

**CEREBROVASCULAR SEGMENTATION
ARCHITECTURE WITH CHANNEL ATTENTION
AND SPATIAL KERNEL FILTERING FOR
TOF-MRA IMAGES**

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by

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"And when you have decided, then rely upon Allah. Indeed, Allah loves those who rely [upon Him]." (Quran 3:159)

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LIST OF SYMBOLS

TP	True Positive
TN	True Negative
FP	False Positive
FN	False Negative
k_i	Key vector
M_c	Channel Attention Map
$\Phi(k)$	Non-Linear Mapping Function
K	Kernel

LIST OF ABBREVIATIONS

ACC	Accuracy
AHD	Average Hausdorff Distance
BVS	Brain Vessel Segmentation
CAD	Computer-Aided Diagnostics
CI	Comprehensive Index
CNN	Convolutional Neural Network
CVD	Cerebrovascular Segmentation
DSC	Dice Similarity Coefficient
ECA	Efficient Channel Attention
FPR	False Positive Rate
HD	Hausdorff Distance
IoU	Intersection-over-Union
MCC	Mathews Correlation Coefficient
MIP	Minimum Intensity Projection
PPV	Positive Predictive Value
PRE	Precision
REC	Recall
SEN	Sensitivity
SKF	Spatial Kernel Filtering
SPE	Specificity
TPR	True Positive Ratio
VS	Volumetric Similarity

**SENIBINA SEGMENTASI CEREBROVASCULAR DENGAN
PERHATIAN SALURAN DAN PENYARING KERNEL RUANG UNTUK
IMEJ TOF-MRA**

ABSTRAK

Tesis ini memperkenalkan pendekatan pembelajaran mendalam untuk membahagikan struktur serebrovaskular dalam gambar angiografi resonans magnetik (MRA) secara automatik. Penyakit serebrovaskular (CVD) adalah keadaan otak yang rosak, yang sering kali mengakibatkan strok iskemik dan memerlukan diagnosis yang tepat. Walaupun ahli radiologi memiliki kepakaran dalam menafsirkan imej MRA, kesilapan dalam penilaian manual masih boleh berlaku dan ini membuktikan kepentingan mengurangkan kesilapan dan meningkatkan kecekapan tafsiran imej MRA dalam sistem diagnosis berbantu komputer (CAD). Di samping pelbagai rangkaian segmentasi wujud untuk pensегmenan serebrovaskular dalam imej MRA, model UNet mempunyai keupayaan pengekstrakan ciri/sifat yang luar biasa. Namun, sifat kompleks pembuluh darah otak menimbulkan cabaran pada senibina U-Net. Penggabungan langsung peta ciri beresolusi tinggi dan rendah dalam U-Net berisiko melemahkan maklumat semantik, mewujudkan variasi rawak, dan mengurangkan ketepatan pensегmenan, terutamanya pada pembuluh darah yang lebih kecil, menyebabkan masalah segmentasi berlebihan dan berkurangan. Untuk mengatasi cabaran-cabaran ini, kajian ini mencadangkan model ECA-SKFNet yang baharu untuk pensегmenan serebrovaskular dalam imej TOF-MRA. Melalui pembinaan atas senibina U-Net, model kajian ini menggabungkan corak penelitian saluran yang efisien (ECA) bertingkat untuk mengekstrak ciri-ciri/sifat-sifat utama dan menggunakan penapis kernel ruang (SKF) untuk memastikan pengekstrakan ciri/sifat yang lebih

tepat dalam segmentasi pembuluh darah otak (BVS). Kajian ini menggunakan pendekatan yang unggul dalam membahagikan seluruh struktur pembuluh darah sambil memberi penekanan yang lebih besar kepada pencerapan pembuluh darah yang kecil (<5 mm radius) dengan ketepatan tinggi. Kaedah yang dicadangkan dinilai dalam dataset MIDAS menunjukkan prestasi yang kompetitif dengan hasil penilaian yang cemerlang. Pendekatan ini mencapai nilai pekali persamaan Dice (DSC) sebanyak 0.6741, pekali Jaccard sebanyak 0.5015, purata jarak Hausdorff (AHD) sebanyak 69.33, dan persamaan isipadu (VS) sebanyak 0.9755, dan mengatasi hasil model lain yang digunakan dalam ujikaji. Keberkesanan pendekatan ini ditekankan, dan mempersembahkan kaedah pensegmenan serebrovaskular yang meyakinkan dan membolehkan visualisasi yang lebih baik terhadap struktur pembuluh darah, terutamanya pembuluh darah yang kecil. Penemuan dalam kajian ini menyumbang kepada kemajuan sistem berkomputer untuk mendiagnosis penyakit serebrovaskular, dengan potensi untuk menyelamatkan nyawa, mengurangkan masa diagnosis, dan menurunkan kos.

CEREBROVASCULAR SEGMENTATION ARCHITECTURE WITH CHANNEL ATTENTION AND SPATIAL KERNEL FILTERING FOR TOF- MRA IMAGES

ABSTRACT

This thesis introduces a deep learning approach to automatically segment cerebrovascular structures in magnetic resonance angiography (MRA) images. Cerebrovascular disease (CVD), a debilitating brain condition often leading to ischemic stroke, necessitates accurate diagnosis. Despite the expertise of human radiologists in interpreting MRA images, the fallibility of manual assessments underscores the importance of computer-aided diagnosis (CAD) systems for error reduction and enhanced efficiency. While various segmentation networks exist for cerebrovascular segmentation in MRA images, the U-Net model stands out for its exceptional feature extraction capabilities. However, the complex nature of brain vessels poses challenges to the U-Net architecture. The direct concatenation of high- and low-resolution feature maps in U-Net risks diluting semantic information, introducing noise, and compromising segmentation accuracy, particularly with smaller vessels, leading to over and under-segmentation. To address these challenges, we propose a novel ECA-SKFNet model for cerebrovascular segmentation in TOF-MRA images. Building upon the U-Net architecture, our model incorporates a cascaded Efficient Channel Attention (ECA) pattern to extract salient features and employs spatial kernel filtering (SKF) to ensure sharper feature extraction in brain vessel segmentation (BVS). This study utilizes an approach that excels in segmenting the entire vessel structure while placing increased emphasis on accurately capturing small vessels (< 5 mm radius). The proposed method was evaluated on the MIDAS dataset,

demonstrating its competitive performance with exceptional evaluation results. The approach achieved a Dice Similarity Coefficient (DSC) score of 0.6741, Jaccard coefficient of 0.5015, Average Hausdorff Distance (AHD) of 69.33, and Volumetric Similarity (VS) of 0.9755 surpassing the results obtained by other models employed in the experiments. The effectiveness of the approach was highlighted, presenting a promising avenue for improved cerebrovascular segmentation, and enabling enhanced visualization of vascular structures, particularly smaller vessels. The findings of this study contribute to the advancement of a computerized system for diagnosing cerebrovascular disease, with the potential to save lives, reduce diagnosing time, and lower expenses.

CHAPTER 1

INTRODUCTION

1.1 Overview

This chapter provides a comprehensive overview of the Cerebrovascular segmentation research, offering insights into its background, motivation, problem statement, research questions, aim, objectives, expected contribution, scope, limitations, and organization. Firstly, it delves into the background of the research, offering context and understanding of the topic. Subsequently, it discusses the motivation behind undertaking this study, shedding light on the driving factors that sparked the research. The problem statement is then presented, clearly articulating the issue and the need for further investigation. Next, the research questions are formulated, outlining the specific inquiries the study aims to address. The aim and objectives of the research are defined, indicating the ultimate goal and the specific milestones to be achieved. Furthermore, the expected contribution of the study is highlighted, emphasizing the potential impact and value it may bring to the field. Additionally, the scope and limitations of the research are elucidated, clarifying the boundaries within which the study operates and acknowledging any potential constraints. Finally, the organization of the work is outlined, providing a roadmap for readers to navigate through the subsequent chapters and sections.

1.2 Background of the Research

Cerebrovascular diseases (CVD) constitute a spectrum of conditions affecting blood vessels in the brain, including ischemic and hemorrhagic strokes, transient ischemic attack (TIA), and vascular dementia. These conditions manifest diverse pathophysiological features within the cerebral vasculature. CVD is a prominent cause

of disability, functional loss, and cognitive decline in adults. Notably, stroke holds a prominent position, prevailing in prevalence and significantly impacting morbidity and mortality within the broader spectrum of cerebrovascular disorders. A stroke is an abrupt blockage of cerebral arteries that compromises brain perfusion. Despite a rise in global stroke prevalence, mortality has declined due to higher life expectancy (Fang et al., 2014). 85% of stroke subtypes are ischemic (due to blockage), while the rest are hemorrhagic (due to rupture) (Mozaffarian et al., 2016). Recognizing and treating a stroke early is crucial for reducing mortality and morbidity. According to research, up to 45% of dementia cases are CVD-related (Pantoni & Gorelick, 2014). Up to 65% of ischemic strokes are attributable to cerebral small vessel disease (CSVD) (Khaku et al., 2021). Hypertension is a leading risk factor for stroke in women, especially. Type-2 diabetes, smoking, obesity, drug use, and atrial fibrillation are other cardio-cerebrovascular risk factors (Khaku et al., 2021). Hypertension can affect anyone, especially those with a family history. Over time, hypertension alters brain vasculature. Clinically, cerebral vascular alterations, including diameter and tortuosity, are often present before hypertension symptoms (Iadecola & Davisson, 2008). Changes in cerebral vasculature and perfusion are also key hypertension indications. Uncontrolled chronic hypertension can cause CSVD, especially in the thalamus, pons, internal capsule, and cerebellum (Shi & Wardlaw, 2016). (Warnert et al., 2016) argued that hypertension-induced remodeling of cerebral vasculature maintains blood circulation equilibrium. In animal models and humans, cerebral vascular remodeling and greater cerebral perfusion pressure occur before hypertension. In contrast, excessive or aberrant blood artery tortuosity is linked to numerous indications of ischemic stroke owing to systemic hypertension (Abdalla et al., 2015; Han, 2012).

1.3 Motivation

Cerebrovascular Disease (CVD) is a collection of cerebrovascular diseases caused by the blood-brain barrier leaking. It is a primary cause of functional loss and cognitive decline in the aged and plays a vital role in ischemic stroke and brain hemorrhages. In 2018, stroke was responsible for one-sixth (1/6) of all fatalities due to cardiovascular disease in the USA. According to researchers, hypertension causes alterations in brain vasculature. It is one of the most common causes of stroke in people of all ages. In rats, chronically high blood pressure was associated with alterations in carotid artery diameter. Excessive or abnormal blood vessel tortuosity has been related to several hazardous conditions, including hypertension. Early detection of hypertension enables people to receive more effective therapy before they become dangerously sick.

Magnetic Resonance Imaging (MRI) and Magnetic Resonance Angiography (MRA) represent non-invasive imaging modalities utilizing magnetic fields and radio waves to produce intricate visualizations of internal anatomical structures. Although both techniques share this foundational principle, MRA is specifically adept at elucidating the intricate details of blood vessels, offering pivotal information regarding vascular anatomy and the dynamics of blood flow. MRA facilitates knowledge of numerous arteries throughout the body, including those in the brain, which aids in diagnosing CSVD. Blood vessel extraction is a complex process due to the prevalence of noise, an intrinsic quality that might distort the MRA images and result in inaccurate classification.

In the diagnosis of cerebrovascular diseases (CVD), patients undergo imaging procedures, and a proficient radiologist meticulously evaluates the images to compose a diagnostic report guiding subsequent medical actions. A pivotal stage in this

diagnostic process entails the segmentation of the vascular network within images, enabling a clear visualization of blood vessels to identify potential ruptures or anomalies. This segmentation procedure plays a crucial role in the thorough evaluation and precise diagnosis of cerebrovascular conditions. The manual segmentation of thousands of images by human professionals for diagnosing Magnetic Resonance Angiography (MRA) images can be both time-consuming and subject to inconsistencies. Even among experts, achieving identical segmentations repeatedly is challenging, leading to variations in outcomes. Consequently, the need for automated brain vessel segmentation is imperative. An automated approach utilizing image segmentation proves advantageous in terms of efficiency and time conservation, aiding clinicians in disease identification through MRA data. Ongoing research endeavors focus on cerebral blood vessel segmentation, with a prominent emphasis on deep learning methodologies as the most promising avenue for accurate and reproducible results.

1.4 Problem Statement

Cerebrovascular system segmentation using magnetic resonance angiography (MRA) has been extensively studied, employing various techniques. Previous approaches included automatic, semi-automated, and manual segmentation methods such as atlas-based algorithms, active contour models, machine learning techniques, and statistical models. Active contour models were widely utilized in clinical practice until recently, but they have limitations when examining microscopic features and their time complexity increases with larger data volumes. The introduction of deep learning to brain vessel segmentation (BVS) in 2017 presented a new and effective solution to address previous limitations. Deep learning models automatically extract complex

features from the data, which is challenging to achieve manually using traditional models. The intricate nature of brain representations, consisting of tissue, blood vessels, and noise, renders hand-crafted features impractical. Deep learning models have proven to be superior in extracting complex image features compared to other strategies.

In recent years, deep learning algorithms have gained significant popularity in medical imaging due to their ability to extract robust features, achieve accurate classification, and demonstrate compatibility. Among the various deep learning architectures, Convolutional Neural Networks (CNNs) have emerged as the most widely used for image processing and segmentation tasks. In the context of segmenting blood arteries in the brain, CNN-based architectures exhibit strong performance and deliver excellent segmentation accuracy. The features extracted from multiple layers, such as convolutional and pooling layers, are inherently robust and challenging to manually construct. One notable network architecture, the Fully Convolutional Network (FCN), introduced by (Long et al., 2015), replaces the final fully connected layer with a fully convolutional layer, enabling pixel-by-pixel prediction. Another advanced design is the U-Net, which combines CNN and FCN models to extract features from images and demonstrates exceptional segmentation performance.

Despite its strengths, U-Net has limitations in the domain of Brain Vessel Segmentation (BVS), specifically in dealing with challenges related to over and under-segmentation. In U-Net, the direct concatenation of high- and low-resolution feature maps poses a risk of diluting semantic information, introducing noise, and compromising segmentation accuracy in fine-grained structures. While skip connections capture local and global features, the absence of a mechanism to selectively prioritize features during concatenation limits seamless integration of

contextual information, potentially including extraneous details or noise. This deficiency impacts accuracy in diverse and complex scenes. Furthermore, it is essential to consider the broader concern of generalization in medical image analysis, as the performance of segmentation models may vary across diverse datasets and imaging modalities.

Accurate feature extraction plays a pivotal role in Brain Vessel Segmentation (BVS), and the U-Net model has demonstrated proficiency in automatically extracting intricate features from brain images, including unintended elements like noise and non-vascular organ structures. However, optimizing its clinical applicability is imperative to address segmentation errors and enhance accuracy while efficiently utilizing computational resources. The integration of an attention mechanism, emphasizing relevant features within the image, proves beneficial in mitigating U-Net's limitations. Additionally, incorporating an intermittent filtering technique to enhance the quality of sharper features provides additional advantages for segmenting complex structures, particularly in cerebrovascular networks. This promising approach holds potential to advance BVS in clinical settings, yielding more reliable and accurate segmentation results. Moreover, it exhibits promise in overcoming segmentation challenges associated with smaller vessels, a common obstacle for existing segmentation models.

1.5 Research Questions

Aligned with the problem statement and the identified research gap, the research addresses the following key questions:

1. What are the impact of integrating an attention mechanism into the U-Net model for BVS?

2. What outcomes arise from incorporating the spatial kernel filter technique into the previously modified U-Net model?

1.6 Research Objective

The objective of this research is given below:

1. To enhance the salient feature extraction of U-Net model through the seamless integration of the channel attention mechanism for improved Brain Vessel Segmentation (BVS).
2. To refine the feature extraction technique by incorporating spatial kernel filtering to extract sharper features for accurate segmentation of small vessels in brain images (MRA).

1.7 Contributions

This work makes a substantial contribution by seamlessly integrating a channel attention-based modification and spatial kernel filter into the U-Net model. The primary objective is to elevate the segmentation accuracy of medical images, particularly in contexts where preserving intricate details is paramount, all while adhering to computational efficiency constraints. Despite the approach entailing the augmentation of attention and spatial filtering within the established U-Net architecture, rather than proposing an entirely new network, these introduced modifications decisively enhance the model's performance in medical image segmentation.

1.8 Scope And Limitations

The proposed research utilizes two-dimensional images, but the MRA data is three-dimensional. The 3D brain scans contain more spatial information regarding the

vessel's anatomy. Due to computing resource limits, research is being conducted on 2D model architecture. Although the proposed model can also be scaled in three dimensions, we failed to conduct a comparative analysis of the three-dimensional model in our ablation study.

1.9 Thesis Organization

The thesis is organized as follows:

Chapter One provides a comprehensive overview of the research on Cerebrovascular segmentation, including its background, motivation, problem statement, research questions, aim, objectives, expected contribution, scope, limitations, and organization, discussing the context, driving factors, specific inquiries, ultimate goal, potential impact, boundaries, and roadmap for readers.

Chapter Two provides an overview of the background of CVD, its diagnosis process, the need for automated segmentation, the advantages and limitations of deep learning methods, current trends in deep learning in BVS, and the theory behind the hypothesis.

Chapter Three outlines the methodology, including dataset description, preprocessing techniques, model selection, architectural design, experimental setup, and relevant considerations.

Chapter Four provides a comprehensive quantitative and visual analysis of our models, comparing their performance based on various metrics, uncovering patterns and trends, and offering insights and implications for future CVD diagnosis studies.

Chapter Five draws conclusion based on the results of the proposed mechanisms and offers insightful suggestions for future research in the academic field.

1.10 Summary

This chapter provides an overview of the research as a whole. It describes the background, motivation, problem description, aims, anticipated contribution, limitations, and scope of the study. The problem's context will be explored in detail in the subsequent chapters. In addition, the emergence of deep learning over other techniques and the current trends of the model used in BVS will be presented in the following chapter, along with the difficulties inherent in deep learning.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

The preceding chapter offer an overview of the direction of the research. This chapter will address the background of CVD and its diagnosis process, the need for automated segmentation approaches, the advantages of deep learning methods over other techniques, and the limitations of deep learning in the domain. This chapter also discusses the current trends in deep learning in CVD and the theory used in developing the hypothesis.

2.2 Cerebrovascular Disease (CVD)

Cerebrovascular diseases (CVD) constitute a diverse range of conditions impacting blood vessels in the brain, including ischemic stroke, hemorrhagic stroke, transient ischemic attack (TIA), and vascular dementia. Each subtype introduces distinct pathophysiological characteristics, contributing to the intricate landscape of cerebrovascular disorders. Of notable significance within this category is stroke, which not only prevails in prevalence but also exerts a considerable influence on morbidity and mortality across the broader spectrum of cerebrovascular ailments. Stroke is an acute interruption of cerebral vasculature leading to a compromised perfusion to the brain parenchyma. Over the past decades, despite an increment in the global stroke prevalence, the rate of mortality is decreasing owing to a longer life expectancy (Fang et al., 2014). CVD also represents a significant cause of disability and mortality, where stroke is recognized as the leading cause of adult's disability or functional loss and cognitive decline (Khaku et al., 2021; Mozaffarian et al., 2016; Pantoni & Gorelick, 2014). Additionally, it is widely accepted that about 85% of stroke subtype are

ischemic in nature (i.e., due to blockage), whilst the remaining are haemorrhagic stroke (i.e., due to rupture) (Mozaffarian et al., 2016). Therefore, recognizing stroke at an early stage and treating it promptly are important to prevent or minimize mortality and/or morbidity. Of note, studies also reported that up to 45% cases of dementia are CVD-related (Pantoni & Gorelick, 2014).

The etiology of ischemic stroke includes microthrombosis, embolism, and lacunar with up to 65% of the etiologies are thought to be due to cerebral small vessel disease (CSVD) (Khaku et al., 2021). There are multiple cardio-cerebrovascular risk factors of stroke, with hypertension (i.e., elevated arterial blood pressure) serves a leading risk factor of stroke, especially in women. Other cardio-cerebrovascular risk factors include type-2 diabetes, smoking, high body mass index (or obesity), drug use and atrial fibrillation (Khaku et al., 2021). Hypertension may afflict anyone at any age, especially someone with a family history of hypertension. Researchers have discovered specific changes in brain vasculature due to hypertension over time. As per a clinical hypothesis, cerebral vasculature changes, such as changes in the diameter and tortuosity, are frequently evident before hypertension develops symptoms (Iadecola & Davisson, 2008). Changes in cerebral vasculature and cerebral perfusion are also important indicators of the aetogenesis of hypertension. Moreover, chronic uncontrolled hypertension may lead to CSVD mainly in deep subcortical region such as thalamus, pons, internal capsule, and cerebellum (Shi & Wardlaw, 2016).

In addition, hypertensive individuals may also have genetic-based cerebrovascular susceptibility than non-hypertensive people according to (Warnert et al., 2016) who proposed the hypertension-induced remodelling of cerebral vasculature to maintain blood circulation balance. Other research reinforces this prior finding, claiming that cerebral vascular remodelling and higher cerebral perfusion pressure

occur before the onset of hypertension. Predictably, chronically elevated blood pressure has been linked to changes in carotid artery diameter while blood artery tortuosity that is excessive or aberrant has been linked to multiple manifestation of ischemic stroke due to the systemic hypertension as reflected by the brain and vasculature imaging (Abdalla et al., 2015; Han, 2012).

2.2.1 Brain Imaging Used For CVD Diagnosis

Neuroimaging of biomarkers is commonly utilized for cerebrovascular diseases (CVD) detection. Despite recent advances, understanding the pathogenesis of vascular disorders remains limited, necessitating human intervention for diagnosis, particularly in techniques like Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) where expert interpretation is vital for discerning subtle cerebral blood vessel anomalies. Recognizing the need for early diagnosis, automating these tasks emerges as a viable option. Presently, medical imaging, a cost-effective diagnostic method, prompts interdisciplinary collaboration to explore automation solutions, particularly in the intricate diagnosis of CVD (Cuadrado-Godia et al., 2018). Image segmentation, precision delineation of cerebral blood vessels, enables quantitative analysis, aiding in the identification of subtle abnormalities and contributing to accurate cerebrovascular disease diagnosis. These studies underscore the importance of achieving high-precision early diagnosis, highlighting the potential of image segmentation techniques in addressing this diagnostic challenge.

Roentgen discovered the first technique of structural imaging in 1895, termed X-ray (Weber, 2001). However, it was not until 1927 that Egas Moniz conducted the first human cerebral angiography (Antunes, 1974). Before 1927, Haschek and Lindenthal used an opaque fluid to inject into human corpses to create radiographs of blood arteries. The latest advances in science and computing have resulted in

increasingly sophisticated systems for acquiring data from the brain. Computed tomography (CT), positron emission tomography (PET), and magnetic resonance imaging (MRI) are the three primary techniques that have been utilized for decades; MRI was created most recently by Nobel laureate Lauterbur and Mansfield. Magnetic resonance angiography (MRA) is a collection of techniques that leverage MRI to depict the brain's blood vessels in detail. TOF-MRA is the most frequently used modality nowadays for cerebrovascular radiography. Together with other imaging modalities, such as digital subtraction angiography (DSA), photoacoustic imaging (PAI), and transcranial doppler (TCD), the techniques above have advanced our comprehension of the brain's vasculature, thereby increasing and improving our knowledge of the central nervous system's complexity (CNS) (Laviña, 2017).

The cerebral network of the brain is intricately connected to different brain tissues, making it difficult to physically identify the tiny arteries, let alone detect Blood Brain Barrier (BBB) leakage. Noise is an inherent component of all magnetic resonance images that degrades the image's resolution and contrast, which are critical for segmenting tiny brain vasculature. Using noise reduction to retrieve the brain's vascular network from an MR image is crucial in medical imaging. Numerous strategies for segmenting the vascular network from MR images have evolved, indicating a good chance of overcoming the problem through recent research. However, such an application is still in its infancy in the clinical setting. As medical imaging modalities advance at a breakneck pace, new application-specific segmentation challenges emerge, and novel approaches are regularly investigated and proposed (Despotović et al., 2015). Choosing the most appropriate method for a particular application is a difficult task.

2.3 Image Processing For Medical Image Segmentation

Image segmentation involves the nuanced task of partitioning images based on attributes like color, intensity, and texture. Embedded within a classification framework, this process entails categorizing N elements into K regions, resembling the intricate resolution of a combinatorial optimization problem (Pham et al., 2000). The efficacy of segmentation techniques hinges on the intrinsic characteristics inherent in processed images, which can be broadly classified into Thresholding, Region-based methods, Clustering, Edge detection, and Model-based methods. Fundamentally, image segmentation in image processing relies on two foundational aspects—discontinuity and similarity. Discontinuity facilitates the separation of regions marked by abrupt intensity changes, while similarity enables the identification of pixels sharing comparable properties within a predefined range. This dual framework serves as the bedrock for various segmentation techniques, offering a nuanced and adaptable approach to image analysis. The subsequent sections will delve into traditional image processing approaches for the segmentation of medical images.

2.3.1 Thresholding Method

Thresholding is a crucial image segmentation method, converting greyscale images into binary representations using a chosen threshold value. Standard techniques include the maximum entropy method (Gonzalez & Woods, 2002), Otsu's method, and K-means clustering (Haralick & Shapiro, 1985). Efficacy is influenced by noise and indistinct boundaries, prompting strategies like Thresholding with Edge detection for improved performance.

2.3.2 Region-Based Method

Region-based techniques present diverse approaches to image segmentation, each method tailored to address specific challenges and offer application-specific

advantages. The region-growing algorithm, initiated by a seed pixel, expands regions based on connectivity and similarity criteria, such as greyscale intensity or color (J. Wu et al., 2009). Adaptive algorithms enhance segmentation by incorporating statistical information and prior knowledge (Thakur & Anand, 2007). The region Split and Merge method, utilizing quadtree information, involves splitting an image into quadrants and merging uniform neighboring segments, effectively eliminating high-frequency artifacts. This approach proves valuable in the evaluation of breast and cyst masses (Thakur & Anand, 2007). The Watershed Approach treats the image as a topographic surface, interpreting low-intensity pixels as valleys and high-intensity pixels as hills or peaks (McElhaney, 1983). Using water sources (seeds), this algorithm floods valleys and constructs barriers to prevent merging. While standard watershed methods encounter challenges with noise, power watershed algorithms effectively address these issues, showcasing efficacy in tasks such as breast tumor (Huang & Chen, 2004), contour extraction from ultrasound images (López-Mir et al., 2014) and liver segmentation (Benson C. C. et al., 2015).

2.3.3 Clustering Method

Clustering, a process of grouping homogeneous data, is exemplified by the foundational "K-means clustering" algorithm assigning each dataset component to a single cluster. In contrast, soft clustering, as seen in Fuzzy C-Means (FCM), permits pixel membership in multiple groups. FCM, applicable to both grey and color images, employs fuzzy community function values for membership determination, guided by an objective function measuring squared Euclidean and fuzzy community distances (Ahmed et al., 2002). Addressing challenges like noise in MR images, enhancements such as Kernelized Fuzzy C-Means (KFCM) (D.-Q. Zhang & Chen, 2004) and Fast Generalized Fuzzy C-Means (FGFCM) (Cai et al., 2007) have been introduced. FCM

variations, including Type-II Fuzzy C-Means (T2FCM) and Intuitionist Fuzzy C-Means (IFCM), demonstrate efficacy in noise removal and image segmentation. Innovations like Fuzzy-based Artificial Bee Colony (FABC) (Aneja & Rawat, 2013) integrate Artificial Bee Colony Optimization with FCM for efficient synthetic and medical image clustering.

2.3.4 Edge Detection Method

Edge detection, a conventional approach for identifying image irregularities, focuses on distinguishing boundaries between regions with distinct intensity or grey levels. Employing derivative operations through convolution functions, the Canny edge detector stands out for its efficiency, relying on gradient extent thresholds, non-maximal suppression, and hysteresis thresholding (Mahmood et al., 2015). Critical pre-processing steps, including Gaussian smoothing, are essential to address noise impact. Thoughtful consideration of image pre-processing is imperative to prevent inaccurate edge detection, thereby facilitating the implementation of multi-resolution edge detection and tracing techniques (Lopez-Molina et al., 2013).

2.3.5 Model-Based Method

Model-based approaches in image analysis, characterized by integrating models encapsulating shape and structure information, demonstrate enhanced robustness against artifacts compared to conventional algorithms. Markov Random Field (MRF) models, drawing inspiration from the Ising model (Kindermann & Snell, 1980), find widespread application in image segmentation, preserving edges through parameter approximation (Held et al., 1997). The Hidden Markov Random Field (HMRF) (Y. Zhang et al., 2001) introduces a stochastic process with unobservable states, enhancing segmentation precision through an Expectation Maximization (EM) framework. The combination of MRF and Self-Organizing Feature Map (SOFM)

contributes to improved smoothness in region partitioning (Li & Chi, 2005). Atlas-based approaches leverage images with anatomical details for segmentation, employing image registration to ensure accurate partitioning (H. Park et al., 2003). Graph cut algorithms, rooted in graph theory, effectively partition images into foreground and background based on pixel similarities. This technique is demonstrated in photo, video editing, and medical image processing applications (Boykov & Jolly, 2001). The Lattice Boltzmann Method (LBM), a simulation technique bridging microscopic and macroscopic scales, proves influential in image analysis, encompassing tasks such as image smoothing, inpainting, and segmentation (Grunau et al., 1993). Anisotropic diffusion models based on LBM exhibit efficacy in clinical image segmentation.

2.4 Recent Growth Of Deep Learning In Medical Imaging

Deep learning-based techniques for medical imaging have grown in popularity in recent years due to their robust feature extraction, accurate classification, and compatibility compared to the traditional image processing techniques. The Convolutional Neural Network (CNN) architecture is the most frequently used deep learning architecture for image processing and segmentation. The feature extracted using many layers (convolutional layer, pooling layer) is highly robust and impractical to produce manually. Depending on the input data, 2D, 2.5D, and 3D CNNs are utilized for medical imaging. In 2D CNN, the input picture is given in a two-dimensional format to apply a two-dimensional filter for segmentation. With transfer learning, a similar architecture was used, in which pre-trained 2D models on ImageNet were used in conjunction with low-level filters (Bar et al., 2015). 2.5D architecture delivers much more spatial information than 2D design at a lower computational cost

than 3D architecture prompted its development. According to some studies, the 2.5D training technique with 2D labelled data is more compatible with present technology than the 3D training technique (Moeskops et al., 2016; Prasoon et al., 2013; Roth et al., 2018). They cannot employ 3D filters that require 3D CNN since 2D architecture is still limited to 2D kernels. The voxels from 3D patches are used in 3D architecture to predict the label, like 2D CNN but with more spatial information. Most medical images are in 3D format, and researchers preferred the architecture because of the availability of processing capacity (Vaidhya et al., 2016).

Fully convolutional network (FCN) is another network proposed by (Long et al., 2015). FCN substitutes the final fully connected layer with a fully convolutional layer, enabling the network to make pixel-by-pixel predictions. This layer enhances the dense pixel-wise prediction in a single forward pass from a full-sized image compared to a patch-wise prediction. High-resolution activation maps are linked with upsampled outputs and fed into the convolution layers to create a more precise result by enhancing localization performance. FCN is frequently utilized to segment organs (X. Zhou et al., 2016, 2017) using 2.5D and 3D images. There are more FCN versions, including Cascade FCN (Christ et al., 2016), Focal FCN (X. Y. Zhou et al., 2018), and Multi-stream FCN (Zeng & Zheng, 2018), that are widely used in medical imaging with high accuracy. One of the most commonly used architectures in medical imaging today is U-Net, which was proposed by (Ronneberger et al., 2015). This model employs deconvolution and FCN to create a U-shaped architecture comprising 19 layers. Two steps are included in the model: encoding and decoding. The encoding step makes use of a CNN structure with layers for downsampling. The decoding is accomplished by a series of upsampling layers followed by a deconvolution layer. Though the first structure was designed for 2D pictures, it lacked localization

capability. Later, (Çiçek et al., 2016) created the 3D U-Net to provide additional spatial information to the network, employed in vascular border identification (Kleesiek et al., 2016). 3D U-Net is a memory-intensive algorithm. V-net is the most well-known adaptation of U-Net, presented by (Milletari et al., 2016). Other potential deep learning models are being applied in medical imaging, including Convolutional Residual Networks (CRNs) (He et al., 2016), Recurrent Neural Networks (RNNs) and their variations, long short-term memory (LSTM), Contextual LSTM (J. Chen et al., 2016), Gated recurrent unit (GRU), and clockwork RNN (CW-RNN). More details on the models and their application were discussed in (Hesamian et al., 2019). Figure 2.1 illustrates the FCN network which is briefly explained above.

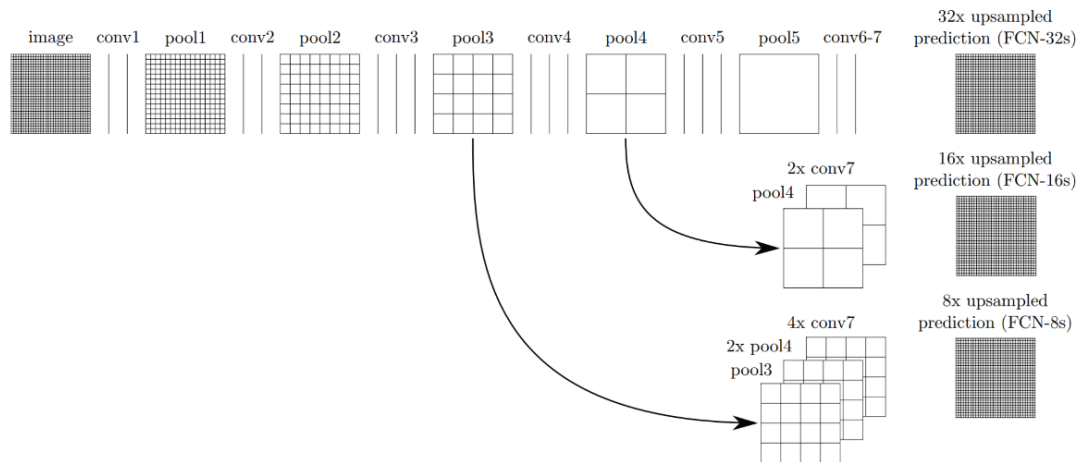


Figure 2.1 FCN architecture proposed by (Long et al., 2015)

2.4.1 Emergence Of Deep Learning For CVD

Numerous studies on segmentation have been conducted, including atlas-based algorithms (Cuadra et al., 2004; Kirisli et al., 2010; H. Wang et al., 2013), active contour models (Mishra, 2010; Tian et al., 2013), machine learning techniques (Othman & Tizhoosh, 2011; H. Wang et al., 2013), and statistical models (Chung et al., 2004; Gao et al., 2011). A previous review on blood vessel segmentation discussed in detail the mentioned methods (Zhao et al., 2017). Some proposed models can be classified as manual, semi-automated, or automated. However, of all the models, the

Active contour model (ACM) is the most extensively used clinically, where images can be identified based on their edges, regions, or higher knowledge (Shang et al., 2011) – until recently. When it comes to microscopic features, the ACM has limitations, and time complexity increases as data volume grows. Since the problem is well-known, researchers are looking for a more robust solution, and deep learning is becoming more popular as an alternative. The First deep learning-based segmentation was performed very recently by (Phellan et al., 2017) in 2017.

2.4.2 Computer-Aided Diagnostic (CAD) And Deep Learning

Since 2017, a lot of deep learning-based research has been done on brain blood vessel segmentation (BVS), leading to the focus on developing Computer-Aided Diagnostic (CAD). Radiologists employ CAD tools to recognize and evaluate medical images automatically. It provides a crucial second opinion and reduces Intra and Interobserver variability, allowing for faster, more accurate, and consistent diagnosis. Conventional CAD systems can automatically diagnose various CVD disorders, including intracranial aneurysms (IA). Due to low sensitivity and high false positive (FP) rates, such methods are not commonly used in medical practice. However, thanks to the advancement of deep learning models and computer vision in medical imaging, CAD systems have recently evolved. MRA has been regularly used in CAD-based systems for IA incorporating various deep learning architectures in recent years. 2D CNN model to detect IA on maximum intensity MRA (Nakao et al., 2018), DeepMedic CNN on TOF-MRA (Faron et al., 2019) and CTA (Shahzad et al., 2020), 18-layers CNN Residual network on MRI (Ueda et al., 2019), 3D Resnet on TOF-MRA (Sohn et al., 2021), 3D U-Net on TOF-MRA (G. Chen et al., 2020), HeadXNet model on CTA (A. Park et al., 2019) all are the current methods used in the CAD system to diagnose IA with sensitivity ranging from 70% to 94%. Recent advancements in CAD

systems suggest an increase in medical research. More on the development of CAD based system for IA can be found in this article (Mensah et al., 2022). Assume that a CAD-based system can be enhanced to the point where the system's sensitivity and accuracy are therapeutically beneficial. In that situation, it will improve radiologists' capacity to diagnose brain imaging.

2.5 Deep Learning For Brain Vessel Segmentation (BVS)

Recent advances in deep learning are transforming medical imaging, particularly cerebrovascular vessels' segmentation. A substantial amount of research is being conducted on this topic utilizing deep learning. Generally, a deep learning model for vessel segmentation follows a generalized pipeline which is shown in Figure 2.2. The pipeline is developed based on the multiple works done on the topic as a summary.

2.5.1 Dataset Used In BVS

The study of brain vascular segmentation (BVS) needs Magnetic Resonance Imaging (MRI), and MRA is a particular type of MRI. Because of its short echo time and utilization of flow correction, TOF-MRA is the most widely used technology for non-contrast bright-blood imaging of the human vasculature. Concerned with privacy and ethics, most BVS research uses TOF-MRA data acquired by the research team. As a result, the majority of the datasets utilized in earlier studies were private. Table 2.1 is an overview of the dataset widely utilized by academics, including the resolution and quantity of the data.

Table 2.1 Summary of MRA datasets used in brain blood vessel segmentation

Dataset	Modality	Source	Resolution (mm ³)	Total subject
Swedish CardioPulmonary bioImage Study (SCAPIS) (Bergström et al., 2015)	CE-MRA	Private	0.48×0.48×0.50	194
PEGASUS (Martin et al., 2015)	TOF-MRA	Private	0.50x0.50x0.70	74
7UP (Madai et al., 2012)	TOF-MRA	Private	0.60x0.60x0.60	9
1000PLUS (Hotter et al., 2009)	Multimodal (Including TOF-MRA)	Private	0.52x0.52x0.65	1200
MIDAS (Bullitt et al., 2005)	TOF-MRA	Public	0.51x0.51x0.80	109

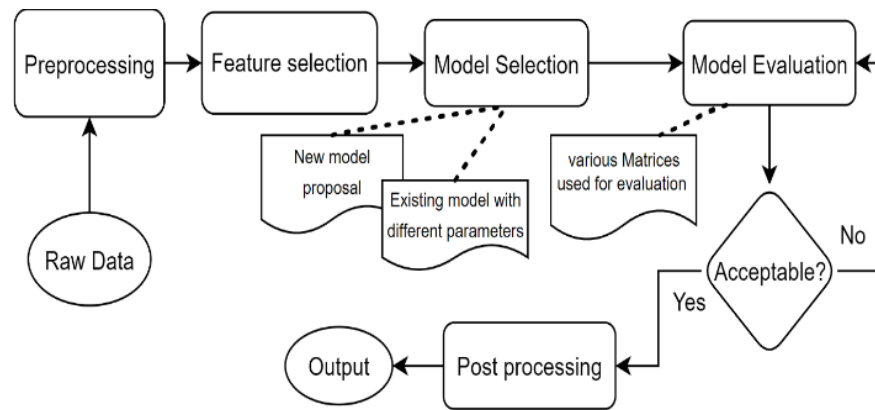


Figure 2.2 Summarized pipeline of the cerebrovascular segmentation using deep learning model

2.5.2 Evaluation Metrics

In medical imaging, image voxels are categorized as vessel voxel (Positive) or non-vessel voxel (Negative). To determine the identity of each voxel, ground truth labels are compared with voxel identification. True positive (TP), true negative (TN), false positive (FP), and false-negative (FN) are the four fundamental measurements. The metrics are presented in Table 2.2 below.

Table 2.2 Pixel measure in vessel segmentation

		Ground truth	
		Vessel	Non-vessel
Segmentation result	Vessel	TP	FP
	Non-vessel	FN	TN

In BVS using deep learning, data annotation is a significant component of the process. As most of the study follows a supervised technique, the ground truth of the data is mandatory. Even though some research tries to adopt an unsupervised method, ground truth is still essential to qualitatively examine the unsupervised output to measure the model's performance. In most situations, the annotation is done manually by experienced observers with several years of expertise in Radiology. The observer utilizes software to segment each voxel manually. Some software is used frequently for ground truth segmentation, i.e., ITK-SNAP (Yushkevich et al., 2006), MevisLab (Ritter et al., 2011), etc.

Usually, the annotation process is determined by the data collection technique. Before segmenting the actual mask, image processing, active contour techniques, or statistical models are employed to identify the Region of Interest (ROI). For example, in the paper (Liu et al., 2022), the observer used ITK SNAP software to generate a pre-segmentation mask using the active contour segmentation pipeline. Later, domain experts utilized the pre-segmentation mask for post-manual enhancement. In the study (Cheng et al., 2021), the grey transformation was utilized as a method of image processing to help distribute grey image values for improved annotation. In a different study (de Vos et al., 2021), histogram-based thresholding on maximum image intensity was employed to select the ROI, which was then manually annotated by an observer. Manual segmentation may require post-processing to guarantee that the mask has no discontinuous regions or holes (Ziegler et al., 2021).

Table 2.3 Evaluation metrics regularly used in BVS

Metrics	Expression
Sensitivity	$\frac{TP}{(TP + FN)}$
Specificity	$\frac{TN}{(TN + FP)}$
Precision	$\frac{TP}{TP + FP}$
Dice Similarity Coefficient	$\frac{2 * TP}{(FP + FN + 2 * TP)}$
Accuracy	$\frac{TP + TN}{TP + TN + FP + FN}$
False Positive Rate	$\frac{FP}{TN + FP}$
Average Hausdorff Distance	$\left(\frac{1}{X} \sum_{x \in X, y \in Y} \min d(x, y) + \frac{1}{Y} \sum_{x \in X, y \in Y} \min d(x, y) \right)$

Some of the principal assessment matrices typically utilized in the BVS study are listed in Table 2.3 a few matrices may have distinct names but equivalent expressions; for instance, DSC and F1 scores are equivalent, and the true positive rate (TPR) is equivalent to Recall and Sensitivity. The average Hausdorff distance from point set X to Y is the sum of all minimum distances between all points in X and Y, divided by the number of points in X where X is the ground truth, and Y is the segmentation.

2.5.3 Preprocessing Used In BVS

Deep learning algorithms typically extract features from unprocessed data, with researchers mainly focusing on model optimization rather than data preprocessing. However, some standard preparation is required for the medical image because it contains noise. Following is a discussion of some standard approaches utilized to solve this issue.