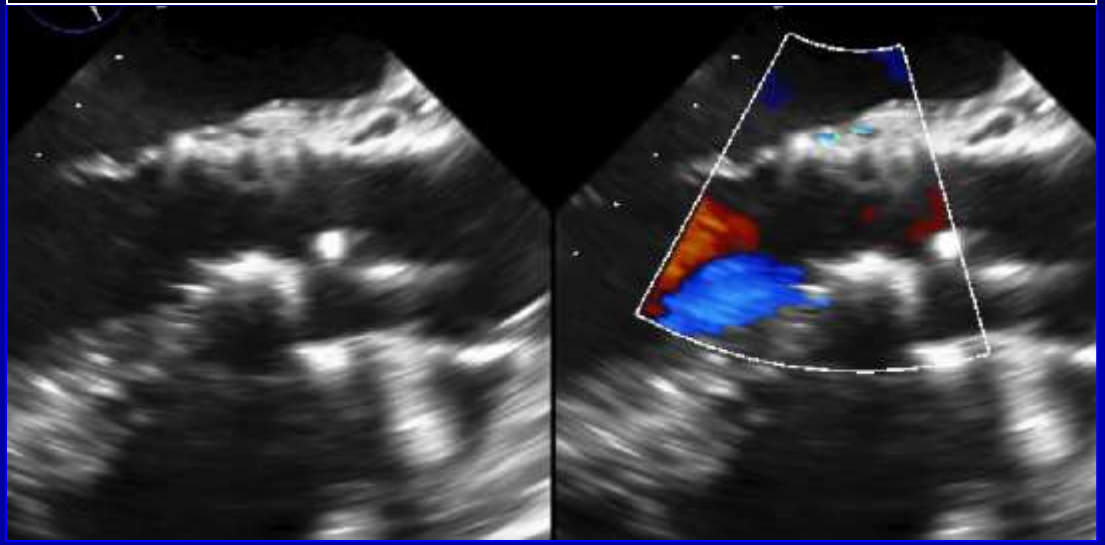
Persistent diastolic flow reversal



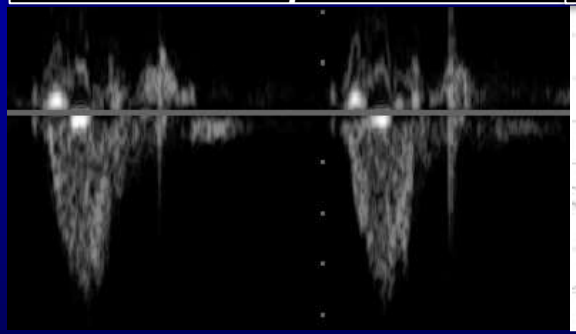
Valve-in valve with Sapien XT 26 mm

Valve deployment

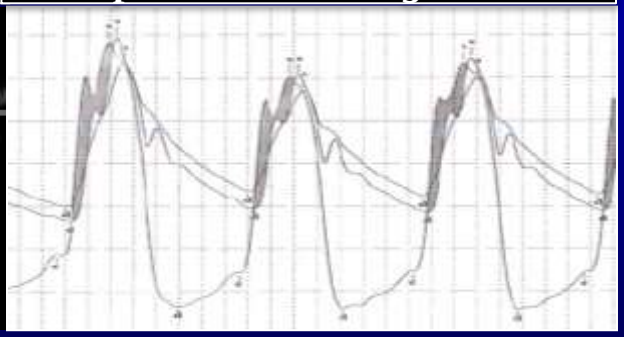
Mild residual PVL



No diastolic flow reversal

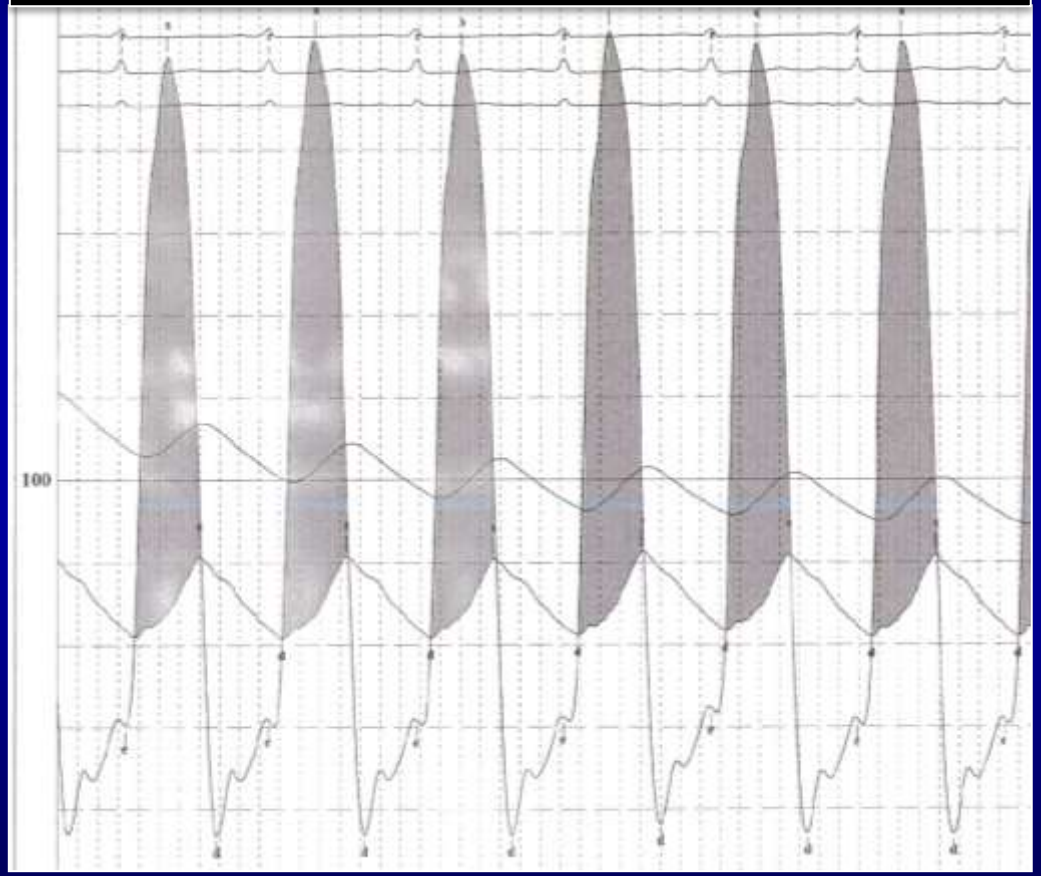


Improved diastolic gradient

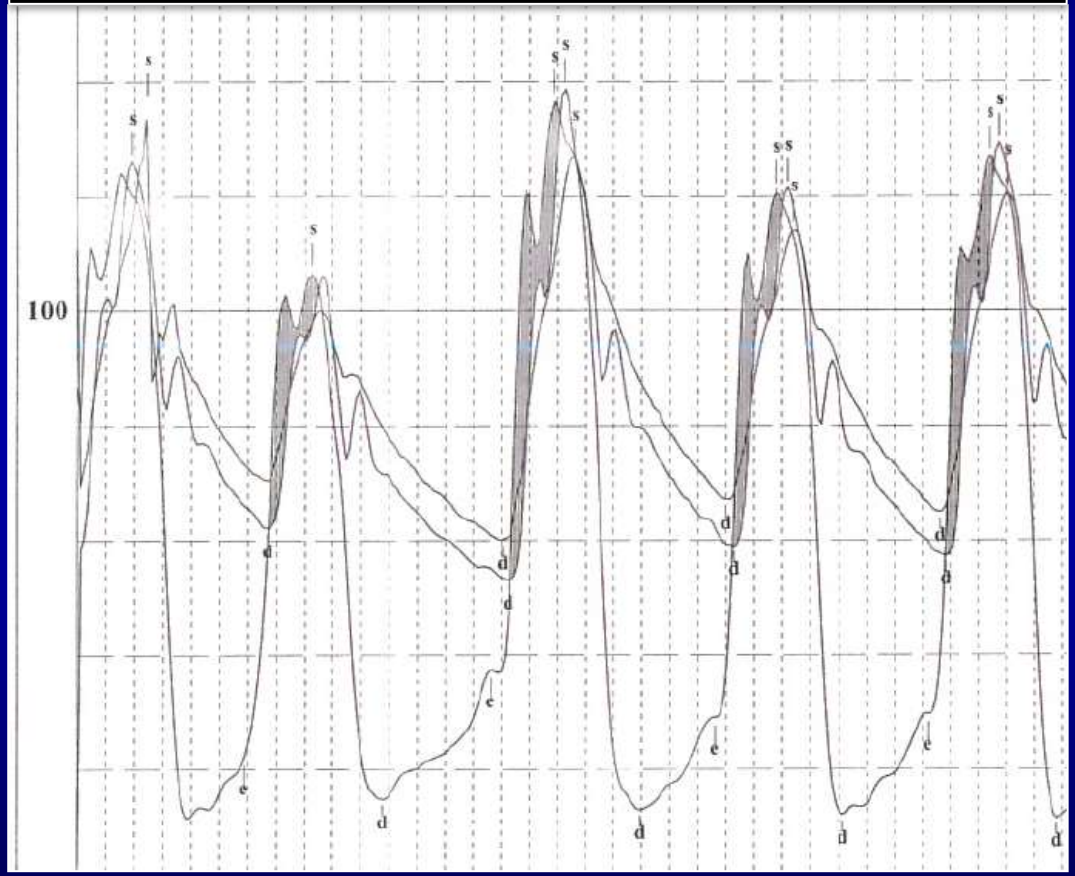


Hemodynamics improvement post TAVR

Pre valve replacement



Post valve replacement



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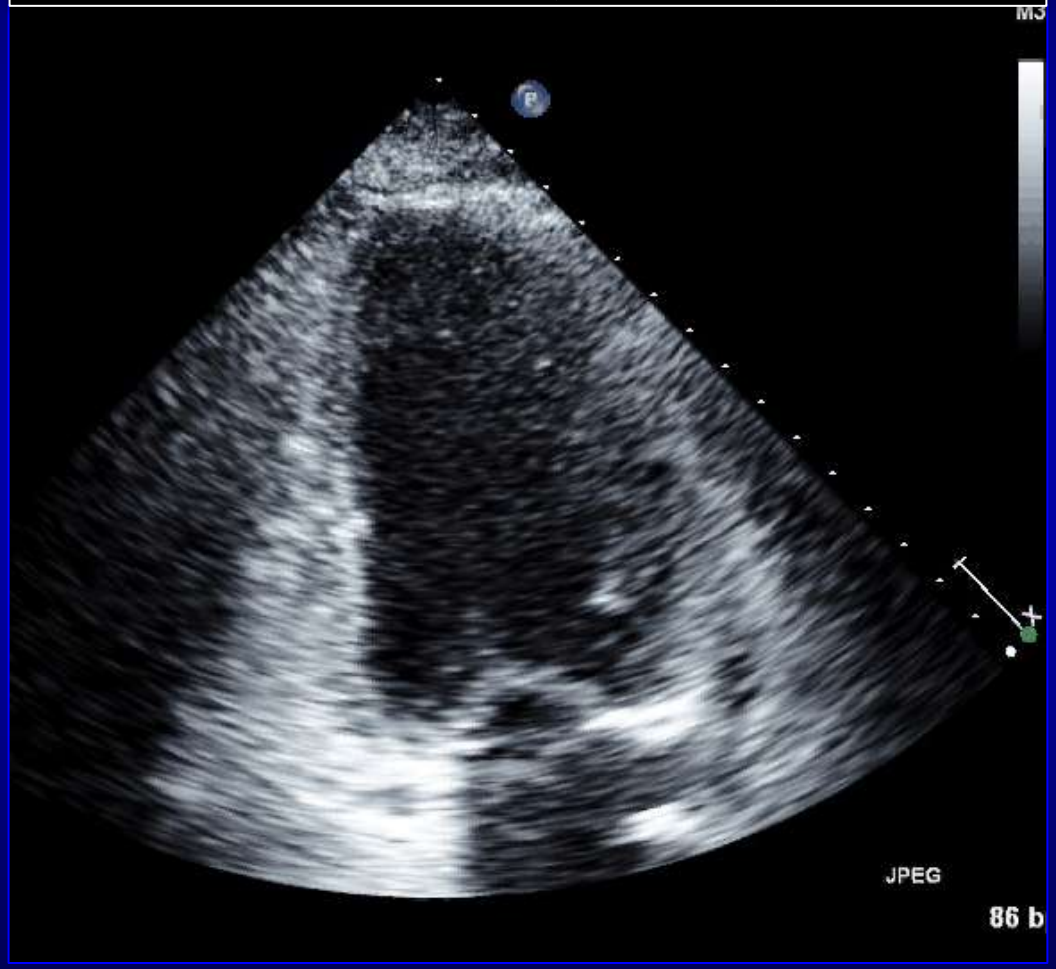
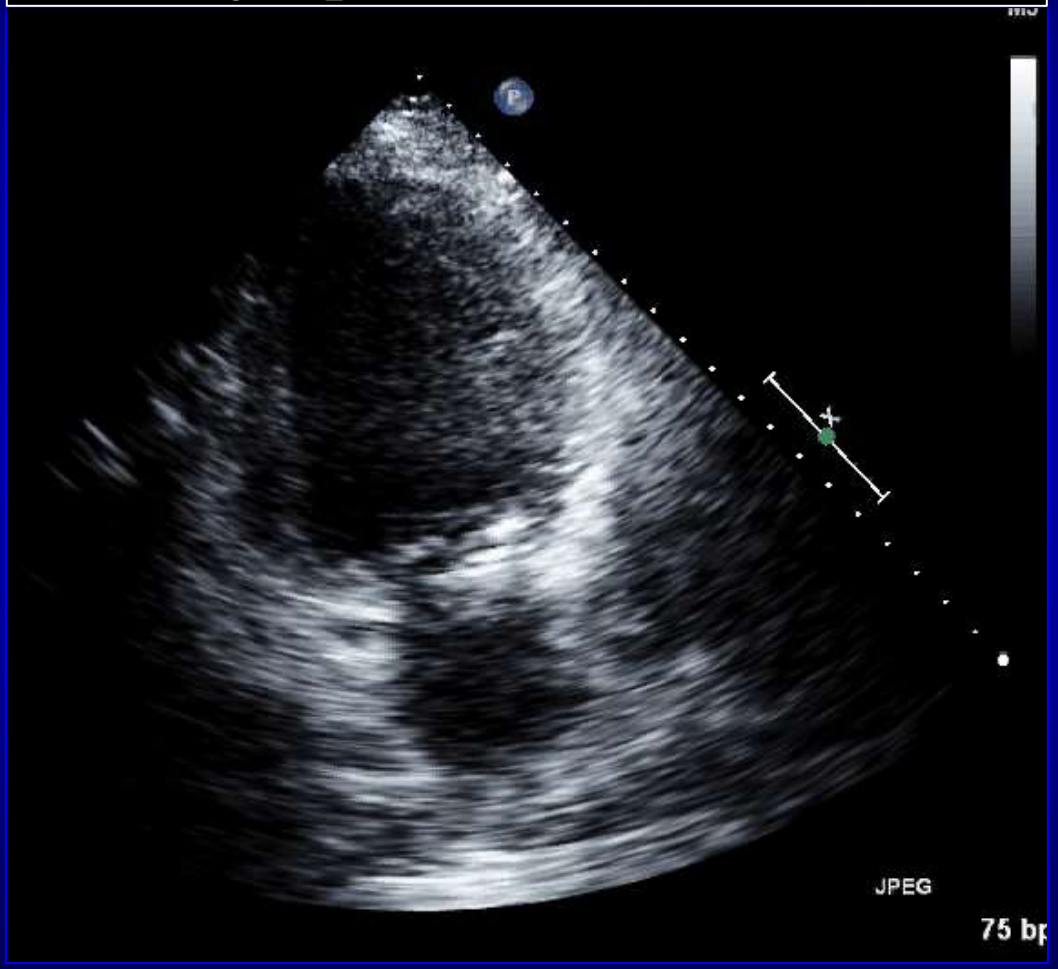
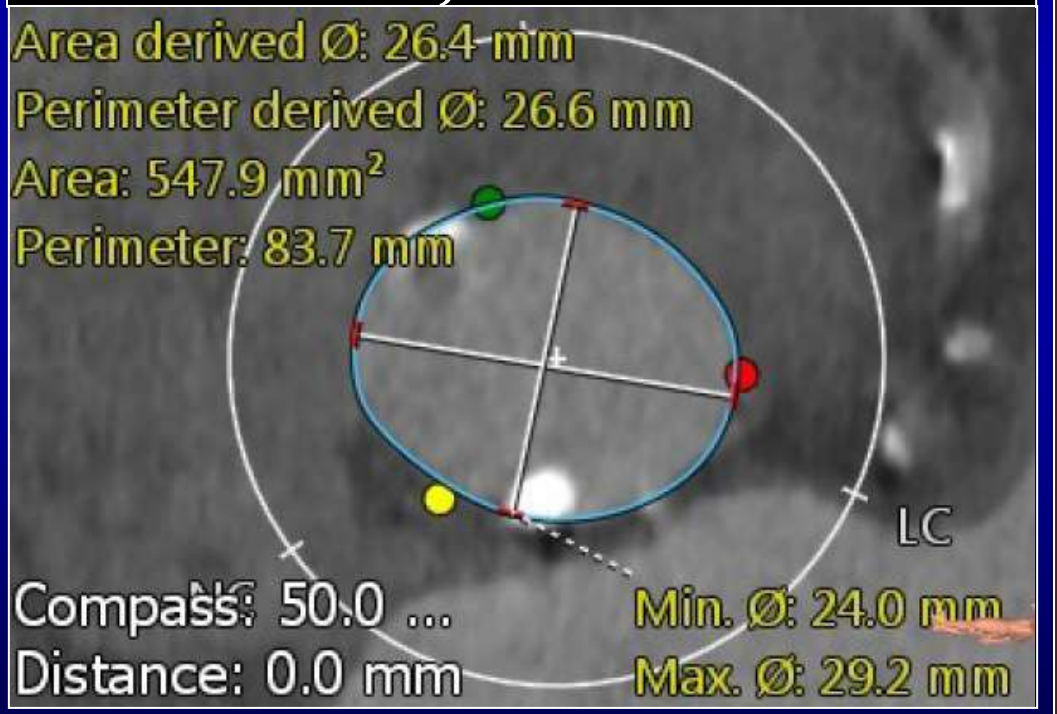
Continuous improvement of LV systolic function post TAVR

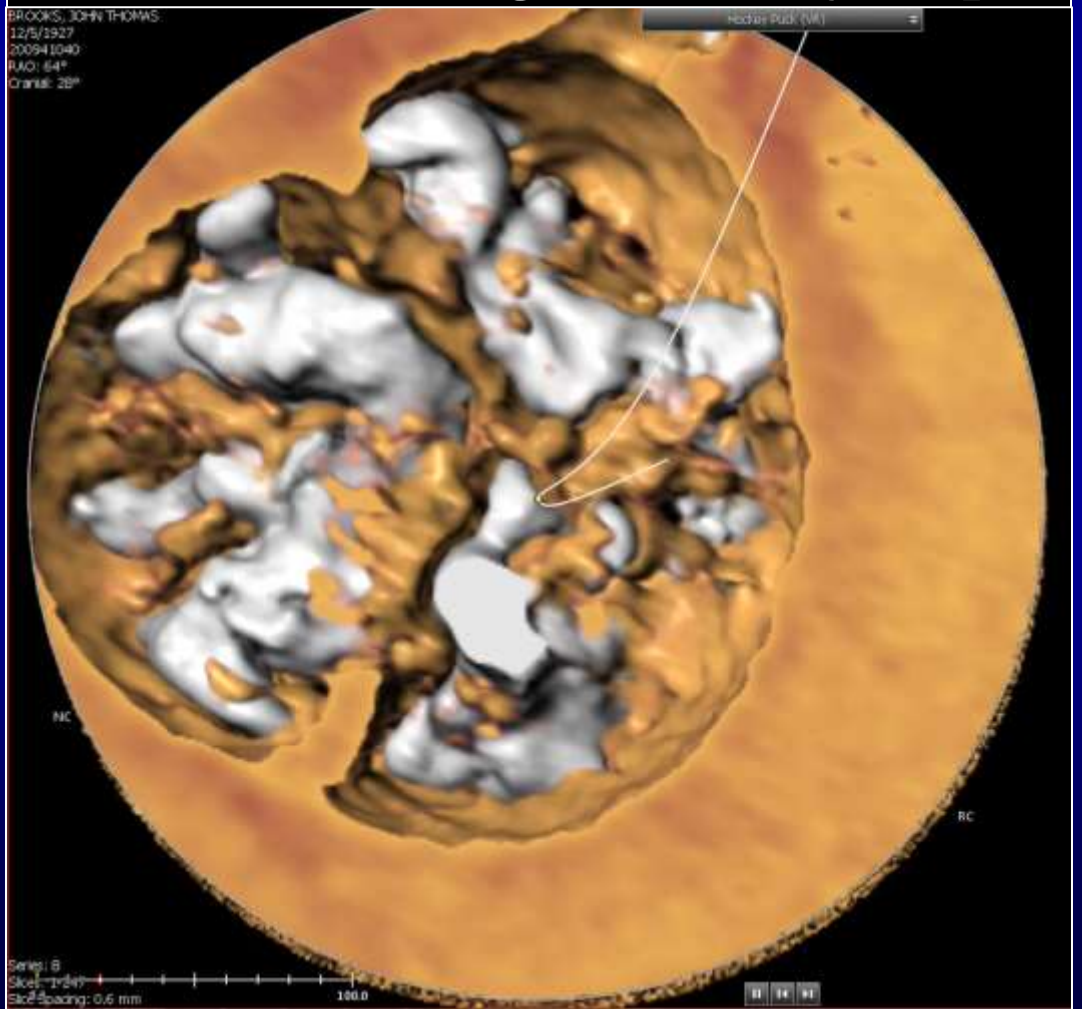
Pre-TAVR (EF 15%)	*Day 1 post-TAVR (EF 40%)*
	

88 y/o male undergoing TAVR

Annulus Area 547.9 mm²
Dmin 24.0, Dmax 29.2 mm

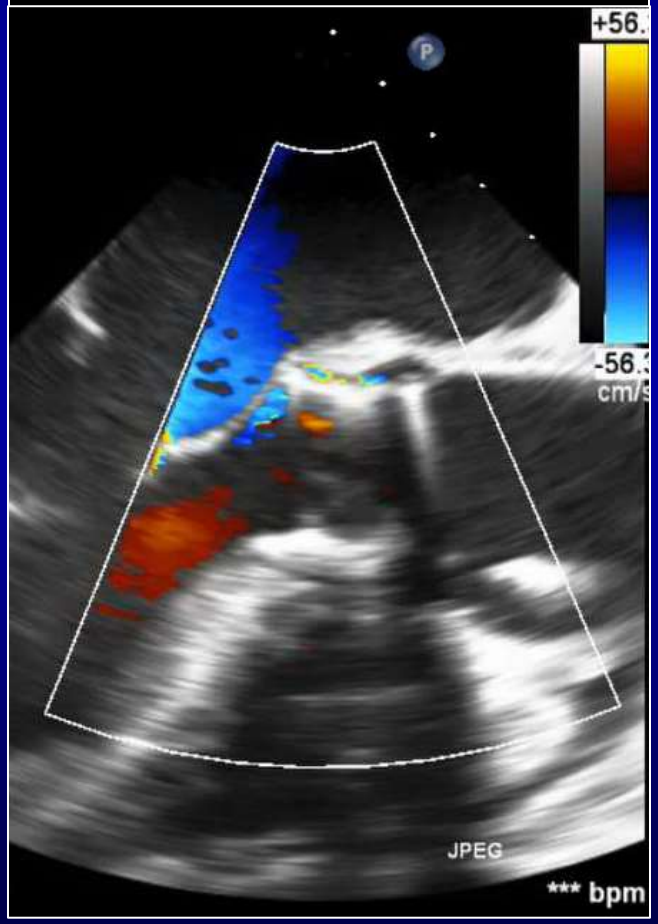


Bicuspid raphe type, heavily calcified
Fused left and right coronary cusps

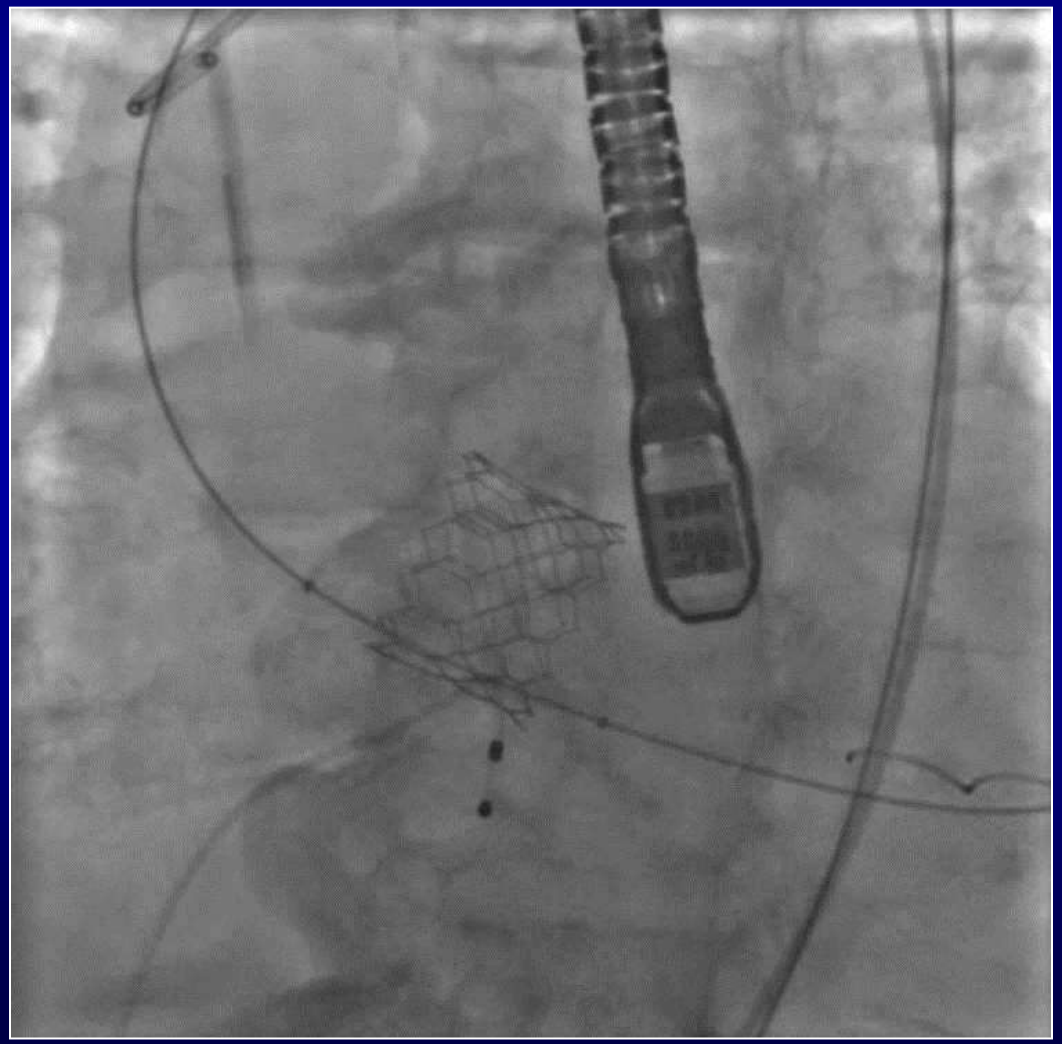


TAVR with 26mm Sapien3

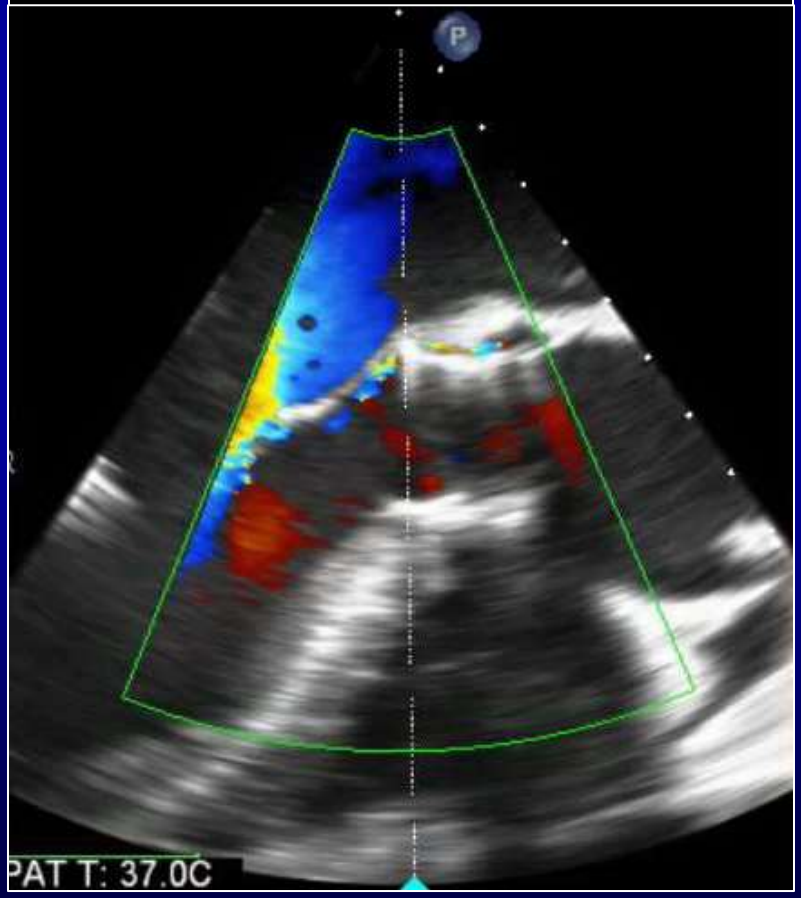
Moderate PVL after valve deployment



Post-dilation performed with a Z-Med II 26 x 4 cm Balloon

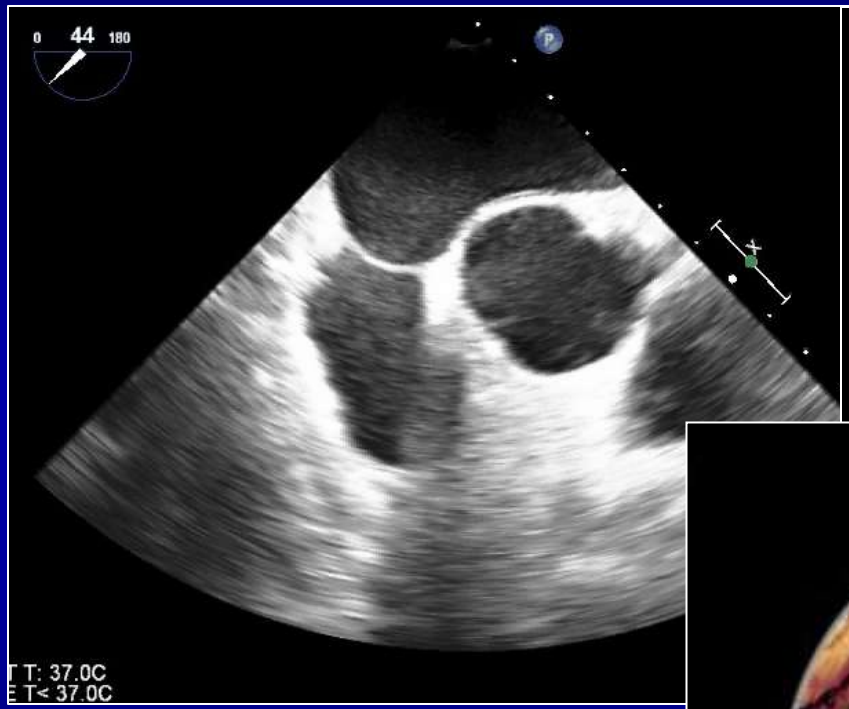


Final result
Trivial PVL

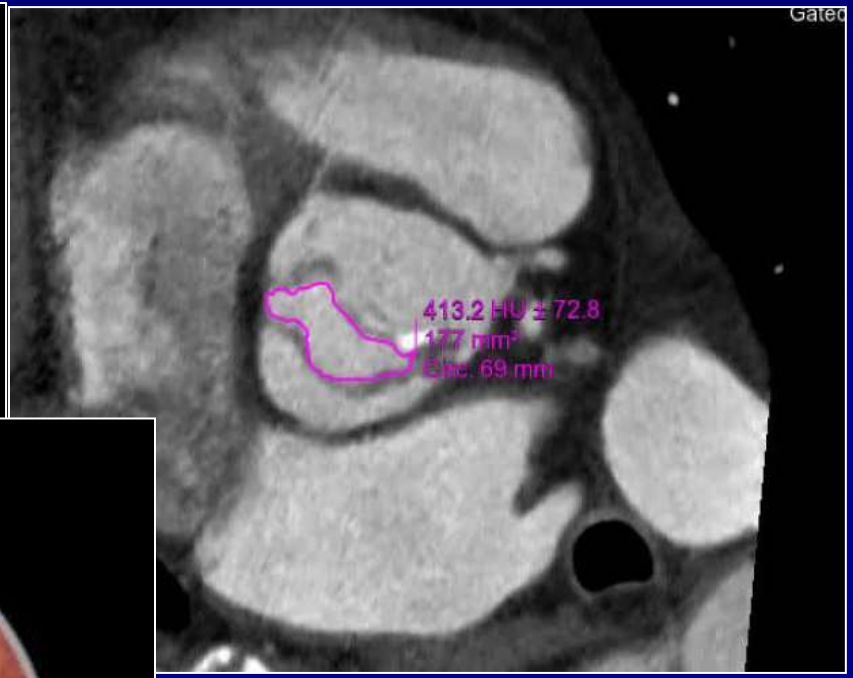


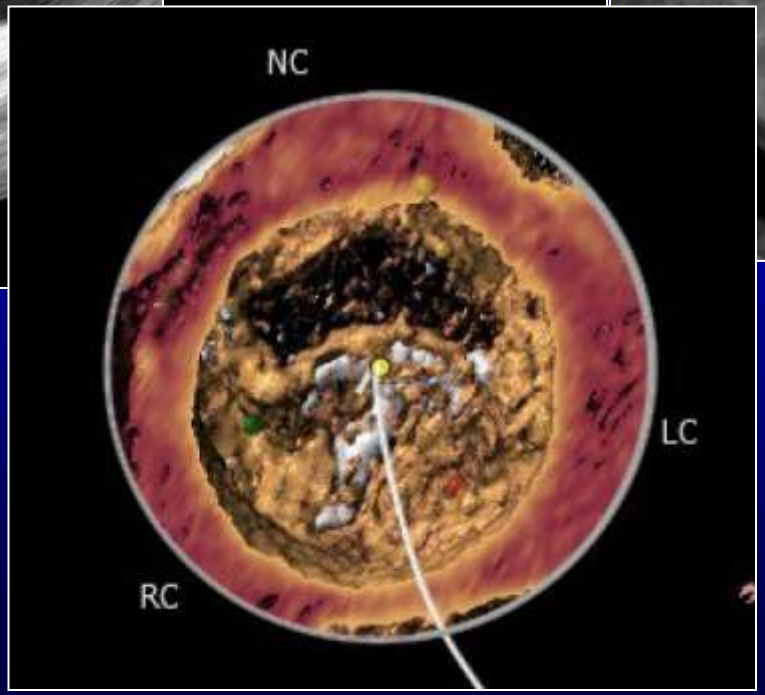
78 y/o male with severe AS referred for TAVR

High risk due to morbid obesity



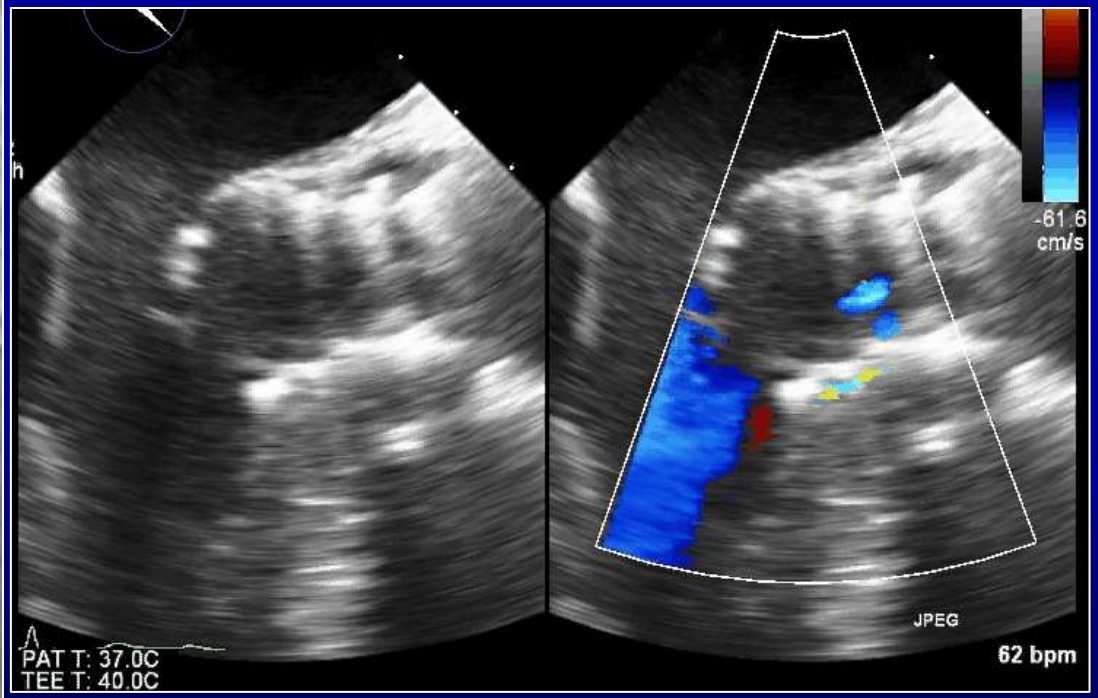
Bicuspid valve





s/p successful transfemoral TAVR with 31-mm Medtronic CoreValve

Mild residual paravalvular AR



Practical considerations..

- Be careful of unfavorable anatomical features on CT: excessive calcium, raphe type especially calcified raphe
- Positioning is harder than the tricuspid valve. Cross check with echo. TEE guidance is is preferable due to higher rates of AI and risk of aortic root rupture
- Predilation is generally a good idea; avoids difficult crossing and stresses on aorta which may be diseased; also can help with sizing.
- Post dilation and rarely valve in vavle may be needed to optimize the expansion and procedural outcomes.

Conclusions

- Despite “exclusion” of Bicuspidy in clinical trials TAVR is currently being performed in real life setting with reasonably good outcomes. Its incidence depends on use of CT; (104 cases out of 1850+TAVRs at Cedars-Sinai)
- Though the mortality may be “similar” to the tricuspid TAVR, the acute outcomes in the published literature are worse with respect to AI, and pacemaker implantation with the first generation devices
- The data with Sapien 3 valve are impressive, no comparative studies are available with other next generation valves (Evolut R, Lotus, Portico)
- While Bicuspid TAVR is justifiable in higher surgical risk patients, high risk anatomical features (extreme calcium, heavy-calcified raphe), concomitant aortopathy should prompt consideration for surgical AVR in low risk patients
- Randomized trials/prospective registries especially in patients with lower surgical risk are needed.