From Theory to Practice: Differences of ACURATE neo2 from Other Valves & Blending the Best for Superior Performance

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ACURATE neo2™
Aortic Valve System

Design features

Open upper frame

Stablilization anchor & Provides unrestricted access for future coronary interventions[1]

Supra-annular leaflets

Porcine pericardium leaflet (BioFix anti-calcification)
Achieves large EOAs and single-digit gradients[2]

ACTIVE PVseal™

Extended (60% larger*) sealing skirt conforms to the native aortic annulus minimizing PVL[3]

Annulus treatment range

Treats 20 mm to 27 mm annulus diameters

Accurate positioning

Top-down deployment with upper- and lower- crown anchoring provides precise procedures[2]

* ACURATE *neo*2 Valve vs. ACURATE *neo*™ Valve

1. Reobtain Coronary Ostia Cannulation Beyond Transcatheter Aortic Valve Stent (RE ACCESS); NCT04026204. *J Am Coll Cardiol Intv*. 2020
2. Möllmann H, Holzhey DM, Hilker M, et al. The ACURATE *neo*2 Valve System for transcatheter aortic valve implantation: 30-day and 1-year outcomes. *Clin Res Cardiol*. 2021;110:1912–1920.
3. Early *neo*2 Registry. Full Core-Lab Results of TAVI with the New ACURATE *neo*2 Valve. TVT Congress. Presenter: Andreas Rück. July 20, 2021.

ACURATE *neo*2™ Aortic Valve System

Contents

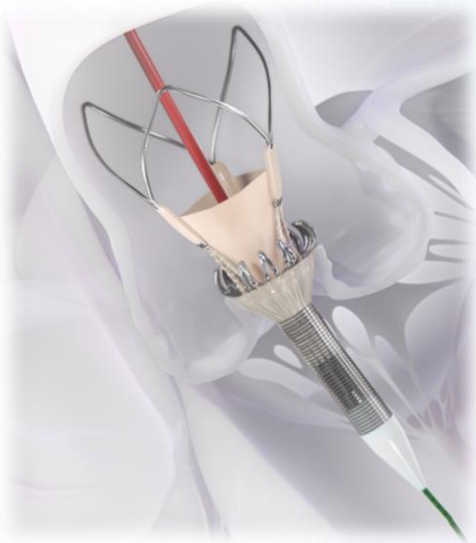
1. Lowest PPI rate
2. Single digit gradients and Large EOAs
3. Upgraded active Pvseal technique to decrease PVL
   (60% larger sealing skirt compared to previous generation)
4. Unrestricted coronary access
5. Smooth deliverability
6. Case (horizontal aorta, very severe AS..)

Best-in-class PPI

Lower patients' pacemaker risk

- Patients who receive PPI after TAVI experience higher mortality and rehospitalization risk[1]
- With top-down deployment and upper- and lower-crown anchoring, the ACURATE *neo2*™ Aortic Valve System minimizes LVOT protrusion

6%
new permanent pacemaker rate*[2]
***in hospital**



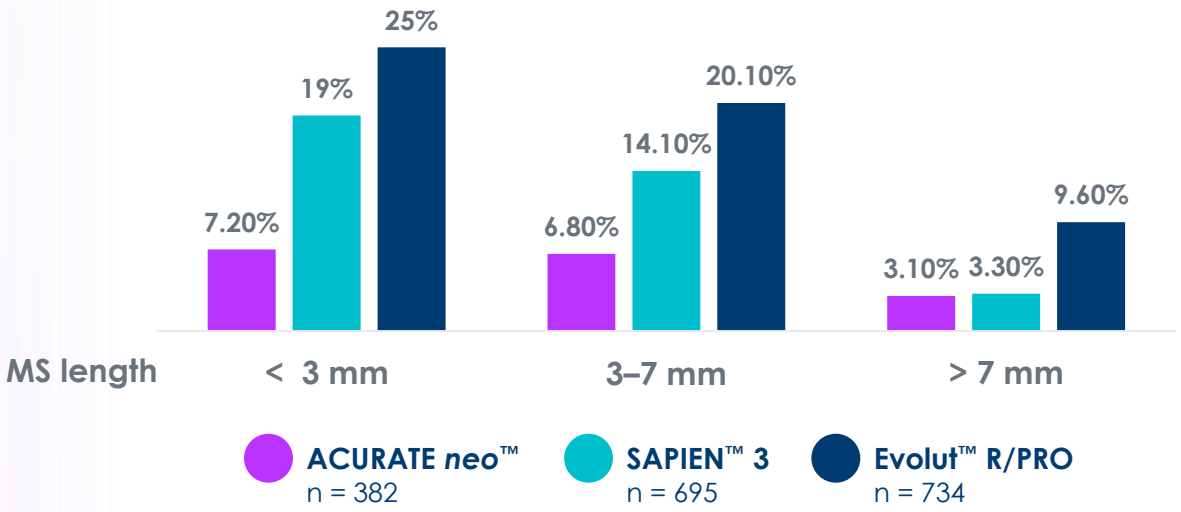
1. Pompeu M, et al. Late outcomes of permanent pacemaker implantation after TAVR: Meta-analysis of reconstructed time-to-event data, *JSCAI.* 2022. doi:https://doi.org/10.1016/j.jscai.2022.100434.
2. Rück A. Early *neo2* Registry. Full Core-lab Results of TAVI with the New ACURATE *neo2* Valve. TVT Congress. 2021.

ACURATE *neo2*™ Aortic Valve System

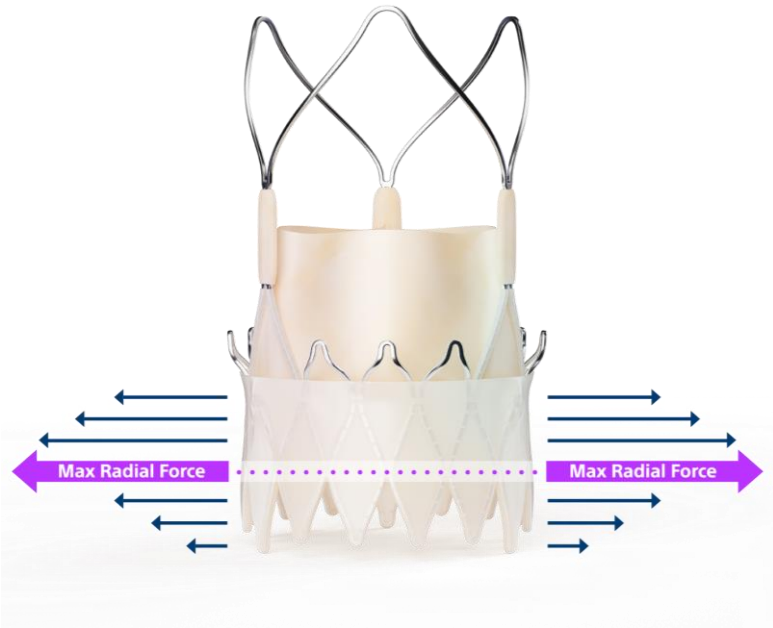
Best-in-class PPI

ACURATE *neo2*™ Aortic Valve System demonstrates the lowest PPI rates for patients at the highest risk of conduction injury[1]

Post-TAVI pacemaker implantation rate by THV type and membranous-septum length (n = 1811)



Optimized radial outward force distribution minimizes conduction system injury[1]



1. Thijmen W. Hokken et al., The INTERSECT Registry 2022.

ACURATE *neo2*™ Aortic Valve System

Single-digit gradients

Supra-annular valve design maximizes leaflet opening for single-digit gradients and large EOAs[1]

Single-digit gradients[2]

8.0 mmHg

Large EOAs[1]

1.7 cm^2

1. Möllmann H, Holzhey DM, Hilker M, et al. The ACURATE *neo2* Valve System for transcatheter aortic valve implantation: 30-day and 1-year outcomes. *Clin Res Cardiol*. 2021;110:1912–1920.
2. Early *neo2* Registry. Full Core-Lab Results of TAVI with the New ACURATE *neo2* Valve. TVT Congress. Presenter: Andreas Rück. July 20, 2021.

ACURATE *neo2*™ Aortic Valve System

Single-digit gradients

Protect patients' futures[1]

- Severe PPM is associated with increased mortality post-TAVR[2]
- Minimize the risk of prosthesis-patient mismatch, even in patients with small annuli

Reduced rates of elevated gradients and severe PPM vs. SAPIEN™ 3 Ultra[3]

ACURATE *neo2*™ Aortic Valve System	SAPIEN™ 3 Ultra
Elevated gradients*	
p < 0.001	
2.4%	**7.7%**
Severe PPM	
2.9%	**15.0%**

*(≥ 20mmHg)

1. Pibarot P, Dumesnil JG. Prosthesis-patient mismatch: Definition, clinical impact, and prevention. *Heart*. August 2006;92(8);1022-1029.
2. Mompeu M. Impact of Prosthesis-patient mismatch after TAVR: JACC CI Sep 16, 2022.
3. Pellegrini C. ACURATE *neo2* versus SAPIEN 3 Ultra. Interventions for valvular disease and heart failure.

ACURATE *neo2*™ Aortic Valve System

ACURATE *neo2*™ *vs* SAPIEN 3 Ultra™ Head-to-Head Comparison

ACURATE *neo2* Aortic Valve System	SAPIEN 3 Ultra Transcatheter Heart Valve
Porcine Pericardium, Supra Annular Leaflets	Bovine Pericardium, Intra-annular Leaflets
Self-Expanding (Top-down) Nitinol frame	Balloon-Expanding Cobalt-Chromium Frame
CE marked 2020	CE marked 2018
Not FDA Approved, Investigational Device in the US	FDA Approved 2018

CAUTION: In Europe, ACURATE neo and *neo2* Aortic Valve Systems are CE-marked. In the USA, ACURATE *neo2* is an investigational device and restricted under federal law to investigational use only. Not available for sale.

Study Design

1st head-to-head comparison of ACURATE *neo2* & SAPIEN 3 Ultra

Objective: To compare VARC-3 device and technical success (Primary Endpoint) and 30-day VARC-3 clinical endpoints (Secondary Endpoint) of ACURATE *neo2* to SAPIEN 3 Ultra

Head-to-Head Transfemoral TAVR

n = 1356 Patients | 4 German Centers | Procedures performed: March 2019 – December 2021

ACURATE *neo2*
n=608

SAPIEN 3 Ultra
n=748

1:1 nearest neighbour matching

Age
Female gender
EuroScore I
NYHA III/IV
Coronary artery disease

Previous PCI
Mean transvalvular gradient
LVEF < 35%
Bicuspid aortic valve

Mean annulus diameter
Severe calcification
Asymmetric calcification
Indexed Effective Orifice Area (iEOA)

ACURATE *neo2*
n=472

SAPIEN 3 Ultra
n=472

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Pellegrini C. ACURATE neo2 versus SAPIEN 3 Ultra. EuroIntervention 2022.

Baseline Characteristics
ACURATE *neo2* & SAPIEN 3 Ultra

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	Entire population			Matched population		
	ACURATE *neo2* n=608	SAPIEN 3 Ultra n=748	p-value	ACURATE *neo2* n=472	SAPIEN 3 Ultra n=472	p-value
Age, years	82.0 [78.7 – 85.0]	81.4 [77.1 – 85.0]	**0.032**	82.0 [78.7 – 85.0]	81.6 [77.6 – 85.1]	0.584
Female gender	289 (47.5)	398 (53.2)	**0.038**	239 (50.6)	246 (52.1)	0.696
Logistic EuroScore, %	14.4 [8.1 – 23.4]	12.3 [7.7 - 21.3]	**0.008**	13.8 [7.9 – 23.0]	12.5 [7.9 - 21.9]	0.184
NYHA III/IV	420 (69.1)	429 (57.4)	**<0.001**	305 (64.6)	297 (62.9)	0.636
Coronary artery disease	376 (61.8)	558 (74.6)	**<0.001**	340 (72.0)	336 (71.2)	0.829
Previous myocardial infarction	58 (9.5)	87 (11.6)	0.251	50 (10.6)	54 (11.4)	0.755
Previous stroke	77 (12.7)	94 (12.6)	0.999	57 (12.1)	55 (11.7)	0.920
COPD	74 (12.2)	86 (11.5)	0.735	57 (12.1)	56 (11.9)	0.999
Peripheral artery disease	84 (13.8)	130 (17.4)	0.085	61 (12.9)	81 (17.2)	0.083
eGFR, ml/min	65.0 [47.0 – 83.0]	64.0 [48.5 – 79.5]	0.684	65.0 [47.0 – 84.3]	62.0 [47.7 – 79.0]	0.198
Previous pacemaker	75 (12.3)	71 (9.5)	0.095	57 (12.1)	46 (9.7)	0.296
Atrial fibrillation	256 (42.1)	291 (38.9)	0.243	190 (40.3)	191 (40.5)	0.999
Right bundle-branch block	56 (9.2)	85 (11.4)	0.211	50 (10.6)	60 (12.7)	0.361
LVEF <35%	17 (2.8)	42 (5.6)	**0.011**	17 (3.6)	13 (2.8)	0.579
Mean gradient, mmHg	42.0 [31.3 – 50.0]	44.0 [37.0 – 54.0]	**<0.001**	43.0 [34.0 – 52.0]	42.5 [34.8 – 51.0]	0.940
Bicuspid aortic valve	20 (3.3)	97 (13.0)	**<0.001**	20 (4.2)	25 (5.3)	0.542
Severe aortic valve calcification	126/606 (20.8)	206/747 (27.6)	**0.004**	114 (24.3)	115 (24.4)	0.954
Asymmetric calcification	123 (20.2)	336 (44.9)	**<0.001**	120 (25.4)	135 (28.6)	0.305
Mean annulus diameter, mm	23.7 [22.4, 25.1]	24.9 [23.4, 26.2]	**<0.001**	23.8 [22.4, 25.2]	24.9 [23.4, 26.2]	<0.001

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Pellegrini C. ACURATE neo2 versus SAPIEN 3 Ultra. EuroIntervention 2022.

Essential Outcomes
ACURATE *neo2* & SAPIEN 3 Ultra

Boston Scientific

	ACURATE *neo2* n=608	SAPIEN 3 Ultra n=748	p-value	ACURATE *neo2* n=472	SAPIEN 3 Ultra n=472	p-value
Pre-dilatation, n (%)	534 (87.8)	268 (35.8)	**<0.001**	434 (91.9)	148 (31.4)	**<0.001**
Post-dilatation, n (%)	250 (41.4)	111 (14.8)	**<0.001**	211 (44.7)	69 (14.6)	**<0.001**
Procedural time, min	44.0 [35.0 – 59.0]	46.0 [35.0 – 58.0]	0.867	45.0 [36.0 – 59.0]	46.0 [35.0 – 57.0]	0.472
Fluoroscopy time, min	9.4 [7.0 - 13.3]	10.2 [7.1 - 14.6]	**0.033**	9.8 [7.3 - 13.8]	10.2 [6.9 - 14.1]	0.974
Technical success (VARC-3)	575 (94.6)	714 (95.5)	0.529	448 (94.9)	450 (95.3)	0.880
Device success (VARC-3)	557 (91.6)	626 (83.7)	**<0.001**	434 (91.9)	401 (85.0)	**0.001**
Contrast agent, ml	40.0 [20.0, 116.0]	115.0 [36.0, 160.0]	**<0.001**	40.0 [22.0, 130.0]	117.5 [37.8, 160.0]	**<0.001**
Pre-discharge moderate/severe PVL n (%)*	4 (0.7)	6 (0.8)	1.000	3 (0.6)	5 (1.1)	0.723
Pre-discharge Mean gradient ≥ 20mmHg, n (%)	11 (1.8)	69 (9.3)	**<0.001**	11 (2.4)	36 (7.7)	**<0.001**
Indexed effective orifine area (cm^2)**	0.9 [0.8, 1.1] (n=453)	0.8 [0.7, 0.9] (n=261)	**<0.001**	0.9 [0.8, 1.1] (n=342)	0.8 [0.7, 0.9] (n=167)	**<0.001**
Severe PPM, n (%)**	10/453 (2.2)	39/261 (14.9)	**<0.001**	10/342 (2.9)	25/167 (15.0)	**<0.001**
Major vascular complication (VARC-3)	39 (6.4)	66 (8.8)	0.122	29 (6.1)	45 (9.5)	0.069
Coronary obstruction requiring PCI	1 (0.2)	3 (0.4)	0.768	1 (0.2)	2 (0.4)	0.999
Annular rupture, n (%)	1 (0.2)	2 (0.3)	1.000	1(0.2)	0 (0)	0.999
Acute kidney injury St 2-4, n (%)	18 (3.0)	23 (3.1)	0.999	15 (3.2)	15 (3.2)	0.999
30-day All-stroke**	18/598 (3.0)	23/734 (3.1)	0.999	16/464 (3.4)	11/465 (2.4)	0.435
30-day Pacemaker implantation, n (%)**	40/522 (7.7)	70/664 (10.5)	0.090	33/406 (8.1)	43/419 (10.3)	0.289
30-day mortality, n (%)**	11/598 (1.8)	18/734 (2.5)	0.566	8/464 (1.7)	11/465 (2.4)	0.646

* Pre-discharge echocardiogram assessed. 10/1356 assessed by angio ** Data not available for full population. Sample sizes as indicated.

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Pellegrini C. ACURATE neo2 versus SAPIEN 3 Ultra. EuroIntervention 2022.

Essential Matched Cohort Outcomes
ACURATE *neo2* & SAPIEN 3 Ultra

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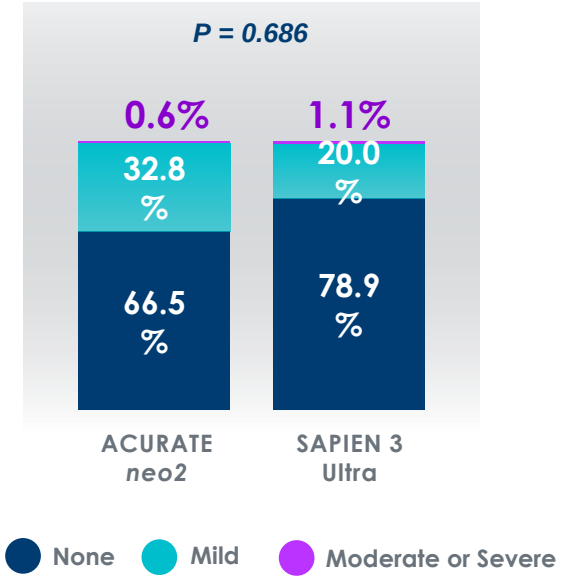
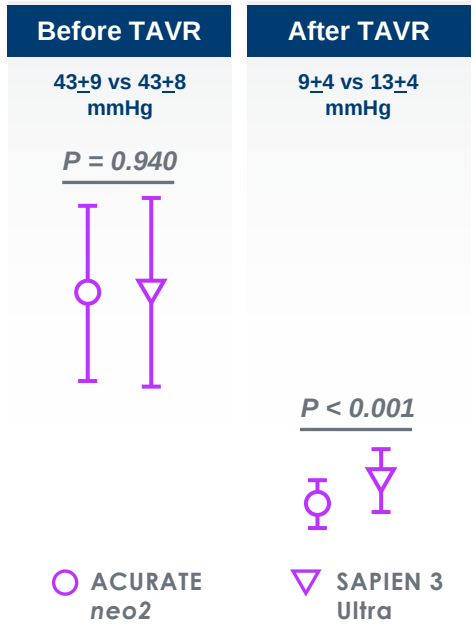
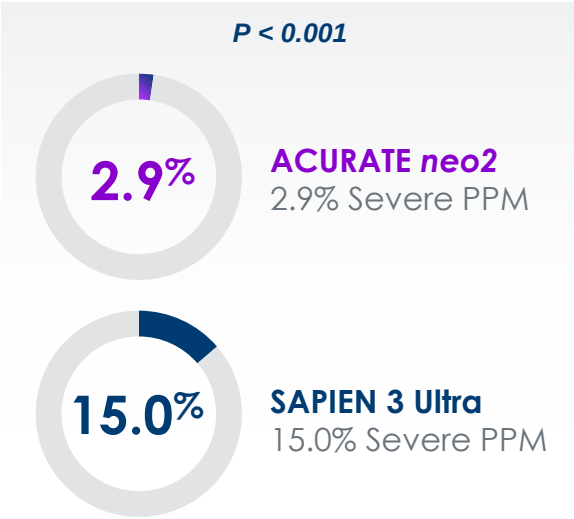
Similar and low Rates of PVL



Lower Mean Gradients



Lower Severe Prothesis-Patient Mismatch



0.6%
Moderate to Severe PVL
vs. 1.1% with SAPIEN 3 Ultra
p=0.723

2.4%
Elevated Gradients*
vs. 7.7% with SAPIEN 3 Ultra
p < 0.001
*(≥ 20mmHg)

91.9%
Device success
vs. 85.0% with SAPIEN 3 Ultra
p = 0.001

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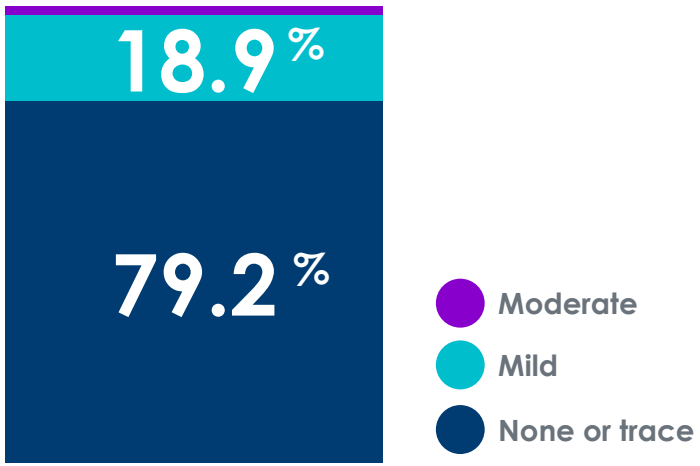
Pellegrini C. ACURATE neo2 versus SAPIEN 3 Ultra. EuroIntervention 2022.

Advanced PVL performance

Protect against PVL with the ACURATE *neo2*™ Aortic Valve System's advanced sealing skirt.

1.9%
Moderate PVL[1]*
(0% > Moderate)



Inner and outer ACTIVE PVseal™ extends the full waist of the ACURATE *neo2* Valve, maximizing sealing efficacy

* At 30-days, Echocardiographic and CT imaging Independently core lab adjudicated

1. Kim W., et al; Clinical outcomes of the ACURATE neo2 transcatheter heart valve: a prospective, multicenter, observational, post-market surveillance study, EuroIntervention 2022. DOI: 10.4244/EIJ-D-22-00914

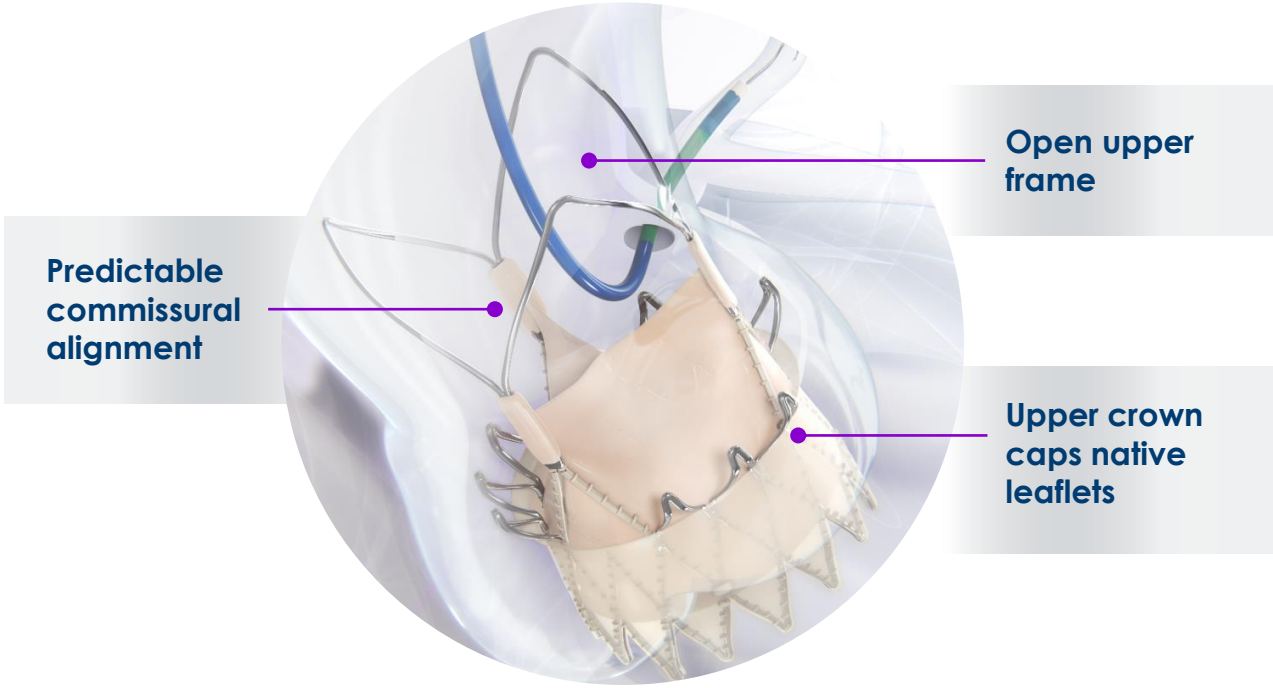
ACURATE *neo2*™ Aortic Valve System

Unrestricted coronary access

Lower-risk TAVI requires preserved future access.[1] STEMI following TAVI resulted in[2]:

- **4x higher PCI failure rate**
- **33% increased mortality rate**

100%	82%	99%
ACURATE *neo*™ Valve platform	**Evolut™ R/PRO**	**SAPIEN™**
100% successful coronary cannulation n = 72	82% successful coronary cannulation n = 123	99% successful coronary cannulation n = 96



The ACURATE *neo2* design is associated with favorable post-TAVI coronary access[1]

1. Reobtain Coronary Ostia Cannulation Beyond Transcatheter Aortic Valve Stent (RE-ACCESS); NCT04026204. J Am Coll Cardiol Intv. 2020.
2. Faroux L, et al. ST-Segment Elevation Myocardial Infarction Following Transcatheter Aortic Valve Replacement. "https://www.jacc.org/journal/jacc" J Am. Coll. Cardiol. 2021 May, 77 (17) 2187 -2199.

ACURATE *neo2*™ Aortic Valve System

Smooth deliverability

Low-profile, highly flexible catheter

Atraumatic nosecone
Optimized nosecone taper and guidewire transition for smooth atraumatic tracking

360° flexibility
Spineless delivery system for enhanced flexibility

14F iSLEEVE compatible for all sizes

Intuitive handle design
Two-step implantation

Extended stability layer
Stable, predictable valve deployment

ACURATE neo2™
Aortic Valve System

ACURATE *neo*™ Aortic Valve System investigator initiated or sponsored trial

NEOPRO Multicenter Comparison Registry[1]

Outcomes of two next-generation self-expanding TAVI valves in real-world patients

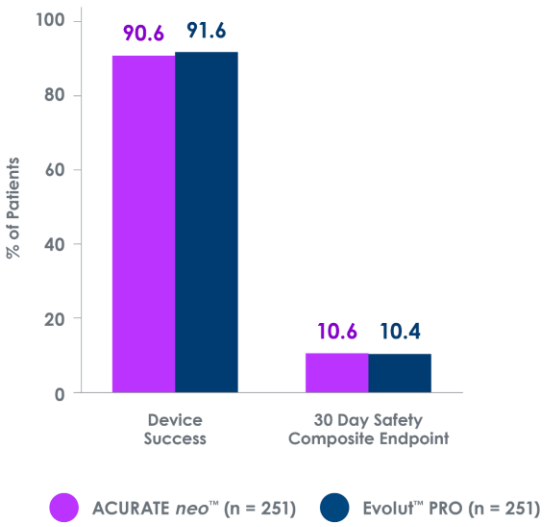
STUDY DESIGN: 1:1 propensity score matched multicenter comparison of ACURATE *neo* (n = 251) and Evolut™ PRO (n = 251) from 24 international centers

ACURATE *neo* demonstrated in PS-matched cohort

- Comparable VARC-2 device success and 30-day clinical outcomes
- Similar PVL rates with no PVL greater than moderate in ACURATE *neo* group

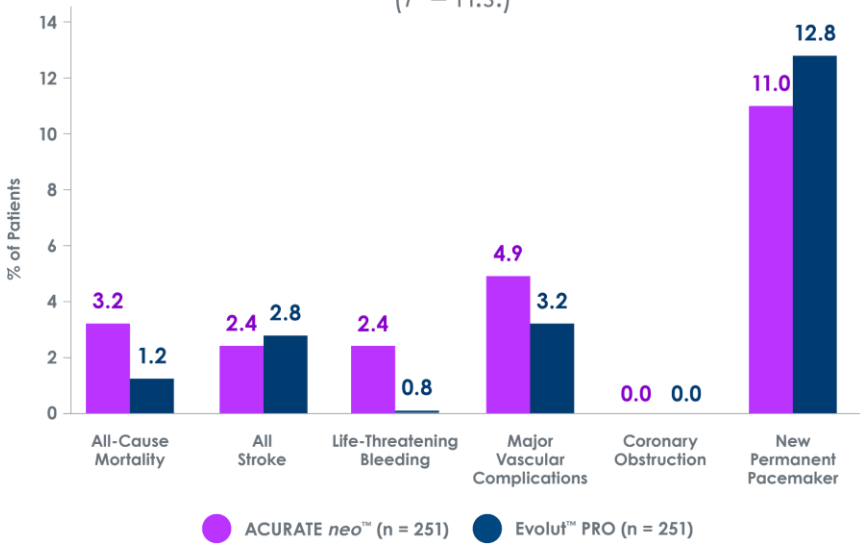
VARC-2 Endpoints

(*P* = n.s.)



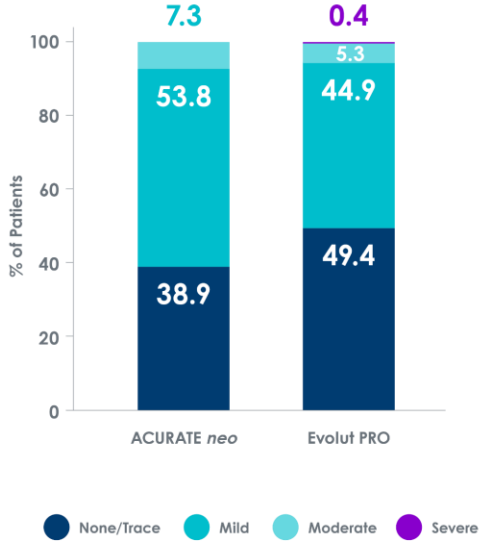
Propensity Score Matched Cohort Summary 30-Day Clinical Outcomes

(*P* = n.s.)



Paravalvular Leak Rates

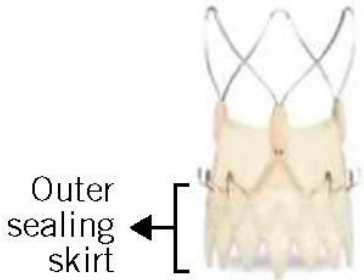
(*P* = 0.055)



1. Pagnesi M, et al. Transcatheter aortic valve replacement with next-generation self-expanding devices: A multicenter, retrospective, propensity-matched comparison of Evolut PRO versus ACURATE *neo* transcatheter heart valves. *JACC: Cardiovascular Interventions.* Mar 2019, 12(5)433-443; doi:10.1016/j.jcin.2018.11.036.

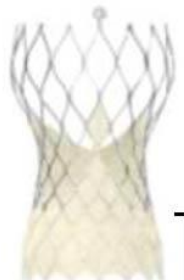
ACURATE *neo2*™ Aortic Valve System

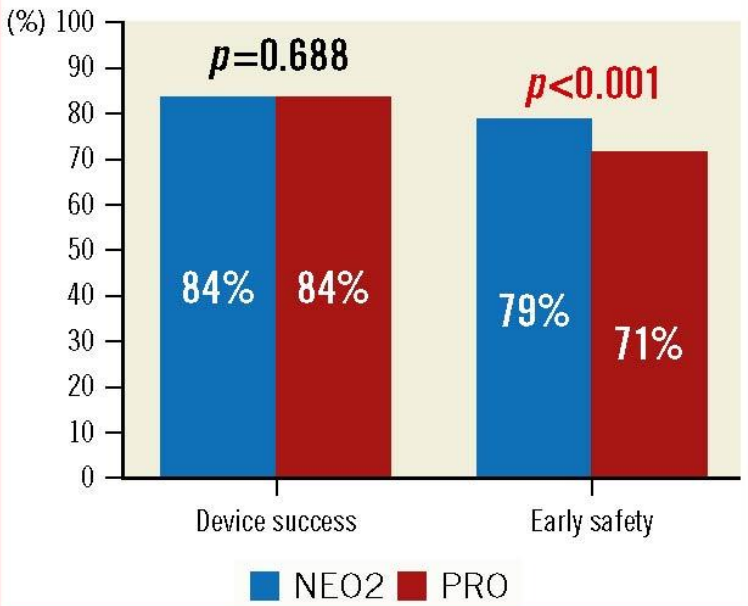
Comparison of Transcatheter Aortic Valve Replacement with the ACURATE neo2 *vs* Evolut PRO/PRO+ devices



TAVR with
ACURATE *neo2* vs Evolut PRO/PRO+
*Insights from the **NEOPRO-2 registry***

N=2,175
20 centres
VARC-3-defined outcomes



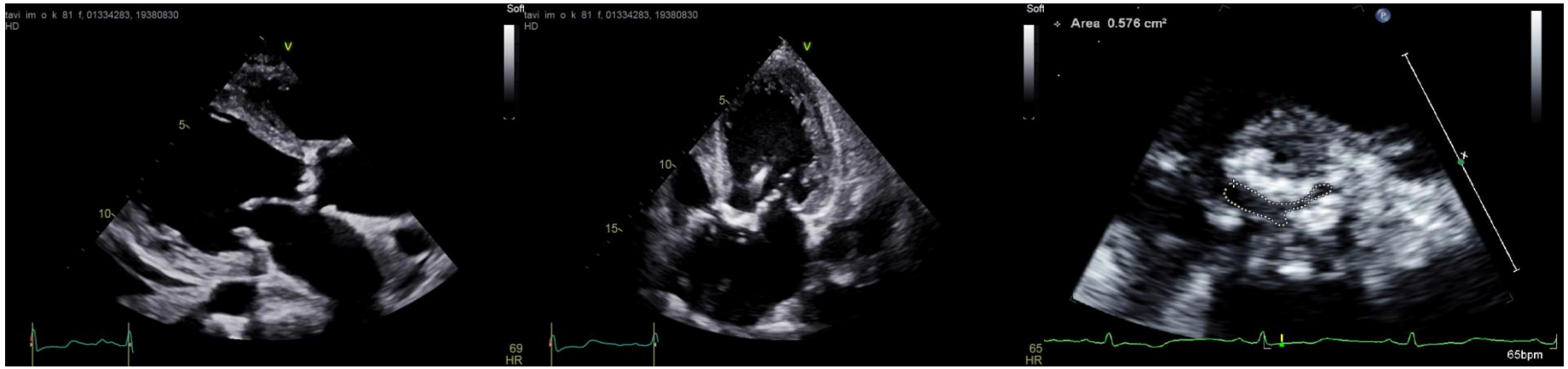
In-hospital outcomes	30-day device success and early safety	30-day outcomes
High technical success NEO2: 93.1% vs PRO: 94.1% (*p*=NS) **Comparable pre-discharge valve performance** NEO2: 96.0% vs PRO: 94.1% (*p*=NS)		**All-cause death:** 2.5% **Stroke:** 2.9% (NEO2 vs PRO: *p*=NS) ***neo2*: Lower rates of new PPI** Entire population: NEO2: 7.7% vs PRO: 15.6% **(*p*<0.001)** PS-matched analysis (n=452): NEO2: 6.7% vs PRO: 16.7% **(*p*<0.001)**

Baggio S, et al. EuroIntervention 2023

Case of TAVR

91 y/o Female

1. Very severe AS with moderate AR (AV area 0.58cm^2)
2. Chronic AF, type 2 DM, HTN

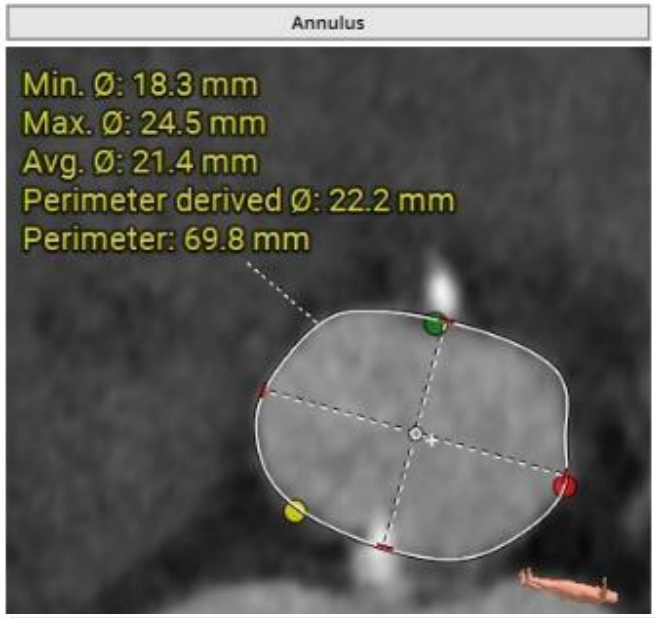


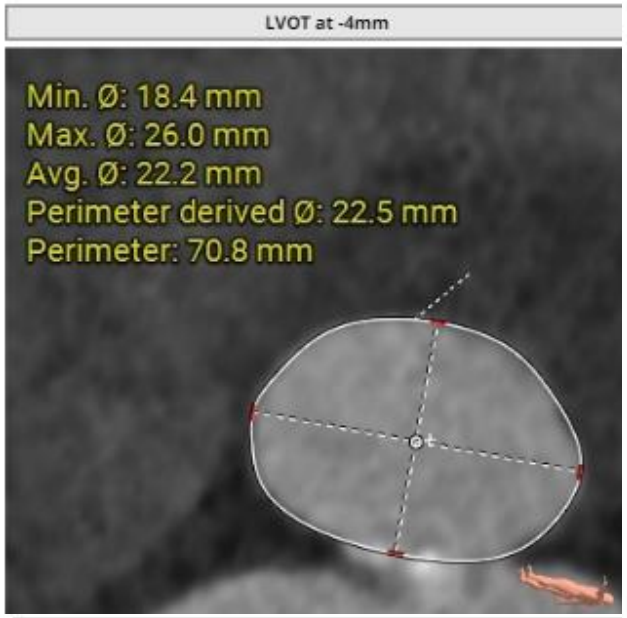
transaortic PG 139/72 mmHg, AV Vmax 6.0 m/s

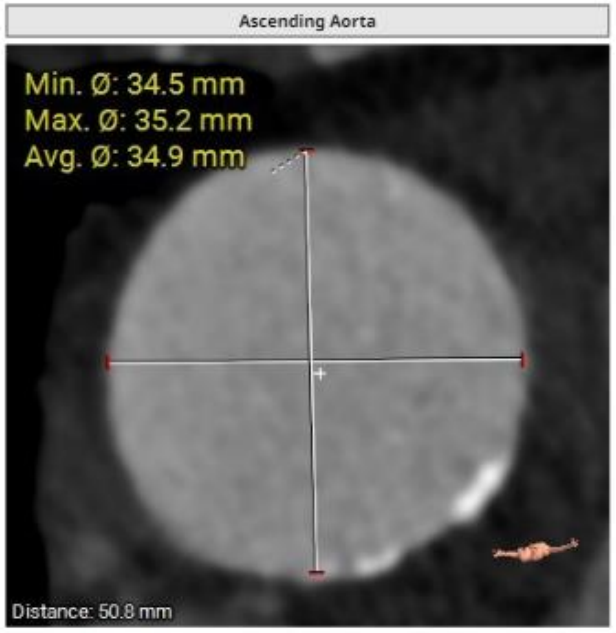
aortic valve area 0.58 cm^2

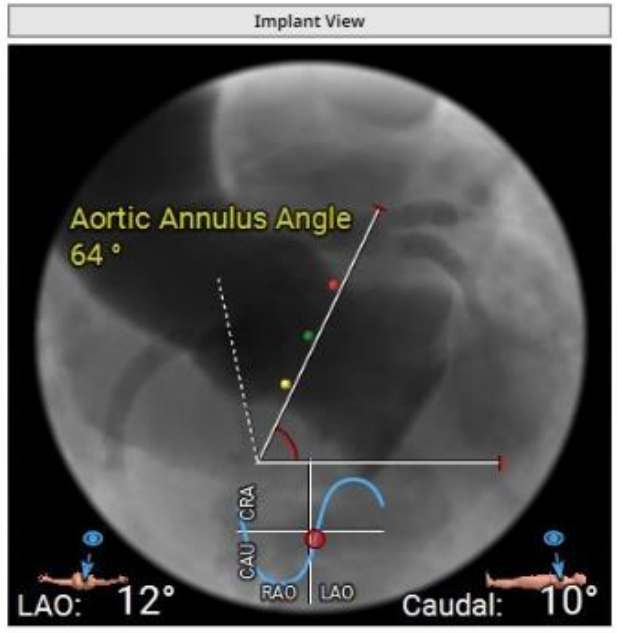
severe LV systolic dysfunction (EF 25 %),
borderline LV dilatation (56/53 mm) with moderate AR

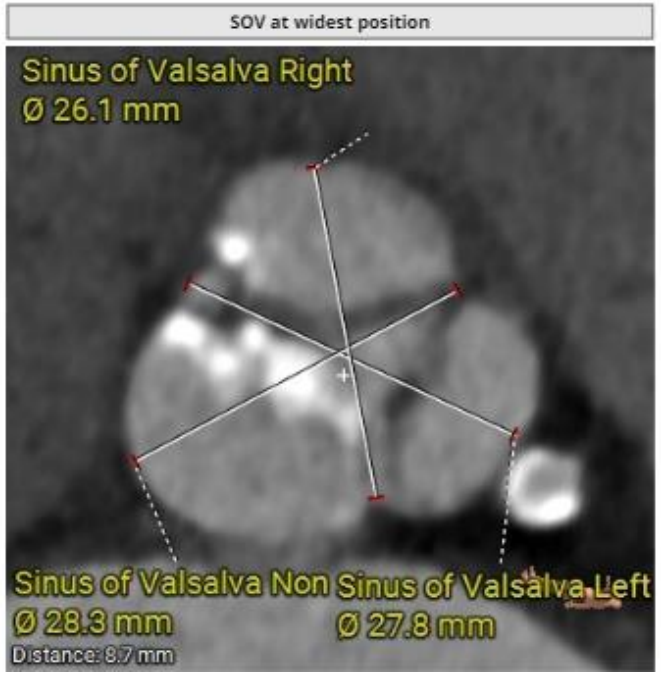
CT of Severe AS

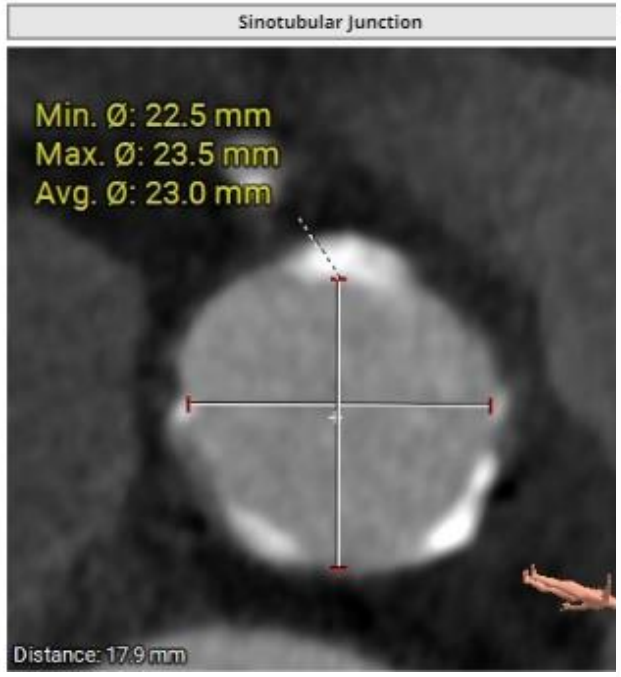


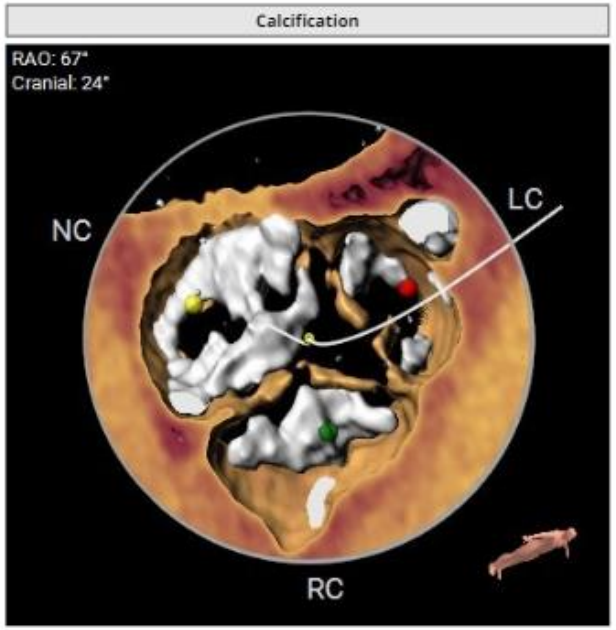


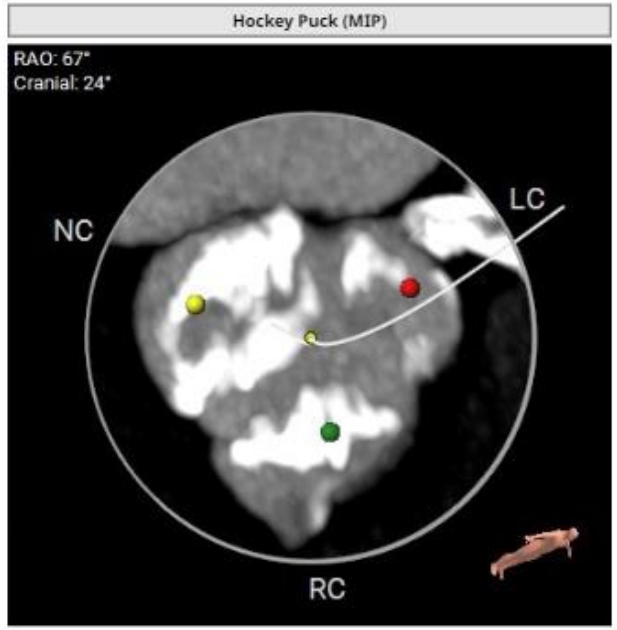






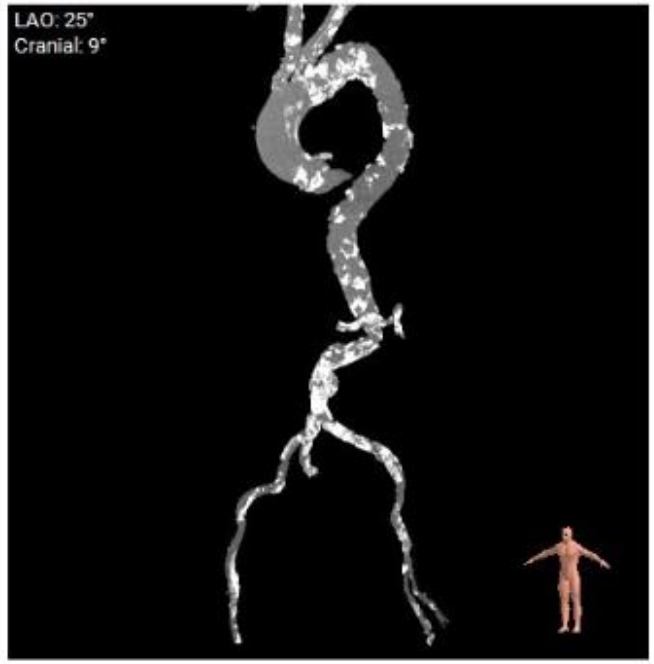




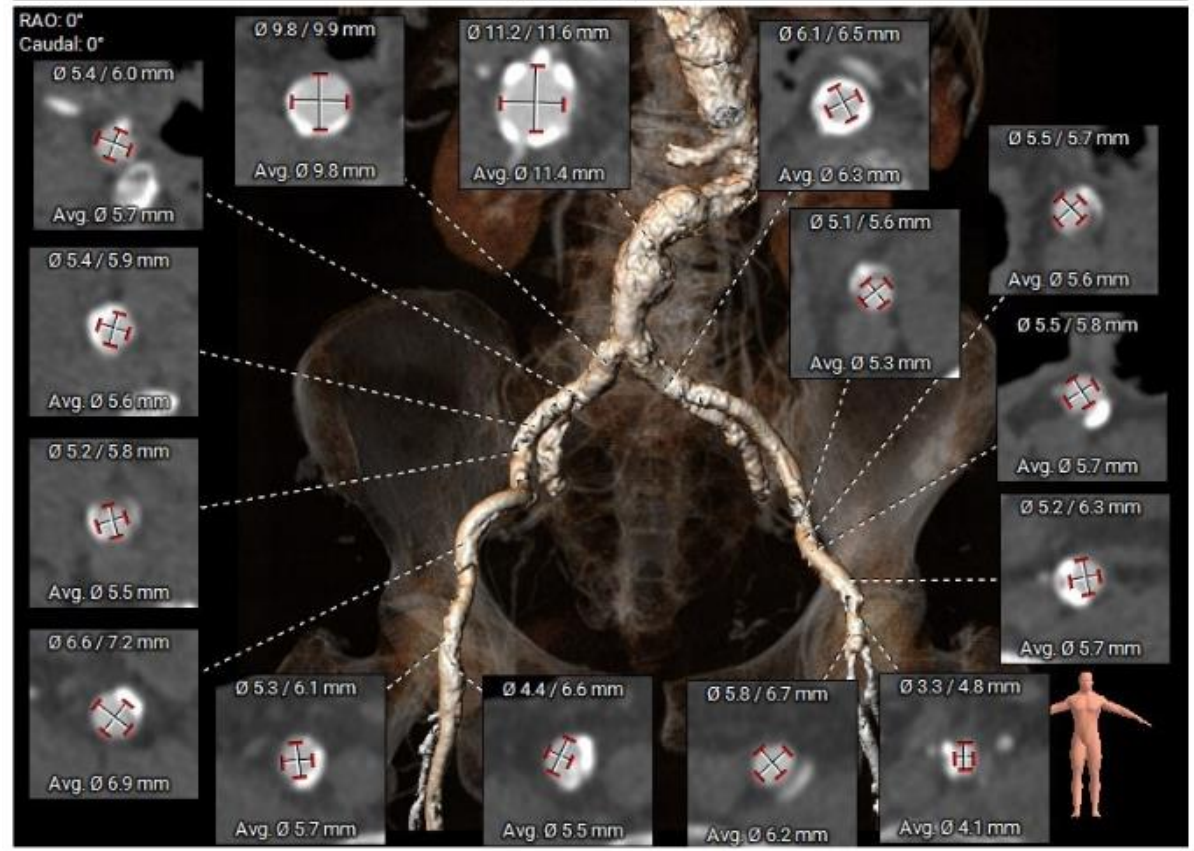


Aorto Ilio Femoral tract

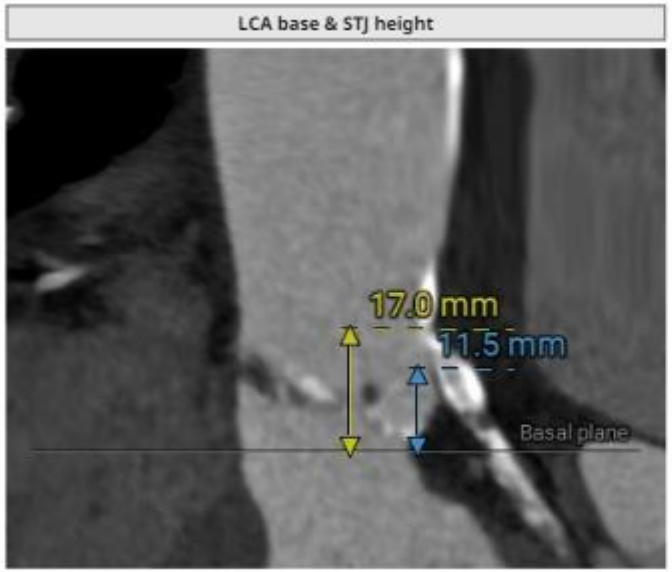
Calcifications

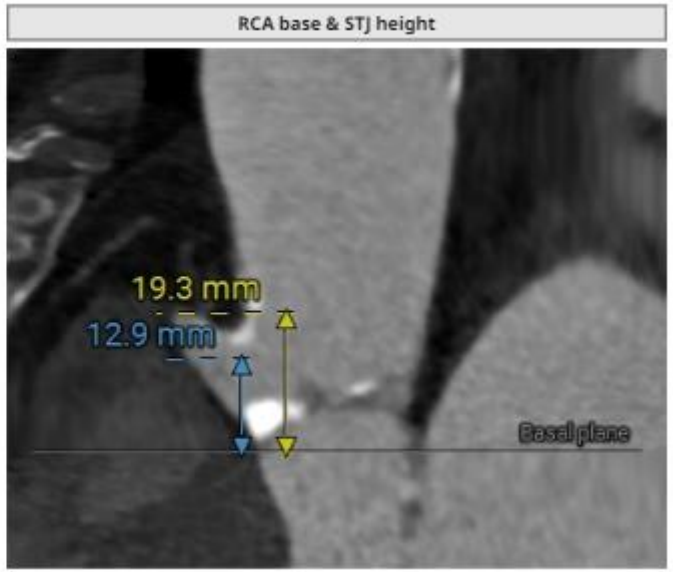


Aorto Ilio Femoral tract



CT of Severe AS

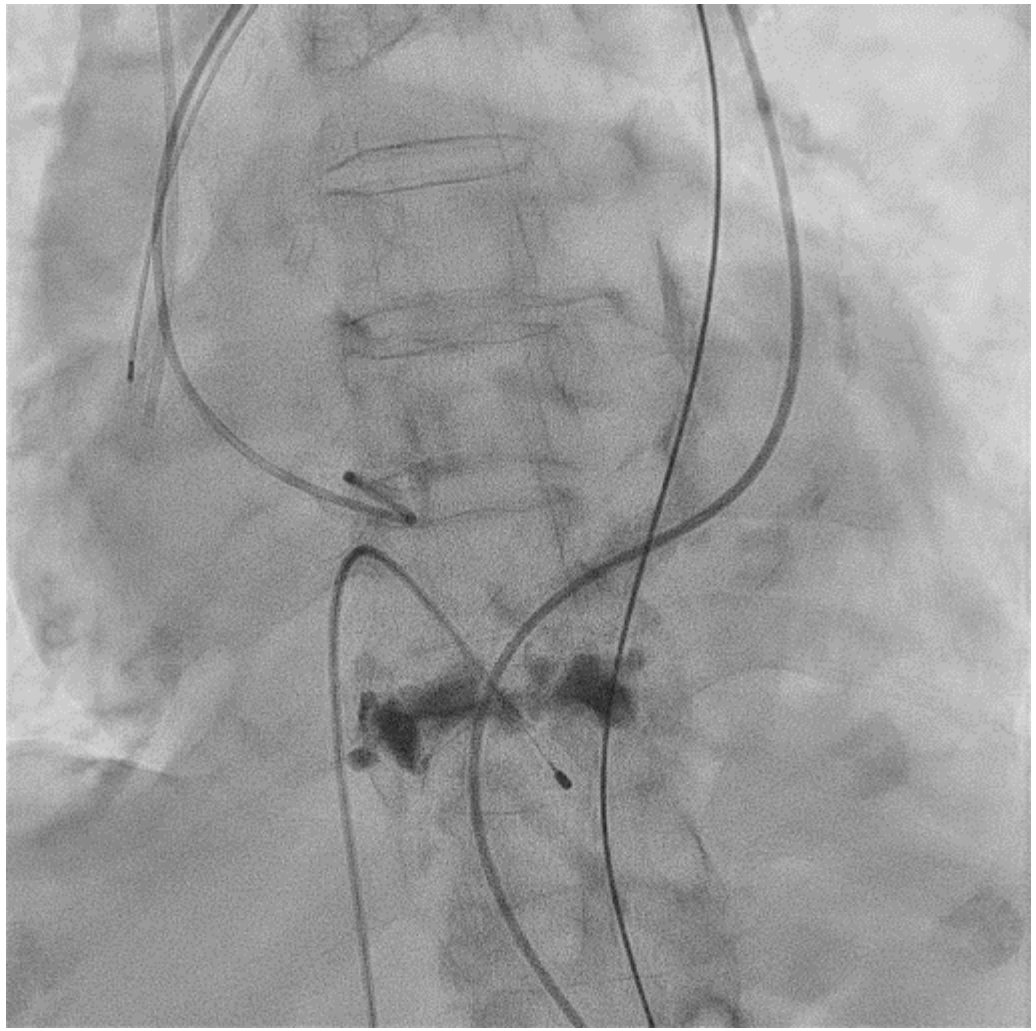


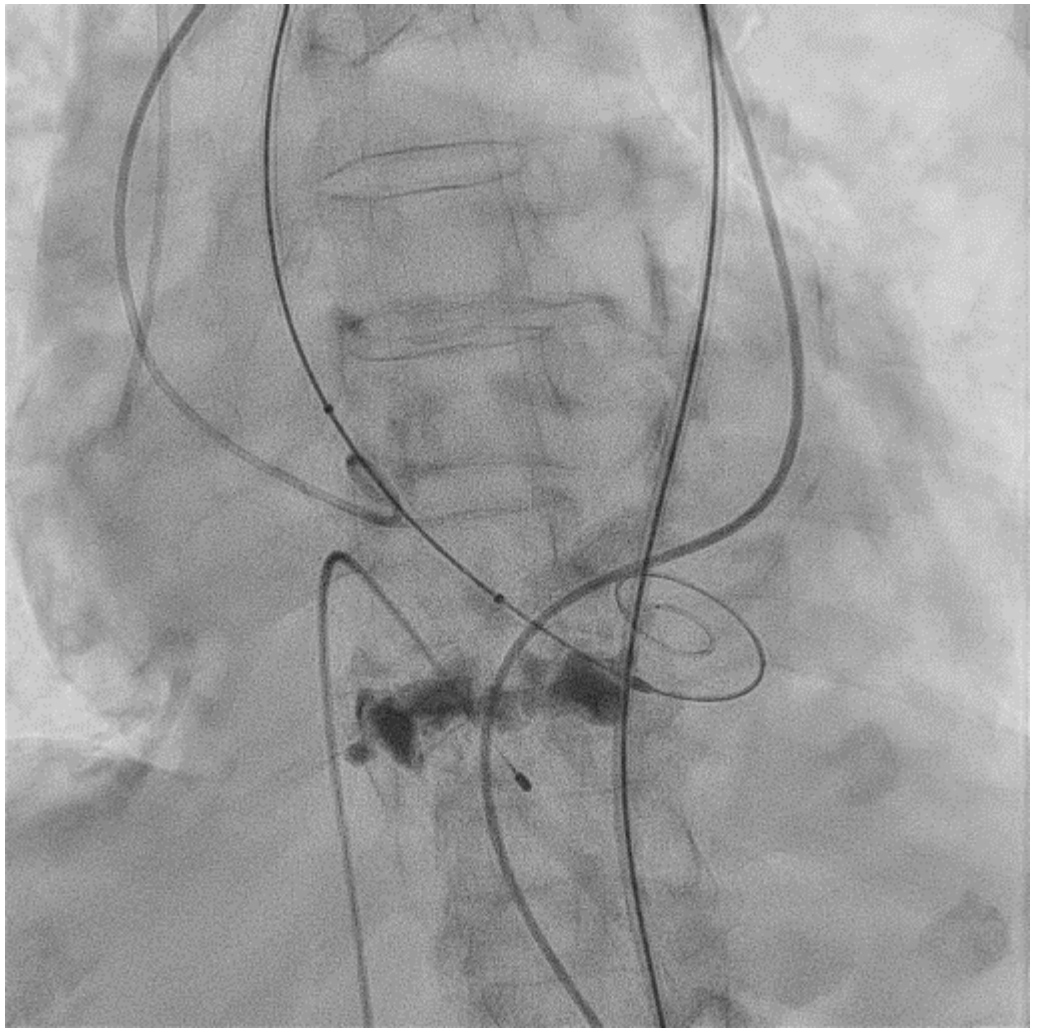


Annulus Perimeter : 69.8mm (ACURATE neo2 23mm)
Perimeter derived diameter = 22.2mm
LVOT Perimeter : 70.8mm (LVOT Diameter : 22.5mm)
SOV : 30.8mm, STJ : 23.0mm
Coronary height : Lt. = 11.5mm, Rt. = 12.9mm
3 Cusp view : LAO 12° CAU 10°
Ascending aorta : 35.2mm
Aorta angulation : 64°

Valve Size	S – 23 mm	M – 25 mm	L – 27 mm
Aortic annulus diameter*	21 mm ≤ annulus ≤ 23 mm	23 mm < annulus ≤ 25 mm	25 mm < annulus ≤ 27 mm
Aortic annulus perimeter	66 mm ≤ annulus ≤ 72 mm	72 mm < annulus ≤ 79 mm	79 mm < annulus ≤ 85 mm

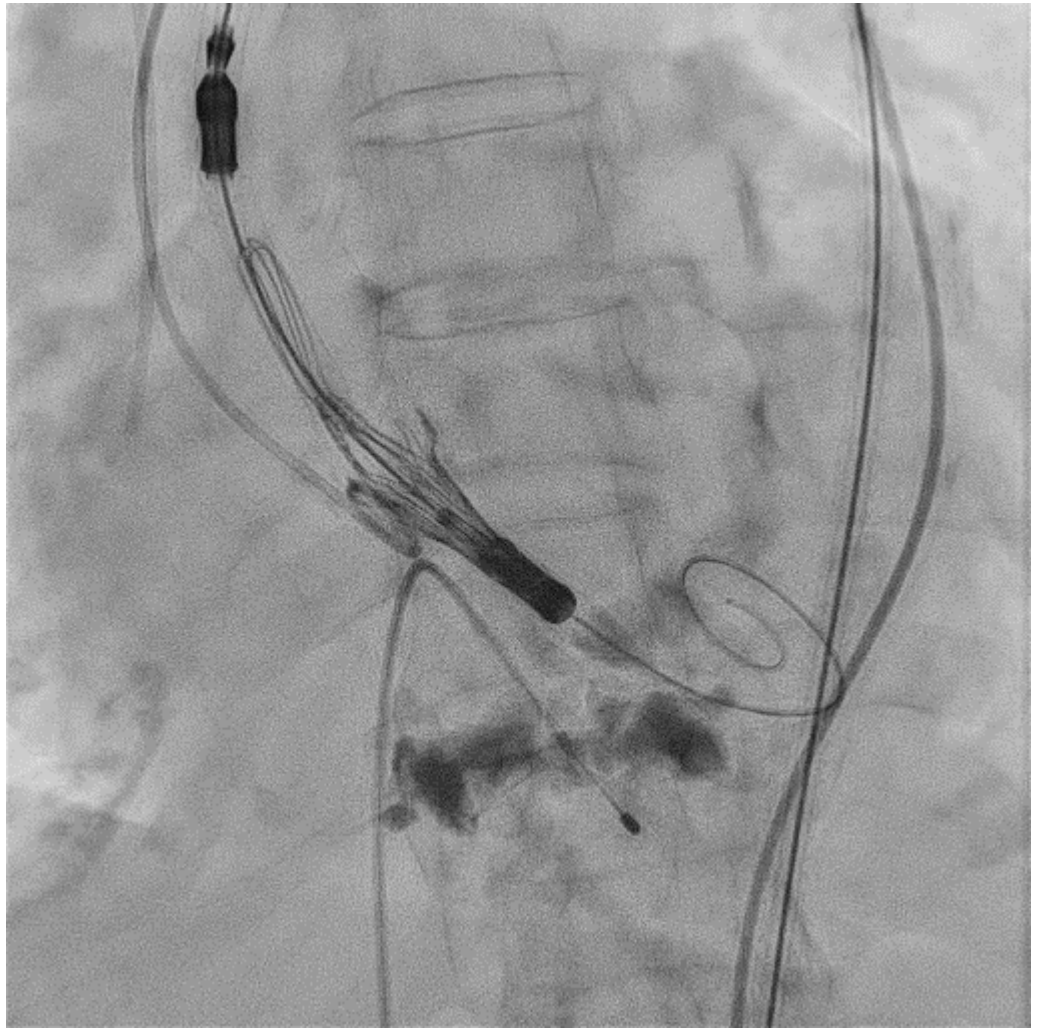
ACURATE neo2 23mm

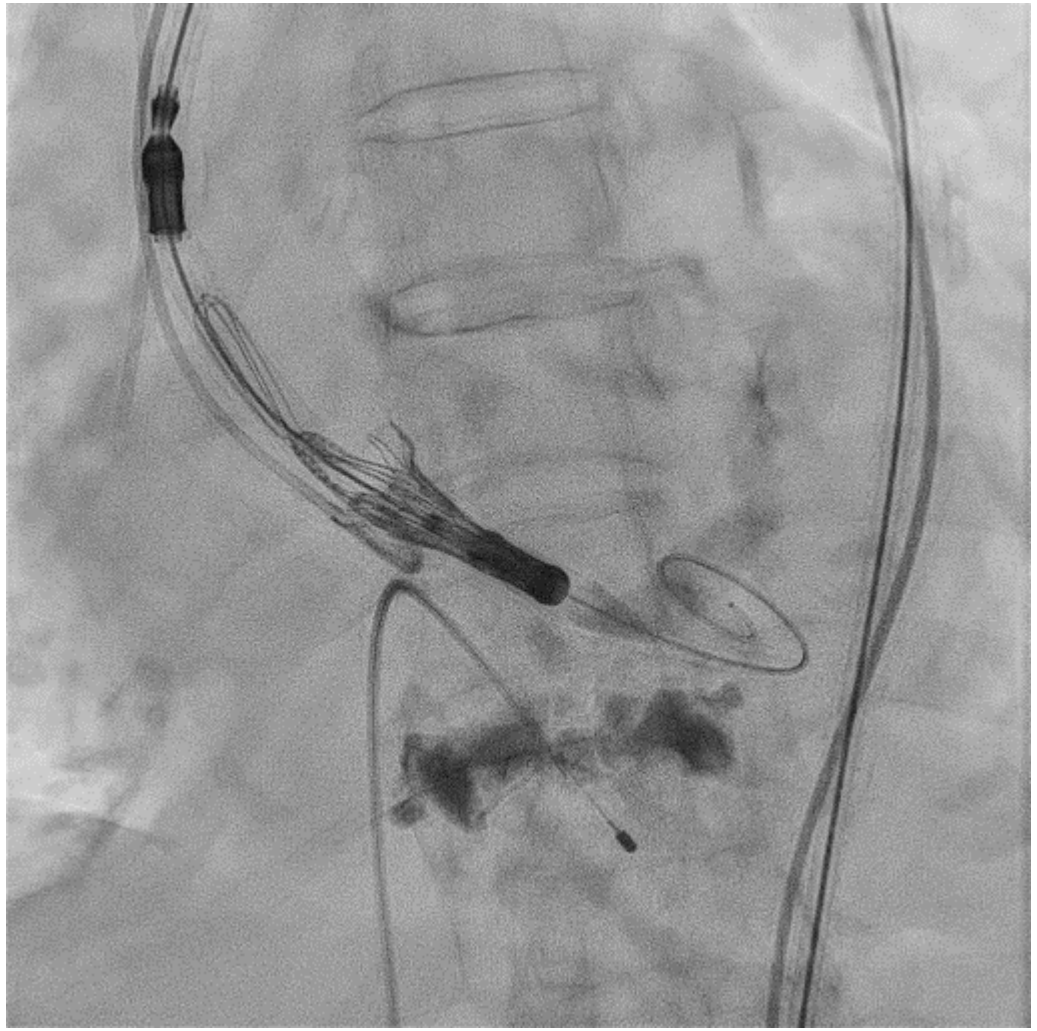




22(21)mm Atlas Gold balloon

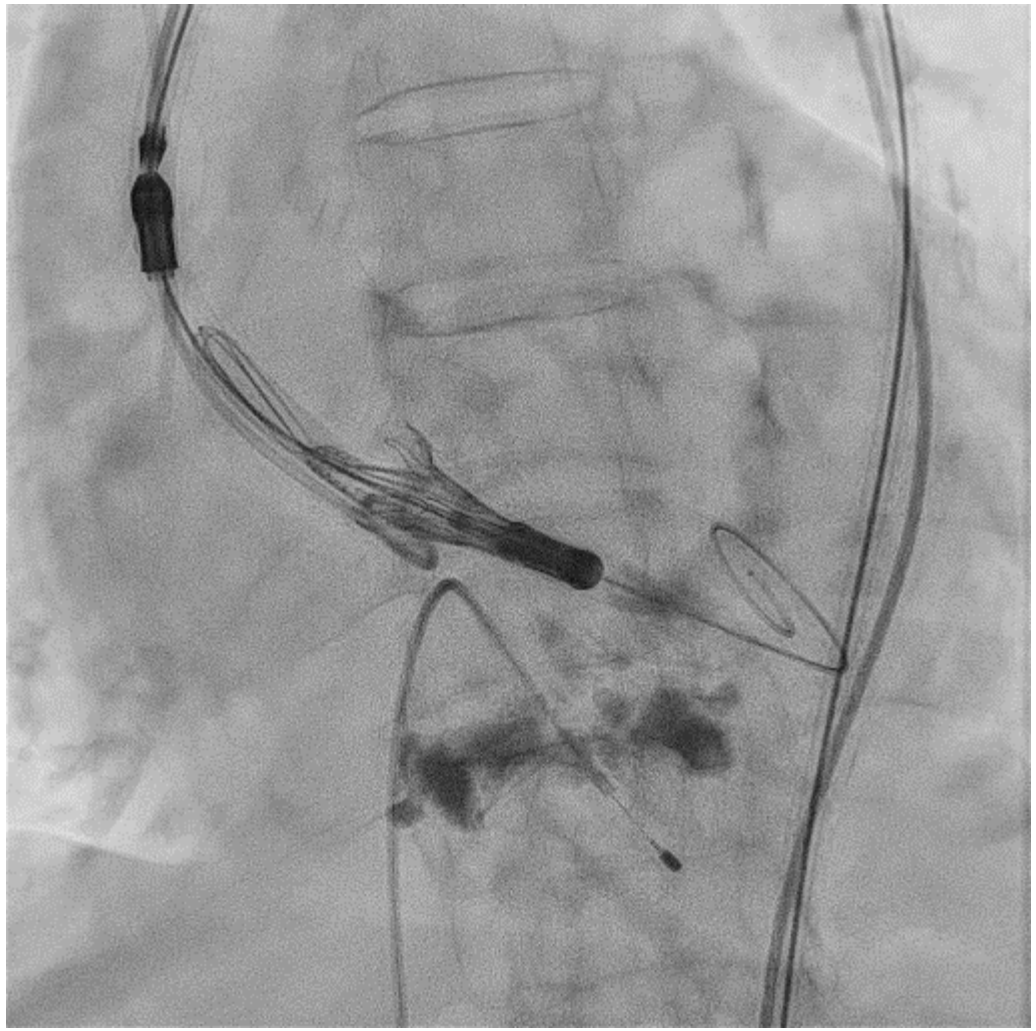
ACURATE neo2 23mm



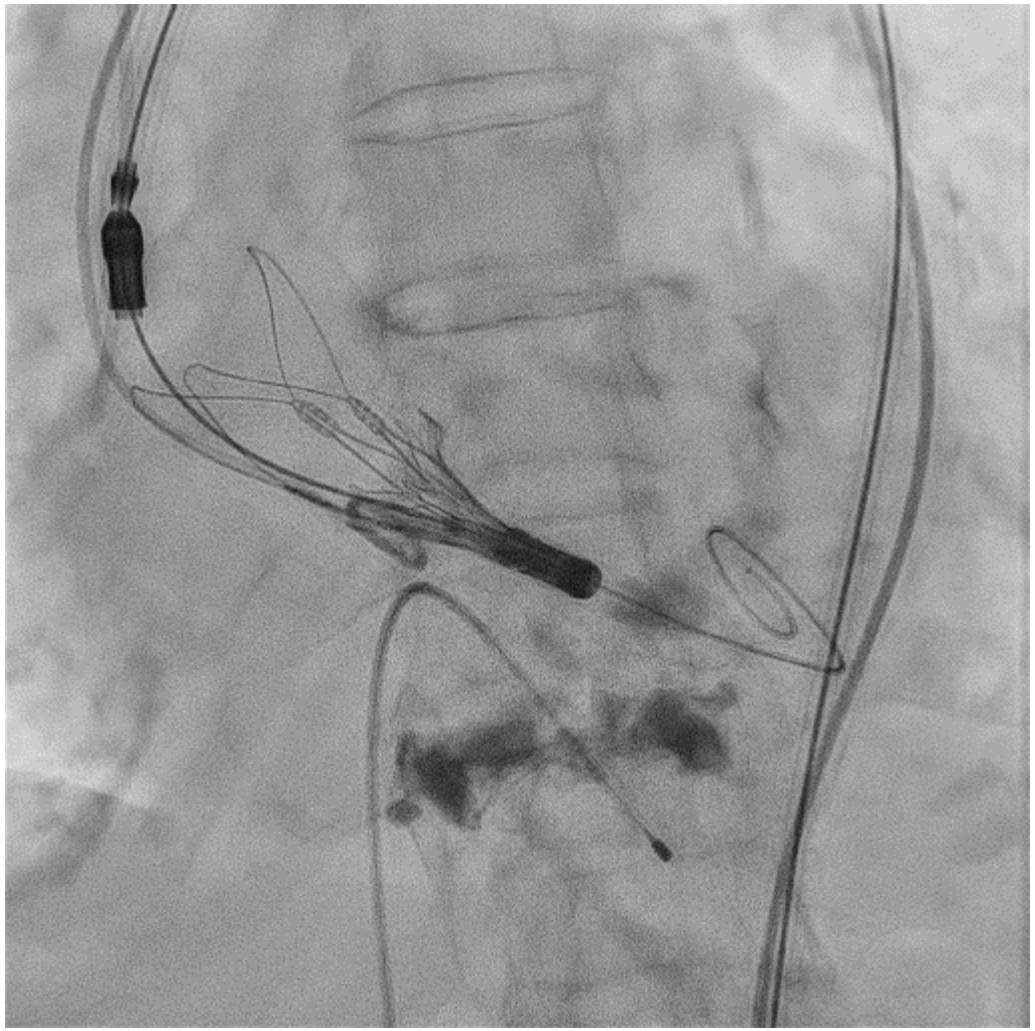


Upward movement

ACURATE neo2 23mm

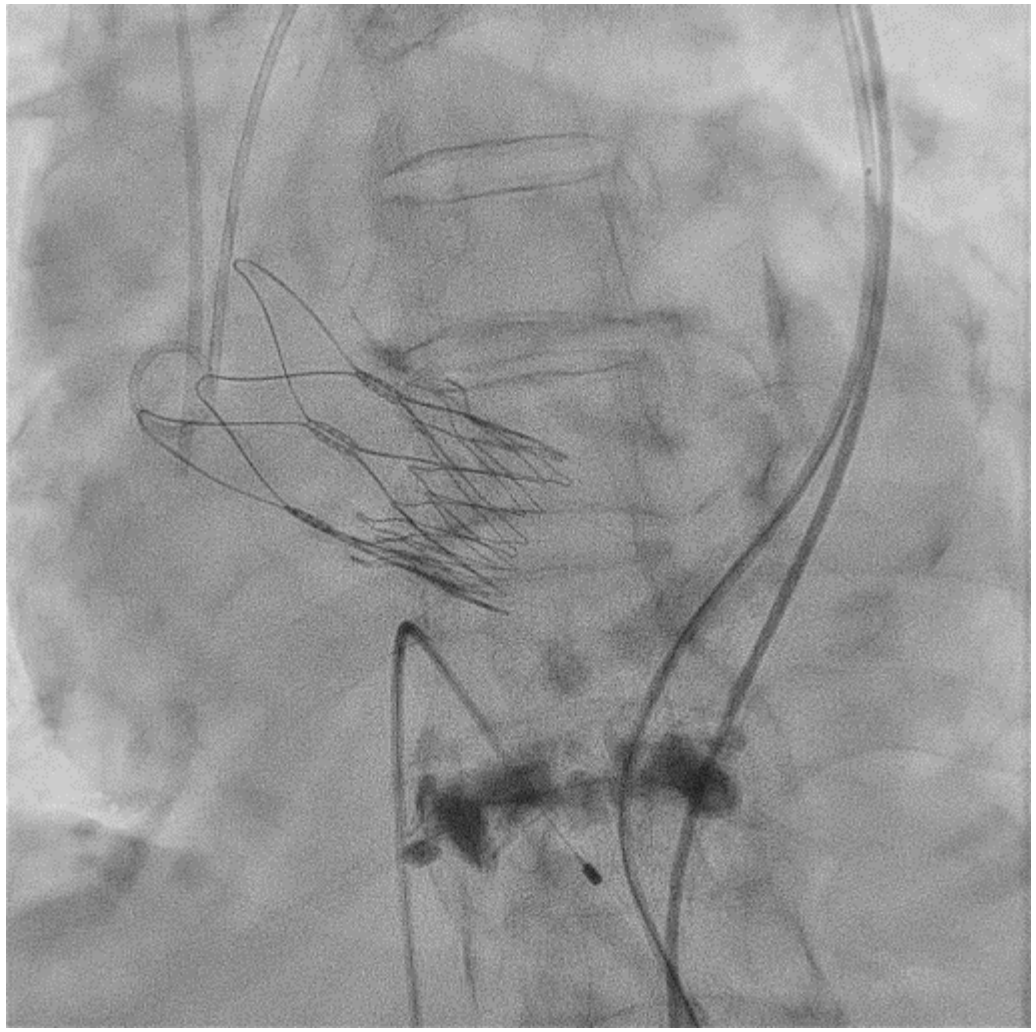


Push



Step2

ACURATE neo2 23mm



Conclusions

1. Lowest PPI rate Yes
2. Single digit gradients and Large EOAs Yes
3. Upgraded active PVseal technique to decrease PVL Yes
   (60% larger sealing skirt compared to previous generation)
4. Unrestricted coronary access Yes
5. Smooth deliverability even in severe angulated horizontal aorta