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## Four-dimensional computed tomography-guided valve sizing for transcatheter pulmonary valve replacement

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**TITLE:**

# Four-Dimensional Computed Tomography-Guided Valve Sizing for Transcatheter Pulmonary Valve Replacement

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**KEYWORDS:**

computed tomography, 4-dimensional, transcatheter pulmonary valve replacement, dynamics

**SUMMARY:**

This study assessed a new methodology with a straightened model generated from the four-dimensional cardiac computed tomography sequence to obtain the desired measurements for valve sizing in the application of transcatheter pulmonary valve replacement.

**ABSTRACT:**

The measurements of the right ventricle (RV) and pulmonary artery (PA), for selecting the optimal prosthesis size for transcatheter pulmonary valve replacement (TPVR), vary considerably. Three-dimensional (3D) computed tomography (CT) imaging for device size prediction is insufficient to assess the displacement of the right ventricular outflow tract (RVOT) and PA, which could increase the risk of stent misplacement and paravalvular leak. The aim of this study is to provide

a dynamic model to visualize and quantify the anatomy of the RVOT to PA over the entire cardiac cycle by four-dimensional (4D) cardiac CT reconstruction to obtain an accurate quantitative evaluation of the required valve size. In this pilot study, cardiac CT from sheep J was chosen to illustrate the procedures. 3D cardiac CT was imported into 3D reconstruction software to build a 4D sequence which was divided into eleven frames over the cardiac cycle to visualize the deformation of the heart. Diameter, cross-sectional area, and circumference of five imaging planes at the main PA, sinotubular junction, sinus, basal plane of the pulmonary valve (BPV), and RVOT were measured at each frame in 4D straightened models prior to valve implantation to predict the valve size. Meanwhile, dynamic changes in the RV volume were also measured to evaluate right ventricular ejection fraction (RVEF). 3D measurements at the end of the diastole were obtained for comparison with the 4D measurements. In sheep J, 4D CT measurements from the straightened model resulted in the same choice of valve size for TPVR (30 mm) as 3D measurements. The RVEF of sheep J from pre-CT was 62.1 %. In contrast with 3D CT, the straightened 4D reconstruction model not only enabled accurate prediction for valve size selection for TPVR but also provided an ideal virtual reality, thus presenting a promising method for TPVR and the innovation of TPVR devices.

**INTRODUCTION:**

Dysfunction of the right ventricular outflow tract (RVOT) and pulmonary valve abnormalities are two of the most frequent consequences of severe congenital heart disease, for example, patients with repaired tetralogy of Fallot (TOF), certain types of double outlet right ventricle (DORV), and transposition of the great arteries[1–3]. The majority of these patients face multiple operations throughout their lives and along with advancing age, the risks of complexity and comorbidities increase. These patients may benefit from transcatheter pulmonary valve replacement (TPVR) as a minimally invasive treatment[4]. To date, there has been a steady growth in the number of patients undergoing TPVR and several thousands of these procedures have been performed worldwide. Compared with traditional open-heart surgery, TPVR requires a more accurate anatomical measurement of the xenograft or homograft from the right ventricle (RV) to pulmonary artery (PA), as well as the repair of pulmonary and RVOT stenosis *via* transannular patch, by computed tomography angiography (CTA) prior to intervention and to ensure that the patients are free from stent fracture and paravalvular leak (PVL)[5,6].

A prospective, multicenter study demonstrated that a multidetector CT annular sizing algorithm played an important role in selecting the appropriate valve size, which could decrease the degree of paravalvular regurgitation[7]. In recent years, quantitative analysis has been more and more applied in clinical medicine. Quantitative analysis has enormous potential to enable objective and correct interpretation of clinical imaging and to verify that patients are free of stent fracture and paravalvular leak, which can enhance patient-specific therapy and treatment response evaluation. In previous clinical practice, it was feasible to reconstruct CT imaging from three planes (sagittal, coronal, and axial) with two-dimensional (2D) CT to obtain a visualization model[8]. Contrast-enhanced electrocardiogram (ECG)-gated CT has become more important in the evaluation of RVOT/PA 3D morphology and function, as well as in the identification of patients with a suitable RVOT implantation site that is capable of maintaining TPVR stability throughout the cardiac cycle[9,10].

However, in the contemporary standard clinical and preclinical settings, the acquired 4D CT data are usually translated into 3D planes for manual quantification and visual evaluation which cannot show 3D/4D dynamic information[11]. Furthermore, even with 3D information, the measurements obtained from multiplanar reconstruction (MPR) have various limitations, such as poor quality of visualization and lack of dynamic deformation due to the different directions of blood flow in the right heart[12]. Measurements are time-consuming to gather and prone to mistakes, as 2D alignment and sectioning can be imprecise, resulting in misinterpretation and distensibility. Currently, there is no consensus on which measurement of RVOT–PA could reliably provide accurate information about the indications and valve sizing for TPVR in patients with dysfunctional RVOT and/or pulmonary valve disease.

In this study, the method for measuring RVOT-PA using a straightened right heart model *via* a 4D cardiac CT sequence is provided to determine how best to characterize the 3D deformations of RVOT-PA throughout the cardiac cycle. The spatio-temporal correlation imaging was completed by including the temporal dimension and, therefore, were able to measure variations in RVOT-PA magnitude. Additionally, the deformation of the straightened models could positively impact TPVR valve sizing and procedural planning.

**PROTOCOL:**

All cardiac CT data were obtained from GrOwnValve preclinical trials with the approval of the legal and ethical committee of the Regional Office for Health and Social Affairs, Berlin (LAGeSo). All animals received humane care in compliance with the guidelines of the European and German Societies of Laboratory Animal Science (FELASA, GV-SOLAS). In this study, the Pre-CT from sheep J was chosen to illustrate the procedures.

## 1. Perform 3D cardiac CT in sheep

### 1.1 Intravenous anesthesia

1.1.1 Tranquilize sheep (3 years, 47 kg, female, *Ovis aries*) with premedication of midazolam (2 mg/mL, 0.4 mg/kg), butorphanol (10 mg/mL, 0.4 mg/kg), and glycopyrronium bromide (200 mcg/mL, 0.011 mg/kg) by intramuscular injection.

1.1.2 Check the physical condition of the sheep when they became docile, 15 min after the injection.

1.1.3 Place an 18 G catheter with injection port aseptically in the cephalic vein with perfusion lines jointed to a T-connector for anesthesia and contrast agent.

1.1.4 Anesthetize the sheep by intravenously injecting propofol (20 mg/mL, 1–2.5 mg/kg) and fentanyl (0.01 mg/kg). Check for symptoms of tranquilization like jaw relaxation, loss of swallowing, and ciliary reflex. Intubate the sheep with a 6.5 mm – 8 mm tracheal tube, and place a gastric tube into the stomach for gastric fluid aspiration followed by intravenous injection

of propofol (20 mg/mL, 1–2.5 mg/kg) and fentanyl (0.01 mg/kg).

1.1.5 Achieve total anesthesia by injecting propofol (10 mg/ml, 2.5–8.0 mg/kg/h) and ketamine (10 mg/mL, 2–5 mg/kg/h) intravenously, in preparation for cardiac CT.

1.2 Cardiac CT

1.2.1 Transfer the sheep from the Research Institutes for Experimental Medicine (FEM) to the CT room of the German Heart Center Berlin (DHZB) after the preparations. Scan all sheep in the prone position after securely fixing them on the CT bed with 3 bandages on the arms, abdomen, and legs.

1.2.2 Perform cardiac CT on a 64-slice dual-source multidetector CT system with ECG-gating using the following parameters. Set the standard acquisition technical parameters as follows: gantry rotation time 0.33 s, 100–320 mAs per rotation, 120 kV tube voltage, matrix 256 with a 16-bit depth, deviation effective x-ray dose 15.5± 11.6 mSv, slice thickness 0.75 mm.

1.2.3 Achieve contrast enhancement by administering 2 –2.5 mL/kg of iodinated contrast agent at the rate of 5 mL/s *via* the T- connector on the arm.

1.2.4 Perform the 4D CT scanning protocol in sequential. Divide the entire cardiac cycle into 11 frames from 0% to 100% with 10% of R-wave to R- wave (RR) interval covering the cardiac cycle. Carry out an end-diastolic phase at approximately 70% of the RR-interval for analysis for the 3D series. Obtain sagittal, coronal, and axial data in each frame of 4D CT, as well as in 70% 3D series.

1.2.5 Use a bolus tracking method for contrast bolus timing in the region of interest on the main pulmonary artery to achieve ideal synchronization. Do not administer beta-blocker in any sheep.

1.2.6 Transfer the sheep back to the FEM and stop the perfusion of propofol, and ketamine after scanning. The sheep regained consciousness 10 – 20 min after the extubation. Anesthesiologists and veterinarians oversaw the entire anesthesia treatment until the sheep were completely awake and able to move freely.

## 2. **Open-source 3D reconstruction software application settings and extension installments**

2.1 Click **Edit** in the top menu to modify the application settings after launching 3D reconstruction software.

2.1.1 Click on **DICOM**, then **Acquisition Geometry Regularization,** and select **Apply Regularization Transform** in the **DICOM Scalar Volume Plugin** section. Select **Volume Sequence** as the preferred multi-volume import format in the **Multi Volume Importer Plugin** section.

2.1.2 Click on **Views**, select **Small Axes.** In the **Orientation marker**, select **Thin Ruler**.

2.1.3 Restart the 3D slicer software to save the application settings.

2.2 Click the **Extension Manager** in the toolbar to open the extensions page.

2.2.1 Find the required extensions and left-click to install them. Use the following extensions in this study: **Sequence Registration, Slicer Elastix, Sandbox, Slice Heart, Slicer IGT, Slicer VMTK, DICOM web Browser, Intensity Segmenter, Markups To Model, Easy Clip, mp Review, Slicer Prostate, and VASSTAUgorithms**.

2.2.2 Restart the 3D slicer software to confirm the installation of the selected extensions.

3. **Load cardiac CT data into 3D slicer from the DICOM files**

3.1 Use one of the two steps described below to load the cardiac CT data into 3D slicer from the DIOCM files (**Figure 1**).

3.2 Import CT data: Add cardiac CT data (the Pre-CT from sheep J was selected to illustrate the procedures) into the application's database by switching to the **DICOM** module and dragging-and-dropping files to the application window.

3.3 Load CT data: Load data objects into the scene by double-clicking on items (In sheep J, the EKG- Ao asc 0.75 126f 3 70% is the 3D sequence at the end-diastolic phase, and Funkion EKG- Ao asc 0.75 126f 3 0- 100% Matrix 256 is the 4D sequence as an 11-frame volume sequence by cardiac cycle).

3.4 Left-click the **Eye** icons in the data tree to show the 3D and 4D sequences from the axial, sagittal, and coronal views in the 2D viewers.

3.5 Left-click the **Slicer layout** icon on the top toolbar and select **Four-Up or Conventional layout**.

3.6 Click on the **Links** icon in the top left corner to link all three viewers, and on the **Eye** icon to display the slices in 3D Viewer.

3.7 Click on the **Save** icon and save all the data loaded into the 3D slicer in a selected destination to build a dataset for the segmentation and volume editing.

4. **Create 4D beating heart volume and beating right heart volume**

4.1 Select **Volume Rendering** in the modules drop-down menu, then select the 4D sequence in the **Volume** drop-down menu.

4.2 Select **CT-Cardiac3** in the Preset drop-down menu to display the 4D heart. Adjust the

cursor below the **Preset** drop-down menu to show the heart only.

4.3 Click on **Sequence Browser** in the modules drop-down menu to select and display the 4D sequence. The beating heart is in the scene. Drag the 4D heart into the 3D scene to observe the heart from various directions.

4.4 Select the **Enable and Display ROI** functions in the **Crop** options below the shift bar to crop the 4D volume of the beating heart in order to better observe the structures of the heart.

4.5 Create the 4D beating heart volume as outlined above. Select **Segment Editor** in the modules drop-down menu, then click the **Scissors** effect with the **Fill Inside** operation to cut one single frame.

4.6 Click on the **Mask Volume** effect and apply it to link the segmentation to the 4D heart as a masked volume. The input volume and output volume in the mask volume effect are the 4D sequences.

4.7 Select the **Scissors** effect with the **Erase inside** operation to remove the bones and other unexpected areas. Select the **Islands** effect with the **Keep Largest Island** operation to remove small areas.

4.8 Choose the **Erase** effect with the **1-3% Sphere Brush** to remove the tissues at the aortic arch with attachments to the main pulmonary artery, as well as the tissue between the ascending aorta and the superior vena cava. After each step, apply the **Mask Volume** effect to mask the 4D volume.

4.9 Repeat steps 4.7 – 4.8 to carry on removing the areas until the right heart model is shown in the 3D scene.

4.10 Click on the **Sequence Browser** and go to the next frame. Use the **Scissors** effect with the **Erase Inside** operation to cut any area in the 3D scene; the right heart model will automatically appear in the contemporary frame. Apply the same method to the rest of the frames until the entire 4D sequence has been segmented.

4.11 Click on the **Sequence Browser** button to display the right heart 4D volume.

NOTE: When removing the left anterior descending coronary artery in some frames as well as the bifurcation of the left coronary artery, it will remove a tiny portion of the right ventricle. Because of this, it is highly recommended to keep a tiny piece of these coronaries to maintain the right ventricular volume in each frame.

## 5. Create straightened models from the 4D sequence

NOTE: It is highly recommended to build each 10% of the cardiac cycle frame in a single 3D slicer

folder, otherwise there will be too many data trees aligned in the DATA module, making it inefficient to create the straightened models. To get the single 3D slicer folder of each 10% frame, it needs to load the 4D sequence several times, choose every frame and save them in a single folder.

5.1 Create right heart segmentations for each frame by selecting the **Segment Editor** module in the toolbar. Add two segmentations for each 10% frame of the 4D sequence, and name them accordingly, e.g., 60% segmentation and Other.

5.2 Select the **Paint** effect tool in the **Segment Editor** module with **Editable Intensity Range** which depends on the CT images to paint the right heart with the sequence superior vena cava, right atrium, right ventricle, and pulmonary artery.

5.3 Click on **Other Segmentation**, use the paint tool to paint other areas to trace the boundaries of the right heart in general.

5.4 Select the **Grow From Seeds** effect, select **Initialize** and **Apply** to apply the effect. Click on the **Show 3D** button in the **Segment Editor** module to display the 3D model of the contemporary frame.

5.5 Repeat steps 4.7 – 4.8 to remove or improve the 3D model according to the CT images in the three directions. Remove the left and right branches of the pulmonary artery at the bifurcation. The right heart 3D model will then show the 3D scene in each frame.

NOTE: It is highly recommended to paint the boundaries of the right heart with a 1% – 2% diameter sphere brush at the attachments between the pulmonary artery and coronary arteries, as well as the pulmonary artery and the superior vena cava.

5.6 Clone the segmentations in the DATA tree as a backup, name the segmentations, for example, 10% Segmentation Original and 10% Segmentation for Straightened Model.

5.7 Add a centerline to the right heart model as described below.

5.7.1 Select **Extract Centerline** in the modules drop-down menu.

5.7.2 Select **Segmentation** in the surface drop-down menu in the Inputs section of the extract centerline module. This creates a segmentation, such as 10% segmentation for straightened model as a segment. Click on **Create New Markups Fiducial** in the endpoints drop-down menu. Click on the **Place a Markup Point** button to add endpoints on the top plane of the SVC and the end plane of the main pulmonary artery.

5.7.3 Select **Create a New Model as a Centerline** model and **Create New Markups Curve** as a centerline curve in the Tree of the Outputs menu. Click on **Apply** to show the centerline right heart model.

5.7.4 Click on the **DATA** module, then right-click on the **Centerline Curve** to edit its properties. Click on the **Eye** icon to display the control points, and in the **Resample** section set the number of resampled points to 40 to lower the computer load.

5.8 Create a straightened model

5.8.1 Select **Curved Planar Reformat** in the modules drop-down menu.

5.8.2 Shift the cursor after **Curve resolution** and **Slice resolution** to 0.8 mm, set the **Slice Size** to 130-140 mm which was according to the range of the right ventricle displayed on the images, and then select **Create a New Volume as Output Straightened Volume**.

5.8.3 Click on **Apply** to obtain the straightened volume.

5.8.4 Select **Volume Rendering** in the module drop-down menu to show the straightened volume. Select the **Straightened Volume** in the volume drop-down menu and click on the **Eye** icon. Select **CT-Cardiac3** as the Preset, move the Shift cursor to show the straightened right heart volume in the 3D scene.

5.8.5 Column the straightened volume in the DATA tree in the name of straightened volume for segmentation, and right-click to segment this straightened volume.

5.8.6 Select the **Threshold** effect in the segment editor module to color the desired straightened right heart and click **Apply** to apply the operation. Select the **Mask Volume** effect to mask the straightened volume by choosing the **Straightened Volume for Segmentation,** volume as **Input Volume and Output Volume** and click **Apply** to apply the operation.

5.8.7 Click **Apply** to apply the same operation as outlined above in steps 4.7- 4.8 to keep the straightened right heart segmentation only. Check the straightened right heart volume and 3D model of the straightened right heart segmentation in the 3D scene.

5.8.8 Click **Apply** to apply the same operation outlined above for other frames to obtain the straightened right heart volume rendering and straightened segmentations and save them in the folder of each frame.

6. **Export the figures and STL files**

6.1 Export the figures of the straightened volume rendering by clicking on the **Capture** and name a scene view effect on the toolbar and saving the scenes in 3D view.

6.2 Export the STL files of the straightened 3D segmentations by clicking on the **Segmentation** module.

7. **Perform five planar measurements**

7.1 Perform a five planar measurement of the perimeter, cross-sectional area, and circumference in the straightened models from the 4D sequence and right ventricular volume measurements in the straightened model as described below.

7.2 Apply the following five planar settings: Plane A: at the main pulmonary artery 2 cm offset from the plane of the sinotubular junction; Plane B: at the sinotubular junction; Plane C: at the sinus; Plane D: at the base of the leaflet; Plane E: at RVOT 1 cm offset from D.

7.3 Add all the above five planes into the straightened models in each frame by holding the Shift key on the keyboard and using the crosshair function in the toolbar to the five planes. Click on the **Create and Place** module in the toolbar to select the **Plane** effect.

7.4 Select the **Line** effect to measure the perimeters, select the **Closed Curve** effect to obtain the circumferences and cross-sectional area. Copy the data to build the dataset.

7.5 Perform right ventricular volume measurements in the straightened model as described below.

7.5.1 Column the straightened segmentation in each frame obtained from the 4D sequence, and label the segmentation according to the matching frame for volume measurement.

7.5.2 Select the **Segment Statistics** module in the module drop-down menu. Select the **X% Segmentation** for volume measurement after **Segmentation and Scalar Volume** in the inputs menu. Select **Create New Table as the Output Table** and then click on **Apply** to apply the operations to get the volume table.

7.5.3 Copy the volume data to create the volume measurement dataset for each frame of the straightened segmentation.

8. **3D multiplanar reconstruction (MPR) measurements and right ventricular volume measurement from the 3D sequence (the best-reconstructed phase at the end of diastole)**

NOTE: In this study, the sheep J Pre-CT was chosen to illustrate the MPR measurement procedures.

8.1 Load the diastolic 3D sequence as illustrated in the following steps. Select the downward arrow next to the crosshair effect, choose **Jump Slices- Offset, Basic+ Intersection, Fine Crosshair, and The Slice Intersections** for crosshair settings.

8.2 Shift + left-click to drag the crosshair to the plane, for instance, the sinus. Press Ctrl+Alt to adjust the crosshair to the desired position in the axial, sagittal, and coronal scenes perfectly in the center of the targeted position.

8.3 Select the **Line** effect to perform the measurements in each plane as illustrated in step 7.4. Copy the data to build the 3D MPR measurement dataset.

8.4 Click on the **Segment Editor** module to create a right ventricular segmentation as outlined above in step 5.8.6.

8.5 Click on the **Segment Statistics** module to perform the right ventricular volume measurement as outlined above in step 7.5.2.

8.6 Copy the volume information to build the diastolic 3D right ventricular volume dataset.

## 9. Calculation for stented heart valve selection

NOTE: In this section, the measurements of the sinotubular junction were used to illustrate the procedure.

9.1 Calculate the mean of the long axial ($d_1$) and short axial perimeters ($d_2$) = ($d_3$), followed by the mean of $d_1$, $d_2$, and $d_3$ to obtain $d_4$, as shown in formulas (1) – (2).

$$\frac{\mathrm{d1} + \mathrm{d2}}{2} = d3 \quad (1)$$

$$\frac{d1 + d2 + d3}{3} = d4 \quad (2)$$

9.2 Divide the calculation of the cross-sectional area ($S_1$) by $\pi$ to obtain $d_5$ followed by the square root of $d_5$ to obtain $d_6$, and then the mean of $d_5$ and $d_6$, as shown in formulas (3) – (5).

$$\frac{S1}{\pi} = d5 \quad (3)$$

$$\sqrt{d5} = d6 \quad (4)$$

$$\frac{d5 + d6}{2} = d7 \quad (5)$$

9.3 Divide the circumference ($C_1$) by $\pi$ to obtain $d_8$, as shown in formula (6).

$$\frac{C1}{\pi} = d8 \quad (6)$$

9.4 Obtain the overall general diameter $d_9$ by calculating the mean of $d_4$, $d_7$, and $d_8$, as shown in formula (7).

$$\frac{d4 + d7 + d8}{3} = d9 \quad (7)$$

9.5 Apply formula (8) to calculate the best choice of valve size (h).

$$100\% - \frac{d8}{3} = h \quad (8)$$

NOTE: The stented heart valve is available in diameters 30 mm, 26 mm, and 23 mm. The valve size (h) shows the match as a percentage for the three diameters, namely an ideal match as 10–20%, big for implantation as 30% and above, and small for implantation below 10%.

10. Import the 3D and 4D data into a versatile statistics software to build the trend diagrams of the measurements in the five planes and export the diagrams in TIFF format. Import all the figures into graphics software for organization.

**REPRESENTATIVE RESULTS:**

In sheep J, the 4D total heart and right heart models were successfully generated from the 4D cardiac CT sequence which showed the deformation throughout the entire cardiac cycle. For better visualization, the whole deformation of the beating heart and right heart is exhibited in every direction in **Figure 3 – Figure 4** and in **Video 1 – Video 2.**

The straightened right heart models were obtained following the mask volume in each 10% of the segmentation to illustrate the deformations of the right heart in a straightened model in sheep J Pre-CT **(Figure 5)**.

Five planes were added in the desired locations to perform the measurements as shown in **Figure 2A**, as well as the MPR measurements in 3D reconstruction software and not the conventional method of cropping the 4D volume in sheep J Pre-CT shown in **Figure 2B**. The changes in cross-sectional area, perimeter, and circumference were obtained in different phases of the cardiac cycle to generate the tendency diagrams as shown in **Figure 6**. Original data from 4D CT measurements and 3D CT measurements are shown in **Supplementary file 1**. In sheep J, 4D CT measurements from the straightened model resulted in the same choice of valve size for TPVR (30 mm) as the MPR measurements from the end-diastolic series, with the advantages of remarkable virtual reality and reliable results. There were significant differences in the measured cross-sectional area (RVOT: 3.42 $cm^2$ in 4D versus 4.28 $cm^2$ in 2D, BPV: 2.96 $cm^2$ in 4D versus 3.92 $cm^2$ in 2D), and circumference (RVOT: 76.1 mm in 4D versus 87.06 mm in 2D, BPV: 67.65 mm in 4D versus 75.73 mm in 2D) in RVOT and the basal plane of the pulmonary valve. The right ventricular ejection fraction of sheep J from the pre-CT was 62.1%.

**FIGURE AND TABLE LEGENDS:**

**Figure 1. User interface in 3- dimensional reconstruction software.** Toolbar, data tree, and other functional menus of the 3- dimensional reconstruction software are shown for operating the program.

**Figure 2. Five planes in the straightened model for measurement and multiplanar reconstruction measurements in the 3-dimensional sequence (end-diastolic phase).** (**A**) Plane a: main pulmonary artery, 20 mm offset from plane b; plane b: sinotubular junction; plane c: sinus of the pulmonary valve; plane d: bottom of pulmonary valve; plane e: in the right ventricular outflow tract, 10 mm offset from plane d. (**B**) MPR measurements in the 3D sequence of the end-diastolic phase at five planes: 10 mm offset from the bottom of the pulmonary valve, bottom of the pulmonary valve, sinus of the pulmonary valve, sinotubular junction, and main

pulmonary artery (20 mm offset from sinotubular junction).

**Figure 3. 4-dimensional heart deformations throughout the cardiac cycle.** Total heart deformations of sheep J pre-computed tomography shows the shape changes from 0% to 100% of the cardiac cycle.

**Figure 4. 4- dimensional right heart deformation throughout the cardiac cycle.** Right heart deformations of sheep J pre- computed tomography shows the shape changes from 0% to 100% of the cardiac cycle.

**Figure 5. Straightened right heart deformation of the sheep J pre- computed tomography throughout the cardiac cycle.** Straightened right heart deformations of sheep J pre- computed tomography shows the shape changes from 0% to 100% of the cardiac cycle.

**Figure 6. Changes in circumference, average diameter, cross-sectional area, and right ventricular volume throughout the cardiac cycle.** (**A**) Changes in circumference during the cardiac cycle at the five planes. (**B**) Changes in average diameter (calculated using formula 1 in step 9.1) during the cardiac cycle at the five planes. (**C**) Changes in the cross-sectional area during the cardiac cycle at the five planes. (**D**) Change in right ventricular volume during the cardiac cycle.

**Video 1. 4- dimensional total heart deformation.** Throughout the cardiac cycle, the 4-dimensional entire heart reconstruction can be visualized in every direction.

**Video 2. 4- dimensional right heart deformation.** The beating heart (superior vena cava, right atrium, right ventricle, and pulmonary artery) can be visualized in every direction throughout the entire cardiac cycle.

**Supplementary file 1.** The table presents the original data from 4D CT measurements and 3D CT measurements generated by following the protocol described including the parameters from the pulmonary artery, right ventricular volume, and the measurements of the aorta from sheep J pre-computed tomography.

**DISCUSSION:**

To date, this is the first study to illustrate a patient-specific measurement of the morphology and dynamic parameters of RVOT-PA with a straightened cardiac model generated from a 4D CT sequence, which can be applied to predict the optimal valve size for TPVR. This methodology was illustrated using sheep J Pre-CT imaging to obtain the dynamic deformations, right ventricular volumes, right ventricular function, and magnitude of RVOT/PA change from the RVOT to the pulmonary trunk in five planes at every 10% reconstruction of the cardiac cycle. Compared with 3D imaging, the straightened models not only predicted the same valve size as the MPR measurements from the end-diastolic 3D images but also allowed for a more intuitive model to extract the desired information about the right heart. According to the findings of a previous study[13], the proposed method allows for a better understanding of *in vivo* loading conditions in patients with dysfunctional RVOT and/or pulmonary valve disease, as well as the development

of new TPVR devices that are morphologically adapted to the different RVOT anatomies of patients requiring TPVR and may exhibit improved mechanical performance in the long run. However, the current methodology of quantitative measurement for a pre-interventional evaluation of TPVR is based on MPR measurements in the 3D sequence, which could result in unexpected errors during evaluations based on the anatomical curve of the RVOT and PA. Furthermore, detailed information can be lost in the 3D models generated from the 4D sequence in terms of the heart's overall movement[14].

In this study, a 4D beating heart model was created to observe and visualize the heart's total deformation throughout the cardiac cycle by using a mask for the 4D volume of the segmentation in 3D reconstruction software and not the conventional method of cropping the 4D volume in sheep J. This method can provide an accurate and efficient way of building a 4D model as a 3D reconstruction from a 3D sequence to visualize the heart and select the valve size. Furthermore, the same method was used to reconstruct the right heart model as a dynamic model from the segmentations in each 10% of the cardiac cycle segmented using the **Grow From Seeds** effect in 3D reconstruction software. The 4D right heart model can visualize the entire anatomical morphology throughout the RR interval, based on which cardiologists can develop a patient-specific strategy for TPVR. In addition, the 3D straightened right heart models obtained from the 4D sequence in each 10% of the cardiac cycle can furnish a precise, morphological, and functional quantification of the right heart, especially in the five planes applied for the stented heart valve selection. Prior to creating the straightened models, a manual and exact 3D segmentation of the right heart from each 10% cardiac cycle is required. When doing right heart segmentations, after the volume from one frame has been masked, the 3D segmentation in the current frame will emerge automatically by using the **Scissor** function for the undesirable structures. In order to retain the whole volume of RVOT, a tiny piece of the left coronary artery must be kept in the segmentations. To create a straightened model, it is pivotal to add a centerline into the original right heart model to ensure the quality of the straightened model and decrease the computational load. The straightened right heart model accurately reflected all the correlations of the cardiac anatomy, including perimeters, circumferences, and cross-sectional areas, allowing a subsequent extraction of morphological information and direct measurements in a holistic fashion. In this study, the measurements from the 4D straightened model resulted in the same choice of valve size (30 mm in diameter) as the 3D measurements in MPR, but with the advantages of remarkable virtual reality and reliable results in sheep J. It also enables the collection of data on right ventricular volumes during the whole cardiac cycle, which can be then applied to calculate the right ventricular ejection fraction.

Previous clinical studies have shown significant differences in the measured cross-sectional areas of RVOT-PA between static and dynamic section planes secondary to large 3D displacements and rotations[15]. In sheep J Pre-CT, the significant differences in measured cross-sectional areas and circumferences in the RVOT plane and basal plane of the pulmonary valve were also observed in the RVOT: 3.42 $cm^2$ in 4D versus 4.28 $cm^2$ in 3D, BPV: 2.96 $cm^2$ in 4D versus 3.92 $cm^2$ in 3D, and RVOT circumferences: 76.1 mm in 4D versus 87.06 mm in 3D, BPV: 67.65 mm in 4D versus 75.73 mm in 3D. To obtain data for the measurements, the five dynamic planes were applied instead of fixed planes; here, the sinotubular plane and the basal plane of the pulmonary valve

were chosen as the lines of reference. These five planes included all the space that can be utilized to deploy the stented heart valve. The RVOT plane exhibited the largest deformation throughout the cardiac cycle in the five planes, highlighting the need for a versatile TPVR device that enables adaptability to various anatomies and retains the designed geometry of the stented heart valve for long-term durability without fracture and migration. The nitinol stent with shape memory is a promising candidate for mounting a tri-leaflet valve for future TPVR. For the clinical application, especially for the patients who have had transannular patch repair or TPVR, it would need more efforts to reconstruct the anatomy as there are artifacts from the adhesion between the pericardium and myocardium, stent, and the deformed anatomy. It needs higher resolution CT data, well-developed reconstruction software, and abundant experience of CT analysis to translate this method for clinical use. But this method can be used for large animal trials as well as for the peri-operative evaluation for patients with Tetralogy of Fallot, isolated pulmonic stenosis who haven't had any open-heart surgeries or interventional therapies.

The described method for the 4D straightened model can enable accurate and visual identification and calculation of all segments of the heart from the RVOT to PA, which can help not only cardiologists to obtain a precise pre-interventional evaluation, but also cardiac engineers to innovate novel TPVR devices for future applications.

The main limitation of the methodology for the 4D straightened model measurement in this study is that the data were obtained from only one sheep pre-CT without a large sample population. Additionally, post-implantation CT imaging was not performed to follow up on the valve size and structural changes in the right heart. Lastly, for the patients who have had transannular patch repair or TPVR, it is more difficult to reconstruct the anatomy as there are artifacts from the adhesion between the pericardium and myocardium, stent, and the deformed anatomy.

Conclusion

In contrast with 3D CT, the straightened 4D reconstruction model not only enabled an accurate prediction of valve size selection for TPVR, but also provided ideal virtual reality in sheep J, and therefore will be a promising method for TPVR and the innovation of TPVR devices.

**ACKNOWLEDGMENTS:**

Xiaolin Sun and Yimeng Hao contributed equally to this manuscript and share first authorship. Heartfelt appreciation is extended to all who contributed to this work, both past and present members. This work was supported by grants from the German Federal Ministry for Economic Affairs and Energy, EXIST – Transfer of Research (03EFIBE103). Xiaolin Sun and Yimeng Hao are supported by the China Scholarship Council (Xiaolin Sun- CSC: 201908080063, Yimeng Hao-CSC: 202008450028).

**DISCLOSURES:**

The authors declare no conflict of interests.

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Figure 1. 3D Slicer User Interface

Click here to access/download;Figure;Figure 1. 3D Slicer User Interface.tif

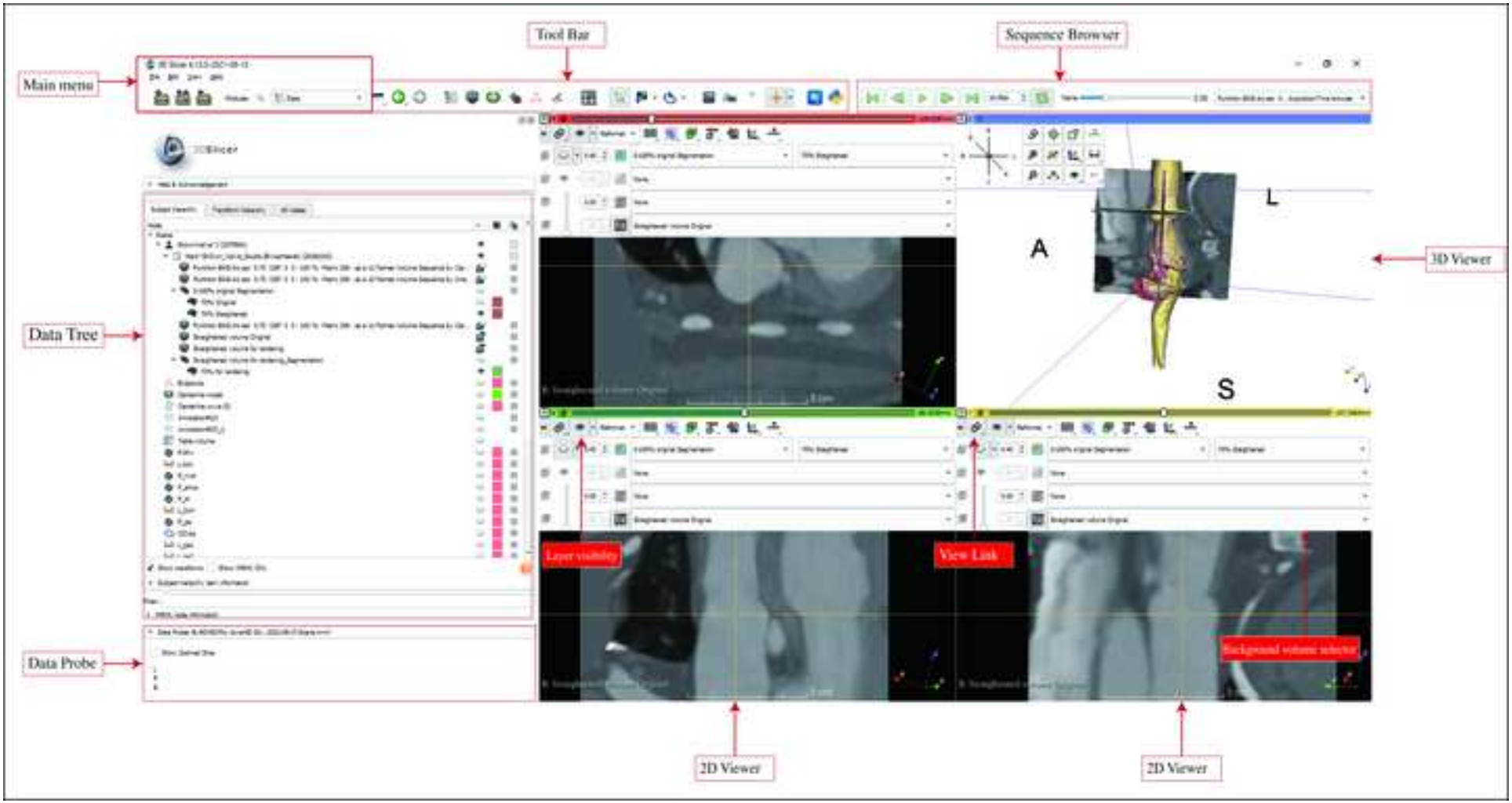


Figure 2. Planes in straightened model and MPR measurement

Click here to access/download;Figure;Figure 2. Planes in straightened model and MPR measurement.tif

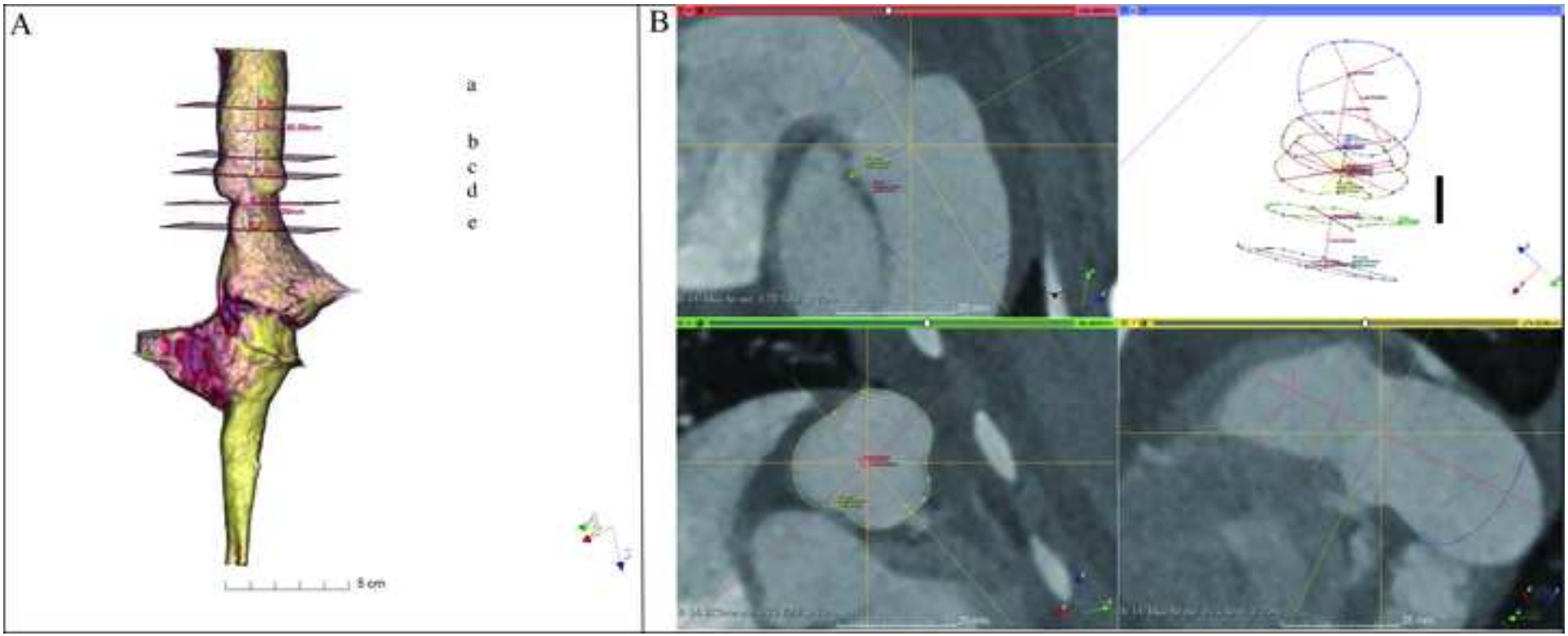


Figure 3. 4D heart deformations of the sheep J Pre-CT throughout the cardiac cycle

Click here to access/download;Figure;Figure 3. 4D heart deformations.tif

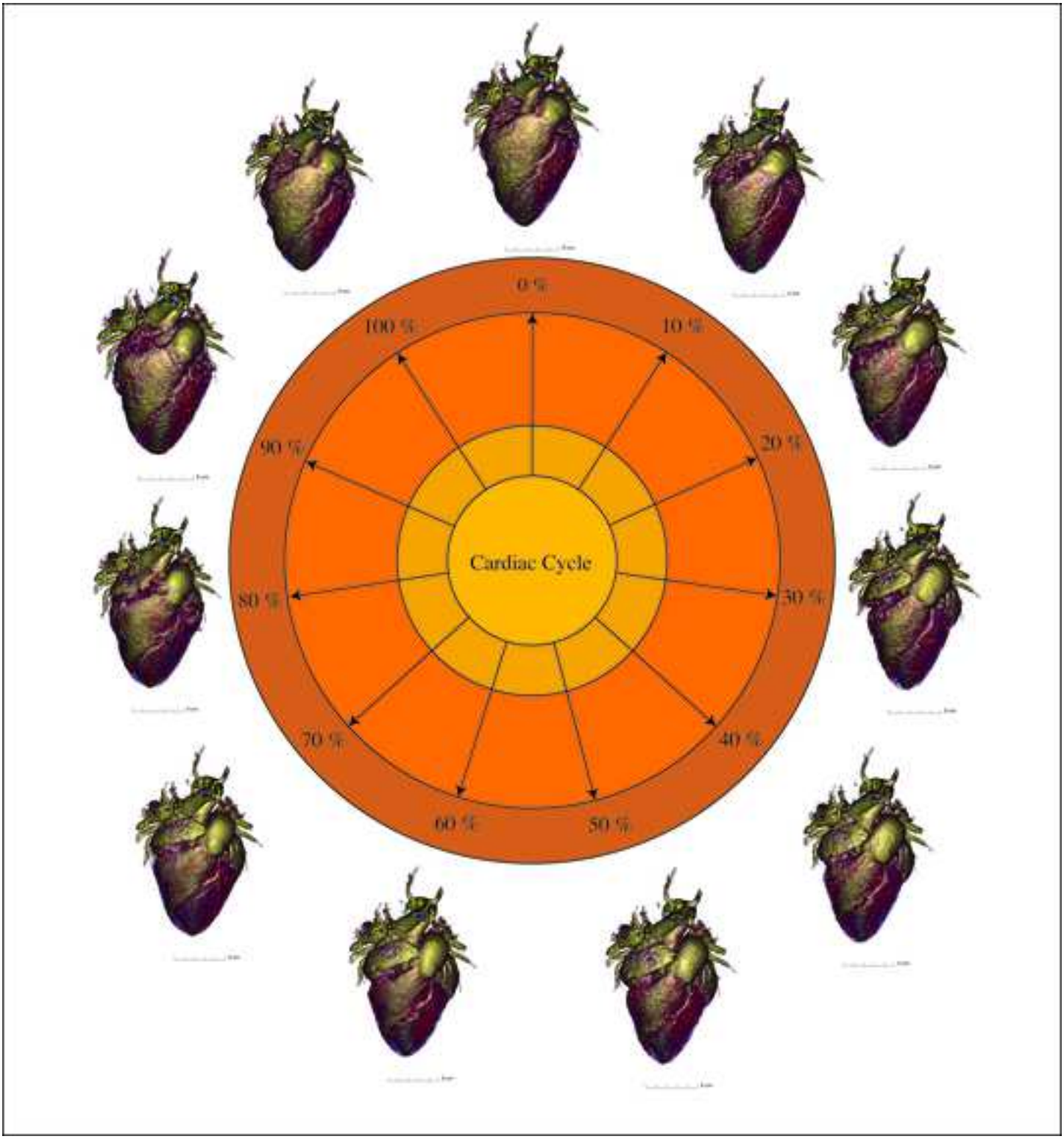


Figure 4. 4D right heart deformation of the sheep J Pre-CT throughout the cardiac cycle

Click here to access/download;Figure;Figure 4. 4D right heart deformation.tif

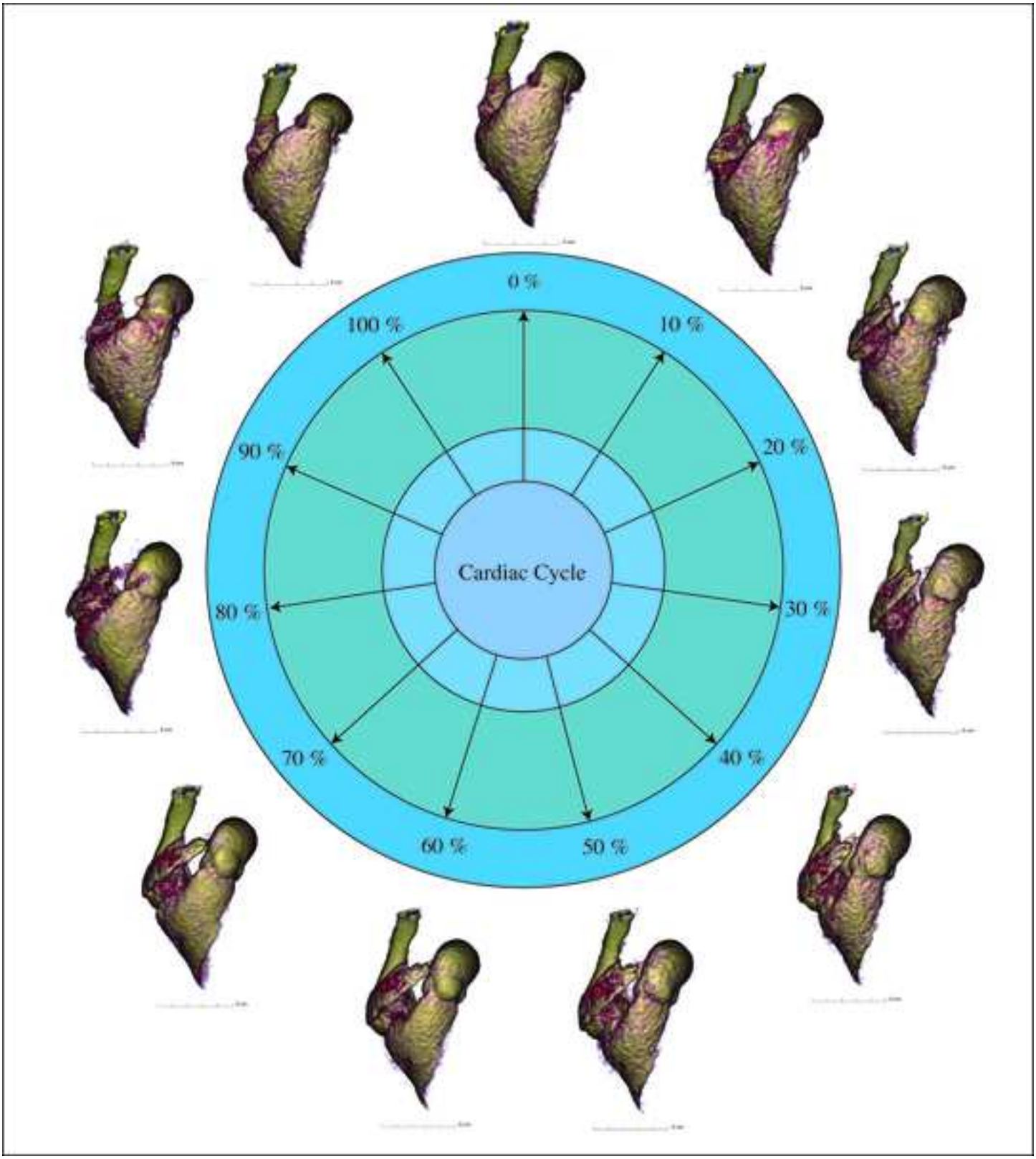


Figure 5. Straightened right heart deformation of the sheep J Pre-CT throughout the cardiac cycle

Click here to access/download;Figure;Figure 5. Straightened right heart deformation.tif

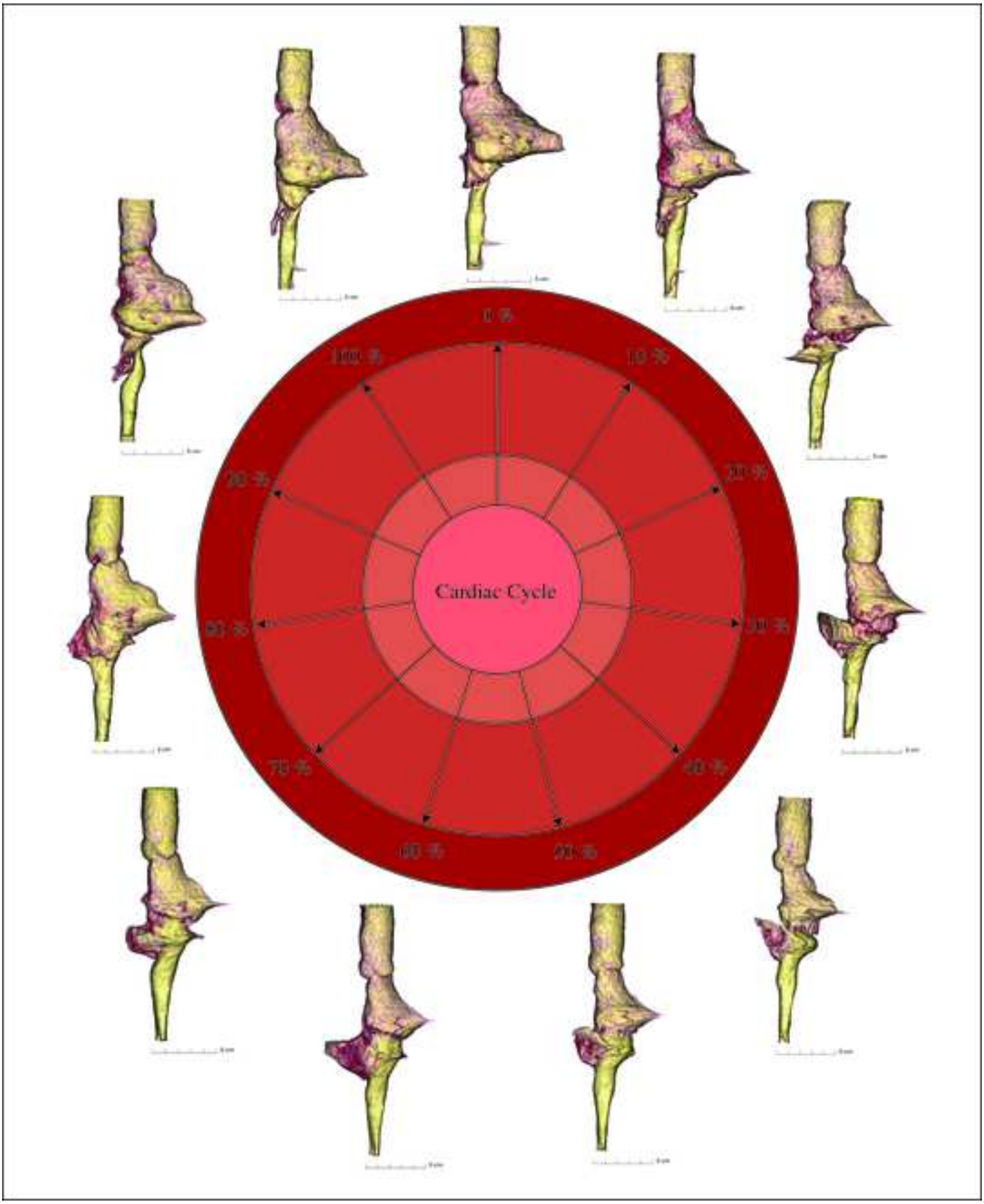
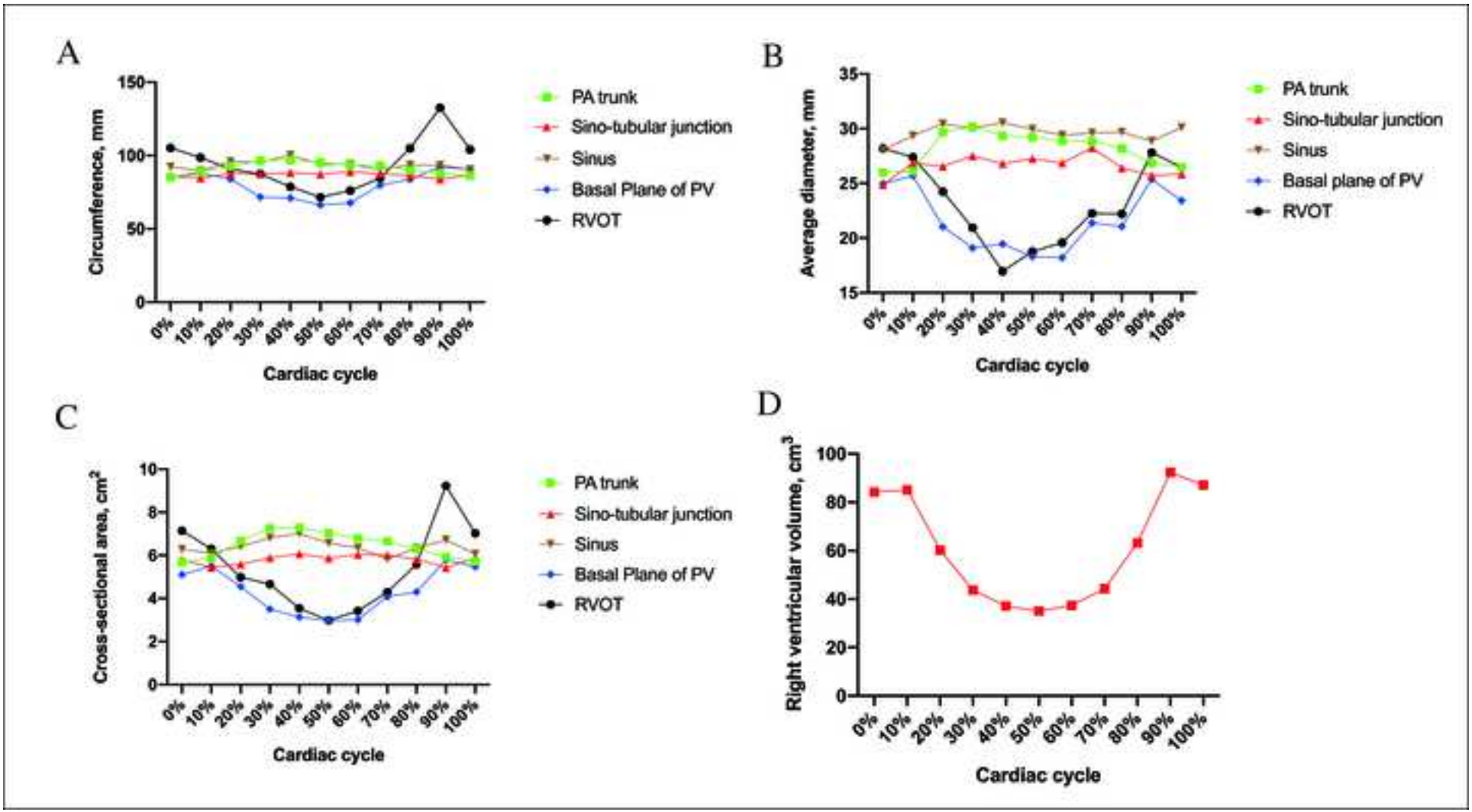


Figure 6. Changes of Cir- Dia-Area-RHV





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**Video or Animated Figure**

Video 1. 4D Total Heart Deformation- JoVE.mp4

Click here to access/download

**Video or Animated Figure**

Video 2. 4D-Right Heart Deformation-JoVE.mp4

Click here to access/download

**Table of Materials**

Xiaolin Sun- JoVE- Table of Materials.xlsx

To the Editor,

Dear editor,

Many thanks for your review and comments for my manuscript.

Regarding the " Editorial comments":

1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues.

-- Spelling and grammar have been check. All modifications and improvements made in response to editor and reviewers' comments are highlighted in yellow throughout the text.

2. Please provide an abstract between 150 -300 words. The current abstract is 348 words.

--The abstract has been shortened to 300 words.

3. Please revise the text to avoid the use of any personal pronouns (e.g., "we", "you", "our" etc.).

--The words "we, you, and our" have been removed from the manuscript.

4. JoVE cannot publish manuscripts containing commercial language. This includes trademark symbols (™), registered symbols (®), and company names before an instrument or reagent. Please remove all commercial language from your manuscript and use generic terms instead. All commercial products should be sufficiently referenced in the Table of Materials.
For example: Imeron 400 MCT, Excel, 3D Slicer, etc.

--All commercial language has been removed from the manuscript and put in the table of materials.

5. Please ensure that all text in the protocol section is written in the imperative tense as if telling someone how to do the technique (e.g., "Do this," "Ensure that," etc.). The actions should be described in the imperative tense in complete sentences wherever possible. Avoid usage of phrases such as "could be," "should be," and "would be" throughout the Protocol. Any text that cannot be written in the imperative tense may be added as a "Note." However, notes should be concise and used sparingly.

-- All text in the protocol section has been checked in the imperative tense followed by this instruction.

6. Please add more details to your protocol steps. Please ensure you answer the "how" question, i.e., how is the step performed? Alternatively, add references to published material specifying how to perform the protocol action. Step 1.1.2, 1.1.3: How was proper tranquilization and anesthetization confirmed?
Step 1.2.1: How was the sheep secured in the prone position? How was scanning and contrast infusion done? Please provide all associated steps.
Step 3: How was the cardiac CT data acquired? Please provide in brief.
Step 3.2: Is Funkion a company name? if yes, please remove it from the text.

--All steps have been revised with comprehensive information in the protocol. "Funkion EKG-Ao asc 0.75 126f 3 0- 100 % Matrix 256" is the name of 4D CT sequence, not a company name.

7. Please note that your protocol will be used to generate the script for the video and must contain everything that you would like shown in the video. Please add more specific details (e.g. button clicks for software actions, numerical values for settings, etc) to your protocol steps. There should be enough detail in each step to supplement the actions seen in the video so that viewers can easily replicate the protocol.

--Figure 1 has been added to show the user interface of the software, as well as comprehensive information in each step.

8. Please include a one-line space between each protocol step and then highlight up to 3 pages of the Protocol (including headings and spacing) that identifies the essential steps of the protocol for the video, i.e., the steps that should be visualized to tell the most cohesive story of the Protocol. Remember that non-highlighted Protocol steps will remain in the manuscript, and therefore will still be available to the reader.

-- A one-line gap has been added between each protocol step, and highlighted words have been altered to a more generic style in the document.

9. Please revise the Representative results to a paragraph instead of points. Ensure that the text explains the Representative Results in the context of the technique you have described, e.g., how do these results show the technique, suggestions about how to analyze the outcome, etc.

-- The representative results were converted to paragraph format instead of points, and adheree to the technique described in the protocol.

10. As we are a methods journal, please ensure that the Discussion explicitly covers the following in detail in 3-6 paragraphs with citations:

a) Critical steps within the protocol

b) Any modifications and troubleshooting of the technique

c) The significance with respect to existing methods

--Discussion has been revised followed by instructions a, b, and c.

11. Please do not use the &-sign or the word “and” when listing authors in the references. Authors should be listed as last name author 1, initials author 1, last name author 2, initials author 2, etc. Title case and italicize journal titles and book titles. Do not use any abbreviations. Article titles should start with a capital letter and end with a period and should appear exactly as they were published in the original work, without any abbreviations or truncations.

-- All references have been changed into JoVE format according to the “Instructions for Authors”.

12. Please remove the titles and Figure Legends from the uploaded figures. The information provided in the Figure Legends after the Representative Results is sufficient.

-- Titles and figure legends have been removed from the uploaded figures and all figures have been reorganized.

13. Please consider including screenshots of the graphical user interface/software as supplemental figures to help readers understand and follow the important steps of the protocol.

-- Figure 1 has been added to show the user interface of the software, as well as comprehensive information in each step.

14. Figure 1: Please include a scale bar in all the images of panel B to make it more informative.

-- A scale bar has been added into the newly organized figure.

15. Do the animated figures ”4D-right heart deformation and 4D Total heart deformation” represent Figure 2, if so, please include a statement regarding the animated figures in the Figure 2 legend? Else, please include a separate title and description for them in the Figure Legends. The scale bars in the figures are not clearly visible.

-- All figures have been reorganized followed by this instruction.

16. Each Figure Legend should include a title and a short description of the data presented in the Figure and relevant symbols. Please describe all abbreviations used in the figure in the figure legends.

-- All figures have been reorganized followed by this instruction.

17. Please ensure that the Table of Materials includes all the supplies (reagents, chemicals, instruments, equipment, software, etc.) used in the study. Please sort the table in alphabetical order.

-- The structure of Table of materials has been revised followed by this instruction.

Thanks for your comments and all the best.

Xiaolin Sun, on behalf of all authors in this manuscript.

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To reviewer 1:

Dear reviewer,

Many thanks for your review and comments for my manuscript.

Regarding the "Major concern":

The study only documents a single CTA in a sheep model with a normal pulmonary valve anatomy and although this is mentioned briefly in weaknesses, it needs to be stressed more in the introduction, discussion, and mentioned in the abstract. It is hard to translate this to an adult human patient with native outflow tract after transannular patch repair.

1. Due to the method was only illustrated using sheep J Pre-CT, this situation has been enhanced in the abstract, introduction, and discussion as suggested by viewer 1.

2. For the patients who have had transannular patch repair or TPVR, it is more difficult to reconstruct the anatomy as there are artefacts from the adhesion between the pericardium and myocardium, stent, and the deformed anatomy. It needs higher resolution CT data, well developed reconstruction software which should be certified by FDA, and abundant experience of CT analysis to translate this method for clinical use. But this method can be used for large animal trial as well as for the peri-operative evaluation for patients with Tetralogy of Fallot, isolated pulmonic stenosis who haven't had any open-heart surgeries or interventional therapies.

Regarding the "Minor concern":

1. The introduction needs to clarify the difference between patients requiring TPVR who have an RV-PA conduit versus patients with what we call the "native" pulmonary outflow which typically represents patients with trans annular patch repair of ToF or repair of valvar PS - this represents the largest population of patients needing TPVR and represents a very different anatomy than a surgically placed "RV-PA conduit".

-- The difference between RV-PA conduit and "native" RVOT with transannular patch repair has been clarified in the 1st paragraph of introduction. Surgical replacement of RVOT with xenograft or homograft is totally different from transannular patch repair with pericardium (autologous, bovine, or porcine).

2. Page 4 line 80 - The study referenced (reference number 7) was for TAVR and not TPVR - needs to be clarified.

-- The aim of citing Reference 7 is to expound the importance of CT measurements for valve sizing in transcatheter heart valve replacement in general and introduce the following text about CT for TPVR. Compared to TAVI, there is no big data of CT for TPVR valve sizing in multicenter clinical trial worldwide.

3. The sheep were under general anesthesia with PPV - would awake spontaneously breathing patients alter the anatomy?

-- The anesthesia was maintained with continuous infusion of propofol and ketamine, spared propofol was used in case that some sheep awaked during the CT scanning. We have performed plenty of CTs in sheep with large-scale heart rate from 70 to 140, the anatomical information from CT had little impact due to the ECG-gated protocol.

4. Please provide more info on how the CTA was performed, assuming this was gated - was it through the entire cycle - how much radiation dose will this be in humans compared to the typical gated studies currently performed for TPVR assessment.

--Detailed information of CT has been added into the protocol- from step 1.2.1 to step 1.2.4.

5. The evaluation for the Harmony valve utilizes superimposed valve structures within the model from the CTA to show what a "virtual" implant would look like - did the authors consider trying to do that with some of the valves that are currently available.

--Yes. We assume that we can use the Pre-CT + post-CT + self-designed stent CAD file + 3D heart valve CAD file to perform the structural analysis of the deployment of stent and 4D flow simulation of the stented heart valve implantation in pulmonary valve position. From the simulation, "virtual patients" would be good to evaluate the performance of autologous stented heart valve and could be parts of evidence to achieve clinical trial even the global medical market in the future.

Thanks for your comments and all the best.

Xiaolin Sun, on behalf of all authors in this manuscript.

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www.kidcathlab.com
www.grownvalve.de

To reviewer 2:

Dear reviewer,

Many thanks for your review and comments for my manuscript.

Regarding the "Major concern":

The study has been conducted on a single ovine model. Drawing conclusions applicable to human patients is, therefore, a big leap.

-- We have applied the method in this article for many CTs measurements from our previous animal trial, not only pulmonary artery but also aorta. We use this data for the iterations of our medical devices. 4D measurement data of pulmonary artery and aorta is available in the supplementary table.

For the clinical application, especially for the patients who have had transannular patch repair or TPVR, it is more difficult to reconstruct the anatomy as there are artefacts from the adhesion between the pericardium and myocardium, stent, and the deformed anatomy. It needs higher resolution CT data, well developed reconstruction software which should be certified by FDA, and abundant experience of CT analysis to translate this method for clinical use. But this method can be used for large animal trial as well as for the peri-operative evaluation for patients with Tetralogy of Fallot, isolated pulmonic stenosis who haven't had any open-heart surgeries or interventional therapies. We are full of confidence to achieve this with the revolutions of AI in medicine and medical devices.

Regarding the "Minor concern":

It would be appropriate to explain the choice of valve size if between two different sizes and how this novel method is superior to the normal one is this case.

-- The data from the 5 planes in the 4D sequence and the 70 % cardiac cycle sequence were used for valve selection via step 9, where the diameter in the Sino-tubular junction plane is highly significant for valve sizing. To achieve excellent anchoring at the proper spot, the new stented heart valve should be 10% to 20% bigger than the parameters in the Sino-tubular junction plane for optimal valve size. In this study, the calculations from the 4D sequence and 70 % sequence predicted the same valve selection. The described method for the 4D straightened model can not only enable accurate and visual identification and calculation of all segments of the heart from the RVOT to PA as the MPR measurements from the end-diastolic sequence, but also provided ideal virtual reality which helped not only cardiologists to obtain a precise pre-interventional evaluation, but also cardiac engineers to innovate novel TPVR devices for future applications.

It would be useful to explain more in detail the CT acquisition details and better define the terms '3D CT' and '4D CT'.

-- Detailed information of CT has been added into the protocol- from step 1.2.1 to step 1.2.4, as well as the definitions of "3D CT" and "4D CT".

--"carried out" has been eliminated in Line 56.

-- Lines 83-86 has been rephrased as "Quantitative analysis has enormous potential to enable objective and correct interpretation of clinical imaging and to verify that patients are free of stent fracture and paravalvular leak, which can enhance patient-specific therapy and treatment response evaluation".

-- "succus gastricus evacuation" has been substituted with "gastric fluid aspiration" in Line 119 as the reviewer's suggestion.

-- "...a layer thickness " has been substituted with " slice thickness " in Line 126 as the reviewer's suggestion.

--Due to the instructions for authors, JoVE cannot publish manuscripts containing commercial language. All "3D Slicer" s in the manuscript have been substituted with "3D reconstruction software", furthermore the 3D Slicer information was put in the "Table of materials".

-- "these tiny coronaries " has been substituted with " tiny piece of these coronaries" in Line 192 as the reviewer's suggestion.

-- The GraphPad Prism manufacturer has been added in the "Table of materials".

-- "intuitionistic" has been substituted with "intuitive" in Line 370 as the reviewer's suggestion.

-- "methods" has been substituted with "method" in Line 372 as the reviewer's suggestion.

-- The sentence between Line 372- 376 has been rephrased as the reviewer's suggestion.

-- Because the 4D model is equally accurate and efficient as the 3D model from the results, the sentence has been rewritten to correct the erroneous term.

-- Figures have been reorganized and detailed information of Figure 2B (previous Figure 1B) has been added in the “Figure and Table Legends” in the manuscript. Xiaolin Sun, on behalf of all authors in this manuscript.

Thanks for your comments and all the best.

Xiaolin Sun, on behalf of all authors in this manuscript.

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W: www.dhzb.de
www.kidcathlab.com

www.grownvalve.de

To Reviewer 3:

Dear reviewer,

Many thanks for your review and comments for my manuscript.

Regarding the "Major concern":

1. It is not clear that measurements from a unfolded heart are more appropriate than measurements from a heart in its native state - one would assume that measurements should be made in as native a state as possible. Impact of this method is unclear since valve sizes estimated from these measurements are same as valve sizes estimated from the traditional measurement.

--This is the first study to illustrate a "patient-specific" measurement of the morphology and dynamic parameters of RVOT-PA with a straightened cardiac model generated from a 4D CT sequence, which can be applied to predict the optimal valve size for TPVR. This study provided a new methodology with a straightened model generated from the 4D cardiac CT sequence to obtain the desired measurements with ideal virtual reality for valve sizing in the application of TPVR in a sheep model. It will take a lot of effort and expertise to show that it is feasible for animal experiments. With developments in 3D reconstruction software, CT resolution, and CT segmentation experience, we are focusing on this issue and attempting to optimize measurements.

2. There is not enough information given on the CT protocol from the image acquisition perspective (and perhaps too much from the sheep perspective) -- in Step 1, info should be given re: ECG gating, coronal, sagittal, axial sequences needed, arterial-venous phase(s) needed, cine protocol needed, etc.

-- Detailed information of CT has been added into the protocol- from step 1.2.1 to step 1.2.4, as well as the definitions of "3D CT" and "4D CT".

3. It was extremely difficult to follow the steps like 'click on eyeball icon' since there are several eyeball icons in the GUI. A simple screen-capture video of mouse movements (even just for review phase while awaiting a production video) would have been extremely helpful.

-- User interface has been added in Figure 1. With Figure 1, it might be better to get practiced operation on 3D Slicer. The authors in this paper spent weeks to get familiar and skillful with the software and consulted many issues on the 3D Slicer forum.

4. It is not clear what the '11-image 4D sequence' is -- is one sagittal, one axial, and one coronal series for each of 11 timepoints in the ecg-gating? If so, please clarify.

-- Detailed information of 4D CT has been added into the protocol as a definition- from step 1.2.1 to step 1.2.4.

5. CTs can be manipulated in multi-planar reformats, so that one can make a measurement on the appropriate plane even if it is oblique to axial, coronal etc. Why isn't this enough?

--Imaging technique is improving quickly. Current methods of CT measurements for clinical use are accurate and efficient, but not flawless, especially for the patients with severe RVOT dysfunction. Compared with 3D imaging, the straightened 4D models not only predicted the accurate valve size as the MPR measurements from the end-diastolic 3D images, but also allowed for a more intuitive model to extract the desired information about the right heart. It would be promising for the doctors to get full information from the CT to make a patient-specific strategy.

Regarding the "Minor concern":

Detailed names of CT sequences pertinent to the example CT (ie "EKG- Ao asc 0.75 126f 3 70 %: The 3D end-diastolic phase, and Funkion EKG- Ao asc 0.75 126f 3 0- 100 % Matrix 256") will be completely different series names for a different CT or different user, in the instructions these should be generalized.

--It has been clarified the names of the 3D sequence and 4D sequence in Protocol step 3.2 as the reviewer's suggestion.

Thanks for your comments and all the best.

Xiaolin Sun, on behalf of all authors in this manuscript.

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Supplemental File:4D and 3D MPR data- PA+Aorta-Sheep J-Pre-CT

Click here to access/download;Supplemental File (Figures, Permissions, etc.);4D and 3D MPR data- PA+Aorta-Sheep J-

| Sheep J Pulmonary artery 4D + 3D MPR | | 0% |
|---|---|---|
| PA trunk | Length | 85.8 |
| | Area | 5.688 |
| | Perimeter 1 | 24.96 |
| | Perimeter 2 | 27.02 |
| | Perimeter (Average) | 25.99 |
| Sub-tubular junction | Length | 85.83 |
| | Area | 5.784 |
| | Perimeter 1 | 27.03 |
| | Perimeter 2 | 22.71 |
| | Perimeter (Average) | 24.87 |
| Sinus | Length | 92.34 |
| | Area | 6.285 |
| | Perimeter 1 | 30.57 |
| | Perimeter 2 | 25.53 |
| | Perimeter (Average) | 28.05 |
| Basal plane of PV | Length | 85.28 |
| | Area | 5.102 |
| | Perimeter 1 | 21.81 |
| | Perimeter 2 | 28.13 |
| | Perimeter (Average) | 24.97 |
| RVOT | Length | 105.2 |
| | Area | 7,149 |
| | Perimeter 1 | 22.53 |
| | Perimeter 2 | 33.89 |
| | Perimeter (Average) | 28.21 |
| Total volume | | 115.686 |
| | | 139.707 |
| | | 84.2101 |

| 10% | 20% | 30% | 40% | 50% | 60% | 70% |
|---|---|---|---|---|---|---|
| 89.12 | 92.63 | 96.6 | 96.92 | 95.36 | 93.3 | 93.13 |
| 5.89 | 6.673 | 7.268 | 7.29 | 7.028 | 6.797 | 6.654 |
| 28.05 | 27.11 | 32.04 | 26.81 | 31.58 | 29.66 | 26.19 |
| 24.14 | 32.23 | 28.3 | 31.92 | 26.86 | 28.09 | 31.5 |
| 26.095 | 29.67 | 30.17 | 29.365 | 29.22 | 28.875 | 28.845 |
| 84.68 | 87.72 | 87.48 | 88.37 | 87.36 | 88.96 | 87.55 |
| 5.439 | 5.591 | 5.888 | 6.067 | 5.871 | 6.035 | 6.011 |
| 27.13 | 27.53 | 27.6 | 26.54 | 28.45 | 27.04 | 28.14 |
| 26.59 | 25.6 | 27.41 | 27.08 | 26.07 | 26.68 | 28.38 |
| 26.86 | 26.565 | 27.505 | 26.81 | 27.26 | 26.86 | 28.26 |
| 89.66 | 95.82 | 95.41 | 100.3 | 93.95 | 94.06 | 90.35 |
| 6.108 | 6.416 | 6.814 | 7.012 | 6.57 | 6.349 | 5.837 |
| 29.74 | 28.24 | 31.54 | 28.85 | 29.02 | 27.92 | 32.73 |
| 28.96 | 32.69 | 28.55 | 32.23 | 30.9 | 30.89 | 26.47 |
| 29.35 | 30.465 | 30.045 | 30.54 | 29.96 | 29.405 | 29.6 |
| 87.89 | 83.9 | 71.73 | 71.04 | 66.29 | 67.65 | 79.85 |
| 5.507 | 4.558 | 3.502 | 3.135 | 2.965 | 3.015 | 4.078 |
| 22.86 | 20.75 | 19.03 | 20.77 | 16.14 | 15.75 | 23.15 |
| 28.51 | 21.32 | 19.16 | 18.14 | 20.49 | 20.66 | 19.59 |
| 25.685 | 21.035 | 19.095 | 19.455 | 18.315 | 18.205 | 21.37 |
| 98.62 | 90.8 | 87.31 | 78.66 | 71.55 | 76.1 | 84.57 |
| 6.304 | 4.99 | 4.66 | 3.542 | 2.979 | 3.42 | 4.294 |
| 25.3 | 27.73 | 19.67 | 18.46 | 20.2 | 19.78 | 23.76 |
| 29.5 | 20.74 | 22.22 | 15.45 | 17.32 | 19.37 | 20.77 |
| 27.4 | 24.235 | 20.945 | 16.955 | 18.76 | 19.575 | 22.265 |
| 115.874 | 101.33 | 127.761 | 98.6383 | 106.153 | 135.628 | 140.581 |
| 142.64 | 137.965 | 127.761 | 127.252 | 131.663 | 136.198 | 141.046 |
| 85.0958 | 60.1682 | 43.7034 | 37.1384 | 35.0442 | 37.4133 | 44.3288 |

| 80% | 90% | 100% | |
|---|---|---|---|
| 89.95 | 87.85 | 86.27 | |
| 6.301 | 5.931 | 5.716 | PA trunk |
| 30.46 | 28.46 | 28.34 | |
| 25.94 | 25.21 | 24.6 | |
| 28.2 | 26.835 | 26.47 | |
| 86.26 | 83.75 | 86.83 | |
| 5.818 | 5.433 | 5.873 | Sub-tubular junction |
| 27.86 | 26.56 | 26.3 | |
| 24.95 | 24.9 | 25.38 | |
| 26.405 | 25.73 | 25.84 | |
| 93.51 | 93.49 | 90.42 | |
| 6.34 | 6.723 | 6.06 | Sinus |
| 29.5 | 26.56 | 31.89 | |
| 29.88 | 31.16 | 28.34 | |
| 29.69 | 28.86 | 30.115 | |
| 83.66 | 92.14 | 90.58 | |
| 4.306 | 5.787 | 5.468 | |
| 22.94 | 25.84 | 23.96 | |
| 19.17 | 24.9 | 22.89 | |
| 21.055 | 25.37 | 23.425 | Basal plane of PV |
| 104.9 | 132.5 | 104.1 | |
| 5.59 | 9.226 | 7.023 | |
| 21.85 | 24.9 | 24.55 | |
| 22.56 | 30.71 | 28.41 | |
| 22.205 | 27.805 | 26.48 | RVOT |
| 140.756 | 113.609 | 137.369 | |
| 143.148 | 161.057 | 143.378 | |
| 63.2092 | 92.3633 | 87.1203 | |
| | | | volume |

3D MPR

| | |
|---|---|
| Length | 93.47 |
| Area | 6.806 |
| Perimeter 1 | 27.2 |
| Perimeter 2 | 30.35 |
| Perimeter (Average) | 28.775 |
| Length | 86.89 |
| Area | 5.916 |
| Perimeter 1 | 25.8 |
| Perimeter 2 | 26.48 |
| Perimeter (Average) | 26.14 |
| Length | 93.87 |
| Area | 6.469 |
| Perimeter 1 | 29.65 |
| Perimeter 2 | 27.56 |
| Perimeter 3 | 27.25 |
| Perimeter 4 | 28.17 |
| Perimeter 5 | 26.52 |
| Perimeter (Average) | 27.83 |
| Length | 75.73 |
| Area | 3.924 |
| Perimeter 1 | 23.11 |
| Perimeter 2 | 18.38 |
| Perimeter (Average) | 20.745 |
| Length | 87.06 |
| Area | 4.281 |
| Perimeter 1 | 15.66 |
| Perimeter 2 | 27.87 |
| Perimeter (Average) | 21.765 |

41.8704

| Sheep J Aorta 4D+ 3D MPR | | 0% |
|---|---|---|
| Plane 1: LVOT (0,5 cm off-set from plane 2) | Cross-sectional Area ($cm^2$) | 5.75 |
| | Circumference (cm) | 87.39 |
| | Length 1 (cm) | 30.45 |
| | Length 2 (cm) | 23.92 |
| Plane 2: Basal plane of AV | Cross-sectional Area ($cm^2$) | 4.44 |
| | Circumference (cm) | 76.53 |
| | Length 1 (cm) | 26.41 |
| | Length 2 (cm) | 22.8 |
| Plane 3: Sinus | Cross-sectional Area ($cm^2$) | 4.39 |
| | Circumference (cm) | 78.68 |
| | Length 1 (cm) | 21.52 |
| | Length 2 (cm) | 24.83 |
| | Length 3 (cm) | 24.38 |
| | LCA height (mm) off-set from plane2 | 6.039 |
| | RCA height (mm) off-set from plane2 | 5.736 |
| Plane 4: Sino-Tubular Junction | Cross-sectional Area ($cm^2$) | 3.52 |
| | Circumference (cm) | 67.16 |
| | Length 1 (cm) | 21.99 |
| | Length 2 (cm) | 20.08 |
| lane 5: Acending aorta (1 cm off-set from Plane 4 | Cross-sectional Area ($cm^2$) | 4.61 |
| | Circumference (cm) | 78.24 |
| | Length 1 (cm) | 28.09 |
| | Length 2 (cm) | 20.41 |

| 10% | 20% | 30% | 40% | 50% | 60% | 70% |
|---|---|---|---|---|---|---|
| 5.04 | 5.06 | 5.21 | 3.72 | 3.64 | 3.1 | 2.83 |
| 85.02 | 92.43 | 85.5 | 69.45 | 69.65 | 68.68 | 65.13 |
| 29.85 | 33.53 | 20.18 | 23.11 | 19.24 | 15.93 | 15.32 |
| 21.34 | 21.19 | 30.58 | 20.49 | 23.73 | 22.47 | 20.69 |
| 3.99 | 3.97 | 3.45 | 3.52 | 3.2 | 2.92 | 2.98 |
| 73.6 | 72.06 | 67.73 | 67.69 | 65.39 | 63.1 | 63.42 |
| 26.05 | 24.45 | 22.59 | 22.81 | 16.98 | 16.72 | 22.59 |
| 21.7 | 20.38 | 19.97 | 19.91 | 22.34 | 22.13 | 16.82 |
| 4.2 | 5.13 | 5.47 | 5.43 | 4.86 | 5.33 | 4.6 |
| 76.57 | 88.18 | 87.99 | 88.21 | 82.79 | 91.73 | 81.54 |
| 23.43 | 23.8 | 25.75 | 25.47 | 25.33 | 23.85 | 23.35 |
| 23.52 | 25.73 | 26.19 | 27.17 | 24.3 | 25.17 | 24.31 |
| 22.62 | 25.41 | 26.01 | 25.31 | 25.45 | 26.5 | 24.48 |
| 6.274 | 5.089 | 7.152 | 3.751 | 6.124 | 7.323 | 5.209 |
| 7.668 | 6.188 | 5.817 | 6.831 | 6.042 | 7.942 | 7.223 |
| 2.48 | 3.87 | 3.89 | 3.97 | 3.61 | 3.57 | 3.43 |
| 56.72 | 70.69 | 70.1 | 71.07 | 67.66 | 67.54 | 66.02 |
| 19.1 | 21.25 | 22.23 | 23.17 | 21.71 | 20.23 | 20.53 |
| 16.5 | 21.07 | 21.85 | 21.47 | 21.04 | 21.72 | 19.74 |
| 4.11 | 4.24 | 4.65 | 4.25 | 4.17 | 4.13 | 3.98 |
| 73.7 | 73.74 | 76.97 | 73.38 | 72.86 | 72.26 | 70.99 |
| 24.34 | 23.65 | 24.55 | 24.35 | 24.17 | 23.1 | 23.18 |
| 20.31 | 21.78 | 23.64 | 22.67 | 21.59 | 22.75 | 21.92 |

| 80% | 90% | 3D MPR |
|---|---|---|
| 3.4 | 5.17 | 3,14 |
| 67.43 | 89.8 | 69,76 |
| 17.19 | 17.67 | 25,67 |
| 24.04 | 30.46 | 14,52 |
| 3.55 | 3.44 | 3,24 |
| 68.74 | 68.88 | 66,32 |
| 23.2 | 23.98 | 23,88 |
| 19.72 | 18.4 | 15,71 |
| 5.23 | 4.52 | 4,87 |
| 86.03 | 82.95 | 85,80 |
| 27.12 | 21.83 | 22,93 |
| 24.05 | 24.66 | 25,70 |
| 25.41 | 25.54 | 23,76 |
| 6.756 | 3.252 | 5,98 |
| 8.29 | 6.444 | 7,06 |
| 3.36 | 3.16 | 3,39 |
| 65.89 | 65.38 | 65,63 |
| 21.2 | 20.35 | 20,59 |
| 20.44 | 19.55 | 20,05 |
| 3.95 | 3.47 | 3,90 |
| 71.01 | 66.52 | 70,35 |
| 23.08 | 20.69 | 21,71 |
| 20.44 | 21.41 | 23,38 |