## Literature Review

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The 3D reconstruction of patient-specific vascular network is the process of building 3D geometric model that captures the general structure and essential details of a patient's blood vessels out of medical images. Normally, it is impossible to obtain complete information about the blood vessel structure due to the relatively low quality of the images. Hence, only partial models can be created by most of the existing reconstruction techniques. Discontinuities of vessels are inevitable. Motivated by this situation, we are encouraged to develop a framework for the construction of vascular systems that transforms raw image input to an augmented 3D vascular model without major discontinuities.

In general, the construction of geometric model of blood vessels involves the following procedures: medical image viewing, pre-processing, image segmentation, centerline extraction, mesh generation, and post-processing [1]. Among them, image segmentation and mesh generation receive the most research attention. In previous works, approaches introduced for vessel segmentation mainly employ model-based methods, graph-based methods, and tracking-based methods [2]. However, these methods are computationally expensive and face the difficulty of segmenting different sizes of vessels. Failure to detect small vessels may result in missing the central parts of vessels. Moreover, with the presence of close vessels and crossover points, partial merging of two vessels and the spurious segmentation at the crossover points are commonly found in the model produced by the above methods [3]. Nevertheless, in search of an effective segmentation approach, we found that a recently developed multi-scale line detection (MSLD) method seems to solve these problems [4]. The MSLD method utilizes a linear combination of line detectors at different scales to produce the vessel segmentation for each clinical image. A basic line detector uses a set of approximated rotated straight lines to detect the vessels at different angles. By changing the length of the aligned lines, line detectors at different scales are achieved. While long length line detectors have shown to be effective in distinguishing close vessels, short length line detectors are able to reduce vessel merging. The problem is that MSLD has only been implemented in 2D image segmentation. To incorporate it in our 3D reconstruction framework, we could utilize centerline projections from all three cut planes (coronal, sagittal, and axial) to track the path of the blood vessel of interest from one end to the other.

However, even with the MSLD method, the resulting vessel lines can be discontinuous, especially in regions connecting different vascular trees. Thus, we

propose to reconnect the vessel trees by searching for an optimal hypothetical configuration that minimizes the material cost (MC) and the power cost (PC) while obeying crucial physiological principles. A recent work of Elif Tekin et al. proposed a mathematical way of finding optimal branching points based on MC and PC optimization [5]. On one hand, MC optimization takes into consideration the two types of material needed for the vascular system: blood vessels (endothelial cells) and blood (plasma and white and red blood cells). The amount of material necessary for vessel construction primarily depends on the surface-area of the vessel  $(2\pi rl)$ , and the material devoted to the blood is proportional to the blood volume  $(\pi r^2 l)$ . On the other hand, PC optimization minimizes the total power for circulating blood and the additional power beyond what is used to move the blood. Assuming the blood as smooth, Poiseuille flow, researchers computed the total volume flow rate and equivalent impedance in an attempt to quantify the power loss. Physiological principles of human bodies, such as the maximum wall shear stress and circumferential stretch that the vessel walls can sustain [6], enforce other constraints to the optimization problem. Sudhir B. J. and Santhosh Kumar K. simulated blood flow using computational fluid dynamics methodology and found that the location of branching points indirectly influences wall shear stress in the vicinity of bifurcation by changing the angle between the branching edges [7]. Increased wall shear stress may explain the pathogenesis of cardio vascular diseases such as Moyamoya disease. Pressure-shear hypothesis also states that vessels adapt to shear stress as a function of local pressure [8]. Hence, we propose to take the pressure and the corresponding force equilibrium as one of the factors in our optimization. Furthermore, previous studies have showed that it is feasible to use optimization in reconnecting the vessels. Francesco Caliva et al. designed a zero-dimensional model and a fluid-dynamics-based cost function to simulate the hemodynamics in the vascular network and successfully reconnected disconnected vascular segments [9].

For vascular volume generation, there are two main approaches: (1) 2D crosssectional segmentations along approximate vessel centerlines and (2) direct 3D volumetric segmentation [1]. For the first technique, after digitizing the lumen centerlines, 2D cross-sectional segmentations are performed perpendicular to the centerlines. The approximated centerlines need to be relatively smooth for robust perpendicular cross-sectional segmentation, so this step may require manual adjustment of particular path points and smoothing functions. With the cross-sectional information such as vessel radius and vessel wall thickness, the next step is to rebuild the 3D structure slice by slice. As for direct 3D volumetric segmentation, the process is much more automatic, but requires more complex and computationally expensive segmentation algorithms. Predominant 3D segmentation methods utilize signal thresholding and active contours. Yet at present, these techniques are not robust enough due to image leaking and computational stability issues. Medical images are simply too noisy and contain too much variety in signal. As a result, we can adopt 2D cross-sectional segmentation in our own method for the following reasons: (1) from centerline extraction, we already have a 3D line model in hand, so the main issue is to extend the line model into a tubular model; (2) apart from exploiting the power of optimization to construct the tubular model, previous studies showed that machine learning approaches have also demonstrated satisfiable results in 3D vascular network construction [10][11], so it is worth trying machine learning approaches in enhancing the model. In a recent study, a deep feature regression (DFR) method is proposed for 3D vessel segmentation, which is based on a convolutional regression network and a stable point clustering mechanism [11]. Given that vessel tracking is limited to areas near the considered vessel, 2D vessel cross-sections extracted near the vessel centerlines are utilized as the training samples, and the pose parameters of these sections are identified as regression results. The proposed DFR-based 3D vessel construction method is summarized as follow. First, a vessel section generator and deviation parameter estimators are designed. The generator provides sample images with specified pose parameters for the training and predicting processes, while the estimators calculate pose parameters of an input vessel section. Second, deep vessel features are extracted by a series of convolutional recurrent networks. Translation estimator, direction estimator, and radius estimator are obtained respectively. Third, the estimators are combined into a deep vascular state estimator. The vascular structure segmentation is finally completed through seed analysis, vessel tracking, termination checking, and segment selection. Experiments demonstrate that the proposed method is effective and reliable. As an extension to the above mentioned method, we can use the same cross-sectional method to generate the training samples in order to reduce the amount of medical images needed. Meanwhile, it is possible to modify the parameter settings to further simplify the learning process while maintaining the relative positional relation of contiguous cross-sectional samples. Therefore, the structural information of the blood vessels, such as radius and curvature, can be fully explored to build the tubular model.

The last step of the reconstruction is to validate the resulted 3D model. Since we utilize constrained constructive optimization based on biological principles and fluid dynamics in reconnecting the vessel centerlines, and use neural networks in building the tubular model, it is necessary to confirm that the hypothetical optimal structure is reasonable. We intend to simulate blood flow in the proposed model and check for potential problems in order to confirm whether the hypothetical optimal structure is reasonable [7]. If not, we plan to further employ correction methods and improve our model as needed.

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