# Impact of aortic landing zone geometry on TAVI implantation depth: comparison between Acurate *neo2* and Portico/Evolut

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## SUPPLEMENTARY MATERIAL

### Theoretical implantation depth

The implantation depth was defined averaging the maximal distance (expressed in millimeters) between the intraventricular end of the bioprosthesis and the aortic annulus as the level of both the noncoronary cusp (NCC) and the left coronary cusp (LCC). A theoretical mean implantation depth of 4 mm below annular level, which is the target implantation depth of the ACURATE *neo* valve, was assumed for the comparative analysis of landing zones in terms of curvature and angulation.[1] The optimal implant position for the Portico corresponds to an implantation depth between 3 mm and 6 mm.[2] Also, instructions for use for the Evolut R/PRO specify an implant depth between 3 and 5 mm.[3] Hence, for the sake of comparison, a theoretical implantation depth of 4 mm was considered appropriate. According to Breitbart and co-workers,[4] a mean implantation depth of at least 4mm demonstrated to be effective in reducing the occurrence of new conduction disturbances post-TAVI. Furthermore, correct implantation was defined by Petronio *et al*.[5] as a depth ≤ 6 mm below the annulus plane.

[1] Toggweiler S, Nissen H, Mogensen B, Cuculi F, Fallesen C, Veien KT, Brinkert M, Kobza R, Rück A. *Very low pacemaker rate following ACURATE neo transcatheter heart valve implantation.* EuroIntervention 2017; 13(11):1273-1280. DOI: 10.4244/EIJ-D-17-00252
[2] Manoharan G, Spence MS, Rodés-Cabau J, Webb JG. *St Jude Medical Portico valve*. EuroIntervention 2012: 8 Suppl Q:Q97-101. DOI: 10.4244/EIJV8SQA18
[3] Jilaihawi H, Zhao ZG, Williams M. *Sizing for self-expanding transcatheter aortic valve implantation*. EuroIntervention 2018; 14(5):e490-e493. DOI: 10.4244/EIJV14I5A86
[4] Breitbart P, Minners J, Hein M, Schröfel H, Neumann FJ, Ruile P. *Implantation depth and its influence on complications after TAVI with self-expanding valves*. Int J Cardiovasc Imaging 2021; 37(10):3081-3092. DOI: 10.1007/s10554-021-02275-3
[5] Petronio AS, Sinning JM, Van Mieghem N, Zucchelli G, Nickenig G, Bekeredjian R, Bosmans J, Bedogni F, Branny M, Stangl K, Kovac J, Schiltgen M, Kraus S, de Jaegere P. *Optimal Implantation Depth and Adherence to Guidelines on Permanent Pacing to Improve the Results of Transcatheter Aortic Valve Replacement With the Medtronic CoreValve System: The CoreValve Prospective, International, Post-Market ADVANCE-II Study*. JACC Cardiovasc Interv 2015; 8(6):837-846. DOI: 10.1016/j.jcin.2015.02.005.

Nonetheless, according to our data, the measure of intended mean implantation depth was overall a bit deeper than 4 mm, with Acurate and Portico/Evolut reporting median values of 5.7 mm (IQR: 4.9 ÷ 6.3 mm) and 6.0 mm (IQR: 5.0 ÷ 7.0 mm). Taking the nominal length of each device into account, this implies that the effective aortic landing zone was about 2 mm proximally repositioned. Specifically, at the level of ascending aorta, it was on average 2 mm shorter than the one calculated and analyzed on CT angiography and on average 2 mm longer at the level of LVOT.

For the sake of clarity and to assess the impact of this discrepancy, both angulations and curvature variables obtainable from the analysis of the landing zone centerline were extracted also considering a theoretical mean implantation depth of 6 mm. The distributions of the recalculated variables are reported below:

| **Variables** | **Overall** (n = 207) | **Acurate** (n = 106) | **Portico + Evolut** (n = 101) | ***P value*** |
|---|---|---|---|---|
| $k_{LZ,tot}$ ($10^{-1}\cdot mm^{-1}$) | 1.30 (1.08, 1.51) | 1.33 (1.19, 1.54) | 1.24 (0.98, 1.47) | **0.006** |
| $\alpha_{LZ,Proximal}$ (°) | 3.5 (1.9, 5.0) | 2.8 (1.8, 4.5) | 3.8 (2.0, 6.5) | **0.009** |
| $\alpha_{LZ,Distal}$ (°) | 31.9 (24.1, 39.7) | 37.7 (29.5, 42.5) | 25.8 (20.3, 34.4) | **< 0.001** |
| Values expressed as median (IQR). [§]Acurate vs. Portico+Evolut. Significant values (P < 0.05) are in bold. | | | | |

Also, the median variation between the two different configurations ($H_{mean,Pre}$ = 4 mm *vs.* $H_{mean,Pre}$ = 6 mm) is reported below for the recalculated variables:

| **Variables** | **$H_{mean,Pre}$ = 4 mm** (n = 207) | **$H_{mean,Pre}$ = 6 mm** (n = 207) | **Median variation** |
|---|---|---|---|
| $k_{LZ,tot}$ ($10^{-1}\cdot mm^{-1}$) | 1.31 (1.09, 1.52) | 1.30 (1.08, 1.51) | - 0.01 |
| $\alpha_{LZ,Proximal}$ (°) | 2.1 (1.1, 3.1) | 3.5 (1.9, 5.0) | + 1.4 |
| $\alpha_{LZ,Distal}$ (°) | 34.0 (25.9, 42.9) | 31.9 (24.1, 39.7) | - 2.1 |
| Values expressed as median (IQR). | | | |

Hence, assuming a mean implantation depth of 6 mm, we noticed a slight decrease in curvature ($k_{LZ,tot}$), while the distal reduction in $\alpha_{LZ,Distal}$ was accompanied by an increase in $\alpha_{LZ,Proximal}$. Nonetheless, despite these minor variations in the magnitude of each variable, the overall trends and statistical significance remained consistent between the two groups.

**Portico and Evolut subgroups**

In the design phase of the study, we chose to group the Portico and Evolut platforms based on several shared characteristics. Notably, both are self-expandable platforms featuring a similar cell-based stent frame and a same

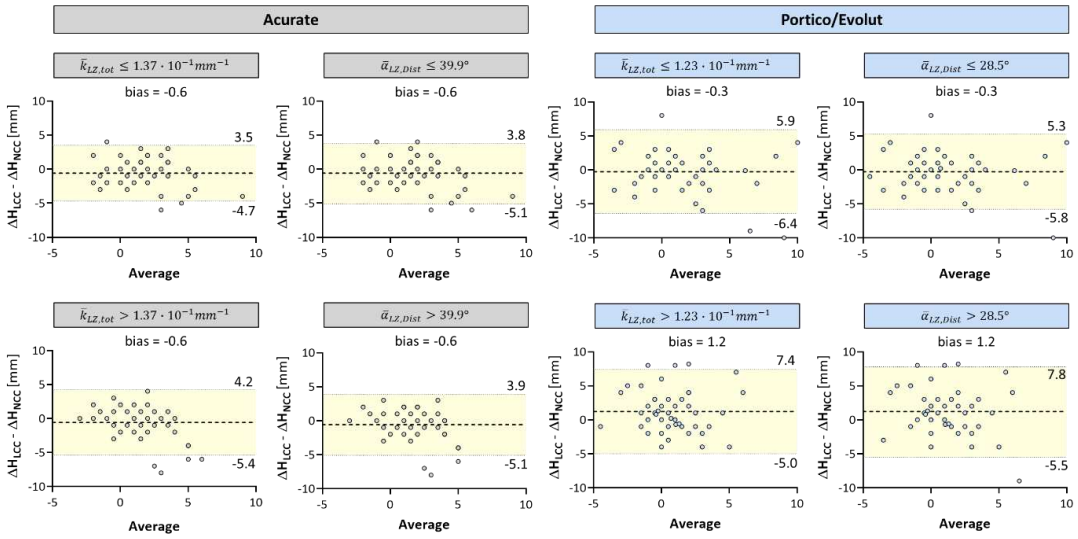
bottom-up deployment mechanism. Nonetheless, there are differences between the two platforms warranting attention. The main difference lies in the flexibility of their delivery system: the Portico FlexNav$^{TM}$ system is made of a single spine technology, enabling multi-directional flexion, whereas the Evolut R/Pro+ Enveo system consists of a dual-spine configuration, restricting flexion to two directions. Furthermore, Portico stent is slightly longer than the Evolut-R/Pro+ (50-53 mm *vs.* 45-46 mm). While these differences could theoretically influence implantation depth, particularly in patients with a severely angulated aorta, current scientific literature does not offer evidence on this matter.

Therefore, we performed a sub-analysis of baseline and procedural characteristics stratifying the study population also by Portico (n = 26) and Evolut (n = 75) platforms. The results of this additional analysis are now included as Supplementary Table S1 and S2.

Specifically, baseline anatomical characteristics (Table S1) indicated that the Portico platform was preferred over Evolut for patient with smaller aortic dimension. Notably, no significant differences specifically arose between the Portico and Evolut platforms in terms of baseline curvature ($k_{LZ,tot}$) and angulations ($\alpha_{LZ,Proximal}$ and $\alpha_{LZ,Distal}$). In terms of procedural variables, the Evolut platform reported a deeper intended implantation depth ($H_{Pre}$) at the LCC level with respect to the Portico platform, i.e., 7.0 (5.0, 8.0) *vs*. 5.0 (4.0, 7.0) mm, $P = 0.003$ at post hoc analysis.

## Supplementary Figures

**Figure S1.** Bland-Altman plots of the differences between $\Delta H_{LCC}$ and $\Delta H_{NCC}$ evaluated within the Acurate and the Portico/Evolut groups clustering ΔH data according to the median value of $\kappa_{LZ,tot}$ and $\alpha_{LZ,Dist}$, respectively.



## Supplementary Tables

**Table S1**. Baseline patient characteristics for Accurate, Portico and Evolut patient subgroups.

| **Variables** | **Acurate** (n = 106) | **Portico** (n = 26) | **Evolut** (n = 75) | ***P value*** |
|---|---|---|---|---|
| Age (years) | 84 (80, 87) | 80 (74, 86)[§] | 82 (78, 85)[§] | **0.007** |
| Female sex | 69 (65.1) | 15 (57.7) | 23 (30.7) | **< 0.001** |
| BSA ($m^2$) | 1.80 ± 0.19 | 1.83 ± 0.2 | 1.88 ± 0.20 | **0.02** |
| Hypertension | 91 (85.9) | 16 (61.5) | 57 (76.0) | **0.02** |
| Diabetes | 27 (25.5) | 3 (11.5) | 24 (32.0) | 0.12 |
| Dyslipidemia | 51 (48.1) | 7 (26.9) | 36 (48.0) | 0.13 |
| COPD | 8 (7.6) | 3 (11.5) | 12 (16.0) | 0.20 |
| CAD | 16 (15.1) | 7 (26.9) | 21 (28.0) | 0.08 |
| Prior AF | 37 (34.9) | 5 (19.2) | 22 (29.3) | 0.28 |
| Prior CABG | 7 (6.6) | 3 (11.5) | 12 (16.0) | 0.13 |
| Prior AMI | 10 (9.4) | 2 (7.7) | 4 (5.3) | 0.60 |
| STS score (%) | 2.5 (2.0, 3.2) | 3.2 (1.7, 6.6) | 3.3 (2.1, 5.2) | 0.15 |
| Creatinine clearance (mL/min/1.73 $m^2$) | 65 (46, 79) | 56 (42, 77) | 57 (43, 72) | 0.21 |
| Haemoglobin (g/dL) | 12.9 ± 1.6 | 12.4 ± 1.9 | 12.5 ± 1.7 | 0.21 |
| Ejection fraction (%) | 61.0 (55.0, 67.0) | 62.0 (53.5, 69.5) | 58.0 (50.0, 64.0) [§] | **0.02** |
| Mean AV gradient (mmHg) | 43.5 ± 12.2 | 46.7 ± 14.9 | 45.4 ± 14.9 | 0.46 |
| Aortic regurgitation ≥ moderate | 15 (14.2) | 3 (11.5) | 14 (18.7) | 0.60 |
| LM height (mm) | 13.1 ± 2.9 | 14.5 ± 2.7 | 15.8 ± 4.0 [§] | **< 0.001** |
| RCA height (mm) | 16.8 ± 3.0 | 18.7 ± 2.7 [§] | 19.4 ± 4.2 [§] | **< 0.001** |
| Annulus minimal diameter (mm) | 20.7 ± 1.9 | 21.0 ± 2.3 | 21.7 ± 3.1 [§] | **0.03** |
| Annulus maximal diameter (mm) | 25.8 ± 1.9 | 26.5 ± 2.1 [ǂ] | 27.8 ± 2.7 [§] | **< 0.001** |
| Annulus mean diameter (mm) | 23.3 ± 1.6 | 23.6 ± 1.9 [ǂ] | 24.8 ± 2.5 [§] | **< 0.001** |
| Annulus perimeter (mm) | 73.5 ± 5.0 | 74.3 ± 5.5 [ǂ] | 78.2 ± 7.7 [§] | **< 0.001** |
| Annulus area ($mm^2$) | 418.5 ± 59.5 | 425.5 ± 65.3 [ǂ] | 474.3 ± 98.3 [§] | **< 0.001** |
| LVOT diameter (mm) | 23.1 ± 1.9 | 22.8 ± 2.8 [ǂ] | 24.3 ± 3.1 [§] | **0.002** |
| Valsalva diameter (mm) | 31.5 ± 3.2 | 31.6 ± 2.8 [ǂ] | 33.9 ± 3.8 [§] | **< 0.001** |
| Calcium volume 800 HU ($mm^3$) | 223 (119, 384) | 147 (69, 358) | 227 (125, 573) | 0.10 |
| Aortic angulation (°) | 53.1 ±10.8 | 45.6 ± 8.3 [§] | 48.6 ± 9.5 [§] | **< 0.001** |
| Index of eccentricity | 0.19 (0.16, 0.23) | 0.21 (0.18, 0.25) | 0.21 (0.17, 0.27) | 0.18 |
| $L_{AR}$ (mm) | 20.0 ± 3.3 | 21.0 ± 3.2 | 21.9 ± 3.7 [§] | **0.001** |
| $k_{AR,tot}$ ($10^{-1}\cdot mm^{-1}$) | 0.30 (0.21, 0.40) | 0.35 (0.26, 0.42) | 0.35 (0.25, 0.48) | 0.08 |
| $k_{LZ,tot}$ ($10^{-1}\cdot mm^{-1}$) | 1.37 (1.22, 1.59) | 1.30 (1.02, 1.60) | 1.19 (0.96, 1.47) [§] | **0.001** |
| $\alpha_{STJ}$ (°) | 9.1 (5.4, 12.7) | 8.2 (4.8, 12.3) | 8.3 (5.2, 12.0) | 0.64 |
| $\alpha_{LZ,Proximal}$ (°) | 1.7 (1.1, 2.8) | 2.4 (1.1, 4.0) | 2.5 (1.3, 3.9) [§] | **0.02** |
| $\alpha_{LZ,Distal}$ (°) | 40.0 (31.1, 45.7) | 32.9 (21.1, 41.4) [§] | 27.8 (21.4, 34.0) [§] | **< 0.001** |

Values expressed as mean ± SD, median (IQR) or n (% of column total). AF, atrial fibrillation; AMI, acute myocardial infarction; BSA, body surface area; CABG, coronary artery bypass grafting; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; HU, Hounsfield units; $k_{AR,tot}$, total (cumulative) curvature of the aortic root centerline; $k_{LZ,tot}$, total (cumulative) curvature of the landing zone centerline; $L_{AR}$, aortic root length; LM, left main; LVOT, left ventricle outflow trunk; LZ, landing zone; RCA, right coronary artery; STJ, sinotubular junction; STS, Society of Thoracic Surgeons; $\alpha_{STJ}$, angulation of the STJ plane with respect to the aortic annulus plane; $\alpha_{LZ,Proximal}$, angulation of the proximal LZ plane with respect to the aortic annulus plane; $\alpha_{LZ,Distal}$, angulation of the distal LZ plane with respect to the aortic annulus plane. Post hoc analysis: [§] $P < 0.05$ *vs.* Acurate, [ǂ] $P < 0.05$ *vs.* Evolut; significant values ($P < 0.05$) reported in bold.

**Table S2**. Procedural and in-hospital outcome for Accurate, Portico and Evolut patient subgroups.

| **Variables** | **Acurate** (n = 106) | **Portico** (n = 26) | **Evolut** (n = 75) | ***P* value**[§] |
|---|---|---|---|---|
| Femoral route | 106 (100) | 20 (76.9) | 68 (90.7) | **< 0.001** |
| Subclavian route | 0 (0.0) | 4 (15.4) | 5 (6.7) | **0.001** |
| EPS | 0 (0.0) | 1 (3.8) | 1 (1.3) | 0.18 |
| Any vascular complications | 10 (9.4) | 1 (3.8) | 3 (4.0) | 0.29 |
| PTA with stenting of access site | 5 (4.7) | 0 (0.0) | 3 (4.0) | 0.53 |
| PCI with stenting | 1 (0.9) | 3 (11.5) | 4 (5.3) | **0.03** |
| Predilatation | 104 (98.1) | 16 (61.5) | 34 (45.3) | **< 0.001** |
| **Implantation depth** | | | | |
| NCC $H_{Pre}$ (mm) | 5.1 (4.3, 5.7) | 6.0 (5.0, 8.0) | 5.0 (4.0, 7.0) | 0.06 |
| LCC $H_{Pre}$ (mm) | 6.2 (5.3, 7,2) | 5.0 (4.0, 7.0) [ǂ] | 7.0 (5.0, 8.0) [§] | **0.002** |
| NCC $H_{Post}$ (mm) | 6.5 (4.8, 8.3) | 6.5 (4.0, 8.3) | 7.0 (5.0, 8.6) | 0.75 |
| LCC $H_{Post}$ (mm) | 7.2 (6.2, 8.8) | 7.0 (6.0, 8.3) | 8.0 (6.0, 10.0) | 0.15 |
| $\Delta H_{NCC}$ (mm) | 1.3 (0.1, 3.0) | 0.0 (-1.0, 1.0) [§] | 0.0 (-1.0, 3.0) | **0.01** |
| $\Delta H_{LCC}$ (mm) | 1.0 (-0.1, 2.8) | 1.5 (0.0, 3.0) | 1.0 (0.0, 3.0) | 0.79 |
| $\Delta H_{mean}$ (mm) | 1.6 (0.2, 2.8) | 0.5 (0.0, 2.0) | 0.7 (- 0.5, 3.0) | 0.22 |
| Postdilatation | 48 (45.3) | 15 (57.7) | 37 (49.3) | 0.51 |
| Emergent cardiac surgery | 0 (0.0) | 0 (0.0) | 0 (0.0) | - |
| Need for second valve | 0 (0.0) | 0 (0.0) | 0 (0.0) | - |
| Contrast volume (mL) | 157 (130, 200) | 135 (110, 179) | 160 (130, 190) | 0.11 |
| Radiation time (min) | 21.4 (17.5, 26.9) | 19.8 (14.5, 23.4) | 23.0 (17.4, 29.5) | 0.09 |
| **In-hospital outcome** | | | | |
| Ejection fraction (%) | 62.0 (56.0, 67.0) | 64.5 (54.5, 69.0) | 58.0 (51.0, 63.0) [§] | **0.009** |
| Mean gradient (mmHg) | 9.0 (7.0, 12.0) | 7.0 (6.0, 10.3) | 7.0 (4.0, 10.0) [§] | **0.002** |
| PVL ≥ moderate | 2 (1.9) | 1 (3.8) | 6 (8.0) | 0.14 |
| Device success | 102 (96.2) | 25 (96.2) | 69 (92.0) | 0.43 |
| PPI | 4 (3.8) | 2 (7.7) | 14 (18.7) | **0.004** |
| Stroke | 2 (1.9) | 1 (3.8) | 2 (2.7) | 0.83 |
| In-hospital mortality | 0 (0.0) | 0 (0.0) | 0 (0.0) | - |

Values expressed as mean ± SD, median (IQR) or n (% of column total). Mismatch in implantation depth (ΔH) calculated as $H_{Post} - H_{Pre}$. EPS, embolic protection system; $H_{Post}$, final implantation depth; $H_{Pre}$, pre-implantation intended depth; LCC, left coronary cusp; NCC, non-coronary cusp; PCI, percutaneous coronary intervention; PPI, permanent pacemaker implantation; PTA, percutaneous transluminal angioplasty; ΔH, variation of implantation depth.

Post hoc analysis: [§] $P < 0.05$ *vs.* Acurate, [ǂ] $P < 0.05$ *vs.* Evolut; significant values ($P < 0.05$) reported in bold.