Validation of a Robust Method for Quantification of Three-Dimensional Deformation of the Thoracic Aorta Using Diffeomorphic Image Registration

Zhangxing Bian[1,2], Jiayang Zhong[1,2], Jeffrey Dominic[1,2], Gary E. Christensen[3], Charles R. Hatt[1,4], and Nicholas S. Burris[1,5].

1. Department of Radiology, University of Michigan
2. Department of Electrical Engineering and Computer Science, University of Michigan
3. Department of Electrical and Computer Engineering, University of Iowa
4. Imbio, LLC
5. Department of Biomedical Engineering, University of Michigan

Version typeset February 21, 2021

Correspondence author: Nicholas S. Burris. Email: nburris@med.umich.edu

Abstract

Purpose: Accurately assessing thoracic aortic aneurysm growth is important. Maximal aortic diameter is the primary metric that is used to assess growth, but it suffers from substantial measurement variability. The recently proposed method, Vascular Deformation Mapping (VDM), quantifies three-dimensional aortic growth using an approach based on deformable image registration. However, VDM has not yet been validated to support the improved accuracy of VDM-derived measurements compared to standard of diameter assessments.

Methods: Thus, we created a group of synthetic cases with great diversity to systematically test and validate the robustness of VDM under a variety of variables that influence clinical CTA data, such as respiratory motion, slice thickness and image noise. Furthermore, by comparing the VDM-derived measurement with the manual measurement from two perspectives – the accuracy and localization ability of maximal diameter change, we demonstrate the superiority and practical use of our method on clinical growth assessments.

Results:

Conclusions:

Contents

I. Introduction

The thoracic aorta is the largest artery in the body, carrying blood from the heart to the rest of the systemic circulation. A variety of degenerative and inflammatory processes cause degrade the structural integrity of the normally elastic aortic wall resulting in thoracic aortic aneurysm (TAA). Aneurysms of the thoracic aorta are often asymptomatic and indolent, either remaining stable or growing slowly over a period of years or decades; however, a small fraction of patients experience acute complications such as rapid growth, aortic dissection or aortic rupture, all of which necessitate urgent surgical repair and are potentially fatal. Current clinical guidelines recommend routine imaging surveillance of TAA and surveillance regimens typically consist of annual or biannual computed tomography angiography (CTA) examinations to assess for interval growth for other aortic complications. Maximal aortic diameter is the primary metric that is used to assess growth and determine candidacy for surgical repair, with measurements typically performed either manually or in a semi-automated fashion using analysis software that allows for multi-planer or centerline based measurements in planes orthogonal to the aortic axis.

Despite optimal measurement technique and operator experience, current diameter measurement techniques are associated with substantial measurement variability – on the order of ±2-5 mm – often limiting confident assessment of aortic growth at typical aortic growth rates (<1mm per year). There are many potential sources of error/variability with diameter measurements, however, common issues involve differences in measurement location along the length of the aorta, differences in angulation of the 2-dimensional measurement planes, and differences in radial position of the diameter calipers (especially when the aortic cross-section is non-circular/elliptical). Without improved methods to measure aortic growth, confident determination of disease progression, accurate assessment of patient risk and fully informed treatment decisions will not be possible.

To address this problem, our group has recently proposed a method, termed Vascular Deformation Mapping (VDM)[?] , to quantify aortic growth in a more accurate and comprehensive fashion using an approach that employs deformable image registration to quantify three-dimensional changes in the aortic wall morphology using high-resolution volumetric computed tomography angiography (CTA) data. Preliminary reports of shown that the VDM technique may be useful for more complete depiction of the extent of TAA growth to inform surgical planning and for the assessment of growth during imaging surveillance, however, the VDM approach and key algorithms have not yet been validated in a manner to that supports the improved accuracy of VDM-derived measurements compared to standard of care diameter assessments. While b-spline based techniques for deformable image registration are well-validated, and can achieve submillimeter registration accuracy using clinical CT data, a variety of factors related to physiologic motion and image reconstruction may influence the accuracy of registration results between serial aortic CTA examinations, and thus a comprehensive evaluation of the influence of these factors is warranted.

The aim of this study was twofold: 1) examine the influences of a variety of variables that influence clinical CTA data such as respiratory motion, slice thickness and image noise

on the accuracy of VDM-derived deformation assessment using a representative sample of synthetic CTAs, and 2) compare the accuracy of growth measurements between VDM and experienced manual raters using synthetic phantoms to better quantify the potential benefit on clinical growth assessments.

II. Methods

In this section, we will first introduce the VDM registration pipeline and the procedure to create the synthetic cases for testing the VDM. Then, we elaborate the approach of comparing the manual measurement and VDM-based measurement on the clinical task – measuring the maximal diameter change.

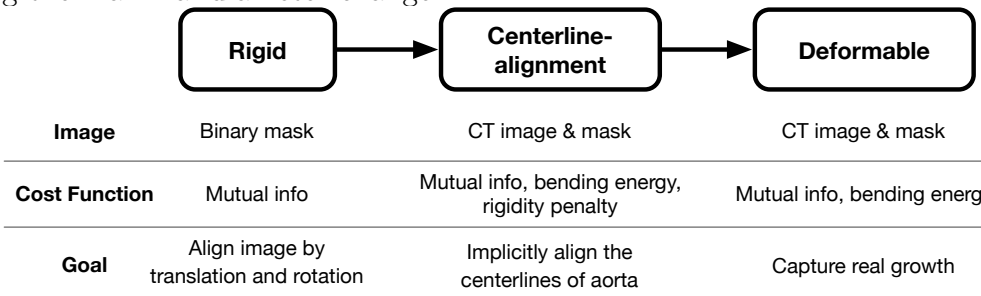


Figure 1: The registration pipeline.

II.A. VDM Registration

Given two CT images, we use the VDM, a deformable image registration pipeline, as shown in Fig.1, to capture the deformation of the aortic wall. The registration consists of three main steps: rigid, centerline-alignment, and deformable registration. The rigid registration only uses the mask of the aorta to rigidly align the images; the centerline-aligning and deformable registration use a multi-image multi-cost strategy, with each pair of images focusing on a different cost. Specifically, centerline-aligning, which can be more formally stated as highly-regularized deformable image registration with aortic rigidity penalty, will help align the centerlines of the aortas implicitly, allowing the later deformable registration to only focus on growth, without needing to fix any bulk motion or affine scaling. The aorta in the moving image will still move rigidly as in rigid registration, but the remaining areas of the moving image outside the aorta can move in a non-linear manner, which will help align the aortas more precisely. The last step, deformable registration, performs B-spline-based registration to capture the real growth.

During the registration, three cost functions involve – mutual information, bending energy, and rigidity penalty. Mutual information[1] is a widely used metric in image registration to measure the image similarity; bending energy[2] is used to penalize the sharp changes in the deformation field and regularise the nonrigid transformation; and rigidity penalty[3] will

penalize the large deformation and can be used to enforce a part of image transform in a rigid manner when using with a mask. The registration tool we used is Elastix[4].

II.B. Create Synthetic Deformation

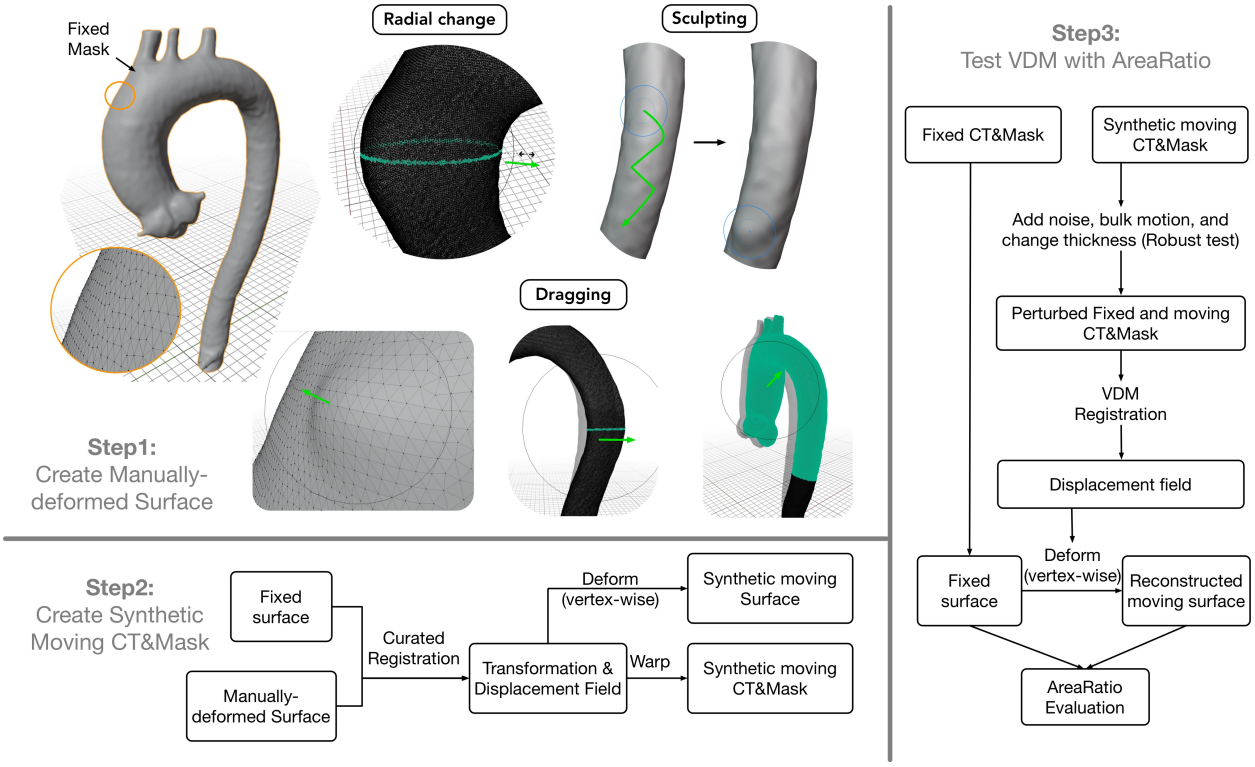


Figure 2: The pipeline for creating synthetic images and validation process with AreaRatio. In step1, we use three ways to create the deformations on 3D meshes, which are radial changing, sculpting, and dragging. In step2, we take the manually-deformed surface to a curated registration process and use the resulting transformation to warp the CT and mask to obtain the synthetic images, and use the displacement field to deform the fixed surface to create the synthetic moving surface. In Step3, we test our VDM registration pipeline using synthetic images with various disturbances. We deform the fixed surface by the resulting displacement field from VDM registration and compare the AreaRatio against the ground-truth AreaRatio computed from the fixed surface and synthetic moving surface. The results of registration and robust test can be found in Fig.4.

Step1: create manually-deformed surface. We first build the 3D fixed surface from the fixed image's mask, and then we use the Blender (www.blender.org), an open-source 3D modeling software to create synthetic deformation. In this paper, we use the vertex-vertex type mesh, meaning a mesh can be presented by of a set of vertices $\mathcal{V} = v_1, v_2, ..., v_N$, and each face is constructed by three vertices and can be written as $f_{\{v_i,v_j,v_k\}}$. Each vertex v_i has a position (x_i, y_i, j_i) in the 3D space. When making manual deformation to the surface using Blender, we change the position of a few vertices, and we denotes the vertices

in deformed surface as $\tilde{\mathcal{V}}$ and note that the vertex-wise correspondence is maintained, i.e. $v_i \leftrightarrow \tilde{v_i}, v_i \in \mathcal{V}, \tilde{v_i} \in \tilde{\mathcal{V}}$. Since a surface can be represented by a set of vertices, for convenience, we will simply use the same notation to represent surface, for example, $\mathcal{V}_{fixed}$ representing the fixed surface.

We created 31 synthetic cases in various locations on the aorta and with various degrees of deformation (the displacement magnitudes range from 0-7mm), which cover most situations we observed in the real clinical scenario, to guarantee the diversity of our synthetic dataset. For example, we created the manually-deformed surface in three ways, with each mimicking a scenario: radial changing mimics the aortic aneurysm growth in the radial direction; sculpting mimics some random irregular deformation and the bulge with strip shape, which often develops in descending aorta; and dragging single vertex or a group of vetices can give examples of local growth, bending, longitudinal stretch, and respiratory effect.

Step2: create synthetic moving CT&Mask. This step aims to obtain the synthetic moving surface and synthetic moving CT&Mask given the manually-created surface. We perform a curated registration procedure on the fixed surface and manually-deformed surface to generate the transformation that can be used to warp the fixed image/mask to obtain synthetic moving image/mask and the displacement field that can be used to vertex-wisely deform the fixed surface $\mathcal{V}_{fixed}$ to obtain the synthetic moving surface $\mathcal{V}_{smoving}$. Specifically, we construct a binary image where the voxel that contains any vertex is one (otherwise zero) for both fixed and manually-deformed moving surfaces. These two binary images indicate the silhouette of the aorta, so we refer to them as boundary images. Then we register these two boundary images and use the resulting transformation to warp the fixed CT and mask to obtain the synthetic images, and also use the resulting displacement field to deform the fixed surface to create the synthetic moving surface. Note that the fixed surface and the synthetic moving surface have vertex-wise correspondence, which allows us to compute the AreaRatio for each face. We take the AreaRatio computed from $\mathcal{V}_{smoving}$ and $\mathcal{V}_{fixed}$ as ground truth for the later evaluation step (Step3 in Fig.2).

Step3: Test VDM with AreaRatio. After obtaining the synthetic moving image&mask, we take the fixed image&mask and synthetic moving image&mask to test our VDM registration under various disturbances which can be encountered in the real clinical scenarios, such as image noise, bulk motion, and various thickness of the image slice. We take the AreaRatio as the metric to measure the registration performance.

AreaRatio is defined as the ratio of the area of a face in one mesh to that of the corresponding face in another mesh.

$$AreaRatio_f = \frac{S(f_{\{\tilde{v_i},\tilde{v_j},\tilde{v_k}\}})}{S(f_{\{v_i,v_j,v_k\}})}, \tag{1}$$

where the $S(\cdot)$ indicates the area of a face. The reasons we prefer using AreaRatio over the Jacobian determinant are three-fold: (1) the AreaRatio is more straightforward and intuitive to represent surface expansion and compression. (2) the visual effect of AreaRatio plot is more consistent with the humans' perception of growth (deformation) when plotting

the values onto the surface. (3) ???

After registration, we take the resulting displacement field to vertex-wisely deform the fixed surface $\mathcal{V}_{fixed}$ to get reconstructed moving surface $\mathcal{V}_{recons}$ and comapre the AreaRatio against the ground truth AreaRatio that are computed by $\mathcal{V}_{fixed} and \mathcal{V}_{smoving}$. The results are reported in Section.III.A..

II.C. Maximal Diameter Measurement: Raters v.s. VDM

In this section, we focus on the clinical task, i.e., measuring the maximal diameter change (representing the maximal deformation), and introduce the procedure used to compare VDM-based measurement and manual measurement.

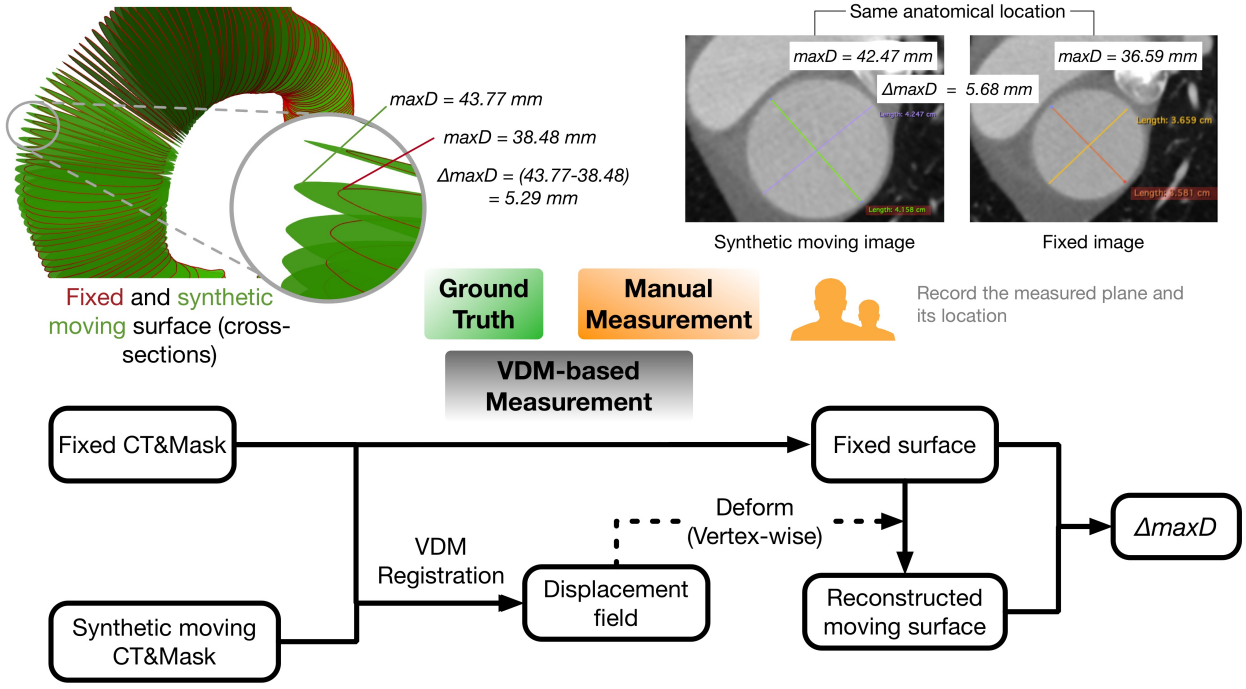


Figure 3: Validation process on maximal diameter change.

We invite two experienced raters to measure the maximum deformation (i.e., the maximal diameter change) following the common practice and record three points in the measured plane. During the measurement, raters put the synthetic moving image and fixed image side by side and try their best to locate the position where the maximum deformation appears while keeping the measured plane corresponding to the same anatomical location. Since the other parts of the CT image rarely change, which provides raters with clear landmarks, finding the same anatomical location and maximal diameter change can be a much easier task than in real clinical scenarios. Thus, the rater's performance on the synthetic cases is considered as the upper bound that manual measurement can possibly achieve.

To get the ground-truth maximal diameter change, we first extract the centerline of the fixed image and sample the centerline with 0.5mm spacing and the maximum diameter of each cross-section (orthogonal to the centerline) at each sampled point in both fixed surface and synthetic moving surface is automaitcally computed by the open-source Vascular Modeling Toolkit (VMTK, www.vmtk.org). We denotes the results as two one-dimentional arrays $\mathbf{d}_{\mathcal{V}_{fixed}}$ and $\mathbf{d}_{\mathcal{V}_{smoving}}$, with each having the length of the number of samples on the centerline. Then we take $max(|\mathbf{d}_{\mathcal{V}_{fixed}} - \mathbf{d}_{\mathcal{V}_{smoving}}|)$ as the ground-truth maximal diameter chaneg and record the location of the cross-section that achieves the maximal diameter change.

In the VDM-based measurement, we obtain the reconstructed moving surface by deforming the fixed surface using the displacement field resulting from registering the original CT image and synthetic moving image. Similarly, we take the same sampled centerline and measure the maximum diameter of cross-sections for both fixed surface and reconstructed moving surface, and record the largest difference (i.e., $max(|\mathbf{d}_{\mathcal{V}_{fixed}} - \mathbf{d}_{\mathcal{V}_{recons}}|)$) and location where it happens.

We compare VDM-based and manual maximal diameter measurement against the ground truth, and the results can be found in Seciton.III.B..

III. Results

III.A. Test VDM with AreaRatio

Robust Test. We test our VDM registration method with three types of disturbance, image noise, various thickness of the image slice, and bulk motion. These sub-ideal scenarios can always be seen in real clinical settings. We add various Gaussian noise levels for noise attack, with the magnitude of 50, 100, and 150 (in HU), to the CT image before VDM registration. Also, to test the robustness of VDM to various thicknesses of image slice (in the z-direction), we resample the image using three thicknesses: 1.0, 1.5, and 2.0 (mm). Furthermore, to mimic the bulk motion, we rotate the image along three axes by randomly selecting from $\{+5, -5\}$ degree and translate the image to the direction $(+x, +y, +z)$ by various distances, 20, 40, 60 (mm). The results in Fig.4 shows that VDM is robust to various disturbances.

Test on Respiratory Effect. Whenever taking CT scans, a patient can't hold their breath at the same level, which leads to the respiratory effect. Besides the 31 synthetic cases that mainly focus on the local deformation, we created another 4 cases with respiratory effect to test VDM. Fig.5 shows VDM can perform well on such cases and achieve low error on AreaRatio.

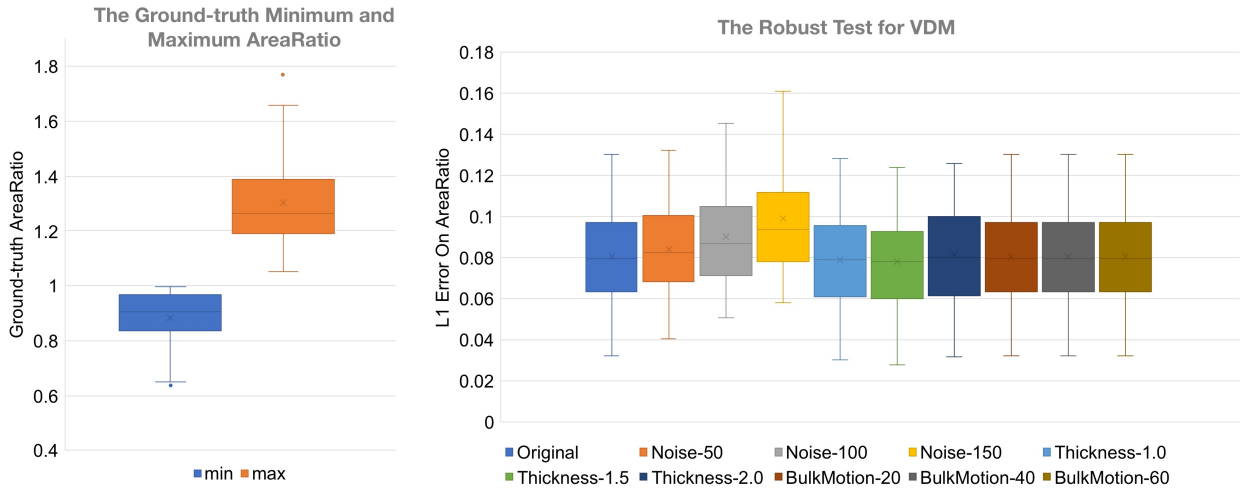
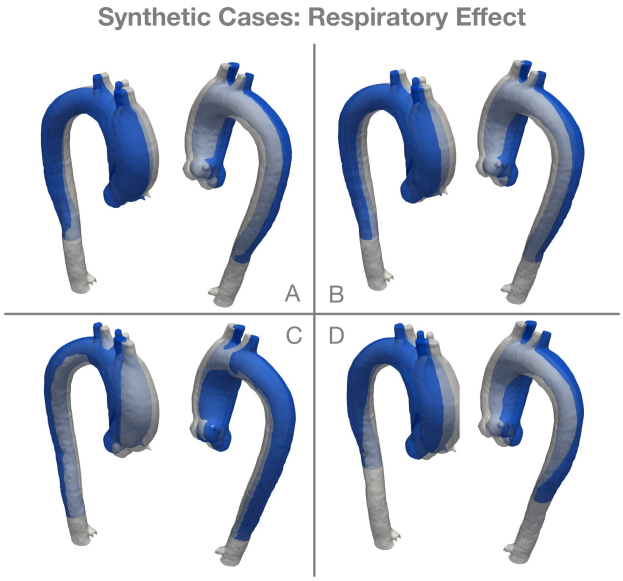


Figure 4: The left figure shows the statistics of the max and min value of the AreaRatio for the 31 synthetic cases. In the right plot, the "original" indicates the test with the original CT image and mask w/o any disturbance. For the rest of the test, we add one and only one disturbance to the original image pair to test the VDM. The 95^{th} percentile of L1 error on AreaRatio is reported.

III.B. Comparision: VDM v.s. Raters

Following the procedure described in Fig.3, we compare VDM-based measurement with manual measurement from two aspects to show our superiority – the variability of the measurement and the ability to locate the region where the maximal diameter change happens. Fig.6 shows the VDM-based measurement achieve much smaller variability than that of both raters, and also shows more accurate localization for maximal diameter change.



Test VDM Respiratory Effect

CaseName	Ground-truth AreaRatio		L1 Error
	minimum	maximum	
A	0.932	1.120	0.040
B	0.954	1.076	0.033
C	0.856	1.084	0.050
D	0.800	1.113	0.055

Figure 5: On the left, we show four synthetic cases created for testing respiratory effect with two angle of views each. The white surface is fixed surface while the blue surface is the synthetic moving surface. On the right, we reported the statistics of the ground-truth AreaRatio and the 95^{th} percentile of L1 error on AreaRatio.

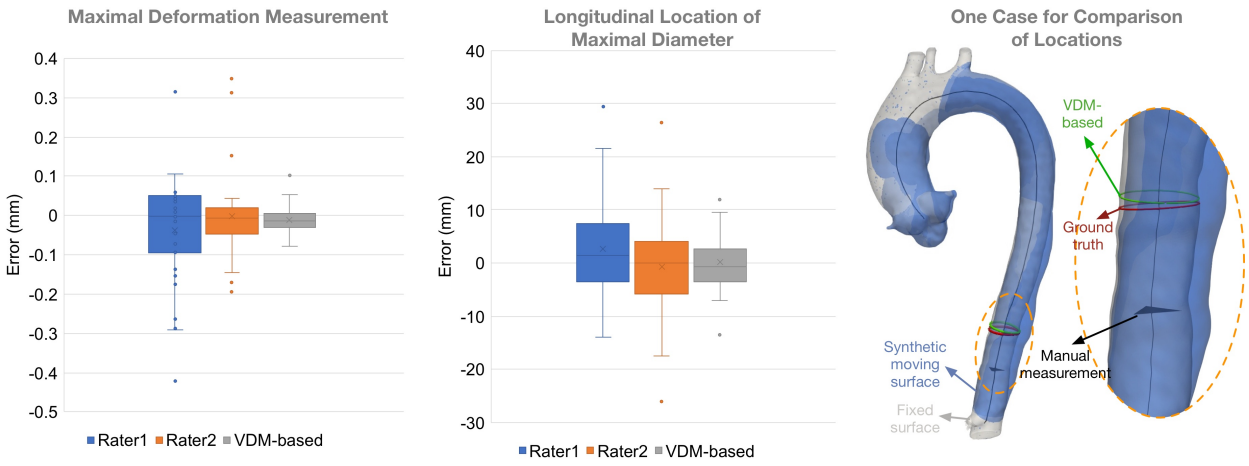


Figure 6: Two box-plots on the left show the error of maximal deformation and longitudinal localization by two raters and the VDM-based method. The right figure gives an example of the three locations: ground-truth location, the one found by rater1, and the one found by the VDM-based measurement.

Appendix

Appendix text goes here if needed.

References

[1] P. Thévenaz and M. Unser, Optimization of mutual information for multiresolution image registration, IEEE transactions on image processing **9**, 2083–2099 (2000).

[2] M. Staring and S. Klein, Itk: Transforms supporting spatial derivatives, Insight J (2010).

[3] M. Staring, S. Klein, and J. P. Pluim, A rigidity penalty term for nonrigid registration, Medical physics **34**, 4098–4108 (2007).

[4] S. Klein, M. Staring, K. Murphy, M. A. Viergever, and J. P. Pluim, Elastix: a toolbox for intensity-based medical image registration, IEEE transactions on medical imaging **29**, 196–205 (2009).