Aortic Annular Sizing Using a Novel 3-Dimensional Echocardiographic Method: Utility and Comparison to Cardiac Computed Tomography

Khalique et al: Aortic Annulus Sizing Using a Novel 3-D TEE Method

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Abstract

Background—Previous studies have shown cross-sectional three-dimensional (3D) transesophageal echocardiography (TEE) measurements to severely underestimate multi-detector row computed tomography (MDCT) measurements for the assessment of aortic annulus prior to transcatheter aortic valve replacement (TAVR). This study compares annulus measurements from 3D-TEE employing off-label use of commercially available software to MDCT measurements, and assesses their ability to predict paravalvular regurgitation (PVR).

Methods and Results—100 patients with severe, symptomatic aortic stenosis who had both contrast MDCT and 3D-TEE for annulus assessment prior to balloon-expandable TAVR were analyzed. Annulus area, perimeter, and orthogonal maximum and minimum diameters were measured. Receiver-operating characteristic (ROC) analysis was performed with mild or greater PVR as the classification variable. 3D-TEE and MDCT cross-sectional perimeter and area measurements were strongly correlated ($r = 0.93-0.94$, $p < 0.0001$), however, the small differences ($\leq 1\%$) were statistically significant ($p = 0.0002$ and 0.0074, respectively). Discriminatory ability for $\geq$ mild PVR was good for both MDCT (area under the curve for perimeter and area cover index = 0.715 and 0.709, respectively) and 3D-TEE (area under the curve for perimeter and area cover index = 0.709 and 0.694, respectively). Differences in ROC analysis between MDCT and 3D-TEE perimeter and area cover indexes were not statistically significant ($p = 0.15$ and 0.35, respectively).

Conclusions—Annulus measurements using a new method for analyzing 3D-TEE images closely approximate those of MDCT. Annulus measurements from both modalities predict mild or greater PVR with equivalent accuracy.

Key Words: aortic stenosis, echocardiography, tomography, paravalvular regurgitation
Abbreviations

2D = 2-Dimensional

3D = 3-Dimensional

AUC = area under the curve

CI = Cover Index

D_{area} = diameter calculated from area

D_{max} = maximum orthogonal diameter

D_{min} = minimum orthogonal diameter

D_{mean} = average of the maximum and minimum orthogonal diameters

D_{perim} = diameter calculated from perimeter

LVOT = left ventricular outflow tract

MDCT = multi-detector row computed tomography

PARTNER = Placement of Aortic Transcatheter Valves

PVR = paravalvular regurgitation

ROC = receiver-operating characteristic

TAVR = transcatheter aortic valve replacement

TEE = transesophageal echocardiography

THV = transcatheter heart valve
Transcatheter aortic valve replacement (TAVR) has emerged as a therapeutic option for patients with symptomatic, severe aortic stenosis and elevated surgical risk.\textsuperscript{1,2} The aim of TAVR implantation is to employ accurate sizing to optimize valvular hemodynamics while creating a tight seal around the transcatheter heart valve (THV) to minimize paravalvular regurgitation (PVR). Accurate imaging assessment of the aortic valve annulus is critical for THV sizing. Although the traditional measurement of annular diameter has been performed on the two-dimensional (2D) echocardiographic long-axis view (sagittal plane)\textsuperscript{3}, multiple studies have demonstrated the oval shape of the annulus\textsuperscript{4-6} with the shortest dimension typically lying in the sagittal plane. Studies across multiple modalities have also shown the advantages of three-dimensional (3D) assessment of the annulus over 2D assessment. Both echocardiography\textsuperscript{7-11} and multi-detector row computed tomography (MDCT)\textsuperscript{5, 6, 9, 12-19} have been used for annular sizing prior to TAVR and have been shown to be predictive of post-implantation paravalvular aortic regurgitation.\textsuperscript{7, 8, 13, 18, 20} Because transesophageal echocardiography (TEE) is a relatively safe procedure\textsuperscript{21} which does not require iodinated contrast and can be used intra-procedurally during TAVR, it is desirable to develop reproducible and accurate 3D-TEE measurements of the aortic valve annulus. Although recent reviews have suggested that 3D-TEE can be used for cross-sectional area and perimeter measurements,\textsuperscript{3, 22} studies to date have shown clinically significant differences in 3D-TEE and MDCT measurements.\textsuperscript{10, 11, 23, 24}

The goal of the current study is to compare a novel 3D-TEE method for annular assessment to MDCT measurements and to compare the predictive value of the two modalities for the development of PVR.
Methods

Patient population and procedure

This analysis included 100 patients who underwent TAVR with a balloon-expandable Edwards SAPIEN or SAPIEN XT THV from (Edwards Lifesciences, Irvine, CA) November 2011 to January 2013 who also underwent both pre-procedural MDCT and intraprocedural TEE. Patients were non-consecutive, as patients who had not undergone both MDCT and intraprocedural TEE were excluded. The procedural access route (transfemoral, transapical or transaortic) was determined by standard protocols. THV sizing was decided at the discretion of the treating physicians with the use of all available imaging modalities (MDCT and 3D-TEE). No patients were excluded from imaging analysis based on image quality. All patients gave informed consent and the study was approved by the institutional review board for human research.

Image Acquisition

Echocardiography

Patients underwent intra-procedural TEE using commercially available equipment (iE33, Philips Medical Imaging, Andover, MA), according to standard protocols. A full 2D-TEE imaging protocol was performed including pulsed-wave and continuous-wave Doppler recordings. User-defined 3D-TEE volumes of the aortic valve complex were acquired (single-beat acquisition) by obtaining long-axis or short-axis 2D-TEE views from imaging windows which minimized acoustic shadowing of the annular plane (Online AVI 1). The 3D volumes contained the left ventricular outflow tract (LVOT), aortic annulus and valve, and aortic root to the sinotubular
junction. Multi-beat, spliced images were avoided. 2D measurements of the annulus were performed from long-axis views with particular attention to avoiding acoustic shadowing of the hinge-point of the right coronary cusp; frequently this required imaging from a deeper esophageal window.

**MDCT**

Prior to the TAVR procedure, patients underwent cardiac computed tomographic angiography using a 320-slice system (Toshiba Medical Systems, Otawara, Japan). The protocol used was specially designed in our institution to minimize iodinated contrast administration while providing cardiac and vascular pre-TAVR assessment during a single contrast bolus administration. During an inspiratory breathhold, single-volume acquisition was performed with prospective electrocardiographic triggering. Data were acquired with collimation of 240-360 x 0.5 mm and a gantry rotation time of 350 ms. Intravenous injection of 39 to 60 ml of non-ionic contrast agent (Iodixanol) was performed at a rate of 3.5 ml/s. The decision regarding the volume of contrast used was at the discretion of the physician conducting the scan. Tube current and potential were determined by the physician conducting the scan or by software automation according to the patient’s body habitus. Real-time bolus tracking with automated peak enhancement detection in the descending aorta was used for timing the scan. Data acquisition was initiated based on a threshold of 180 Hounsfield Units. The 3-dimensional dataset from the contrast-enhanced scan was reconstructed at 5% increments throughout the cardiac cycle. Images were reconstructed with a slice thickness of 0.5 mm or 0.25 mm. CT datasets were transmitted to a dedicated workstation and analyzed using 3mensio valve software (version 5.1, Pie Medical Imaging, Netherlands). Window width and level were optimized by the reader.
Aortic annulus measurements and calculations

The aortic annulus was defined as the plane of the virtual circumferential ring containing the basal attachment points of the three aortic valve leaflets. For both echocardiography and CT, the following annular measurements were performed: perimeter, area, and orthogonal maximum and minimum diameters. Average diameter was calculated from perimeter \( D_{\text{perim}} = \frac{\text{perimeter}}{\pi} \) and from area \( D_{\text{area}} = 2 \times \sqrt{\text{area} \div \pi} \). Mean diameter \( D_{\text{mean}} \) was calculated as the average of the maximum diameter \( D_{\text{max}} \) and minimum diameter \( D_{\text{min}} \). Absolute differences \( \Delta \) in nominal THV diameter and measured or calculated annular diameters were determined.

Eccentricity index was calculated using the formula maximum diameter/minimum diameter. The cover index (CI) representing the % oversizing of the THV as compared to the measured annulus size and was calculated separately for mean diameter, perimeter, and area. Diameter CI was calculated as \( \frac{\text{[nominal THV diameter – measured diameter]}}{\text{nominal THV diameter}} \times 100\% \). Perimeter CI was calculated as \( \frac{\text{[nominal THV perimeter – 3D perimeter]}}{\text{nominal THV perimeter}} \times 100\% \). Area CI was calculated as \( \frac{\text{[nominal THV area – 3D area]}}{\text{nominal THV area}} \times 100\% \). All measurements were performed in mid-systole, using the most optimal image at or near maximum aortic valve excursion. Initial echocardiographic measurements were performed intra-operatively at the time of THV implant by an echocardiographer experienced in TAVR imaging (RTH). MDCT measurements were performed retrospectively by a CT reader experienced in TAVR imaging (OKK). For each modality, readers were blinded to results of measurements from the other modality. For inter- and intra-observer reproducibility, readers were blinded to the previous measurements.
Echocardiographic Measurements

2D-TEE annular diameter measurements were performed from the long axis view which maximally bisected the diameter of the aortic annulus. To ensure optimal selection of this plane, simultaneous biplane imaging was performed or meticulous attention was paid to visualization of the hinge point of the right coronary cusp and the commissure between the left and non-coronary cusps (Figure 1).

3D echocardiographic reconstruction for measurement of the aortic annulus was performed by off-label use of commercially available Q-lab™ MVQ software (version 8.1, Philips Medical Imaging, Andover, MA) (Figure 2). This allowed for precise identification of the annular plane from orthogonal long-axis views utilizing adjacent anatomy to accurately identify the annular plane, minimizing the effect of acoustic shadowing on measurement of the annulus. Once the plane was defined, the following annular measurements were obtained: area, perimeter, and orthogonal maximum and minimum dimensions.

MDCT Measurements

Commercially available 3mensio software (Pie medical imaging) was used for MDCT annular measurements (Figure 3). The 3mensio software requires the user to select a point at the caudal attachment of each aortic valve leaflet in order to generate the annular plane (Figure 3A-C). Following generation of the annular plane, a polygonal line was traced circumscribing the annulus, and the perimeter and area were automatically calculated by the software (Figure 3D). Orthogonal maximum and minimum diameters were measured manually by the reader (Figure 3E). The plane was kept at the level of the true virtual basal annulus regardless of calcification, since avoiding calcification could lead to inaccuracies in measurement. For annular...
measurements, the annular border was traced outside any visualized calcium. The appearance of partial volume averaging artifacts (“blooming”) due to calcification was reduced by adjusting window and level settings (Figure 3F). Images with suboptimal contrast opacification were enhanced by adjusting window and level settings to better delineate the boundaries of the annular lumen (Figure 3G). In cases of both suboptimal contrast opacification and calcified hinge points, window and level settings were adjusted to alternately decrease partial volume averaging or increase lumen/tissue contrast, in order to optimize visualization of the annular boundaries.

**Post-procedural assessment**

Assessment of PVR was performed by planimetry of 3D-TEE color Doppler reconstruction with direct planimetry of EROA (Figure 4) as the method of choice. When 3D color Doppler reconstruction was not possible, assessment was performed by a combination of visual estimation of 2D color Doppler imaging and quantitative Doppler assessment of relative stroke volumes across the LVOT and right-ventricular outflow tract. In cases where 3D Color Doppler was performed, grading of PVR was performed using the following EROA cutoffs: trace > 0-4 mm²; mild 5-9 mm²; moderate: 10-19 mm²; moderate-severe 20-29 mm²; and severe ≥ 30 mm². The need for post-dilatation was decided by the treating physicians and was typically based on the immediate post-deployment TEE imaging of more than mild paravalvular regurgitation, relying primarily on the short-axis view just apical to the THV stent.

**Statistical Analysis**

Analyses were performed using SPSS 19.0 (IBM, Armonk, New York), StataSE version 12 (StataCorp LP, College Station, TX), and MedCalc version 12.4.0.0 (MedCalc Software, Belgium). Statistical significance was defined as p < 0.05. Continuous variables are reported as
mean ± standard deviation. Comparisons between two measurements were performed using a paired 2-sided student’s t-test. Normality of distributions for continuous variables was tested using the Kolomogorov-Smirnov test prior to performing t-tests. Pearson correlation coefficients were used to assess the correlation between measurements from echocardiography and MDCT. Intra-class correlation coefficients were used to assess inter-observer (RTH and OKK for TEE, OKK and JMP for MDCT) and intra-observer (RTH for TEE, OK for MDCT) variability. Receiver-operating characteristic (ROC) curves were generated using ≥ mild PVR as a classification variable, employing the method of Delong et al. Agreement between measurement methods was displayed with plots using the Bland-Altman method.

Study Population. The population consisted of 55 females and 45 males with a mean age of 87.8 ± 8.3 years. Mean pre-TAVR calculated aortic valve area and peak transaortic velocity were 0.67 ± 0.17 cm² and 4.1 ± 0.76 m/s, respectively. TAVR was performed in 85 patients via transfemoral access, 9 via transapical access, and 6 via transaortic access. 60 patients received a SAPIEN THV, and 40 received a SAPIEN XT THV. 10 patients received a 29 mm THV, 57 patients received a 26 mm THV, and 33 patients received a 23 mm THV. Balloon post-dilatation was performed in 27 patients.

Paravalvular regurgitation. Immediate post-procedural echocardiographic assessment revealed no paravalvular regurgitation in 50/100 patients. In the 50 patients with PVR, assessment was performed by 3D color Doppler reconstruction in 43/50 patients. In 7/50 patients with PVR, assessment was performed by a combination of visual estimation by 2D color
Doppler and quantitative Doppler assessment of relative stroke volumes across the LVOT and right-ventricular outflow tract. In 6 of these 7 patients, the visual assessment was trace, and the difference between LV and RV stroke volumes was < 10 cc; therefore, regurgitation was categorized as trace. In one of these 7 patients, the visual assessment was trace-to-mild and the difference between LV and RV stroke volumes was 29 cc with regurgitant fraction = 25%, so regurgitation was categorized as mild. At the conclusion of the procedure, 50 patients had no PVR, 28 had trace PVR, 15 had mild PVR, and 7 had moderate PVR. No patient had more than moderate PVR.

**Comparison of 2D and 3D measurements.** The mean 2D-TEE sagittal annulus measurement was 23.0 ± 2.0 mm. The sagittal annulus measurement significantly underestimated 3D-TEE and MDCT measurements (Table 1).

**Comparison of 3D-TEE and MDCT measurements.** Table 1 compares 3D-TEE and CT annulus measurements. Both area and perimeter measurements showed excellent correlation between the modalities (r = 0.93 and 0.94, respectively). Although absolute differences were small (MDCT – 3D-TEE for D_{perimeter} = 0.99 ± 2.9 mm, for D_{area} = 0.22 ± 0.78 mm), 3D-TEE measurements were statistically significantly smaller than MDCT measurements (p = 0.0002 for perimeter, p = 0.0074 for area). Eccentricity Index was greater for CT measurements (1.18 ± 0.07 vs. 1.16 ± 0.09, p = 0.004). Figure 5 shows Bland-Altman plots for agreement between methods. For the mean diameter measurement, 3D -TEE measurements were smaller than MDCT measurements with the following mean differences: mean diameter difference = -0.1 mm (range 1.9 to -2.0 mm); perimeter difference -1.0 mm (range 4.0 to -6.0 mm; area difference = - 8.0 mm² (range 49.1 to -65.0 mm²).
The intra-class correlation coefficients for interobserver variability were 0.86-0.95 for 3D-TEE measurements and 0.89-0.95 for MCDT measurements. The intra-class correlation coefficients for intraobserver variability were 0.90-0.98 for 3D-TEE measurements and 0.91-0.98 for MCDT measurements.

**ROC curve analyses for predicting paravalvular regurgitation.** Table 2 summarizes ROC analyses with area under the curve (AUC) values for pre-procedural 2D-TEE, 3D-TEE, and MDCT absolute differences (Δ) between THV size and measured annulus diameter, as well as cover indexes, using ≥ mild PVR as a classification variable. The upper cutoff values for oversizing with the highest combination of sensitivity and specificity are also listed. Discriminatory ability for ≥ mild PVR was good for both MDCT (AUC for perimeter and area CI = 0.715 and 0.709, respectively) and 3D-TEE (AUC for perimeter and area CI = 0.709 and 0.694, respectively). Figure 6A shows an ROC curve for the 2D-TEE annulus CI using ≥ mild PVR as a classification variable. Figures 6B and 6C show comparisons of 3D-TEE and MDCT perimeter and area CI, respectively, using ≥ mild PVR as the classification variable. There is no significant difference in AUC values between 3D-TEE and MDCT for perimeter CI or area CI, (p = 0.15 and 0.35, respectively). AUC values for discrimination of ≥ mild PVR for Dmean CI between modalities also showed no statistically significant difference (p = 0.45).

**Discussion**

The principal findings of this analysis are: 1) Novel, off-label use of commercially-available software allows 3D-TEE annulus measurements to be made which closely approximate MDCT
measurements, 2) MDCT and 3D-TEE cross-sectional measurements predict post-TAVR PVR with equivalent accuracy.

MDCT cross-sectional area and perimeter measurements are commonly used for aortic valve annulus sizing prior to TAVR. Numerous studies have shown the advantages of three-dimensional (3D) assessment of the annulus over 2D assessment using multiple modalities, including MDCT, 3D-TEE, and cardiac magnetic resonance imaging. Cross-sectional 3D-TEE annulus measurements have generally been shown to be smaller than MDCT measurements, and a recent study demonstrated that MDCT overestimated, while 3D-TEE underestimated in vitro phantom annulus diameters. Using a novel, semi-automated 3D-TEE method with widely available software, our study shows excellent correlation between 3D TEE and MDCT measurements with a small absolute difference (≤1%), with 3D-TEE measurements underestimating MDCT measurements. Although statistically significant, these differences are not clinically relevant. As suggested in the study by Tsang et al., there may be systematic, methodologic reasons for these differences. 3D-TEE and MDCT clearly have different imaging limitations which may lead to the selection of slightly different transverse planes for annulus assessment. In addition, ectopic calcification may introduce significant measurement errors which differ by technique. Finally, the two modalities differ in temporal resolution, and thus measurements may be performed in slightly different points in the cardiac cycle.

PVR which is ≥ mild in severity may be associated with increased mortality after TAVR. In our analysis, area- and perimeter-based measurements by each modality had statistically similar predictive value for the presence of ≥ mild PVR at the end of the procedure. Jilaihawi et al. recently found both MDCT and 3D-TEE cross-sectional measurements to be
superior to 2D-TEE annulus for the prediction of PVR. Although not directly compared, the AUC and specificity for prediction of PVR by 3D-TEE cross-sectional measurements were much lower in that study compared to MDCT. This could be explained by a number of factors: there were fewer PVR events in the 3D-TEE group as compared to the MDCT group, the technique for cross-sectional 3D-TEE annulus measurement relied on tracing the annulus on a single short-axis view, and MDCT was used to prospectively size the THV with 3D-TEE measurements performed retrospectively. In the patient population used in the current study, treatment decisions were primarily made at the time of implantation using 3D-TEE cross-sectional measurements, and MDCT measurements were performed retrospectively. Our current practice is to use both MDCT and 3D-TEE for sizing, and in the event of a discrepancy, to use the method that provides the best image for data analysis for that individual patient.

In our study, the MDCT and 3D-TEE yield comparable measurements of the annulus with equal accuracy in predicting > mild PVR. It is not surprising that the AUC for both modalities is much less than perfect. There are multiple determinants of PVR, including device positioning, and left ventricular outflow tract/annulus/leaflet calcification, and although the predictive value of annulus sizing is significant, it is unlikely that any method will yield a higher AUC than shown in this and other studies. In addition, annulus sizing is only one parameter used to determine THV size; transfemoral access, sinus effacement, sinus height, coronary ostial height, and left ventricular outflow tract anatomy are some of the other important considerations.

Both MDCT and 3D-TEE $D_{\text{area}}$ calculations slightly underestimated $D_{\text{perimeter}}$. This is likely due at least in part to the polygonal line method used in many software packages for annulus tracing (including the 3mensio and MVQ programs used in our study) which creates a disproportionately truncated area as compared to perimeter. Although the area CI cutoff would
mathematically be expected to be twice the perimeter CI cutoff, the actual area CI cutoff (by either modality) is larger than expected because of a systematic under-measurement of the true annular area.

Recent studies\textsuperscript{10,11,23} have shown a severe underestimation of 3D-TEE of annulus cross-sectional measurements as compared to MDCT measurements. An error in the 10\% range which was found in these prior reports is clinically significant and potentially devastating for the patient. The current study also shows smaller measurements by 3D-TEE than by MDCT, however, the difference between 3D-TEE and MDCT measurements is \( \leq 1\% \), which is much smaller than observed in studies by Jilaihawi et al,\textsuperscript{11} Tsang et al,\textsuperscript{10} Husser et al,\textsuperscript{24} or Ng et al.\textsuperscript{23} Possible reasons for the stronger correlation between 3D-TEE and MDCT measurements in the current study include the novel, off-label use of 3D-TEE software as well as improvements in MDCT 3D software. Particularly limiting in these previous studies was that the 3D echocardiographic analysis was performed with manual measurements on a single short axis 3D plane. Given the significant echocardiographic artifacts that may occur (such as acoustic shadowing and side-lobe artifacts) the technique described in the current report allows a more accurate identification of and thus measurement of the annulus. The method does not rely only on the transverse plane of the annulus for this measurement, but uses the adjacent structures in the orthogonal long-axis views as an additional guide. We have shown 3D-TEE to be a reliable alternative to MDCT for the assessment of aortic valve annulus. This may allow for critical assessment of the annulus in cases of where MDCT angiography is not feasible or desirable, such as in the setting of significant renal insufficiency. Furthermore, if TAVR is employed in younger populations in the future, radiation from MDCT will become an increasingly important issue.
Certainly, 3D-TEE and MDCT each have distinct strengths and weaknesses. 3D-TEE has superior temporal resolution, which oftentimes allows for differentiation of the basal aortic valve hinge point attachments on the basis of visualized separation of calcium, provides physiologic information, and essentially eliminates motion based artifacts. However, 3D-TEE is hampered by suboptimal lateral resolution in the coronal plane which reduces the ability to measure the blood/tissue interface in this plane. On the other hand, MDCT typically provides superior tissue/lumen contrast but may be limited by artifacts due to partial volume averaging effects (“blooming”), heart/lung motion, patient motion (especially in this elderly group of patients who may have difficulty remaining still or holding their breath even for brief periods), and arrhythmias. Both modalities are user-dependent, and optimal image acquisition and analysis is always paramount for adequate annular assessment. Given these differences, we believe that echocardiography and MDCT are best thought of as complementary imaging modalities. Indeed, the current study suggests that these two modalities are equally accurate and highly correlative.

Limitations

The limitations of 3D-TEE and MDCT imaging have been previously discussed. All measurements were performed by experienced readers. In addition, the acquisition protocol for the 3D-TEE volume sets was also refined in order to acquire images with the least amount of acoustic shadowing of the annulus. The high reproducibility of these measurements is likely dependent on training and experience, and thus our findings cannot necessarily be generalized to less-experienced readers. Automation of the process for both modalities would be useful. Finally, this analysis included only patients receiving a balloon-expandable Edwards THV, and results regarding PVR should not be generalized to other valve platforms. Given the mismatch between the SAPIEN and SAPIEN XT patients in our study, we did not analyze these separately.
Although studies to date have shown similar short-term paravalvular regurgitation and hemodynamic performance data using the SAPIEN and SAPIEN XT valves, there are potential differences between them which will require further study.

**Conclusions**

Aortic annulus mean diameter, perimeter and area can be accurately and reproducibly measured by 3D-TEE. MDCT and 3D-TEE measurements are equally predictive of mild PVR. As more automated use-specific software algorithms become commercially available for 3D echocardiography, widespread use will become more feasible.

**Disclosures**

Dr. Williams has received consultant fees from Edwards Lifesciences. Dr. Kodali has received consulting fees from Edwards Lifesciences and Medtronic, and is a member of the Scientific Advisory Board of Thubrikar Aortic Valve, Inc., the Medical Advisory Board of Paieon Medical, and the TAVI Advisory Board of St. Jude Medical. Dr. Einstein has received grants for other research from GE Healthcare and Philips Healthcare, and owns stock in Medtronic. Dr. Leon is a nonpaid member of the Scientific Advisory Board of Edwards Lifesciences and Medtronic Vascular. Drs. Khalique, Paradis, Grubb, Harjai, George, Pearson, and Hahn have no disclosures.

**References**


Table 1. Comparison Between TEE and MDCT Aortic Annulus Measurements (n = 100 for both MDCT and 3D TEE measurements)

<table>
<thead>
<tr>
<th>Measurement</th>
<th>3D TEE</th>
<th>MDCT</th>
<th>Δ 3D TEE*</th>
<th>Δ MDCT TEE*</th>
<th>R**</th>
<th>P **</th>
</tr>
</thead>
<tbody>
<tr>
<td>D&lt;sub&gt;max&lt;/sub&gt; (mm)</td>
<td>25.3 ± 2.6</td>
<td>25.6 ± 2.6</td>
<td>2.32 ± 1.54</td>
<td>2.67 ± 1.29</td>
<td>0.34 ± 1.6</td>
<td>0.80</td>
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<tr>
<td>D&lt;sub&gt;min&lt;/sub&gt; (mm)</td>
<td>21.9 ± 2.2</td>
<td>21.7 ± 2.1</td>
<td>-1.07 ±</td>
<td>-1.25 ±</td>
<td>-0.20 ±</td>
<td>0.85</td>
</tr>
<tr>
<td>D&lt;sub&gt;mean&lt;/sub&gt; (mm)</td>
<td>23.6 ± 2.3</td>
<td>23.7 ± 2.1</td>
<td>0.63 ± 0.95</td>
<td>0.74 ± 0.92</td>
<td>0.09 ± 1.0</td>
<td>0.90</td>
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<tr>
<td>Perimeter (mm)</td>
<td>74.8 ± 7.0</td>
<td>75.8 ± 6.6</td>
<td>-1.07 ±</td>
<td>-1.02 ±</td>
<td>1.03 ± 1.9</td>
<td>0.85</td>
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<tr>
<td>D&lt;sub&gt;perimeter&lt;/sub&gt; (mm)</td>
<td>23.8 ± 2.2</td>
<td>24.1 ± 2.1</td>
<td>0.85 ± 0.87</td>
<td>1.17 ± 0.95</td>
<td>0.34 ± 0.82</td>
<td>0.93</td>
</tr>
<tr>
<td>Area (mm&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>434.9 ± 81.3</td>
<td>442.8 ± 78.9</td>
<td>8.0 ± 29.1</td>
<td>0.99 ± 2.9</td>
<td>0.94</td>
<td>0.0002</td>
</tr>
<tr>
<td>D&lt;sub&gt;area&lt;/sub&gt; (mm)</td>
<td>23.4 ± 2.2</td>
<td>23.7 ± 2.1</td>
<td>0.47 ± 0.82</td>
<td>-0.70 ±</td>
<td>0.22 ± 0.78</td>
<td>0.94</td>
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3D = 3-Dimensional; TEE = transesophageal echocardiography; MDCT = multi-detector row computed tomography; Δ 2D TEE = listed diameter – 2D TEE diameter; D<sub>area</sub> = average diameter based on area; D<sub>max</sub> = maximum orthogonal diameter; D<sub>mean</sub> = (D<sub>max</sub> + D<sub>min</sub>) / 2; D<sub>min</sub> = minimum orthogonal diameter; D<sub>perimeter</sub> = average diameter based on perimeter; R = Pearson’s correlation coefficient

*all with p <0.0001 compared to 3D TEE or MDCT based data; ** for 3D TEE vs. MDCT
Table 2. ROC Analyses for Prediction of ≥ Mild PVR

<table>
<thead>
<tr>
<th></th>
<th>AUC</th>
<th>P-value</th>
<th>Cutoff</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tr>
<td><strong>2D TEE</strong></td>
<td></td>
<td></td>
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<tr>
<td>Δ 2D Annulus (mm)</td>
<td>0.667</td>
<td>0.007</td>
<td>2.3</td>
<td>77.2</td>
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<td>Annulus CI (%)</td>
<td>0.669</td>
<td>0.005</td>
<td>9.1</td>
<td>77.3</td>
<td>59.0</td>
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<td><strong>3D TEE</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Δ D&lt;sub&gt;max&lt;/sub&gt; (mm)</td>
<td>0.689</td>
<td>0.002</td>
<td>0.0</td>
<td>68.2</td>
<td>52.6</td>
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<tr>
<td>Δ D&lt;sub&gt;min&lt;/sub&gt; (mm)</td>
<td>0.589</td>
<td>0.24</td>
<td>3.2</td>
<td>59.1</td>
<td>59.0</td>
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<td>Δ D&lt;sub&gt;mean&lt;/sub&gt; (mm)</td>
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<td>1.85</td>
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<td>57.7</td>
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<td>Δ D&lt;sub&gt;perim&lt;/sub&gt; (mm)</td>
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<td>0.001</td>
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<td>77.3</td>
<td>59.0</td>
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<td>7.1</td>
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<td>57.8</td>
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<tr>
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<td>59.0</td>
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<td>0.0001</td>
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<td>66.7</td>
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<td>59.0</td>
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<tr>
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<td>0.97</td>
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<td>59.0</td>
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<td>Perimeter CI (%)</td>
<td>Area CI (%)</td>
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<tr>
<td>Dmean CI (%)</td>
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<td>0.709</td>
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<td>Perimeter CI (%)</td>
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<td>77.3</td>
<td>77.3</td>
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<td>64.0</td>
<td>57.8</td>
<td>60.3</td>
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ROC = Receiver-Operating Characteristic; PVR = paravalvular regurgitation; AUC = area under the curve; CI = cover index; Δ2D Annulus = Nominal THV diameter – 2D Annulus measurement; ΔDarea = Nominal THV diameter – Darea; ΔDmax = Nominal THV diameter - Dmax; ΔDmean = Nominal THV diameter - Dmean; ΔDmin = Nominal THV diameter - Dmin; ΔDperimeter = Nominal THV diameter – Dperimeter; other abbreviations as in Table 1.
Figure Legends

Figure 1. Use of Biplane Imaging for 2D-TEE 3-chamber Linear Annulus Measurement

The white line bisecting the mid-systolic short-axis image on the 2-dimensional transesophageal echocardiographic (2D-TEE) view on the left is used to find a long-axis image which maximally bisects the aortic annulus. The measurement is then performed on the orthogonal long-axis view (red arrow).

Figure 2. Determination of Annulus Size by 3D-TEE MVQ software

Panel A shows a 3-Dimensional (3D) volume set is acquired from a long-axis 2-Dimensional transesophageal echocardiographic (2D-TEE) view. Acquisition with multiplane 2D visualization is recommended if available to ensure minimization of acoustic shadowing of aortic valve hinge points.

Panel B: After identification of mid-systole, the blue panel is used to identify the transverse plane of the annulus by alignment of the two orthogonal long-axis views. This can be done by “grabbing” the blue line in the sagittal or long-axis plane, and rotating the plane approximately 90 degrees counterclockwise (white arrow).

Panel C: The location of the two orthogonal long-axis views (in the green and red panels, yellow arrows) can be seen in the transverse plane (blue panel). These orthogonal planes are rotated around the center of the annulus in the transverse plane (blue panel) in order to confirm that this
transverse plane is at the virtual annulus. To confirm this, (Panels D1-3) the hinge-point of the cusps (red arrows) should be imaged in the orthogonal long-axis views during this rotation.

Panel E: Once the user has confirmed that the annulus is imaged in the transverse (blue) plane, the initial 4 points which define 2 orthogonal planes of the annulus are placed along the maximum and minimum diameters of the annulus in the orthogonal long-axis views.

Panel F: The user scrolls through a total of 16 points (total of 4 pair of orthogonal long-axis images in the green and red planes) and confirms all points lie at the blood-tissue interface, and at the annulus. Confirmation of the location of these points will be seen on the transverse plane. The points can be adjusted manually if needed.

Panel G: Once all points have been confirmed, perimeter, area, maximum and minimum diameters are then automatically determined by the MVQ package.

**Figure 3. Annulus Measurement by Multi-detector Row Computed Tomography**

Panel A-C: Localization and selection of the 3 aortic valve hinge points is performed to form the annular plane

Panel D: The resulting annular plane is shown. A polygonal line is drawn circumscribing the annulus for area and perimeter measurements.

Panel E: Orthogonal maximum and minimum measurements are performed.
Panel F: Adjustment of window and level settings is performed to reduce the appearance of partial volume averaging effects from calcification. The reduced appearance of annulus calcium can be seen in comparison to Panel G.

Panel G: Adjustment of window and level settings is performed to enhance the appearance of intraluminal contrast. The enhanced appearance of intraluminal contrast can be seen in comparison to Panel F.

**Figure 4. 3-Dimensional Transesophageal Echocardiographic Assessment of Paravalvular Regurgitation**

Panel A: Paravalvular regurgitation is localized using 3-Dimensional color Doppler reconstruction. Panel B: An effective regurgitant orifice area is traced on the 3-Dimensional color Doppler reconstruction.

**Figure 5. Bland Altman Plots for Comparison of 3D-TEE and MDCT Annulus Measurements.**

Comparison of 3-Dimensional (3D) transesophageal echocardiographic (TEE) vs. Multi-detector row computed tomography (CT) annulus mean diameter (top), perimeter (middle), and area (bottom) measurements.

**Figure 6. ROC Analysis Curves for Prediction of Mild or Greater Paravalvular Regurgitation**
Panel A shows Receiver-Operating Characteristic (ROC) analysis for the 2-Dimensional Transesophageal Echocardiographic (TEE) Annulus Cover Index measurement with the associated area under the curve and p-value. Panel B shows a comparison of 3-Dimensional (3D) TEE vs. multi-detector row computed tomography (MDCT) Perimeter Cover Index measurements with the difference in AUC values and p-value for the difference. Panel C shows a comparison of 3D-TEE vs. MDCT Area Cover Index measurements with the difference in AUC values and p-value for the difference.
Aortic Annular Sizing Using a Novel 3-Dimensional Echocardiographic Method: Utility and Comparison to Cardiac Computed Tomography
Omar K. Khalique, SusHEEL Kodali, Jean-Michel Paradis, Tamim M. Nazif, Mathew R. Williams, Andrew J. Einstein, Gregory D. Pearson, Kishore Harjai, Kendra Grubb, Isaac George, Martin B. Leon and Rebecca T. Hahn

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