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Gap-free segmentation of vascular networks with automatic image processing pipeline

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ABSTRACT

Current image processing techniques capture large vessels reliably but often fail to preserve connectivity in bifurcations and small vessels. Imaging artifacts and noise can create gaps and discontinuity of intensity that hinders segmentation of vascular trees. However, topological analysis of vascular trees require proper connectivity without gaps, loops or dangling segments. Proper tree connectivity is also important for high quality rendering of surface meshes for scientific visualization or 3D printing. We present a fully automated vessel enhancement pipeline with automated parameter settings for vessel enhancement of tree-like structures from customary imaging sources, including 3D rotational angiography, magnetic resonance angiography, magnetic resonance venography, and computed tomography angiography. The output of the filter pipeline is a vessel-enhanced image which is ideal for generating anatomical consistent network representations of the cerebral angioarchitecture for further topological or statistical analysis. The filter pipeline combined with computational modeling can potentially improve computer-aided diagnosis of cerebrovascular diseases by delivering biometrics and anatomy of the vasculature. It may serve as the first step in fully automatic epidemiological analysis of large clinical datasets. The automatic analysis would enable rigorous statistical comparison of biometrics in subject-specific vascular trees. The robust and accurate image segmentation using a validated filter pipeline would also eliminate operator dependency that has been observed in manual segmentation. Moreover, manual segmentation is time prohibitive given that vascular trees have more than thousands of segments and bifurcations so that interactive segmentation consumes excessive human resources. Subject-specific trees are a first step toward patient-specific hemodynamic simulations for assessing treatment outcomes.

1. Introduction

Medical imaging data acquired from Magnetic Resonance Imaging (MRI), Computed Tomography Angiography (CTA), and Interventional Digital Subtraction Angiography (DSA) provide valuable information regarding patient vascular health for clinical diagnosis of cerebral vascular diseases (CVD) [1]. Currently, biometrics of the vasculature cannot be readily accessed from the medical images, because manual segmentation of the entire arterial tree would require weeks of labor which is impractical. What is needed is an automatic image processing pipeline for the robust and reliable extraction of patient-specific vascular biometrics to characterize the patient's cerebral angioarchitecture. A critical property for automatic image segmentation is preservation of tree connectivity needed to perform topological and statistical analysis of cerebrovascular trees. The connectivity is often lost due to four reasons: (i) large variations in image intensity along centerlines, (ii) sign changes in the eigenvalues close to bifurcations, (iii) artificial gaps introduced into vessel segments due to finite image slice spacing, and (iv) artifacts due to overlapping structures, such as cortical surfaces or cerebrospinal fluid spaces. In addition, 3D visualization of vascular trees may be helpful for treatment planning [2], education of medical students or patients before intervention to lower anxiety, and for 3D printing of vascular networks. There is also a pressing need for subject-specific vasculature segmentation for computational fluid dynamics (CFD) studies. Researchers and physicians utilize cerebral hemodynamic simulations to acquire more insight in

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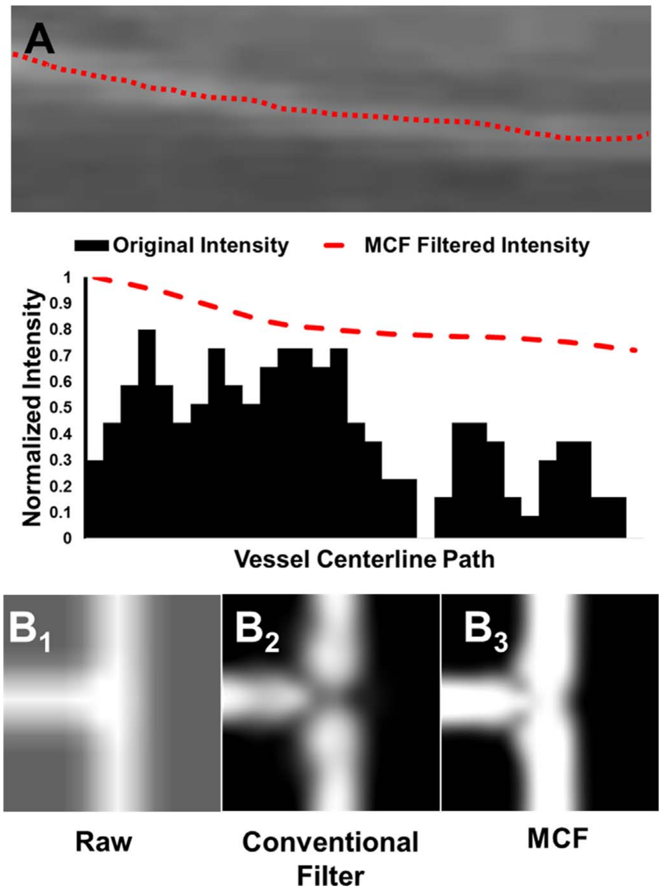

Fig. 1. Imaging artifacts, noise and image processing techniques introduce gaps and result in incomplete segmentation of blood vessels. A. Imaging artifacts such as motion and scattering suppresses image intensities leading to premature termination of vessel segmentation. After filtering with MCF, the intensities are more equalized in vascular segments indicated by the red dotted lines. B_1 shows a digital bifurcation phantom exhibiting high intensity inside the tubular segments. After application of a conventional vesselness filter, artificial gaps around the bifurcation are introduced in B_2, causing incomplete segmentation of vascular structures. The MCF preserves connectivity in bifurcations without creating gaps in B_3. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

the cause of CVDs. Patient-specific CFD also enables planning of endovascular interventions such as bypass surgery [3,4], aneurysm clipping [5] and arteriovenous malformation rupture risk [6]. Prior CFD studies were often limited to small sections such as the carotid bifurcation [7–10] or the Circle of Willis (CoW) [11–13]. However, since CFD affect the entire circulation, it is important to reconstruct larger portions of the cerebrovascular angioarchitecture.

Despite the contrast enhancement with iodine or gadolinium or specialized imaging protocols (Time-of-Flight, TOF, and Phase Contrast, PC) [14–17], signals belonging to the cerebral vasculature often coincide with information from other anatomical structures including skull, grey or white matter, this overlap deteriorates the specificity of blood vessel detection. Especially, small vessels like communicating arteries in the CoW are easily obfuscated in medical images due to image scattering artifact or relatively weak contrast compared to surrounding tissues. Furthermore, imaging artifacts and unavoidable noise often introduce discontinuity or gaps that hinder automatic segmentation of vascular structures as shown in Fig. 1. The gap between image slices also tend to severs blood vessels unless the spacing is much smaller than the thinnest blood vessel. Since, the smallest capillaries measure only 4 µm in diameter, severed vessel between slice are inevitable in most modalities. In practice, several dedicated software use probability and logic to reconnect severed vessels to maintain connectivity [18]. Here we propose an alternative without the need to reconnect severed vessels or fill erroneous gaps. We show that intensity equalization drastically reduces the probability of artificial gaps, suppresses information that does not belong to tree-like structures. Moreover, the use of Gaussian smoothing to propagate intensity information across gaps between image slices to avoid broken vessel segments.

Numerous prior studies presented excellent *vesselness* filters [19–25], using the eigenvalues of the Hessian matrices of the image intensity to identify blood vessels. Vesselness filters enhance intensity of voxels whose eigenvalues correspond to elongated structures while suppressing signals from other anatomical features and noise. However, the eigenvalues of the Hessian matrix changes sign and magnitude at bifurcations. This phenomenon causes vesselness filters to erroneously weaken the contrast in bifurcations which results in disconnected segments in the network. To address this issue, a filter was designed to enhance the contrast in bifurcations [23,24]. However, this improvement for bifurcations has the side effect of suppressing neighboring segments in the vicinity, which introduces artificial gaps [25]. This side effect is undesirable because bifurcations near other branches frequently occur in the convoluted pial network. Moreover, all prior filters were designed for a specific image modality which limits their general applicability. It would be ideal to have a filter which highlights vessels, preserves bifurcations, maintains connectivity in highly-branched networks, and is applicable to any imaging modality. We recently introduced the mathematical operation for a multi-scale vessel contrast enhancement filter for magnetic resonance angiography images. However, our previous work was not automated, required manual tuning and was used for research only. Here we present the fully automated processing pipeline with customized settings and a software implementation ready for general use by the scientific community.

In our experience based on reconstructing hundreds of vascular datasets, we found it easier to eliminate false connections than guessing correct connections where gaps are present. Therefore, it is paramount to avoid introducing gaps. The critical need for circumventing the artificial introduction of gaps is achieved by several procedures: Gaussian smoothing at multiple length scales, intensity equalization, and contrast enhancement in bifurcations. To offer optimal filter performance for each dataset, the filter pipeline has three adjustable parameters that control shape detection and background level. The automated filter pipeline performs intensity histogram equalization throughout the image to preserve connectivity of tree-like structures. It segments the subject-specific cerebral angioarchitecture without gaps, broken bifurcations, dangling segments and loops.

This paper is organized as follows. First, image acquisition protocols for four different imaging modalities are introduced. Then, the mathematical background of the automatic image processing pipeline and its implementation is provided. Next, we compare filter performance in different case studies from multiple imaging modalities. Finally, we discuss potential applications and indicate future research directions.

2. Methods

First, we outline the methods for acquiring medical image of vascular structures. Specifically, we introduce methods for acquiring high resolution images of the cerebral vasculature using clinical 3D rotational angiography (3DRA). Moreover, computed tomography angiography (CTA), magnetic resonance angiography (MRA) and venography (MRV) procedures will be described briefly. In addition, a tubular phantom was created to demonstrate introduction of artificial gaps. Finally, we provide an overview of the automatic image processing pipeline and a brief description for filtering the information from 3DRA, CTA, MRA, and MRV.