IEEE Access
Multidisciplinary ⋮ Rapid Review ⋮ Open Access Journal

Received May 5, 2017, accepted May 22, 2017, date of publication June 22, 2017, date of current version August 22, 2017.

Digital Object Identifier 10.1109/ACCESS.2017.2718590

A Review on Segmentation and Modeling of Cerebral Vasculature for Surgical Planning

AZIMAH AJAM[1], AZRINA ABD. AZIZ[1], (Member, IEEE), VIJANTH SAGAYAN ASIRVADAM[1], (Member, IEEE), AHMAD SOBRI MUDA[2], IBRAHIMA FAYE[3], (Senior Member, IEEE), AND S. JAMAL SAFDAR GARDEZI[3], (Student Member, IEEE)

[1]Center for Intelligent Signal and Imaging Research, Department of Electrical and Electronic Engineering, Universiti Teknologi PETRONAS, 32610 Bandar Seri Iskandar, Perak, Malaysia
[2]Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia
[3]Center for Intelligent Signal and Imaging Research, Department of Fundamental and Applied Sciences, Universiti Teknologi PETRONAS, Perak, Malaysia

Corresponding author: Azrina Abd. Aziz (azrina_aaziz@utp.edu.my)

This work was supported by the Higher Institution Centre of Excellence (HICoE), Ministry Education of Malaysia (MOE) for the Center of Intelligent Signal and Imaging Research (CISIR) under Grant 0153CA-003.

ABSTRACT Visualization of cerebral blood vessels is vital for stroke diagnosis and surgical planning. A suitable modality for the visualization of blood vessels is very important for the analysis of abnormalities of the cerebrovascular system, as it is the most complex blood circulation system in the human body and vulnerable to bleeding, infection, blood clot, stenosis, and many other forms of damage. Images produced by current imaging modalities are not promising because of noise, artifacts, and the complex structure of cerebral blood vessels. Therefore, there is a requirement for the accurate reconstruction of blood vessels to assist the clinician in making an accurate diagnosis and surgical planning. This paper presents an overall review of modeling techniques that can be classified into the three categories, i.e., image-based modeling, mathematical modeling, and hybrid modeling. Image-based modeling deals directly with medical images and which involves preprocessing, segmentation, feature extraction, and classification. Mathematical modeling exploits existing mathematical laws and equations, an example being an arterial bifurcation, which is assumed to follow a fractal and cube law, and a system of ordinary differential equations are solved to obtain pressure and velocity estimates in a branching network. Whereas, Hybrid modeling incorporates both image-based and mathematical modeling to attempt to produce a more detailed and realistic arterial structure. From the literature review and the analysis of the results, it can be summarized that hybrid models provide a faster and more robust technique, which can significantly help in diagnosis and surgical planning, such as for finding the shortest path for a stenting procedure.

INDEX TERMS Cerebrovascular imaging, cerebral vessel modeling, image-based modeling, mathematical modeling, hybrid modeling, segmentation.

I. INTRODUCTION

Visualization of the vascular structure of the human brain is very important for the diagnosis of abnormalities and surgical planning. Currently, it is a vital part of the early detection, diagnosis, and treatment of diseases such as cancer and vascular disease [1]. According to the Institute of Health Metrics and Evaluation (IHME) [2], cerebrovascular disease is the third leading cause of death in Malaysia.

Analysis of blood vessels is very challenging due to size, amount, and overlapping blood vessels, the intensity between background and blood vessels, tortuosity and complexity of blood vessels. There exist several imaging modalities available for stroke research including computed tomography (CT), magnetic resonance imaging (MRI), conventional X-ray, and positron emission tomography (PET) [3]. These modalities are capable to visualize either lesions in brain tissue or blood vessel abnormalities. For example, there are many different MRI sequences for the visualization of different types of tissues, including angiography, which uses contrast agents to visualize blood vessels in any human organ. X-ray angiography (XA), CT angiography (CTA), and MR angiography (MRA) are capable of visualizing blood flow in real time. The quality of images produced by these current modalities is often

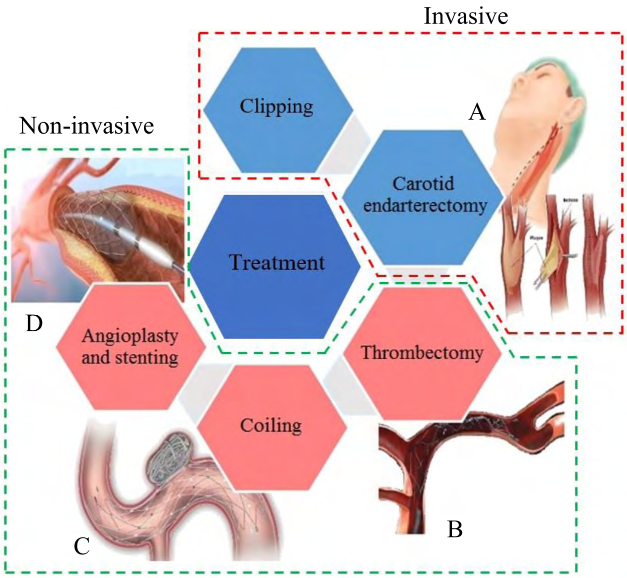


FIGURE 1. Cerebrovascular disease treatments. A. Invasive procedures include clipping and carotid endarterectomy [10]. Non-invasive procedures include B. thrombectomy [11], C. coiling (for an aneurysm) [12], and D. intracranial angioplasty and stenting (for thrombosis and embolism) [13].

unsatisfactory because of noise, artifacts, and low intensity. This leads to a need for reconstruction techniques to overcome the limitations. Reconstruction techniques may be classified into the three groups of image-based modeling, mathematical modeling, and hybrid modeling. Image-based modeling consists of several steps, including image acquisition, preprocessing, segmentation, and feature extraction. Current reviews on image-based modeling techniques include Suri *et al.* [4] and Kirbas and Quek [5] who cover the segmentation part and Lesage *et al.* [6] who provide a further review on vessel segmentation models together with feature extraction techniques using CTA and MRA images. Mathematical models for generating arterial structure without the use of medical images have also been described [7]. Even though mathematical modeling does not provide better accuracy than previous techniques, it can provide important features such as the geometrical structure of blood vessels. By implementing a hybrid model, which is the combination of both image-based and mathematical modeling, the reconstruction of blood vessels can be modeled with the inclusion of much case-specific information.

This study deals with the most common type of modeling technique which is image-based modeling. Although most of the points discuss in this paper related to image-based modeling, we break the modeling technique to another two parts, mathematical modeling and hybrid modeling. A thorough review on all three modeling techniques is provided and should help readers in choosing suitable techniques for the reconstruction of cerebral blood vessels. Sections II.A, II.B, and II.C discuss the different techniques further. The reconstruction of blood vessels in a model can be used for surgical planning for operations such as stenting procedures.

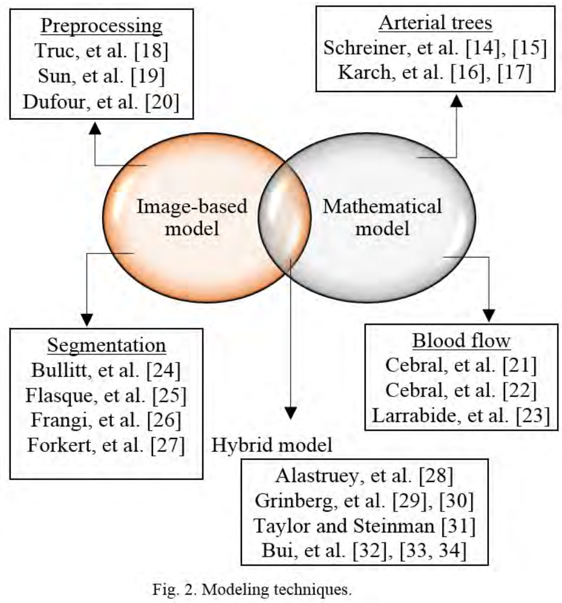


FIGURE 2. Modeling techniques.

Although there are many treatments available for stroke as shown in Fig. 1, intracranial angioplasty and stenting (IAS), which have been used for several decades, still represent an effective and safe treatment method for acute ischemic stroke and aneurysms. They have been shown to be successful for treating acute stroke ($>$ 70% level of stenosis) with a success rate of more than 90%, with clinical implications of around 0–20% [8], [9]. However, there are some conditions where IAS cannot be performed, including in those patients with the abnormal cerebral vasculature.

Therefore, the aid of a system employing the information from an appropriate imaging modality is required for accurate diagnosis and surgical planning. Because of the complex structure of cerebral vessels, the virtual reconstruction of them may assist in diagnosis and may help find the shortest path for IAS treatment when the standard approach is not possible. This review covers several techniques that can potentially be used to acquire useful information for construction of a cerebral vasculature model, including CTA, MRA, and XA.

II. CLASSIFICATION OF MODELING TECHNIQUES

Modeling techniques for blood vessels may be classified into three types, namely image-based modeling, mathematical modeling, and hybrid modeling, as illustrated in Fig. 2. These three modeling techniques are discussed in detail in Sections II.A, II.B, and II.C respectively.

A. IMAGE-BASED MODELING

Image-based modeling requires a data set from an imaging modality that can be used to reconstruct the blood vessel network. The basic steps of image-based modeling begin with image acquisition, followed by prepro-

TABLE 1. Comparison of CTA and 4D-CTA.

	Advantages	Disadvantages	Clinical Applications
CTA [39]	Not all aneurysms may be observable in the image (experiment in Cai, et al. [40])	• Not as accurate as 4D-CTA • Exposure to radiation	Vascular disease (i.e. cerebrovascular, cardiovascular, lung and kidney disease)
4D-CTA [35, 38]	• More accurate than CTA • Aneurysms observable in every scanning procedure for high numbers of patients • Higher prediction of hematoma expansion and prognosis	Higher exposure to radiation than CTA, as the cumulative radiation dose is higher	Intracranial vascular malformation, hemorrhagic and ischemic stroke

cessing and segmentation, and finally, feature extraction. Sections II.A.1, II.A.2, II.A.3, and II.A.4, discuss the techniques involved in constructing a blood vessel model.

1) IMAGE ACQUISITION

Although many imaging modalities are available, angiography is the most suitable method for the visualization of abnormalities in blood vessels, whether it is performed using X-ray, CT, or MRI. The images are captured after a contrast agent has been injected into the blood vessels. Each modality has its own characteristics, as described in Table 1. It is important to choose a suitable modality, as otherwise the reconstruction or modeling process may be problematical owing to a lack of information.

X-ray angiography (XA) or catheter angiography is capable of combining diagnosis and treatment in a single procedure, as it can produce very detailed and accurate images of blood vessels. It is typically used to evaluate and diagnose the abnormalities of blood vessels in various part of the body, including the heart, brain, kidney, and lungs. Narrowed, enlarged, and blocked arteries can be clearly seen with this technique. A catheter, which is a thin plastic tube, is inserted through a small incision in the skin to the body area of interest to highlight blood vessels. A contrast agent is then injected to render the blood vessels visible on X-ray. The advantage of XA is that it produces a detailed, clear, and accurate image of blood vessels. The images produced are very helpful for deciding on a surgical procedure or percutaneous intervention. An advantage of XA is that the use of the catheter makes

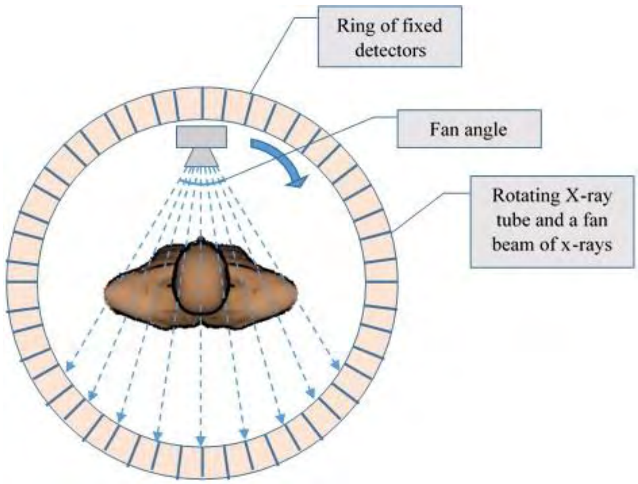


FIGURE 3. CT scanner diagram.

it possible to perform diagnosis and treatment in a single procedure. For example, a surgeon can find the location of an arterial narrowing and then perform an IAS procedure in a single intervention. The limitations of XA include an allergic reaction to the contrast agents, which may lead to a skin reaction, blood pressure drop, breathing difficulties, and loss of consciousness. There is also a risk of a blood clot forming at the tip of the catheter.

Computed tomography (CT) is a medical imaging technique that uses X-rays to acquire images from various type of organ. As with other modalities, angiography techniques are also possible with CT and allow the acquisition of blood vessel images. CTA imaging uses a thin X-ray beam to provide images of organs in the human body. Fig. 3 provides an illustration of a CT scanner, with the dotted arrows indicating the X-ray beams that capture the image. CT can be used to visualize abnormalities, such as a blood clot inside a blood vessel. The use of contrast agent enables CTA to be used for distinguishing between bone, soft tissues, and blood vessels, within the same images. CTA can be performed quickly and may be very beneficial in emergency situations. It can show any abnormalities in brain structure, including brain swelling or bleeding caused by ruptured aneurysms, hemorrhagic stroke, and head injury. However, one drawback of using CT is that patients are exposed to radiation from the X-ray beam.

There exist a new protocol that employs non-invasive CTA with a dynamic acquisition of digital subtraction angiography (DSA) or XA, called Dynamic CTA sometimes also referred as four-dimensional-CTA (4D-CTA Kortman, *et al.* [35] also conducted a study using 4D-CTA. It is capable of visualizing the location of aneurysms, and the technique was shown to be likely to have a high predictive value for hematoma (a collection of blood outside of the blood vessels) expansion [36]. In ischemic stroke cases, 4D-CTA provided a better evaluation of the extent and dynamics of collateral flow when flow to certain regions was occluded [37]. 4D-CTA also provides better visualization of collateral circulation than CTA, thereby providing a

TABLE 2. The advantages and disadvantages of non-contrast-enhanced MRA.

<table>
<tr><th></th><th>Advantages</th><th>Disadvantages</th><th>Clinical applications</th></tr>
<tr><td>2D TOF-MRA [42]</td><td>• Non-invasive
• Capable of capturing slow flow
• Capable of capturing a large volume of tissue
• Reproducible if suboptimal
• Will be accessible after contrast administration but is slightly degraded by venous signal
• Suitable for studying a large intracranial artery</td><td>• Over-interpretation of vessel stenosis
• Has in-plane artifactual signal loss, susceptible to signal loss from flow turbulence
• Limited spatial resolution
• Misregistration artifacts on MIP reconstructions</td><td rowspan="2">• Used as backup in case a CE-MRA is suboptimal
• Used routinely in MR venography
• Used routinely to evaluate the circle of Willis and to detect intracranial stenoses and occlusions
• Estimation of carotid bifurcation stenoses</td></tr>
<tr><td>3D TOF-MRA [42]</td><td>• High spatial resolution
• Displaying complex vascular flow
• Less susceptible to intravoxel dephasing
• Reproducible if suboptimal
• Will be accessible after contrast administration but is slightly degraded by venous signal
• Suitable for studying a large intracranial artery</td><td>• Capable of capturing only a small volume because of saturation artifact
• Has poor background suppression; fat or blood may appear bright on the MRA
• Unable to capture slow flow because of saturation effects
• Time-consuming and susceptible to patient motion</td></tr>
<tr><td>2D PC-MRA [39]</td><td rowspan="2">• Shorter acquisition time for 2D
• Provides anatomic images of vessels, besides hemodynamic information and flow
• Identifies the direction and velocity of flow
• Better background suppression than TOF</td><td>• Cannot capture slow blood flow
• Sensitive to slow blood flow
• Limited spatial resolution</td><td rowspan="2">• Image-guided therapy
• Vascular imaging with non-contrast injection
• Vascular disease (i.e. cerebrovascular, cardiovascular, lung, and kidney disease)
• Evaluation of intracranial collateral flow distal to a stenosis [42]</td></tr>
<tr><td>3D PC-MRA [39]</td><td>• Time-consuming
• Limited to single-frame static images</td></tr>
<tr><td>4D-MRA [43, 44]</td><td>• High spatial and temporal resolution
• Large coverage
• Lack of radiation exposure
• Qualitative evaluation of complex flow patterns</td><td>• Large image datasets</td><td>Intracranial vascular malformation, hemorrhagic and ischemic stroke</td></tr>
</table>

better evaluation of thrombus burden in an anterior circulation occlusion [38].

Magnetic resonance angiography (MRA)

There are two categories of MRA: contrast-enhanced (CE-MRA) and non-contrast-enhanced (NCE-MRA) methods. NCE-MRA methods, such as phase contrast (PC) and time-of-flight (TOF) are the most commonly used techniques to visualize blood vessels. TOF-MRA is more common and is widely used to produce 2D and 3D angiographic images without the injection of contrast agent [41]. The approach is better than PC-MRA for studying large intracranial arteries, as image slices can be thinner and the echo times minimize phase shift that contributes to signal loss. PC-MRA is generally insensitive to slow flow, but it can capture slow flow near the occlusion site [42]. Furthermore, PC-MRA is suitable for visualizing collateral blood flow and can identify the direction and velocity of flow.

Hartung *et al.* [39] discussed the development of advanced techniques using both CE-MRA and NCE-MRA methods. They found that NCE-MRA methods require longer acquisition times than CE-MRA methods. However, they still offer several advantages over CE-MRA, including reduced risks of patients and lower costs. Phase-contrast NCE-MRA methods offer the potential to provide additional hemodynamic information to that currently obtained using invasive methods. However, these imaging techniques are limited to single-frame static images or in the spatial resolution [43]. Therefore, NCE time-resolved 4D-MRA has been developed to visualize the vascular morphology and blood flow dynamic simultaneously in 3D [43]. It is suitable for the study of vascular blood flow but results in larger datasets ($>$ 2000 2D images) than conventional MRI scans [44]. The use of a contrast agent is avoided by performing alternating magnetization preparation

TABLE 3. The comparisons between modalities.

Characteristics	Advantage	Drawback	Spatial resolution	Contrast	Acquisition time	Acquisition cost	Application	Projection
X-ray angiography (XA)	Fast and easy method of imaging	Superposition of structures creates difficulties for interpretation; it cannot pass through bone	Highest	Low	Fast	Low cost	Anatomical	2D
Computed tomography Angiography (CTA)	Provides information about collateral circulation and improves contrast	High contrast agent dose per examination	High	High	Faster and causes less discomfort in comparison with MRA	Intermediate cost	Anatomical Functional	2D and 3D
Magnetic resonance angiography (MRA)	Relies on magnetic properties of body tissues moreover, blood in an external magnetic field	• Strong magnetic field may disturb implants • Can exaggerate the narrowing which leads to inaccuracy in quantification of the degree of stenosis	High	High	Long acquisition time	Intermediate cost	Anatomical Functional	2D and 3D

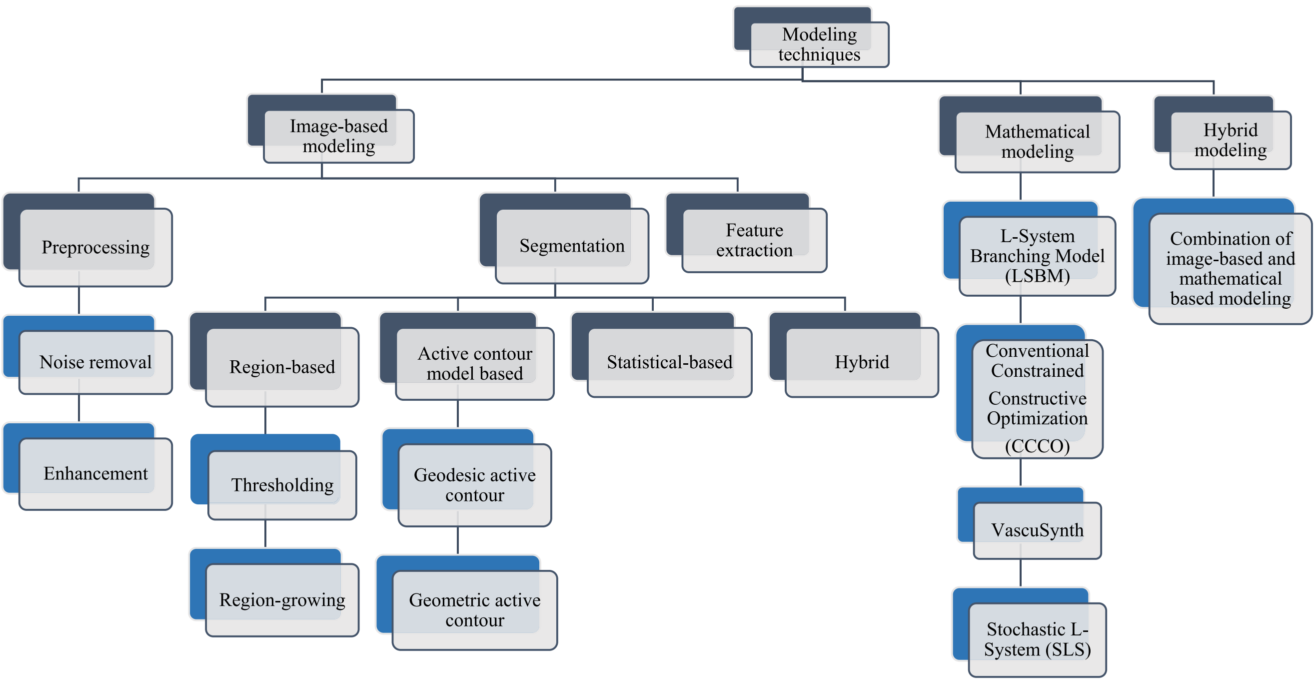


FIGURE 4. The overall picture of the modeling techniques.

schemes in two consecutive acquisitions of each measurement.

Every imaging modalities have their advantages and disadvantages according to what we want to see and solve. There is type of modalities that are not suitable for a certain disease.

Therefore, Table 3 provides a comparison of three types of modalities that commonly used for stroke problem. It includes the comparison of spatial resolution among modalities as well as the contrast, acquisition time, cost, application and also the projection of the modality.

2) PREPROCESSING

The quality of the images produced by imaging modalities is affected by local intensity abnormalities and background noise. Therefore, preprocessing steps like noise reduction and vessel enhancement are necessary on medical images. The results from preprocessing steps help to provide meaningful information about the geometry, position, and topological structure of vessels.

Noise reduction is a process of removing noise in the image which involves several filtering techniques. There are two types of filtering techniques namely conventional (fixed) and unconventional (multiscale or mix).

The conventional filtering techniques such as mean, median, Weiner, Gaussian [45], [46], and low-pass filters [47] have long been used to reduce noise in images. In linear spatial filtering, the content of a pixel is given the average brightness value of its immediate neighbors. The spatial averaging technique referred to as low-pass filtering reduces the level of noise, but results in poor feature preservation because it degrades important information such as lines or edges. The filtering neglects region boundaries and small vessel

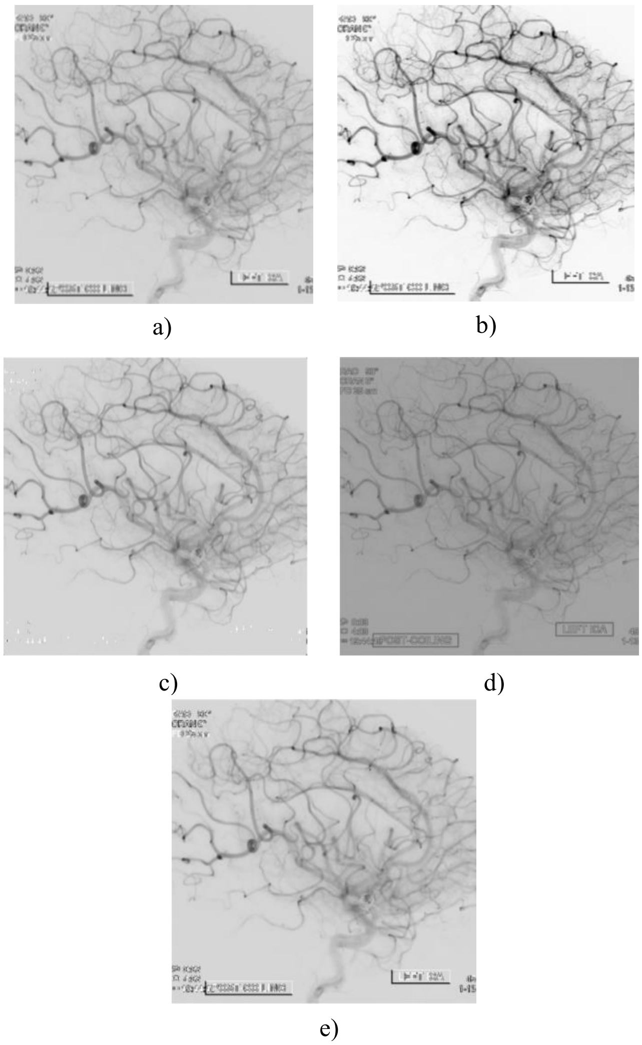


FIGURE 5. **Preprocessing steps for an XA image as a) is an original image, b) stretched image, c) median filtered image, d) low-pass filtered image, and e) anisotropic diffusion filtered image.**

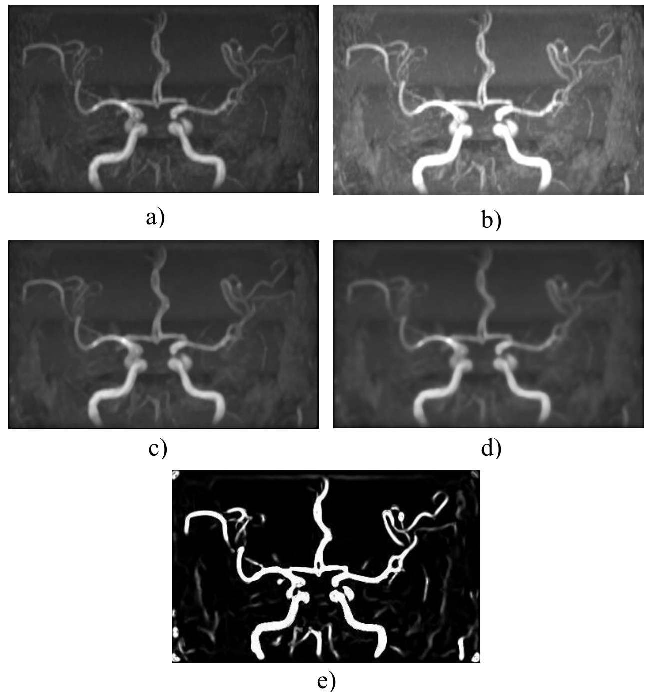


FIGURE 6. **Preprocessing steps for an MRA image. a) original image, b) stretched image, c) median filtered image, d) anisotropic diffusion filtered image by Perona and Malik [47], and e) Frangi filtered image by Frangi *et al.* [59].**

structures, with the result that images produced from this filtering technique appear blurred and diffused. These undesirable effects can be reduced or avoided by modifying the nonlinear filters. The most common technique is median filtering, which results in the edges being preserved, although the filtering causes a loss of resolution by suppressing fine details. Fig. 5 and 6 show the examples of fixed scale techniques as well as a non-linear filtering technique. As we can see, the fixed scale technique is not capable of enhancing but blurring the images. However, in Fig. 6, the Frangi's filter can enhance the vesselness structure but need more preprocessing steps to deal with the gap between vessels.

Although previous filtering techniques may have been somewhat lacking, several authors have introduced an adaptive filter, which can address the problems of blurred edges, disconnected vessels, and undesirable removal of important information. The diameters of cerebral vessels vary according to the depth level of each vessel; this is called multiscale structure. A multiscale filtering technique can deal with any vessel size, as required.

Fixed scale techniques, such as median filtering, have a problem in detecting small vessels. Many studies have used unconventional techniques such as nonlinear anisotropic filtering, Hessian-based filter [48], [49], morpho-Hessian filter [20], and directional bank filter [18], [50] to overcome this problem.

Nonlinear anisotropic filtering was introduced by Perona and Malik [47], where they developed a multiscale smoothing and edge detection scheme that was a powerful new concept for image processing. Canero and Radeva [51] introduced an improved anisotropic diffusion filter to enhance multiscale vessel structure. The proposed filter was inspired by crease enhancement diffusion (CED), [52] but the diffusion strength employed in the study was based on a vesselness measure and named as vesselness enhancement diffusion (VED). Since the VED is a multiscale approach, the results can deal with multiple vessel sizes. Moreover, the VED filter can smooth the background better than CED, and suppress the blob structure (a region that has similar properties to the surrounding regions and represents an artifact or unwanted region). The disadvantage of this technique is that it does not preserve the vessel edges.

Du *et al.* [53] developed a nonlinear anisotropic filtering method capable of significantly reducing noise while preserving the edge structures of blood vessels. This technique introduced a parameter called the exponential diffusion function that could control the smoothing process and was demonstrated to be much more efficient than previous techniques. It was able to improve the contrast-to-noise ratio (CNR) by 50 to 100 percent. Although this technique is capable of suppressing image noise in most cases, it does have the potential to create streak artifacts and enhance noise spikes. The suppression of streak artifact use the interleaved projection angles, but the presence of noise spike enhancement may reduce the CNR in the image.

In later work, bilateral filters were introduced by several authors [45], [54]–[56]. These adapt the idea behind anisotropic diffusion filters, of smoothing the image while preserving the edges of vessel structures. Bhonsle *et al.* [57] demonstrated that bilateral filtering effectively removes additive white Gaussian noise but shows a poor performance in reducing salt and pepper noise. Salt and pepper noise can be caused by disturbances in the image signal. However, the formulation and performance of this technique depended upon the choice of parameter, which was not automated.

Vessel enhancement is widely used in computer graphics where the principle is to enhance an image to facilitate accurate segmentation and reconstruction of vessels for many medical imaging applications [18]–[20], [48]–[50], [58].

The Hessian-based filter was introduced [59]–[63] for vessel enhancement. One advantage of this filter is that it can capture a range of diameters owing to the multiscale analysis. Furthermore, it is not only capable of detecting tubular structures, but also blob-like and sheet-like structures within the image. The Hessian-based filter used a Hessian matrix obtained from the Gaussian second derivative of the 3D image [20] to analyze second-order variation in image intensity to determine the type of local structure (tubular-like) present in the image [20].

Hessian-based filters have been applied in several vessel-enhancement approaches [20], [49], [50]. This technique has been shown to be applicable to various imaging modalities, such as DSA [24], [59], [61], CTA [64], and MRA [25], [26], [41], [49], [65]. It has also been applied to several types of vessels, for example cerebral [27], [66]–[68], peripheral [59], hepatic [60], pulmonary [60], and cardiac [48], [69] vasculature.

Olabarriaga *et al.* [48] presented a method that applied a Hessian-based filter to multi-detector CT images acquired with contrast injection. The study compared three filters for central vessel axis (CVA) enhancement: the Lorenz filter [61], Sato filter [60], and Frangi filter [59]. It found that the Frangi filter provided better enhancement, as it was able to filter a larger area than the other filters.

One of the drawbacks of the Hessian-based approach is that it is very sensitive to noise, and sometimes the vessels appear discontinued because of junction suppression. To address this problem Truc *et al.* [18], [50] proposed a method of adapting the Hessian-based filter to directional images, which they termed the directional bank filter. In comparison with the Frangi filter and Shikata filter, this method can provide superior enhancement of small vessels and distinguish all vessels at bifurcation and crossing points. However, the directional bank filter only currently works with 2D images, while the Frangi filter has been established for 3D images. In general, the proposed filter only generates better performance in 2D images in comparison with the two Hessian-based approaches.

Dufour *et al.* [20] then proposed a morpho-Hessian approach, which involved the combination of two filtering methods, namely mathematical morphology, and Hessian-based approaches. It shows that the proposed method could reconnect vessel-like structures, as one of the basic operations of mathematical morphology is closing (joining disconnect vessel structure parts by filling the gaps between them and smoothing their outer edges). This method was compared with the Frangi filter, and the results were in favor of the morpho-Hessian approach for both low and high noise, although with images showing the highest level of noise, the Frangi filter provided more accurate results. One advantage of the morpho-Hessian approach is that the combined technique led to time-savings.

The Hessian-based filter has been demonstrated to be a powerful technique for vessel enhancement [49]. The technique results in suppression of non-vascular tissues and enhancement of small vessels. However, another challenge of vessel extraction is the problem of background disturbance. To address this problem, Sun *et al.* [19] introduced top hat enhancement to normalize the background, as vessel images may have a non-uniform background. By normalizing the background image the filtering of the vessel structure is improved, as well as the segmentation process.

From the literature survey, it can be analyzed that the Hessian-based filter is found to be a powerful technique for the enhancement of blood vessels. It is very useful for detecting small blood vessels and the line structures (centerlines) within blood vessels.

The next section will discuss the segmentation methods available for brain vessels.

3) SEGMENTATION

Cerebrovascular segmentation is one of the most challenging tasks in vessel segmentation and plays an important role in medical diagnosis. It separates an input image into several non-overlapping regions [74]. The technique is necessary to perform a three-dimensional (3D) visualization of cerebral vessels to facilitate diagnosis, quantification, and grading of vascular abnormalities, such as stenosis and aneurysm [75].

Over the decades, various techniques have been proposed for the segmentation of blood vessels from MRA. Systematic analyses given by Sur *et al.* [4], Kirbas and Quek [5], Luo and Zhao [68], and Lesage *et al.* [6] present recent progress in cerebrovascular segmentation. Vessel segmentation in MRA is challenging because of (1) the low contrast of an MRA image, (2) the weak contrast between the arteries and background, (3) an unknown and easily deformable vessel-tree shape, (4) overlapping and strong bone shadows [76], (5) the small size of the vessels [66], and (6) noise and gaps in vessels and hemodynamic changes [65]. Moreover, blood

TABLE 4. **Image filtering techniques.**

Filtering techniques	Type of filter	Descriptions	Advantages	Drawbacks
Conventional image filter	• Wiener filter • Median filter • Low-pass filter	• Weiner filter will filter out noise corrupting an image • Median and low-pass filter smooth the image and are useful in reducing noise	Simple	Not suitable for MR images analysis, where it is important to preserve partial volume and edge information
Unconventional image filters	Adaptive histogram equalization (AHE)	Maps the grey values of pixels by using the relationships obtained from the local histograms	• Improves image contrast • Enhances the high frequency signals to improve visual perception	• Requires intensive computation • Noise over enhancement • Ringing artifacts
	• Threshold [20, 64, 70, 71] • Hysteresis threshold [72] • Hessian-based filter [48, 49] • Sato filter [60] • Shikata filter • Directional filter bank [18, 50] • Hybrid [73]	Vessel enhancement is an important preprocessing step to achieve accurate vessel-tree reconstruction that is necessary in many medical imaging applications	• Improves small vessel visibility • Able to decompose the spectral region of an input image into wedge-shapes, which correspond to linear features in a specific direction in the spatial domain [18]	Large vessel signal is decreased
	• Anisotropic diffusion filter [53] • Bilateral filter [45, 56] • Trilateral filter [46]	A robust nonlinear filter proposed by Perona and Malik [47]	• Reduce noise and preserves edge properties simultaneously • Works well for 3D MR angiographic • Effective in suppressing noise and improving CNR in MRA with isotropic spatial resolution • Higher CNR was achieved using spatial frequency dependent anisotropic filtering	Limited noise reduction close to edges

vessels may contain low or complex flow that can lead to low signal-to-noise ratio (SNR) [77].

Image segmentation techniques may be classified into four main categories: a) region-based, b) active contour-based model, c) statistical-based, and d) hybrid techniques as shown in Fig. 4.

Region-based approaches: Region-based approaches segment the image into regions of voxels with a certain similarity. The region based can be further characterized into two categories, mainly thresholding based and region growing based segmentations.

- **Thresholding-based vessel segmentation:** Thresholding is used to divide an image into several regions such as background, soft tissues, vessels, and bone structure. The capability of this technique depends on the selection of an appropriate threshold value, since non-uniform illumination may complicate the process. Many authors [20], [64], [70], [71] have used thresholding techniques to extract blood vessels. The thresholding methods are applied before application of any segmentation technique, so that unwanted background and soft tissues are separated from the vessels areas. For example, Suran *et al.* [70] performed a skeletonization technique (as was introduced in [4]) after thresholding to obtain a centerline of the vessels for graph generation. However, Wang *et al.* [71] demonstrated that their proposed method was able to efficiently obtain accurate cerebral vessels from MRA images, whereas Otsu's method divided the image into two parts named as foreground and background regions, and thresholding was then performed to obtain a more accurate segmentation than achieved with manually segmented vessels.
- **Region growing:** Region growing segmentation benefits from fast algorithms and is the most common technique for segmentation [78]. The technique results in vessel segmentations having good connectivity and preserves the topological structure, which is very important for cerebral vessel analysis [79]. This technique requires a seed point from which to initiate the extraction of similar pixels. It builds the arterial and venous trees by iteratively checking neighboring voxels that are selected according to their grayscale value [80].

Active contour-based model: This approach applies an energy minimization connectivity-preserving relaxation process to an image to obtain the boundary of an object. There are two types of active contour models; parametric models (snakes) and geometric models (level sets).

- **Geodesic active contour:** Yang *et al.* [81] proposed a method that adaptively configures the parameters for a geodesic active contour. Active contours are a very popular technique that evolves a closed curve or surface through a combination of several forces, namely external and internal forces, where the objective is to deform the initial geometry until a total energy is minimized [82]. Even though active contours have widespread interest in geometric analyses, the approach has several drawbacks. First, the results obtained might not be significantly associated with the desired boundary. Second, the topology of a vessel's structure might be different from the original image. Therefore, the geodesic active contour can solve the drawbacks, with improvements to the local shape analysis and preservation of topology.
- **Geometric active contour:** This model is largely implemented using level sets and has been extensively applied

in medical image computing. An MRA segmentation using the level sets technique was proposed by Farag *et al.* [75]. The level sets segmentation approach solves a set of partial differential equations (PDEs) to minimize an energy value, and can preserve the topology and recovering shape. The disadvantage of the proposed method is that no detail was provided on how many initial points were used and how many branches were extracted using this technique.

Statistical-based Compared with conventional clustering algorithms such as k-Nearest Neighbors and fuzzy C-Means, the statistical model can naturally describe both the homogeneity and heterogeneity of materials. A segmentation algorithm based on a statistical model was first introduced by Wilson and Noble [83], [84] when they applied an expectation-maximization (EM) algorithm to statistically classify voxels into vessels or other brain tissue classes. The algorithm could segment the structure of the circle of Willis (CoW) but had difficulties extracting vessels with a small diameter. Based on this statistical model. Hassouna *et al.* [85] divided voxels into vascular and non-vascular classes. They used one normal distribution to model the blood vessels, while the low-level process of the background was modeled using one Rayleigh and two normal distributions. The parameters were estimated using an EM algorithm, as this algorithm is sensitive to the initial estimation. This model can accurately fit the overall intensity histogram distribution of medical images; however, in cerebrovascular segmentation, it can only overcome short gaps and fill holes. Recently, Wen *et al.* [79] presented an automatic statistical intensity-based approach to extract cerebrovascular structure. They found that the proposed algorithm, called the particle swarm optimization (PSO) algorithm, was faster and more robust than traditional algorithms such as EM and stochastic models. It was also capable of accurate segmentation of small-sized blood vessels.

A whole brain blood vessel model was reconstructed from a 3T MRA image by Nowinski *et al.* [86], but the utility of the model for predicting diseases such as stroke was not evidenced. Furthermore, the model was inaccurate and imprecise, because the length and angles did not match when compared with the real distances of each artery in the brain. Such a blood vessel model can be improved by retrieving the image from PC-MRA to validate the accuracy, as introduced by El-Baz *et al.* [66], thus allowing representation of a more accurate 3D blood vessel system. Their study used a statistical-based approach to obtain an accurate extraction of a 3D cerebrovascular system obtained from TOF-MRA or PC-MRA. El-Baz *et al.* [66] claimed that the approaches used in the study were more accurate than those of Gao *et al.* [67].

Hybrid vessel segmentation Hybrid approaches combine two or more techniques to achieve segmentation. Jian and Amini [87] combined the three techniques of multi-scale filtering, level set methods, and deformable geometric modeling, to achieve automatic and accurate quantification of vessel structures from 3D MRA images. Bullitt *et al.* [24] segmented vessels by defining seed points for automatic extraction of image intensity ridges representing a vessel's central skeleton. The advantage of this technique is that it can link disconnected vessels from low-intensity images. A disadvantage of the method is it use many seed points, which will be picked manually at the beginning of the process.

Flasque *et al.* [25] proposed a method for detection, representation, and visualization of the cerebral vascular tree on MRA images. The vessel centerlines were modeled by second-order B-splines to obtain the complete description of the vascular networks. The vascular tree was built by iteratively tracking the centerlines of vessel on candidate voxels. The candidate voxels were selected by combining intensity correction, diffusion filtering, and region growing. The method could only provide topological information, not morphological, as it was unable to measure parameters such as diameter and cross section. The method was also only able to extract the main vessels. Moreover, a fixed thresholding selection in the process may restrict its application.

4) FEATURE EXTRACTION

Understanding the features for blood vessels analysis is very crucial steps. An accurate measurement of the features will meaningfully represent the information that we want to gather for further analysis. Several attributes or parameters [88], [89] used by physicians to diagnose vascular diseases are:

- *Blood vessel morphology*: The shape of blood vessels and the interrelationships between them are the basic information used to detect eventual anomalies. Blood vessels provide evidence of cerebrovascular disease regarding changes in diameter, branching angles, or tortuosity. Previously described preprocessing and segmentation techniques are used to increase the quality of the images to facilitate the accurate extraction of blood vessel structure.
- *Diameter*: The diameters of vessels' cross sections are used to detect malformations that may form constraints to stent-path planning. There are limitations on how wide a diameter to consider for the stent's path, as there are various sizes of the stent device.
- *Velocity*: Blood velocity varies in different regions because of the multiscale structure of vessels. Moreover, the differences are measured to identify regions with stagnancy, which can indicate abnormal vascular regions. The blood flow near occluded areas tends to change from laminar to turbulent flow. This is because the direction of blood flow is changed by obstructions ahead. Therefore, there is a possibility that velocity changes in the blood vessels are caused by an abnormality inside the vessels.
- *Blood Pressure*: Cerebrovascular disease is caused by many factors, which include hypertension. The pressure of the blood, which is related to its velocity, enables the detection of hypertension in zones with an obstruction. Higher blood pressure may affect the stent's path, as it

can affect the stability of the device. This may be taken into consideration to reduce the risk of the device colliding with the wall of the vessels.

- *Tortuosity*: Tortuosity is defined as twists and turns to vessels, where the abnormality in the vessels may affect the level of tortuosity. There are three types of tortuosity metric that can be measured: the distance metric, infection count metric, and sum of angles metric [90]. Tortuosity is measured to specify the level of disease severity related to the vasculature. More twisted vessels indicate that disease is more severe.

The above attributes are important for diagnosis purpose. These can be measured either using image-based, mathematical, or hybrid modeling method. Mathematical and hybrid modeling are discussed in detail in Section II.B and II.C, respectively.

Quantitative analysis of the above attributes can be obtained after blood vessel reconstruction. Diameter and velocity are obtained by averaging results of multiple adjacent extracted blood vessel velocity profiles [91]. Another relevant parameter such as blood flow, wall shear stress can be calculated based on the quantified diameter and velocity. Besides, there are many approaches in measuring the diameter of vessel and majority of them are using skeleton method. The method by Sukanya *et al.* [92] skeletonize the vascular structure then map the vessel boundary to obtain the branching point, the end point of the vessel, and vessel width or diameter. The proposed method is better when compared with manual measurement, and the errors are less than 0.1%. Sankowski and Materka [93] use a similar method in Zhou *et al.* [94] with a slightly different approach but based on binary ball structuring element. The ball is located at the center line in vessel image with an initial smallest radius ball. It will grow until the ball contains a background voxels. Vessel diameter then will be computed based on some iteration and percent of voxels in the last iteration. Tortuosity of vessels can be evaluated using tortuosity metrics.

The most common method is using the distance metrics [96] which provides a ratio of the actual path length to the linear distance between curve endpoints. Bullitt and Guido [90] provide the abnormal type of tortuosity consist of type I until type III. Type I occur when vessels elongate so that a normally straight vessel started to curve. Type II occur in the presence of highly vascular tumors and type III appear in malignant brain tumors when imaged by high-resolution MR.

The other attributes or parameters like velocity, blood pressure, and blood flow may be extracted during segmentation process by mathematical modeling techniques in Section II.B.

B. MATHEMATICAL MODELING

Mathematical models are used to analyze the structure of blood vessels in human organs computationally. The mathematical model is usually based on assumptions made for certain conditions, such as blood is assumed to be a time-dependent viscous incompressible fluid [21], homogeneous Newtonian fluid [16] as the density of blood remains nearly constant. There are also several types of boundary conditions, such as pressure boundary conditions, which may affect the flow distribution in bifurcations.

The basic theory of arterial trees follows the concept of graph theory. A graph, $G = (V, E)$ consists of nodes, V which represent the branching points of the vascular map, while the edges E that connect each branching point are called segments. The branching systems of vascular structures are characterized by their fractal nature, which results in a self-similarity and bifurcation pattern [97]. This fractal nature employs Horton-Strahler's order to describe the structure of human arterial trees [15], [98]. The Strahler order was originally devised to classify river networks, although it can be applied to vascular trees with the arterial bifurcations corresponding to river tributaries, although it does require some modifications, such as blood flow is in the opposite direction to water flow.

Zamir [99] used an L-System Branching Model (LSBM) to generate tree structures incorporating a branching law. The results show that the branching structure patterns of arteries can be mimicked by LBSM if appropriate branching parameters are chosen. However, LBSM could not reproduce all the branching characteristics of arterial trees because of the chosen value of the asymmetry ratio. Conservation of flow rate at the bifurcation follows a cube law, where flow rate in the parent vessel equals the sum of flow rate in the two branches (refer to equation 1).

$$d_0^3 = d_1^3 + d_2^3 \tag{1}$$

Where the variables d_0, d_1, and d_2 indicate a measurement of diameter as in Fig. 7. The diameter ratios can be defined in term of α in equation 2

$$\lambda_1 = \frac{d_1}{d_0} = \frac{1}{(1+\alpha^3)^{\frac{1}{3}}}, \lambda_2 = \frac{d_2}{d_0} = \frac{\alpha}{(1+\alpha^3)^{\frac{1}{3}}}. \tag{2}$$

The ratio of branch length to the length of the parent vessels at the bifurcation is another important parameter to consider. There is no standard way of determining the ratio, but biologically, the length of a vessel segment has a relationship with its diameter. Smaller diameter indicates shorter length and vice versa. The ratio of branch length, γ for the two branches, can be defined as

$$\gamma_1 = \frac{l_1}{l_0} = \frac{d_1}{d_0} = \lambda_1, \quad \gamma_2 = \frac{l_2}{l_0} = \frac{d_2}{d_0} = \lambda_2. \tag{3}$$

Finally, the defined angles, θ_1 and θ_2, complete the arterial bifurcation structure. The angles can be defined as

$$\cos\theta_1 = \frac{(1+\alpha^3)^{\frac{4}{3}} + 1 - \alpha^4}{2(1+\alpha^3)^{\frac{2}{3}}}, \cos\theta_2 = \frac{(1+\alpha^3)^{\frac{4}{3}} + \alpha^4 - 1}{2\alpha^2(1+\alpha^3)^{\frac{2}{3}}} \tag{4}$$

Later, a technique called constraint constructive optimization (CCO) [14], [15], [32], [33], [100]–[104] was adapted

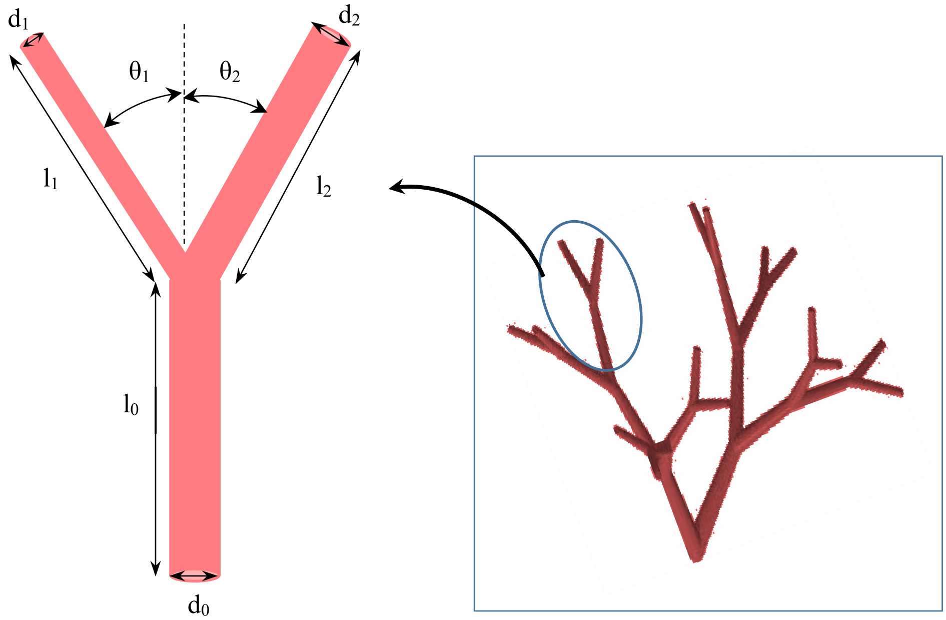


FIGURE 7. The theory of mathematical modeling approaches for arterial tree bifurcation area.

to the fractal scaling concept [99], [105] to produce fractal tree structures. This method involves geometric and structural optimization, which minimizes the total volume of blood vessels and ensures uniform blood perfusion in the designated domain. The arterial tree is generated without the input of anatomical data, for example, from the images from MRA, CTA, or another imaging modality, where it starts from the main artery that supplies blood to the smaller arteries. The advantage of CCO is that the method allows the generation of arterial tree models with many vessel segments (about 10^4 in number), although accuracy remains a challenge. Furthermore, CCO trees display realistic vessels and reproduce the properties of real arterial trees, such as branching angle statistics, diameter ratios of parent and daughter segments, and the volumes of large arteries quite satisfactorily [103]. CCO also follows the bifurcation law in equation 1, and the vessels are generated in a circular area with a radius r_{perf} that is assumed to represent the tissue or perfusion area. The total perfusion flow, Q_{perf} is assumed to enter the root segment at a constant pressure, p_{perf} and it requires to deliver equal flow for all terminal segments, N_{term}.

$$Q_{term} = Q_{perf}/N_{term}, \tag{5}$$

where $Q_{perf} = p_{perf} - p_{term}$ is the total perfusion flow across overall pressure drop.

Flow models using fractal techniques may consider the distribution of pressure and velocity in a vascular branching network and the hydrodynamic resistance, R_j of each segment, j is given by Poiseuille's law

$$R_j = \left(\frac{8\eta}{\pi}\right)\frac{l_j}{r_j^4}, \tag{6}$$

These can be obtained by solving a system of ordinary differential equations (ODEs) describing the flow conservation at bifurcation points [33]. Cebral *et al.* [21] also generated cerebral arterial trees using an image-based CCO method as in Karch *et al.* [17], [103], with the trees exhibiting geometrical properties such as bifurcation angles, area and symmetry ratios, and branch diameters. The results showed good agreement with the real vascular system.

Arteries can be modeled as tree-like structures with blood flowing from the largest to the smallest artery. Hence, Schreiner [100] and Neumann *et al.* [106] developed a 2D arterial tree model. Their studies found that the segment diameters and branching angles were in good agreement with the real structure of the human heart. A 2D model is not fully reliable in medical applications. Therefore, with consideration of this limitation, Karch *et al.* [16] constructed a 3D model of the arterial tree structure of hemodynamic simulation studies. Recently, Blanco *et al.* [104] also used a computational approach to generate the arterial network in each separately partitioned vascular territory to avoid overlapping. For example, the brain is divided into four lobes (frontal, parietal, occipital and temporal lobe), and there are three arterial networks that supply each lobe; these are specifically named as the anterior cerebral artery (ACA), middle cerebral artery (MCA), and posterior cerebral artery (PCA).

Alastruey *et al.* [28] utilized a 1D equation of pressure and flow wave propagation to investigate the behavior of blood flow when a part of a blood vessel was missing. This study found that the anterior communicating artery (ACoA) is a more important path than the posterior communicating artery (PCoA) when the ICA is occluded. The equation also provided physiological data such as the length, radius, and

TABLE 5. Summary of segmentation methods.

Authors	Segmentation: Region-based	Active contour	Statistical-based	Hybrid	Advantages	Disadvantages	Result
Wilson and Noble [83]			√		Accurate initial estimation of vessels and aneurysm	Less extraction of vessels	8% of automatically segmented voxels are not appeared as in manual segmentation
Wilson and Noble [84]			√		• Works well for intracranial arteries near the circle of Willis (CoW) • May not capture many of the distal arteries	The segmentation underestimates large and giant aneurysms	Automatic segmentation failed to segment a large and giant aneurysm but works well for a small aneurysm
Bullitt, et al. [24]	√				Linking disconnected vessels	• Lacks information on the blood flow in the CoW • Time-consuming	High level of accuracy with above 90% correct vessel segmentation and clinically acceptable
Flasque, et al. [25]	√				• Low-computation cost • Accurate	Unable to measure parameters such as diameter and cross section	Accuracy is better than 0.7 voxels and 5° on synthetic images
Hassouna, et al. [85]			√		High-quality segmentation	• Only overcomes short gaps and fills holes in cerebrovascular segmentation • Fixed modality	Not provided
Forkert, et al. [27]		√		√	Accurate		0.42mm accuracy compared with initial segmentation. Detects an average of 35 additional connection, whereby 92.7% declared as correct by medical expert.
El-Baz, et al. [66]				√	Fast and accurate	Difficult to estimate the number of objects when there is a dominant low-weighted mode	0.18–1.34% erroneous voxels compared to 3.97–9.52% for the Wilson–Noble approach on the synthetic TOF-MRA data and 0.14–0.79% of erroneous voxels comparing to 2.12–4.01% for the Chung–Noble approach on the synthetic PC-MRA data
Almi'ani and Barkana [65]	√				Provides a parameter-free environment	2D	Produced more vessels compared with the ground truth
Tian, et al. [62]		√			• Able to extract the entire cerebral tree • Efficient and robust	Unable to precisely segment abnormal vessels	Low error rate and time cost for 9 datasets 24.63% error rate 3.12m 31.42% error rate 4.26m 20.18% error rate 2.61m 36.57% error rate 3.21m 19.83% error rate 1.76m 17.65% error rate 3.03m 18.51% error rate 4.04m 29.93% error rate 3.81m 21.32% error rate 2.17m
Forkert, et al. [95]				√	Exhibits most vessel structure	Not capable of segmenting turbulent and fast blood flow in a vessel (low intensity)	Mean dice coefficient of 0.806
Suran, et al. [70]	√				Provides a way to find the shortest path	• Semi-automated • Lack of information on the shortest path provided	The shortest path is not accurate as the brain vessels reconstruction is not realistic
Wang, et al. [71]	√				Fast when running the segmentation on one slice of an image (0.13 s)		Dice similarity coefficient is 0.84 with run time per slice 0.13s
Dufour, et al. [20]				√	• Reconnects vessel-like structures • Time-saving	Cannot filter well in high noise	Sensitivity 99.9%, 100%, and 65.77% for 3 type of 3D datasets

thickness of arterial segments from the aortic arch to the intracranial arteries. The method used was able to predict the hemodynamic effect of clinical interventions such as carotid endarterectomy, angioplasty, and stenting. It would have been beneficial if this study had included sufficient experimental confirmation of their findings for validation and accuracy purposes.

In 2013, Galarreta-Valverde *et al.* [7] used the stochastic L-system (SLS) to generate arterial structure by incorporating stochastic and parametric rules that can be used to simulate CTA and MRA datasets. The authors attempted to produce a realistic-looking synthetic arterial tree in 3D by taking into account the arbitrary surface as a physical constraint. The results were visually very convincing, with them resembling images from CTA or MRA. However, it would be improved if there was an additional constraint added like tortuosity level, which might be very important for diseased arteries.

Hamarneh and Jassi [107] introduced VascuSynth with an algorithm similar to the CCO method. VascuSynth produces a simulation of a realistic vascular tree structure but does not provide the specific human organ. However, it does give an insight into how an algorithm capable of producing a cerebral blood vessel model could be implemented.

The reconstruction of artificial vessels using a mathematical model offers advantages such as lower acquisition time, lower cost, and the flexibility to create vessels with

TABLE 6. The summary of mathematical modeling techniques.

Authors	Mathematical model/equation	Description	Disadvantages	Results
Zamir [102]	L-System Branching Model (LSBM)	Employs several equations as follows: (1) Cube Law (2) Diameter ratios equation (3) Ratio of branch length (4) Angles	• Based on assumptions at all levels of the tree • The vessel structure is assumed to be a straight line	L-systems can be used to produce fractal tree structures that have some but not all the branching characteristics of arterial trees.
Schreiner, et al. [14], Schreiner, et al. [15], Schreiner [103], Schreiner, et al. [104], Schreiner, et al. [105]	Constrained Constructive Optimization (CCO)	Follows fractal laws to produce a branch structure	• Generates the arterial structure in circular, square, and elliptical shapes (not the real shapes of a human organ) • The locations of major arteries are randomly generated	Cover larger range of mother diameters (≈ from $5\mu m$ to $2000\mu m$) while the model data only extend from $100\mu m$ to $2500\mu m$
Alastruey, et al. [29]	1-D model of pulse wave propagation	Able to predict the hemodynamic effect of clinical interventions such as carotid endarterectomy, angioplasty, and stenting.	• Lack of experimental confirmation • Limited to the most frequent anatomical variation of cerebrovascular network	• ACoA is important path than PCoA when ICA is occluded • Magnitude of the velocity is low
Galarreta-Valverde, et al. [7]	Stochastic L-System (SLS)	• Extended version of conventional L-system by Zamir [102] • Introduces a stochastic rule	• Involves tedious and intricate handwork • Needs suitable parameter tuning to match the real vascular tree properties	221998 vascular tree created within the liver surface took 55 minutes for 11 iterations, and the vascular tree within the thigh surface took 10 minutes for nine iterations.
Hamarneh and Jassi [110], Jassi and Hamarneh [111]	VascuSynth	Simulates volumetric images of vascular trees and generates the corresponding ground-truth segmentations, bifurcation locations, branch properties, and tree hierarchy.	• Only produces straight branches • Without surrounding organs like brain, liver, lungs, and kidney	The vascular structure is curvy, similar with real vessels but not realistic as it does not have a background tissue

different growth configurations and the possibility to incorporate anomalies [7]. Besides which, the synthetic vessels could also contribute to the simulation of surgical techniques. Downsides of the method include inaccuracies and that it lacks information from real data, although it can preserve the geometrical structure of blood vessels. The source of the variables used for the parameters is also unknown. Table 6 summarizes the mathematical modeling techniques.

C. HYBRID MODELING

The distinction between mathematical and hybrid model is a mathematical model using several mathematical laws and assumptions to reconstruct vessel tree. Meanwhile, the hybrid modeling combines two or more methods such as image-based and mathematical model such as computational fluid dynamics (CFD) [3], [11], [109], [111], [112] and multiscale modeling of cerebral blood flow [32], [33] to reconstruct blood vessel structures. The information from the reconstructed vessel will be used as a perfusion site or boundary conditions for CFD simulation. It can provide detailed predictions of hemodynamics using input parameters derived from medical imaging, blood sampling, and other patient information. Computational fluid dynamics has become a practical and reliable tool for the study of time-varying 3D blood flow behavior in complex arterial geometries. CFD has been used by many groups to investigate possible correlations between hemodynamics and the risk of rupture or growth of intracranial arteries.

Bui *et al.* [34] conducted a study that facilitates a fractal approach to reconstruct brain blood vessels including small blood vessels. The study employs a concept of CCO (refer II.B) to develop the optimized structure by combining with a generated surface of brain tissue using a level sets method from CT or MRI as a staged growth perfusion site. The vascular simulation will only occur inside the brain tissues area.

The computational modeling of blood flow in complex vascular models can help researchers to quantify the relationships between hemodynamic changes and the path used to insert a stent. It is essential to understand the hemodynamic changes occurring in aneurysms and arterial stenoses, for both their diagnosis and their treatment. Blood flow direction within arteries can be considered as a constraint to the stent-path, as the blood flow will alter its direction if there is a blood clot obstructing the arteries. Changes in the topology and geometry of the vascular tree may also directly impact the risk of later severe clinical events such as ischemic and hemorrhagic stroke. The stability of the hemodynamic pattern post-stenting is linked to the success of the stenting procedures [22], [23] because the stent inserted into a blood vessel will divert the flow from entering the aneurysm. It can reduce the pressure inside an aneurysm and minimize the likelihood of post-treatment rupture [113].

Cassot *et al.* [114] conducted a study to investigate how changes in the diameter of arteries may affect the circulation inside the brain. They found that small changes in diameter may induce a dramatic pressure drop in cerebral vascular territories. In their study, they focused more on the CoW, as it is the main source of collateral flow to the brain. The advantage of using a linear mathematical model was that its computation

TABLE 7. The summary of hybrid modeling techniques.

Authors	Methods	Description	Disadvantages	Results
Bui, et al. [33], Bui, et al. [34], Bui, et al. [35]	Constrained Constructive Optimization (CCO) and CT or MRI	Generates the arterial structure following the real shape of a human organ CFD by solving ODEs	The mathematical model for small blood vessels cannot be employed to simulate flow in large blood vessels due to an assumption that ignores oscillatory pressure propagation and reflection	Provide detailed descriptions of the flow and pressure distributions of blood vessel sizes at different levels and simulate the variations of the blood flow in the major cerebral arteries
Cebral et al., [21]	Component-based approach and tubular deformable model (image-based method) and CFD simulation	This work combine an image-based method such as tubular deformable model, and the flow velocity was computed using CFD simulation	No tissue perfusion model for the construction arterial tree model	Comparison of three models shows that the mean wall shear stress (WSS) of Newtonian and Casson models agree quite well while for the Newtonian and vascular bed model produced slightly higher oscillatory shear index (OSI) and low WSS.
Grinberg et al.,[31]	Finite-element (FE) discretization and MRA, CT, and DSA	Review some issue to reconstruct 3D image from MRA and CTA using CFD model	Require large scale of computers	A single multiscale simulation of the human brain vascular network is estimated approximately 27.7 wall-clock hours per cardiac cycle on 110000 processors
Anor et al. [118]	CFD and CT	Reviewed models for blood flow, and efficient numerical methods for performing large-scale simulations. Specifically, we focused on simulations in large arterial networks, such as the intracranial tree	Time-consuming from medical image acquisition to post-processing of the CFD results	A high 3D simulation is possible since there exist an advanced computer hardware and numerical methods. It can minimize processing time
Grinberg et al.,[30]	CFD and CT	Developed and implemented a two-level domain decomposition method, and a new type of outflow boundary condition	Focus only on MaN network (large vessel network)	• Strong development of secondary flows in the communicating arteries and ICA • High-pressure drop along the PCA-P1 artery • Requires setting the peripheral resistance to high values • The high-pressure variation correlated with the phase shift at the inlet flow points to a new direction in diagnosing cranial vasculature disorders

time was very low and that it might be an accurate assessment tool for cerebral hemodynamics in carotid disease. The dynamics of blood flow in the human brain are determined by a complex network of vessels, especially in the CoW area, because in many cases the CoW is incomplete or missing an arterial segment. Therefore, studies [31], [115]–[117] have been conducted to examine patient-specific blood flow.

In recent years, there have been many attempts to investigate the blood flow in the CoW, because this circle connects the internal carotid arteries with other cerebral arteries, and the CoW is a common location for aneurysms. The importance of the CoW has been demonstrated by many studies [21], [28]–[30], [114], and the blood pressure and velocity are determined by the completeness or incompleteness of the circle [28], [29]. Cebral *et al.* [21] investigated blood flow models of the CoW from MRA surface reconstruction. This work combines an image-based method such as tubular deformable model, and the flow velocity was computed using CFD simulation. The final surface triangulation is used as a support surface to define the computational domain whereby a hybrid method is used to develop patient-specific models of the cerebral circulation. The hybrid method included anatomical and physiological imaging techniques with computer simulation technology. However, the remaining challenge for this physiologic technique was that the material properties of the arterial wall and physiologic pressure waveforms that drive the wall motion were difficult to measure non-invasively. Therefore, the use of a hybrid method to describe the blood flow appeared promising.

Blood vessels are modeled mathematically to identify their direction. In engineering fields, CFD is also used to simulate blood flow in arteries, stented vessels, and vascular disease, but this is limited to only one or two arteries [118], [119]. Therefore, the work by Grinberg *et al.* [30] enhances the technique to investigate features for different levels of vessel networks, although it requires high amounts of computer processing power to reduce the time required for generation of the results. They provide a review of some issue to reconstruct a 3D image from MRA and CTA using CFD model. Anor *et al.* [115] also provide a review of models for blood flow and effective numerical methods for performing large-scale simulations. They focused on simulations in large arterial networks, such as the intracranial tree.

Grinberg *et al.* [29] studied blood vessel simulation in large arteries. The flow simulation may replace the dye injection procedures currently used for visualizing blood flow, as injection of dye is an invasive procedure. The work is divided into two stages, with the first stage concerned with reconstructing vascular networks from a combination of medical images obtained from CT, DSA, and MRA. The purpose of

TABLE 8. Advantages and disadvantages of the different reviewed modeling techniques.

	Image-based modeling	Mathematical modeling	Hybrid modeling
Description	Reconstruction of blood vessel models directly from imaging data	Generates arterial model using computational algorithm without the input of anatomical model information	Analyzing the hemodynamic changes in the blood vessels
Data acquisition	XA, CTA, MRA	• Random numbers to define the nodes in the graph • Mathematical equation	• XA, CTA, MRA • Mathematical equation
Accuracy	Better accuracy	• Less accurate • Realistic vessel models	Most accurate
Processing time	Based on the image and technique used	Based on the number of iterations	Considers processing time of both image-based and mathematical modeling
Performance	Can be measured using PSNR or CNR	Can be measured using the number of vessels obtained	Can be measured by comparing the intensity value in the image with the velocity and pressure in the vessels
Features	• Diameter of vessels • Tortuosity	• Branching angles • Length of vessels • Diameter of vessels • Symmetry ratio • Flow rate	Geometrical structure from both modeling techniques and the behavior of blood flow inside the vessels
Application	Assists clinician in diagnosing disease by providing an accurate reconstruction of vessels	Provides surgical simulation for decreasing the risks involved in real surgical procedures	Provide cerebral vessel models capable of simulating the blood flow in diseased arteries

processing the medical data was to obtain information such as boundary conditions, velocity, and the resistance of blood flow for use in CFD simulations. The second stage was to incorporate all the information gathered in stage one into several numerical models designed to visualize the blood flow. The results show the development of strong secondary flows in the communicating arteries and internal carotid artery (ICA), for both complete and incomplete CoWs. This provides a new direction in the diagnosis of vasculature disorders by patient-specific information, especially for a patient with an incomplete CoW. Table 7 summarizes the hybrid modeling techniques.

III. COMPARISON OF THE MODELING TECHNIQUES

This paper has discussed modeling techniques and classified them into three groups based on the different algorithms employed in the techniques. Therefore, this section will provide an overall comparison of the three modeling classes, namely image-based modeling, mathematical modeling, and hybrid modeling, as depicted in Table 7.

Reconstructing blood vessels from medical images is difficult due to the complex nature of cerebral vessels. It can be more tedious for low-resolution images. Therefore, in image-based modeling, many techniques have been developed to deal with many types of noise and artifact within the images. As these approaches deal directly with the images from XA, CTA, or MRA, the results are more accurate than mathematical modeling approaches. Thus, the hybrid model can result in better accuracy, as it employs features from both modeling techniques to reconstruct models of cerebral vessels. For example, tortuosity may complicate the image processing part, but this feature is difficult to reproduce using a mathematical approach. Therefore, the vessel structure may be completed by combining both types of information.

Image-based modeling can be applied to assist clinicians in diagnosing disease by providing accurate reconstructions of vessels, while mathematical modeling can generate synthetic arterial structures that can be used for surgical simulations. By incorporating both modeling techniques, hybrid modeling may produce a reliable diagnosis and surgical planning tool for clinicians.

IV. OPEN ISSUES

The challenges of reconstructing cerebral vessel models have given rise to a tremendous amount of research on modeling techniques, such as providing the fastest and most robust algorithm. Mathematical modeling may be inaccurate at first, but by incorporating information obtained from medical images, it may become the most accurate model for cerebral blood vessels. Construction of a blood vessel model is important to enable the clear visualization of abnormal structures in cerebral vessels, in either 2D or 3D projections, especially for surgical planning. The future direction of this research will be towards developing faster, more accurate, and more automated techniques for reconstruction of the vasculature so that the shortest path for a stenting procedure can be more reliably found.

To the best of our knowledge, little work has been performed on finding the shortest path for stenting procedures. Schafer *et al* [120] proposed a graph representation technique to calculate the shortest pathways for a guidewire in a phantom of the carotid artery. The simulation results show that their proposed algorithm yielded a good agreement with the actual guidewire path. However, this work was limited to only the carotid artery, while this study will accommodate the whole structure of the cerebral vasculature. Suran *et al.* [70] performed a study on finding the shortest path in the cerebral vascular system, but it lacked information regarding the blood vessels. Supposedly, there are several parameters that should be taken into consideration, such as the vessel centerline, the diameter of the corresponding vessel, and tortuosity [120]. Non-inclusion of these parameters will affect the accuracy of the planning of the shortest path for stent placement.

Therefore, more research work should be performed to combine cerebral vasculature information with the parameters mentioned previously. It includes accurate and realistic 3D reconstruction of cerebral blood vessels to offer accurate and reliable diagnosis and indicate the shortest path for stenting procedures. It would then become a great tool for assisting clinicians.

V. CONCLUSIONS

This paper has outlined three techniques, namely image-based, mathematical, and hybrid modeling. The image-based techniques were shown to be more accurate than mathematical modeling techniques, but we believe that incorporating both techniques allows more satisfying results to be achieved. Hybrid models provide a faster and more robust technique, which can significantly help in diagnosis and surgical planning, such as finding the shortest path for a stenting procedure. Faster analysis of medical images can be achieved by developing a robust filtering and segmentation algorithm.

Faster segmentation can be achieved by employing multiscale processing to cover the different sizes of blood vessels [5]. Another way to achieve fast processing is to implement a processing technique in high-resolution images.

Accuracy in the modeling of cerebral vessels and definition of the shortest path is vital for accurate diagnosis and surgical planning. Implementation of hybrid modeling can help to achieve both with increased accuracy. By taking advantage of image-based and mathematical modeling, it is possible to introduce new constraints, which can later be used for stent-path planning.

REFERENCES

[1] G. Dougherty, *Medical Image Processing: Techniques and Applications*. New York, NY, USA: Springer, 2011.

[2] *Institute for Health Metrics and Evaluation. Leading Causes of YLDs in 2015 and Percent Change, 2005–2015*. [Online]. Available: http://www.healthdata.org/malaysia

[3] H.-Y. Wey, V. R. Desai, and T. Q. Duong, "A review of current imaging methods used in stroke research," *Neurol. Res.*, vol. 35, no. 10, pp. 1092–1102, 2013.

[4] J. S. Suri, K. Liu, L. Reden, and S. Laxminarayan, "A review on MR vascular image processing: Skeleton versus nonskeleton approaches: Part II," *IEEE Trans. Inf. Technol. Biomed.*, vol. 6, no. 4, pp. 338–350, Dec. 2002.

[5] C. Kirbas and F. Quek, "A review of vessel extraction techniques and algorithms," *ACM Comput. Surv.*, vol. 36, no. 2, pp. 81–121, 2004.

[6] D. Lesage, E. D. Angelini, I. Bloch, and G. Funka-Lea, "A review of 3D vessel lumen segmentation techniques: Models, features and extraction schemes," *Med. Image Anal.*, vol. 13, no. 6, pp. 819–845, Aug. 2009.

[7] M. A. Galarreta-Valverde, M. M. G. Macedo, C. Mekkaoui, and M. P. Jackowski, "Three-dimensional synthetic blood vessel generation using stochastic L-systems," *Proc. SPIE*, vol. 8669, pp. 86691I-1–86691I-6, Mar. 2013.

[8] T. Mori, K. Kazita, K. Chokyu, T. Mima, and K. Mori, "Short-term arteriographic and clinical outcome after cerebral angioplasty and stenting for intracranial vertebrobasilar and carotid atheroscleroticocclusive disease," *Amer. J. Neuroradiol.*, vol. 21, no. 2, pp. 249–254, 2000.

[9] R. T. Higashida *et al.*, "Intracranial angioplasty & stenting for cerebral atherosclerosis: A position statement of the american society of interventional and therapeutic neuroradiology, society of interventional radiology, and the american society of neuroradiology," *J. Vascular Intervent. Radiol.*, vol. 16, no. 10, pp. 1281–1285, 2005.

[10] (2017). *Carotid Artery Surgery/Endarterectomy—MyMedicPlus*, accessed on May 2, 2017. [Online]. Available: http://www.mymedicplus.com/index.php?option=com_k2&view=item&id=1696:carotid-artery-surgery-endarterectomy&Itemid=142

[11] The Stroke Blog. (2017). *Stroke Clinical Trials Archives—The Stroke Blog*, accessed on May 2, 2017. [Online]. Available: https://strokeblog.net/category/stroke-clinical-trials/

[12] (2017). *Stryker Neurovascular | Neuroform EZ Stent System*, accessed on May 2, 2017. [Online]. Available: http://www.strykerneurovascular.com/products/hemorrhagic/neuroform-ez-stent-system

[13] P. Animation. (2017). *Polygon Medical Animation | Angioplasty Medical Illustration*, accessed on May 2, 2017. [Online]. Available: Polygonmedical.com and http://www.polygonmedical.com/angioplasty.html

[14] W. Schreiner, F. Neumann, M. Neumann, A. End, S. M. Roedler, and S. Aharinejad, "The influence of optimization target selection on the structure of arterial tree models generated by constrained constructive optimization," *J. Gen. Physiol.*, vol. 106, no. 4, pp. 583–599, 1995.

[15] W. Schreiner, F. Neumann, M. Neumann, A. End, and M. R. Müller, "Structural quantification and bifurcation symmetry in arterial tree models generated by constrained constructive optimization," *J. Theor. Biol.*, vol. 180, no. 2, pp. 161–174, May 1996.

[16] R. Karch, F. Neumann, M. Neumann, and W. Schreiner, "A three-dimensional model for arterial tree representation, generated by constrained constructive optimization," *Comput. Biol. Med.*, vol. 29, no. 1, pp. 19–38, Jan. 1999.

[17] R. Karch, F. Neumann, M. Neumann, and W. Schreiner, "Staged growth of optimized arterial model trees," *Ann. Biomed. Eng.*, vol. 28, no. 5, pp. 495–511, May 2000.

[18] P. T. H. Truc, M. A. U. Khan, S. Lee, and T.-S. Kim, "A new approach to vessel enhancement in angiography images," in *Proc. IEEE/ICME Int. Conf. Complex Med. Eng.*, May 2007, pp. 878–884.

[19] K. Sun, Z. Chen, S. Jiang, and Y. Wang, "Morphological multiscale enhancement, fuzzy filter and watershed for vascular tree extraction in angiogram," *J. Med. Syst.*, vol. 35, no. 5, pp. 811–824, Oct. 2011.

[20] A. Dufour *et al.*, "Filtering and segmentation of 3D angiographic data: Advances based on mathematical morphology," *Med. Image Anal.*, vol. 17, no. 2, pp. 147–164, Feb. 2013.

[21] J. R. Cebral, M. A. Castro, O. Soto, R. Löhner, and N. Alperin, "Blood-flow models of the circle of Willis from magnetic resonance data," *J. Eng. Math.*, vol. 47, nos. 3–4, pp. 369–386, Dec. 2003.

[22] J. R. Cebral *et al.*, "Aneurysm rupture following treatment with flow-diverting stents: Computational hemodynamics analysis of treatment," *Amer. J. Neuroradiol.*, vol. 32, no. 1, pp. 27–33, 2011.

[23] I. Larrabide *et al.*, "Intra-aneurysmal pressure and flow changes induced by flow diverters: Relation to aneurysm size and shape," *Amer. J. Neuroradiol.*, vol. 34, no. 4, pp. 816–822, 2013.

[24] E. Bullitt, S. Aylward, K. Smith, S. Mukherji, M. Jiroutek, and K. Müller, "Symbolic description of intracerebral vessels segmented from magnetic resonance angiograms and evaluation by comparison with X-ray angiograms," *Med. Image Anal.*, vol. 5, no. 2, pp. 157–169, Jun. 2001.

[25] N. Flasque, M. Desvignes, J.-M. Constans, and M. Revenu, "Acquisition, segmentation and tracking of the cerebral vascular tree on 3D magnetic resonance angiography images," *Med. Image Anal.*, vol. 5, no. 3, pp. 173–183, Sep. 2001.

[26] A. F. Frangi, W. J. Niessen, P. J. Nederkoorn, J. Bakker, W. P. T. M. Mali, and M. A. Viergever, "Quantitative analysis of vascular morphology from 3D MR angiograms: *In vitro* and *in vivo* results," *Magn. Reson. Med.*, vol. 45, no. 2, pp. 311–322, Feb. 2001.

[27] N. Forkert *et al.*, "Automatic correction of gaps in cerebrovascular segmentations extracted from 3D time-of-flight MRA datasets," *Methods Inf. Med.*, vol. 51, no. 5, p. 415, 2012.

[28] J. Alastruey, K. Parker, J. Peiró, S. Byrd, and S. Sherwin, "Modelling the circle of Willis to assess the effects of anatomical variations and occlusions on cerebral flows," *J. Biomech.*, vol. 40, no. 8, pp. 1794–1805, 2007.

[29] L. Grinberg, T. Anor, E. Cheever, J. R. Madsen, and G. E. Karniadakis, "Simulation of the human intracranial arterial tree," *Philos. Trans. Roy. Soc. London A, Math. Phys. Sci.*, vol. 367, no. 1896, pp. 2371–2386, 2009.

[30] L. Grinberg, T. Anor, J. R. Madsen, A. Yakhot, and G. E. Karniadakis, "Large-scale simulation of the human arterial tree," *Clin. Experim. Pharmacol. Physiol.*, vol. 36, no. 2, pp. 194–205, Feb. 2009.

[31] C. A. Taylor and D. A. Steinman, "Image-based modeling of blood flow and vessel wall dynamics: Applications, methods and future directions," *Ann. Biomed. Eng.*, vol. 38, pp. 1188–1203, 2010.

[32] A. Bui, R. Manasseh, I. Šutalo, and K. Liffman, "Multiscale modeling of cerebral blood flow," in *Proc. 7th Int. Conf. CFD Minerals Process Ind.*, Melbourne, VIC, Australia, Dec. 2009, pp. 145–147.

[33] A. Bui, I. D. Šutalo, R. Manasseh, and K. Liffman, "Dynamics of pulsatile flow in fractal models of vascular branching networks," *Med. Biol. Eng. Comput.*, vol. 47, no. 7, pp. 763–772, Jul. 2009.

[34] A. V. Bui, R. Manasseh, K. Liffman, and I. D. Šutalo, "Development of optimized vascular fractal tree models using level set distance function," *Med. Eng. Phys.*, vol. 32, no. 7, pp. 790–794, Sep. 2010.

[35] H. G. J. Kortman, E. J. Smit, M. T. H. Oei, R. Manniesing, M. Prokop, and F. J. A. Meijer, "4D-CTA in neurovascular disease: A review," *Amer. J. Neuroradiol.*, vol. 36, no. 6, pp. 1026–1033, 2015.

[36] S.-J. Sun *et al.*, "ŞDynamic spot signŤ on CT perfusion source images predicts haematoma expansion in acute intracerebral haemorrhage," *Eur. Radiol.*, vol. 23, no. 7, pp. 1846–1854, Jul. 2013.

[37] A. M. Frölich *et al.*, "Time-resolved assessment of collateral flow using 4D CT angiography in large-vessel occlusion stroke," *Eur. Radiol.*, vol. 24, no. 2, pp. 390–396, Feb. 2014.

[38] A. M. J. Frölich, D. Schrader, E. Klotz, R. Schramm, K. Wasser, M. Knauth, and P. Schramm, "4D CT angiography more closely defines intracranial thrombus burden than single-phase CT angiography," *Amer. J. Neuroradiol.*, vol. 34, no. 10, pp. 1908–1913, 2013.

[39] M. P. Hartung, T. M. Grist, and C. J. François, "Magnetic resonance angiography: Current status and future directions," *J Cardiovascular Magn. Reson.*, vol. 13, no. 1, p. 19, 2011.

[40] W. Cai, B. Zhao, D. Conover, J. Liu, and R. Ning, "Dynamic cone beam CT angiography of carotid and cerebral arteries using canine model," *Med. Phys.*, vol. 39, no. 1, pp. 543–553, Jan. 2012.

[41] D.-Y. Kim, "3D volume extraction of cerebrovascular structure on brain magnetic resonance angiography data sets," *J. Biomed. Sci. Eng.*, vol. 5, no. 10, p. 574, 2012.

[42] D. Vu, R. G. González, and P. W. Schaefer, "Conventional MRI and MR angiography of stroke," in *Acute Ischemic Stroke*. Berlin, Germany: Springer, 2006, pp. 115–137.

[43] X. Bi, P. Weale, P. Schmitt, S. Zuehlsdorff, and R. Jerecic, "Non-contrast-enhanced four-dimensional (4D) intracranial MR angiography: A feasibility study," *Magn. Reson. Med.*, vol. 63, no. 3, pp. 835–841, Mar. 2010.

[44] N. D. Forkert, J. Fiehler, T. Illies, D. P. F. Möller, H. Handels, and D. Säring, "4D blood flow visualization fusing 3D and 4D MRA image sequences," *J. Magn. Reson. Imag.*, vol. 36, no. 2, pp. 443–453, Aug. 2012.

[45] K. N. Chaudhury and K. Rithwik, "Image denoising using optimally weighted bilateral filters: A sure and fast approach," in *Proc. IEEE Int. Conf. Image Process. (ICIP)*, Sep. 2015, pp. 108–112.

[46] H.-H. Chang, T.-J. Hsieh, Y.-N. Ting, and W.-C. Chu, "Rician noise removal in MR images using an adaptive trilateral filter," in *Proc. 4th Int. Conf. Biomed. Eng. Inform. (BMEI)*, Oct. 2011, pp. 467–471.

[47] P. Perona and J. Malik, "Scale-space and edge detection using anisotropic diffusion," *IEEE Trans. Pattern Anal. Mach. Intell.*, vol. 12, no. 7, pp. 629–639, Jul. 1990.

[48] S. D. Olabarriaga, M. Breeuwer, and W. J. Niessen, "Evaluation of Hessian-based filters to enhance the axis of coronary arteries in CT images, in: Computer assisted radiology and surgery," *Proc. 17th Int. Congr. Exhib.*, vol. 1256. London, U.K., 2003, pp. 1191–1196.

[49] C.-Y. Hsu, B. Schneller, M. Ghaffari, A. Alaraj, and A. Linninger, "Medical image processing for fully integrated subject specific whole brain mesh generation," *Technologies*, vol. 3, no. 2, pp. 126–141, 2015.

[50] P. T. H. Truc, M. A. U. Khan, Y.-K. Lee, S. Lee, and T.-S. Kim, "Vessel enhancement filter using directional filter bank," *Comput. Vis. Image Understand.*, vol. 113, no. 1, pp. 101–112, Jan. 2009.

[51] C. Cañero and P. Radeva, "Vesselness enhancement diffusion," *Pattern Recognit. Lett.*, vol. 24, no. 16, pp. 3141–3151, Dec. 2003.

[52] A. F. Solé, A. López, and G. Sapiro, "Crease enhancement diffusion," *Comput. Vis. Image Understand.*, vol. 84, no. 2, pp. 241–248, Nov. 2001.

[53] J. Du, S. B. Fain, T. Gu, T. M. Grist, and C. A. Mistretta, "Noise reduction in MR angiography with nonlinear anisotropic filtering," *J. Magn. Reson. Imag.*, vol. 19, no. 5, pp. 632–639, May 2004.

[54] C. S. Anand and J. S. Sahambi, "MRI denoising using bilateral filter in redundant wavelet domain," in *Proc. IEEE Region Conf. (TENCON)*, Nov. 2008, pp. 1–6.

[55] B. Zhang and J. P. Allebach, "Adaptive bilateral filter for sharpness enhancement and noise removal," *IEEE Trans. Image Process.*, vol. 17, no. 5, pp. 664–678, May 2008.

[56] R. Riji, J. Rajan, J. Sijbers, and M. S. Nair, "Iterative bilateral filter for Rician noise reduction in MR images," *Signal, Image Video Process.*, vol. 9, no. 7, pp. 1543–1548, Oct. 2015.

[57] D. Bhonsle, V. Chandra, and G. Sinha, "Medical image denoising using bilateral filter," *Int. J. Image, Graph. Signal Process.*, vol. 4, no. 6, pp. 36–43, 2012.

[58] M. Erdt, M. Raspe, and M. Süehling, "Automatic hepatic vessel segmentation using graphics hardware," in *Proc. 4th Int Workshop Med. Imag. Augmented Reality (MIAR)*, vol. 5128. 2008, pp. 403–412.

[59] A. F. Frangi, W. J. Niessen, K. L. Vincken, and M. A. Viergever, "Multiscale vessel enhancement filtering," in *Medical Image Computing and Computer-Assisted Intervention—MICCAI*. Springer, 1998, pp. 130–137.

[60] Y. Sato *et al.*, "Three-dimensional multi-scale line filter for segmentation and visualization of curvilinear structures in medical images," *Med. Image Anal.*, vol. 2, no. 2, pp. 143–168, 1998.

[61] C. Lorenz, I.-C. Carlsen, T. M. Buzug, C. Fassnacht, and J. Weese, "Multi-scale line segmentation with automatic estimation of width, contrast and tangential direction in 2D and 3D medical images," in *Proc. CVRMed-MRCAS*, 1997, pp. 233–242.

[62] Y. Tian *et al.*, "A flexible 3D cerebrovascular extraction from TOF-MRA images," *Neurocomputing*, vol. 121, pp. 392–400, Dec. 2013.

[63] S. Hassan and J. Yoon, "A hybrid approach for vessel enhancement and fast level set segmenatation based 3d blood vessel extraction using MR brain image," in *Proc. 7th IEEE Int. Conf. Nano/Mol. Med. Eng.*, Nov. 2013, pp. 77–82.

[64] D. Babin, E. Vansteenkiste, A. Pižurica, and W. Philips, "Segmentation of brain blood vessels using projections in 3-D CT angiography images," in *Proc. Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, Aug. 2011, pp. 8475–8478.

[65] M. M. Almi'ani and B. D. Barkana, "Automatic segmentation algorithm for brain MRA images," in *Proc. IEEE Long Island Syst., Appl. Technol. Conf. (LISAT)*, May 2012, pp. 1–5.

[66] A. El-Baz *et al.*, "Precise segmentation of 3-D magnetic resonance angiography," *IEEE Trans. Biomed. Eng.*, vol. 59, no. 7, pp. 2019–2029, Jul. 2012.

[67] X. Gao, Y. Uchiyama, X. Zhou, T. Hara, T. Asano, and H. Fujita, "A fast and fully automatic method for cerebrovascular segmentation on time-of-flight (TOF) MRA image," *J. Digit. Imag.*, vol. 24, no. 4, pp. 609–625, Aug. 2011.

[68] S. Luo and Y. Zhong, "Extraction of brain vessels from magnetic resonance angiographic images: Concise literature review, challenges, and proposals," in *Proc. IEEE Eng. Med. Biol. 27th Annu. Conf.*, Jan. 2005, pp. 1422–1425.

[69] O. Wink, W. J. Niessen, and M. A. Viergever, "Fast delineation and visualization of vessels in 3-D angiographic images," *IEEE Trans. Med. Imag.*, vol. 19, no. 4, pp. 337–346, Apr. 2000.

[70] S. Suran, V. Pattanaik, and D. Malathi, "Discovering shortest path between points in cerebrovascular system," in *Proc. 6th IBM Collaborative Acad. Res. Exchange Conf. (I-CARE)*, Oct. 2014, pp. 1–3.

[71] R. Wang *et al.*, "Threshold segmentation algorithm for automatic extraction of cerebral vessels from brain magnetic resonance angiography images," *J. Neurosci. Methods*, vol. 241, pp. 30–36, Feb. 2015.

[72] G. Gerig, T. Koller, G. Székely, C. Brechbühler, and O. Kübler, "Symbolic description of 3-D structures applied to cerebral vessel tree obtained from MR angiography volume data," in *Information Processing in Medical Imaging*. 1993, pp. 94–111.

[73] X. Xu, B. Liu, and F. Zhou, "Hessian-based vessel enhancement combined with directional filter banks and vessel similarity," in *Proc. IEEE Int. Conf. Complex Med. Eng.*, China, May 2013, pp. 80–84.

[74] S. S. Kumar and R. Amutha, "Edge detection of angiogram images using the classical image processing techniques," in *Proc. IEEE-Int. Conf. Adv. Eng., Sci. Manage. (ICAESM)*, Mar. 2012, pp. 55–60.

[75] A. A. Farag, H. Hassan, R. Falk, and S. G. Hushek, "3D volume segmentation of MRA data sets using level sets: Image processing and display," *Acad. Radiol.*, vol. 11, no. 4, pp. 419–435, Apr. 2004.

[76] W. Kang, W. Kang, W. Chen, B. Liu, and W. Wu, "Segmentation method of degree-based transition region extraction for coronary angiograms," in *Proc. 2nd Int. Conf. Adv. Comput. Control*, Mar. 2010, pp. 466–470.

[77] A. C. S. Chung, "Image Segmentation methods for detecting blood vessels in angiography," in *Proc. 9th Int. Conf. Control, Autom., Robot. Vis. (ICARCV)*, Dec. 2006, pp. 1–6.

[78] R. Adams and L. Bischof, "Seeded region growing," *IEEE Trans. Pattern Anal. Mach. Intell.*, vol. 16, no. 6, pp. 641–647, Jun. 1994.

[79] L. Wen, X. Wang, Z. Wu, M. Zhou, and J. S. Jin, "A novel statistical cerebrovascular segmentation algorithm with particle swarm optimization," *Neurocomputing*, vol. 148, pp. 569–577, Jan. 2015.

[80] N. Passat, C. Ronse, J. Baruthio, J.-P. Armspach, C. Maillot, and C. Jahn, "Region-growing segmentation of brain vessels: An atlas-based automatic approach," *J. Magn. Reson. Imag.*, vol. 21, no. 6, pp. 715–725, Jun. 2005.

[81] X. Yang, K. T. T. Cheng, and A. Chien, "Geodesic active contours with adaptive configuration for cerebral vessel and aneurysm segmentation," in *Proc. 22nd Int. Conf. Pattern Recognit.*, Aug. 2014, pp. 3209–3214.

[82] K. C. Wang, R. W. Dutton, and C. A. Taylor, "Improving geometric model construction for blood flow modeling," *IEEE Eng. Med. Biol. Mag.*, vol. 18, no. 6, pp. 33–39, Nov. 1999.

[83] D. L. Wilson and J. A. Noble, "Segmentation of cerebral vessels and aneurysms from MR angiography data," in *Information Processing in Medical Imaging*. 1997, pp. 423–428.

[84] D. L. Wilson and J. A. Noble, "An adaptive segmentation algorithm for time-of-flight MRA data," *IEEE Trans. Med. Imag.*, vol. 18, no. 10, pp. 938–945, Oct. 1999.

[85] M. S. Hassouna, A. A. Farag, S. Hushek, and T. Moriarty, "Cerebrovascular segmentation from TOF using stochastic models," *Med. Image Anal.*, vol. 10, no. 1, pp. 2–18, Feb. 2006.

[86] W. L. Nowinski, I. Volkau, Y. Marchenko, A. Thirunavuukarasuu, T. T. Ng, and V. M. Runge, "A 3D model of human cerebrovasculature derived from 3T magnetic resonance angiography," *Neuroinformatics*, vol. 7, no. 1, pp. 23–36, Mar. 2009.

[87] J. Chen and A. A. Amini, "Quantifying 3-D vascular structures in MRA images using hybrid PDE and geometric deformable models," *IEEE Trans. Med. Imag.*, vol. 23, no. 10, pp. 1251–1262, Oct. 2004.

[88] A. P. Puig, "Cerebral blood vessels modeling," Polytech. Univ. Catalonia, Barcelona, Spain, Tech. Rep. LSI-98-21-R, 1998.

[89] E. Bullitt, K. E. Müller, I. Jung, W. Lin, and S. Aylward, "Analyzing attributes of vessel populations," *Med. Image Anal.*, vol. 9, no. 1, pp. 39–49, Feb. 2005.

[90] E. Bullitt, G. Gerig, S. M. Pizer, W. Lin, and S. R. Aylward, "Measuring tortuosity of the intracerebral vasculature from MRA images," *IEEE Trans. Med. Imag.*, vol. 22, no. 9, pp. 1163–1171, Sep. 2003.

[91] A. Kloosterman, B. Hierck, J. Westerweel, and C. Poelma, "Quantification of blood flow and topology in developing vascular networks," *PLoS ONE*, vol. 9, no. 5, p. e96856, 2014.

[92] S. Sukanya, S. Abinaya, and D. Tamilselvi, "Detection of blood vessels and measurement of vessel width for diabetic retinopathy," *Comput. Sci. Inf. Technol.*, pp. 233–246.

[93] A. Sankowski and A. Materka, "Mathematical morphology analysis of 3D MRA images of human brain for estimation of blood vessels parameters," in *Proc. Joint Conf. New Trends Audio Video Signal Process., Algorithms, Archit., Arrangements Appl. (NTAV/SPA)*, Sep. 2012, pp. 49–52.

[94] J. Zhou, S. Chang, D. Metaxas, and G. Mageras, "3D-3D tubular organs registration based on bifurcations for the CT images," in *Proc. 30th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, Aug. 2008, pp. 5394–5397.

[95] N. D. Forkert *et al.*, "3D cerebrovascular segmentation combining fuzzy vessel enhancement and level-sets with anisotropic energy weights," *Magn. Reson. Imag.*, vol. 31, no. 2, pp. 262–271, Feb. 2013.

[96] M. Helmberger *et al.*, "Quantification of tortuosity and fractal dimension of the lung vessels in pulmonary hypertension patients," *PLoS ONE*, vol. 9, no. 1, p. e87515, 2014.

[97] A. Kamiya and T. Takahashi, "Quantitative assessments of morphological and functional properties of biological trees based on their fractal nature," *J. Appl. Physiol.*, vol. 102, no. 6, pp. 2315–2323, 2007.

[98] G. Finet *et al.*, "Fractal geometry of arterial coronary bifurcations: A quantitative coronary angiography and intravascular ultrasound analysis," *EuroIntervent., J. EuroPCR Collaboration Work. Group Intervent. Cardiol. Eur. Soc. Cardiol.*, vol. 3, no. 4, pp. 490–498, 2008.

[99] M. Zamir, "Arterial branching within the confines of fractal L-system formalism," *J. Gen. Physiol.*, vol. 118, no. 3, pp. 267–276, 2001.

[100] W. Schreiner, "Computer generation of complex arterial tree models," *J. Biomed. Eng.*, vol. 15, no. 2, pp. 148–150, Mar. 1993.

[101] W. Schreiner, F. Neumann, M. Neumann, A. End, and S. M. Roedler, "Anatomical variability and functional ability of vascular trees modeled by constrained constructive optimization," *J. Theor. Biol.*, vol. 187, no. 2, pp. 147–158, Jul. 1997.

[102] W. Schreiner, F. Neumann, R. Karch, M. Neumann, S. M. Roedler, and A. End, "Shear stress distribution in arterial tree models, generated by constrained constructive optimization," *J. Theor. Biol.*, vol. 198, no. 1, pp. 27–45, May'1999.

[103] R. Karch, F. Neumann, M. Neumann, P. Szawlowski, and W. Schreiner, "Voronoi polyhedra analysis of optimized arterial tree models," *Ann. Biomed. Eng.*, vol. 31, no. 5, pp. 548–563, 2003.

[104] P. Blanco, R. A. B. de Queiroz, and R. Feijóo, "A computational approach to generate concurrent arterial networks in vascular territories," *Int. J. Numer. Methods Biomed. Eng.*, vol. 29, no. 5, pp. 601–614, 2013.

[105] M. Zamir, "On fractal properties of arterial trees," *J. Theor. Biol.*, vol. 197, no. 4, pp. 517–526, Apr. 1999.

[106] F. Neumann, W. Schreiner, and M. Neumann, "Computer simulation of coronary arterial trees," *Adv. Eng. Softw.*, vol. 28, no. 6, pp. 353–357, Aug. 1997.

[107] G. Hamarneh and P. Jassi, "*VascuSynth*: Simulating vascular trees for generating volumetric image data with ground-truth segmentation and tree analysis," *Comput. Med. Imag. Graph.* , vol. 34, no. 8, pp. 605–616, Dec. 2010.

[108] P. Jassi and G. Hamarneh, "VascuSynth: Vascular tree synthesis software," *Insight J.*, pp. 1–12, Jun. 2011.

[109] T. Hassan *et al.*, "Computational replicas: Anatomic reconstructions of cerebral vessels as volume numerical grids at three-dimensional angiography," *Amer. J. Neuroradiol.*, vol. 25, no. 8, pp. 1356–1365, 2004.

[110] R. Torii, M. Oshima, T. Kobayashi, K. Takagi, and T. E. Tezduyar, "Fluid–structure interaction modeling of blood flow and cerebral aneurysm: Significance of artery and aneurysm shapes," *Comput. Methods Appl. Mech. Eng.*, vol. 198, nos. 45–46, pp. 3613–3621, 2009.

[111] A. Marzo *et al.*, "Computational hemodynamics in cerebral aneurysms: The effects of modeled versus measured boundary conditions," *Ann. Biomed. Eng.*, vol. 39, no. 2, pp. 884–896, Feb. 2011.

[112] S. Hirsch, J. Reichold, M. Schneider, G. Székely, and B. Weber, "Topology and hemodynamics of the cortical cerebrovascular system," *J. Cerebral Blood Flow Metabolism*, vol. 32, no. 6, pp. 952–967, 2012.

[113] S. Oeltze, D. J. Lehmann, A. Kuhn, G. Janiga, H. Theisel, and B. Preim, "Blood flow clustering and applications invirtual stenting of intracranial aneurysms," *IEEE Trans. Vis. Comput. Graphics*, vol. 20, no. 5, pp. 686–701, May 2014.

[114] F. Cassot, M. Zagzoule, and J.-P. Marc-Vergnes, "Hemodynamic role of the circle of Willis in stenoses of internal carotid arteries. An analytical solution of a linear model," *J. Biomech.*, vol. 33, no. 4, pp. 395–405, Apr. 2000.

[115] T. Anor, L. Grinberg, H. Baek, J. R. Madsen, M. V. Jayaraman, and G. E. Karniadakis, "Modeling of blood flow in arterial trees," *Wiley Interdiscipl. Rev., Syst. Biol. Med.*, vol. 2, no. 5, pp. 612–623, Sep./Oct. 2010.

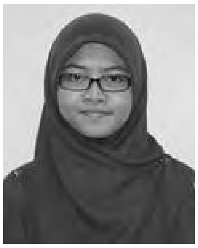
[116] C. A. Taylor and C. A. Figueroa, "Patient-specific modeling of cardiovascular mechanics," *Annu. Rev. Biomed. Eng.*, vol. 11, pp. 109–134, Aug. 2009.

[117] C. A. Taylor, T. J. Hughes, and C. K. Zarins, "Computational investigations in vascular disease," *Comput. Phys.*, vol. 10, no. 3, pp. 224–232, 1996.

[118] I. Marshall, S. Zhao, P. Papathanasopoulou, P. Hoskins, and X. Y. Xu, "MRI and CFD studies of pulsatile flow in healthy and stenosed carotid bifurcation models," *J. Biomech.*, vol. 37, no. 5, pp. 679–687, May 2004.

[119] S. Lorthois and F. Cassot, "Fractal analysis of vascular networks: Insights from morphogenesis," *J. Theor. Biol.*, vol. 262, no. 4, pp. 614–633, Feb. 2010.

[120] S. Schafer, V. Singh, K. R. Hoffmann, P. B. Noël, and J. Xu, "Planning image-guided endovascular interventions: Guidewire simulation using shortest path algorithms," *Proc. SPIE*, vol. 6509, pp. 65092C-1–65092C-10, Mar. 2007.



AZIMAH AJAM received the bachelor's degree (Hons.) in mathematical sciences from Universiti Teknologi MARA, Malaysia, in 2012, and the M.Sc. degree from Universiti Sains Malaysia, Malaysia, in 2014. She is currently pursuing the Ph.D. degree with the Department of Electrical and Electronic Engineering, Universiti Teknologi PETRONAS, Malaysia. Her current research interests include medical image analysis for cerebrovascular disease and stroke images.

AZRINA ABD. AZIZ received the B.Sc. degree (Hons.) in electrical and electronic engineering from The University of Queensland, Australia, in 1997, and the M.Sc. degree in system level integration from the Institute for System Level Integration, Scotland, in 2003, and the Ph.D. degree in electrical and computer systems engineering from Monash University, Melbourne, Australia. She is currently a Senior Lecturer with the Department of Electrical and Electronics Engineering, Universiti Teknologi PETRONAS, Perak, Malaysia. Her research interests include wireless sensor networks and biomedical engineering.

VIJANTH SAGAYAN ASIRVADAM (M'04) received the B.Sc. degree (Hons.) in statistic from Universiti Putra Malaysia, Malaysia, in 1997, and the M.Sc. degree (Hons.) in engineering computation and the Ph.D. degree, with a focus on online and constructive neural learning methods, from Queen's University Belfast, Belfast, U.K. He joined the Intelligent Systems and Control Research Group, Queen's University Belfast, in 1999. He serves as an Associate Professor with the Department of Electrical and Electronics Engineering, Universiti Teknologi Petronas, Perak, Malaysia, where he is also the Head of the Center of Intelligent Signal and Imaging Research, Health Informatics Modeling Group. His current research interest includes linear and nonlinear system identification and model validation in computational intelligence, control, and signal, and image processing. He is a member of the Institute of Engineering Technology. He also serves as an Executive Committee Member of the IEEE Signal Processing Society and the IEEE Control System Society for Malaysian chapters.

AHMAD SOBRI MUDA received the medical degree in medicine from UKM, followed by specialist training in radiology from USM. He pursued his sub-speciality training in interventional Neuroradiology with the Foundation Rothschild Hospital, Paris. He was an interventional Neuroradiologist Consultant. He is currently a Professor of Radiology with the Imaging Department, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Malaysia. His research interest includes neurointervention, neuroradiology and interventional radiology. He is a member of the Malaysian Society of Neuroscience and the Ex-Chairman for Malaysian Neuroradiology Section. He is also one of the Founding Member of Endovascular and Interventional Radiology UKM Malaysian Society of Interventional Radiology and teaching workshop in neurointervention.

IBRAHIMA FAYE (SM'12) received the B.Sc., M.Sc., and Ph.D. degrees in mathematics from the University of Toulouse, and the M.S. degree in engineering of medical and bio-technological data from École Centrale Paris. He is currently an Associate Professor with the Department of Fundamental and Applied Sciences of Universiti Teknologi PETRONAS. His research interests include engineering mathematics, signal & image processing, pattern recognition, and dynamical systems. He is member of the EMBS and the French Mathematical Society.

S. JAMAL SAFDAR GARDEZI received the B.Sc. and M.Sc. degrees in applied mathematics from the COMSATS Institute of Information Technology, Islamabad, Pakistan, in 2008 and 2010, respectively. He is currently pursuing the Ph.D. degree with the Department of Fundamental and Applied Sciences, University Teknologi PETRONAS. He is currently a Research Scientist with the Center for Intelligent signals and Imaging Research, Universiti Teknologi PETRONAS. His research interests include developing an automatic lesion segmentation algorithm to reduce false positive rates in medical images analysis in particular for breast and skin cancer images.