A method for standardized computed tomography angiography-based measurement of aortic valvar structures

Raquel del Valle-Fernández¹, Vladimir Jelnin¹, Georgia Panagopoulos¹, Yuriy Dudiy¹, Laurence Schneider¹, Peter T. de Jaegere², Carl Schultz², Patrick W. Serruys², Eberhard Grube³, and Carlos E. Ruiz¹*

¹Lenox Hill Heart and Vascular Institute, 130 East 77th Street, 9th Floor Blackhall, New York, NY 10075, USA; ²Thoraxcenter, Rotterdam, The Netherlands; and ³HELIOS Heart Center, Siegburg, Germany

Received 17 July 2009; revised 9 February 2010; accepted 22 February 2010; online publish-ahead-of-print 25 May 2010

Aims
Reliable assessment of the aortic valvar apparatus (AVAp) is essential as it may facilitate consistent outcomes with percutaneous aortic valvar therapies. The commonly referenced aortic annulus is problematic since this measurement does not correspond to any actual anatomic structure. We aim to describe a reliable method of measuring relevant structures of the AVAp based on widely available computed tomography analyses.

Methods and results
Retrospective analysis of computed tomograms of 75 patients with severe aortic stenosis (45 females, age 81.2 ± 7.8 years). Curved multiplaner reconstruction technique was used to measure average diameters of the ‘Aortic Leaflets Basal Attachment Plane’ (ALBAP), sinuses of Valsalva (SV), sinutubular junction (STJ), ascending aorta (AA), and distance from coronary arteries to the base of the cusps. Angulation between the AA and the left ventricle (LV) was measured in one plane that included the LV inflow long axis and the maximum visualization of the aortic root. Inter-rater reliability and absolute agreement among three raters were evaluated. Intra-class correlation coefficients for ALBAP, SV, STJ, and AA diameters were 0.90, 0.99, 0.95, and 0.94, respectively (\(P < 0.001\)) with 95% limits of agreement of the observed differences falling in the less than 1 mm range. Intra-class correlation coefficients were 0.82 for the angle and 0.61 and 0.78 for distances to the right and left coronary arteries (\(P < 0.001\)).

Conclusion
This method showed a high degree of inter-rater reliability and absolute agreement for AVAp diameters. Agreement was lower for AA–LV angle and distance to coronary artery measurements, emphasizing the need for software improvements and standardized image acquisition protocols.

Keywords
Aortic valve • Stenosis • Aortic • Computed tomography • Valves • Prosthetic

Introduction
Successful procedural outcomes in transcatheter aortic valve implantation (TAVI) have been linked to a steep learning curve.¹ This likely reflects a combination of procedural skill acquisition for the various device technologies available and, perhaps more importantly, learning how to select the most appropriate candidates for these interventions.

Anatomic characteristics of the aortic valvar apparatus (AVAp) are of relevance for patient selection. Therefore, it is essential to understand the true anatomical structures that constitute this apparatus in order to measure them in an accurate and reproducible manner. These structures include the sinutubular junction (STJ), sinuses of Valsalva (SV), leaflet attachment, interleaflet triangles, aortic leaflets, the ventriculo-arterial junction, and the left ventricle outflow tract (LVOT).²⁻⁸ Various imaging modalities have attempted to measure the ‘aortic annulus’. However, this is a non-existent anatomical structure, as the insertion of the aortic leaflets into the aortic root simulates a crown-like shape²⁻⁸ (Figure 1), with no distinctive tissue at
Inclusion criterion in TAVI protocols.1,10–13 Prior to surgical aortic valve replacement and more recently as these well-known limitations, this measurement has been reported using multidetector computed tomography (MDCTA) in patients with severe aortic stenosis. Therefore, we evaluated the inter-rater reliability based on actual anatomic landmarks easily defined with computed tomography angiography. The aim of this study is to define a method of consistent and reliable measurement of the AVAp in patients with aortic stenosis, based on actual anatomic landmarks easily defined with computed tomography. Therefore, we evaluated the inter-rater reliability and degree of agreement among three raters of a defined post-processing protocol using multidetector computed tomography angiography (MDCTA) in patients with severe aortic stenosis.

Methods

Patients
This retrospective study was undertaken following Institutional Review Board approval and a waiver of informed consent.

This is a retrospective analysis of 75 patients with severe degenerative aortic stenosis (diagnosed by echocardiography and angiography), who underwent MDCTA as part of routine evaluation prior to TAVI, from January 2005 to May 2008. Computed tomography angiography was performed on 31 patients at the Thoraxcenter, Rotterdam (The Netherlands) using a Dual Source CT (Somatron Definition, Siemens Medical Solutions, Farachheim, Germany); on 27 patients at the HELIOS Heart Center, Siegburg (Germany) using a Philips 16 Brilliance CT (Philips Healthcare, Amsterdam, The Netherlands); and on 17 patients at Lenox Hill Heart and Vascular Institute (New York) using a Philips Brilliance 64 CT (Philips Healthcare, Cleveland, OH, USA). Standard protocols at each centre were used for image acquisition, and for gated studies, beta-blockers were administered as necessary (i.e. metoprolol 1 mg i.v. up to three times) until a heart rate of <70 b.p.m. was achieved (except contraindications). Data were de-identified and sent to a core-lab (Lenox Hill Heart and Vascular Institute, New York) for further analysis, where measurements and data collection were blindly performed by three experienced cardiologists.

Twenty-one studies were not ECG-gated and in the remaining studies, the phases analysed were 75% in 30 patients, 40% in 9 patients, 30% in 5 patients, 60, 55, and 45% in 2 patients each, and 70, 35, 25, and 0% in 1 patient each.

The Extended Brilliance Workspace workstation v.3.5 (EBW, Philips Medical, Cleveland, OH, USA) was used for data reconstruction and analysis.

Image post-processing
A curved planar reconstruction technique (Advanced Vessel Analysis module, Philips EBW, Philips Medical) was used to measure the diameters of the AVAp structures and the distance from the inferior limit of the origin of each coronary artery to the basal attachment of the corresponding leaflet. An aorta-LVOT centerline was constructed that defined the aorta-LVOT long axis (Figure 2A). Distances from the inferior limit of the right coronary artery (RCA) and the left main (LM) ostia to the basal attachment of each corresponding leaflet were measured along this centerline (Figure 2B and C). Perpendicular planes were automatically built at pre-specified points along the straightened view of the aorta-LVOT long axis (Figure 2D): (i) at the lowest point of attachment of the aortic leaflets into the LVOT, which defined the Aortic Leaflet Basal Attachment Plane (ALBAP); (ii) at every consecutive cross-section through the sinuses of Valsalva; (iii) at the STJ, defined as the ridge between the sinuses of Valsalva and the site of leaflet insertion. This concept was derived from two-dimensional (2D) imaging techniques (echocardiography, angiography), which make the evaluation of three-dimensional (3D) structures difficult. Furthermore, owing to the 2D nature of these imaging techniques, the measurement of this ‘annulus’ is performed in planes generated from random tangents across the aortic root (depending on the angulation or slicing of the root).14 As a result, significant differences in the sizing of the aortic annulus have been reported between different imaging techniques.5 Despite these well-known limitations, this measurement has been reported prior to surgical aortic valve replacement and more recently as inclusion criterion in TAVI protocols.1,10–13

Figure 1 The ‘aortic annulus’ misconception. (A) The insertion of the aortic leaflets simulates a crown-like structure (yellow curved lines), with part of the leaflets attached to the aorta and part attached to the left ventricle. There is no distinctive tissue at the site of insertion. Therefore, the traditional measurement of the aortic annulus does not correspond to any actual anatomical structure, so the measurement can vary widely. Nevertheless, three ‘rings’ can be identified in the aortic valvar apparatus. (i) A real anatomic ring that corresponds to the sinotubular junction (green ring 1); (ii) a virtual ring obtained when the lowest points of attachment of the aortic leaflets into the LV are joined (green ring 2) and that can be assimilated to the ‘aortic leaflet basal attachment plane’; and (iii) a second real ring that corresponds to the ventriculo-arterial junction (red ring 3). (B) The entire circumference of the ventriculo-arterial junction cannot be accurately identified using MDCTA. The red line shows the level of the ventriculo-arterial junction (the transformation of the arterial wall into the ventricular wall), with the lateral aspect in relation to the myocardium of the left ventricle. (A, adapted from Anderson2).
where the normal tubular configuration of the ascending aorta (AA) is attained; and (iv) at the AA, arbitrarily measured at 40 mm distance from the ALBAP level. In each of the above cross-sections, vessel areas were carefully drawn and manually adjusted. In those cases in which the vessel wall was calcified, the calcified segments were visually compared with the adjacent, non-calcified wall, and vessel area was drawn through the centre of the calcium. Average diameters were automatically calculated for each area (Figure 2E–H). For the SV, the maximum among all the average diameters obtained was used for analysis.

The Functional Analysis module in the Comprehensive Coronary Analysis software (Philips EBW, Philips Medical) was used to assess the angulation between the left ventricle (LV) and the aorta. Initially, the left ventricular inflow long axis was built as the straight line that transected the LV from the apex to the centre of the mitral valve (Figure 3A, C, and D). The plane that included this LV inflow long axis was then rotated until it included the maximum visualization of the aortic root (Figure 3B). The angle between the LV inflow long axis and a line through the centre of the aorta was measured in this plane (Figure 3D).

**Statistics**

Inter-rater reliability: The degree of consensus among the three raters on the seven measures obtained (average diameters of the ALBAP, SV, STJ, and AA, distances from RCA and LM to the basal attachment of the corresponding leaflet and angulation between the aortic root and the LV) was assessed in two ways. First, using reliability analysis, the intra-class correlation coefficient (ICC) was estimated as an indicator of inter-rater reliability for each measurement. Since systematic variability due to the raters was a relevant issue, the model utilized the absolute agreement option, which measures whether raters assign the same absolute score. We present the single measure intraclass coefficient, since we expect further research to use the measurements of a single rater rather than the average of multiple raters. Second, the exact degree of agreement for each of three combinations

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**Figure 2** Diameter and distance measurements using curved multiplaner reconstruction (CPR) technique. An aorta-LVOT centerline is constructed (A). The straightened view of the vessel can be rotated on its centerline until the desired structures are identified (B–D). Once the planes of the left main or the right coronary arteries (purple lines in B and C, respectively) are identified, the distances to the basal attachment of the related leaflet (blue lines in B and C) are measured (distance between both lines). (D) The aortic leaflet basal attachment plane (ALBAP, blue line), sinuses of Valsalva (green line), sinutubular junction (purple line), and ascending aorta at 40 mm from the ALBAP (yellow line) are identified. Their respective cross-sectional area measurements are shown in H, G, F, and E, respectively. (G) The picture shows how measuring diameters of this clover-leaf shaped structure in 2D-oblique planes may lead to significant differences in the values obtained. This may be overcome by the estimation of an average diameter.
of two raters (rater1–rater2, rater1–rater3, rater2–rater3) on the seven measures was obtained by calculating the 95% limits of agreement.\(^\text{14}\) We calculated the differences between two raters and the mean and the standard deviation of these differences. The 95% limits of agreement were obtained using the formula: \((\text{mean difference} \pm 1.96 \times \text{standard deviation of the differences})\). Normality of the distributions was tested using the Kolmogorov–Smirnoff and the Shapiro–Wilk tests. The degree of agreement between each set of two raters across all measures was also evaluated using Bland-Altman plots, whereby differences between the two raters’ measurements on each variable for each patient were plotted against the mean of the measurements. The purpose of this analysis was to determine whether between-rater differences increased as the size of the measurement increased.

We set out to determine whether the various resolution levels of scanner technology processing and whether performing a gated vs. a non-gated study could impact inter-rater reliability and exact degree of agreement. We hypothesized that this would be most clearly evident in the examination of the results between the following two groups: non-gated/MDCT16 and gated/MDCT64, since we expected their combination to represent the extremes of the continuum of data in this study. The ICCs as well as the exact degree of agreement for each of the three combinations of the two raters on each of the seven measures for both groups was obtained by calculating the average difference and the 95% limits of agreement. In order to examine the equivalence of the median difference among the three raters between the two groups on all seven measures, we performed the non-parametric Mann–Whitney test and we adjusted the level of significance (0.05) for the 21 multiple comparisons: \(0.05/21 = 0.0023\). Therefore, a difference between the two groups would be considered statistically significant, if it was observed to occur at \(P < 0.0023\).

All statistical analyses were performed utilizing SPSS version 16.2 (SPSS, Inc., Chicago, IL, USA) statistical software. \(P < 0.05\) was considered a priori to indicate statistical significance.

The authors had access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript.

Results

Baseline clinical characteristics of the patients were unknown except for age and sex and for the fact that all had severe aortic stenosis and were evaluated for percutaneous valve implant. There were 45 women and 30 men and the mean age of the patients was 81.2 ± 7.8 years.

The ICC was observed to be consistently high for AVAp diameter measurements, indicating little variation among the scores given to each subject by the raters. The single measures ICC for ALBAP diameter was 0.90, for SV was 0.99, for STJ was 0.95, and for AA was 0.94, \((P < 0.001)\). The single measures ICC for the angle was 0.82 and for the distance from the RCA and LM to the basal attachment of the corresponding leaflet were 0.61 and 0.78, respectively \((P < 0.001)\). These lower ICC values indicate that, although significant, these measures were less reliable (Table 1).

The limits of agreement for each set of two raters across these sites were calculated and they are presented in Table 2. It is

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**Figure 3** Measurement of the angulation between the left ventricle (LV) and the aorta. The inflow long axis of the LV is constructed as the line that transects the centre of the mitral valve and the LV apex (vertical green lines in A, C, and D). Figure (B) shows a plane that is perpendicular to this LV inflow long axis. The three axis identified in (B) are always separated by 60°, and they correspond to the planes shown in (A) (blue axis), (C) (red axis), and (D) (green axis). These planes are rotated on the LV long axis (green curved arrow in B) until the maximum visualization of the aortic root is obtained (D). The angle between the LV long axis and the line that passes through the centre of the aorta is measured in this plane.
noteworthy that the observed differences were minimal, frequently <1 mm. Visual inspection of the majority of the plots indicated that the magnitude of the differences remained independent of the magnitude of the variable.

The distributions of the difference scores were tested for normality and we observed that the distributions of some of the differences were not normal. As a result, we present both the mean ± 95% confidence interval as well as the median with the inter-quartile range (Table 3) to describe the data with greater accuracy.

There were 14 cases in the non-gated/MDCT16 group and 17 cases in the gated/MDCT64 group. The ICCs are presented in Table 1; the great majority of them was similar in both groups. The median and inter-quartile range are also presented in Table 3, since some of the data were not normally distributed. None of the 21 comparisons between the two groups was observed to be statistically significant as per the multiple comparisons corrected level of significance (P > 0.02).

### Discussion

The 3D anatomic complexity of the AVAp is poorly depicted by 2D imaging technologies. In fact, the universally accepted misconception of an ‘aortic annulus’ has evolved from a simplistic interpretation of those 2D modalities and does not apply to any true anatomical structure, due to the crown-shape insertion of the aortic leaflets into the LVOT (Figure 1). With the advent of 3D imaging technologies, we have the opportunity to more appropriately describe the aortic valvar complex. In the present study, we validate a simple MDCTA post-processing method that reliably measures real anatomic landmarks relevant to the AVAp.

Imaging modalities currently used to assess the aortic valve have clear and concise limitations. The most commonly used, 2D echocardiography, is operator dependent and limited by the angle of incision of the ultrasound array. Furthermore, shadowing caused by heavy calcification (frequently observed in aortic stenosis patients) is a significant limitation of this technology. Among the limitations of computed tomography, motion artefacts and non-adequate image acquisition and post-processing are probably the most relevant ones. In fact, prior studies using MDCTA to assess aortic root dimensions, distance from the ‘annulus’ to the coronary arteries and valve area have been limited by the use of measurements obtained in standard 2D (axial, saggital, and coronal) or in multiple oblique planes. Therefore, these studies faced some of the limitations of measuring in two dimensions (Figure 4).

In addition, earlier MDCTA reports did not analyse inter-rater variability and reliability of the measurements. It would be most prudent to validate the accuracy and reproducibility of the method of measurement prior to its application in the clinical setting. Following this validation, the method could be assessed in well-designed prospective studies. The current study, therefore, is the first of several steps and a good beginning in attempting to validate this MDCTA methodology for accurate and clinically important aortic apparatus characterization. Prior MDCTA protocols have not been subjected to such scrutiny and validation, but nonetheless have been used clinically.

We decided to analyse patients with aortic stenosis because severely degenerative valves are the most difficult to characterize

### Table 1 Intra-class correlation coefficients for the seven different measurements

<table>
<thead>
<tr>
<th>ICC</th>
<th>ALBAP</th>
<th>SV</th>
<th>STJ</th>
<th>AA</th>
<th>RCA</th>
<th>LM</th>
<th>α (°)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>0.90</td>
<td>0.99</td>
<td>0.95</td>
<td>0.94</td>
<td>0.61</td>
<td>0.78</td>
<td>0.82</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MDCT64/gated</td>
<td>0.90</td>
<td>0.99</td>
<td>0.98</td>
<td>0.97</td>
<td>0.62</td>
<td>0.71</td>
<td>0.87</td>
<td></td>
</tr>
<tr>
<td>MDCT16/non-gated</td>
<td>0.95</td>
<td>0.99</td>
<td>0.95</td>
<td>0.94</td>
<td>0.64</td>
<td>0.73</td>
<td>0.75</td>
<td></td>
</tr>
</tbody>
</table>

ICC, intra-class correlation coefficient; ALBAP, aortic leaflet basal attachment plane; MDCT, multidetector computed tomography; SV, sinuses of Valsalva; STJ, sinutubular junction; AA, ascending aorta (at 40 mm from the ALBAP); RCA, right coronary artery; LM, left main; α, angle between the aorta and the left ventricle inflow long axis.

### Table 2 Limits of agreement (95%) of the differences between raters

<table>
<thead>
<tr>
<th>Rater</th>
<th>ALBAP</th>
<th>SV</th>
<th>STJ</th>
<th>AA</th>
<th>RCA</th>
<th>LM</th>
<th>Angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (mm)</td>
<td>Lower bound</td>
<td>Upper bound</td>
<td>Mean (mm)</td>
<td>Lower bound</td>
<td>Upper bound</td>
<td>Mean (mm)</td>
</tr>
<tr>
<td>1–2</td>
<td>−0.52</td>
<td>−0.04</td>
<td>0.17</td>
<td>−0.21</td>
<td>−0.13</td>
<td>1.40</td>
<td>0.27</td>
</tr>
<tr>
<td>1–3</td>
<td>−0.41</td>
<td>0.02</td>
<td>0.26</td>
<td>−0.71</td>
<td>−0.45</td>
<td>0.37</td>
<td>−0.44</td>
</tr>
<tr>
<td>2–3</td>
<td>−0.36</td>
<td>0.05</td>
<td>0.21</td>
<td>−0.49</td>
<td>−0.31</td>
<td>−1.03</td>
<td>−0.71</td>
</tr>
</tbody>
</table>

The 95% limits of agreement are presented for each set of two raters across all sites. Diameters and distances are presented in millimetres (mm), angle in grades (°). Abbreviations as in Table 1.
using echocardiography and CTA due to the high prevalence of calcium, which introduces discrepancies in the measurements. A protocol that demonstrates good inter-rater variability in non-diseased valves may not be as good for measuring calcified ones, but if the inter-rater reliability is good for calcified valves, it is expected to be even better for non-diseased ones, the real borders of which are easier to identify. Furthermore, characterization of non-diseased valves has by now no more than diagnostic implications. On the other hand, characterization of severely stenotic valves has a more immediate therapeutic implication, as in the selection of device size for TAVI.

To accurately measure diameters along a vessel, measurements need to be performed in a perpendicular plane to the long axis of this vessel. Therefore, we used a curved multiplaner reconstruction technique to measure diameters since this technique allows for generation of strictly perpendicular planes to a centerline at each point along the length of the vessel under study, reducing angulation errors inherent with the techniques used in previous reports. We only measured clearly identifiable landmarks that correspond to actual anatomic structures (ALBAP, SV, STJ, AA), and for angle measurements we constructed a virtual reference plane from actual anatomic structures. ‘Diameter’ measurements for the SV are not straightforward, due to the clover-leaf shape of their cross-sections and to the different sizes of each of the sinuses (Figure 2G). In oblique reconstructions, the distance measured across the SV may correspond to the distance from commissure to commissure in one patient and to the distance from cusp to cusp in the next one, therefore introducing heterogeneity in the measurements.

To standardize the observed values, our methodology takes into consideration all available distances between opposite points (passing through the centerline) at the level of the SV, and it integrates them into a single value, which is the average distance (‘diameter’). The ‘ALBAP’ may be interpreted as the evolution of the 2D derived ‘aortic annulus’ misconception. Nevertheless, this 3D concept encompasses the fact of the oval shape of the LVOT and the multiple axes (‘diameters’) that can be obtained from it. The ventriculo-arterial junction, so clearly identifiable in pathological specimens, could not be reliably identified using this imaging modality. Since a portion of this landmark is in continuity with the fibrous mitro-aortic structure, its radiological density is similar to that of the adjacent tissue, which prevents accurate identification of its exact location. Therefore diameters of this structure were not calculated.

We confirmed the high level of reproducibility of our post-processing methodology for measuring diameters, despite the handicap of performing the measurements in sub-optimal image-quality sets (non-gated studies, extended use of 16 MDCT, and analysis of systolic phases). A high degree of inter-rater reliability and absolute agreement was demonstrated among the three raters.

The distance from the origin of the coronary arteries to the aorta and the LV using a single angle is a simplistic approach of performing the measurements in sub-optimal image-quality sets (non-gated studies, extended use of 16 MDCT, and analysis of systolic phases). A high degree of inter-rater reliability and absolute agreement was demonstrated among the three raters.

Finally, we evaluated the angulation between the LV and the aorta by measuring the angle of insertion of the aorta into the LV. Although clinical implications of this angulation in the setting of percutaneous aortic valve implantation are unknown, it has been suggested by experienced operators that it might influence the success of the implant. Characterizing the spatial relation of the aorta and the LV using a single angle is a simplistic approach.

### Table 3 Median and inter-quartile range of the differences among each two raters

<table>
<thead>
<tr>
<th>Rater</th>
<th>ALBAP</th>
<th>SV</th>
<th>STJ</th>
<th>AA</th>
<th>RCA</th>
<th>LM</th>
<th>Angle (°)</th>
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</thead>
<tbody>
<tr>
<td>All 1–2</td>
<td>Median (mm)</td>
<td>0.15</td>
<td>0.00</td>
<td>0.20</td>
<td>0.10</td>
<td>1.70</td>
<td>0.20</td>
</tr>
<tr>
<td></td>
<td>IQR</td>
<td>1.00</td>
<td>0.68</td>
<td>0.97</td>
<td>1.17</td>
<td>2.47</td>
<td>2.9</td>
</tr>
<tr>
<td>1–3</td>
<td>Median (mm)</td>
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<td>0.10</td>
<td>0.60</td>
<td>0.30</td>
<td>0.00</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>IQR</td>
<td>1.25</td>
<td>0.68</td>
<td>0.88</td>
<td>1.17</td>
<td>2.68</td>
<td>2.95</td>
</tr>
<tr>
<td>2–3</td>
<td>Median (mm)</td>
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<td>0.05</td>
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<td>1.1</td>
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<tr>
<td></td>
<td>IQR</td>
<td>0.95</td>
<td>0.60</td>
<td>0.90</td>
<td>0.82</td>
<td>3.03</td>
<td>3.82</td>
</tr>
<tr>
<td>16/NG</td>
<td>Median (mm)</td>
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<td>0.20</td>
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<td>0.20</td>
<td>1.80</td>
<td>1.00</td>
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<tr>
<td></td>
<td>IQR</td>
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<td>0.60</td>
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<td>2.40</td>
<td>4.00</td>
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<td>1–3</td>
<td>Median (mm)</td>
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<td>0.9</td>
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<tr>
<td></td>
<td>IQR</td>
<td>1.30</td>
<td>1.00</td>
<td>1.20</td>
<td>1.10</td>
<td>6.60</td>
<td>4.30</td>
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<tr>
<td>2–3</td>
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<td>0.00</td>
<td>1.70</td>
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<tr>
<td></td>
<td>IQR</td>
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<td>0.90</td>
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<td>0.30</td>
<td>2.60</td>
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<tr>
<td>64/G</td>
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<td>0.00</td>
<td>1.90</td>
<td>0.70</td>
</tr>
<tr>
<td>1–2</td>
<td>IQR</td>
<td>1.40</td>
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<td>0.80</td>
<td>1.60</td>
<td>3.9</td>
<td>3.10</td>
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<td>0.00</td>
<td>0.70</td>
<td>1.40</td>
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<tr>
<td></td>
<td>IQR</td>
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<td>0.40</td>
<td>1.30</td>
<td>0.90</td>
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<td>4.20</td>
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<tr>
<td>2–3</td>
<td>Median (mm)</td>
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<td>0.10</td>
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<td>0.20</td>
<td>2.10</td>
<td>1.40</td>
</tr>
<tr>
<td></td>
<td>IQR</td>
<td>1.20</td>
<td>0.80</td>
<td>0.90</td>
<td>0.60</td>
<td>3.30</td>
<td>6.10</td>
</tr>
</tbody>
</table>

The median and inter-quartile range (IQR) of the differences are presented for each set of two raters across all sites. Diameters and distances are presented in millimetres (mm), angle in grades (°). Abbreviations as in Table 1. NG, non-gated. G, gated.
to this anatomic interaction and relies on assumptions that may explain the lower reliability of the measurements. The aortic long axis is curved, and assimilating it to a straight line introduces a potential limitation of the technique. Furthermore, the lines of the LV inflow long axis and the aortic long axis will never cross because they lie in different planes, and therefore an imaginary 2D plane must be constructed to create an intersect (Figure 5). This requires building a plane that includes the inflow long axis of the LV and a second plane that includes the long axis of the aorta (Figure 5A–C), and these two planes must be rotated on their axes (Figure 5D) until they are parallel to each other. Once they are parallel, they can be projected onto a single imaginary plane (Figure 5E) where angle measurements can be made (Figure 5F). Current software limitations do not support such complex manipulation, and we defined a surrogated method for achieving this (Figure 3). The software module used allows accurate construction of the LV inflow long axis (Figure 3A, C, and D), but does not allow simultaneous construction of the centerline of the aorta. Therefore, angle measurements were not performed between these two centerlines. Instead of the centerline of the aorta, we used the line that followed the aorta in the plane in which the maximum visualization of the aortic root was achieved (Figure 3B and D) for angle measurements. We believe that future software should take into account the ideal method previously proposed for a more accurate measurement of the angle.

We specifically investigated whether the degree of agreement among the three raters was different depending upon the processing level of the scanner and whether a study was gated by
examining two groups representing the extremes of the data measurement continuum (non-gated/MDCT16 and gated/MDCT64). We believe that this data analysis served our purpose well from a statistical analysis viewpoint because it limited the number of multiple comparisons to 21 and thus, made the interpretation of results more manageable and reduced the potential or erroneous findings due to type I error. Despite these precautions, however, we must be mindful of the fact that these results are based on a substantially smaller subgroup sample size and they are, therefore, more likely to show greater variability than the total group results. The great majority of the ICCs was observed to be similar in both groups, as were the median differences on each of the seven measures obtained by all three raters. This indicates that we currently do not have enough evidence to suggest that the degree of agreement among our raters is different between the two groups. As we mentioned earlier, this may very well be the result of not having enough power to detect this difference due to the small subgroup size. Future research efforts may help elucidate the answer to this question.

The first of several steps towards the clinical validation of any diagnostic technique should always be, in our opinion, the validation of the post-processing/measuring protocols by demonstrating that they provide consistent and reliable measurements. Only when this has been proven should we climb the next steps of validation against established diagnostic modalities and clinical evaluation. Given the high reliability demonstrated by this protocol, we consider this analysis an important step in establishing standard criteria for the evaluation of the complex AVAp. Nevertheless, only well-designed prospective studies will determine if pre-procedural definition of the aortic anatomy and aorta–LV relationship are important determinants of percutaneous procedural success, and if these variables may be of use in patient and device selection in order to optimize the results.

**Study limitations**

Image acquisition protocols differed between centres, non-gated studies were included in the analysis and only a single, non-standardized phase of the cardiac cycle was analysed. These may
have contributed to greater variability in our measurements, and sub-optimal quality images might have in particular influenced the measurement of the distance to the coronary arteries. However, even under these unfavourable conditions, most of the structural measurements were highly reliable. Although the analysis of different phases of the cardiac cycle may present a major limitation to the conclusions of clinical studies assessing the relationship between anatomy and outcomes, it does not limit the justification for conducting a reliability study as long as all readers measure the same data set.

Finally, software advances may in the future allow greater accuracy in the evaluation of the angulation between the aorta and the LV.

**Conclusion**

Accurate measurements of the structures involved in the AVAap are essential in planning surgical and percutaneous valve therapies, and most likely impact patient selection and outcomes.

We describe a protocol for computed tomography image post-processing that uses actual anatomic landmarks of the aortic apparatus and avoids measurements that do not have a clear anatomic correlation. This simple methodology demonstrates a high degree of inter-rater reliability and absolute agreement for diameter measurements, with <1 mm absolute differences between raters, despite the use of non-standardized image acquisition protocols from several centres from several countries. Absolute agreement was observed to be lower for distance to coronary arteries and for the estimation of the angulation between the aorta and the LV, emphasizing that further work and software improvement are needed to better assess these complex relations.

Prospective clinical studies should evaluate whether aortic and aorta–LV anatomical variances are related to percutaneous procedural success, and determine if these variables are useful in patient and device selection and procedural planning.

**Acknowledgements**

We are grateful to Dr. Nicolo Piazza, MD (Thoraxcenter, Rotterdam, The Netherlands) and Dr. Kirk Garratt (Lenox Hill Heart and Vascular Institute, New York, US) for their valuable contribution in preparing and editing this manuscript.

**Funding**

R.d.V.-F. was supported by a research Grant from the Spanish Society of Cardiology, Madrid, Spain.

**Conflict of interest:** none declared.

**References**