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BSc of Science in Biomedical Engineering

IMAGE ENHANCEMENT AND CORONARY SEGMENTATION

THE FIRST STEPS TOWARD THREE-DIMENSIONAL RECONSTRUCTION
OF THE CORONARY ARTERIES

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Image Enhancement and Coronary Segmentation

The First Steps Toward Three-Dimensional Reconstruction of the Coronary Arteries

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ABSTRACT

Cardiovascular diseases, including Coronary Artery Disease (CAD), account for a significant portion of global morbidity and mortality rates. While Coronary Angiography (CA) still remains the standard diagnostic technique for CAD, some advancements in non-invasive imaging techniques are being made.

Despite the lack of non-commercial programs capable of creating a Three-Dimensional (3D) coronary model and performing real-time co-registration with non-invasive models, progress towards its development is crucial for guiding coronary intervention procedures and help planning coronary surgeries.

This work aims to serve as a starting point for the development of such a program by presenting a method for selecting coronary angiographic frames and performing both image enhancement and coronary segmentation in CA and Computed Tomography Coronary Angiography (CTCA) images.

In pursuit of such objectives, electrocardiographic signals were analysed, and the R peaks were detected. The CA frames chosen to be further processed were the ones that were in the same moment of the cardiac cycle as when the CTCA images were taken.

For CA image enhancement, both global and local manipulations of image quality, such as brightness, contrast, and gamma adjustments, histogram equalisations, contrast-limited adaptive histogram equalisations, and edge-aware local contrast manipulations, were tested. Edge-aware local contrast manipulation was found to be the most effective for distinguishing coronary arteries from surrounding tissues. In order to segment these images, three different methods were followed: thresholding, region growing, and multi-scale vessel enhancement filtering methods, with the last one being the one with better outcomes.

Finally, to enhance the CTCA images, the windowing technique was used, and then the Frangi Vesselness Filter for 3D volumes was applied, along with a simple thresholding to remove darker regions.

Keywords: Coronary Arteries, Coronary Angiography, Computed Tomography Coronary Angiography, Image Enhancement, Image Segmentation

RESUMO

As doenças cardiovasculares, incluindo a doença arterial coronária (DAC), representam uma parte significativa das taxas globais de morbidade e mortalidade. Embora a angiografia coronária (AC) ainda seja a técnica padrão de diagnóstico da DAC, alguns avanços nas técnicas de imagem não invasivas têm vindo a ser feitos.

Apesar da falta de programas não comerciais para criar modelos tridimensionais (3D) das coronárias e os co-registar em tempo real com modelos 3D de técnicas não invasivas, é crucial começar a trabalhar nesse sentido, pois permitiria guiar procedimentos de intervenção coronária e ajudaria a planejar as cirurgias cardiovasculares coronárias.

Este trabalho tem como objetivo servir de ponto de partida para o desenvolvimento de um programa deste tipo, apresentando um método para a escolha das imagens de AC e realizando quer a melhoria de imagem quer a segmentação coronária em imagens de AC e angiografia coronária por tomografia computadorizada (Angio-TC).

Para alcançar esses objetivos, os sinais eletrocardiográficos foram analisados e os picos R foram detectados. Foram escolhidas para ser analisadas as imagens de AC que se encontravam no mesmo momento do ciclo em que as imagens de Angio-TC foram obtidas.

Para a melhoria das imagens de AC, foram testadas tanto manipulações globais quanto locais da qualidade da imagem, como ajustes de brilho, contraste e gamma, equalizações de histograma, equalizações de histograma adaptativo limitado por contraste e manipulações de contraste local consciente de contornos. Esta manipulação foi considerada a mais eficaz para distinguir as artérias coronárias dos tecidos envolventes. Para segmentar essas imagens, três métodos diferentes foram utilizados: limiarização, crescimento de regiões e métodos de filtragem de realce de vasos em múltiplas escalas, sendo este último o que apresentou os melhores resultados.

Finalmente, para melhorar as imagens de Angio-TC, foi utilizada a técnica de janelamento e, após a aplicação do Filtro de Frangi para volumes 3D, foi aplicada uma simples limiarização para eliminar regiões mais escuras.

Palavras-chave: Artérias Coronárias, Angiografia Coronária, Angiografia Coronária por Tomografia Computadorizada, Melhoria de Imagem, Segmentação da Imagem

CONTENTS

List of Figures	viii
Abbreviations	xiv
1 Introduction	1
1.1 Motivation	1
1.2 Main Goals	2
1.3 Outline	2
2 Theoretical Concepts	3
2.1 Coronary Anatomy	3
2.1.1 Coronary Arteries	3
2.1.1.1 Left Coronary Artery	4
2.1.1.2 Right Coronary Artery	4
2.1.2 Histology of Coronary Arteries	5
2.2 Coronary Artery Disease	5
2.2.1 Pathophysiology of Coronary Artery Disease	5
2.2.2 Risk Factors	6
2.2.3 Symptoms	7
2.2.4 Imaging Techniques for Diagnosing Coronary Artery Disease	7
2.2.4.1 Coronary Angiography	7
2.2.4.2 Computed Tomography Coronary Angiography	8
2.2.5 Therapeutic Techniques in Coronary Artery Disease	9
2.3 Image Processing	9
2.3.1 Image Enhancement	10
2.3.2 Image Segmentation	10
2.3.2.1 Thresholding Approach	10
2.3.2.2 Region-Based Approach	11
2.3.2.3 Edge-Based Approach	11
2.3.2.4 Clustering-Based Approach	11

2.3.2.5	Model-Based Approach	11
2.3.2.6	Deep Learning Approach	11
3	State of Art	12
3.1	Coronary Angiography and Computed Tomography Coronary Angiography Image Enhancement and Segmentation	12
3.2	Available Softwares for 3D Cornary Reconstruction and Co-Registration of Coronary Models	14
4	Methodology	15
4.1	Data Source	15
4.2	Programming Environment	15
4.3	Data Pre-processing	16
4.4	Data Processing	16
4.4.1	Electrocardiogram Signal Processing	16
4.4.2	Coronary Angiography Image Enhancement	17
4.4.3	Segmentation in Coronary Angiography Images	18
4.4.3.1	Thresholding Method	18
4.4.3.2	Region-Based Method	18
4.4.3.3	Multi-scale Vessel Enhancement Filtering	18
4.4.4	Computed Tomography Coronary Angiography Image Enhancement	19
4.4.5	Segmentation in Computed Tomography Coronary Angiography Images	20
5	Results and Discussion	21
5.1	Electrocardiogram Signal Processing	21
5.2	Coronary Angiography Image Enhancement	23
5.3	Coronary Angiography Image Segmentation	30
5.3.1	Thresholding Method	30
5.3.2	Region-Based Method	33
5.3.3	Multi-scale Vessel Enhancement Filtering Method	35
5.4	Computed Tomography Coronary Angiography Image Enhancement . .	36
5.5	Computed Tomography Coronary Angiography Image Segmentation . .	37
6	Conclusion	39
6.1	Main Findings	39
6.2	Future Work	40
	Bibliography	41
	Appendices	

A	Electrocardiogram Signal Processing	49
B	Coronary Angiography Image Enhancement	50
C	Coronary Angiography Image Segmentation	66

LIST OF FIGURES

2.1	Aortic Sinuses.	4
2.2	Anterior view of the main coronary arteries and their branches.	4
2.3	Arterial wall and its three tunicas: the intima, the media and the adventitia.	5
2.4	Demonstration of plaque build-up within the arteries, commonly called atherosclerosis, that leads to coronary artery disease.	6
2.5	Example of an coronary angiographic image.	8
2.6	Example of a computed tomography coronary angiography.	9
5.1	Final result, after correction, of R peaks detection algorithm in different CA projections. (a) First projection of individual 1; (b) Second projection of individual 2; (c) Eighth projection of individual 10.	21
5.2	Final identification, after correction, of the optimal frames of projections to further consider in the CA image analysis. (a) First projection of individual 1; (b) Second projection of individual 2; (c) Eighth projection of individual 10.	22
5.3	All frames selected from first CA projection of individual 1.	22
5.4	All frames selected from second CA projection of individual 2.	22
5.5	All frames selected from eighth CA projection of individual 10.	23
5.6	CA images prior and after removing a registered version of the first frame, for the first projection of individual 1. (a) Image 2; (b) Image 3; (c) Image 4.	23
5.7	CA images prior and after removing a registered version of the first frame, for the second projection of individual 2. (a) Image 2; (b) Image 3; (c) Image 4.	24
5.8	CA images prior and after removing a registered version of the first frame, for the eighth projection of individual 10. (a) Image 2; (b) Image 3; (c) Image 4; (d) Image 5.	24
5.9	Best results of performing single manipulations in the first CA projection of individual 1. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.	25
5.10	Best results of performing single manipulations in the second CA projection of individual 2. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.	25

5.11	Best results of performing single manipulations in the eighth CA projection of individual 10. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.	26
5.12	Best results of performing two sequential manipulations in the first CA projection of individual 1. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.	26
5.13	Best results of performing two sequential manipulations in the second CA projection of individual 2. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.	27
5.14	Best results of performing two sequential manipulations in the eighth CA projection of individual 10. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.	27
5.15	Best results of performing three sequential manipulations in the first CA projection of individual 1. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.	28
5.16	Best results of performing three sequential manipulations in the second CA projection of individual 2. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.	28
5.17	Best results of performing three sequential manipulations in the eighth CA projection of individual 10. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.	28
5.18	Results of performing Histogram Equalisation (HE), Contrast-Limited Adaptive Histogram Equalisation (CLAHE) and Edge-Aware Local Contrast Manipulation (EALCM) in the images from first CA projection of individual 1. . .	29
5.19	Results of performing Histogram Equalisation (HE), Contrast-Limited Adaptive Histogram Equalisation (CLAHE) and Edge-Aware Local Contrast Manipulation (EALCM) in the images from second CA projection of individual 2.	29
5.20	Results of performing Histogram Equalisation (HE), Contrast-Limited Adaptive Histogram Equalisation (CLAHE) and Edge-Aware Local Contrast Manipulation (EALCM) in the images from eighth CA projection of individual 10.	30
5.21	Results of the thresholding method with different threshold values on the first CA projection of individual 1.	31
5.22	Results of the thresholding method with different threshold values on the second CA projection of individual 2.	31
5.23	Results of the thresholding method with different threshold values on the eighth CA projection of individual 10.	31
5.24	Results of Otsu's method on (a) Image 2, (b) Image 3, and (c) Image 4 of the first CA projection of individual 1.	32

5.25	Results of otsu's method on (a) Image 3, and (b) Image 4 of the second CA projection of individual 2.	32
5.26	Results of otsu's method on (a) Image 3, (b) Image 4, and (c) Image 5 of the eighth CA projection of individual 10.	33
5.27	Results of the region growing algorithms on the first CA projection of individual 1, where the white dot marks the pixel used as a seed and the blue coloured portion is the region segmented.	34
5.28	Results of the region growing algorithms on the second CA projection of individual 2, where the white dot marks the pixel used as a seed and the blue coloured portion is the region segmented.	34
5.29	Results of the region growing algorithms on the eighth CA projection of individual 10, where the white dot marks the pixel used as a seed and the blue coloured portion is the region segmented.	35
5.30	Final results of the multi-scale vessel enhancement filtering method on (a) Image 2, (b) Image 3, and (c) Image 4 of the first CA projection of individual 1, where the blue colored region corresponds to what was segmented.	36
5.31	Final results of the multi-scale vessel enhancement filtering method on (a) Image 3 and (b) Image 4 of the second CA projection of individual 2, where the blue colored region corresponds to what was segmented.	36
5.32	Final results of the multi-scale vessel enhancement filtering method on (a) Image 3, (b) Image 4, and (c) Image 5 of the eighth CA projection of individual 10, where the blue colored region corresponds to what was segmented.	37
5.33	Results of windowing performance on the some CTCA slices of individual 1. WL: <i>WindowLevel</i> ; WW: <i>WindowWidth</i>	37
5.34	3D CTCA models from individual 1 considering (a) Original slices, (b) Slices after windowing process with <i>WindowLevel</i> = 200 and <i>WindowWidth</i> = 600, and (c) Slices after windowing process with <i>WindowLevel</i> = -600 and <i>WindowWidth</i> = 1300.	38
5.35	3D CTCA models from individual 1 (a) after applying the Frangi filter, (b) after applying the Frangi Filter and followed by thresholding, and (c) after applying the Frangi Filter and followed by thresholding, with an appropriate rotation to better visualise internal arteries.	38
A.1	R peak detection in the ECG signals of different coronary angiography projections. (a)First projection of individual 1; (b)Second projection of individual 2; (c)Eighth projection of individual 10.	49
A.2	Identification of the optimal frames of different coronary angiography projections to further consider in the coronary angiography image analysis. (a) First projection of individual 1; (b) Second projection of individual 2; (c) Eighth projection of individual 10.	49

B.1	Results of brightness adjustments on the first CA projection of individual 1.	50
B.2	Results of brightness adjustments on the second CA projection of individual 2.	50
B.3	Results of brightness adjustments on the eighth CA projection of individual 10.	51
B.4	Results of contrast adjustments on the first CA projection of individual 1. . .	51
B.5	Results of contrast adjustments on the second CA projection of individual 2.	51
B.6	Results of contrast adjustments on the eighth CA projection of individual 10.	52
B.7	Results of gamma adjustments on the first CA projection of individual 1. . .	52
B.8	Results of gamma adjustments on the second CA projection of individual 2.	52
B.9	Results of gamma adjustments on the eighth CA projection of individual 10.	53
B.10	Results of contrast adjustments on the first CA projection of individual 1 with brightness decreased by 20%.	53
B.11	Results of contrast adjustments on the second CA projection of individual 2 with brightness decreased by 20%.	53
B.12	Results of contrast adjustments on the eighth CA projection of individual 10 with brightness decreased by 20%.	54
B.13	Results of gamma adjustments on the first CA projection of individual 1 with brightness decreased by 20%.	54
B.14	Results of gamma adjustments on the second CA projection of individual 2 with brightness decreased by 20%.	54
B.15	Results of gamma adjustments on the eighth CA projection of individual 10 with brightness decreased by 20%.	55
B.16	Results of brightness adjustments on the first CA projection of individual 1 with contrast increased by 40%.	55
B.17	Results of brightness adjustments on the second CA projection of individual 2 with contrast increased by 40%.	55
B.18	Results of brightness adjustments on the eighth CA projection of individual 10 with contrast increased by 40%.	56
B.19	Results of gamma adjustments on the first CA projection of individual 1 with contrast increased by 40%.	56
B.20	Results of gamma adjustments on the second CA projection of individual 2 with contrast increased by 40%.	56
B.21	Results of gamma adjustments on the eighth CA projection of individual 10 with contrast increased by 40%.	57
B.22	Results of brightness adjustments on the first CA projection of individual 1 with gamma value of 2.	57
B.23	Results of brightness adjustments on the second CA projection of individual 2 with gamma value of 2.	57
B.24	Results of brightness adjustments on the eighth CA projection of individual 10 with gamma value of 2.	58

B.25 Results of contrast adjustments on the first CA projection of individual 1 with gamma value of 2.	58
B.26 Results of contrast adjustments on the second CA projection of individual 2 with gamma value of 2.	58
B.27 Results of contrast adjustments on the eighth CA projection of individual 10 with gamma value of 2.	59
B.28 Results of gamma adjustments on the first CA projection of individual 1 with brightness decreased by 20% and contrast increased by 45%.	59
B.29 Results of gamma adjustments on the second CA projection of individual 2 with brightness decreased by 20% and contrast increased by 45%.	59
B.30 Results of gamma adjustments on the eighth CA projection of individual 10 with brightness decreased by 20% and contrast increased by 45%.	60
B.31 Results of contrast adjustments on the first CA projection of individual 1 with brightness decreased by 20% and gamma value of 1.5.	60
B.32 Results of contrast adjustments on the second CA projection of individual 2 with brightness decreased by 20% and gamma value of 1.5.	60
B.33 Results of contrast adjustments on the eighth CA projection of individual 10 with brightness decreased by 20% and gamma value of 1.5.	61
B.34 Results of gamma adjustments on the first CA projection of individual 1 with contrast increased by 40% and brightness decreased by 30%.	61
B.35 Results of gamma adjustments on the second CA projection of individual 2 with contrast increased by 40% and brightness decreased by 30%.	61
B.36 Results of gamma adjustments on the eighth CA projection of individual 10 with contrast increased by 40% and brightness decreased by 30%.	62
B.37 Results of brightness adjustments on the first CA projection of individual 1 with contrast increased by 40% and gamma value of 2.	62
B.38 Results of brightness adjustments on the second CA projection of individual 2 with contrast increased by 40% and gamma value of 2.	62
B.39 Results of brightness adjustments on the eighth CA projection of individual 10 with contrast increased by 40% and gamma value of 2.	63
B.40 Results of contrast adjustments on the first CA projection of individual 1 with gamma value of 2.0 and brightness decreased by 10%.	63
B.41 Results of contrast adjustments on the second CA projection of individual 2 with gamma value of 2.0 and brightness decreased by 10%.	63
B.42 Results of contrast adjustments on the eighth CA projection of individual 10 with gamma value of 2.0 and brightness decreased by 10%.	64
B.43 Results of brightness adjustments on the first CA projection of individual 1 with gamma value of 2 and contrast increased by 15%.	64
B.44 Results of brightness adjustments on the second CA projection of individual 2 with gamma value of 2 and contrast increased by 15%.	64

B.45	Results of brightness adjustments on the eighth CA projection of individual 10 with gamma value of 2 and contrast increased by 15%.	65
C.1	Results of modified Frangi Vesselness Filter function with different sigma parameters on the first CA projection of individual 1.	66
C.2	Results of modified Frangi Vesselness Filter function with different sigma parameters on the second CA projection of individual 2.	67
C.3	Results of modified Frangi Vesselness Filter function with different sigma parameters on the eighth CA projection of individual 10.	67
C.4	Results of selecting the regions based on their properties on the first CA projection of individual 1.	68
C.5	Results of selecting the regions based on their properties on the second CA projection of individual 2.	68
C.6	Results of selecting the regions based on their properties on the eighth CA projection of individual 10.	69

ABBREVIATIONS

3D	Three-Dimensional (<i>pp.</i> iii , 1 , 2 , 8 , 12 , 14 , 16 , 37 , 40)
CA	Coronary Angiography (<i>pp.</i> iii , 1 , 2 , 7 , 8 , 12 , 13 , 15–21 , 36 , 39 , 40)
CABG	Coronary Artery Bypass Graft Surgery (<i>pp.</i> 9)
CAD	Coronary Artery Disease (<i>pp.</i> iii , 1 , 3 , 5–9 , 12 , 39)
CLAHE	Contrast-Limited Adaptive Histogram Equalisation (<i>pp.</i> 18 , 29 , 39)
CTCA	Computed Tomography Coronary Angiography (<i>pp.</i> iii , 1 , 2 , 7 , 8 , 12 , 13 , 15–17 , 19–22 , 36 , 37 , 39 , 40)
DICOM	Digital Imaging and Communications in Medicine (<i>pp.</i> 15 , 16)
EALCM	Edge-Aware Local Contrast Manipulation (<i>pp.</i> 18 , 29 , 30)
ECG	Electrocardiogram (<i>pp.</i> 2 , 16 , 17 , 21 , 22 , 39)
LCA	Left Coronary Artery (<i>pp.</i> 3 , 4)
PCI	Percutaneous Coronary Intervention (<i>pp.</i> 8 , 9)
RCA	Right Coronary Artery (<i>pp.</i> 3 , 4)

INTRODUCTION

This chapter describes the motivation behind this dissertation, outlines its ultimate purposes, and clarifies the overall structure of the present document.

1.1 Motivation

For several years, studies have consistently highlighted the significant impact of cardiovascular diseases on high mortality and morbidity rates in developed countries, including Portugal [2, 3]. Cardiovascular diseases encompass a wide range of heart and blood vessel conditions, with Coronary Artery Disease (CAD) being the most prevalent and often associated with fatal complications [4, 5].

Coronary Angiography (CA) is the standard technique used to locate and assess the severity of coronary artery stenosis in individuals with CAD. However, the currently available softwares for the Three-Dimensional (3D) reconstruction of two-dimensional angiographic images are expensive and non-automatic, requiring a specialized technician to operate it. Consequently, interventional cardiologists must rely on their knowledge and experience to mentally create a 3D model of the arteries.

To fill this gap in cardiovascular imaging, there is an urgent need to develop a program that can autonomously reconstruct the coronary arteries from angiographic images. Moreover, taking advantage of the fact that Computed Tomography Coronary Angiography (CTCA) is often performed before invasive CA, the program should also allow to co-register these two image modalities, exploring the advantages of both techniques.

This advancement would improve the accuracy of catheter placement during interventional cardiology procedures, assist clinicians in identifying pathological anatomical alterations, and provide valuable information for surgical planning. Thus, it is crucial to create the necessary conditions for the development of this tool. It is imperative to begin by studying the particularities of both imaging modalities, enhancing their quality, and precisely segmenting the coronary arteries in both.

1.2 Main Goals

This work serves as a starting point for the development of a robust program capable of reconstructing a 3D model of the coronary arteries from CA images and co-registering this model with a 3D model derived from CTCA images. To achieve this, it is necessary to focus on two main objectives:

- Improve image quality by enhancing the distinction between the tissues of interest and the surrounding tissues in both imaging modalities;
- Segment the coronary arteries in both CA and CTCA images.

To accomplish these two challenging goals, several steps must be followed. First, it is necessary to study the Electrocardiogram (ECG) signal contained in the metadata of the CA images to locate the frames with the least cardiac activity. After selecting the frames for processing, image enhancement must occur. Finally, different segmentation techniques need to be tested and evaluated to identify the one that best delineates the coronary arteries.

1.3 Outline

This work is divided into five main chapters. Chapter 2 explains some important theoretical concepts for fully understanding this project. It describes the coronary anatomy in relation to dependent heart zones and provides an overview of the pathophysiological mechanisms of CAD. Additionally, it explores imaging techniques used for its diagnosis and outlines various therapeutic interventions. Finally, it discusses image processing, with a particular focus on image enhancement and segmentation.

Chapter 3 presents the available literature on image enhancement and coronary segmentation for CA and CTCA. Since this work initiates the development of a robust program for three-dimensional coronary artery reconstruction and co-registration of two coronary imaging modalities, it also reviews similar programs.

Chapter 4 provides a detailed description of the methodology for this work, explaining the data sources, the choice of programming environment, and the steps involved in data pre-processing and processing.

Chapter 5 presents all the results obtained throughout this work and includes an analysis of those results.

Finally, Chapter 6 summarises this research's core results and outlines possible directions for future work in the same area.

The research work described in this dissertation was carried out in accordance with the norms established in the ethics code of Universidade Nova de Lisboa. The work described and the material presented in this dissertation, with the exceptions clearly indicated, constitute original work carried out by the author.

THEORETICAL CONCEPTS

The present chapter establishes a theoretical framework that contextualises this dissertation. To fully acknowledge the clinical context, it is relevant to understand the basics of coronary anatomy, CAD pathophysiology, and the most commonly used image techniques for CAD diagnosis and therapeutics. It is equally pertinent to address the theoretical concepts related to image processing, particularly in the medical context, containing the grounds and techniques employed for image enhancement and segmentation.

2.1 Coronary Anatomy

Like all other muscles in the human body, the myocardium relies on an uninterrupted supply of oxygen and vital nutrients to sustain its contractile functions. This crucial process is referred to as coronary circulation and is facilitated by an intricate network of essential blood vessels, including the coronary arteries, coronary veins, and related capillaries [6].

2.1.1 Coronary Arteries

The coronary arteries are crucial in delivering oxygenated blood to the heart muscle. These vessels arise from dilations in the ascending aorta's wall located above the aortic semilunar valve, commonly known as aortic sinuses. There are three aortic sinuses, commonly called the non-coronary sinus, the right coronary sinus, and the left coronary sinus, and their classification is representative of the existence or not of generated vessels. Thereby, the two main coronary arteries, the Right Coronary Artery (RCA) and the Left Coronary Artery (LCA), originate in the right and left coronary sinuses, respectively [7]. This is shown in Figure 2.1.

These two main coronary arteries have their ramifications that allow for efficient perfusion of the whole cardiac muscle [7]. Figure 2.2 illustrates the coronary arteries.

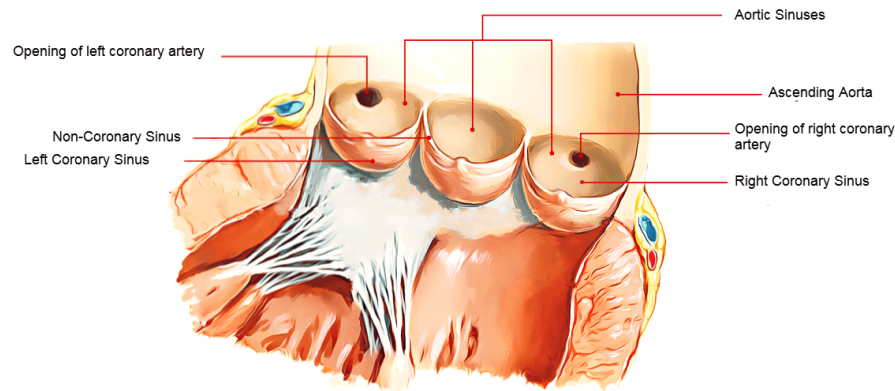


Figure 2.1: Aortic Sinuses. Adapted from [8].

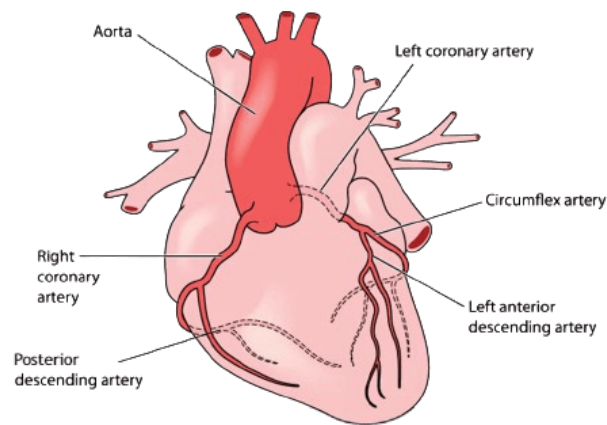


Figure 2.2: Anterior view of the main coronary arteries and their branches. Adapted from [9].

2.1.1.1 Left Coronary Artery

The LCA supplies oxygenated blood to the left atrium and left ventricle. The LCA further branches out into two arteries: the left anterior descending artery and the circumflex artery. The left anterior descending artery supplies blood to the front of the left side of the heart, while the circumflex artery encircles the heart muscle and provides blood to the outer side and back of the heart [7].

2.1.1.2 Right Coronary Artery

The RCA is responsible for delivering oxygen-rich blood to essential regions of the heart, including the right ventricle, right atrium, and some parts of the conducting system, like the sinoatrial and atrioventricular nodes. It follows the coronary sulcus and may give rise to various marginal arteries that distribute blood to the superficial regions of the right ventricle.

The Posterior Descending Artery is a branch of the RCA that runs along the posterior

interventricular sulcus to the apex of the heart. It provides blood to the posterior interventricular septum and the posterolateral branch, which supplies the posterior and inferior walls of the left ventricle [7].

2.1.2 Histology of Coronary Arteries

Coronary arteries have three tunics, which are the intima, media, and adventitia. As shown in Figure 2.3, intima is the innermost layer and is made up of endothelial cells, a network of connective tissue and an elastic layer that creates a selectively permeable barrier. The media consists of involuntary smooth muscle cells and some elastic fibers, and the adventitia is mainly composed of fibrous tissue. The adventitia plays a crucial role in regulating the diameter of the coronary artery by orienting its collagen fibers [10, 11].

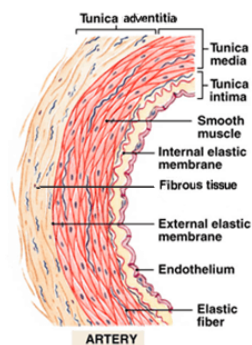


Figure 2.3: Arterial wall and its three tunics: the intima, the media and the adventitia. Adapted from [12].

2.2 Coronary Artery Disease

Maintaining the structural and functional well-being of the coronary arteries is an essential aspect of preserving cardiovascular health. These arteries play a crucial role in ensuring the integrity and optimal functioning of the heart. Therefore, it is imperative to take appropriate measures to protect these arteries, as any notable blockage or constriction can result in inadequate blood flow to the cardiac tissues [13].

CAD is a pathological condition that originates from the gradual accumulation of atherosclerotic plaque in the coronary arteries, leading to the narrowing or blockage of blood vessels, which can ultimately result in myocardial ischemia or infarction. Managing this inflammatory disorder can be quite intricate due to the diverse range of risk factors and blood cell interactions involved [4].

2.2.1 Pathophysiology of Coronary Artery Disease

Atherosclerosis is an inflammatory disease that starts with the activation of arterial endothelium cells, which can stimulate leucocyte migration from the bloodstream to

the inner layer of the coronary artery wall. The leucocytes then interact with arterial media cells, encouraging the migration of smooth muscle cells from tunica media to intima. This leads to their proliferation and triggers extracellular matrix production. Some specific constituents of the extracellular matrix bind to lipoproteins, which prolong their residence in the intima and sustain and propagate the inflammatory response. As the lesion progresses, calcification may occur. The process of CAD involves combining various factors like the injured vascular wall, an activated inflammatory response, the buildup of cholesterol, and the retention of cells [5]. The accumulation of cholesterol creates atherosclerotic plaques that are illustrated in Figure 2.4. These plaques are responsible for reducing blood flow in the arteries, as the lumen of the artery also has its diameter decreased.

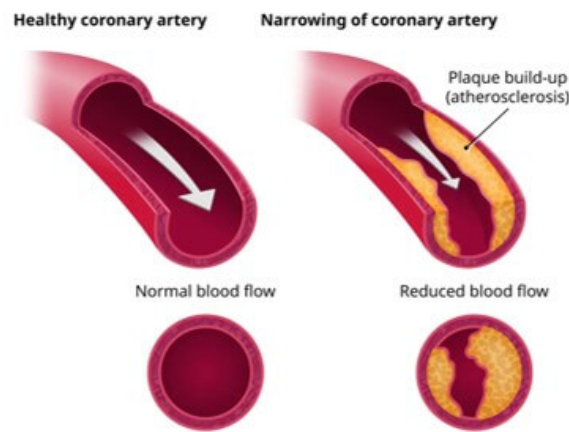


Figure 2.4: Demonstration of plaque build-up within the arteries, commonly called atherosclerosis, that leads to coronary artery disease. Adapted from [14].

2.2.2 Risk Factors

Various risk factors for CAD can be classified either as modifiable or non-modifiable. Among the non-modifiable ones are age, gender, ethnicity, and family history. Over the years, it is normal to gradually build up fats, cholesterol, and some other substances in and on the arterial walls. Besides age, gender is also considered a risk factor, and when compared to women, men have a higher risk of having this disease at an early age [15]. Aside from that individuals with a family history of premature cardiac disease younger than fifty years of age have an increased CAD mortality risk [16, 17]. Among the modifiable factors, hypertension, hyperlipidemia, diabetes mellitus, obesity, smoking, a sedentary lifestyle, and an unbalanced diet are the most relevant and the most studied [18–20].

2.2.3 Symptoms

Since CAD can develop slowly over the years, it can be asymptomatic for a long time until symptoms begin to manifest when blockages are already considered severe and life-threatening. This means that those who have this disease can be stable for long periods and, due to an acute atherothrombotic event, turn unstable at any time. This is usually associated with plaque ruptures or erosion.

To avoid life-threatening situations, it is important to detect this inflammatory response early, and so there are some symptoms to watch out for, like crushing chest pain or pressure, shoulder or arm pain, shortness of breath, and sweating. Usually, the first symptoms appear during physical exercises due to the poor perfusion of cardiac muscle [16].

2.2.4 Imaging Techniques for Diagnosing Coronary Artery Disease

As with most pathologies, early detection of CAD is crucial to treating the lesion before it becomes severe. Throughout the years and with technological development, CAD diagnosis has become more efficient because of the advances in clinical imaging tools, from invasive to non-invasive techniques.

To assess if an individual's symptoms are caused by CAD, usually, in clinical practice, a non-invasive evaluation is primarily carried out. There are a lot of non-invasive image techniques to help with CAD diagnosis and to assess the event risk in each individual, such as CTCA or functional imaging tests like single-photon emission computed tomography, stress cardiovascular magnetic resonance, or stress echocardiography.

However, in some cases where there is a high suspicion or there has already been an event of an acute coronary syndrome, invasive techniques, like CA, take precedence since they allow for a revascularization procedure if needed. Both invasive and non-invasive techniques are very helpful in diagnosing CAD, although they give different information about the arteries. While CTCA produces static images, CA creates real-time dynamic images [21, 22]. Being anatomical tests, simple CTCA and CA may not be enough to fully evaluate the coronary circulation. Intermediate stenosis may provoke ischaemia, which is possible to evaluate with physiologic studies [23], and even non-obstructive plaques can be responsible for acute coronary syndromes, which is possible to evaluate with intracoronary imaging techniques [24, 25].

2.2.4.1 Coronary Angiography

Initially developed by Egas Moniz in 1929 for the study of various cerebral vascular conditions, angiography involves the injection of a contrast element into the patient. This increases the contrast between the blood vessels and the surrounding tissues, enabling better discrimination between different anatomical structures [26].

CA is an invasive diagnostic exam designed to visualise the blood circulation in the coronary arteries, intending to identify potential alterations or lesions that explain the

symptoms presented. The procedure involves placing catheters through the radial or femoral arteries into the coronary arteries. The selective injection of iodinated contrast allows for coronary lumen visualisation with a high spatial and temporal resolution [27, 28]. Figure 2.5 exemplifies the images acquired in CA technique, where the coronary arteries appear in a darker tone than the surrounding tissues.



Figure 2.5: Example of an coronary angiographic image.

Despite being mainly a diagnostic test, in some cases, angiography can be used to perform therapeutic measures such as angioplasty, clot removal, or coronary stent placement, and in those cases, it is very useful to have a program that can reconstruct the whole coronary system with the minimum image projections possible [27].

Although it has remained the standard technique for assessing the severity of coronary artery disease, the available softwares to create a 3D model of the coronaries are still not widely used in clinical practice. In recent years, several studies have appeared in this area. However, a robust, user-friendly 3D reconstruction tool is still to be developed, which will have great potential for Percutaneous Coronary Intervention (PCI) planning and wire-free physiologic evaluation.

2.2.4.2 Computed Tomography Coronary Angiography

Despite invasive CA remaining the standard technique in CAD diagnosis, the CTCA has emerged as a reliable non-invasive strategy to assess the severity of vessel stenosis without having the implicit risks associated with an invasive image procedure.

CTCA is an advanced imaging diagnostic procedure that generates detailed 3D images of coronary arteries. This exam assesses the blood flow throughout these vessels, helping to accurately diagnose any potential cardiovascular diseases, especially CAD [29, 30]. A typical CTCA image is represented in Figure 2.6. As can be seen, unlike what happens in CA images, in this imaging modality the arteries appear with higher intensity values, that is, in lighter shades.

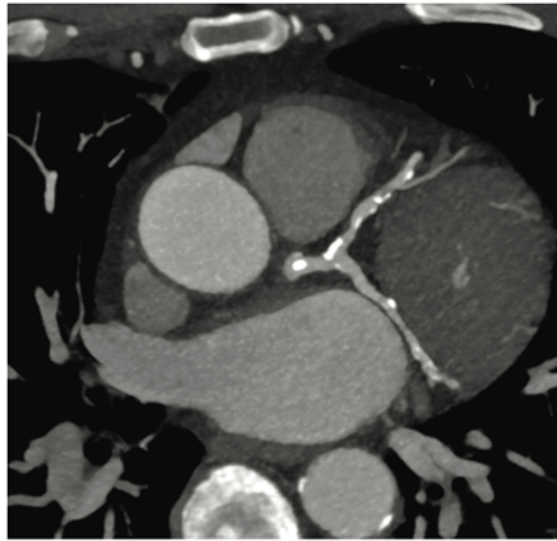


Figure 2.6: Example of a computed tomography coronary angiography.

2.2.5 Therapeutic Techniques in Coronary Artery Disease

Usually, there are three treatment options for individuals with CAD: Coronary Artery Bypass Graft Surgery (CABG), PCI, and optimal medical treatment [31].

- CABG is an open chest surgery that aims to treat the blocked or narrowed artery by bypassing that region with a healthy blood vessel, taken from elsewhere in the body. In this surgical procedure, one end of the graft is attached above the blockage and the other end below that same blockage, creating a channel for blood circulation [32].
- PCI is a less invasive method that treats CAD by opening the blocked coronary artery. This technique is also known as coronary angioplasty with stenting and uses a small balloon in the distal end of a catheter. When the catheter arrives at the narrowed artery, the interventional cardiologist inflates the balloon, and a permanent stent is placed within the artery to keep her open. Often, this stent has medication to improve the efficiency of this technique by preventing the risk of re-narrowing [33].
- Usually, the optimal medical treatment consists of antiplatelet therapy, angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers, β -blockers, and statins. This is usually indicated even when PCI or CABG are performed [34].

2.3 Image Processing

Image processing encompasses a range of techniques that utilise computer algorithms to modify and manipulate digital images. These techniques are employed either to enhance the quality of an existing image or to extract valuable information from it [35]. There

are several techniques of image processing, among them image enhancement and image segmentation.

2.3.1 Image Enhancement

Image enhancement is understood as the application of a set of techniques aimed at improving the quality and overall appearance of the image and better distinguishing its details [35, 36].

Whenever working with images, regardless of the purpose, it is always recommended to enhance their quality. Since this is a work in medical imaging, this step is even more important. Improving the quality of a medical image is especially relevant for achieving a good identification of the structures that one intends to analyse. Yet, it is crucial that they not alter the diagnostic information contained in those images.

There are several image enhancement techniques, such as denoising, histogram equalisation, filtering, contrast, gamma, and brightness adjustment, and deblurring [36–38].

In the images of CA and CTCA that we intend to improve, the goal is the same: to enhance the difference in intensities between the coronary arteries and the surrounding tissues. Although contrasting agents are applied in both imaging modalities, since the vessels of interest have very small diameters, it is crucial to differentiate this region from the background, especially as we approach the edges that take on even smaller sizes.

2.3.2 Image Segmentation

Image segmentation is understood as the process of dividing an image into distinct regions based on the characteristics presented, such as colour, texture, and intensity. As pixels are grouped according to similar properties, this technique enables object detection and recognition, feature extraction, and image analysis. It is therefore very useful in various fields, such as robotics, autonomous vehicles, intelligent video analytics, and medical imaging, as is the case in this work. There are numerous segmentation techniques that can be employed, which can be categorised as thresholding methods, region-based methods, edge-based methods, clustering-based methods, model-based methods and deep learning methods [39–43].

2.3.2.1 Thresholding Approach

The thresholding approach is perhaps the simplest and the most used in the field of image segmentation. It consists of transforming a greyscale image into a binary image by classifying each pixel based on a comparison with a predefined threshold value. The choice of the value to be used as a threshold can be made manually by the user, or automatic threshold selection alternatives can be tested, such as Otsu’s method [44]. This tool allows for an automatic selection of the threshold value based on the histogram information of the image in order to minimise the intraclass variance [39, 40, 45].

2.3.2.2 Region-Based Approach

The region-based segmentation approach involves looking for similar characteristics in neighboring pixels to group them into a single region. The most common approach in this type of method is to follow the reasoning of region growing, where one or more pixels are defined as seeds and their adjacent ones are classified as similar or different. The neighbours are then treated as seeds, and their adjacent ones are analysed until the entire image has been segmented [39, 40, 46].

2.3.2.3 Edge-Based Approach

Edge-based segmentation, also known as edge detection, entails determining which pixels constitute sharp differences in intensity, as these mark the boundary between two different regions. These pixels are subsequently highlighted in a separate class from the classification assigned to the rest of the image. For this type of approach, it is usually necessary to apply high-pass filters to the image, such as the Canny filter or the Laplacian [39, 40, 47].

2.3.2.4 Clustering-Based Approach

Clustering-based segmentation algorithms work unsupervised, dividing the image into clusters based on the properties they share, such as colour, texture, and intensity. Pixels with comparable features are grouped together, whereas those with more distinguishing characteristics are divided into different regions. The k-means algorithm is probably the most used in this group and works by dividing the image into k different regions [39, 40, 48].

2.3.2.5 Model-Based Approach

Model-based segmentation uses predictive models developed with information from the regions of interest, namely, the structure, appearance, or characteristics of that region. The model is then modified to fit the image data and can proceed with segmentation using the knowledge it acquired beforehand [39, 40].

2.3.2.6 Deep Learning Approach

Deep learning-based segmentation uses algorithmic architectures, such as neural networks, to learn features about the image. With the trained models, it is possible to automatically identify and delineate regions of interest in images [49]. However, in order for them to be effectively trained, it is necessary to provide these models with a large amount of annotated data that is not always accessible.

STATE OF ART

Despite the evolution of non-invasive cardiovascular imaging techniques, invasive strategies remain common in clinical practice, particularly when there is a high suspicion of CAD. This chapter describes the state of the art in image enhancement for both CA and CTCA, as well as the segmentation of the coronary arteries in both modalities. To achieve segmentation, it is essential to first address image enhancement, which is why all authors focusing on segmentation also detail the manipulations they performed on the images beforehand. Since this work serves as a starting point for developing a program capable of reconstructing a 3D model of the coronary arteries from CA images and co-registering that model with a 3D model derived from CTCA images, this chapter also reports the investigation for possible existing programs in this area.

3.1 Coronary Angiography and Computed Tomography Coronary Angiography Image Enhancement and Segmentation

Since the introduction of artificial intelligence for healthcare purposes, notably in the analysis and processing of medical images, a growing number of studies have been conducted in this field. Although a substantial quantity of annotated data is required for this purpose, all of the most recent studies discuss the application of deep learning algorithms for coronary artery segmentation, whether in CA or CTCA images.

The work conducted by Gao et al. [50] involved the segmentation of coronary arteries in 130 sequences of CA images. To achieve that goal, the images underwent processing using noise reduction filters, and contrast modifications were applied using a non-local averaging filter [51] followed by a top-bottom-hat filtering strategy [52]. Coronary segmentation was treated as a pixel-by-pixel problem and was conducted utilising deep learning techniques incorporating filter-based characteristics. Their best-performing model used a gradient boosting decision tree classifier [53] and achieved a precision of 0.857, sensitivity of 0.902, specificity of 0.992, F1 score of 0.874, AUROC of 0.947, and IoU of 0.779.

Yang et al. [54] presented a study to perform major vessel segmentation using also deep learning models, based on convolutional neural networks. The ground-truth images were obtained using computer-aided tools with manual corrections performed by specialists. Several algorithms were tested, such as SimpleUNet [55], ResNet101 [56], DenseNet121 [57], and InceptionResNet-v2 [58]. SimpleUNet attained the lowest F1 score of 0.871, whereas the highest F1 score of 0.917 was reached by DenseNet121. In this study, image enhancement techniques are not mentioned since some of the image adjustments are performed by the neuronal model.

Another study was run by Cheung et al. [59], whose purpose was to train a two-dimensional UNet model [60] capable of performing segmentation of the aorta and the coronary arteries on CTCA images. They proposed two models. The first one performs the segmentation of the aorta and the coronary arteries simultaneously, and the reported F1 score was 91.20%, whereas the second model aims to segment only the coronary arteries, achieving an F1 score of 88.80%. Before being provided to the models, the images underwent brightness adjustments using a windowing technique and intensity normalisation using the linear histogram stretch technique.

A study with promising results was presented by Du et al. [61], who employed deep learning methods to create a diagnostic tool for evaluating CA images. To accomplish this, 20612 images with annotations of the coronary arteries and their lesions were used, and two different deep neural networks were trained. Only the first model aimed at coronary segmentation, achieving average accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of 98.4%, 85.2%, 99.1%, 76.2%, and 99.5%, respectively.

Although the aforementioned studies present good segmentation results, they all mention the existence of annotated data that served as ground-truth for training the deep learning architectures and for evaluating the segmentation. However, the models mentioned are not freely accessible, and training such models requires a vast amount of annotated data. Therefore, the use of deep learning, and particularly any of the mentioned architectures or models, in this work was impossible.

Luo et al. [62] introduced a segmentation model based on a multi-scale Hessian matrix analysis of CA images. To preprocess those images, the grayscale was adjusted by a piecewise linear function so that the background grey value was compressed while improving the target grey value. After that adjustment, the multi-scale Hessian matrix enhancement algorithm is applied.

In a study conducted by Qian et al. [63], a modification to the multi-scale Hessian matrix approach was proposed. It was modified by the addition of non-local rotation-invariant weights to the derivations of the Hessian Matrix, which helps in noise suppression.

Although these studies utilised a multi-scale Hessian analysis algorithm, which did not require annotated data as deep learning algorithms do, they could not be directly applied in this work without modification, since the parameters might vary according to the set of images being used.

3.2 Available Softwares for 3D Cornary Reconstruction and Co-Registration of Coronary Models

The biggest motivation for this work is to fill the existing gap in cardiovascular imaging. The existing softwares to reconstruct the 3D structure of the coronary arteries are not used in clinical practice because they usually require manual inputs from a specialist. There are a few mentioned in the literature, such as QAngio XA 3D (Medis Medical Imaging System) [64] and CAAS Workstation (Pie Medical Imaging) [65], but they are commercial softwares which means that nearly all information available about them is the one publicly available on the company's websites [66, 67].

These programs are semi-automated since they usually can autonomously reconstruct the 3D model of the coronaries if the contour detection is accurate (in cases where this condition is not verified, manual corrections are needed), and if optimal viewing angles of the artery are considered. In addition to requiring manual corrections from a specially trained user, which limits their autonomy, these software tools demand significant computational resources, potentially restricting their use in some clinical settings.

METHODOLOGY

This chapter contains a description of the source and nature of the data used in this work, as well as all the processing that was applied, from the choice of the CA images to be analysed to the enhancement and segmentation of both CA and CTCA images.

4.1 Data Source

The images used in this work were provided by Dr. David Neves, cardiologist at the Hospital do Espírito Santo de Évora. This dataset pertains to the images from CA and CTCA of 16 individuals, 5 of them female and 11 male, aged between 45 and 90 years.

The CTCA folders contained 350 to 850 tomographic slices, depending on the subject, whereas the CA one held 5 to 35 projections, each consisting of 20 to 40 temporally sequential frames. While both images were the same size, 512-by-512 pixels, in the CA images only 8 bits were allocated for intensity description, whereas in the CTCA images 12 bits were allocated.

Despite differing in content, both image modalities came in Digital Imaging and Communications in Medicine (DICOM) file format, a standard in the medical imaging area.

4.2 Programming Environment

An appropriate programming environment had to be selected to process these images and carry out the coronary segmentation.

Before even starting to develop programs to accomplish the goals proposed, RadiAnt DICOM Viewer [68] was employed to examine the images, get acquainted with them and comprehend their unique characteristics before further processing.

MATLAB [69] was the program of choice as a programming environment because it is an intuitive platform that performs well with data in array format, and because it already has several features and algorithms designed specifically for image processing, especially for medical imaging, as is the case. This study required the installation of

various MATLAB add-ons, namely, the signal processing [70], the image processing [71, 72], the medical imaging [71, 73], and the computer vision toolboxes [71, 74].

4.3 Data Pre-processing

Although DICOM images often include sensitive metadata, to ensure anonymity, all fields related to the patient (except age and sex, which are non-identifiable and potentially valuable for statistical analysis), the hospital, and the technicians engaged in the examination were removed.

As this work will serve as the starting point for a bigger one that aims to reconstruct a 3D model of the coronary arteries from CA images and to co-register the 3D models of the two modalities of cardiovascular imaging, it was required that both models were at the same point in the cardiac cycle. It was known a priori that the CA images contained the ECG signal corresponding to the acquisition in their metadata, and upon examining the CTCA scans in RadiAnt Viewer, it was perceived that they included, for each individual, an annotation with a proportion that indicates the moment in the cardiac cycle where these images were acquired. Therefore, the synchronisation requirement could be considered.

4.4 Data Processing

4.4.1 Electrocardiogram Signal Processing

Instead of analysing all the CA images, it was chosen to select specifically the frames that were at the same moment of the cardiac cycle that appeared annotated in the CTCA images. Hence, a function was developed to use the ECG signal contained in the metadata of the CA images and determine the temporal location of the frames that can be used in the construction of the 3D model. In order to do this, the function detects the R peaks of each signal, through the *findpeaks* function [75], whose arguments 'MinPeakProeminence' and 'MinPeakDistance' have been adjusted. For the MinPeakProeminence, the value considered was a fixed percentage of the difference between the maximum amplitude of the signal ($maxAmp_{ECGsignal}$) and the average amplitude value ($meanAmp_{ECGsignal}$), as can be seen in Equation 4.1. This percentage was studied (considering values between 0.5 and 1) to optimise the detection of peaks.

$$MinPeakProeminence = 0.68 \times (maxAmp_{ECGsignal} - meanAmp_{ECGsignal}) \quad (4.1)$$

Similarly, a study was carried out to determine a percentage of the sampling frequency, f_s , as the optimal value of MinPeakDistance. Percentages between 0.1 and 1 were tested. Equation 4.2 describes the formula used for this calculation.

$$MinPeakDistance = 0.5 \times f_s \quad (4.2)$$

Despite accurately detecting the R peaks in individuals with elevated heart rates, the algorithm occasionally identified large-amplitude aberrant tracings as R peaks. Therefore, it was crucial to include a function that, upon receiving the position of all detected R peaks, filtered them based on the shape of the beat in question. Thus, it was decided to remove R peaks whose respective beats correlated with the others significantly below a certain threshold. This new function eliminated erroneous detections of R peaks.

After identifying the true R peaks at each signal, it was necessary to determine the frames wanted from each interval of two consecutive R peaks (RR interval). At this point, the best choice was to allow the user to specify the percentage of the RR interval that should be employed. Nevertheless, to test the built program, it was assumed that the value recorded in the CTCA metadata would be used, and this step was not considered.

Through observation, it was concluded that sometimes there could be relevant images that were not considered because immediately before starting or after finishing the acquisition, R peaks could occur that were not recorded in the ECG signal. Thus, there was a need to readjust the algorithm, and it was realised that by averaging the number of samples corresponding to the detected RR intervals, it would be possible to extrapolate the relative position where the R peak should be located. This way, it could be checked whether more frames from the beginning and the end of the signal could be utilised.

Once the temporal locations of the frames to be analysed have been identified in the ECG, there is a need to perform a conversion to the corresponding image. This conversion is required because there is a discrepancy between the acquisition rate of the cardiac signal contained in the metadata of the CA images and the images themselves.

4.4.2 Coronary Angiography Image Enhancement

After analysing the ECG signal, identifying the relevant temporal locations, and converting these into corresponding images, one can proceed to the actual image processing. Normally, the initial step is to strive to improve the quality of the structure being analysed.

This work aims for a better distinction between the coronary arteries and the adjacent physiological tissues. Although contrast is injected directly into these vessels during CA, there is not always a sufficiently contrasted image to ensure good segmentation. Moreover, because of the narrow diameters of the arteries, particularly at their extremities, they also exhibit reduced contrast towards those ends. Consequently, it becomes crucial to strive for enhancement of the intensity disparities between the arteries and the surrounding tissues.

Prior to any efforts to enhance the image quality, it was observed that there were anatomical structures in the images that might potentially result in misidentification errors, especially evident in the images where the contrasted vessels were not visible. Since when trying to enhance details of the coronary arteries, the background information will also be highlighted, it then became apparent that these structures needed to be removed. Therefore, the first frame of each sequence was registered in every frame of that sequence, in order to align the background structures, and then a subtraction between the

registered frame and each frame took place.

After that, the effects of decreasing and increasing brightness, contrast, and gamma in different orders were tested to encompass all possible combinations of those adjustments. Another method of global image manipulation that was tested was histogram equalisation.

Moreover, considering that general modifications normally do not yield such good outcomes, it was decided to further explore local image manipulation approaches. For this strategy, a technique known as Contrast-Limited Adaptive Histogram Equalisation (CLAHE) was utilised, and an Edge-Aware Local Contrast Manipulation (EALCM) of images was also tested. The EALCM approach enhances or reduces local contrast while maintaining crucial edge features. This guarantees that the details in the image are highlighted or smoothed without damaging the strong edges, preserving the image's overall structure and clarity.

4.4.3 Segmentation in Coronary Angiography Images

4.4.3.1 Thresholding Method

For the thresholding approach, it is necessary to choose the threshold value, and since the region of interest, in this case, is a darker portion of the image, there is a need to search for lower values than that chosen threshold. Although the manual selection of the value was tested, it was realised that it was not a good option because the intention was for the program to work for any individual. Thus, the use of Otsu's method, which is widely used in image segmentation because it automatically selects the threshold value based on the histogram information of the image, was tested.

4.4.3.2 Region-Based Method

Region-based segmentation emerged as an endeavour to replicate the human visual perception. When looking at CA images, one can see the whole range of the arteries because the darker portion is continuous. The goal was to use this continuity to segment the coronary arteries.

Variations of region growing algorithms were tested by comparing the intensity of each pixel to either the initial seed intensity or the average intensity values of the already-grown region. Nevertheless, the images may exhibit an unequal distribution of lighter and darker areas. Therefore, it was necessary to compare each pixel with the average intensity values of the pixels in the close neighbourhood that are in the previously developed region.

4.4.3.3 Multi-scale Vessel Enhancement Filtering

Lastly, the Frangi Vesselness Filter [76], an algorithm for recognising tubular structures in 2D images or 3D volumes, was tested. Frangi's approach starts by computing the Hessian Matrix. For a given image (I), the Hessian matrix (H) at a point (x) and scale (σ) is defined by the Equation 4.3, where each one of the terms is the second-order partial derivatives of

the image (I) smoothed by a Gaussian kernel with standard deviation (σ).

$$H(x, \sigma) = \begin{bmatrix} \frac{\partial^2 I(x, \sigma)}{\partial x^2} & \frac{\partial^2 I(x, \sigma)}{\partial x \partial y} \\ \frac{\partial^2 I(x, \sigma)}{\partial y \partial x} & \frac{\partial^2 I(x, \sigma)}{\partial y^2} \end{bmatrix} \quad (4.3)$$

Then, the eigenvalues (λ_1 and λ_2) are computed and analysed. For blob-like structures, have $\lambda_1 \approx \lambda_2$, whereas for tubular structures $\lambda_1 \ll \lambda_2$. Therefore, two different metrics, represented in Equations 4.4 and 4.5, are defined to enable vessel detection. The R_B helps the algorithm to discriminate between blob-like or plate-like structures and the tubular structures, while the S metric is the Frobenius norm of the Hessian matrix, which enhances vesselness measure by reducing the influence of noise.

$$R_B = \frac{|\lambda_1|}{|\lambda_2|} \quad (4.4)$$

$$S = \sqrt{\lambda_1^2 + \lambda_2^2} \quad (4.5)$$

The vesselness measure ($V(x, \sigma)$) at scale (σ) is then calculated as described in Equation 4.6, where β and c are parameters that control the filter sensitivity to the metrics R_B and S , respectively.

$$V(x, \sigma) = \begin{cases} 0 & \text{if } \lambda_2 > 0 \\ e^{-\frac{R_B^2}{2\beta^2}} \cdot \left(1 - e^{-\frac{S^2}{2c^2}}\right) & \text{otherwise} \end{cases} \quad (4.6)$$

In order to enhance vessels with different diameters, the filter must be applied at multiple scales (σ) and the final response is computed as the maximum response over all scales, like in Equation 4.7.

$$V(x) = \max_{\sigma_{\min} \leq \sigma \leq \sigma_{\max}} V(x, \sigma) \quad (4.7)$$

Based on the presented method and the function introduced by Dirk-Jan Kroon [77], a new function was developed to identify the dark tubular structures in the two-dimensional CA images. This function received as arguments σ values to be used in the Hessian and two constants (β and c). Normally, the first one tends to have values lower than one, and the other one tends to have higher values, such as ten or fifteen. At this point, a search for better parameters was also conducted, in order to improve the performance of the created algorithm. Specifically, β , c , and σ were tested with values ranging respectively from 0.01 to 1, 5 to 20, and 1 to 6.

4.4.4 Computed Tomography Coronary Angiography Image Enhancement

Although the nature of coronary angiography images and computed tomography angiography images is different, there is also contrast in the blood vessels in CTCA images. However, contrary to what is observed in CA images, in this type of image, the blood vessels take on lighter tone colours. Even so, it is equally important to enhance the contrast between the coronary arteries and the other tissues. For this purpose, a technique known

as windowing was employed, which involves adjusting the window level and window width to modify the contrast and brightness of the image. For each individual, there were two different sets of values in the metadata of the CTCA images, and they were both tested. Firstly, it was performed a conversion on the pixel values to transform them into Housfield units, as described by Equation 4.8, where the *RescaleSlope* and *RescaleIntercept* were attained in CTCA images metadata. Then the minimum and maximum value of the window were determined as described in Equation 4.9, using the *WindowLevel* and *WindowWidth* from metadata. In order to remove all the values that might be lower than the *minValue* or higher than *maxValue*, an additional step was taken, which is presented in Equation 4.10. Finally, all the image was normalised using the Equation 4.11.

$$pixel_{HU} = RescaleSlope \times pixel_{value} + RescaleIntercept \quad (4.8)$$

$$\begin{aligned} minValue &= WindowLevel - \frac{WindowWidth}{2} \\ maxValue &= WindowLevel + \frac{WindowWidth}{2} \end{aligned} \quad (4.9)$$

$$\begin{aligned} Image(Image < minValue) &= minValue \\ Image(Image > maxValue) &= maxValue \end{aligned} \quad (4.10)$$

$$ImageNormalized = \frac{Image - minValue}{maxValue - minValue} \quad (4.11)$$

4.4.5 Segmentation in Computed Tomography Coronary Angiography Images

Similar to the procedure used in the segmentation of coronary arteries in CA images, thresholding techniques were also applied in these images to remove the darker areas, along with the Frangi Vesselness filter algorithm in the 3D volume to identify the lighter tubular structures.

RESULTS AND DISCUSSION

This chapter presents the main results obtained, along with the analysis and discussion of said results. As in this work data from 16 different individuals were considered and a lot of images had to be presented, it was chosen to present only the results from three of them in the CA analysis, where the images were more different from individual to individual, and the results of one of the individuals in the case of the CTCA analysis, where the images are very similar. Hence, for CA analysis the first projection of individual 1, the second from individual 2 and the eighth from individual 10 were shown, while only the images from individual 1 were presented in the CTCA analysis.

5.1 Electrocardiogram Signal Processing

Firstly, when analysing the ECG signal contained in the CA metadata, the R peaks had to be identified. After the third second of ECG signal represented in Figure 5.1a, it can be seen an aberrant cardiac tracing portion, which initially was wrongly identified as an R peak (as it can be seen in Figure A.1). To remove the wrong R peaks detected, caused by some abnormal high amplitude events, a rectification was made to the algorithm by comparing all the heartbeat formats detected and removing those that seem different. The final result of R peak detection after the correction can be seen in Figure 5.1.

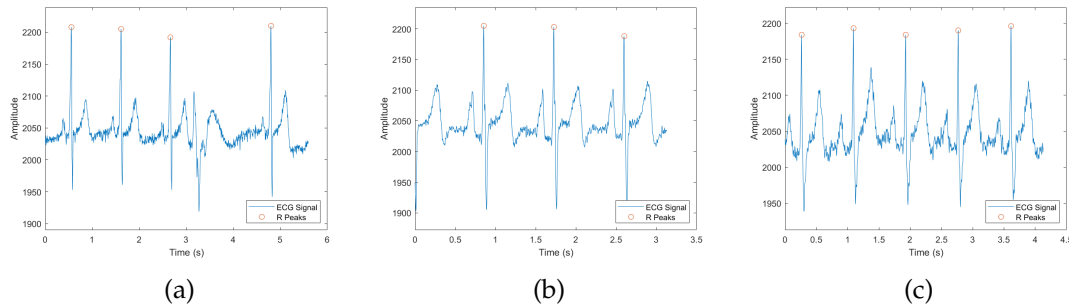


Figure 5.1: Final result, after correction, of R peaks detection algorithm in different CA projections. (a) First projection of individual 1; (b) Second projection of individual 2; (c) Eighth projection of individual 10.

When the R peaks detection was satisfactory, it was necessary to identify the frames that were in the same moment of the cardiac cycle as the one annotated in the CTCA metadata. Then that proportion of each RR interval was assigned with a vertical line. Firstly, it was found that at the beginning and at the end of the ECG signal, there could be considered more images that were in the same moment of the cardiac cycle (reported in Figure A.2). Therefore, a correction was made where that possibility was verified, and as described in the previous chapter, an average of the samples corresponding to the RR interval proportion was considered to extrapolate the location of the extra frames.

In Figure 5.2 can be noted that an extra initial frame was considered in each projection after the readjustment. Thus, it led to a more robust algorithm, since it enabled the analysis of more images in each projection.

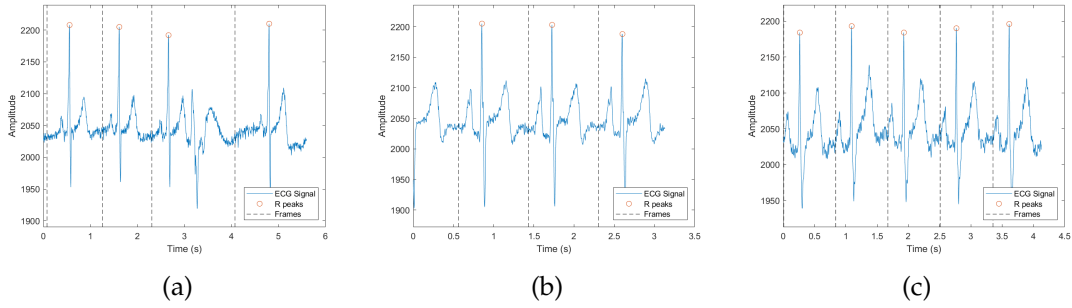


Figure 5.2: Final identification, after correction, of the optimal frames of projections to further consider in the CA image analysis. (a) First projection of individual 1; (b) Second projection of individual 2; (c) Eighth projection of individual 10.

Finally, after all the relevant frames were located in the ECG signal, those could be converted into the images properly said. In Figure 5.3, Figure 5.4 and Figure 5.5 are presented the frames that were selected at this stage.

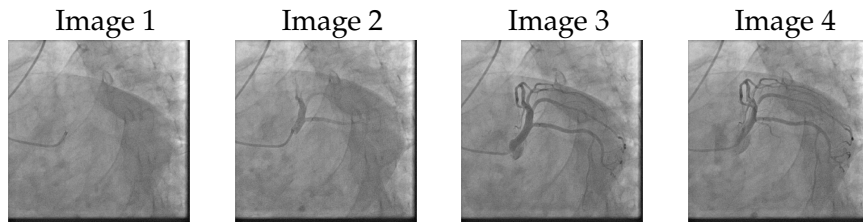


Figure 5.3: All frames selected from first CA projection of individual 1.

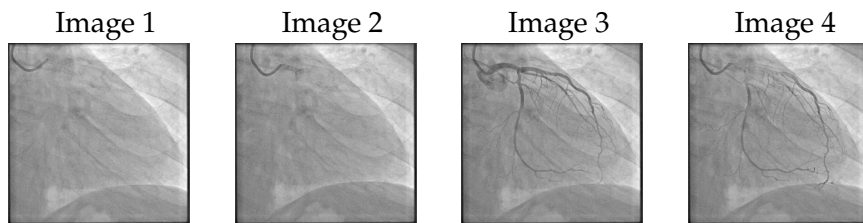


Figure 5.4: All frames selected from second CA projection of individual 2.

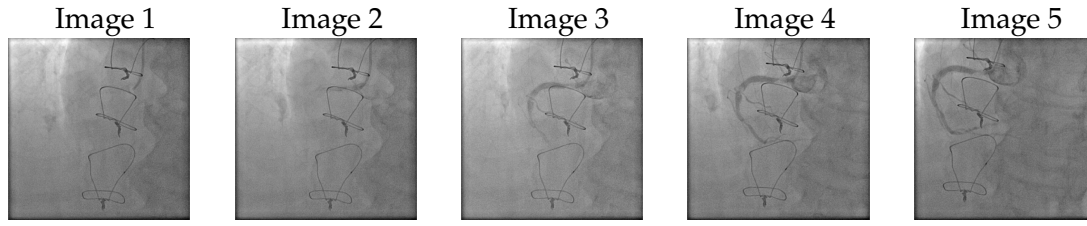


Figure 5.5: All frames selected from eighth CA projection of individual 10.

5.2 Coronary Angiography Image Enhancement

After visualising all the frames chosen, it was observed that images from different individuals have different particularities. The images from individual 1 revealed a darker region in the arterial ends, the frames from individual 2 displayed lighter regions than the others and individual 10 had sternotomy wires that appeared in a similar pixel intensity as the arteries if not lower.

Besides that, it was observed that in the first frames, where there are no coronary arteries evidenced, some other structures appear to be dark and seem to be tubular, similar to the characteristics of the tissues of interest. These structures might cause segmentation problems and so, they need to somehow be eliminated. To do so, the first frame of each sequence of images was registered in every frame of that sequence, and then the registered images were subtracted from the corresponding frames. The result is shown in Figures 5.6- 5.8.

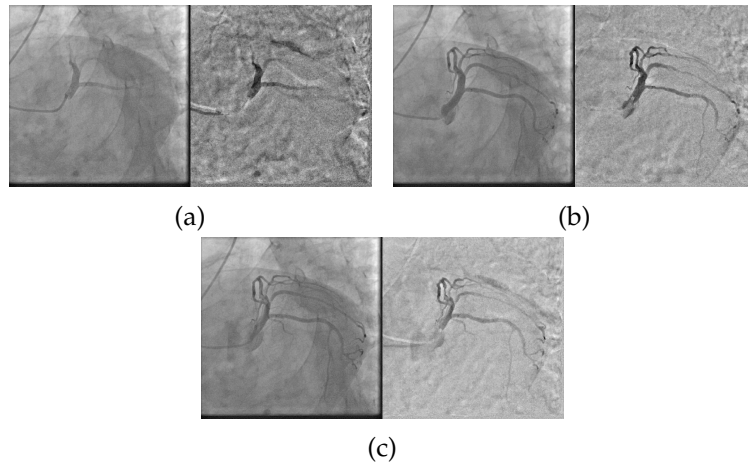


Figure 5.6: CA images prior and after removing a registered version of the first frame, for the first projection of individual 1. (a) Image 2; (b) Image 3; (c) Image 4.

Despite conducting an exhaustive search to choose the parameters that allowed for the best non-rigid registration, it was noticed that although some background details of the image were indeed eliminated, the registration was not perfect for all images. This was confirmed by analysing Figure 5.6 and Figure 5.7, in which some background details present in the images without the contrasted vessels had been removed. However, even

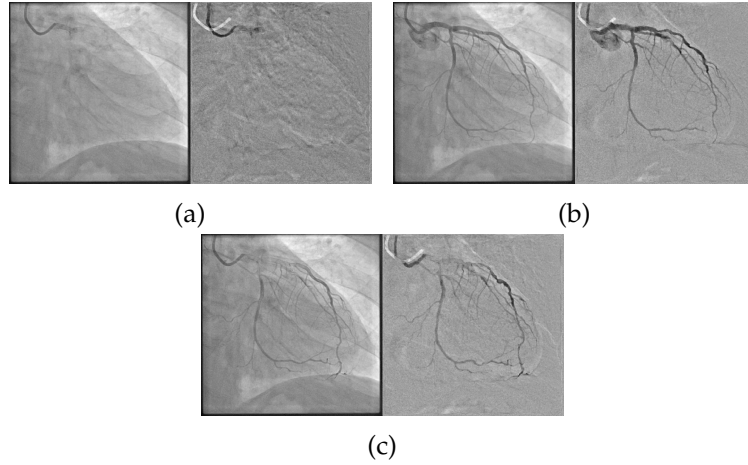


Figure 5.7: CA images prior and after removing a registered version of the first frame, for the second projection of individual 2. (a) Image 2; (b) Image 3; (c) Image 4.

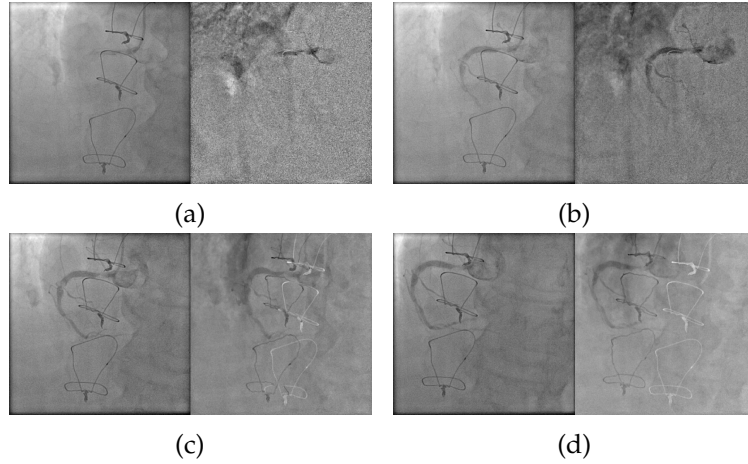


Figure 5.8: CA images prior and after removing a registered version of the first frame, for the eighth projection of individual 10. (a) Image 2; (b) Image 3; (c) Image 4; (d) Image 5.

in these images where the registration seems to have been successful, the catheter is still noticeable. This means that, while this strategy may be effective for preventing the detection of objects outside the coronary arteries, the values to be used as parameters depend from individual to individual and, potentially, even from image to image.

The differences between images of the same individual are noteworthy in Figure 5.8, as images 2 and 3 indicate that the registration was successful, as the subtraction has eliminated the metallic structures that were visible in the image. However, in the remaining two images, the algorithm did not yield the same result, as these images, when compared to the first frame, have more pixels between the identical structures than those considered as parameters during the exhaustive search.

It was decided not to proceed with these images, as no parameters were found to allow for acceptable non-rigid registration in all cases and, consequently, effective subtraction.

After unsuccessfully attempting to remove the background structures from the selected

frames, standard image quality manipulations were tested. Although all the images of each individual were examined, from this point onward, only the frames that clearly show the arteries will be presented. These include the second, third, and fourth frames of individual 1, the third and fourth frames of individual 2, and the third, fourth, and fifth frames of individual 10, as only these yielded relevant results for the development of this work.

Individual modifications to the image's brightness, contrast, and gamma were performed. Through visual examination, the optimal outcomes from each single modification were identified as follows: a 20% decrease in brightness, a 40% increase in contrast, and a gamma value of 2. The best results are reported in Figures 5.9, 5.10 and 5.11 (Figures B.1 to B.9 report all the values tested for each single modification).

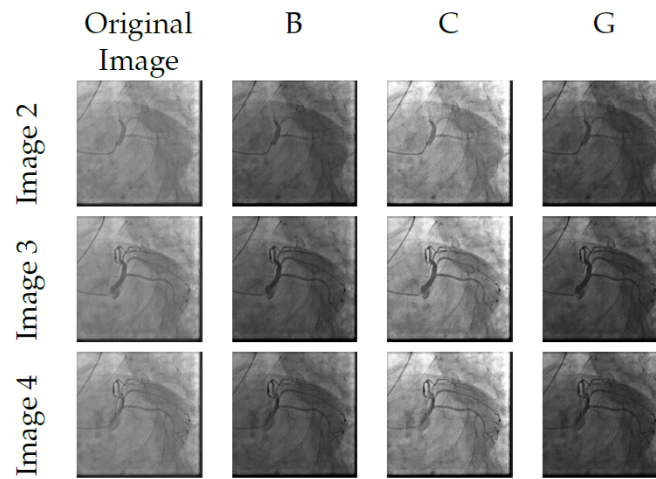


Figure 5.9: Best results of performing single manipulations in the first CA projection of individual 1. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.

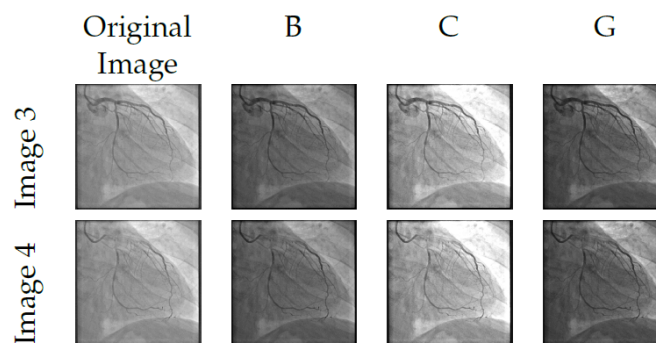


Figure 5.10: Best results of performing single manipulations in the second CA projection of individual 2. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.

Given their performance, these specific single modifications were selected for testing sequences of two global image adjustments as the initial manipulation. The most favourable results were achieved when: 20% decrease in brightness, and 45% increase in contrast; 20% decrease in brightness, and gamma value of 1.5; 40% increase in contrast,

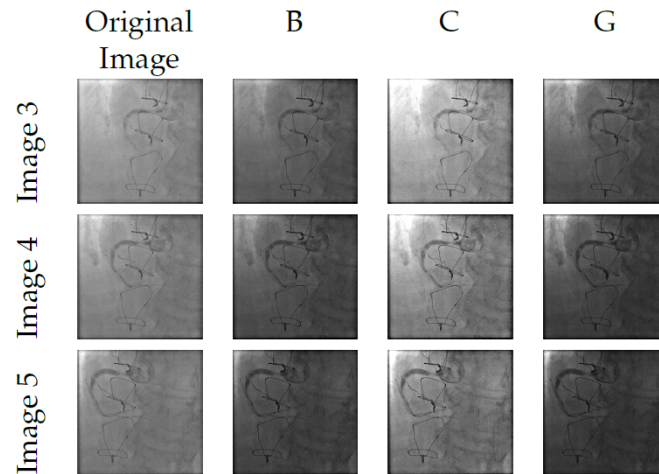


Figure 5.11: Best results of performing single manipulations in the eighth CA projection of individual 10. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.

and 30% decrease in brightness; 40% increase in contrast, and gamma value of 2; gamma value of 2, and 10% decrease in brightness; gamma value of 2, and 15% increase in contrast.

In Figures 5.12 to 5.14, the best results of two sequential manipulations can be seen (images from the detailed study are reported in Figures B.10 to B.27).

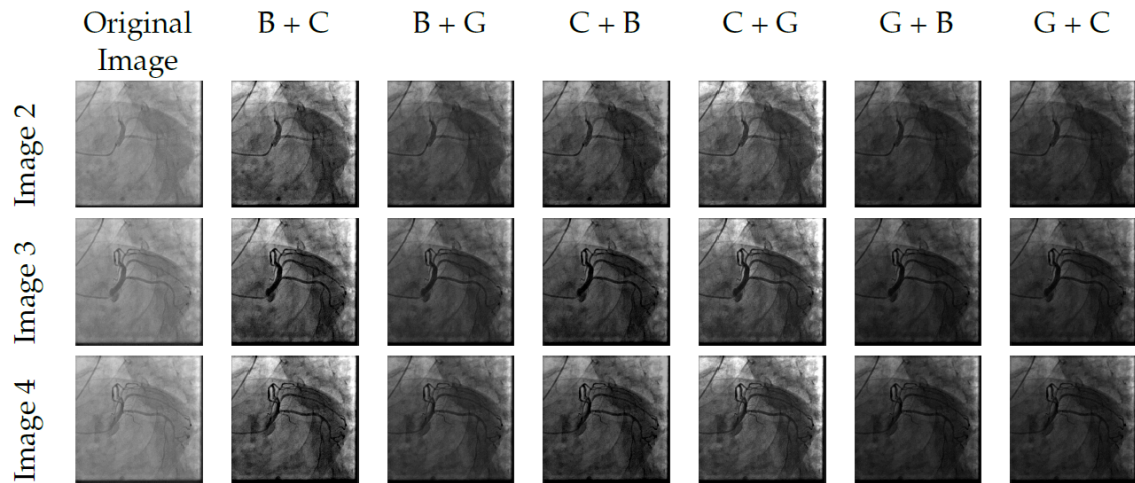


Figure 5.12: Best results of performing two sequential manipulations in the first CA projection of individual 1. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.

Similar to the previous analysis, these served as the first two manipulations in combinations of three manipulations (the detailed results are presented in Figures B.28 to B.45). Through visual assessment, the best sequences were determined to be: 20% decrease in brightness, gamma value of 1.5, and 15% increase in contrast or gamma value of 2, 15% increase in contrast, and 10% decrease in brightness.

As in some cases it was observed that it would be preferable to retain the image

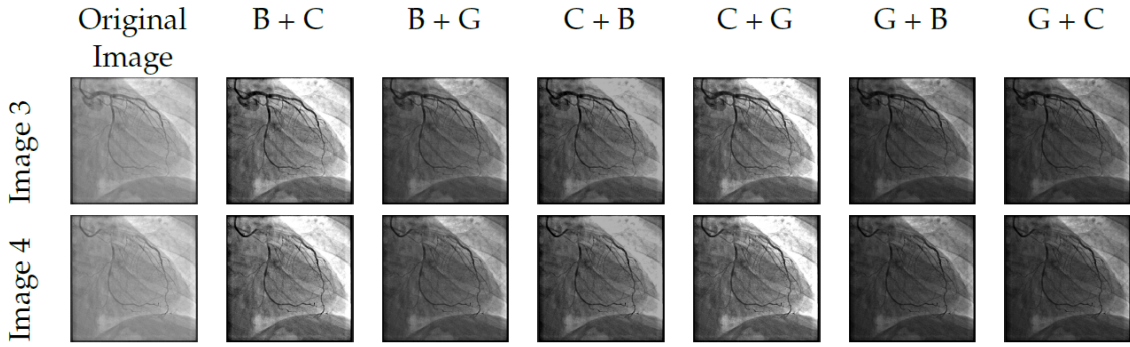


Figure 5.13: Best results of performing two sequential manipulations in the second CA projection of individual 2. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.

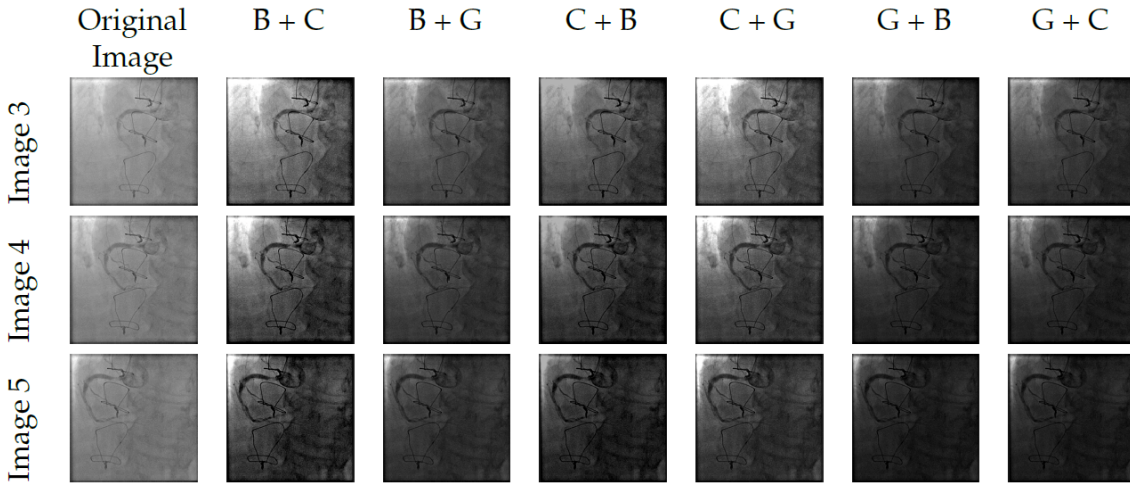


Figure 5.14: Best results of performing two sequential manipulations in the eighth CA projection of individual 10. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.

obtained before adding the third manipulation, those combinations were not included in Figures 5.15, 5.16, and 5.17, where only the best results from the complete sequences of three modifications are presented.

Upon analysing the Figures 5.9 to 5.17, it was observed that for brighter images, such as those of individual 2, image enhancement was easier to perform as the arteries are already well contrasted. Since the arteries of individuals 1 and 10 are less distinguishable in the original images, this task was more complex and in some cases, the image turned out too dark to allow sufficient discrimination between the arteries and the background.

Although some combinations did help to enhance the contrast between the coronary arteries and the surrounding tissues, it can be said that the performance of these global adjustments was not satisfactory.

Continuing with global image manipulations, the histogram equalisation was performed on each frame. The resulting images from this step are presented in the second column of Figures 5.18- 5.20. It can be seen that the histogram equalisation did not perform

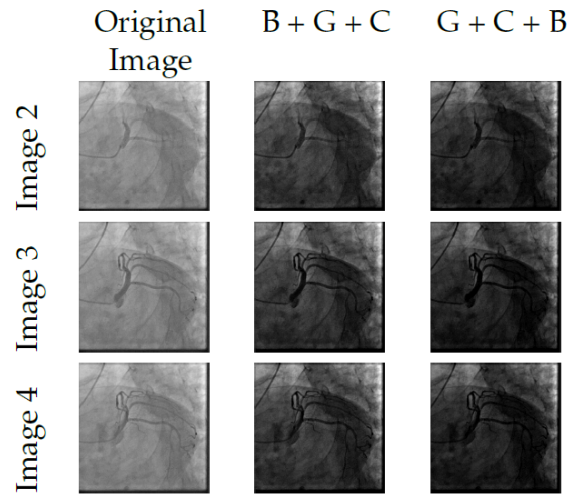


Figure 5.15: Best results of performing three sequential manipulations in the first CA projection of individual 1. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.

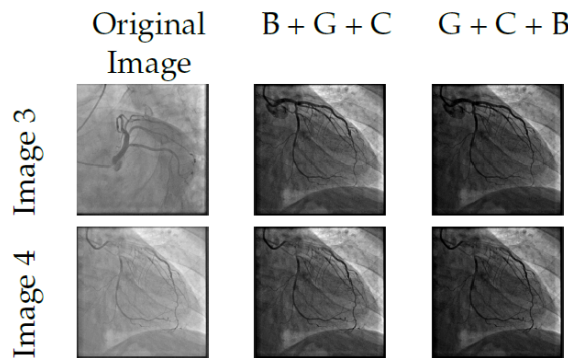


Figure 5.16: Best results of performing three sequential manipulations in the second CA projection of individual 2. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.

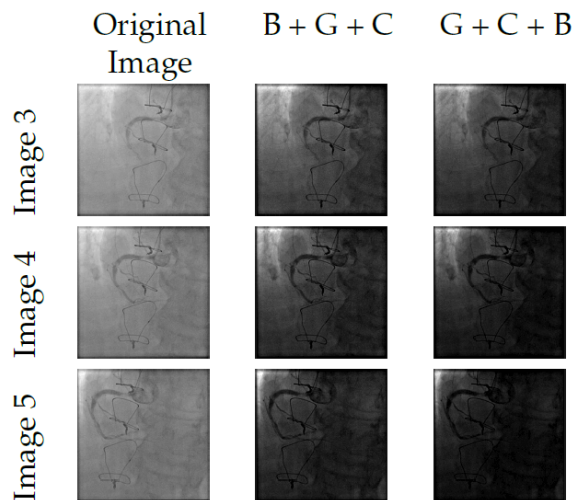


Figure 5.17: Best results of performing three sequential manipulations in the eighth CA projection of individual 10. B: Brightness adjustments; C: Contrast adjustments; G: Gamma adjustments.

well, since it operates globally and attempts to improve contrast uniformly. Given that the images have a non-homogeneous distribution of contrast, the outcome was less than ideal.

Given the expectation that the outcomes of the global manipulations could be sub-optimal, the CLAHE technique was employed and an EALCM was tested, yielding the outcomes illustrated in the third and fourth columns, respectively, of Figures 5.18 to 5.20.

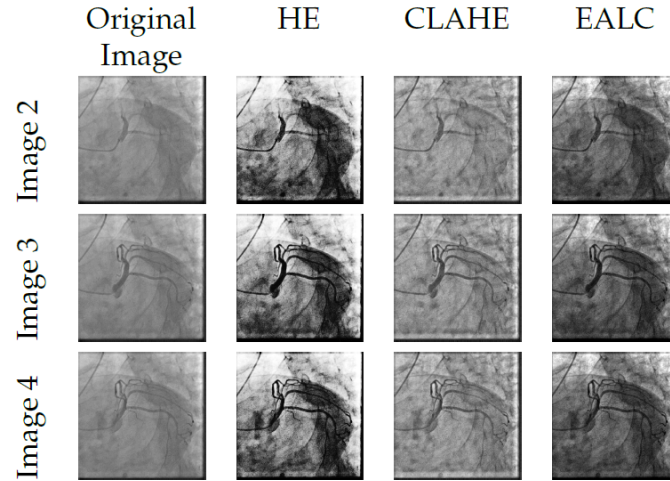


Figure 5.18: Results of performing Histogram Equalisation (HE), Contrast-Limited Adaptive Histogram Equalisation (CLAHE) and Edge-Aware Local Contrast Manipulation (EALCM) in the images from first CA projection of individual 1.

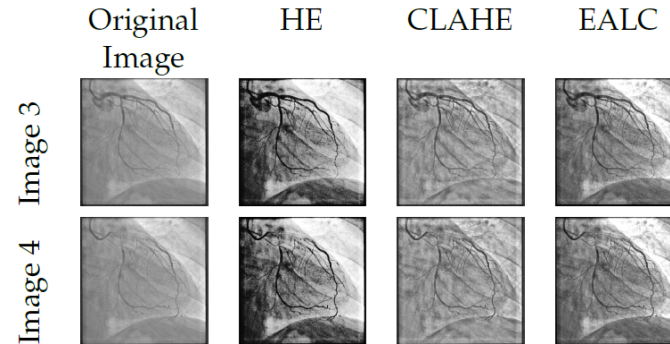


Figure 5.19: Results of performing Histogram Equalisation (HE), Contrast-Limited Adaptive Histogram Equalisation (CLAHE) and Edge-Aware Local Contrast Manipulation (EALCM) in the images from second CA projection of individual 2.

Upon examining all the images acquired after executing the various global and local manipulations, it was evident that, overall, the global manipulations exhibited inferior performance. This fact can be explained by the discrepancy in intensity in the image's various regions, which are all addressed in the same way. The manual global modifications showed a tendency to result in darker images, which led to poor discrimination between the arteries and the other structures. In the case of global histogram equalisation, a new distribution of pixel intensities is enforced in order to improve previously indistinguishable

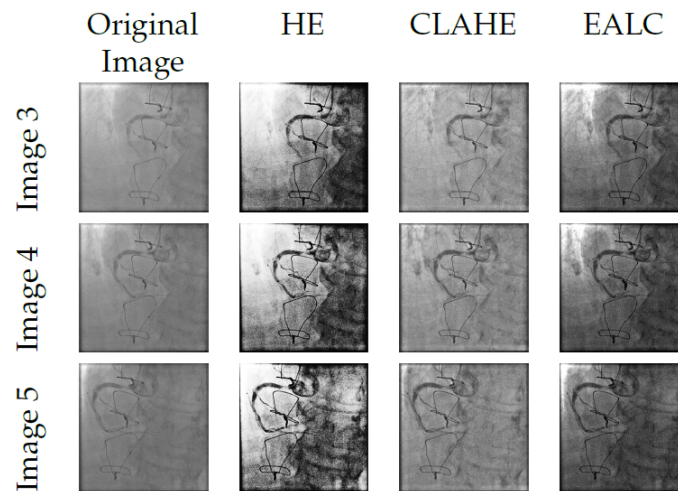


Figure 5.20: Results of performing Histogram Equalisation (HE), Contrast-Limited Adaptive Histogram Equalisation (CLAHE) and Edge-Aware Local Contrast Manipulation (EALCM) in the images from eighth CA projection of individual 10.

features, regardless of whether they are from the region of interest. This brought out features in the surroundings that were meant to be subtle.

On the other hand, the results obtained in the local image enhancing steps seem to have been more fruitful, in the sense that the arteries stand out without overly emphasising the details of the background. The ultimate best outcome was considered to be the application of EALCM.

5.3 Coronary Angiography Image Segmentation

The accurate segmentation of the coronary arteries is perhaps the most crucial component of this work, as artificial intelligence algorithms are increasingly used to find the best segmentation solution in medical imaging. Since the use of such algorithms is beyond the scope of this work, due to the lack of a large amount of annotated data, what was sought to find was a segmentation solution following classical approaches. This point forward the original images remote to the ones that were previously enhanced by the EALCM.

5.3.1 Thresholding Method

The first segmentation method tested was thresholding. This technique involves selecting an optimal threshold value to which the intensity value of each pixel is compared. Thus, various values were tested in order to determine the one that could give better outcomes. By analysing Figures 5.21 5.22, and 5.23, it was possible to see that each individual or each image needed a different threshold value. For individual 1, values between 0.2 and 0.3 seem to be the ones that offer better segmentation. While, for individual 2, the optimal threshold might be close to 0.4, and the optimal value for individual 10 may be between 0.3 and 0.4.

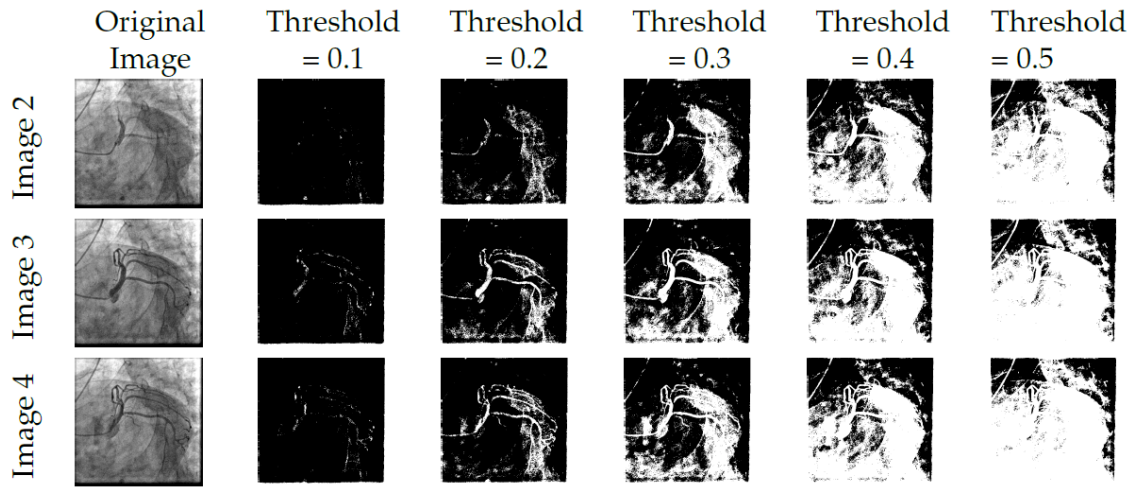


Figure 5.21: Results of the thresholding method with different threshold values on the first CA projection of individual 1.

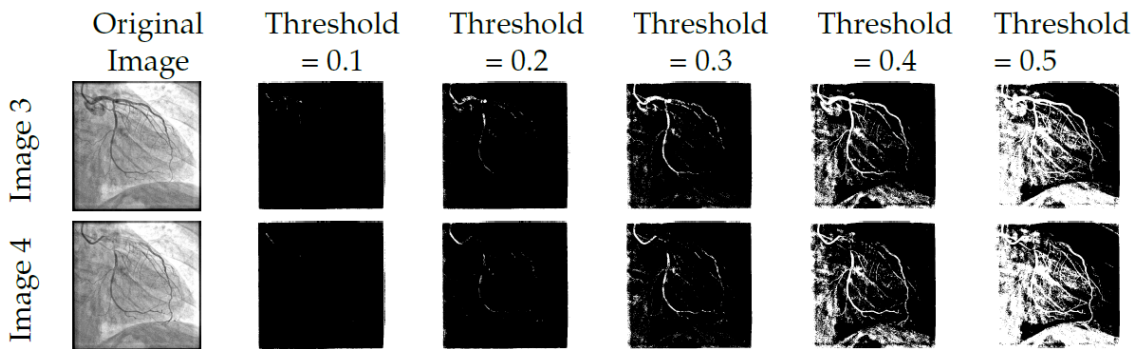


Figure 5.22: Results of the thresholding method with different threshold values on the second CA projection of individual 2.

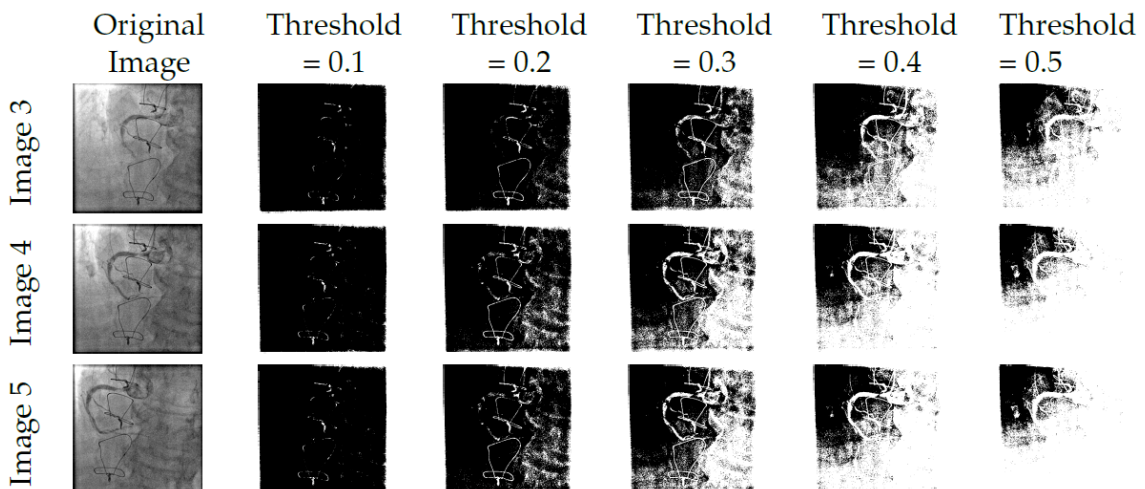


Figure 5.23: Results of the thresholding method with different threshold values on the eighth CA projection of individual 10.

Since the aim of this work is to provide an automatic segmentation solution, manually selecting the optimal threshold value would not be effective. Therefore, the use of the Otsu's method was tested. However, as shown in Figures 5.24, 5.25, and 5.26, the threshold that minimises the intra-class variance of the background and foreground intensities does not effectively isolate the arteries.

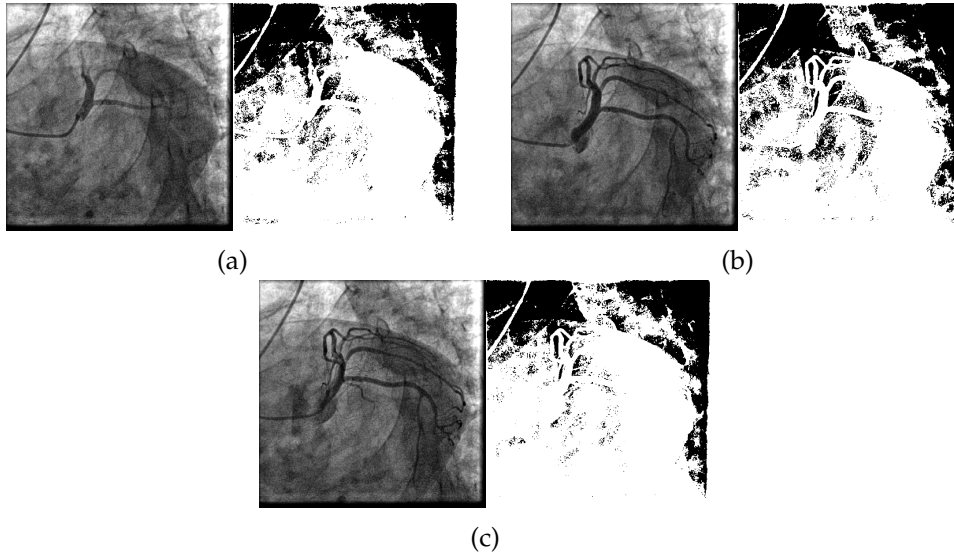


Figure 5.24: Results of Otsu's method on (a) Image 2, (b) Image 3, and (c) Image 4 of the first CA projection of individual 1.

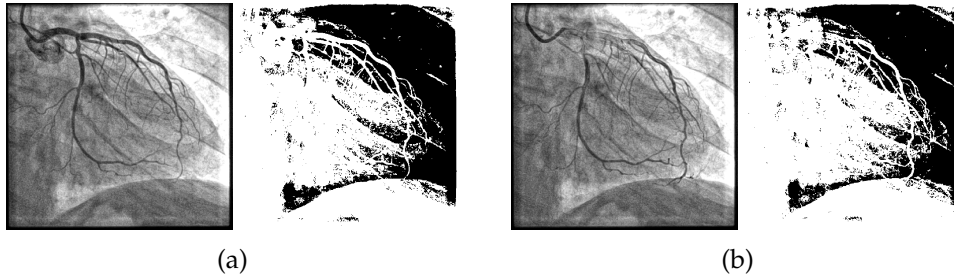


Figure 5.25: Results of Otsu's method on (a) Image 3, and (b) Image 4 of the second CA projection of individual 2.

In both the manual thresholding method and the automatic method using Otsu, the segmentation results were obtained extremely quickly, taking less than a second per image. However, it was evident that both algorithms demonstrate poor performance.

The poor performance of these methods can be attributed to the variation in the global intensity of the image in different regions. Once the background was not uniformly clearer than the arteries, it became difficult to separate them from their surroundings. This problem was particularly relevant in cases like those presented in Figures 5.24 and 5.25, where the darker background region coincides with areas where the arteries are located, resulting in over-segmentation of that region.

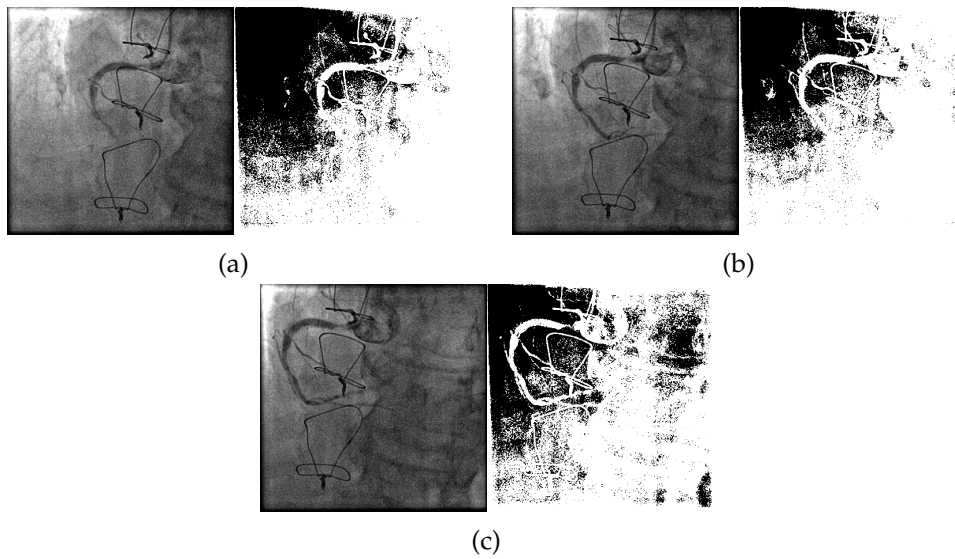


Figure 5.26: Results of Otsu's method on (a) Image 3, (b) Image 4, and (c) Image 5 of the eighth CA projection of individual 10.

5.3.2 Region-Based Method

As described in the previous chapter, three variations of the region growth algorithm were considered. In the first method, the decision to include each pixel in the region depended on a comparison of its intensity with that of the seed pixel. For the second method, the comparison was made with the average intensity values of the previously grown region rather than the original seed intensity. Finally, the third method, a local version of the previous one, involved comparing each pixel's intensity with the average intensity of the adjacent neighbours that were already part of the grown region.

When analysing Figures 5.27 to 5.29, it was evident that the first approach results in less growth of the regions overall, achieving partial segmentation without incorrectly segmenting the background (except for the image in the third column of the first row of Figure 5.29). When considering the results of the second approach, it could be understood that it was more successful than the first, as the grown regions were generally larger than the previous ones. However, despite representing a more robust technique, the third method did not yield such good results, as it continued to grow into the background after leaving the artery region by comparing intensities with the nearest neighbours. While it over-segmented for some individuals, it seemed to be the best approach for individual 10 in terms of region growing.

In general, these results demonstrated that due to the non-uniformity in the intensity of the artery and the possibility of having an image background with intensity comparable to that of the arteries, small changes in the evaluation formula or the threshold value used can alter the outcome. Furthermore, it is possible to notice that for individual 2, none of the three approaches seems to perform satisfactorily, even though the vessels appear to be well highlighted visually. Moreover, the region growing technique itself may not be

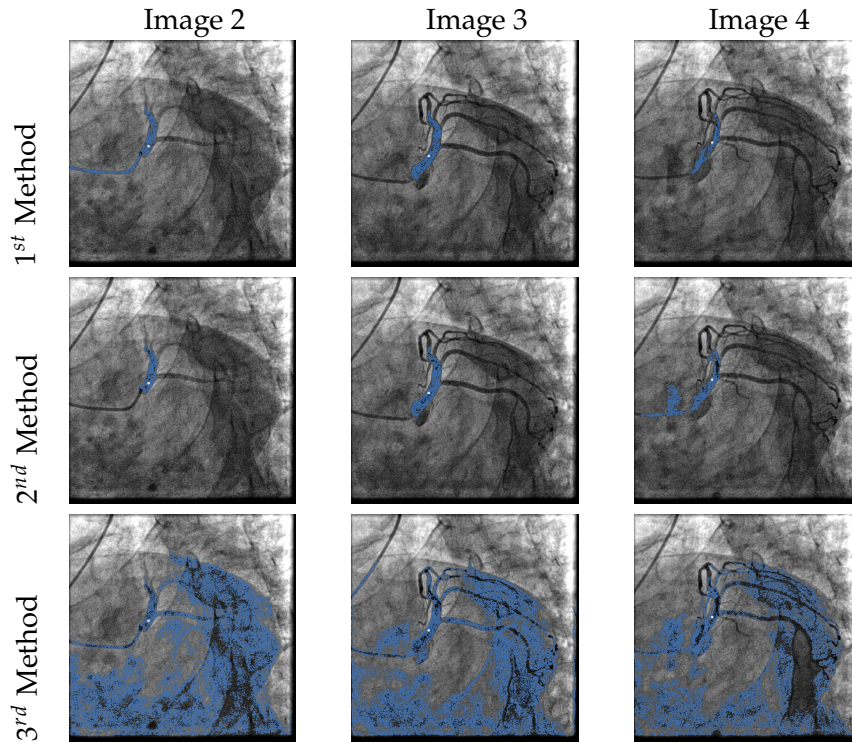


Figure 5.27: Results of the region growing algorithms on the first CA projection of individual 1, where the white dot marks the pixel used as a seed and the blue coloured portion is the region segmented.

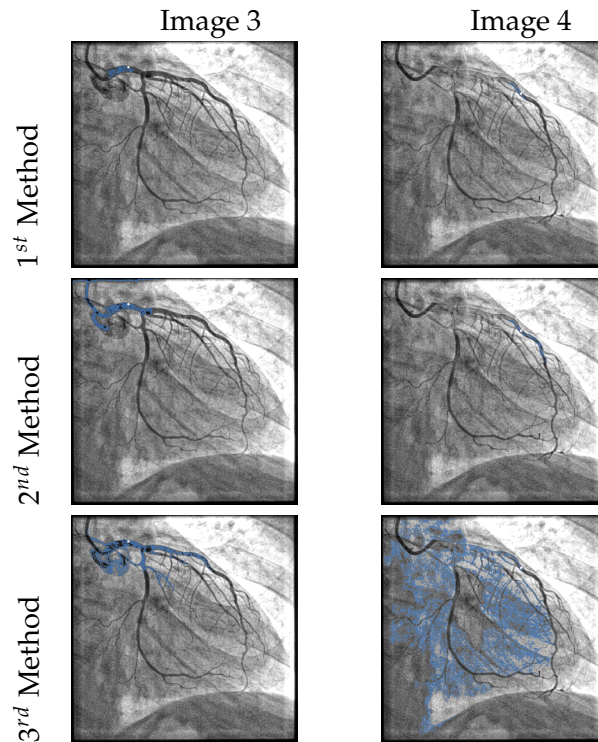


Figure 5.28: Results of the region growing algorithms on the second CA projection of individual 2, where the white dot marks the pixel used as a seed and the blue coloured portion is the region segmented.

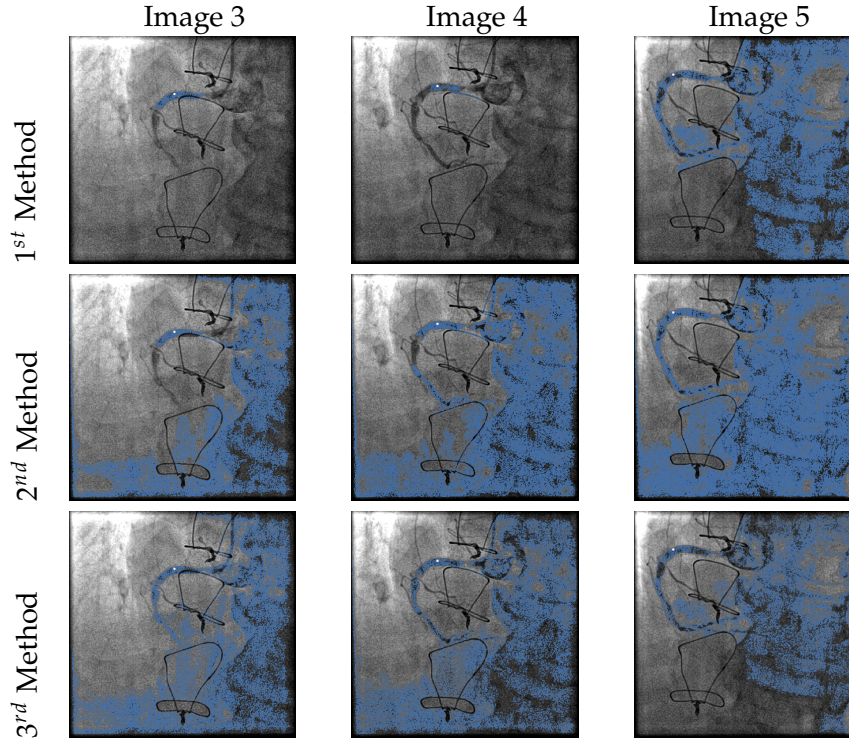


Figure 5.29: Results of the region growing algorithms on the eighth CA projection of individual 10, where the white dot marks the pixel used as a seed and the blue coloured portion is the region segmented.

the best choice for a program intended to be automatic, as it requires the determination of a seed for each frame.

5.3.3 Multi-scale Vessel Enhancement Filtering Method

The final segmentation method evaluated employed Frangi's approach [76]. As this technique searches for dark tubular structures, the arteries were identified, along with some other structures of the background that were misidentified. The function introduced by Dirk-Jan Kroon [77] was applied and the sigma values to use as parameters had to be chosen. Thus, those tests were conducted while considering β and c as 0.5 and 10, respectively. It was concluded that the best outcome was achieved while sigmas between 3 and 4 were used as parameters of the function (for more detailed analysis about the choice of sigma, Figures C.1 to C.3 reported the result of testing different sigma values).

After directly applying the function that described Frangi's approach, an intermediate step of this process took place, where some segmented regions were removed based on their characteristics, such as the area. This step eliminated some smaller segmented regions from the background that were wrongly segmented (in Figures C.4 to C.6, this modification was reported).

The final segmentation obtained by this method was reported in Figures 5.30 to 5.32. On those, it was possible to verify that by searching for dark tubular structures, almost every

portion of the coronary arteries was identified. Despite that, this method misidentified tubular structures in some portions of the background that could not be removed in the intermediate step because they had similar attributes as some portions of the arteries themselves. It is also noticeable that for individual 10, the sternotomy wires were also segmented since they are in fact dark tubular structures in the coronary images.

Overall, when comparing all the segmentation results obtained, those provided by this method seemed to be the best. For future research work, it could be useful to test if an algorithm that combined both region growing and multi-scale vessel enhancement filtering methods would provide better results, as it would join the two key factors of visual perception of the arteries: the identification of the dark tubular structures and the evaluating of their continuity.

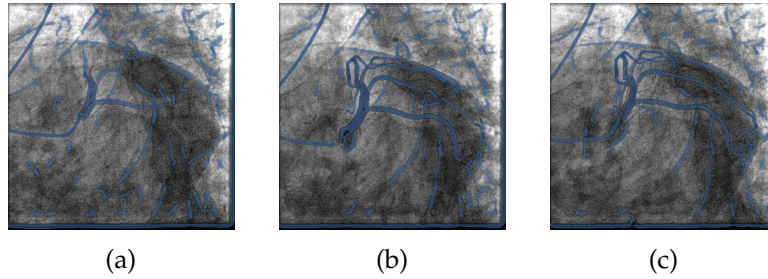


Figure 5.30: Final results of the multi-scale vessel enhancement filtering method on (a) Image 2, (b) Image 3, and (c) Image 4 of the first CA projection of individual 1, where the blue colored region corresponds to what was segmented.

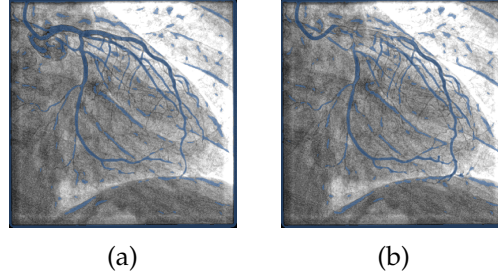


Figure 5.31: Final results of the multi-scale vessel enhancement filtering method on (a) Image 3 and (b) Image 4 of the second CA projection of individual 2, where the blue colored region corresponds to what was segmented.

5.4 Computed Tomography Coronary Angiography Image Enhancement

Improving image quality to enhance the coronary arteries is equally important in both CTCA and CA. The results of applying the Windowing technique are illustrated in Figure 5.33, which shows the outcomes of windowing with two different sets of *WindowLevel* and *WindowWidth* values, as recorded in the images' metadata. From Figure 5.33, it can

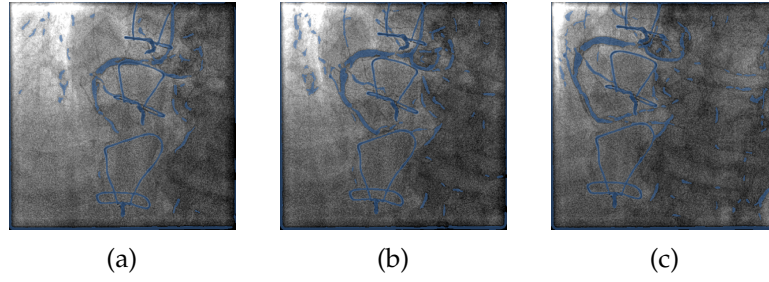


Figure 5.32: Final results of the multi-scale vessel enhancement filtering method on (a) Image 3, (b) Image 4, and (c) Image 5 of the eighth CA projection of individual 10, where the blue colored region corresponds to what was segmented.

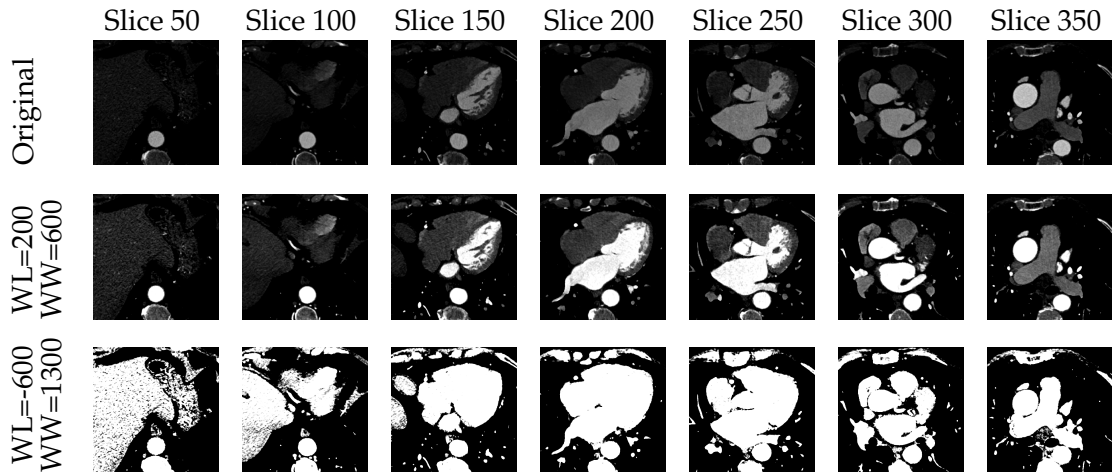


Figure 5.33: Results of windowing performance on the some CTCA slices of individual 1. WL: *WindowLevel*; WW: *WindowWidth*.

be observed that when considering $WindowLevel = 200$ and $WindowWidth = 600$, the best result was achieved, as the arteries appeared lighter than in the original image. In the second set of values used for windowing, it was evident that all structures, whether arteries or not, were highlighted, which complicated the segmentation process. Since segmenting the arteries required using a volume to search for tubular shapes, it was also necessary to visualise the results in their 3D form. The 3D models are presented in Figure 5.34.

5.5 Computed Tomography Coronary Angiography Image Segmentation

Using the 3D CTCA model shown in Figure 5.34b, the Frangi filter was applied and the resulting model is shown in Figure 5.35. The image from Figure 5.35a showed only the tubular structures enhanced but were still present some darker portions. To remove those, a simple threshold was applied and the result of that was shown in Figures 5.35b and 5.35c. These two models have the arteries segmentated in black, but they have more tubular

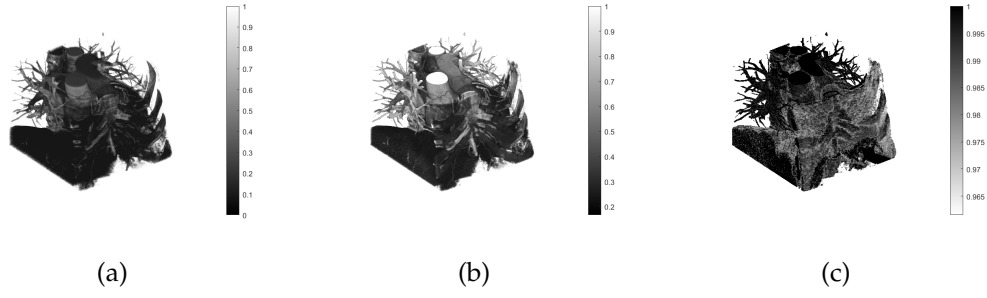


Figure 5.34: 3D CTCA models from individual 1 considering (a) Original slices, (b) Slices after windowing process with $WindowLevel = 200$ and $WindowWidth = 600$, and (c) Slices after windowing process with $WindowLevel = -600$ and $WindowWidth = 1300$.

structures segmented than only the coronary arteries. For future research work, the used technique should be improved or some other segmentation methods should be tested.

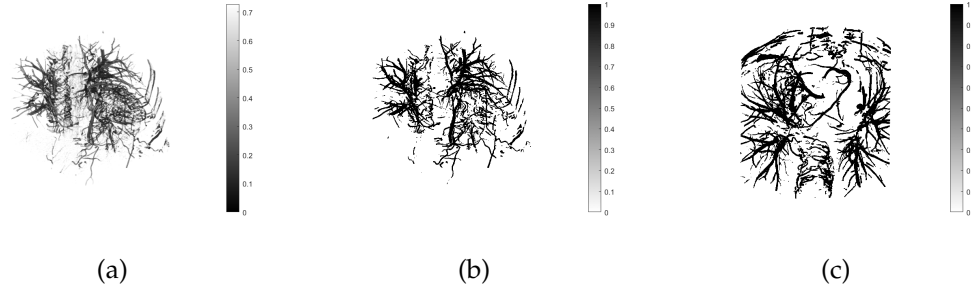


Figure 5.35: 3D CTCA models from individual 1 (a) after applying the Frangi filter, (b) after applying the Frangi Filter and followed by thresholding, and (c) after applying the Frangi Filter and followed by thresholding, with an appropriate rotation to better visualise internal arteries.

CONCLUSION

This chapter presents the main results of this work, which contribute significantly to the advancement of cardiovascular imaging techniques, particularly concerning image enhancement and segmentation of the coronary arteries. In addition, it sets out the implications of these results for clinical practice and suggests directions for future research that could deepen and expand this field, intending to improve the diagnosis and treatment of CAD.

6.1 Main Findings

To achieve the objectives of this work, presented in Section 1.2, it was necessary to develop algorithms capable of selecting frames that were in a precise moment of the cardiac cycle. Thus, they needed to identify and select the R peaks in the ECG signals, remove possible erroneously detected peaks by comparing the heartbeat formats with each other, and locate the temporal position between each two consecutive R peaks that corresponded to the same moment of the cycle where the CTCA images were acquainted. With the marked temporal location, the algorithm should proceed to select the corresponding frames.

Several global and local image enhancement techniques were applied to the selected CA frames, and generally speaking, the local manipulations produced better results. Among the two local image enhancement techniques tested, Edge-Aware Local Contrast was chosen as the better option because, compared to CLAHE, it highlighted the arteries more effectively. In terms of segmentation in CA images, techniques such as thresholding, region growing, and the application of the Frangi vesselness filter were tested. Although the least time-consuming method was thresholding (less than a second per frame), it also yielded the worst results, and it was extremely dependent on the selection of the optimal threshold value. The choice to use region growing derived from the visual tendency to follow the continuity of the dark areas in the image. However, this method would have a very significant limitation in building an automatic or semi-automatic program, as it required the determination of an initial seed. Furthermore, although three different approaches to the method have been tested, none seem sufficiently effective and they

wasted about seven seconds to segment each frame. Finally, the application of a modified Frangi Vesselness Filter algorithm was tested. Although it takes slightly longer than the others, taking about two seconds more than the region growing algorithm, the results obtained were closer to what was expected. The idea of testing this approach was to simulate what the human eye does since it searches for long tubular dark regions.

When the focus shifted to improving the quality of CTCA images, the Windowing technique was applied. Two sets of values were tested, which came as metadata from the images themselves, and it was decided to proceed with segmentation using the 3D model obtained after applying *WindowLevel* = 200 and *WindowWidth* = 600 for windowing.

Finally, to segment the CTCA images, the Frangi Vesselness Filter was used for 3D volumes. However, the results obtained still required some additional processing to eliminate tubular structures that were not coronary arteries.

Thus, it was possible to conclude that the image enhancement goal was accomplished, and the synchronisation requirement was satisfied. Moreover, although using artificial intelligence algorithms, specifically deep learning, to create automatic segmentation models of the coronary arteries was beyond reach for this work, a satisfactory solution was achieved for the CA images using only classical techniques. In the case of CTCA images, although tubular structures have already been identified, there was still a need to isolate only the coronary arteries.

6.2 Future Work

This work serves as an initial foundation for a more robust project that involves the construction of a program capable of performing 3D reconstruction of the coronary arteries from CA and CTCA images, to subsequently co-register them into a single model with more structural information while retaining the functional information of CA. Thus, there were still some steps to take to reach that goal.

Given that there is increasingly more development in the artificial intelligence field and that the future of medicine will likely benefit greatly from this aspect, the results obtained from the CA image enhancement and segmentation may be used as ground truth images. This would allow for a large amount of data to be annotated not by specialists but by programs like the one developed in this work. Furthermore, once the segmentation of the CA images is completed, one can proceed to the reconstruction step. For this, the angular information from which the sequence of frames was made would be used to create an image of the artery in depth, and by combining two or more of these depth images that are sufficiently separated angularly, it would be possible to transition to the 3D model itself.

In the context of CTCA images, there is a need to improve the results obtained in this work so that only the coronary arteries are visible. This step is crucial because to co-register the two models, the arteries will need to be as similar as possible, and the presence of other structures will certainly complicate the alignment of the models.

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ELECTROCARDIOGRAM SIGNAL PROCESSING

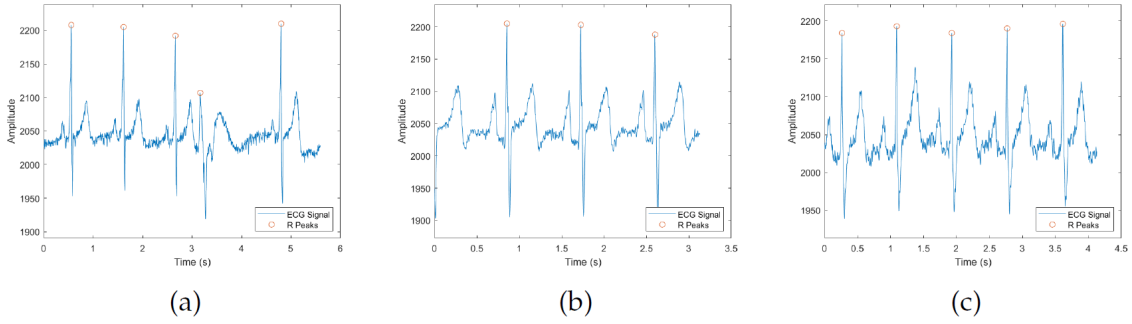


Figure A.1: R peak detection in the ECG signals of different coronary angiography projections. (a) First projection of individual 1; (b) Second projection of individual 2; (c) Eighth projection of individual 10.

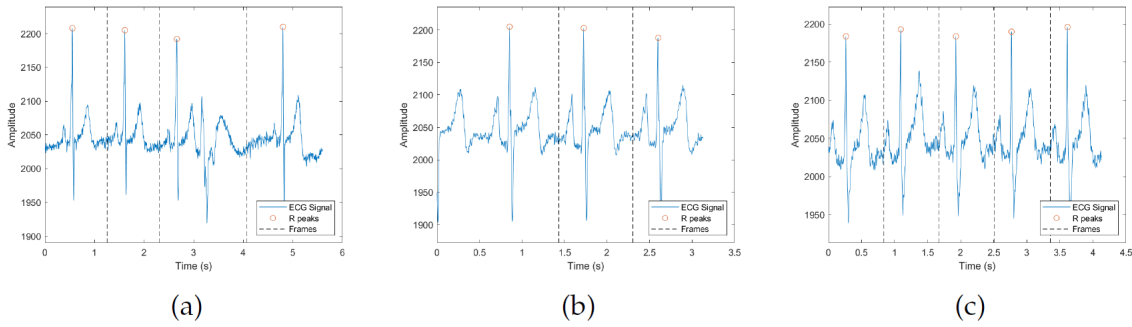


Figure A.2: Identification of the optimal frames of different coronary angiography projections to further consider in the coronary angiography image analysis. (a) First projection of individual 1; (b) Second projection of individual 2; (c) Eighth projection of individual 10.

B

CORONARY ANGIOGRAPHY IMAGE ENHANCEMENT

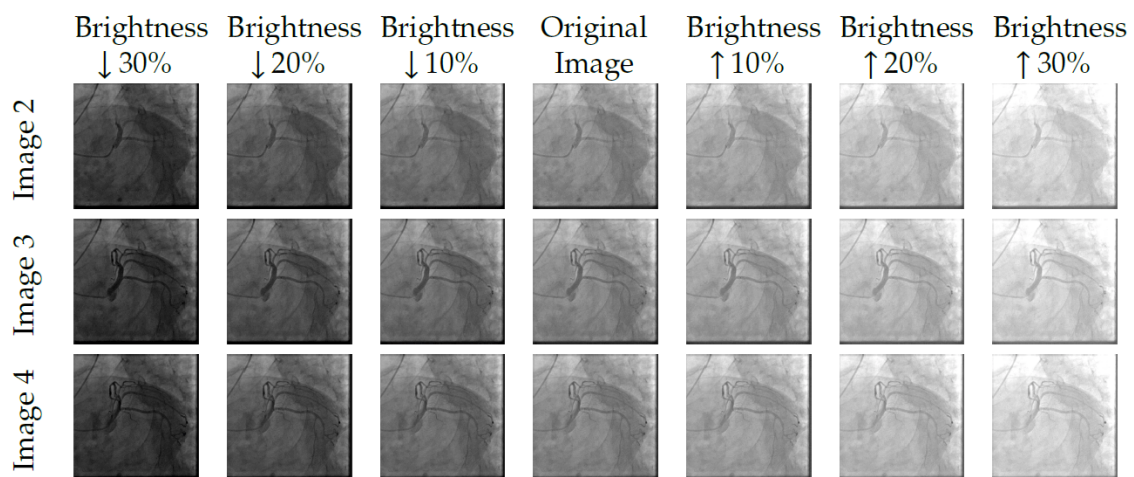


Figure B.1: Results of brightness adjustments on the first CA projection of individual 1.

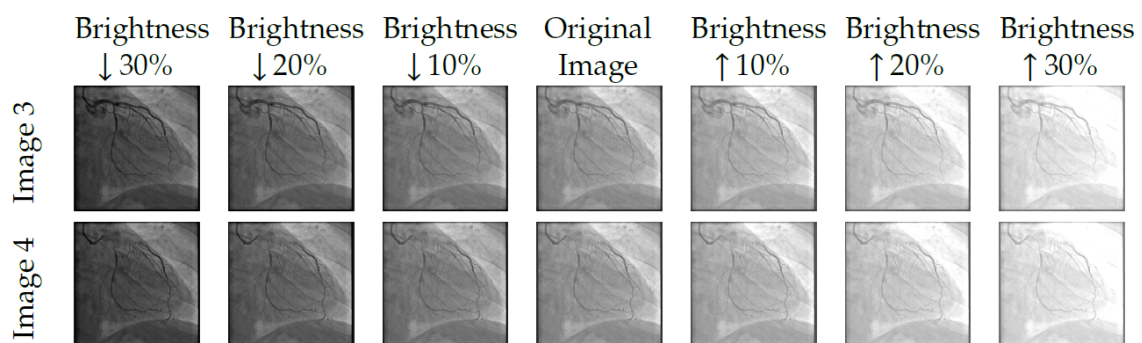


Figure B.2: Results of brightness adjustments on the second CA projection of individual 2.

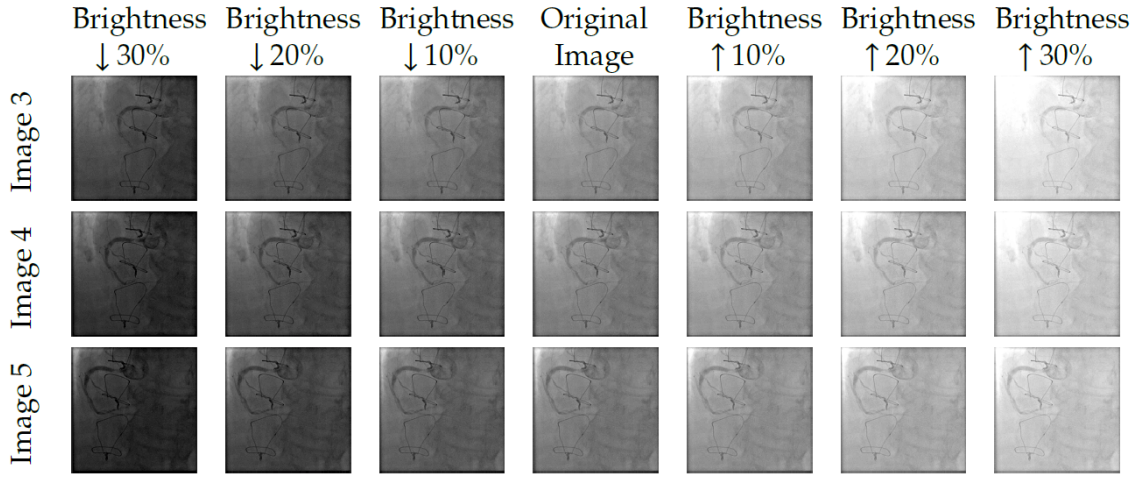


Figure B.3: Results of brightness adjustments on the eighth CA projection of individual 10.

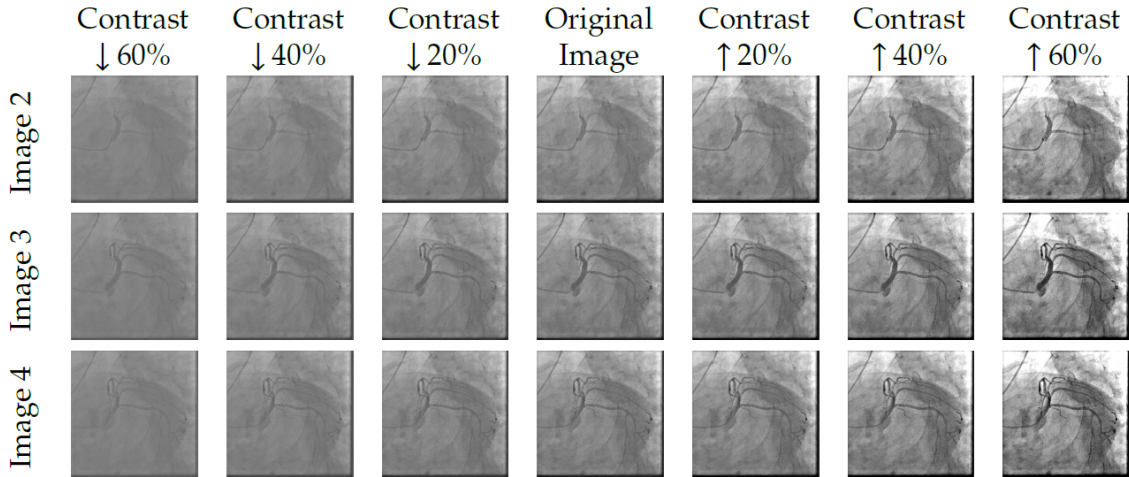


Figure B.4: Results of contrast adjustments on the first CA projection of individual 1.

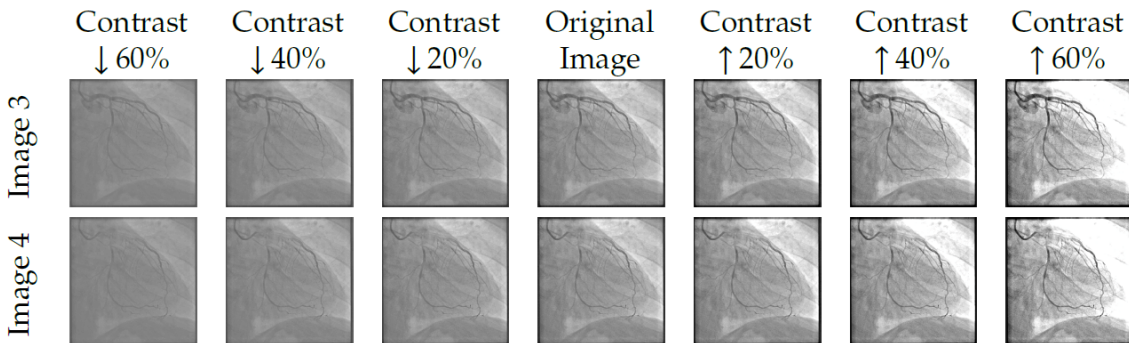


Figure B.5: Results of contrast adjustments on the second CA projection of individual 2.

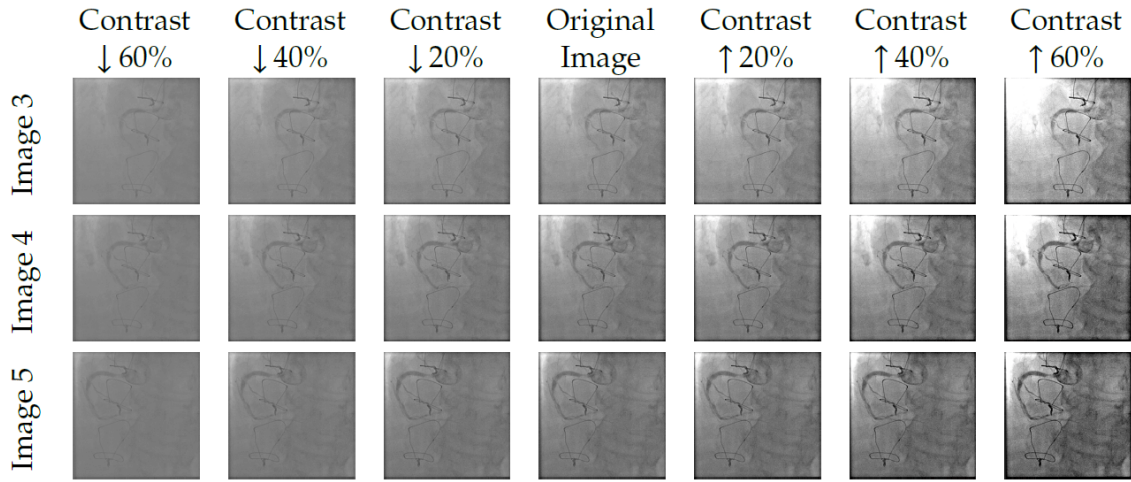


Figure B.6: Results of contrast adjustments on the eighth CA projection of individual 10.

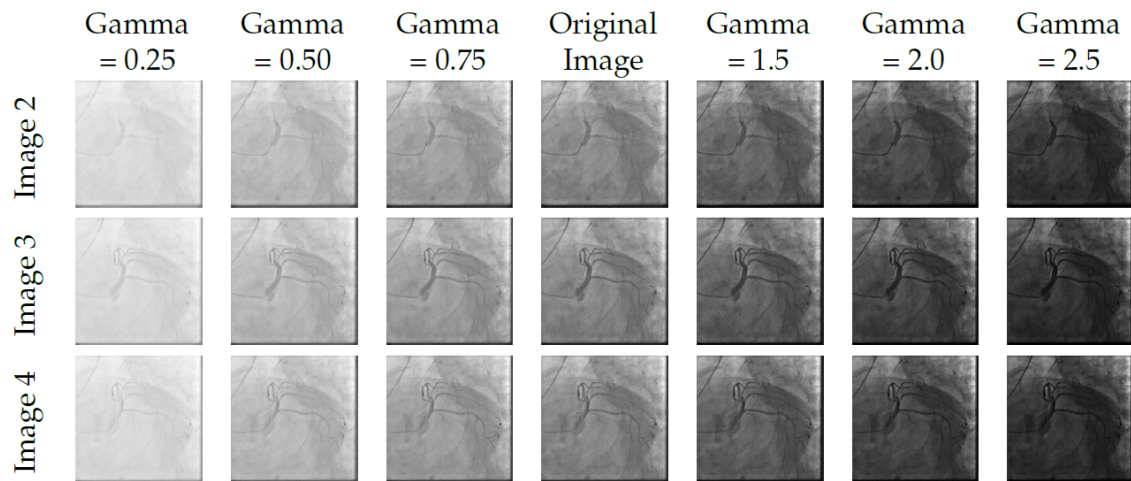


Figure B.7: Results of gamma adjustments on the first CA projection of individual 1.

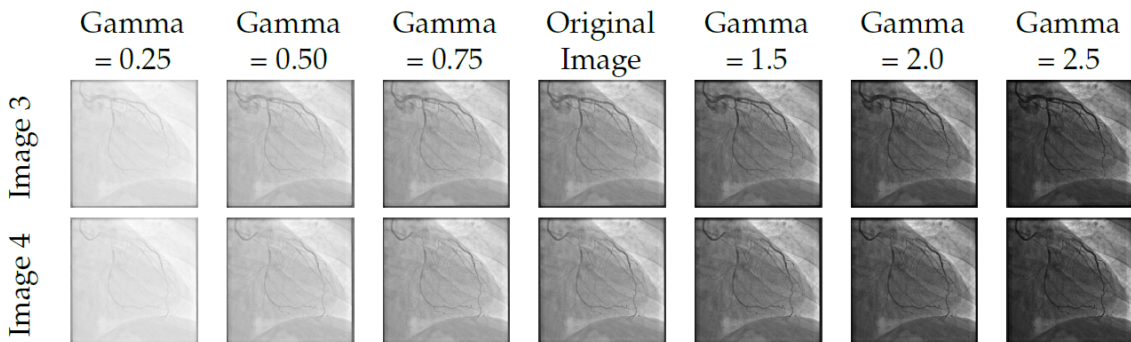


Figure B.8: Results of gamma adjustments on the second CA projection of individual 2.

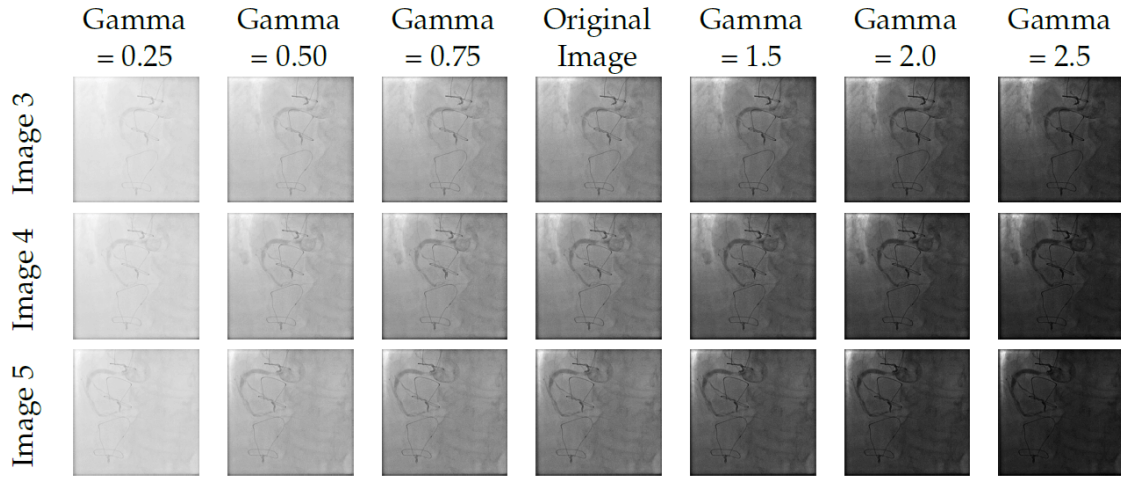


Figure B.9: Results of gamma adjustments on the eighth CA projection of individual 10.

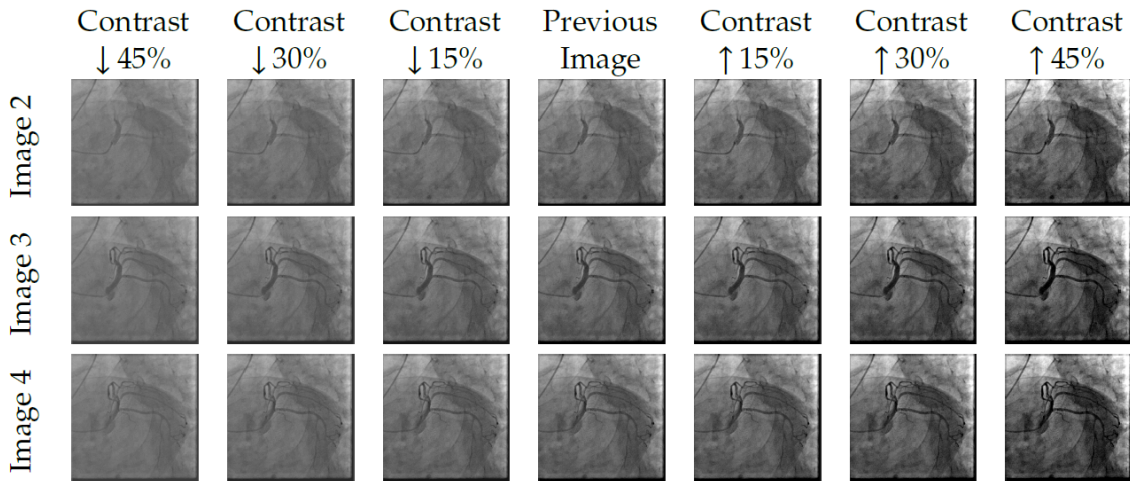


Figure B.10: Results of contrast adjustments on the first CA projection of individual 1 with brightness decreased by 20%.

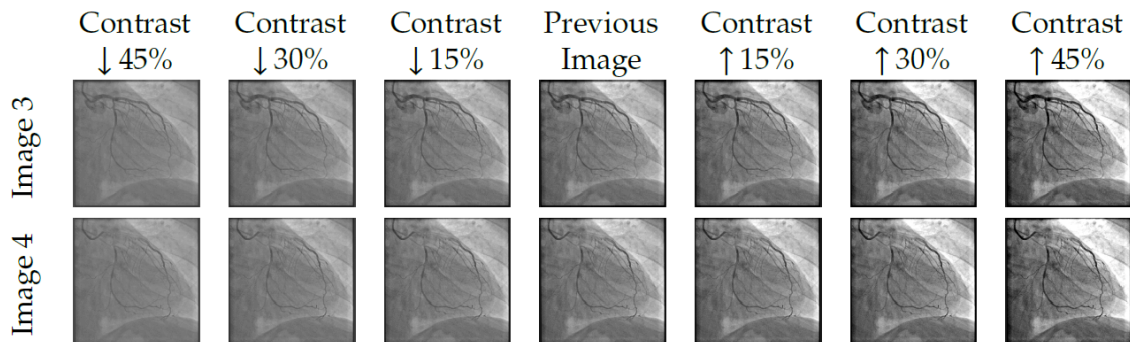


Figure B.11: Results of contrast adjustments on the second CA projection of individual 2 with brightness decreased by 20%.

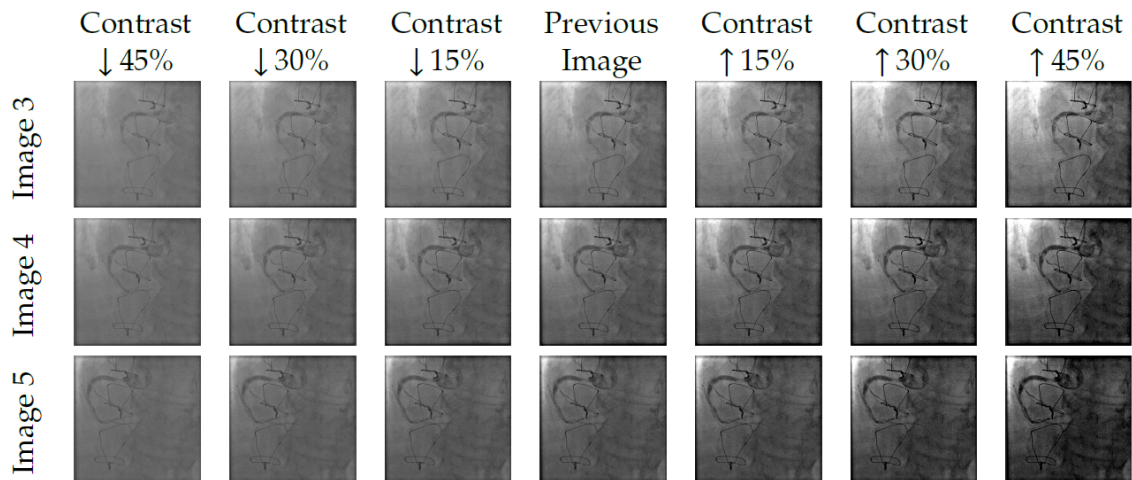


Figure B.12: Results of contrast adjustments on the eighth CA projection of individual 10 with brightness decreased by 20%.

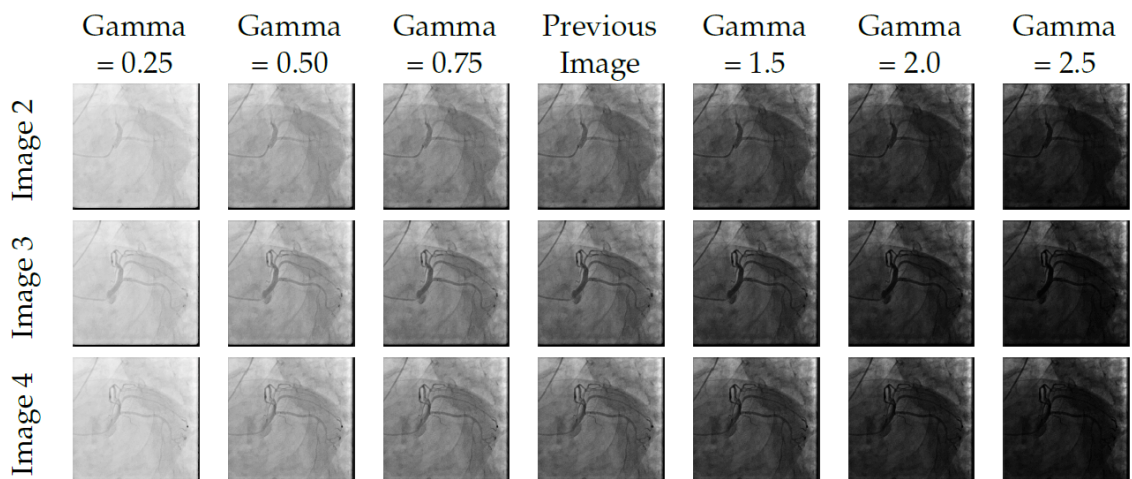


Figure B.13: Results of gamma adjustments on the first CA projection of individual 1 with brightness decreased by 20%.

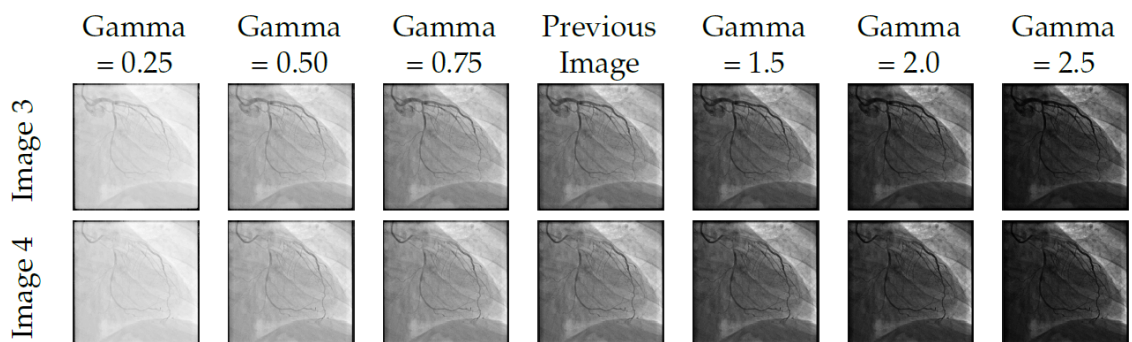


Figure B.14: Results of gamma adjustments on the second CA projection of individual 2 with brightness decreased by 20%.

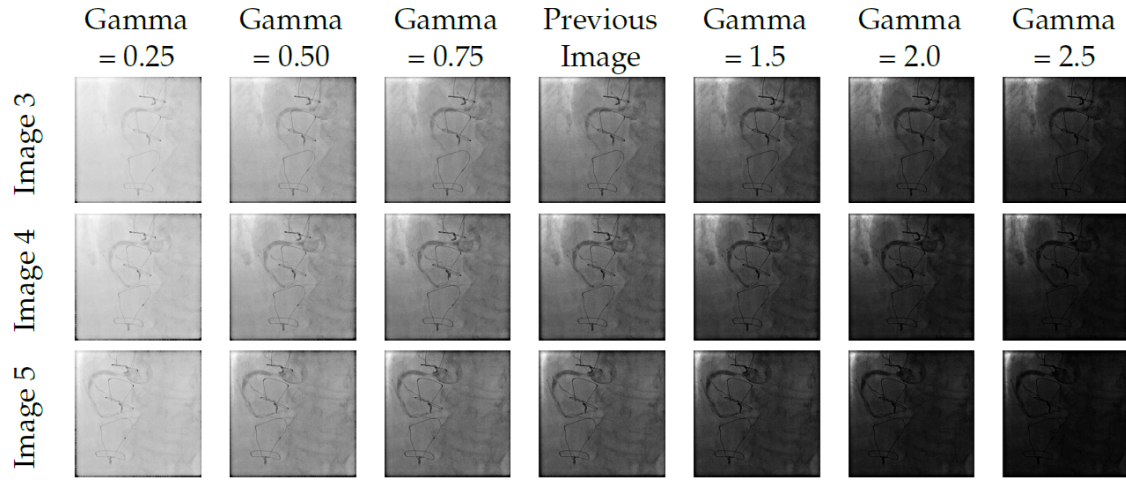


Figure B.15: Results of gamma adjustments on the eighth CA projection of individual 10 with brightness decreased by 20%.

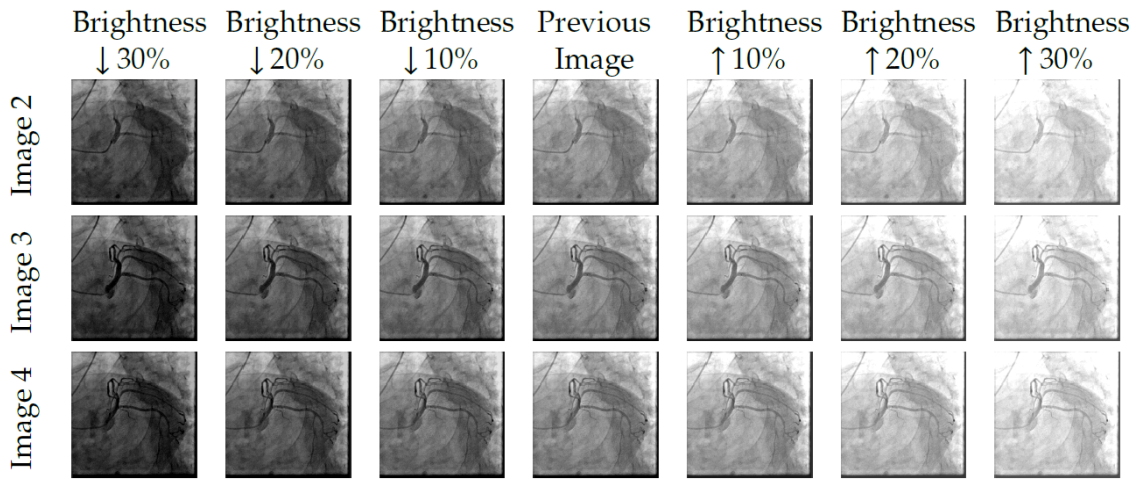


Figure B.16: Results of brightness adjustments on the first CA projection of individual 1 with contrast increased by 40%.

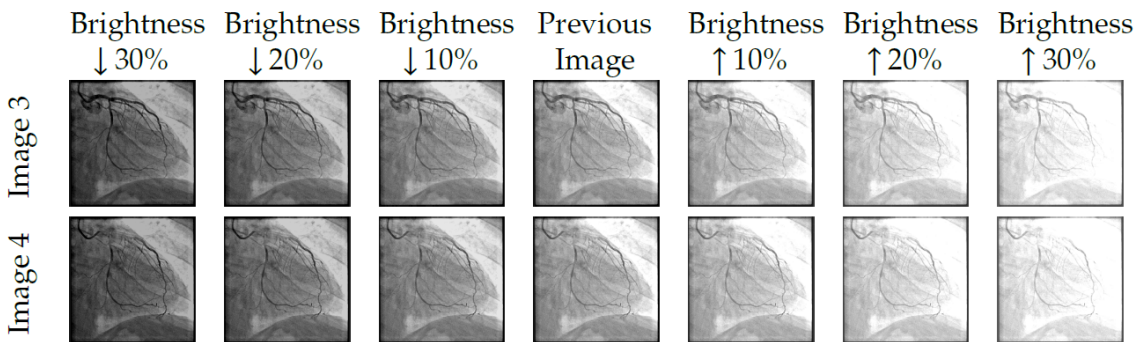


Figure B.17: Results of brightness adjustments on the second CA projection of individual 2 with contrast increased by 40%.

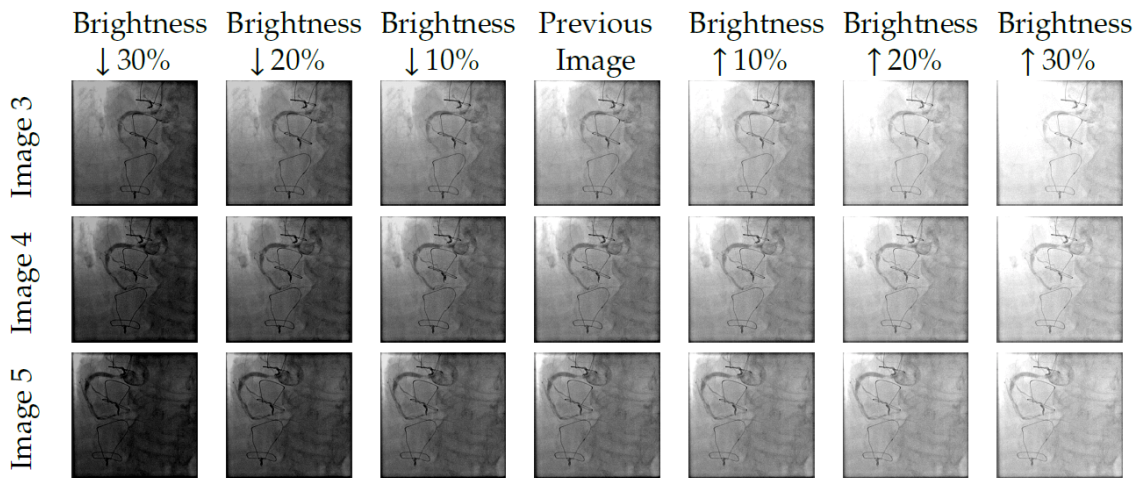


Figure B.18: Results of brightness adjustments on the eighth CA projection of individual 10 with contrast increased by 40%.

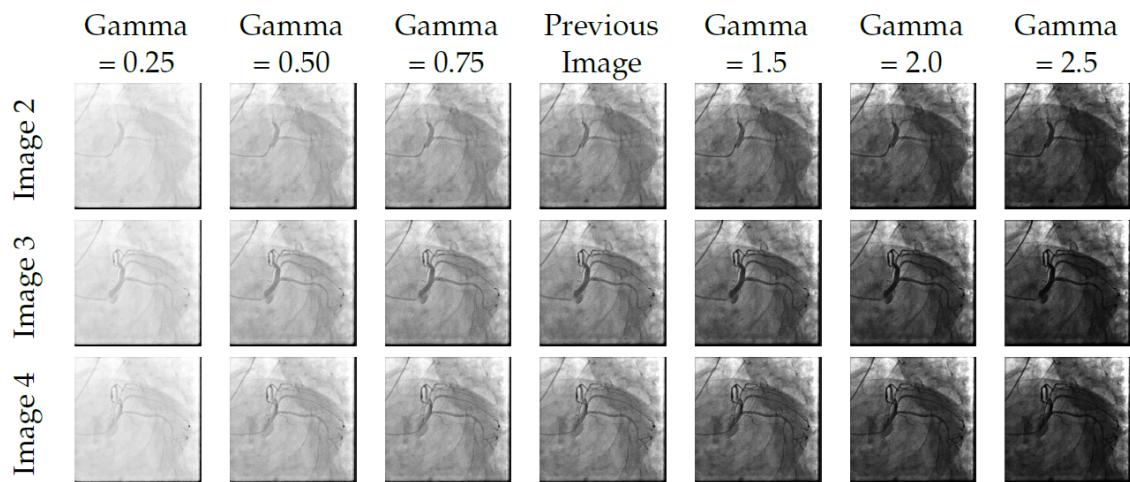


Figure B.19: Results of gamma adjustments on the first CA projection of individual 1 with contrast increased by 40%.

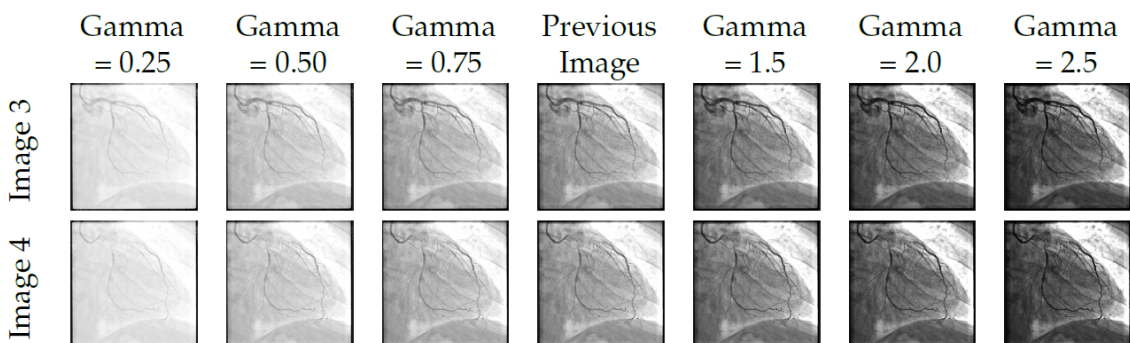


Figure B.20: Results of gamma adjustments on the second CA projection of individual 2 with contrast increased by 40%.

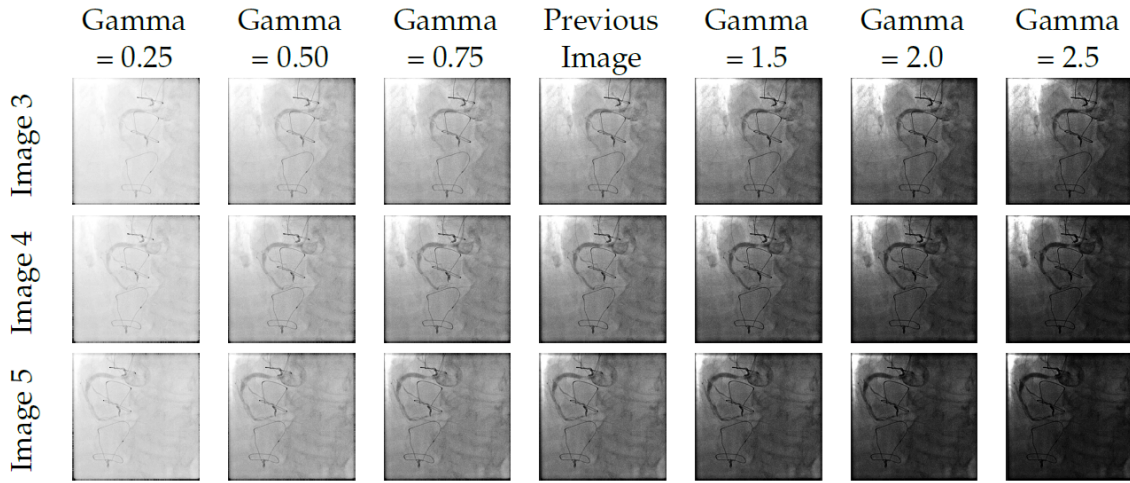


Figure B.21: Results of gamma adjustments on the eighth CA projection of individual 10 with contrast increased by 40%.

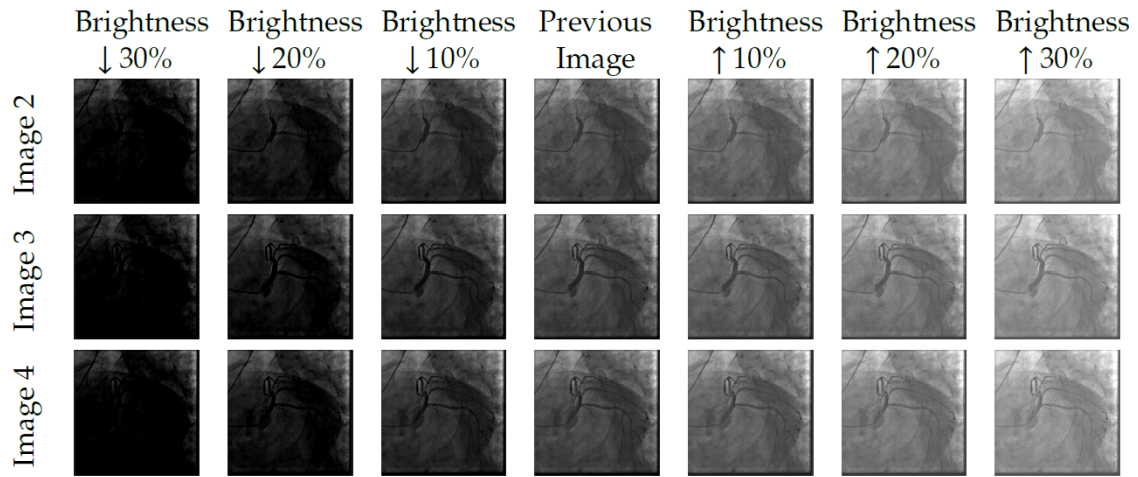


Figure B.22: Results of brightness adjustments on the first CA projection of individual 1 with gamma value of 2.

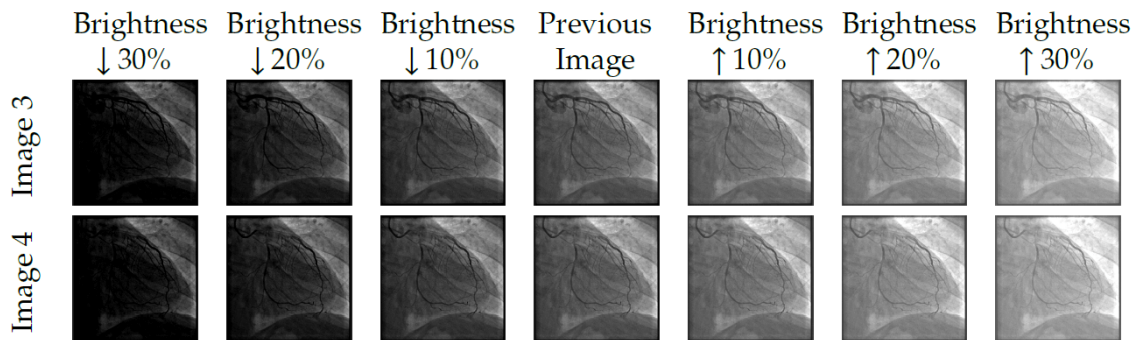


Figure B.23: Results of brightness adjustments on the second CA projection of individual 2 with gamma value of 2.

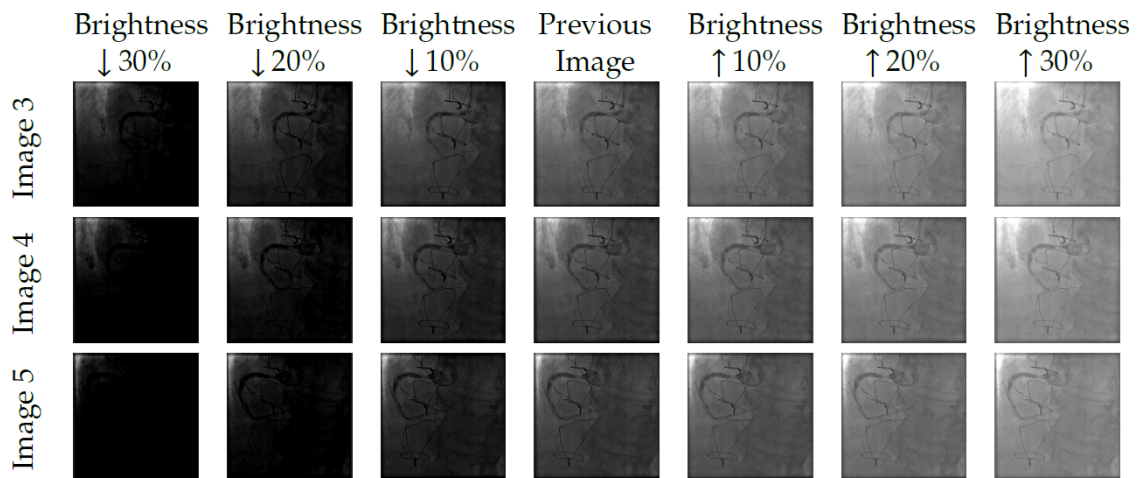


Figure B.24: Results of brightness adjustments on the eighth CA projection of individual 10 with gamma value of 2.

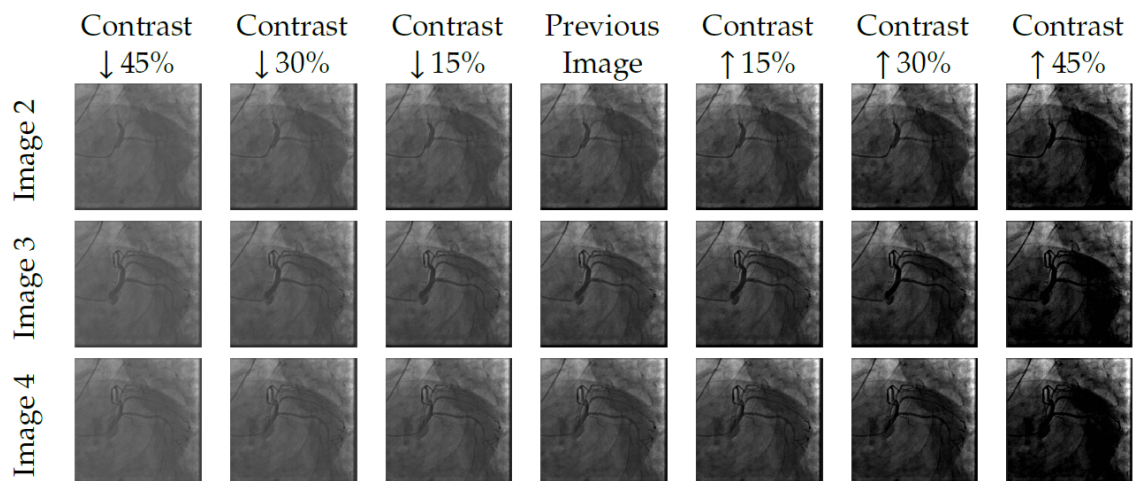


Figure B.25: Results of contrast adjustments on the first CA projection of individual 1 with gamma value of 2.

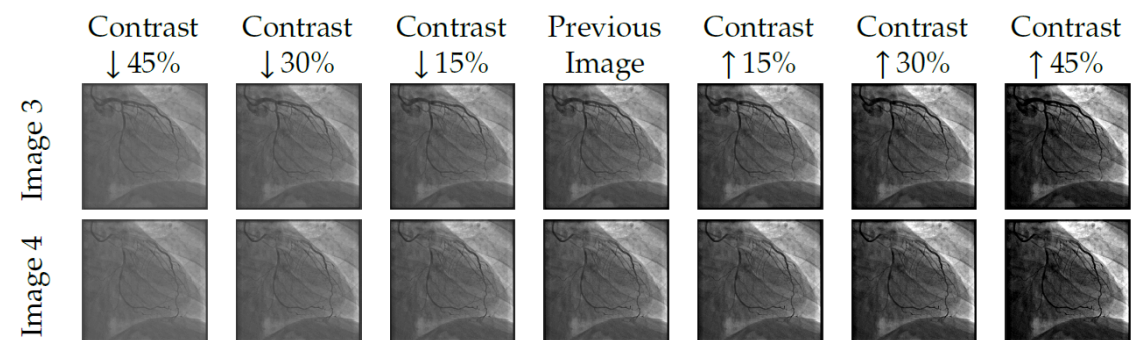


Figure B.26: Results of contrast adjustments on the second CA projection of individual 2 with gamma value of 2.

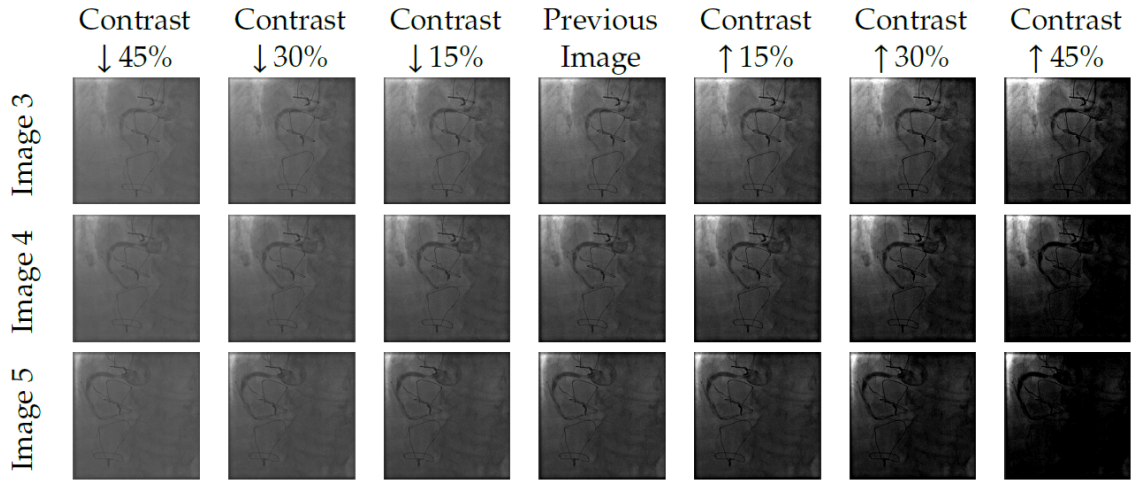


Figure B.27: Results of contrast adjustments on the eighth CA projection of individual 10 with gamma value of 2.

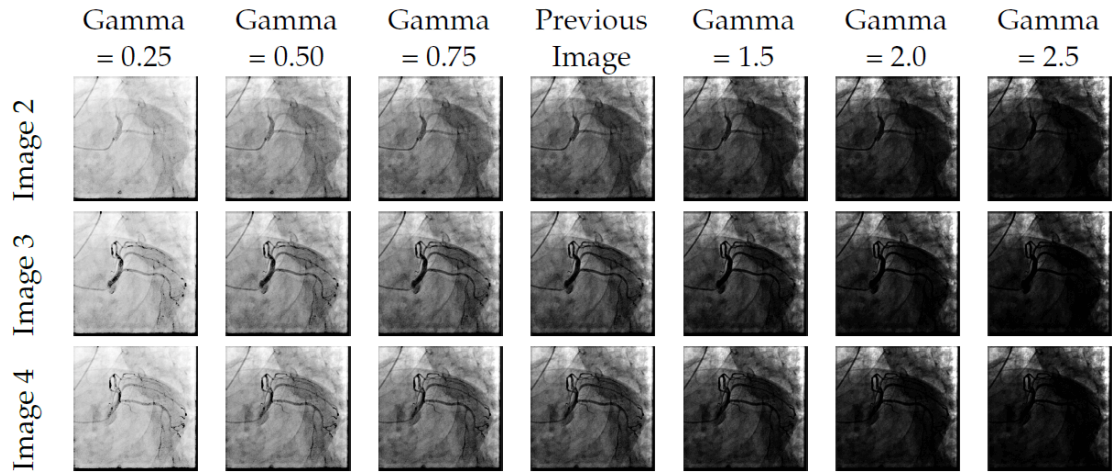


Figure B.28: Results of gamma adjustments on the first CA projection of individual 1 with brightness decreased by 20% and contrast increased by 45%.

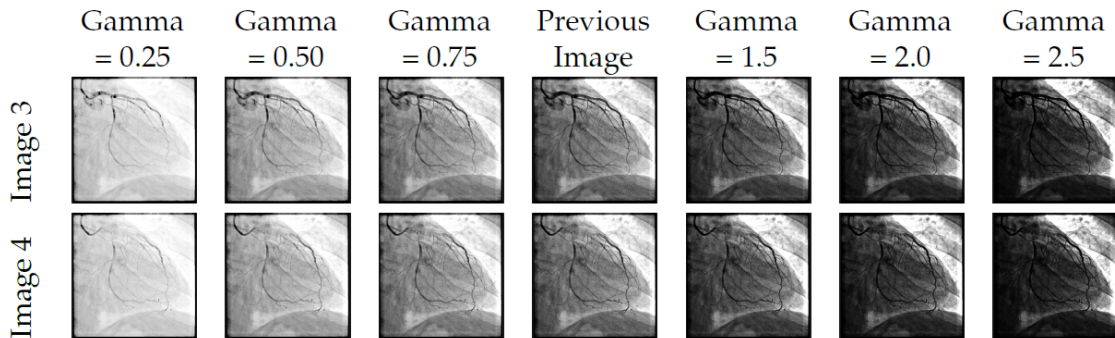


Figure B.29: Results of gamma adjustments on the second CA projection of individual 2 with brightness decreased by 20% and contrast increased by 45%.

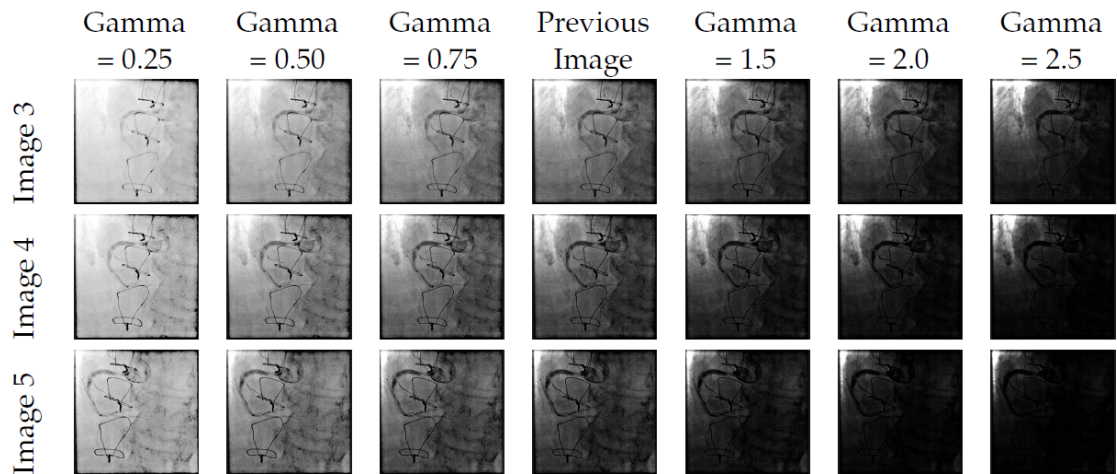


Figure B.30: Results of gamma adjustments on the eighth CA projection of individual 10 with brightness decreased by 20% and contrast increased by 45%.

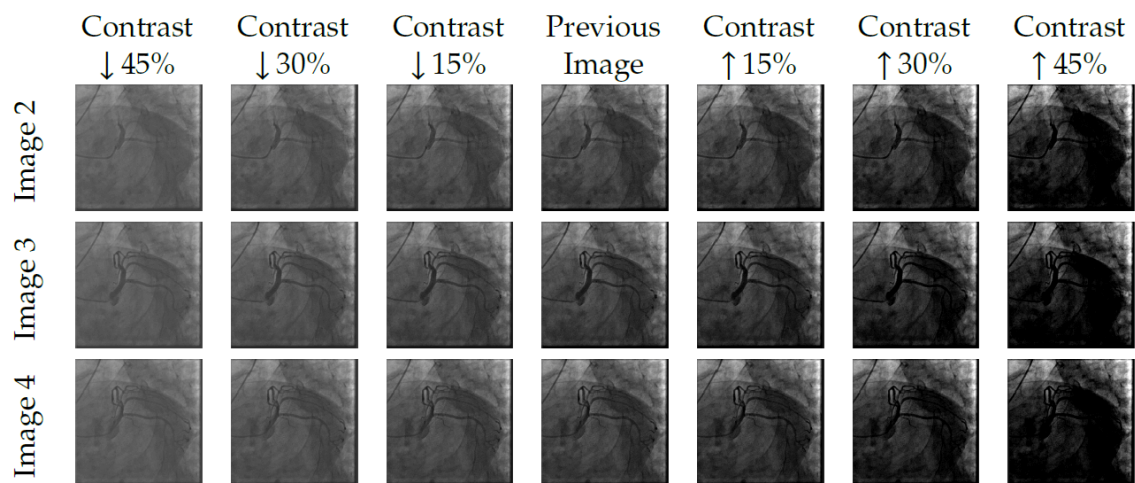


Figure B.31: Results of contrast adjustments on the first CA projection of individual 1 with brightness decreased by 20% and gamma value of 1.5.

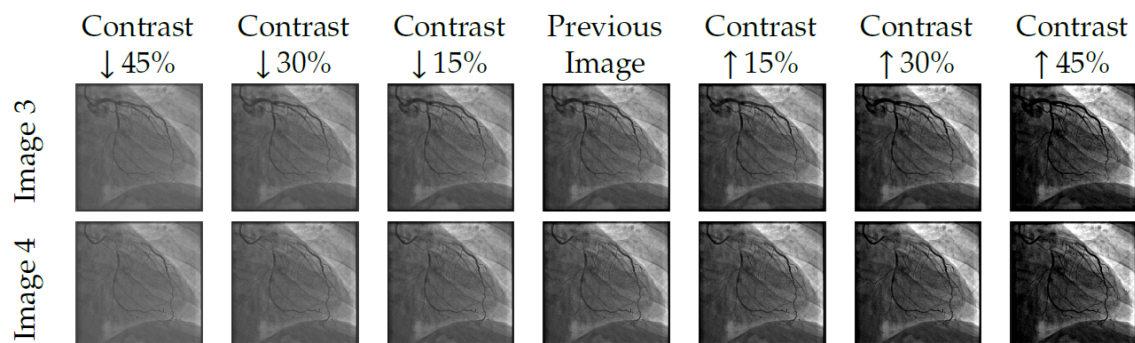


Figure B.32: Results of contrast adjustments on the second CA projection of individual 2 with brightness decreased by 20% and gamma value of 1.5.

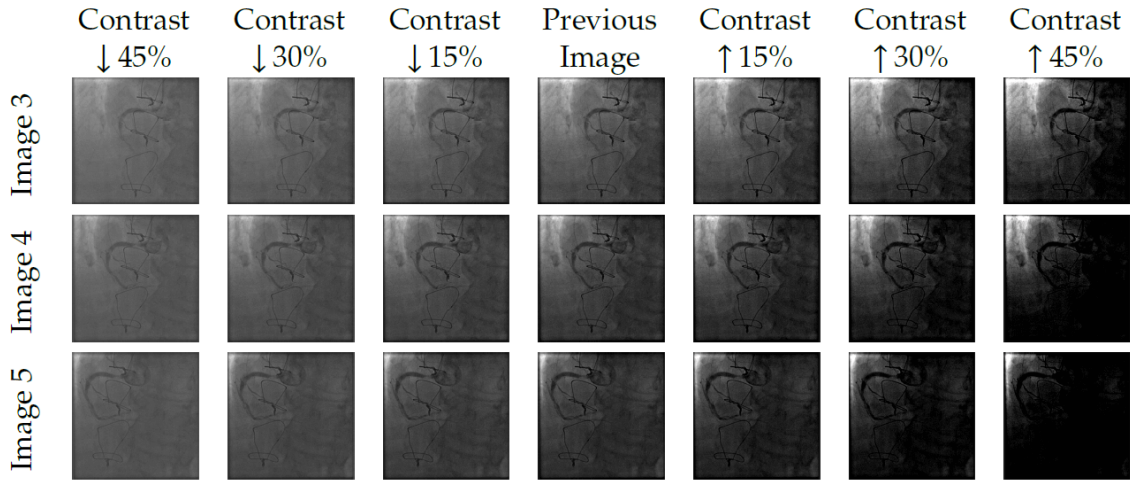


Figure B.33: Results of contrast adjustments on the eighth CA projection of individual 10 with brightness decreased by 20% and gamma value of 1.5.

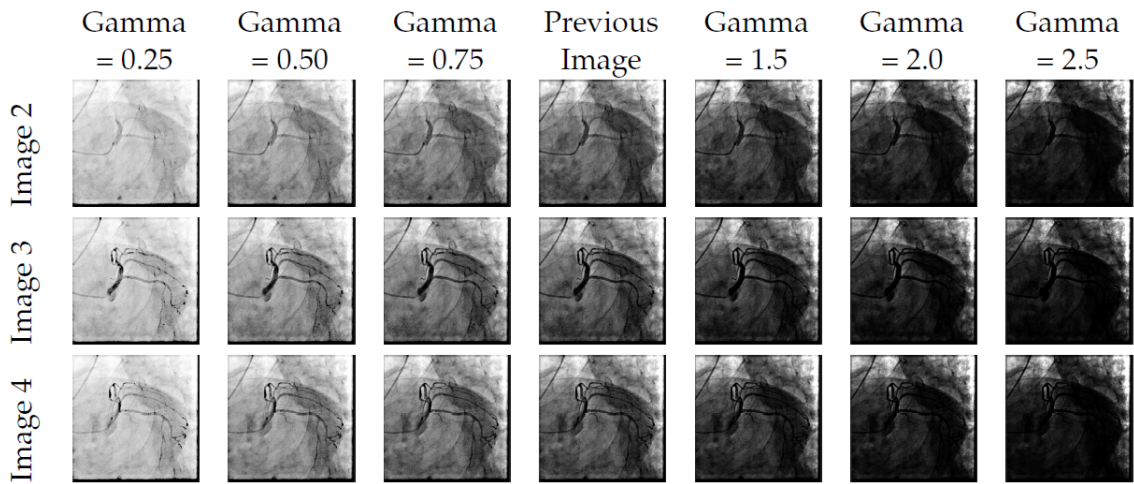


Figure B.34: Results of gamma adjustments on the first CA projection of individual 1 with contrast increased by 40% and brightness decreased by 30%.

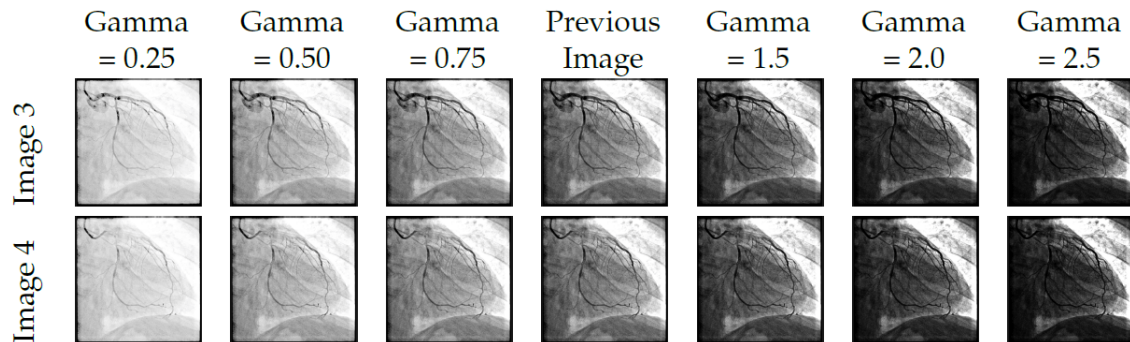


Figure B.35: Results of gamma adjustments on the second CA projection of individual 2 with contrast increased by 40% and brightness decreased by 30%.

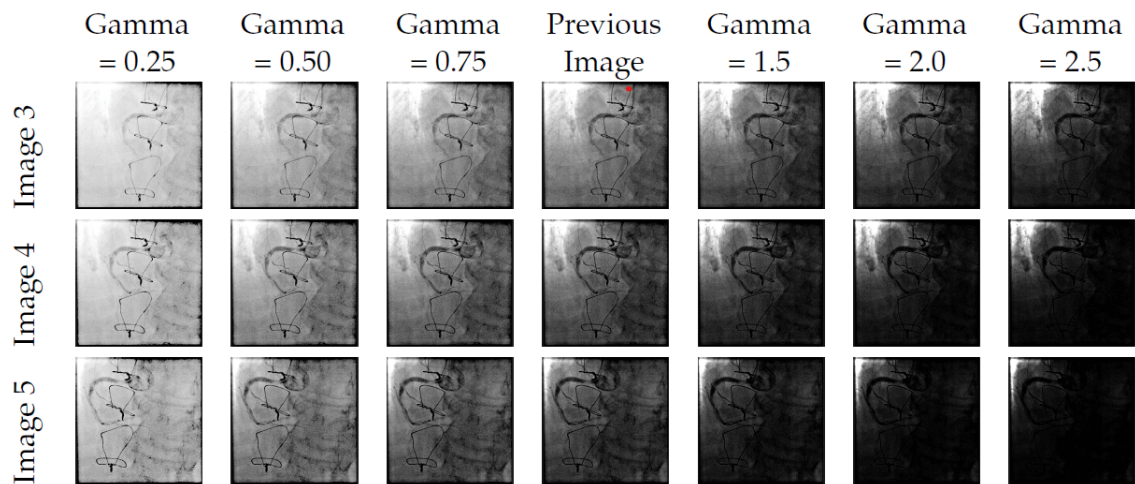


Figure B.36: Results of gamma adjustments on the eighth CA projection of individual 10 with contrast increased by 40% and brightness decreased by 30%.

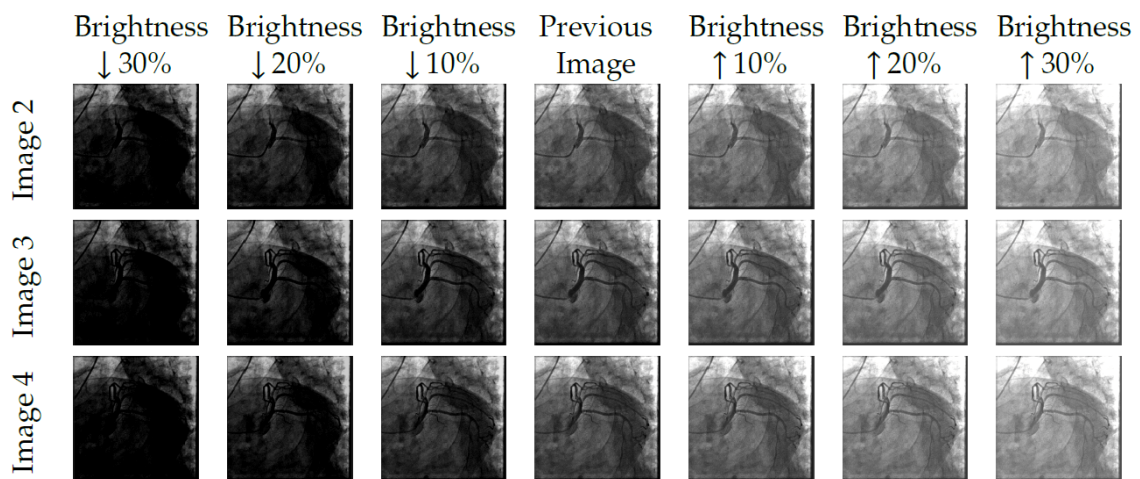


Figure B.37: Results of brightness adjustments on the first CA projection of individual 1 with contrast increased by 40% and gamma value of 2.

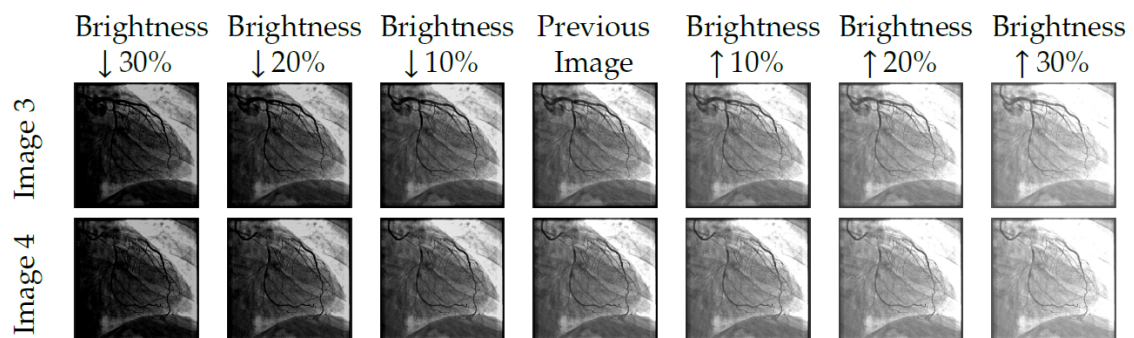


Figure B.38: Results of brightness adjustments on the second CA projection of individual 2 with contrast increased by 40% and gamma value of 2.

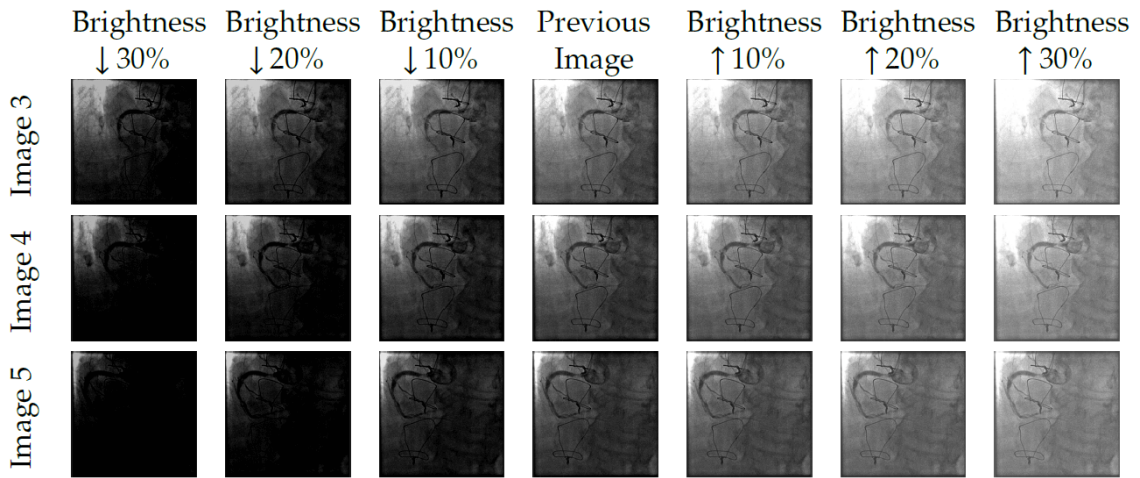


Figure B.39: Results of brightness adjustments on the eighth CA projection of individual 10 with contrast increased by 40% and gamma value of 2.

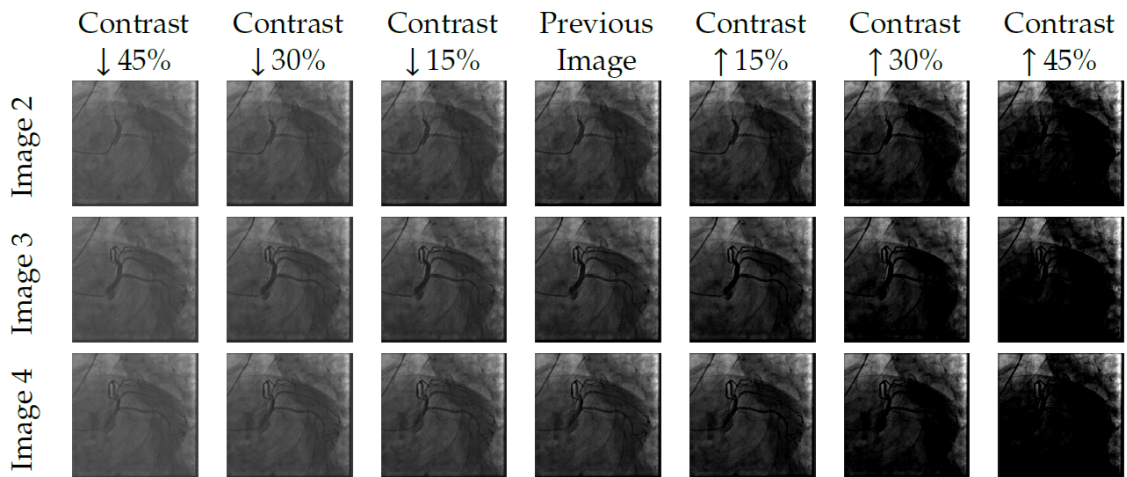


Figure B.40: Results of contrast adjustments on the first CA projection of individual 1 with gamma value of 2.0 and brightness decreased by 10%.

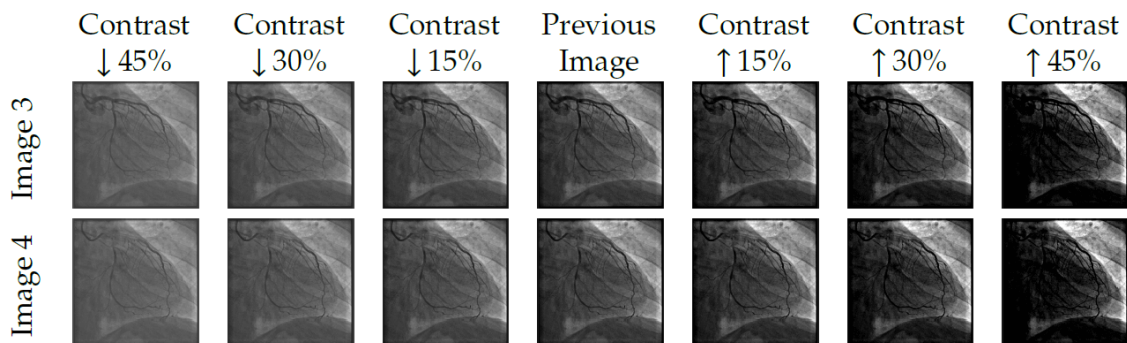


Figure B.41: Results of contrast adjustments on the second CA projection of individual 2 with gamma value of 2.0 and brightness decreased by 10%.

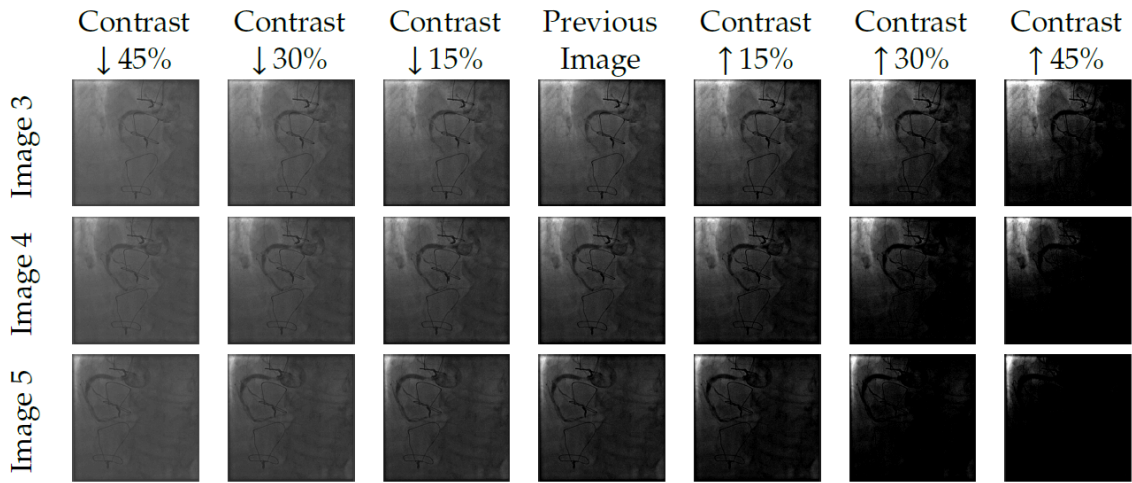


Figure B.42: Results of contrast adjustments on the eighth CA projection of individual 10 with gamma value of 2.0 and brightness decreased by 10%.

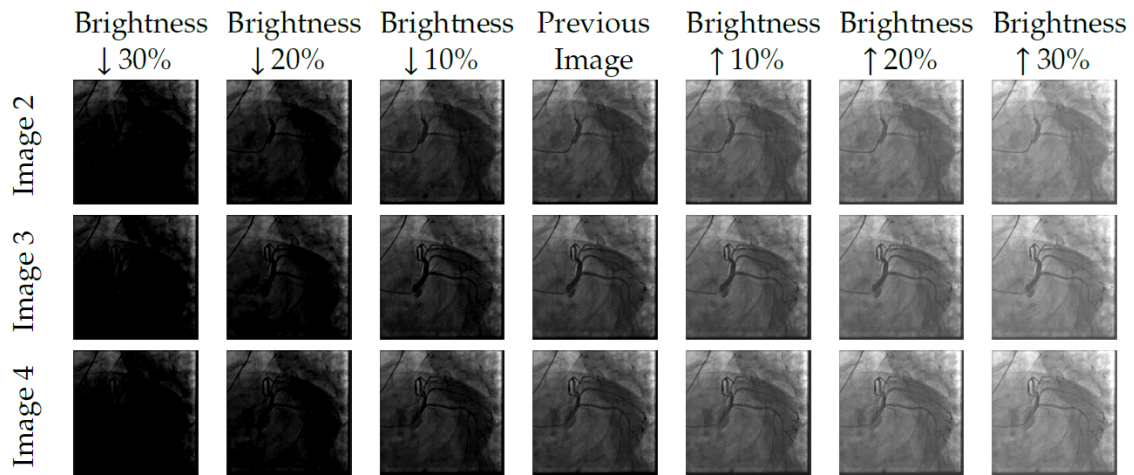


Figure B.43: Results of brightness adjustments on the first CA projection of individual 1 with gamma value of 2 and contrast increased by 15%.

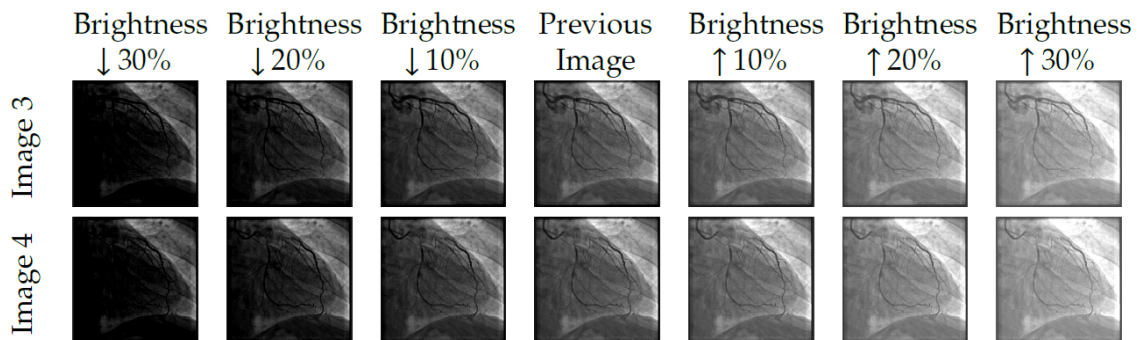


Figure B.44: Results of brightness adjustments on the second CA projection of individual 2 with gamma value of 2 and contrast increased by 15%.

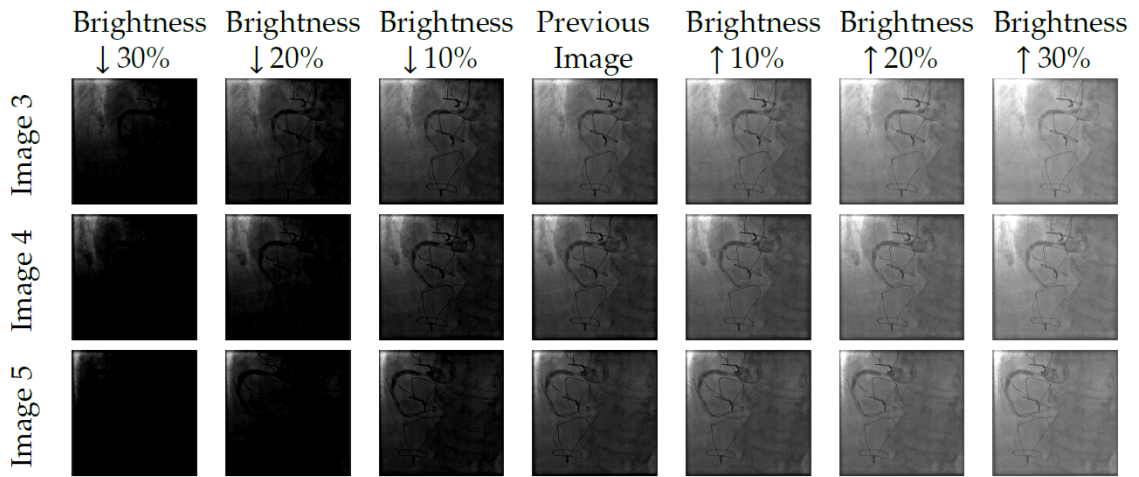


Figure B.45: Results of brightness adjustments on the eighth CA projection of individual 10 with gamma value of 2 and contrast increased by 15%.

CORONARY ANGIOGRAPHY IMAGE SEGMENTATION

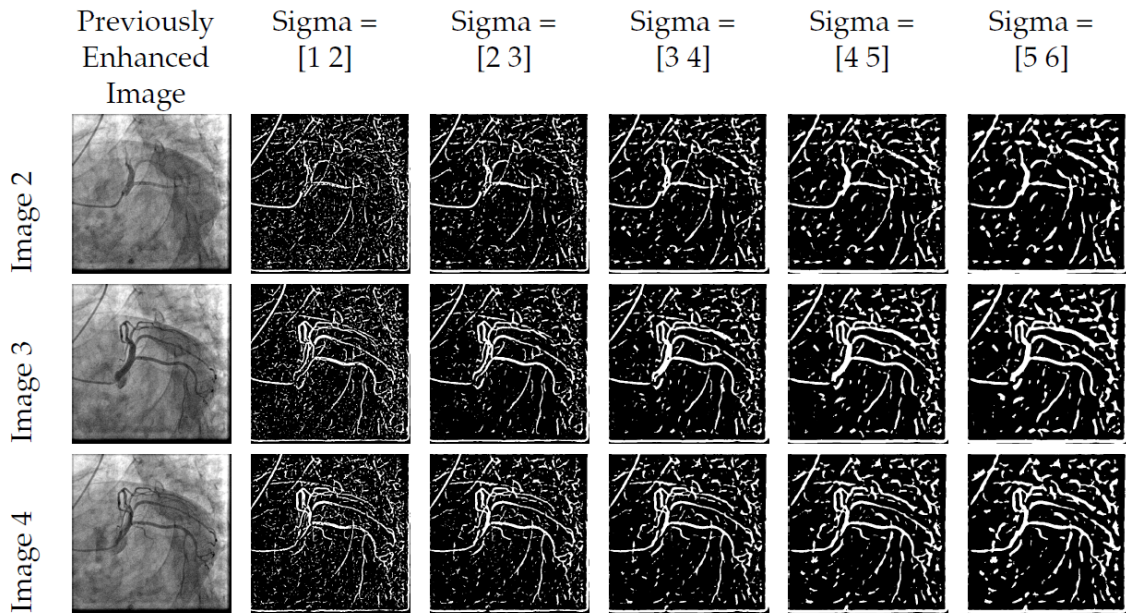


Figure C.1: Results of modified Frangi Vesselness Filter function with different sigma parameters on the first CA projection of individual 1.

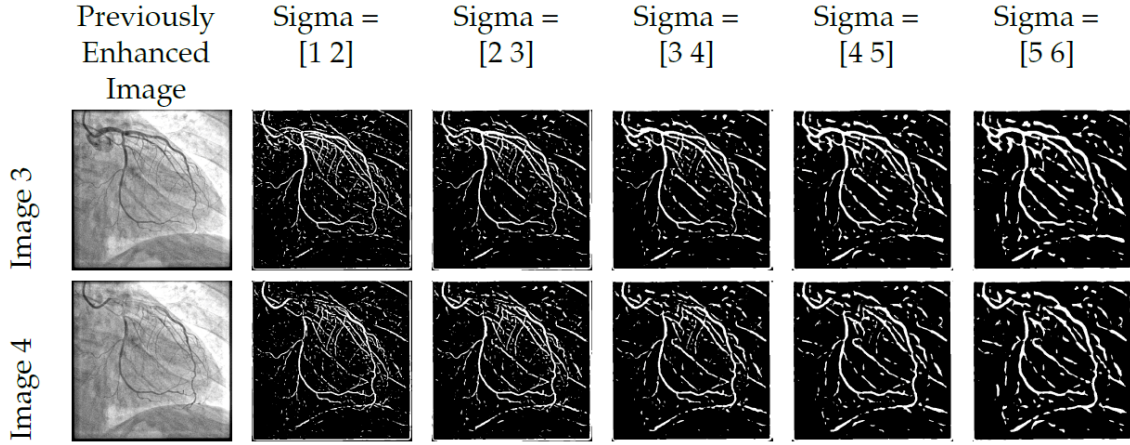


Figure C.2: Results of modified Frangi Vesselness Filter function with different sigma parameters on the second CA projection of individual 2.

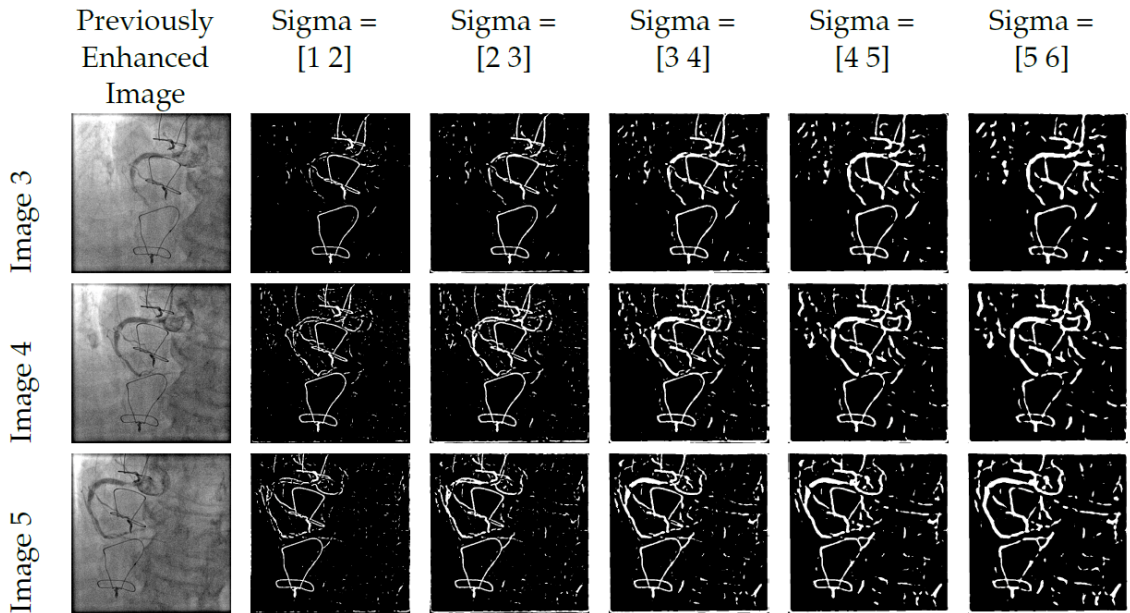


Figure C.3: Results of modified Frangi Vesselness Filter function with different sigma parameters on the eighth CA projection of individual 10.

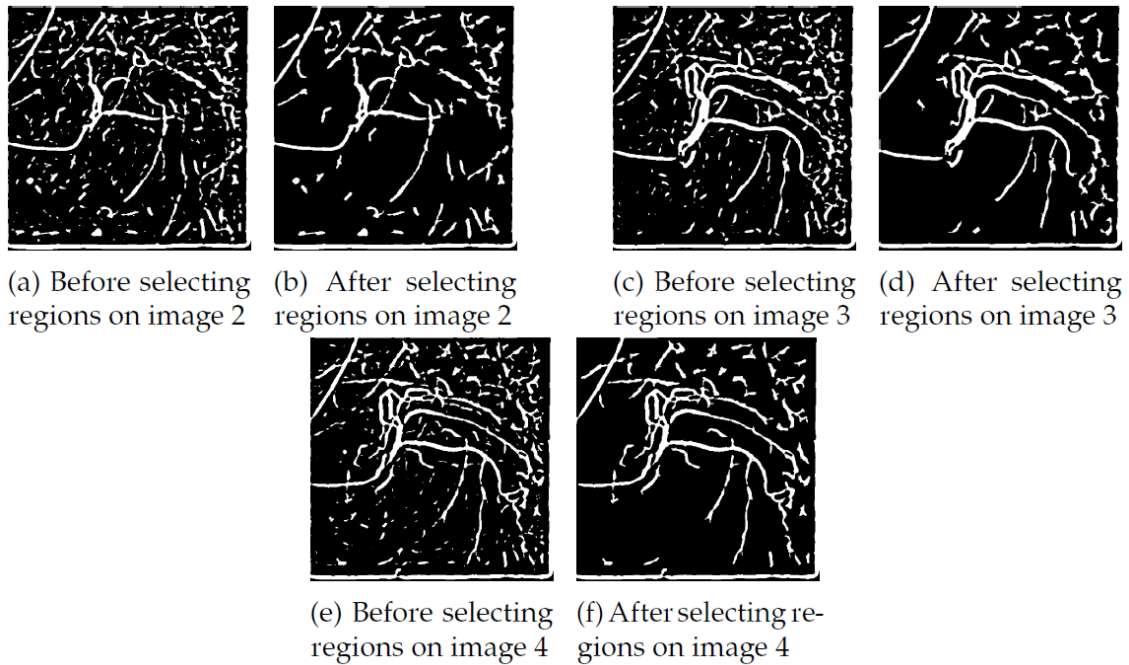


Figure C.4: Results of selecting the regions based on their properties on the first CA projection of individual 1.

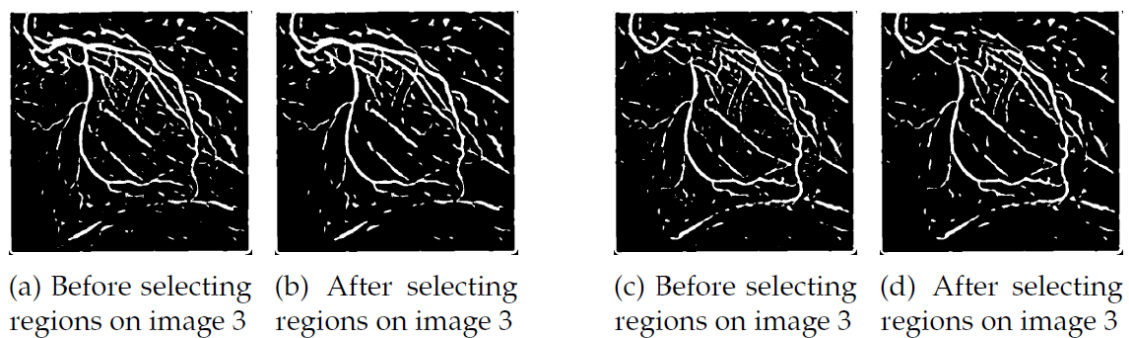


Figure C.5: Results of selecting the regions based on their properties on the second CA projection of individual 2.

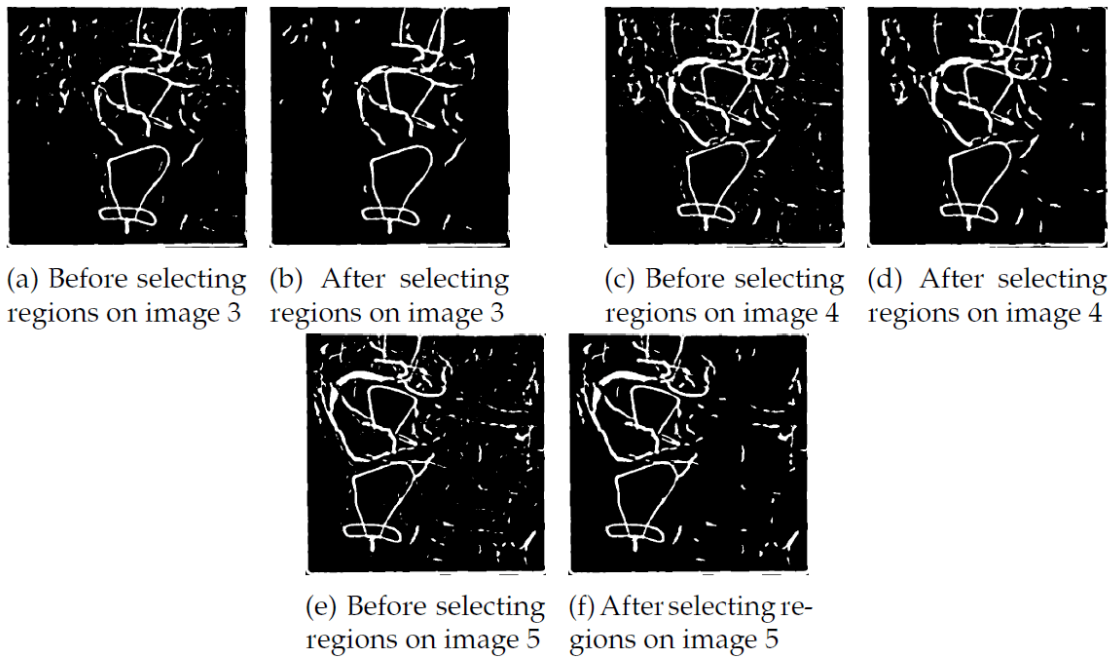


Figure C.6: Results of selecting the regions based on their properties on the eighth CA projection of individual 10.



2024

Image Enhancement and Coronary Segmentation: The First Steps Toward Three-Dimensional Reconstruction of the Coronary Arteries

Adriana Silva



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SCHOOL OF

SCIENCE & TECHNOLOGY