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Authors: Won-Keun Kim, M.D; Christian Hengstenberg, M.D, PhD; Michael Hilker, M.D, PhD; Ulrich Schäfer, M.D, PhD; Tanja K. Rudolph, M.D, PhD; Stefan Toggweiler, M.D, PhD; Andreas Rück, M.D, PhD; Lars Sondergaard, M.D, PhD; Lenard Conradi, M.D, PhD; Christian Hamm, M.D, PhD; Thomas Walther, M.D, PhD; Helge Möllmann, M.D, PhD

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Transcatheter aortic valve implantation with the ACURATE Neo valve: indications, procedural aspects and clinical outcomes

Won-Keun Kim MD[1,2,3], Christian Hengstenberg[4], MD, PhD, Michael Hilker[5], MD, PhD, Ulrich Schäfer[6], MD, PhD, Tanja K. Rudolph[7], MD, PhD, Stefan Toggweiler[8], MD, PhD, Andreas Rück[9], MD, PhD, Lars Sondergaard[10], MD, PhD, Lenard Conradi[11], MD, PhD, Christian Hamm[1,3], MD, PhD, Thomas Walther[12], MD, PhD, Helge Möllmann[13], MD, PhD

A list of study collaborators can be found in the appendix.

[1]Kerckhoff Heart Center, Department of Cardiology, Bad Nauheim, Germany

[2]Kerckhoff Heart Center, Department of Cardiac Surgery, Bad Nauheim, Germany

[3]Justus-Liebig University of Giessen, Department of Cardiology, Giessen, Germany

[4]Department of Medicine II, University Departments of the MedUni, Vienna, Austria

[5]University Medical Center, Department of Cardiothoracic Surgery, Regensburg, Germany

[6]Marienkrankenhaus, Department of Cardiology, Angiology, and Intensive Care Medicine, Hamburg, Germany

[7]Herz- und Diabeteszentrum NRW, Department of Cardiology, Ruhr-University Bochum, Bad Oeynhausen, Germany

[8]Heart Center Lucerne, Lucerner Kantonsspital, Lucerne, Switzerland

[9]Karolinska University Hospital, Stockholm, Sweden

[10]The Heart Center, Rigshospitalet, Copenhagen, Denmark

[11]University Heart Center, Department of Cardiovascular Surgery, University Hospital Hamburg-Eppendorf (UKE), Germany

[12]University Heart Center, Department of Cardiovascular Surgery, Johann-Wolfgang-Goethe University, Frankfurt, Germany

[13]St. Johannes Hospital, Department of Cardiology, Dortmund, Germany

Short running title: ACURATE *neo* best practice

Corresponding Author:

Dr. med. W. Kim

Department of Cardiology

Kerckhoff Heart Center

61231 Bad Nauheim, Germany

Tel: +49(0)6032-996-0; Fax: +49(0)6032-996-2313

Email: w.kim@kerckhoff-klinik.de

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ABSTRACT

The ACURATE *neo* aortic valve system is a self-expanding transcatheter device that was granted CE mark in 2014 and since has been widely adopted in the treatment of patients with severe aortic stenosis. The ACURATE *neo* can be used in a wide clinical spectrum, but there are some specific indications and anatomies where this device is particularly suitable. Recently it was shown that with appropriate patient screening, size selection, and optimized positioning, results can be improved substantially. This review provides an overview of existing data and compiles a standardized manual of best practice for the implantation of this device based on both evidence and individual experience.

ABBREVIATIONS

ACURATE$_{neo}$: ACURATE *neo*

PVL: paravalvular leakage

INTRODUCTION

The ACURATE *neo* (ACURATE$_{neo}$; Boston Scientific, Marlborough, MA) is a self-expanding transcatheter heart valve with a supra-annular design and porcine pericardial leaflets that has been commercially available in Europe since 2014. It is characterized by a top-down deployment, which allows for precise positioning and minimizes flow obstruction during deployment (1). Three stabilization arches provide for a better co-axial alignment, and the upper crown supports anchoring (Figure 1). The transfemoral delivery system incorporates two knobs in the handle that can be turned to deploy the device in two steps. The smallest diameter of the delivery system is 15 Fr and increases to 18 Fr at the site of the valve attachment. The ACURATE$_{neo}$ valve can be implanted via either transvascular or transapical access routes and has a dedicated transapical delivery system. Since CE-mark in 2014, it has been widely adopted in Europe, Canada, South America, and the Asia-Pacific region. A recent study illustrated that results are considerably subject to appropriate patient screening, size selection, and optimized positioning (2).

The purpose of this manuscript is to review the growing amount of clinical data on the ACURATE$_{neo}$ and to present a sophisticated approach for sizing and patient selection by highlighting suitable anatomies and indications. Moreover, we aim to provide a best-practice manual going through each procedural step of transfemoral implantation based on insights from experienced operators.

CLINICAL DATA

CE-mark study. This prospective series included the first 89 patients that were implanted with the ACURATE$_{neo}$ prosthesis (age 83.7±4.4 years; logistic EuroSCORE 26.5±7.7%) (3). Procedural success was 94.4%. At 30 days, all-cause mortality was 3.4%, the rate of moderate paravalvular leakage (PVL) was 4.5%, major stroke occurred in 2.2%, and the frequency of permanent pacemaker implantation (PPI) was 10.3%.

SAVI-TF registry. The purpose of this prospective, international registry was to demonstrate efficacy and safety of the ACURATE$_{neo}$ in a real-world setting (4). A total of 1,000 patients from 25 centers (age 81.1±5.2 years; STS score 6.0±5.6%) were included. Procedural success was obtained in 98.7%, mean

gradient was 8.4±4.0 mmHg, and more-than-mild PVL 4.1%. At 30 days, all-cause mortality was 1.4%, PPI occurred in 8.3%, and there was no case of coronary obstruction requiring intervention.

MORENA. Data from 3 high-volume centers in Germany were merged for a comparison of the ACURATE*neo* and the balloon-expandable SAPIEN 3 (5). From a total of 1,121 patients, a matched cohort of patients (SAPIEN 3 n=622; ACURATE*neo* n=311) was identified. Rates of in-hospital complications were similar between both groups, including major stroke, major vascular complications, or life-threatening bleeding. Thirty-day mortality (2.3% vs. 1.9%; p=0.74) and overall device failure were similar (10.9% vs. 9.6%; odds ratio: 1.09; p=0.71) between groups, with increased rates of more-than-mild PVL (4.8% vs. 1.8%; p=0.01), but less elevated gradients (3.2% vs. 6.9%; p=0.02) and less frequent PPI (9.9% vs. 15.5%; p=0.02) in the ACURATE*neo* group.

SCOPE I. In this randomized trial, the ACURATE*neo* was compared with the balloon-expandable SAPIEN 3 system for transfemoral TAVI of patients with severe aortic stenosis (13). A total of 739 patients from 20 European centres (age 82.8±4.1 years; STS score 3.5%) were enrolled. At 30 days, the primary composite endpoint (all-cause death, any stroke, life-threatening or disabling bleeding, major vascular complications, coronary artery obstruction requiring intervention, acute kidney injury (stage 2 or 3), rehospitalisation for valve-related symptoms or congestive heart failure, valve-related dysfunction requiring repeat procedure, moderate or severe prosthetic valve regurgitation, or prosthetic valve stenosis) occurred in 24% in the ACURATE*neo* and in 16% in the SAPIEN 3 group; thus, non-inferiority of the ACURATE*neo* was not met (absolute risk difference 7.1% [upper 95% confidence limit 12.0%], p=0.42), and the secondary analysis suggested superiority of the SAPIEN 3 THV over the ACURATE*neo* device (95% CI for risk difference −1.3 to −12.9, p=0.0156). While all-cause mortality and stroke rates were similar, more-than-mild PVL was more frequent in the ACURATE*neo* group (9% vs. 3%).

NEOPRO registry. In this multicentre observational registry, 1551 patients (mean age 82 years, STS score 5.1%) who underwent transfemoral TAVI with either ACURATE*neo* (n=1263) or Evolut PRO (n=288) valves were included. After propensity score matching, device success (86.9% vs. 89.0%, p=0.48), more-than-mild PVL (10.9% vs. 8.5%, p=0.37), 30-day mortality (3.2% vs. 1.2%, p=0.13), 30-day stroke (2.4% vs. 2.8%, p=0.79), 30-day VARC-2 early safety endpoint (10.6% vs. 10.4%, p=0.96), and new PPI (12.8% vs. 11.9%, p=0.55) were similar between the groups (6).

Comparison of new-generation devices. A total of 346 patients (age 81.4±5.2 years; STS PROM 4.0±2.5%) from a single center treated with a new-generation THV (SAPIEN 3 n=134; Evolut R n=111, ACURATE$_{neo}$ n=101) were compared between each other. At 30 days, all-cause mortality was similar between groups, whereas rates of PVL and PPI and mean gradients differed significantly (SAPIEN 3 vs. Evolut R vs. ACURATE$_{neo}$: more-than-trace PVL 18.8 vs. 47.9 vs. 45.8%, p<0.05; PPI 8.3% vs. 16.7% vs. 2.1%, p<0.05; Pmean 9.7±7.5 mmHg vs. 6.1±2.4 mmHg vs. 8.4±3.5 mmHg, p<0.01). At 1 year, MACCE rates were similar between all groups (7).

Small aortic annuli. In this multicentre study, a total of 92 matched pairs of patients with an aortic annulus area below 400 mm^2 undergoing TAVI with either the supra-annular ACURATE$_{neo}$ or the intra-annular SAPIEN 3 prothesis were studied (8). The ACURATE$_{neo}$ provided larger indexed EOA (0.96 cm²/m² vs. 0.80 cm²/m²; p<0.001) and lower rates of severe PPM (3% vs. 22%; p<0.001) as well as lower mean transvalvular gradients (9.3 mmHg vs. 14.5 mmHg; p<0.001). These hemodynamic findings sustained at 1-year follow-up. Mortality at 30 days and 1 year, and in-hospital rates of stroke, PPI rate, as well as more-than-mild PVL were similar for the two THV systems.

Permanent pacemaker implantation. In a small study that included 175 patients (83±6 years, STS score 4.1±2.4%) from three centres, the PPI rate using the ACURATE$_{neo}$ was as low as 2.5% in pacemaker naïve patients (9). The authors concluded that a less aggressive pre-dilatation to minimize mechanical trauma to the conduction system, peri-procedural avoidance of negative dromotropic drugs, and conservative indication for a new PPI may be strategies that help to achieve a low PPI rate.

SELECT RBBB. This recent multicentre study included 296 patients without previous pacemaker and pre-existing right bundle branch block from 7 centres undergoing TAVI using either the ACURATE$_{neo}$ (n=98) or the SAPIEN 3 device (n=198). The 30-day PPI rate was lower when using the ACURATE$_{neo}$ (29.6% vs. 43.9%; p=0.025; OR 0.54; 95% CI 0.32-0.89; p=0.018). There was no difference in device failure (8.2% vs. 6.6%; p=0.792) (10).

Predictors of PVL. In a comprehensive analysis of anatomical and procedure-related factors of PVL in 500 patients (82.1 years; STS score 4.4%) undergoing transfemoral TAVI with the ACURATE$_{neo}$ in a

single center, more-than-mild PVL was more frequent with increasing device landing zone calcification (mild 0.8% vs. moderate 5.0% vs. severe 13.0%; p<0.001). The degree of peri-annular calcification, oversizing, presence of annular plaque protrusions, inappropriate positioning, and the sino-tubular junction height were identified as independent predictors of more-than-mild PVL. When comparing the first 100 with the last 100 ACURATE*neo* cases performed in this center, more-than-mild PVL decreased from 11% to 3% (p=0.03), an observation that was attributed to increased oversizing, selection of patients with less calcified aortic valve calcification, and improved positioning (2).

Balloon pre-dilatation. Given the comparably moderate radial force of the ACURATE*neo*, an effective balloon pre-dilatation is mandatory. However, feasibility and safety of direct implantation without pre-dilatation was demonstrated in a single-center series of selected patients with mild aortic valve calcification. From a total of 294 patients, 72 (24%) cases were performed without pre-dilation (82.7 years, STS score 4.6%). Device success (VARC-2) was achieved in 94.4%, post-dilation was necessary in 26.4%, and 1 (1.4%) patient had moderate PVL. A propensity matched comparison of patients with vs. without pre-dilatation showed that there were no differences regarding device success, more-than-mild PVL, post-dilation, and post-procedural mean gradients, but procedure and fluoroscopy times were significantly decreased in the group without pre-dilation (11).

Pure aortic regurgitation. The frame of the ACURATE*neo* has an X-shaped design with the upper crown being 5 mm larger than the nominal THV diameter at the waist. This may help to anchor the prosthesis and prevent from embolization into the left ventricle even in the absence of calcification. The current evidence is scarce, but a small series of 20 patients with pure aortic regurgitation showed favourable hemodynamic outcomes (12). This study demonstrated that due to the absence of calcification, more oversizing may be required compared to patients with aortic stenosis. The maximum mean diameter that was treated with the largest available size (ACURATE*neo* L, 27 mm) in the published series was 25 mm. Furthermore, to minimize the risk of ventricular embolization, the initial positioning may be slightly higher than for the implantation in aortic stenosis, and rapid pacing may be used to enhance stability during deployment.

Bicuspid aortic valve. In a multicentre registry, among 712 patients who were treated with the ACURATE*neo* THV, a bicuspid aortic valve (BAV) was identified in 54 (7.5%) cases (13). In comparison

to patients with tricuspid anatomy (n=658; 92.4%), the presence of BAV was associated with more frequent post-dilatation (57.4% vs. 38.7%, p=0.007), more-than-mild PVL (7.4% vs. 3.2%, p<0.001), and major stroke (7.4% vs. 1.8%, p=0.001). After propensity score matching, the rate of post-dilation remained higher in the BAV group, whereas more-than-mild PVL and major stroke were similar between groups.

In summary, a growing body of evidence demonstrates the feasibility and safety of using the ACURATE*neo* for approved indications, but also in off-label situations. The X-shaped design allows for an optimal distribution of the relatively moderate radial force (Figure 2), which translates into a balanced profile of this valve with a low risk of annular rupture, coronary obstruction, and conduction disturbances whilst having an acceptable rate of more-than-mild PVL in most series. However, the unusually high frequency of more-than-mild PVL of 9% in the recent SCOPE I trial is inconsistent to previous data and requires further clarification, before a final recommendation regarding differential device selection can be made. These inconsistencies may be ascribed to the absent core laboratory adjudication in the vast majority of studies and different populations that were examined, but may also reflect the versatility of results that are markedly subject to appropriate patient selection, sizing, and positioning (2) .
There are several ongoing clinical studies that may corroborate existing data and fill knowledge gaps. Among these, the SCOPE II randomized trials for head-to-head comparisons of the ACURATE*neo* with the Evolut R/PRO platform, respectively, and the PROGRESS PVL registry for intra-individual, longitudinal assessment of the degree of PVL, should be mentioned. Enrolment has been completed recently for these studies and initial results will soon be available.

PATIENT SELECTION

The ACURATE*neo* can be used in a wide clinical spectrum of patients, but there are some potential indications and anatomies where this device may be particularly suitable. Supplemental Table 1 provides an overview for the differential selection among commonly used TAVI prostheses.

Short coronary distance. The risk of coronary obstruction is relatively low since the upper crown keeps the native cusps away from the coronary ostia (Video 1). Accordingly, in the SAVI TF registry among

1000 patients no case of coronary obstruction requiring intervention occurred (4). Moreover, coronary re-access may be less challenging due to the short stent-body and the open-cell design of the upper crown (Supplemental Figure 1).

Small aortic annulus. The supra-annular design of the ACURATE*neo* translates into low mean transvalvular gradients, which may be of particular benefit for patients with small annuli to reduce the risk of prosthesis-patient-mismatch (8).

Horizontal aorta and tortuous anatomies. In horizontal aortic configurations, the short stent frame and the stabilization arches provide a better co-axial alignment and thereby facilitate the deployment of the ACURATE*neo*. The flexible delivery system allows for a smooth tracking of tortuous anatomies (Videos 2 & 3).

Low pacemaker rate. The rate of permanent pacemaker implantation is among the lowest for the ACURATE*neo* (7,9,10), which may be attributed to the specific distribution of the moderate radial force (Figure 2) and the less protrusion into the left ventricular outflow tract. However, recent data are not consistent and require further investigation (14).

Gentle procedure. The top-down release of the ACURATE*neo* without any need of rapid ventricular pacing allows for haemodynamic stability throughout the entire implantation, as no outflow obstruction occurs during valve deployment. This may be beneficial in cases with impaired ventricular function or severe heart failure, particularly in the case that no pre-dilatation and no post-dilatation are required (11).

Severe aortic valve calcification. As a caveat, due to its lower radial force, the ACURATE*neo* may be less appropriate in severe aortic valve calcification, where its use can result in higher rates of more-than-mild PVL and more frequent need for balloon post-dilatation (2). However, Supplemental Figure 2 illustrates that the degree of PVL in severe aortic valve calcification not only depends on the total amount of aortic valve calcium, but also on its distribution.

Bicuspid aortic valve. The use of the ACURATE*neo* in bicuspid anatomies is feasible (13). However, in the setting of very severe aortic valve calcification or asymmetric distribution, the use in bicuspid aortic valve may have an increased risk of device failure.

SIZING

The original sizing recommendation was adopted from the experience with the ACURATE TA bioprosthesis, which in fact differs from the ACURATE*neo* in many aspects. Particularly in cases with borderline annulus dimensions, strict adherence to the official sizing chart may lead to relative undersizing. Supplemental Table 2 shows a modified sizing recommendation that was derived from a large, single-centre cohort to discriminate the risk of more-than-mild PVL (2). In contrast to the official recommendation, annulus sizes below 21 mm can be treated without concern to a minimum of 19 mm, whereas the maximum size of 27 mm should not be exceeded, keeping in mind that the risk of residual PVL increases above an annulus size of 26.5 mm.

PROCEDURAL STEPS

A comprehensive overview of all relevant procedural steps for the implantation of the ACURATE*neo* is provided in Table 1 (including Figures 3-5 and Supplemental Figures 3-5). Throughout the procedure, a proper device positioning is key to achieve good results; once correctly positioned, upon full release the prosthesis will commonly stay within the intended landing zone due to predominant lateral extension and only minimal vertical motion.

PERSPECTIVES

(1) The next-generation ACURATE *neo 2* aortic valve system has a dedicated sealing skirt that is designed to further reduce PVL, especially in the setting of heavily calcified annuli; the new system underwent initial clinical testing in 2018.

(2) Implantation of the current version of the ACURATE*neo* is generally perceived as easy and intuitive. Less experienced operators would nonetheless be even more confident if valve repositioning or retrieval would be possible.

(3) The current version officially covers an annular size range from 21 to 27 mm. The smallest size is most probably also suitable for smaller annuli in an off-label fashion, whereas annuli >27 mm cannot be treated. Therefore, additional valve sizes particularly for annulus dimensions above 27 mm would further expand the spectrum of patients that can be treated with this device.

(4) Further clinical data, especially from randomized trials, are awaited as outlined above. This holds especially true for the evolving field of intermediate- to low-risk patients, since this subgroup was not enrolled in the initial ACURATE*neo* trials. Moreover, additional data will be important to clarify inconsistencies that were introduced by the most recent SCOPE I trial.

CONCLUSIONS

The worldwide increasing use of the ACURATE*neo* system is endorsed by a growing body of evidence. The optimal distribution of the relatively moderate radial force and its unique principle of deployment account for its notably balanced profile. Importantly, careful patient selection, proper sizing, and appropriate positioning are premises for optimized outcomes. Nonetheless, at present there is the urgent need for additional data to

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APPENDIX

Collaborators:

Mirko Doss, MD, PhD, Kerckhoff Heart Center, Department of Cardiac Surgery, Bad Nauheim, Germany

Andreas Holzamer, MD; University Medical Center, Department of Cardiothoracic Surgery, Regensburg, Germany

Oliver Husser, MD, PhD; St. Johannes Hospital, Department of Cardiology, Dortmund, Germany

Cindy Belon; Boston Scientific, Ecublens, Switzerland

Stefane Delaloye, PhD; Boston Scientific, Ecublens, Switzerland

CONFLICTS OF INTEREST

WK, Che, MH, US, TR, ST, AR, OH, AH, LC, MD, HM are proctors for Boston Scientific; WK: proctor/speaker honoraria from Abbott, Edwards Lifesciences, Medtronic; US: consultant, proctor, and speaker´s bureau for Abbott Vascular, Boston Scientific, Edwards Lifesciences, Medtronic, Gore, JenaValve, and New Valve Technology, research grant from Abbott Vascular, Boston Scientific, JenaValve, Edwards Lifesciences, and New Valve Technology, TR proctor/speaker honoraria from Boston Scientific, JenaValve, Edwards, Medtronic, Abbott, ST: research grant from Boston Scientific, proctor/consultant for New Valve Technology, speaker fees from Edwards Lifesciences and Medtronic, LS: consultant fees and institutional research grants from Boston Scientific, CHa: advisory board Medtronic, HM: proctor fees and/or speaker honoraria from Abbott, Biotronic, Edwards Lifesciences

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FIGURE LEGENDS

Figure 1: ACURATE *neo* transcatheter heart valve system.

The ACURATE *neo* prosthesis (A) and delivery system (B).

Figure 2: Radial force of the ACURATE *neo*

Distribution of the radial force (chronic outward force, COF) over the height of the lower crown in contact with a cylindrical and compliant annulus model as estimated with the finite element method. The maximum force is located approximately at mid-height of the stent-body.

Figure 3: Introducer sheaths

The ACURATE *neo* system is compatible with various introducer sheaths that have different inner diameters (ID), outer diameters (OD), and insertion profiles.

Figure 4: Positioning

The delivery system should be kept in the outer curvature (small red arrows) for enhanced stability during positioning. A proper device position is accomplished when the radiopaque intersection line (asterisk) is at the level of the annulus (dotted blue line), and the upper crown is in close proximity to the native leaflets (red circle). During step 2, an appropriate amount of forward tension should be maintained (large red arrow), trying to avoid too much (active) push on the device that might lead to ventricular embolization.

Figure 5: Deployment

After initial positioning of the prosthesis (A), turning the 1st rotation-knob counter-clockwise releases the upper crown and the stabilization arches (step 1). Thereafter, turning the 2nd rotation-knob counter-clockwise for step 2 (B) fully releases the prosthesis (C). Panel D shows a complete disengagement of the stent-holder from the prosthesis (yellow double-arrow). For retrieval of the delivery system out of the left ventricle, the guidewire should be pulled until the nosecone centralizes (E).

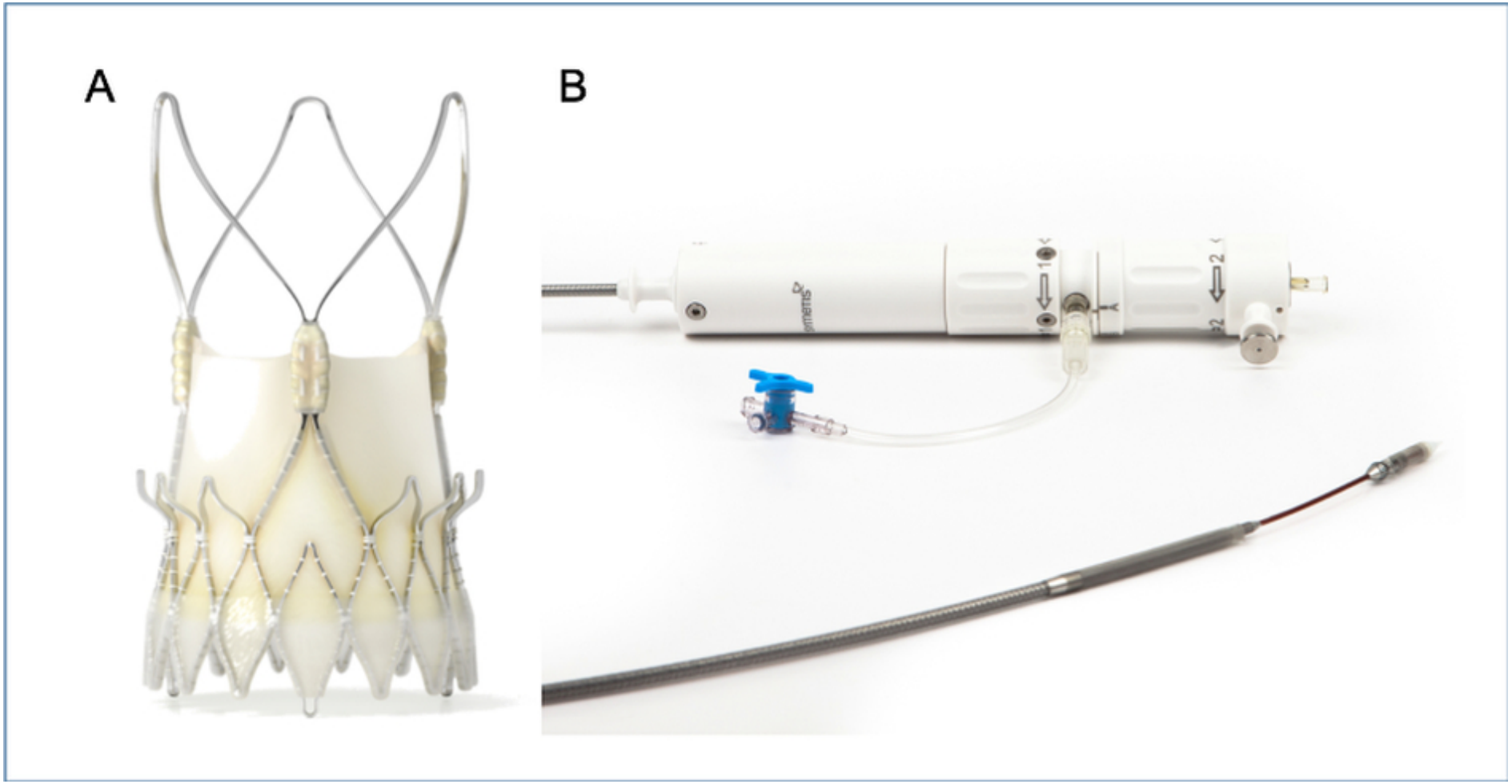
TABLES

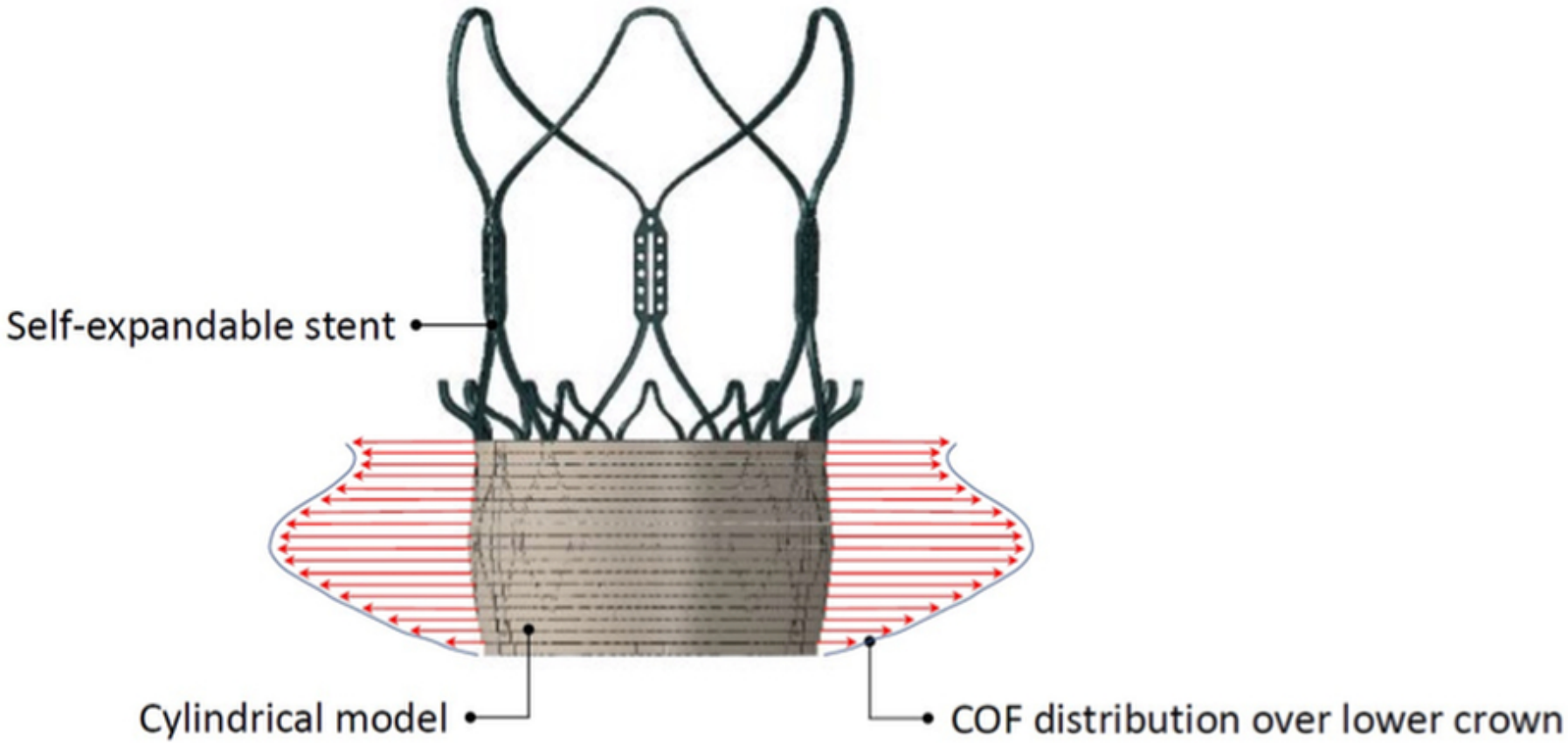
Table 1: Procedural steps

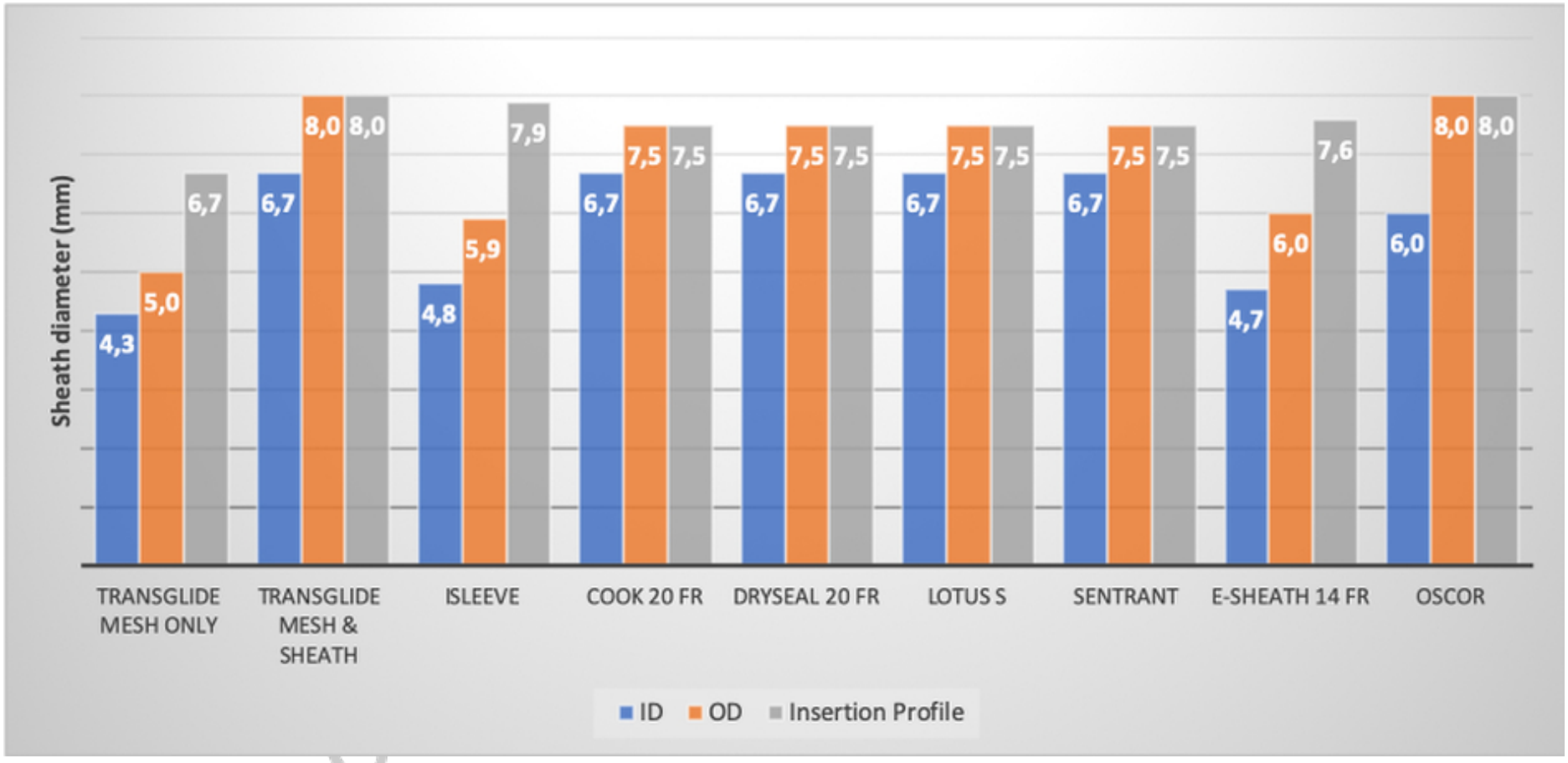
Introducer sheath	A variety of different sheaths are compatible for femoral access using the ACURATE*neo* system (Figure 3). Recently, the expandable iSLEEVE (Boston Scientific, Marlborough, MA) introducer sheath with a 14 Fr inner diameter at the tip has become available (Supplemental Figure 3). The lowest possible insertion profile can be achieved when using only the mesh of the Transglide® expandable introducer system (TransAortic Medical, Morgan Hill, CA), which comes close to a sheathless approach (15), but is currently off-label use.
Co-planar view	In contrast to other self-expanding devices that follow the alignment of the prosthesis, the implantation of the ACURATE*neo* requires a co-planar view on the native annular plane.
Pre-dilatation	Due to the moderate opening force of the ACURATE*neo*, effective balloon pre-dilatation is mandatory to facilitate device expansion. While according to the manufacturer, a relatively aggressive pre-dilatation is recommended, a less aggressive approach (balloon size approximately 2 mm smaller than the perimeter-derived annulus diameter) may decrease the risk of conduction disturbances (9).
Positioning and deployment	A proper position is indicated by the radiopaque intersection line (referred to as "marker band") located in the mid-portion of the stent-body, being in the annular plane. In addition, the upper crown should be located right above the tips of the native leaflets (Figure 4). It is of utmost importance that the final movement for positioning is in a forward motion. When the final motion of the delivery system is in aortic direction, upon full release the stent-holder will move in an aortic direction and may not disengage from the prosthesis. When a good initial position has been achieved, the first step can be initiated by turning knob 1 counter-clockwise, which will release the upper crown and the stabilization arches (Figure 4A). This should be done rather slowly in order to promptly recognize any inappropriate movement of the device. Depending on the wire position, vascular tortuosity, aortic valve calcification, and the amount of push

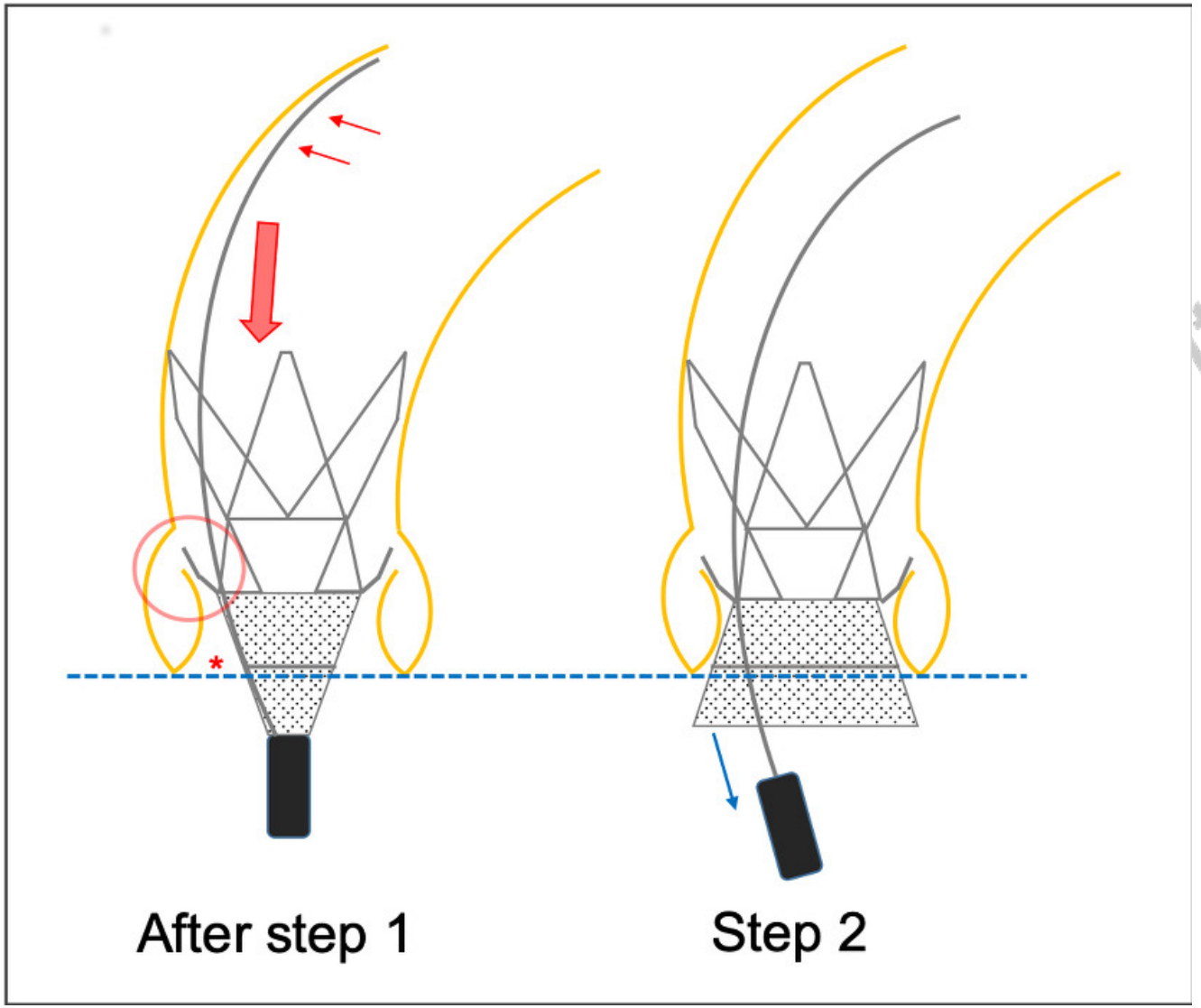
	exerted during this step, there will usually be an upward movement. In this situation, the first operator should try to maintain the position by slightly increasing the pressure on the delivery system. Video 4 shows an example of maintaining an appropriate forward tension during step 2. However, excessive push on the delivery system should be avoided (Video 5). Particularly in mildly calcified aortic valves, the device tends to dive into the left ventricle. If this occurs, the deployment should be stopped immediately to adjust the position. After release of the upper crown, the prosthesis cannot be re-sheathed. However, even after completing step 1, it is still possible to adjust the position. When a proper device position has been verified, knob 2 can be turned counter-clockwise (Figure 4B), which will release the lower crown for full deployment of the valve (Figure 4C).
Retrieval of the delivery system	After completing step 2, a complete disengagement of the prosthesis from the stent-holder should be ascertained. Ideally, the latter shows a slight movement into the left ventricle, leaving space between the stent-body and the radiopaque stent-holder (Figure 4D). In the case that the stent-holder moves in aortic direction, the delivery system should be carefully advanced into the left ventricle to disengage the prosthesis from the stent-holder. Retrieval of the delivery system out of the left ventricle should be done with minimal interaction with the prosthesis by adjusting the guidewire position (Figure 4E). In the descending aorta, the delivery system must be closed by first turning knob 2 clockwise until the hard stop, and then turning knob 1 clockwise until there is a slight contact between the shuttle and the stent-holder. It is important not to turn knob 1 until the hard stop, otherwise there is a risk of over-closing, with the capsule 'riding' on the nosecone, and retrieval out of the sheath may become difficult.
Evaluation of the result	For aortography, the pigtail catheter should be placed just above the stent-posts using a sufficient amount and speed of contrast agent (20–25 ml, 20 ml/s), otherwise paravalvular leakage might be underestimated. Importantly, unless the operator is not satisfied with the result and post-dilatation might become necessary, it is recommended to retain access to the left ventricle, as the re-crossing of the prosthesis can be challenging and bears the risk of re-crossing through one of the

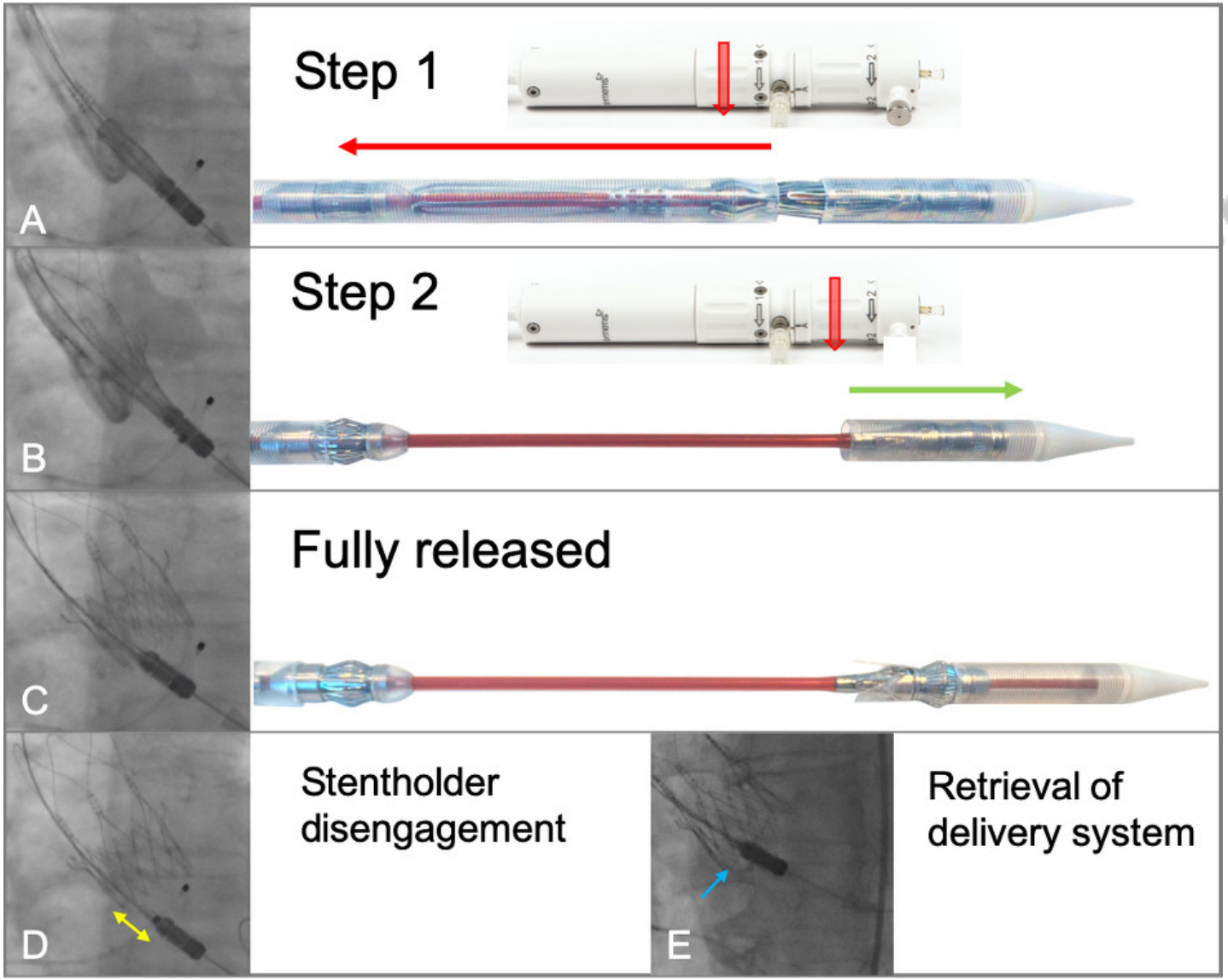
	stabilization arches, which may result in valve migration during retrieval of the balloon catheter (Video 6). In the event of re-crossing, the correct trans-prosthetic wire position should be verified carefully (Video 7 & 8). In case of a suboptimal result despite favourable anatomy and proper device position, it is justified to wait for a few minutes, as the nitinol can further expand (Supplemental Figure 4).
Post-dilatation	For post-dilatation, the balloon should be placed in the mid-part of the stent-body (Supplemental Figure 5). The balloon size should not exceed that of the prosthesis minus 1 mm (ACURATE$_{neo}$ S: max. 22 mm balloon, M: max. 24 mm balloon, L: max 26 mm balloon) to minimize the risk of leaflet damage.











SUPPLEMENTAL MATERIAL

Supplemental Table 1: Differential selection of transcatheter heart valves

THV	Access	Pre-dilatation	Rapid Pacing	Ease of use	PVL	PPI	Gradient	Annulus range (mm)	DLZ calcification	Coronary access
ACURATE neo	+	yes	no	++	o	++	++	20 – 27	-	+
Evolut R	++	no	no	+	+	-	++	18 – 31	+	o
Lotus	o	no	no	-	++	-	-	20 – 27	++	-
Portico	+	yes	no	o	+	o	+	19 – 27	o	o
SAPIEN 3	+	no	yes	++	++	o	-	20 – 32*	++	+

Abbreviations: THV=transcatheter heart valve, PVL=paravalvular leakage, PPI=permanent pacemaker implantation, DLZ=device landing zone

++ very good

+ good

o indifferent

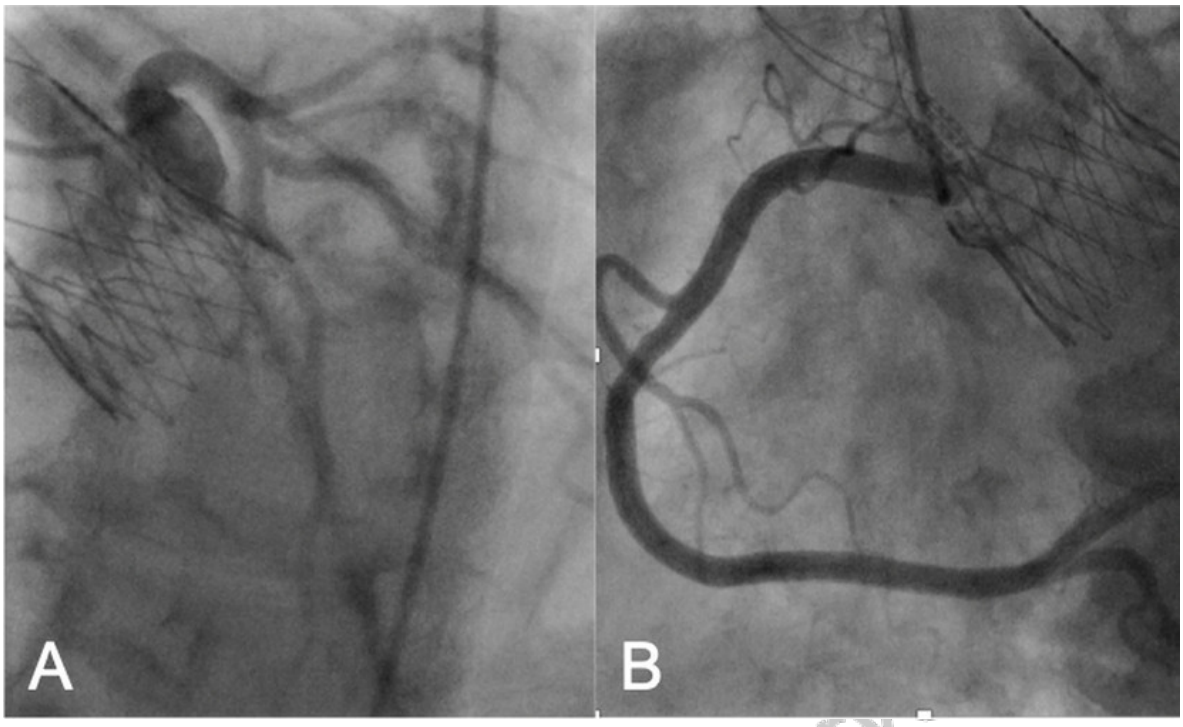
- suboptimal

Supplemental Table 2: Sizing recommendation (modified according to (2))

ACURATE *neo* size	Official sizing recommendation Annulus diameter	Modified sizing recommendation* Perimeter-derived annulus diameter [cover index]
S	21–23 mm	20.0–22.4 mm [13.0-2.6%]
M	23–25 mm	22.5–24.3 mm [10.0-2.8%]
L	25–27 mm	24.4–26.3 mm [9.6-2.6%]

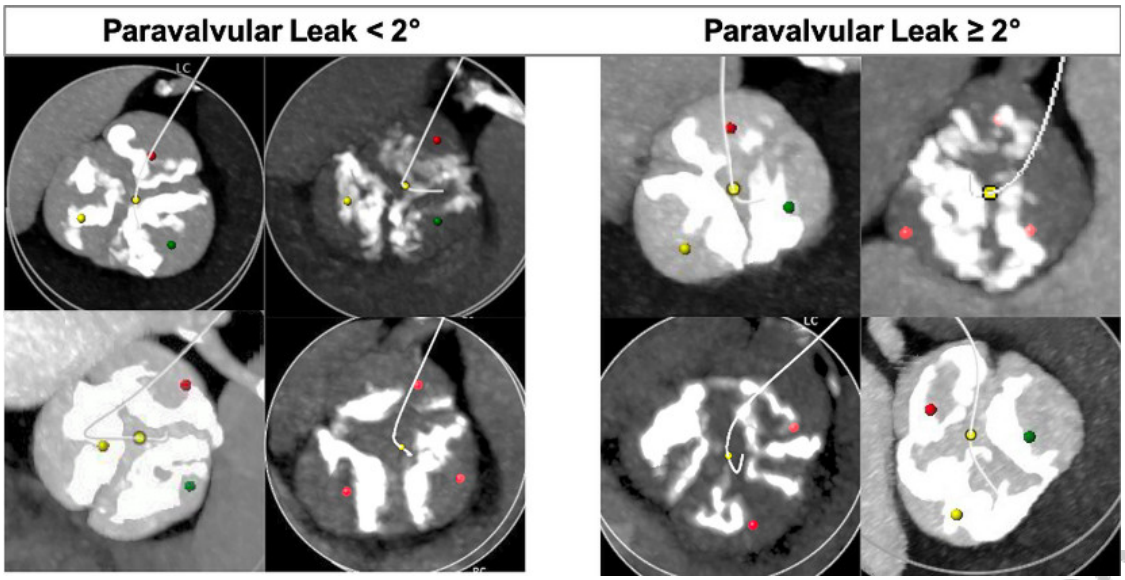
*For discrimination of PVL ≥2°, the threshold of the cover index based on the perimeter-derived annulus in systole was *2.5%* with an area under the curve of 0.645 [95% CI 0.535-0.755]; p=0.01; sensitivity 79.9%, specificity 46.4%.

Supplemental Figure 1: Coronary re-access



Engagement of the left main (A) and the right coronary artery (B) for coronary angiography.

Supplemental Figure 2: Severe aortic valve calcification

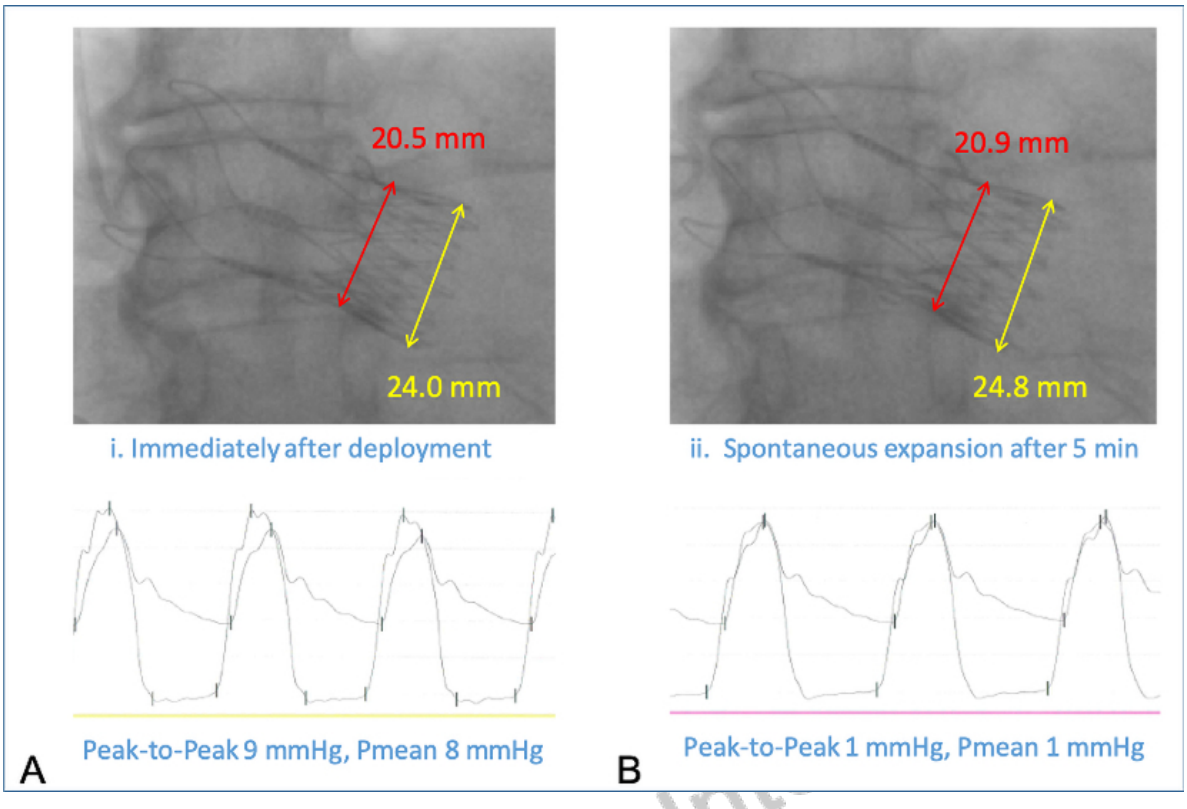


Despite the same total amount of aortic valve calcification (Agatston score >4500 AU) patients in the left panels had no relevant post-procedural paravalvular leakage after implantation of the ACURATE *neo* device, whereas those in the right panels had moderate/severe paravalvular leakage, most likely related to the unfavourable distribution of the calcium.

Supplemental Figure 3: iSLEEVE expandable introducer set

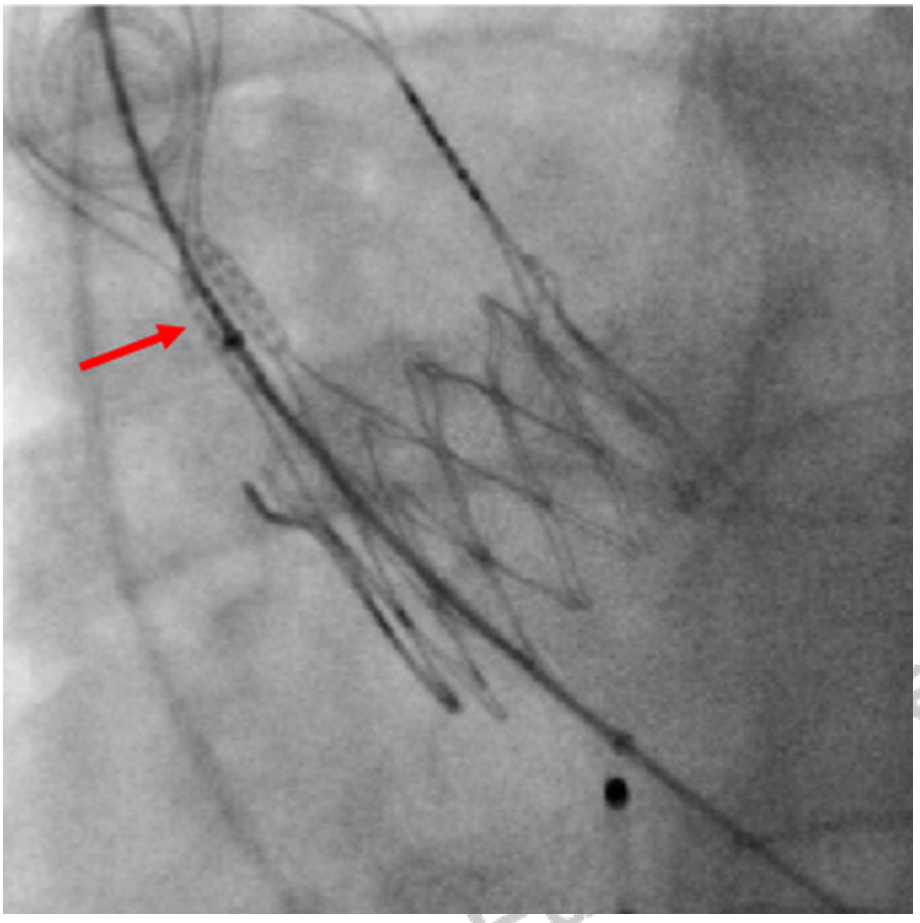
The iSLEEVE introducer sheath has a low profile with an inner diameter (ID) of 4.8 mm and outer diameter (OD) of 5.9 mm at the tip (ID 7.0 mm and OD 7.9 mm at the proximal end of the sheath). The trifold design enables controlled expansion and accommodation to the vessel anatomy during insertion of the delivery system.

Supplemental Figure 4: In vivo expansion of the ACURATE *neo*



Immediately after deployment, gradients are slightly increased (A). After a few minutes, there is a visible expansion of the stent body along with a reduction in the transaortic gradient (B).

Supplemental Figure 5: Post-dilatation



The balloon should be placed in the mid-part of the stent-body just below the stent-posts (red arrow).

ONLINE DATA SUPPLEMENTS

Video 1: The upper crown keeps the native calcified cusp away from the left main ostium.

Video 2: Severe aortic tortuosity and horizontal aorta.

Video 3: Smooth advancement of the ACURATE delivery system through the tortuous aorta and across the aortic arch.

Video 4: Appropriate forward pressure on the delivery system during step 2.

Video 5: Inappropriate push on the delivery system leading to ventricular embolization.

Video 6: Aortic migration of the prosthesis during balloon retrieval after re-crossing through one of the stabilization arches.

Video 7: After re-crossing of the prosthesis, wire manipulation reveals a slight inward bending of the adjacent stabilization arch

Video 8: Correct re-crossing of the prosthesis.