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IMPORTANCE OF UNCERTAINTY IN IMAGE SEGMENTATION IN ONE-DIMENSIONAL VASCULAR NETWORK MODELS

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SUMMARY

Patient-specific models can be used to plan treatments and manage diseases, including chronic thromboembolic pulmonary hypertension (CTEPH). This study examines uncertainty in fluid dynamics and CTEPH vasular networks based on computed tomography (CT) images. We segment the pulmonary arteries and calculate the radius and length for each vessel using centerlines and change points. Networks are created from the centerlines, and are used in a fluid dynamics model, predicting uncertainty in hemodynamics from variations in geometry. We compare two centerline algorithms: VMTK, which uses maximal inscribed spheres, and SGEXT, which uses skeletonization. Results show that centerline placement and vessel radius significantly impact hemodynamics.

Key words: *image segmentation, centerlines, fluid dynamics, uncertainty quantification*

1 INTRODUCTION

Patient-specific vascular models can be used in disease management, e.g., to improve diagnoses or plan treatment strategies. For patients with chronic thromboembolic pulmonary hypertension (CTEPH), patient-specific models can examine what vessels to dilate to reduce pressure and improve perfusion [1]. Typically, generating a patient-specific model involves two core steps: (i) setting up a vascular domain and (ii) calibrating a fluid dynamics model to hemodynamic data. The first step can be accomplished by segmenting arteries captured by computed tomography (CT) or magnetic resonance (MRI) images; the second by solving an inverse problem, estimating model parameters, and minimizing the least square error between computed results and available hemodynamic data. Numerous studies have examined hemodynamics using 3D [8] and 1D [3, 7] computational fluid dynamics (CFD) models. Due to computational challenges, 3D CFD models are most useful for studying flow in localized regions within the network, whereas 1D models are better suited for examining hemodynamics in large networks such as the pulmonary arterial vasculature, which branches rapidly for over 20 generations. However, obtaining a reliable representation of vascular networks is challenging [3]. Significant uncertainty is associated with capturing vascular networks since images typically have multiple intersecting networks (e.g., in the lungs, there are arteries, veins, and airways). Another challenge is that vessels have no ground truth dimensions, and clinical images are often noisy. Networks are typically extracted by segmenting CT or MRI images and constructing a 3D rendered volume. Through this volume, centerlines can be identified using automated algorithms, along with algorithms determining the vessel radius at each point along the centerlines. Based on the centerlines, a labeled tree is generated including information about vessel length and radii, connectivity of vessels along the network, and location in 3D space [3]. Such networks are essential, especially for 1D models, for which the computational domain is constructed from the centerlines [3]. Two methodologies for extracting centerlines include the Vascular Modeling Toolkit (VMTK) [2] and Skeletonization and Spatial Graph Extractor of Images (SGEXT) [5] (github.com/phcerdan/SGEXT). VMTK places maximally inscribed spheres in the lumen of the vessels and determines centerlines by connecting the center of consecutive spheres. SGEXT uses skeletonization, which iteratively removes voxels until a single voxel path remains in each vessel. This study compares hemodynamic predictions in pulmonary arteries segmented from a CT image of a CTEPH patient. The CT image is segmented using

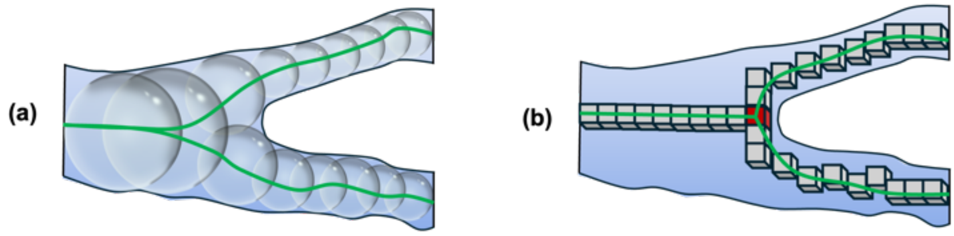

Figure 1: Centerlines obtained with (a) VMTK generated from maximally inscribed spheres and (b) SGEXT via skeletonization.

3D Slicer [4], and vascular networks are generated from centerlines extracted using VMTK [2] and SGEXT [5]. We use statistical change points to quantify the uncertainty of vessel radii distribution for each vessel, sampling radii values from a normal distribution to demonstrate the effects of geometric uncertainty on hemodynamics using a 1D fluid dynamics model.

2 METHODOLOGY

Volume rendering. We analyze a chest CT image from a 57-year-old male CTEPH patient made available from collaborators at Duke Health. The pulmonary arterial network is rendered using the open-source image segmentation software 3D Slicer developed by Kitware, Inc. [4]. To extract the pulmonary arteries, we include intensities from 50 to 3027 Hounsfield units. We identify the main (MPA), right (RPA), and left (LPA) pulmonary arteries through thresholding followed by manual painting, erasing, and cutting to identify the lobar, segmental, and subsegmental vessels.

Centerlines. VMTK [2] determines centerlines in the 3D rendering by placing maximally inscribed spheres along each vessel with boundaries defined by user-specified inlet and outlet points. Centerlines and vessel radii are obtained from the center and radius of each sphere, and when two centerlines intersect, a junction node is placed. Due to challenges associated with placing a sphere at a junction, we utilize an algorithm that moves junction nodes closer to the barycenter of the ostium region [3]. SGEXT [5] generates centerlines using skeletonization, iteratively removing voxels until a single voxel remains in the center of the vessel. In SGEXT, the radius is obtained by constructing a distance map and determining the shortest distance from the center voxel to the background. The latter is done by superimposing the distance map and the single voxel path. After centerlines are generated, we fit change points to each vessel's radius data to determine locations where there is uncertainty within the calculated radius, e.g., the ostium region. We use this to find the segment within each vessel where the radius can be reliably estimated, calculate the mean and standard deviation, and fit a probability density function (PDF). The PDF represents the radius measurement and uncertainty for each vessel, which is used to inform the geometry for fluid dynamics simulations. Examples illustrating the 3D renderings and methodology for centerline generation are shown in Figure 1.

1D fluid dynamics model. In each vessel, we solve the 1D Navier–Stokes equations, ensuring conservation of mass and momentum. This system of equations is obtained assuming vessels are deformable and cylindrical, blood is incompressible, viscous, and homogeneous, and the flow is Newtonian and irrotational. Under these assumptions, volumetric flow $q(x,t)$ (mL/s), blood pressure $p(x,t)$ (mmHg), and vessel area $A(x,t)$ (cm^2) can be computed as

$$\frac{\partial A}{\partial t} + \frac{\partial q}{\partial x} = 0, \quad \frac{\partial q}{\partial t} + \frac{\partial}{\partial x}\left(\frac{q^2}{A}\right) + \frac{A}{\rho}\frac{\partial p}{\partial x} = -\frac{2\pi\nu R}{\delta}\frac{q}{A},$$

where ρ (g/mL) is density, μ (g/cm s) is viscosity, $\nu = \mu/\rho$ (cm^2/s) is the kinematic viscosity, $R(x,t)$ (cm) is the vessel radius, $\delta = \sqrt{\nu T/2\pi}$ (cm) is the boundary layer thickness, and T (s) is the length of the cardiac cycle [3]. The two fluid dynamics equations are coupled with a linearly elastic wall model that relates pressure and vessel area such that

$$p(x,t) = \frac{4}{3}\frac{Eh}{R_0}\left(\sqrt{\frac{A_0}{A}} - 1\right), \quad \frac{Eh}{R_0} = k_1 e^{-k2R_0} + k_3.$$

Here, Eh/R_0 (mmHg) is the vessel stiffness increasing with decreased vessel size, R_0 (cm) is the unstressed radius, and $A_0 = \pi R_0^2$ (cm^2) is the unstressed vessel area. The system of equations is hyperbolic, requiring a boundary condition at the beginning and end of each vessel. The inflow to the network is obtained from measurements, and at the outflow of each vessel, we use a structured tree boundary condition [3, 7]. At junctions, we enforce conservation of flow and continuity of pressure. The system of equations is solved numerically using the two-step Lax Wendroff method.

3 RESULTS AND CONCLUSIONS

Centerlines. Figure 2 shows an example of the centerlines generated in a pulmonary arterial network from a CTEPH patient, where (a) depicts the raw network obtained with VMTK, (b) the network obtained by SGEXT, and (c) an analysis of the vessel radii along its length using change points. Note the significant difference in junction placement between VMTK and SGEXT. In the raw VMTK network, the junctions placed by VMTK [2] are located far from the barycenter, likely due to challenges associated with placing spheres in the junction region, which is not cylindrical. The result is a significant variation in radius along each vessel. In our previous study [3], we designed a junction correction algorithm moving the junction closer to the barycenter. This step is not needed in SGEXT [5], which generates centerlines with vessel junctions that visually appear to be in the barycenter. However, SGEXT is sensitive to ridges in the volumetric model, causing them to arc more than expected.

Moreover, the vessel radius is poorly defined in the ostium region where vessels meet. Therefore, to reliably determine vessel radius, we use statistical change points to identify the part of the vessel that best represents the radius. From this segment, we choose the radius and account for its uncertainty. Figure 2(c) shows an example of a vessel radius and its uncertainty, which is normally distributed.

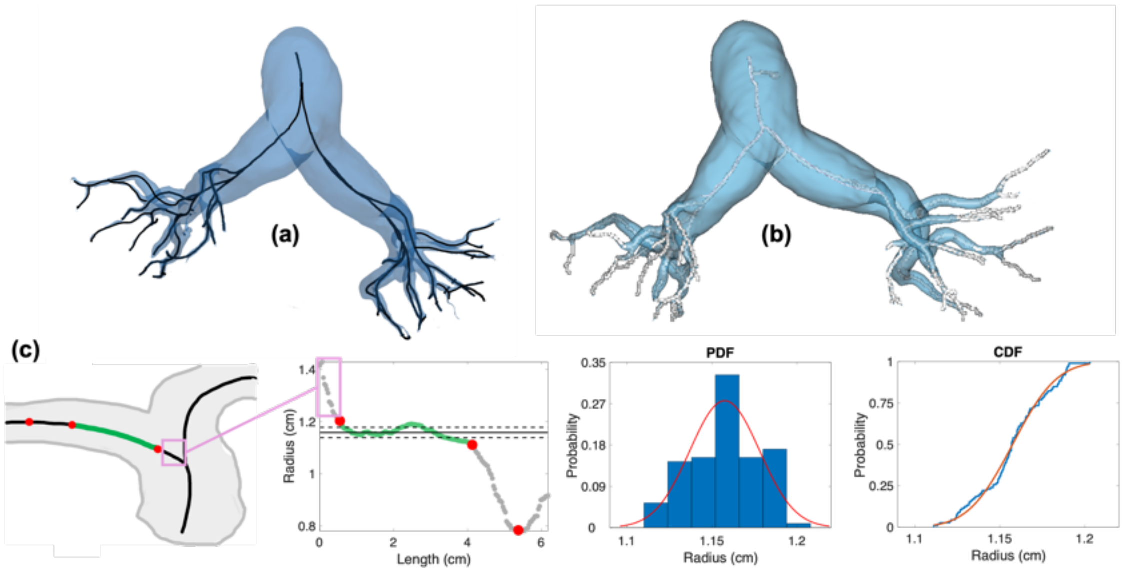

Figure 2: Segmentations and centerlines of a pulmonary vascular network from a CTEPH patient. Centerlines were found using (a) VMTK and (b) SGEXT. In (c), radii values along the length of each vessel are identified using statistical change points, and radius uncertainty is quantified by viewing the probability density function (PDF) and cumulative density functions (CDF).

Fluid dynamics predictions. Figure 3 shows example fluid dynamics predictions in the main (MPA), right (RPA), and left (LPA) pulmonary arteries. Results are obtained by sampling radii from the normal distribution for each vessel. The radius variation (Figure 2(c)) is obtained by fitting a Gaussian curve to the radius samples along each vessel. By sampling the radius from a normal distribtion within physiological bounds, we see a significant impact on blood flow and pressure predictions. The minor flow variations in the MPA result from the boundary condition prescribing a flow profile at the inlet; in contrast, the variation in pressure is similar to the expected measurement error. Results demonstrate the importance of accounting for uncertainty in medical images, variation in centerline placement, and radius estimation. This is because CT images have finite resolution, limiting the

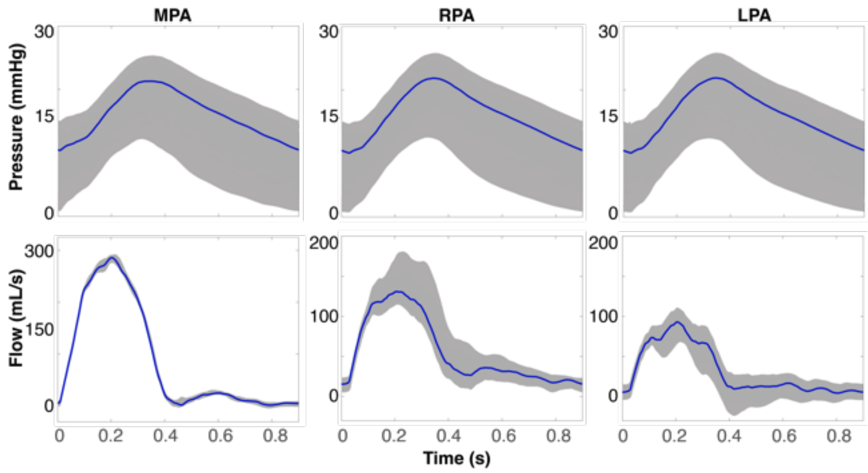

Figure 3: The solid line shows fluid dynamics prediction using the mean radius along each vessel, and the gray lines show predictions running 1000 fluid dynamics simulations sampling the radius from a normal distribution for each vessel.

number of vessels that can be captured reliably by 3D rendering for use in mathematical models. Uncertainty quantification is essential in patients with pulmonary vascular diseases, such as CTEPH, results in remodeling of the vasculature, chronic lesions, and increased tortuosity of vessels. In this study, we demonstrate that using multiple centerline methodologies, such as VMTK and SGEXT, combined with statistical change points to identify representative radii for each vessel, will minimize uncertainty in predictions of hemodynamic quantities. Thus, when using 1D models to generate patient-specific predictions for medical applications, careful image and network extraction process analysis is imperative for accurate results.

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