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A New Precision Measurement Protocol and Parametric Models of Vertebral Endplate

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Dear Prof. Phillip Steindel,

Thanks very much for your kind consideration about our manuscript entitled "A New Precision Measurement Protocol and Parametric Models of Vertebral Endplate" (JoVE59371R3). The reviewers' pertinent remarks and suggestions are also very much appreciated, which have been addressed point by point in the following response. We have studied the comments carefully and have made correction accordingly.

Best regards,

Desheng Wu

TITLE:

Precision Measurements and Parametric Models of Vertebral Endplates

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KEYWORDS:

vertebral endplate, reverse engineering, mathematical modeling, scanner, 3D reconstruction, parameter equation, representation

SUMMARY:

A reverse engineering system is employed to record and obtain detailed and comprehensive geometry data of vertebral endplates. Parametric models of vertebral endplate are then developed, which are beneficial to designing personalized spinal implants, making clinical diagnoses, and developing accurate finite element models.

ABSTRACT:

Detailed and comprehensive geometric data of vertebrae endplates is important and necessary to improve the fidelity of finite element models of the spine, design and ameliorate spinal implants, and understand degenerative changes and biomechanics. In this protocol, a high-speed and highly accurate scanner is employed to convert morphology data of endplate surfaces into a digital point cloud. In the software system, the point cloud is further processed and reconstructed into three dimensions. Then, a measurement protocol is performed, involving a 3D coordinate system defined to make each point a 3D coordinate, three sagittal and three frontal surface curves that are symmetrically fitted on the endplate surface, and 11 equidistant points that are selected in each curve. Measurement and spatial analyses are finally performed to obtain geometric data of the endplates. Parametric equations representing the morphology of curves and surfaces are fitted based on the characteristic points. The suggested protocol, which is modular, provides an accurate and reproducible method to obtain geometric data of vertebral endplates and may assist in more sophisticated morphological studies in the future. It will also contribute to designing personalized spinal implants, planning surgical acts, making clinical diagnoses, and developing accurate finite element models.

INTRODUCTION:

A vertebral endplate is the superior or inferior shell of the vertebral body and serves as a mechanical interface to transfer stress between the disc and vertebral body[1]. It consists of the epiphyseal rim, which is a strong and solid bony labrum surrounding the outer rim of the vertebral body, and the central endplate, which is thin and porous[2].

The spine is subject to a wide array of degenerative, traumatic, and neoplastic disorders, which may warrant surgical intervention. Recently, spinal devices such as artificial discs and cages have been widely used. Accurate and detailed morphometric parameters of endplates are necessary for the design and amelioration of spinal implants with effective prosthesis-vertebra contact and bone ingrowth potential[3]. Furthermore, information on the exact shape and geometry of vertebral endplates is important for understanding the biomechanics. Although the finite element modeling allows for simulation of the real vertebrae and has been widely used to study physiological responses of the spine to various loading conditions[4], this technique is patient-specific and not generalizable to all vertebrae. It has been suggested that the intrinsic variability of vertebrae geometry among the general population should be considered when developing the finite element model[5]. Therefore, the geometric parameters of endplates are conducive to the mesh generation and fidelity enhancement in finite element modeling.

Although the importance of the matching of endplate geometry and implant surface has been discussed in previous studies[6-8], data on the morphology of vertebral endplates is scarce. Most previous studies have failed to reveal the 3D nature of the endplate[9-11]. A spatial analysis is required to better and fully depict endplate morphology[12-14]. In addition, most studies have employed lower precision measurement techniques[10,15,16]. Moreover, significant magnification has been reported when geometry parameters are measured by employing radiography or computed tomography (CT)[17,18]. Though magnetic resonance imaging (MRI) is considered non-invasive, it is less accurate in defining the precise margins of osseous structures[11]. Due to a lack of a standardized measurement protocol, there are large differences among existing geometric data.

In recent years, reverse engineering, which can digitize the existing physical parts into computerized solid models, has been increasingly applied to the field of medicine. The technique makes it feasible to develop an accurate representation of the anatomical character of sophisticated vertebrae surfaces. The reverse engineering system includes two subsystems: the instrumentation system and software system. The instrumentation system adopted in this protocol has a non-contact optical 3D range flatbed scanner, which is high-speed and highly accurate (precision 0.02 mm, 1,628 x 1,236 pixels). The scanner can efficiently (input time 3 s) capture surface morphology information of the target object and convert it into digital point cloud. The software system (i.e., reverse engineering software) is a computer application for point cloud data processing (see **Table of Materials**), 3D surface model reconstruction, free curve and surface editing, and data processing (see **Table of Materials**).

The purposes of the present report are to (1) devise a measurement protocol and algorithm to obtain quantitative parameters of vertebral endplates based on a reverse engineering technique, (2) develop a mathematical model that allows for a realistic representation of vertebral endplates without digitizing too many landmarks. These methods will be beneficial to surgical act planning and finite element modeling.

PROTOCOL:

This study was approved by the health research ethics board of the authors' institute. As cervical vertebral bones have more intricate shapes[19], the protocol uses the cervical vertebrae as an illustration to facilitate relevant research.

1. Preparation of materials, scanning, and image processing

1.1. Collect a dry cervical vertebra without pathologic deformation or broken parts.

1.2. Place the vertebra vertically in the platform of the scanner (**Figure 1**, see **Table of Materials**), with the endplate facing the camera lens. Use the active light source of the scanner. Then, start the scanning process to obtain point cloud data (.ASC format).

NOTE: According to the pre-scan images, adjust the scanner and position of the vertebra to capture as much surface morphology information as possible.

1.3. Open the software specially used for processing point clouds (see **Table of Materials**). Click **Import** to import the point cloud data and generate the digital graphic of the vertebra. Set the sample rate to 100%, select **Keep Full Data On Sampling**, select the unit of data as millimeters, and click **Shade Points**. Use the Lasso Selection Tool to select redundant points on the graphic, then click **Delete** to remove them. Click **Reduce Noise** and set the smoothness level to its maximum to reduce noise and spikes (**Figure 2A,B**).

NOTE: There are basic software operation instructions at the bottom of the GUI (graphical user interface). Noise points with obvious sharp spurs laterally or vertically should be removed to reduce error.

1.4. Click **Wrap** to package the imaging data into .stl format file to transform the point cloud into mesh, which will convert a point object into a polygon object.

NOTE: Reverse engineering software usually accepts .stl-style 3D format.

1.5. Open the software specially used for 3D reconstruction and data processing (see **Table of Materials**). Click **File** then **New** in the submenu. Select **Part** in the List of Types. Click **Start**, then **Shape** in the submenu, then **Digitized Shape Editor**. Click the **Import** icon in the toolbar at the right-hand side of the GUI. In the Import window, select the **.stl** format file, then click **Apply** > **OK.** Click **Fit All** in the icon in the toolbar at the bottom to load the reconstructed image to the main window of the presentation software.

NOTE: Steps 1.5–2.3.3 are performed with the same software.

1.6. Click **Activate** in the toolbar at the right-hand side. In the Activate window, select **Trap Mode** >

Polygonal Type > **Inside Trap**. Then, select the vertebral endplate on the 3D image to remove unneeded vertebral components, such as the posterior elements and osteophytes (**Figure 2C**).

2. Quantification of 3D morphology of the endplate

2.1. Defining the endplate 3D coordinate system

2.1.1. Click **Start** > **Shape** in the submenu, then **Generative Shape Design**. Click the **Point** icon in the toolbar at the right-hand side. Mark three anatomic landmarks on the epiphyseal rim: the first two are the left and right endpoints of the endplate trailing edge, respectively; the third is the anterior median point.

2.1.2. Click the **Line** icon in the toolbar at the right-hand side and select the two trailing edge endpoints to define a posterior frontal line. Click the **Plane** icon, select the plane type to be normal to curve, then select the posterior frontal line and anterior median point to define the mid-sagittal plane.

2.1.3. Click **Start** > **Shape** > **Quick Surface Reconstruction**. Click the **Planar Section** icon, enter **1** in the number option, then select the endplate image and mid-sagittal plane to generate an intersecting curve. Click **Curve** from the Scan icon and select the intersection of the intersecting curve and posterior epiphyseal rim. Define the intersection as the posterior median point.

2.1.4. Click **Start** > **Shape** > **Generative Shape Design**. Click the **Line** icon and select the anterior median point and posterior median point to define a mid-sagittal diameter. Click the **Point** icon, then **Points** and **Planes Repetition** in the submenu. Then, select the mid-sagittal diameter and enter **1** in the Instance(s) option to define the midpoint of the mid-sagittal diameter.

2.1.5. Click the **Axis System** icon in the toolbar at the bottom. Then, select the midpoint of the mid-sagittal diameter as the origin, the line parallel to the posterior frontal line as the x-axis, the mid-sagittal diameter as the y-axis, and the line pointing forward and perpendicular to the x-y plane as the z-axis (**Figure 3**).

NOTE: The two trailing edge endpoints are chosen as reference points because they are consistent and show minimum variation in the presence of osteophytes[10].

2.2. Fitting characteristic curves and points on the endplate surface (**Figure 4A–D**)

2.2.1. Click the **Point** icon, then **Points** and **Planes Repetition** in the submenu. Select the mid-sagittal diameter and enter **3** in the Instance(s) option to divide the mid-sagittal diameter equally into four parts.

2.2.2. Click **Start > Shape > Quick Surface Reconstruction**. Click the **Planar Section** icon, enter **1** in the Number option, then select the endplate image and x-z plane to generate an intersecting curve. Click **Curve** from the Scan icon and select the two intersections of the x-z plane and epiphyseal rim.

2.2.3. Define the line between the two intersections as the mid-frontal diameter. In the same way, divide the mid-frontal diameter equally into four parts.

NOTE: When the endplate is not symmetrical relative to the med-sagittal plane, choose one of the two endpoints of the mid-frontal curve that has a shorter vertical distance to the z-y plane. Then, define the mid-frontal diameter as 2x the length of the shorter, and divide it equally into four parts.

2.2.4. Click the **Measure Between** icon in the toolbar at the bottom to measure the length of a quarter of the mid-sagittal diameter. Click the **Planar Section** icon, enter **2** in the Number option, enter the measured value in the Step option, then select the endplate image and x-z plane to generate two fitting curves on one side of the frontal part. Click **Swap** to generate two fitting curves on the other side. In the same way, obtain the other three fitting curves in the sagittal plane.

NOTE: The two mid-frontal fitting curves overlap with the two mid-sagittal fitting curves.

2.2.5. Select 11 equidistant points in each curve for subsequent measurements. Specific method is as follows:

2.2.5.1. Taking the mid-sagittal curve as an example, divide the mid-sagittal diameter equally into 10 parts, resulting in a sum of 11 points, including nine intermediate points and two endpoints (refer to steps 2.1.3 and 2.2.1).

2.2.5.2. Go through each equidistant point, obtain nine fitting curves on the endplate surface (refer to step 2.2.2). Click **Curve** from the Scan icon and select the intersection of the fitting curves and the mid-sagittal curve. Finally, obtain a total of 66 points on each endplate (11 points per curve multiplied by six curves). Click the **Measure Item** icon in the toolbar at the bottom to measure the coordinates of each point.

2.3. Measurement of endplate morphological parameters

2.3.1. Line parameter:

2.3.1.1. Click the **Measure Between** icon to measure the length of line parameter that is the distance between two measured points.

2.3.2. Concavity parameters:

2.3.2.1. Create a plane parallel to the x-y plane (**Figure 5A**): click **Start** > **Shape** > **Generative Shape Design**. Click the **Sketch** icon in the toolbar at the right-hand side, then click the x-y plane.

Click the **Circle** icon, click **Origin** on the endplate surface, drag the cursor of the mouse to an appropriate distance, then click. Click the **Exit Workbench** icon, then the **Fill** icon, and then click.

2.3.2.2. Click the **Offset** icon, select the filled plane, and enter an appropriate value in the offset option until it is tangent to the most concave part, and zoom in. Click **Start** > **Shape** > **Quick Surface Reconstruction.** Then, click the **3D curve** icon to find and create the most concave point. Click the **Measure Item** icon to measure the coordinates of the most concave point (**Figure 5B**).

2.3.2.3. Click the **Measure Between** icon, then select the most concave point and x-y plane to measure the whole endplate concavity depth. Similarly, find and create the most concave depth on a particular plane and measure its coordinates.

2.3.2.4. Click the **Projection** icon in the toolbar at the right-hand side, then select the most concave point and x-y plane to obtain the projective point. Click the **Measure Item** icon to measure the coordinates of the projective point, and determine its distribution based on the coordinates.

2.3.3. Surface area parameters:

2.3.3.1. Click the **Measure Inertia** icon in the toolbar at the bottom and click **endplate surface** to measure its area. Click the **Activate** icon and select the central endplate along the inner margins of the epiphyseal ring (refer to step 1.6), then click the **Measure Inertia** icon to measure its area (**Figure 5C**). Click the **Activate** icon, then the central endplate, and finally the **Swap** icon in the Activate window to obtain an epiphyseal rim. Then, measure its area.

3. Development of endplate surface mathematical model

3.1. Determining the fit order of the parametric equation

3.1.1. Open the data analysis and visualization software (see **Table of Materials**). Input **x = [corresponding data]** in the command window. Click **Enter**.

NOTE: The “corresponding data” refers to x-coordinate data of the 11 characteristic points in one curve that has been measured in the previous steps. Click **Enter** after inputting each command, with the same applying to subsequent operations. Steps 3.1–5.5 are performed uniformly with the same software.

3.1.2. In the same way, input **z = [corresponding data]**.

3.1.3. Input the code **for i=1:5 z2=polyfit(x,z,i); Z=polyval(z2,x); if sum((Z-z).^2)<0.01 C=I break; end; end**.

NOTE: The protocol sets the error sum of squares below 0.01 to obtain higher precision, the value of which can be readjusted to satisfy various demands.

3.1.4. Click **Enter** to obtain a C value that is the desired fit order.

3.2. Parameter equation fitting

3.2.1. Input **cftool** and click **Enter** to bring up the Curve Fitting Tool.

3.2.2. Input the coordinates of a curve in the command window (refer to steps 3.1.1 and 3.1.2). In the Curve Fitting Tool, select x-coordinate data when fitting frontal plane curves and y-coordinate data when fitting sagittal plane curves in the x data option, select z-coordinate data in the y data option, select **polynomial**, and enter the fit order obtained. Then, the software will output the parametric equation and goodness of fit automatically.

NOTE: As the curve is a 2D image, the default work option is the x and y options in the Curve Fitting Tool when fitting a curve.

3.2.3. In the similar way, input the 3D coordinates of the 66 points and match the coordinate data to the corresponding axis options. Select **polynomial** and enter the fit order to gain the parametric equation of the endplate surface (**Figure 6B**).

4. Acquisition of geometric data based on parametric equation

4.1. Input x- and y-coordinate values of any point on the endplate in the command window.

4.2. Input P_{X1}, P_{X2}, P_{X3}....

NOTE: Px is the parameters of the parametric equation that have been fitted using polynomial in the steps above.

4.3. Input the equation and click **Enter** to obtain the result (i.e., input format: **z = P_{00} + P_{10}*x + P_{01}*y + P_{20}*x^2 + P_{11}*x*y + P_{02}*y^2 + P_{30}*x^3 + P_{21}*x^2*y + P_{12}*x*y^2 + P_{03}*y^3 + P_{40}*x^4 + P_{31}*x^3*y + P_{22}*x^2*y^2 + P_{13}*x*y^3 + P_{04}*y^4**).

5. **Representation of the endplate based on parametric equation**

5.1. Input P_{X1}, P_{X2}, P_{X3}....in the command window.

5.2. Input the code **X=N_1:0.01:N_2;**.

NOTE: N_1–N_2 is the range of X-axis data (i.e., the values of the two endpoints of the themid-coronal curve).

5.3. Input the code “Y=N_3:0.01:N_4;”.

5.4. Input the equation (i.e., $z=@(x,y)P_{00} + P_{10}.*x + P_{01}.*y + P_{20}.*x.\^2 + P_{11}.*x.*y + P_{02}.*y.\^2 + P_{30}.*x.\^3 + P_{21}.*x.\^2.*y+ P_{12}.*x.*y.\^2 + P_{03}.*y.\^3 + P_{40}.*x.\^4 + P_{31}.*x.\^3.*y + P_{22}.*x.\^2.*y.\^2+ P_{13}.*x.*y.\^3 + P_{04}.*y.\^4;$).

5.5. Input the code **ezmesh(z, [N_1,N_2,N_3,N_4])** to obtain 3D simulation graphics (**Figure 6C**).

REPRESENTATIVE RESULTS:

Using the highly accurate optical 3D range flatbed scanner, the endplates were converted into more than 45,000 digital points, which adequately characterize the morphology (**Figure 2A,B**).

In the measurement protocol, the spatial analysis of endplate surfaces was conducted. Representative curves were fitted and quantified on the surface to characterize morphology (**Figure 4B**). The linear parameters were measured by calculating the distance between two endpoints. Measurements obtained include the concavity depth and concavity apex location in mid-sagittal plane, in addition to those of the whole endplate concavity and any specific section (**Figure 5B**). The components of endplates, epiphyseal rim, and central endplate were separated (**Figure 5C**), and their lengths and areas were obtained conveniently.

A total of 138 cervical vertebral endplates were digitized and analyzed, and the mathematical model of the endplate was established. The protocol sets the sums of squared error below 0.01, and it was concluded that using the four-order polynomial function could achieve satisfaction. The parametric equation of each curve was deduced based on the coordinates of 11 points: $f(x) = P_1*x\^4 + P_2*x\^3 + P_3*x\^2 + P_4*x + P_5$. P_1, P_2, P_3, P_4 and P_5 were the parameters, the exact values of which are shown in **Table 1**.

The parametric equation representing the morphological characteristics of endplate surface is:

$$F(x, y) = P_{00} + P_{10}*x + P_{01}*y + P_{20}*x\^2 + P_{11}*x*y + P_{02}*y\^2 + P_{30}*x\^3 + P_{21}*x\^2*y + P_{12}*x*y\^2 + P_{03}*y\^3 + P_{40}*x\^4 + P_{31}*x\^3*y + P_{22}*x\^2*y\^2 + P_{13}*x*y\^3 + P_{04}*y\^4$$

Where: P_{XY}s are the parameters, which were deduced from the pre-measured coordinates of 66 points (**Table 2**).

FIGURE AND TABLE LEGENDS:

Figure 1: The non-contact optical 3D range flatbed scanner. The scanner, which is based on heterodyne multifrequency phase shift 3D optical measurement technology, includes optical measurement (integrating around two cameras and a projector) and control devices. Precision of this instrument is 0.02 mm, and pixels are 1628 x 1236. The scanner can efficiently (input time 3 s) digitize the surface geometry of a target object.

Figure 2: The point cloud of vertebral surface and 3D reconstruction of endplate. (A) and (**B)** are the inferior and superior surfaces of a cervical vertebra generated by the software specially used

for processing point clouds, respectively. (**C)** and (**D)** are the 3D reconstruction of the inferior and superior endplates generated by the software specially used for 3D reconstruction and data processing, respectively. The posterior elements and osteophytes are removed from the vertebrae, leaving only the endplate. The best-fit plane is defined through the anterior-most and posterior-most points of the bilateral uncinate processes, and the two curves formed by the best-fit plane and endplate are the boundaries of the uncovertebral joint and caudal endplate.

Figure 3: Definition of the endplate 3D coordinate system. Marking of three anatomic landmarks on the epiphyseal rim: the first two are the left and right endpoints of the endplate trailing edge, respectively; the third is the anterior median point. The posterior frontal line is formed by the two trailing edge endpoints, which define the mid-sagittal plane with the anterior median point. The posterior median point is determined by the mid-sagittal plane and posterior epiphyseal rim, which form the mid-sagittal diameter with the anterior median point. The origin is the midpoint of the mid-sagittal diameter. The y-axis is determined by mid-sagittal diameter and pointing forward. The x-axis is the line parallel to the posterior frontal line. The z-axis is normal to the x-y plane.

Figure 4: The steps of fitting characteristic curves and points on endplate surface. (A) Divide the mid-sagittal diameter and the mid-frontal diameter equally into four parts. (**B)** Go through every equidistant point, and choose six surface curves symmetrically, three of which are the intersection curves of the frontal plane and the endplate surface, and the other three in the sagittal plane. (**C)** Divide the mid-sagittal diameter equally into 10 parts. (**D)** Going through each equidistant point, the frontal planes and mid-sagittal curve form nine intersections, resulting in a sum of 11 points, together with the two endpoints.

Figure 5: Measurement of endplate concavity depth and surface area. (A) Create a plane parallel to the x-y plane. (**B)** Offset the plane until it is tangent to the most concave point, and the endplate concavity depth is the perpendicular distance between the most concave point and x-y plane. (**C)** Draw a line along the inner margins of the epiphyseal ring to partition the endplate into the central endplate and epiphyseal rim.

Figure 6: The 3D reconstruction and representations of an inferior endplate. (A) The 3D reconstruction of the inferior endplate surface generated by the software specially used for 3D reconstruction and data processing. (**B)** and (**C)** are the representations of the inferior endplate generated by the data analysis and visualization software.

Table 1: The parameters of equation to represent the curve of endplate surface. Only the data of the sixth cervical vertebral endplate is listed. Px = the parameters of the equation. On each end plate, six surface curves were symmetrically chosen; three of these were in the frontal plane and termed the anterior curve (FAC), middle curve (FMC), and posterior curve (FPC); the other three in the sagittal plane were termed the left curve (SLC), middle curve (SMC), and right curve (SRC). Parameters with an absolute value of less than 0.0001 are represented as 0 here.

Table 2: The parameters of parametric equation representing the morphology of endplate

surface. Px = the parameters of the equation; inf = inferior endplate; sup = superior endplate. Parameters with an absolute value of less than 0.0001 are represented as 0 here. This table has been modified from a previous publication[3].

Table 3: Reliability of measurements. Data were mean ± standard deviation (mm). ICC = intra-class correlation coefficient; APD = antero-posterior diameter; CMD = center mediolateral diameter; RE = the reverse engineering system. This table has been modified from a previous publication.[3]

Table 4: The validity of the geometric model representing the endplate morphology. Data are represented as mean ± standard deviation (mm). The original points are 15 randomly selected points on the original 3D reconstruction image. Comparison points = corresponding points auto-generated from parametric equations; R = correlation coefficient.

DISCUSSION:

Reverse engineering has been increasingly and successfully applied to the field of medicine, such as cranioplasty[20], oral[21], and maxillofacial implants[21]. Reverse engineering measurements, namely product surface digitization, refers to the conversion of surface information into point cloud data employing specific measuring equipment and methods. On the basis of such data, complex surface modeling, evaluation, improvements, and manufacturing can be performed. Digital measurement and data processing are a basic and key technology used in reverse engineering.

In this protocol, accurate and detailed morphology information of vertebral endplates are recorded using a non-contact optical 3D range scanning system, which is based on heterodyne multifrequency, phase-shift, 3D optical measurement technology. The scanner is primarily made of control devices and an optical measurement integrating two cameras and a projector. Compared with other measuring instruments, the scanner is highly accurate and efficient and avoids point-by-point scanning. When capturing point-cloud data, the scanning head is usually not in contact with the object, such that there are no deformation effects. The reliability, validity, and precision of the scanner for recording surface morphology have been well-established[2,3,22]. The replicability of these measurements have been verified.

To verify the accuracy of measurements taken by the reverse engineering system, 20 endplates were measured using a digital caliper and evaluated using Cronbach alpha. For intra-test reliability, 16 endplates were randomly selected from the 138 vertebral endplates and measured twice at 2 week intervals, then assessed using an intra-class correlation coefficient. The results showed great agreement and reliability (**Table 3**). Reverse engineering software involves powerful measurements, data processing, error detection, and free curve and surface editing functions. It can also intelligently and efficiently construct and adjust curves and surfaces, and the 3D surface model reconstruction contributes to accurate measurements[23].

There are important and considerable applications for detailed and comprehensive anatomy data of vertebrae, such as designing spinal implants, improving the fidelity of finite element models of the spine, and developing mathematical models. The vertebral endplate is essential to maintaining the integrity and function of the intervertebral disk, and it also serves as a mechanical interface to transfer stress. Therefore, the quantification of endplate geometry is important. With the help of reverse engineering, endplate morphology can be quantified intelligently and comprehensively. In this protocol, six characteristic curves are fitted on the surface of each endplate, and a 3D coordinate system is established to quantify spatial morphology.

In addition, a parametric model of the endplate is developed to institute accurate and reproducible quantitative evaluations and to develop personalized biomechanical finite element models. The parametric model of endplates surface can produce quick, realistic, and accurate representations that can be visualized and conveniently analyzed by researchers.

The inclusion of more landmarks will improve the precision, but it is time-consuming and costly. In this protocol, it is proposed that 66 points from six surface curves are adequate for describing the morphological features. Reliability tests are also conducted by comparing coordinate values of 15 randomly selected points with corresponding values that are auto-generated from parametric equations. The result reveal that the parametric model has good reliability and reproducibility may serve as a realistic representation of endplate surface (**Table 4**). It should be noted that the parametric model can be derived based on other imaging modalities such as CT and MRI.

As non-contact scanners are susceptible to ambient light, it is critical to keep the ambient light steady, and active light sources are recommended. If there is residual grease on the endplate surface, infantile talcum powder should be daubed gently to avoid the risk of being affected by spatial reflectance characteristics of the object surface. The subaxial cervical vertebrae has a special component: the uncovertebral joint. To distinguish it from the endplate, a best-fit plane is defined using the least-squared method. Then, the intersection curve formed by the best-fit plane, and the endplate surface is the boundary between the uncovertebral joint and superior endplate (**Figure 2D**).

The specific operation is as follows: click **Start** > **Shape** > **Generative Shape Design**. Click the **Point** icon in the toolbar at the right-hand side, then select the anterior-most and posterior-most points of the bilateral uncinate processes on the 3D image. Click the **Plane** icon and select **Mean Through Points** in the plane type to define the a best-fit plane. Click **Start** > **Shape** > **Quick Surface Reconstruction**. Click the **Planar Section** icon, then select the 3D image and best-fit plane.

Accurate marking of the three anatomical points on the endplate surface when establishing the 3D coordinate system is critical. The reverse engineering software allows for flexible shifting of the reconstruction image and improves contrast that helps to identify the landmarks. Alternatively, it is important to assess the appropriateness of the coordinate system based on whether the intersecting line of the defined mid-sagittal and coronal planes is perpendicular to the endplate section, and to then adjust the system accordingly. Intra-observer testing was also assessed, and the result indicated good reliability (**Table 3**).

This protocol requires multiple skills and techniques including point cloud data acquisition and processing, image reconstruction and analysis, and parametric model development. For a beginner, it may take time to complete the whole process. However, as only a few modules of the software in this protocol are used and the procedure is modular, it requires a short learning curve to become well-experienced.

In conclusion, the protocol described provides an accurate and reproducible method to obtain detailed and comprehensive geometry data of vertebral endplates. A parametric model is also developed without digitizing too many landmarks, which is beneficial to designing personalized spinal implants, planning surgical acts, making clinical diagnoses, and developing accurate finite element models.

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The authors declare no competing financial interests.

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Figure 1

Figure 2

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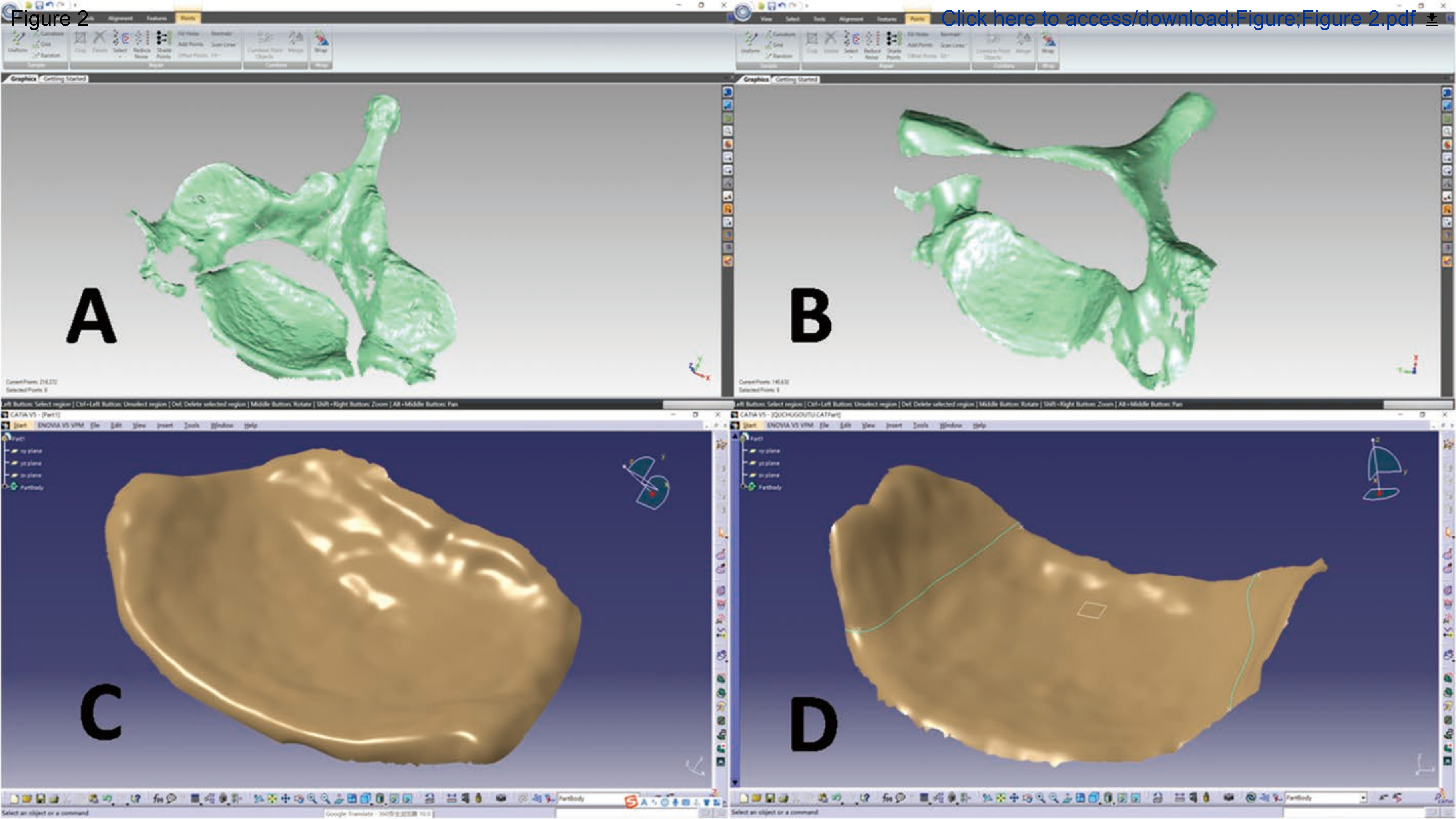
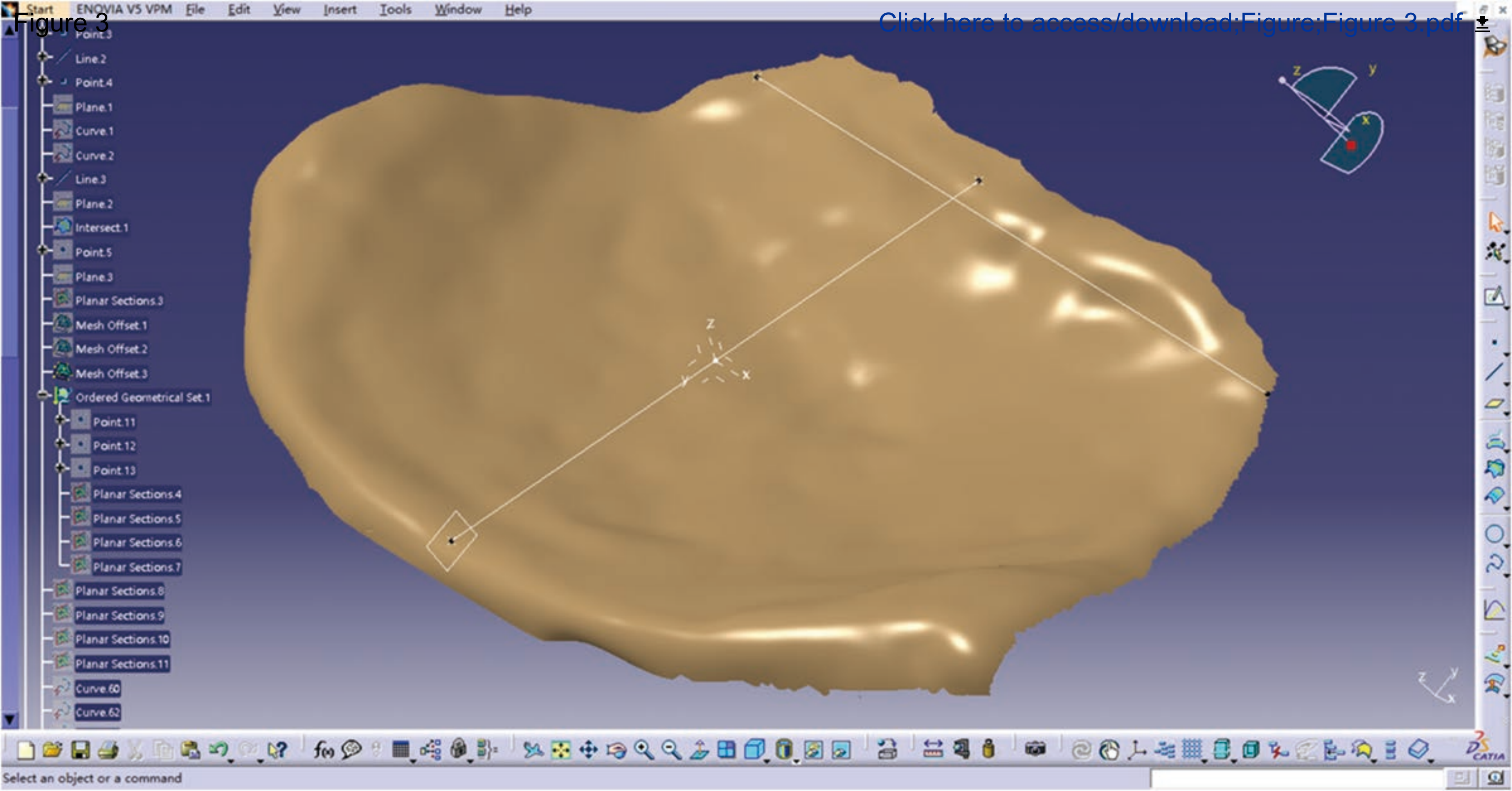


Figure 3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Mesh Offset.1
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Mesh Offset.3
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Figure 4

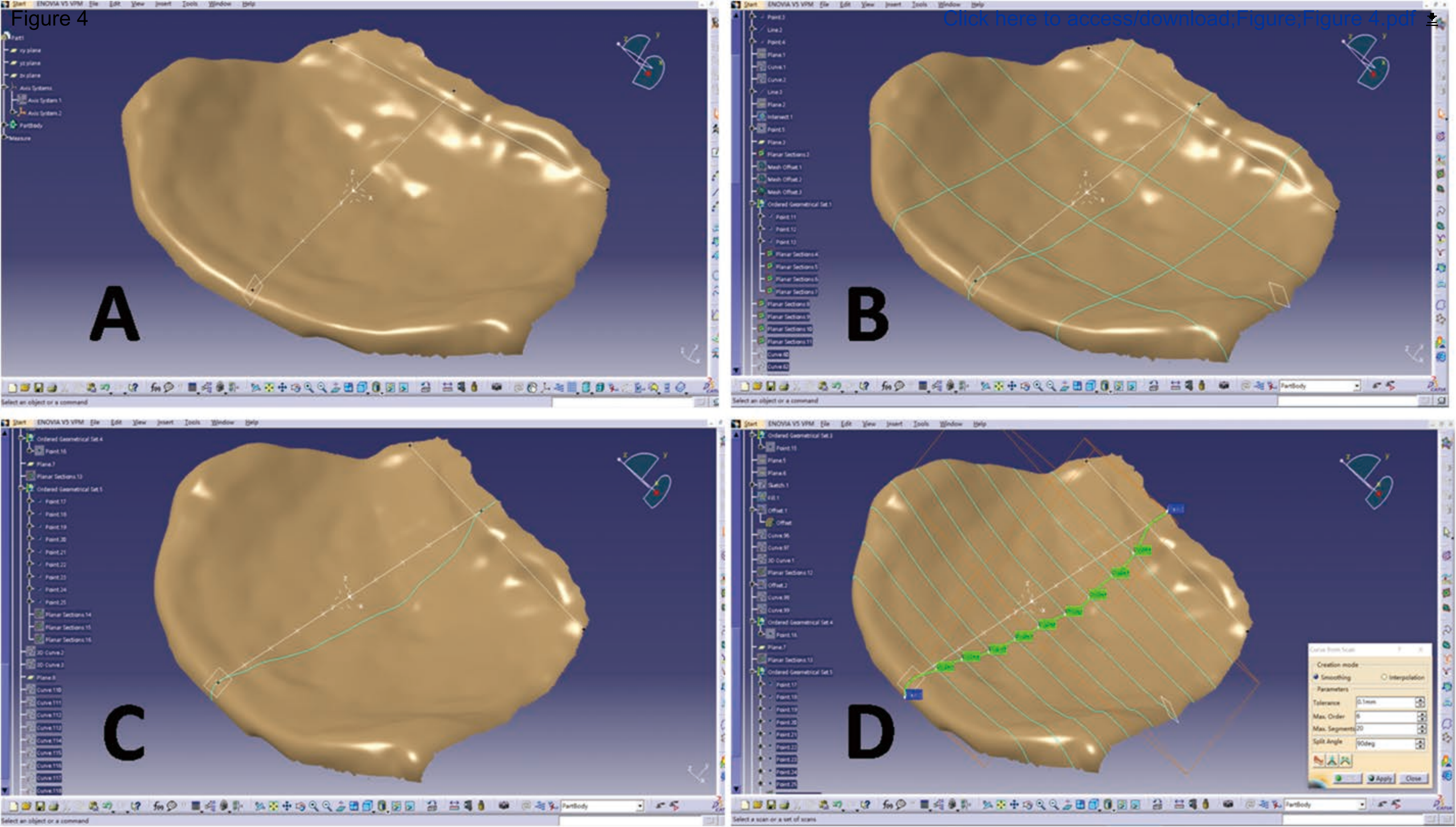
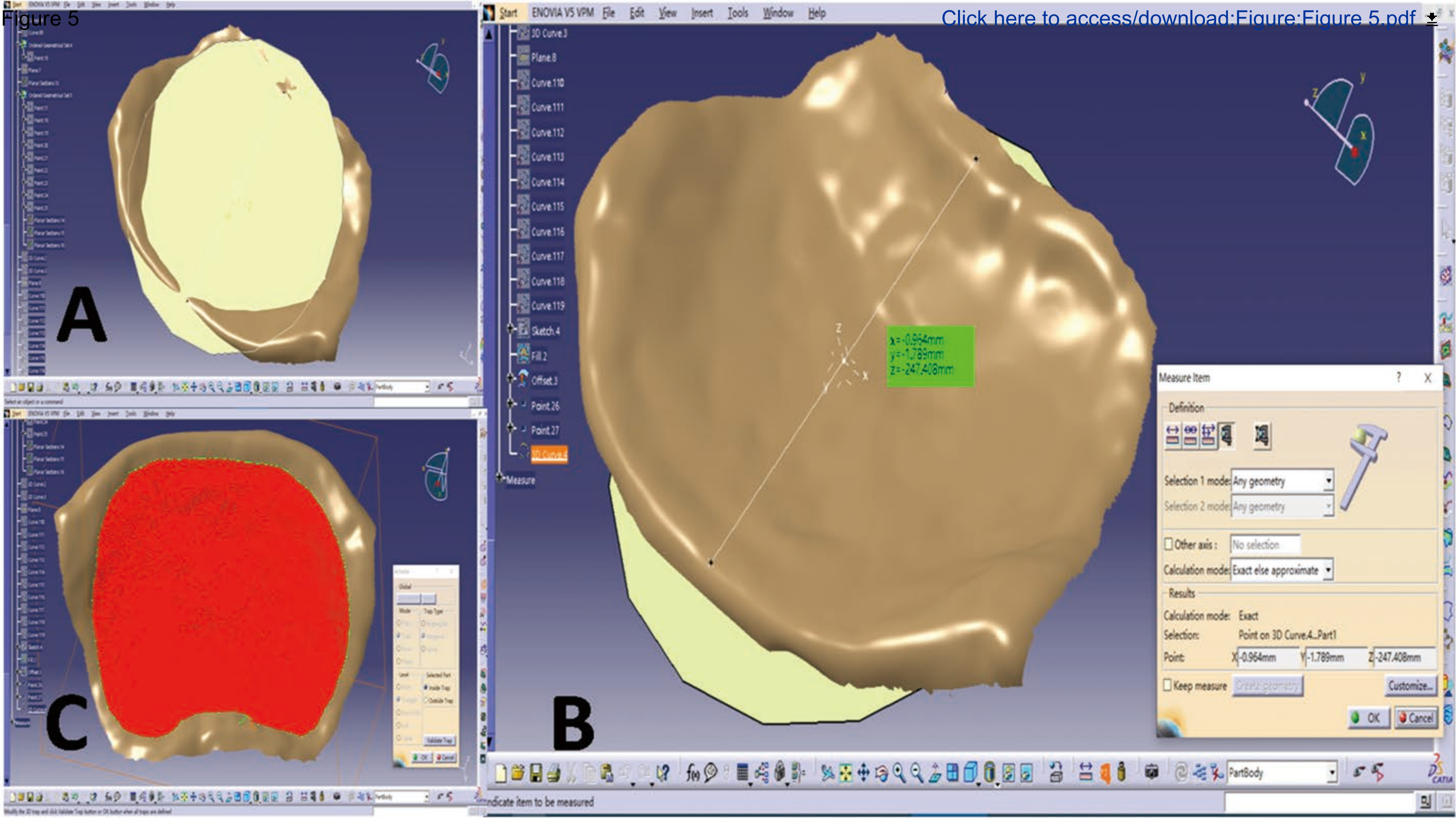


Figure 5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Curve.111
Curve.112
Curve.113
Curve.114
Curve.115
Curve.116
Curve.117
Curve.118
Curve.119
Sketch.4
Fill.2
Offset.3
Point.26
Point.27
3D Curve.4
Measure
x=-0.964mm
y=-1.789mm
z=-247.408mm
Measure Item
Definition
Selection 1 mode: Any geometry
Selection 2 mode: Any geometry
Other axis : No selection
Calculation mode: Exact else approximate
Results
Calculation mode: Exact
Selection: Point on 3D Curve.4_Part1
Point: X -0.964mm Y -1.789mm Z -247.408mm
Keep measure
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OK
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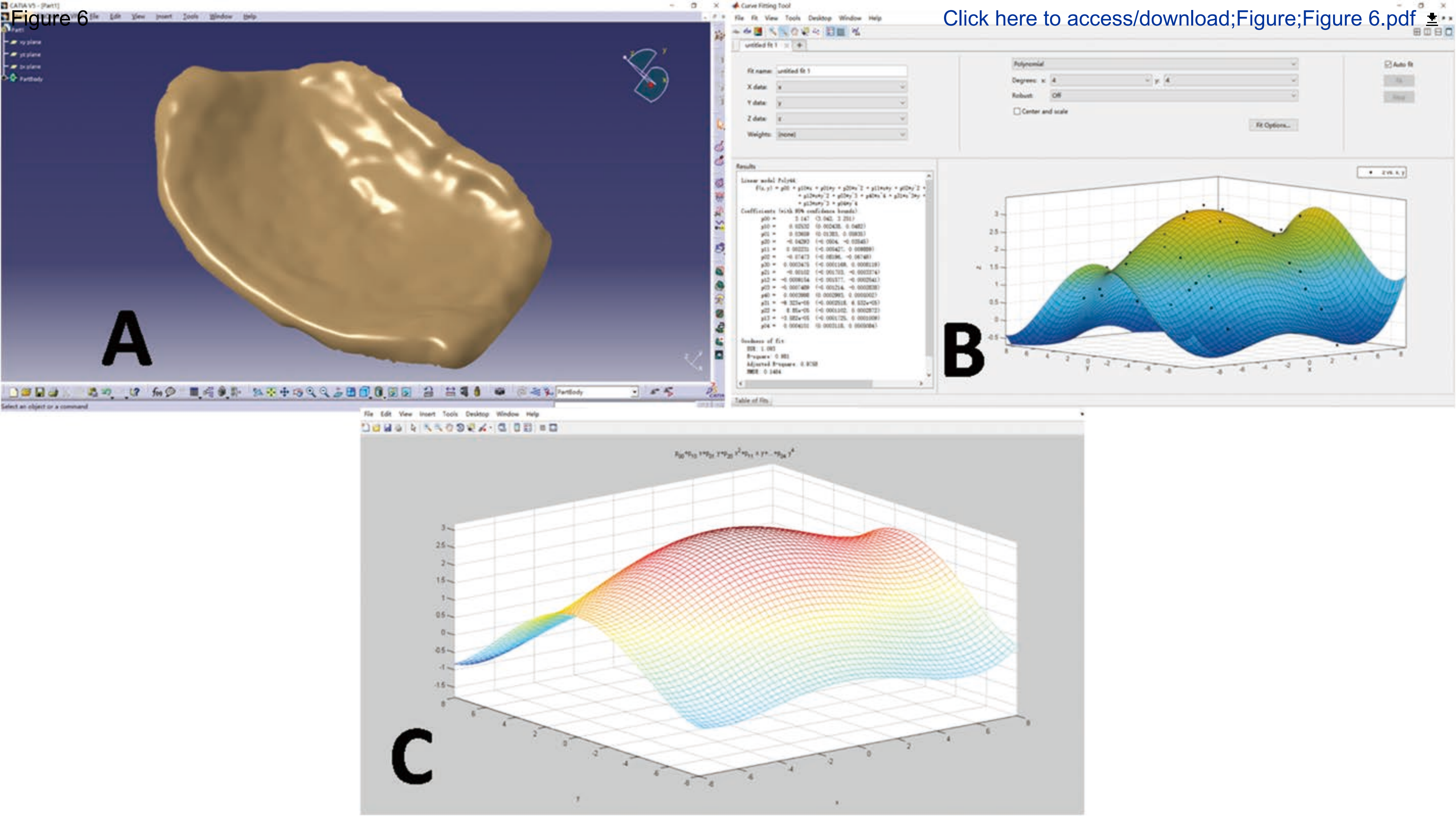
PartBody
Indicate item to be measured

Figure 6



Endplate Level	Curve	Parameters				
		P1	P2	P3	P4	P5
C6 superior	FAC	0	0	-0.01284	-0.00283	0.02523
	FMC	0	0	-0.01989	0.00074	0.3693
	FPC	0	0	-0.03292	0.00739	0.5323
	SLC	0	0.00176	-0.01125	-0.04192	-0.04192
	SMC	0.00011	0.00232	-0.01596	-0.09857	0.4712
	SRC	0	0.00179	-0.00961	0.04451	-0.03941
C6 inferior	FAC	0	-0.00013	-0.02252	0.00594	1.223
	FMC	0	0	-0.01604	-0.00817	1.729
	FPC	0	0	-0.00335	-0.00328	1.404
	SLC	0.00012	0.00087	-0.03468	-0.09623	1.448
	SMC	0.00025	0.00064	-0.0495	-0.03305	1.846
	SRC	0	0.00079	-0.02951	-0.08279	1.362

parameters	C3 inf	C4 sup	C4 inf	C5 sup	C5 inf	C6 sup	C6 inf	C7 sup
p00	1.989	0.4187	2.004	0.3383	1.913	0.4276	1.779	0.5674
p10	-0.00221	-0.00435	0.00542	-0.02082	-0.01108	0.0012	-0.00433	-0.00524
p01	-0.03561	-0.08683	-0.05366	-0.08263	-0.02572	-0.09797	-0.04069	-0.06418
p20	0.01286	-0.02523	-0.01455	-0.02991	-0.0253	-0.02639	-0.01747	-0.00878
p11	0.00092	0.00071	-0.00094	0.00018	-0.00021	-0.00124	0.00117	0.00021
p02	-0.05289	-0.01514	-0.05253	-0.01196	-0.04179	-0.01421	-0.03955	-0.01336
p30	0	-0.0001	0.00013	0.00024	0.00017	0	0	0
p21	-0.00107	0.00299	-0.00119	0.00363	-0.0021	0.00306	-0.00195	0.00194
p12	0	0.00048	-0.00041	0.00033	0.00014	0	-0.00011	0
p03	0.00062	0.00204	0.00089	0.00206	0.00046	0.00208	0.00077	0.00115
p40	0.0002	0	0.0002	0	0.00024	0	0	0
p31	0	0	0	0	0	0	0	0
p22	0.00017	0.00013	0	0.00015	0.00015	0.00017	0.00032	0
p13	0	0	0	0	0	0	0	0
p04	0.00023	0.00013	0.00024	0	0	0	0	0

	Measurements	Intratest reliability		Measurements	RE vs Caliper
APD	First-remeasurement	15.76±1.3	APD	RE	16.47±1.31
	Remeasurement	15.86±1.61		Caliper	16.26±1.27
	ICC	0.85		Cronbach alpha	0.99
CMD	First-remeasurement	19.71±2.47	CMD	RE	20.7±3.05
	Remeasurement	19.41±2.43		Caliper	20.45±3.21
	ICC	0.96		Cronbach alpha	0.99

Measurements value	N	Z coordinate value	T	P	R
Original points	15	1.75±0.87	0.26	0.8	0.98
Comparison points	15	1.74±0.91			

Name of Reagent/ Equipment	Company
Catia	Dassault Systemes, Paris, France
Geomagic Studio	Geomagic Inc., Morrisville, NC
MATLAB	The MathWorks Inc., Natick,USA
Optical 3D range flatbed scanner	Xi’an XinTuo 3D Optical Measurement Technology Co.Ltd., Xi’an, Shaanxi, C

Catalog Number

https://www.3ds.com/products-services/catia/

https://cn.3dsystems.com/software?utm_source=geomagic.com&utm_medium=301

https://www.mathworks.com/

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Comments/Description

3D surface model reconstruction, free curve and surface editing and data processing

point cloud data processing

analyze data, develop algorithms, and create models

acquire surface geometric parameters and convert into digital points

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Responses to Reviewers' Comments

Manuscript number: JoVE59371R2

Dear Editors and Reviewers:

Thank you for your letter and the reviewers' comments concerning our manuscript entitled "A New Precision Measurement Protocol and Parametric Models of Vertebral Endplate" (JoVE59371R1). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied the comments carefully and have made correction accordingly. The main corrections in the manuscript and the responses to the reviewer's comments are as following:

Responses to Editors:

Thank you very much for your pertinent comments and kind suggestions. These suggestions are very important for us to improve the quality of our manuscript. By taking the suggestions into consideration, the responses and revisions in our manuscript are listed below.

1. General comment: Please ensure that the manuscript is formatted according to JoVE guidelines – letter (8.5" x 11") page size, 1-inch margins, 12 pt Calibri font throughout, all text aligned to the left margin, single spacing within paragraphs, and spaces between all paragraphs and protocol steps/substeps.

Authors' response: Thank you very much for your kind suggestion. Following your suggestions, we have carefully checked and revised the manuscript according to JoVE guidelines.

2. General comment: The highlighting is currently very scattered; ideally full substeps should be highlighted (or at least full sentences). Please make the highlighting more cohesive, while remaining under the 2.75-page limit for highlighting.

Authors' response: According to your instructions, all the essential steps we have highlighted are complete sentences, which are no more than 2.75 pages.

3. Tables 1 and 2: What does "the value was too small and approached 0" mean?

Authors' response: We appreciate the editors' comments. The values of some Px (the parameters)were too small and close to zero. For the convenience of subsequent calculations, such as acquiring geometric data based on parametric equations, we set those parameter values to zero. We assessed the validity of the geometric model representing the endplate morphology by comparing coordinate value of 15 randomly selected points with their corresponding value auto-generated from parametric equations. The reliability tests indicated that the parametric equations had good reliability and reproducibility to quantify endplate morphology.

Responses to Reviewer #2:

We fully appreciate your pertinent comments and valuable suggestions. These constructive suggestions are very important to polish the quality of our manuscript. By taking the suggestions into consideration, the responses and revisions in our manuscript are listed below.

1. Line 24: "beneficial to designing personalized spinal implants", is it really true? maybe yes possible, is it useful? To know if it does fit to the person, you will need the information of that particular person like CT scans or MRI (just examples) which means I could just fit a new model to that person without using your parameteric model. The model is polynomial anyway so not that difficult.

Authors’ response: Thank you very much for your pertinent comment. There is a large discrepancy between footprints of currently available disc prostheses and the anatomic dimensions of vertebral endplates [1-3]. Moreover, the surface of almost all prostheses used now is designed relatively flat [4-5], while the osseous endplate geometry is concave [6-7].

Therefore, an ideal device should mirror the three dimensions of endplate morphology. The accurately and comprehensively quantitative data of vertebral endplate is prerequisite for developing and improving spinal implants [8]. However, many previous studies mainly focused on anteroposterior diameter and width, or concavity in midsagittal plane, which could not adequately describe the endplate morphology [5,6,9-12]. In addition, the accuracy and reliability of existing geometric data may be problematic due to the lack of a standardized measurement protocol and lower precision measuring instruments [11,13].

In this protocol, we developed a parametric model representing osseous endplates, which was fitted based on the coordinates data of 66 points from six surface curves on endplate surface, and developed an algorithm capable of describing their 3D morphological characteristics conveniently and efficiently. As we have already stated in the Discussion section, the parametric model can of course be derived base on other imaging modalities such as CT and MRI. Besides, the reliability tests indicated that the 3D model could make a realistic representation of endplate surface, and the parametric equations had good reliability and reproducibility to quantify endplate morphology [8].

The suggested protocol, provides an accurate and reproducible method to obtain geometry data of vertebral endplates, which we think may contribute to designing anatomic spinal implants.

References:

[1] Thaler M, Hartmann S, Gstöttner M, Lechner R, Gabl M, Bach C.Footprint mismatch in total cervical disc arthroplasty. Eur Spine J2013;22:759-65.

[2] Gstoettner, M., Heider, D., Liebensteiner, M. & Bach, C. M. Footprint mismatch in lumbar total disc arthroplasty. Eur Spine J 2008;17: 1470-1475.

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[5] Zhu, Y. H., Cheng, K. L., Zhong, Z., Li, Y. Q. & Zhu, Q. S. Morphologic evaluation of Chinese cervical endplate and uncinate process by three-dimensional computed tomography reconstructions for helping design cervical disc prosthesis. JChin Med Assoc 2016;79:500-6.
[6] Chen, H., Zhong, J., Tan, J., Wu, D. & Jiang, D. Sagittal geometry of the middle and lower cervical endplates. Eur Spine J 2013;22:1570-5.
[7] Wang, Y., Battie, M. C. & Videman, T. A morphological study of lumbar vertebral endplates: radiographic, visual and digital measurements. EurSpine J2012;21:2316-23.
[8] Feng, H. et al. Morphometry evaluations of cervical osseous endplates based on three dimensional reconstructions. Int Orthop, doi:10.1007/s00264-018-4053-1 (2018).
[9] Tan, S. H., Teo, E. C. & Chua, H. C. Quantitative three-dimensional anatomy of cervical, thoracic and lumbar vertebrae of Chinese Singaporeans. EurSpine J 2004;13:137-46.
[10] Kim, M. K. et al. Quantitative anatomy of the endplate of the middle and lower cervical vertebrae in Koreans. Spine2007;32:E376-81.
[11] Tang, R. et al. Morphometry of the lower lumbar intervertebral discs and endplates: comparative analyses of new MRI data with previous findings. Eur Spine J 25, 4116-4131.
[12] Panjabi, M. M., Duranceau, J., Goel, V., Oxland, T. & Takata, K. Cervical human vertebrae. Quantitative three-dimensional anatomy of the middle and lower regions. Spine (Phila Pa 1976) 16, 861-869 (1991).
[13] Pitzen, T. et al. Variation of endplate thickness in the cervical spine. Eur Spine J 13, 235-240.

2. Line 28: You talk about vertebrae, and line 23 you talk about the endplates to say similar things, which one is more accurate?

Authors' response: Thanks very much for your careful check. It should be vertebral endplates. We apologize for this error, and have correct it in revision manuscript.

3. Lines 34: why do you need a 3D coordinate system if you get already a point cloud associated with a coordinate system, that means you are not making a new coordinate system by translating rotating and maybe scaling to a new one?

Authors' response: We appreciate your comment. Since the vertebrae vary in footprint, and it is difficult to make the endplate surface face the camera lens perfectly vertically, the coordinates of the point at the same location on different vertebrae may be different in the system default 3D coordinate system.

In order to make the measurement performed under the unified standard, we established a new 3D coordinate system based on the endplate surface. The detailed steps that how to define the 3D coordinate system was described in the Protocol section.

4. Line 40: characteristic points? what are they? should be probably defined later clearly. Personally I got lost in the text.

Authors' response: Many thanks for your comment. In this protocol, in order to describe the morphological features of vertebral endplates, three sagittal and three frontal surface curves were symmetrically fitted on endplate surface, and 11 equidistant points were selected in each curve. Then, parametric equations of endplate surface were deduced based on coordinates of the 66 points. The detailed steps that how to define the characteristic points were described in the Protocol section.

5. Line 53: "frequent", what does it mean frequent? once a year? or 365 times a year?

Authors' response: We appreciate the reviewer's comment. In order to be prudent, we have adjusted the statement:

"The spine is subject to a wide array of degenerative, traumatic and neoplastic disorders and as a result may need surgical intervention."

6. Line 58: Developing mathematical models of the spine? it is a really "large" statement, why has not been developed yet? is it just a matter of endplates?

Authors' response: Thank you very much for your kind suggestion. In order to be prudent, the tone of related statement has been adjusted in the revised manuscript：

"Furthermore, information on the exact shape and geometry of the vertebral endplates is important for understanding the biomechanics."

7. Line 68: insufficient or unsuitable. Why it is insufficient or unsuitable? Back up? is your model now sufficient and suitable?

Authors' response: Many thanks for your comment. As mentioned above, an ideal device should mirror the three dimensions of endplate morphology. The accurately and comprehensively quantitative data of vertebral endplate is prerequisite for developing and improving disc prostheses. However, many previous studies mainly focused on anteroposterior diameter and width, or concavity in midsagittal plane, which could not adequately describe the endplate morphology. In addition, the accuracy and reliability of existing geometric data may be problematic due to the lack of a standardized measurement protocol and lower precision measuring instruments.

In order to be prudent, the tone of related statement has been adjusted in the revised manuscript:

"data on the morphology of the vertebral endplate is scarce."

8. Line 72: X-ray. Do you mean radiograph?

Authors' response: Thank you very much for your kind suggestion. As you point out, the X-ray means radiograph. According to your comment, the "X-ray" now is revised as "radiograph".

9. Line 93: What does mean too many? 10? 20?.... millions?

Authors' response: Many thanks for your comments. On each endplate, six surface curves were symmetrically chosen that three of these in the sagittal plane and the other three in the frontal plane. Then, 11 equal points were selected in each curve to be measured for their coordinates. Therefore, each endplate could yield a total of 66 point and corresponding coordinates. The parametric equation of each curve was deduced based on coordinates of 11 points using the polynomial fitting method in MATLAB, and the parametric equation of each endplate surface was deduced based on coordinates of 66 points.

10. Line 98: intricate shapes. Back up? or your own opinion, if yes prove?

Authors' response: We appreciate the reviewer's comment. Compared with the thoracic and lumbar vertebrae, the subaxial cervical vertebrae has a special component, uncovertebral joint. In order to distinguish it from the endplate, a best-fit plane was defined using the least squared method. Then, the intersection curve formed by the best-fit plane and the endplate surface was the boundary between the uncovertebral joint and the superior endplate. The specific operation was described in the Discussion section.

Meanwhile, the corresponding literature [1] has also been added in revision manuscript to support the statement.

References:
[1] Langrana NA, Kale SP, Edwards WT, Lee CK, Kopacz KJ. Measurement and analyses of the effects of adjacent end plate curvatures on vertebral stresses. The spine journal : official journal of the North American Spine Society. 2006;6(3):267-78.

11. Line 104: where is the vertebra on the platform facing the camera?

Authors' response: Many thanks for your comment. In the Figure 1, we did not place a vertebra on the platform of the scanner, but showed the non-contact optical 3D range flatbed scanner separately. During scanning, the vertebra was placed vertically on the platform of the scanner, with the endplate facing the camera lens and an active light source used. We obtained 19 cervical spine specimens (16 males and 3 females, average age 53 years; age range 38-64 years), which were spontaneously dried and stored at a constant temperature and humidity to prevent changes in shape or dimension.

According to the publishing process of the JOVE, if the manuscript is accepted, JoVE's Ph.D. scriptwriters will translate the manuscript into a video script, and a professional videographer will shoot the video based on the video script. Everything and detailed steps will be shown in the video.

12. Line 106: if you get a point cloud data (by definition there is a coordinate system) so why do you need to do that later?

Authors' response: Many thanks for your comment. This step was the process of acquiring the point cloud of the vertebral endplate. The scanner is high-speed and highly accurate (precision 0.02 mm, 1,628×1,236 pixels, input time 3 seconds), which can efficiently capture the surface morphology of a targeted object and convert the corresponding information into digital point cloud. Each vertebral endplate was scanned using the scanning system to acquire surface geometric parameters. After scanning, the endplate was converted into digital points called the point cloud. In the software system, the point cloud was further processed and created a 3D surface model.

13. Line 113: redundant points? how do you define redundant points? those have same coordinates? what is the error?

Authors' response: Thank you very much for your suggestion. When scanning, the morphology information of the platform may also be recorded, and the formed point cloud was called redundant points in this protocol. The main purposes of the protocol were to devise a measurement protocol and an algorithm to obtain quantitative parameters of vertebral endplates; to develop a mathematical model that allows for a realistic representation of vertebral endplates without digitizing too many landmarks. Thus, the study focused primarily on the morphology of endplates. In order to show the action steps more intuitively, we removed the redundant points and the unnecessary vertebral components, such as the posterior elements and osteophytes, and only the vertebral endplate was preserved.

Since the information of the target object recorded by the point cloud was three-dimensional, the coordinates of these digital points were different. According to the Operations Guide of Geomagic Studio software, the errors were systematic error and random error. So, noise points with obvious sharp spurs laterally or vertically were removed in this protocol.

14. Line 19: 3D image. Image has many definitions depending on fields. I am not sure the on the use here.

Authors' response: We appreciate your comment. According to your suggestion, we have reorganized the sentence in the revised manuscript：

"Click Fit All In icon in the toolbar at the bottom to load the reconstructed image to the main window of the presentation software."

15. Line 140: mark three anatomic landmarks. Why three? it is not too low? because before you said not too many landmarks.

Authors' response: Many thanks for your comments. Before measurements were conducted, the endplate 3Dcoordinate system was defined to transform the digitized points into local coordinate system. These three anatomicpoints were used to define the coordinate system, and the detailed steps that how to define the coordinate system was described in the Protocol section.

In this protocol, on each endplate, six surface curves were symmetrically chosen that three of these in the sagittal plane and the other three in the frontal plane. Then, 11 equal points were selected in each curve to be measured for their coordinates. Therefore, each endplate could yield a total of 66 point and corresponding coordinates. We developed a parametric model representing osseous endplates, which was fitted based on the coordinates data of the 66 points, and developed an algorithm capable of describing their 3D morphological characteristics conveniently and efficiently.

We think 66 points from six surface curves are adequate to describe the morphological features of endplates. The reliability tests indicated that the 3D model could make a realistic representation of endplate surface, and the parametric equations had good reliability and reproducibility to quantify endplate morphology [1].

References：

[1] Feng, H. et al. Morphometry evaluations of cervical osseous endplates based on three dimensional reconstructions. Int Orthop, doi:10.1007/s00264-018-4053-1 (2018).

16. Line 194: I am definitely lost here. you say 11 points ... plus the two endpoints which means 13 points? and 66 points on each endplate. does it mean you have 79 points on each endplate. The 79 points are in 3D which means 237 values? and you are trying to fit a polynome of degree 4?

Authors’ response: We appreciate the Reviewer’s comment and apologize for the unclear description. On each endplate, six surface curves were symmetrically chosen: three of these were in the sagittal plane and the other three in the frontal plane. Taking the mid-sagittal curve as an example, divide the mid-sagittal diameter equally into 10 parts. Go through each equidistant point, choose nine intersections formed by the frontal planes and the mid-sagittal curve, resulting in a sum of 11 points, together with the two endpoints. So, each endplate has 66 such points.

We apologize for the confusing description again and have revised the relevant description:

“2.2.3.1 Taking the mid-sagittal curve as an example, divide the mid-sagittal diameter equally into 10 parts, resulting in a sum of 11 points, including 9 intermediate points and two endpoints(refer to 2.1.3 and 2.2.1).

2.2.3.2 Go through each equidistant point, obtain nine fitting curves on the endplate surface (refer to 2.2.2). Click Curve from Scan icon and select the intersection of the fitting curves and the mid-sagittal curve. Finally, obtain a total of 66 points on each endplate (11 points per curve multiply 6 curves). ”

17. Line 239: why do 1 to 5? what will happen if Matlab's update get rid of this functions? that means the protocol is not working anymore because the reader does not understand what is going on. I suggest you explain what you are doing and then give details of how to do it.

Authors’ response: Many thanks for your comment. The “i=1:5” is the code language of MATLAB that helps to determine the fit order of the parametric equation. The recommended version of Matlab was listed in the Table of Materials. Besides, this code can work in all the current versions of MATLAB. In the future, if Matlab's update get rid of this functions, we believe that the manufacturer will recommend new code for researchers. Besides, as an alternate method, we can also use the Curve Fitting Tool to determine the fit order of the parametric equation by adjusting the number of order to observe the fitting degree.

18. Line 241: 0.01. How did you get this value?

Authors' response: Many thanks for your comment. When the sums of squared error was set below 0.1, we can observed a good fitting effect in the Curve Fitting Tool. In this Protocol, we recommend to set the sums of squared error below 0.01 to obtain higher precision. After the parametric equation was fitted, we also evaluated the validity of the geometric model representing the endplate morphology, and the results revealed it was accurate and reproducible to represent endplate surface. Besides, other researchers can readjust the value to satisfy different demands.

19. Line 243: you do not need in a new line if you put ";" after the "end".

Authors' response: We appreciate and really agree with your suggestion. Following the reviewer's suggestion, we agree with the comment and re-wrote the sentence in the revised manuscript as the following:

we have reorganized the description of relevant operation codes and deleted the redundant sentence in the revised manuscript：

"Input the code "for i=1:5z2=polyfit(x,z,i); Z=polyval(z2,x); if sum((Z-z).^2)<0.01 C=i break; end; end"."

Thanks your suggestion again.

20. Line 245: C value? not clear to me is it the same c in line 239? one capital one lower case.

Authors' response: We appreciate your comment. As you pointed out, they are really the same. We apologize for the typo. According to the reviewer's suggestion, we have capitalized all the code C in the revised manuscript.

21. Line 257: Least square method reference?

Authors' response: Many thanks for your comment. In this protocol, the Parametric equations of endplate surface were fitted using polynomial fit whose principle was least square method. To avoid ambiguity, we have deleted the redundant sentence (The polynomial fit used in this protocol is based on the least square method).

22. Line 267: the equation. The means already defined of will be just bellow. But I do not know what the "the equation" refers too.

Authors' response: Many thanks for your comment. We apologize for the confusing description. "the equation" refers to the parametric equation that have been fitted using polynomial in the steps above.

According to your comment, we have modified the related description in the revised manuscript:

“Px is the parameters of the parametric equation that have been fitted using polynomial in the steps above.”

23. Line 288: 45000 digital points. is it not too many as you said before or not?

Authors’ response: Many thanks for your comment. The scanner employed in this protocol is high-speed and highly accurate, which can efficiently capture the surface morphology of a targeted object and convert the corresponding information into digital points called the point cloud. Each vertebral endplate was scanned using the scanning system to acquire surface geometric parameters. After scanning, each endplate was converted into point cloud, Which consisted of at least 45,000 digital points.

In the software system, the point cloud was further processed and created a 3D surface model to measure its surface geometry. Before measurements were conducted, a 3D coordinate system was defined using three anatomic points to transform the digitized points into local coordinate system. Then, six surface curves were symmetrically chosen on each endplate, and 11 equal points were selected in each curve to be measured for their coordinates. Therefore, each endplate could yield a total of 66 point and corresponding coordinates. The parameter equation was fitted based on the coordinates data of the 66 points.

Therefore, the number of characteristic points we chose to fit the parametric model is 66.

24. Lines 293 and 294: A distance between two points how can give you linear parameters? I feel there is a problem in the sentence.

Authors’ response: We appreciate your comment and apologize for the language problems. Following your suggestions, we have reorganized the sentence in the revised manuscript:

“The linear parameters were measured by calculating the distance between two endpoints.”

25. Line 301: achieve satisfaction. What is satisfaction? Are any results satisfactory? opinion!

Authors’ response: Many thanks for your comment. When the sums of squared error was set below 0.1, we can observed a good fitting effect in the Curve Fitting Tool. In this Protocol, we recommend to set the sums of squared error below 0.01 to obtain higher precision. After the parametric equation was fitted, the validity of the geometric model representing the endplate morphology was evaluated by comparing coordinate value of 15 randomly selected points with their corresponding value auto-generated from parametric equations (Table 1). The statistical results revealed it was accurate and reproducible to represent endplate surface ($R = 0.98$, $p > 0.5$).

JoVE is a methods-based journal, and publishes expanded descriptions of techniques that have previously appeared in results-based journals. According to the INSTRUCTIONS FOR AUTHORS of JOVE, authors should focus on the protocol and not on the representative results. More information can be available in INSTRUCTIONS FOR AUTHORS of the JoVE's website

(https://www.editorialmanager.com/jove/default.aspx). Besides, for more research results of this Protocol, please refer to the previous study[1].

Table 1. The validity of the geometric model representing the endplate morphology

Measurements value	N	Z coordinate value	T	P	R
Original points	15	1.75±0.87	0.26	0.80	0.98
Comparison points	15	1.74±0.91			

Data were mean±standard deviation (mm). Original points: 15 randomly selected points on the original 3D reconstruction image; Comparison points: corresponding points auto-generated from parametric equations; R: correlation coefficient.

References：

[1] Feng, H. et al. Morphometry evaluations of cervical osseous endplates based on three dimensional reconstructions. Int Orthop, doi:10.1007/s00264-018-4053-1 (2018).

26. Line 303 and lines 308 309 should be written in a mathematic fashion! Line 310: The Px WERE parameters or maybe are better.

Authors' response: Thank you very much for your kind suggestion. In this protocol, the parametric equations were fitted using MATLAB. The number and value of parameters of the equation varies with the amount of data and the fit order. Besides, when acquiring geometric data or representation of endplates based on parametric equation, the equation should be inputted according in the code language format of MATLAB. If the input format was changed, the software may not work. Therefore, we listed the general equation in the output format of the MATLAB in the REPRESENTATIVE RESULTS part and the parameters of parametric equation representing the endplate surface in Table 2 in the manuscript.

27. Line 310: you say 66 coordinates, that means 22 points? Previously you talked about 66 POINTS!

Authors' response: Thanks very much for your careful check. We apologize for this error, and the sentence have been corrected in the revised manuscript:

"The PX was the parameters, which were deduced from the pre-measured coordinates of 66 points."

28. Line 377: manufacturing? Manufacturing what? not sure what means here.

Authors' response: Many thanks for your comment. Based on the morphology data obtained using Reverse engineering measurement, customizing products can be manufactured, for example, personalized artificial intervertebral disc.

29. Lines 377 and 378: are the basic and key technology, sounds like there are other parts to reverse engineering but on line 82 you said there are only two!

Authors’ response: Many thanks for your comment. The reverse engineering system employed in this protocol includes two subsystems: the instrumentation system and the software system. The instrumentation system is a noncontact optical 3D range flatbed scanner, which can efficiently capture the surface morphology of a targeted object and convert the corresponding information into digital point cloud. In the software system, the point cloud is further processed and created a 3D surface model, then the curve and surface editing, measurement and data processing are performed. In terms of technical principles, digital measurement and data processing are the basic and key technology of reverse engineering.

30. Line 380: accurate, it has not been proven to me it is accurate. I do not know what you compared to and with.

Authors’ response: Many thanks for your comment. There have been many excellent studies that were conducted employing 2D CT scan or 3D CT reconstruction to measure endplates geometry. However, some researches reported that CT measurement may overestimate the geometry parameters of endplates [1,2]. Such an overestimation is expected when scanning small, high-contrast objects, and can be attributed to partial volume averaging, beam hardening, and edge effects [1,3]. For these reasons, the quantitative accurate may be affected.

In recent years, reverse engineering has been increasingly applied to medicine field, which can digitize the existing physical parts into computerized solid models. Instead of the actual component, its solid model can be developed and converted into a physical prototype that can be used for testing. The technique makes it feasible to develop an accurate representation of the anatomical character of cervical vertebrae.

The instrumentation system we employed has a relatively high resolution and accuracy (precision 0.02 mm, 1628×1236 pixels, input time 3s). After scanning, a cervical endplate was converted into point cloud consisting of at least 45,000 digital points, which could make a good description of the surface details of the endplate. In the software system, the point cloud was further processed and created a 3D surface computer model allowing more convenient and more accurate measurement.

In previous studies, the reliability, validity and precision of the reverse engineering system for capturing surface geometry have been well established [4,5]. Moreover, Wang et al. [6] and Langrana et al. [7] respectively described lumbar endplate morphology using similar technique, and achieved good results, which offered further proofs that the technique can accurately and comprehensively quantify the three-dimensional anatomic morphology of vertebral endplates.

Besides, we also evaluated the reliability of measurements [8]. For intra-test reliability, 16 samples were randomly selected and measured twice at a two week interval and were assessed using intra-class correlation coefficient (ICC). To verify the accuracy of the measurements taken by the reverse engineering system, 20 samples were measured using a digital caliper (Heng liang tools Co. Ltd., Shanghai, China, Precision ±0.01 mm) and were evaluated using Cronbach alpha. As shown in Table 1, these values showed great agreement, as the value of ICC greater than 0.75 indicates good reliability and alpha values of 0.7-0.8 are regarded as satisfactory.

Hence, we utilized the reverse engineering system to record the morphology information of vertebral endplates, which could be an alternate method to evaluate surface morphology for future.

Table 1. Reliability of measurements

	Measurements	Intratest reliability	Measurements		RE vs Caliper
APD	First-remeasurement	15.76±1.3	APD	RE	16.47±1.31
	Remeasurement	15.86±1.61		Caliper	16.26±1.27
	ICC	0.85	Cronbach alpha		0.99
CMD	First-remeasurement	19.71±2.47	CMD	RE	20.7±3.05
	Remeasurement	19.41±2.43		Caliper	20.45±3.21
	ICC	0.96	Cronbach alpha		0.99

Data were mean±standard deviation (mm).

ICC: intra-class correlation coefficient; APD: antero-posterior diameter; CMD: center mediolateral diameter; RE: The reverse engineering system.

References:

[1] Silva MJ, Wang C, Keaveny TM, Hayes WC (1994) Direct and computed tomography thickness measurements of the human, lumbar vertebral shell and endplate. Bone 15 (4):409-414.

[2] Panjabi MM, Chen NC, Shin EK, Wang JL (2001) The cortical shell architecture of human cervical vertebral bodies. Spine 26 (22):2478-2484.

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[4] Keating AP, Knox J, Bibb R, Zhurov AI (2008) A comparison of plaster, digital and reconstructed study model accuracy. Journal of orthodontics 35 (3):191-201; discussion 175.

[5] Spalding SJ, Kwoh CK, Boudreau R, Enama J, Lunich J, Huber D, Denes L, Hirsch R (2008) Three-dimensional and thermal surface imaging produces reliable measures of joint shape and temperature: a potential tool for quantifying arthritis. Arthritis research & therapy 10 (1):R10.

[6] Wang Y, Battie MC, Videman T (2012) A morphological study of lumbar vertebral endplates: radiographic, visual and digital measurements. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 21 (11):2316-2323.

[7] Langrana NA, Kale SP, Edwards WT, Lee CK, Kopacz KJ (2006) Measurement and analyses of the effects of adjacent endplate curvatures on vertebral stresses. The spine journal : official journal of the North American Spine Society 6 (3):267-278.

[8] Feng, H. et al. Morphometry evaluations of cervical osseous endplates based on three dimensional reconstructions. Int Orthop, doi:10.1007/s00264-018-4053-1 (2018).

31. Line 382: It? what does the it refer to?

Authors' response: We apologize for unclear description. "It" refers to a non-contact optical 3D range scanning system. According to the reviewer's suggestion, we have reorganized the sentence in the revised manuscript:

"The scanner is primarily made up of control devices and an optical measurement integrating two cameras and a projector."

32. Line 384: compared with other measuring instruments. Such as ?

Authors' response: Many thanks for your comments. Please refer to the response to the comment 31.

33. Line 385: avoids point-by-point.... But what does it use? yes I know there are two cameras and projector but which method is using to get the point cloud.

Authors' response: Many thanks for your comments. The input time of the non-contact optical 3D range scanning system is 3 seconds, so it can capture the surface morphology data of the target object efficiently. During scanning, the projector as an active light source was responsible for emitting light, while the two cameras were used to record surface morphology information.

34. Line 388: we also verified the replicability? In another paper, right? if yes I do not think it should be claimed here at all if it was in another paper. so here you did not verify anything.

Authors' response: Many thanks for your comments. Please refer to the response to the comment 25 and comment 31.

35. Line 391: randomly? what is the thing that is random? the measurements? the days?

Authors' response: Many thanks for your comments. We apologize for the ambiguous statement. In this protocol, a total of 138 vertebral endplates were used. For intra-test reliability, 16 endplates were randomly selected from the 138 vertebral endplates and measured twice at a two-week interval, and were assessed using intra-class correlation coefficient.

We apologize for the confusing description and the relevant description have also been corrected in the revised manuscript:

"For intra-test reliability, 16 endplates were randomly selected from the 138 vertebral endplates and measured twice at a two-week interval, and were assessed using intra-class correlation coefficient."

36. General comment: Paragraph starting from line 399 to 408 should be probably rewritten. Line 405: especially important. Compare to what? Line 407: from previous measurement protocol, which ones? It should have been cited more into details and probably

make comparison to show that your protocol is better or worse.

Authors' response: We apologize for the language problem. It has been demonstrated that several cervical vertebra surgery postoperative complications are related with morphologic mismatch between the anatomic geometry of cervical endplates and prostheses [1-3]. Therefore, it is essential to design cervical devices that imitates the shape of endplates adjacent to natural discs in all three dimensions. Accurate and detailed information of vertebral endplates is important and necessary to design appropriate cervical devices.

Many previous studies, mainly focusing on anteroposterior diameter and width, or concavity in midsagittal plane, could not adequately describe the endplate morphology [4-8].

As your mentioned, we didn't provide direct comparison data with other factors. In order to be prudent, the tone of related statement has been adjusted in the revised manuscript, and the language have also been reorganized and refined :

"There are important and considerable applications for detailed and comprehensive anatomy data of vertebrae, such as designing spinal implants, improving the fidelity of the finite element models of spine and developing mathematical models. Besides, the vertebral endplate is essential to maintain the integrity and function of the intervertebral disk, and also serves a mechanical interface to transfer stress. Therefore, the quantification of endplate geometry is important. With the help of reverse engineering, endplate morphology can be quantified intelligently and comprehensively. In this protocol, six characteristic curves were fitted on the surface of each endplate, and a 3D coordinate system was established to quantify the spatial morphology."

References:

[1] Lin CY, Kang H, Rouleau JP, Hollister SJ, Marca FL (2009) Stress analysis of the interface between cervical vertebrae end plates and the Bryan, Prestige LP, and ProDisc-C cervical disc prostheses: an in vivo image-based finite element study. Spine 34(15):1554-1560.

[2] Steffen T, Tsantrizos A, Aebi M (2000) Effect of implant design and endplate preparation on the compressive strength of interbody fusion constructs. Spine 25(9):1077-1084.

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[5] Chen H, Zhong J, Tan J, Wu D, Jiang D (2013) Sagittal geometry of the middle and lower cervical endplates. Europ Spine J 22(7):1570-1575.

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[7] Panjabi MM, Duranceau J, Goel V, Oxland T, Takata K (1991) Cervical human vertebrae. Quantitative three-dimensional anatomy of the middle and lower regions. Spine 16(8):861-869.

[8] Tan SH, Teo EC, Chua HC (2004) Quantitative three-dimensional anatomy of cervical, thoracic and lumbar vertebrae of Chinese Singaporeans. Eur Spine J 13(2):137-146.

37. Line 412 and 413: realistic, and accurate representations. Not convinced. Has not been shown maybe on the surface for you but not for me. Again paragraph from line 416 to 423, are you using the results and discussion of another paper. I don't think it should be claimed here at all even done by same researchers. The wording good reliability and reproducibility is again an opinion not backed up. Line 444: claiming something that is done from previous etude as done here!

Authors' response: Many thanks for your comments. Please refer to the response to the comment 25 and comment 31.

38. Line 390 and 391: You have 20 endplates, why only 16 were used after that? why not using the extra 4? Might make the reliability study stronger!

Authors' response: Thanks for your comment. We obtained a total of 19 cervical spine specimens, which were spontaneously dried and stored at a constant temperature and humidity to prevent changes in shape or dimension. The sample consisted of 16 men and 3 women, and the age varied between 38 years and 64 years with an average age of 53 years. Intact vertebral endplates without pathologic deformation or broken parts were included; 11 endplates were excluded. Because of poorly scanned images, 3 endplates were also excluded, leaving a total number of 138 vertebral endplates (68 inferior and 70 superior endplates).

The measurements were accomplished by two of the authors, who have rich knowledge of spine surgery. Besides, we also conducted some tests to verify the replicability of measurements. To assess the intra-test reliability, 16 samples were randomly selected and measured twice at a two-week interval. To verify the accuracy of the measurements taken by the reverse engineering system, 20 samples were measured using a digital caliper.

39. Line 432 to line 438, is it part of the protocol, I do not see why it should be in the discussion.

Authors' response: We appreciate the reviewer's comment. As you pointed out, the content you mentioned here was actually placed in the protocol part in the initial manuscript. However, In the previous review comments, the editors gave us the following comments and asked us to revise the manuscript:

"Any text that cannot be written in the imperative tense may be added as a "Note". Please include all safety procedures and use of hoods, etc. However, notes should be used sparingly and actions should be described in the imperative tense wherever possible. Please move the discussion about the protocol to the Discussion."

Since the content you mentioned is not necessary steps, but some supplementary steps instruction for special cases, we put them in the Discussion.

40. Line 438 and Line 439, do you use the anatomical points to establish the coordinate system, or the 3D anatomical points are defined in a coordinate system. I do not think the

authors are aware of what is a 3D coordinate system is.

Authors’ response: Many thanks for your comment. Before measurements were conducted, a 3D coordinate system was defined to transform the digitized points into local coordinate system. When defining the endplate 3D coordinate system, the first step was marking three anatomic landmarks on the epiphyseal rim: the first two are the left and right endpoints of the endplate trailing edge; the third is the anterior median point. Then, the mid-sagittal plane was defined using the normal of the line of two trailing edge endpoints and the anterior median point. The intersection of the mid-sagittal plane and the posterior epiphyseal rim was the posterior median point. The midpoint of the line between the anterior median point and the posterior median point was defined as the origin of the coordinate system. The connected line of the anterior-posterior median point formed the Y-axis, pointing forward. The line parallel to the line linking the two trailing edge endpoints formed the X-axis. The Z-axis was perpendicular to the X-Y plane. The detailed steps were described in the Protocol.

The description about the anatomical points in the Discussion was to help mark them accurately. But to avoid ambiguity, we have reorganized the statement in the revised manuscript：

“How to mark the three anatomical points on the endplate surface accurately when establishing the 3D coordinate system is critical.”

41. Line 440: reconstruction imagine? what does it mean?

Authors’ response: We appreciate the Reviewer’s comment and apologize for the typo. It should be “image”, and have been corrected in the revised manuscript.

42. Line 449: novice well experienced! Do we really need to be well experienced, do we really become well experienced when applying the same protocol (same steps) again and again especially if we do not understand them? and well experienced in what? applying a protocol. I do not see the point of trying to become if the idea just to repeat without understanding the main ideas behind the steps which have not been described here.

Authors’ response: Many thanks for your comments. The main purposes of the protocol were to devise a measurement protocol and an algorithm to obtain quantitative parameters of vertebral endplates; to develop a mathematical model that allows for a realistic representation of vertebral endplates without digitizing too many landmarks.

The suggested protocol, which is accurate and reproducible, may be an alternate method to assist in more sophisticated morphological studies in the future. Besides, it can also contribute to designing personalized spinal implants, planning surgical acts, making a clinical diagnosis and develop accurate finite element models.

43. Once again, thanks for your valuable comments and suggestions.

Responses to Reviewer #3:

We fully appreciate your kind comments and valuable suggestions. These constructive suggestions are very important to polish the quality of our manuscript. By taking the suggestions into consideration, the manuscript have been carefully checked and revised.

1. General comment: Process diagram / Flow chart could have given more clarity.

Authors' response: We appreciate your comment. We have carefully checked the manuscript and improved the Protocol to make it clearer and more coherent.

2. Thanks again for your valuable suggestion.

Responses to Reviewers' Comments

Manuscript number: JoVE59371R3

Responses to Editors:

We fully appreciate your kind comments and valuable suggestions. These constructive suggestions are very important to polish the quality of our manuscript. We have studied the comments carefully and have made correction accordingly. The main corrections in the manuscript and the responses to the editors' comments are as following:

1. General comment: Can you include more of your response to Reviewer 2 (in particular, points 25 and 31, including the tables) in the manuscript? While it's true that we are not focused on results, it would be best to have more evidence of repeatability here.

Authors' response: Thank you very much for your kind suggestion. Following your suggestions, the corresponding content, including the tables, have also been added in revision manuscript. Besides, we also obtained the RightsLink Printable License in PDF format on the publisher's website, which also was uploaded in the Editorial Manager account.

2. Protocol 3.1.1/3.1.2: It's still unclear which 'corresponding data' is being input here-please clarify.

Authors' response: We appreciate your comment and apologize for the unclear description. The "corresponding data" refers to X or Z coordinate data of the 11 characteristic points in one curve that has been measured in the previous steps. Meanwhile, we have added the corresponding description in the revised manuscript.

3. 4.3: Is this done the same way as in 5.4?

Authors' response: Many thanks for your comment. The input format of equations is different in the step 4.3 and 5.4.

In the 4.3, the input format is "z= P_{00} + P_{10}*x + P_{01}*y + P_{20}*x^2 + P_{11}*x*y + P_{02}*y^2 + P_{30}*x^3 + P_{21}*x^2*y + P_{12}*x*y^2 + P_{03}*y^3 + P_{40}*x^4 + P_{31}*x^3*y + P_{22}*x^2*y^2 + P_{13}*x*y^3 + P_{04}*y^4".

While, the input format in the step 5.4 is "z=@(x,y)P_{00} + P_{10}.*x + P_{01}.*y + P_{20}.*x.^2 + P_{11}.*x.*y + P_{02}.*y.^2 + P_{30}.*x.^3 + P_{21}.*x.^2.*y+ P_{12}.*x.*y.^2 + P_{03}.*y.^3 + P_{40}.*x.^4 + P_{31}.*x.^3.*y + P_{22}.*x.^2.*y.^2+ P_{13}.*x.*y.^3 + P_{04}.*y.^4;".

We apologize for the unclear description, and have added further explanations in the revised manuscript.

4. Table 1/2: So, is every 0 value one that was small? How small was this, an absolute value of less than .0001?

Authors' response: Many thanks for your comment. As you said, the value of every parameter we set to 0 is too small and close to zero, and all less than 0.0001.

For example, all the original parameter values of the C3 inferior endplate are as follows:

"P_{00} = 1.989, P_{10} = 0.002214, P_{01} = -0.03561 ,P_{20} = -0.01286, P_{11} = 0.0009194, P_{02} =

-0.05289, P_{30} = 1.715e-05, P_{21} =- 0.001071, P_{12} = -2.4e-05, P_{03} = 0.0006198, P_{40} = 0.000204,P_{31} = -1.914e-05 , P_{22} = 0.0001671, P_{13} = -2.928e-05, P_{04} = 0.0002251"

Among them, P_{30}, P_{12}, P_{31}, P_{13}, are too small and close to zero. For the convenience of subsequent calculations, such as acquiring geometric data based on parametric equations, we set those parameter values to zero.

5. Can you provide some example files (e.g., the point clouds) as supplemental material?

Authors' response: Thank you very much for your kind suggestion. Following your suggestion, a point clouds file (.ASC format) of a cervical vertebra and a .stl format file that records the surface information of one endplate have been uploaded in the Editorial Manager account.

6. Thanks again for your valuable suggestion.

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