UNIVERSITI PUTRA MALAYSIA

THREE-DIMENSIONAL CORONARY ARTERY RECONSTRUCTION BASED ON SINGLE-PLANE ANGIOGRAPHY AND INTRAVASCULAR ULTRASOUND REGISTRATION

SUHAILI BINTI BEERAN KUTTY

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By

SUHAILI BINTI BEERAN KUTTY

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Doctor of Philosophy

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DEDICATION

This thesis is dedicated to all members of heart wellness who are always ready to help people and trying so hard to reduce the number of heart failures and cardiovascular disease.

Indeed, we belong to Allah and indeed to Him we will return.

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Doctor of Philosophy

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Chairman : Professor Rahmita Wirza binti O. K. Rahmat
Faculty : Computer Science and Information Technology

The mortality rate of heart failure or heart disease has been increasing all over the world. Coronary artery disease (CAD) is one type of heart disease that is caused by the atherosclerosis process. The process starts with the building up of plaque along the inner walls of the coronary arteries. The obstruction of the artery will reduce the blood flow that circulates through the heart. The reduced blood flow to the heart can cause angina or chest pain and heart attack. X-ray coronary angiography is the gold standard test to investigate the affected artery, however, this modality only visualizes the silhouette of the artery. To help the diagnostic process, Intravascular Ultrasound (IVUS) based on ultrasound technology, is used to show the internal structure of the artery. Coronary angiography and IVUS complement each other. However, to use coronary angiography and IVUS simultaneously, cardiologists view both modalities on the same screen, but in a different window. They are merged mentally using the biological landmarks on the modalities and also based on the cardiologist's knowledge and experiences. Mental registration can cause errors in the interpretation of the plaque and is time-consuming. Because of that, research on the registration of Angiography and IVUS have been highlighted until today. Most of the previous registration approaches are based on the bi-plane Angiography that required greater radiation dose and a common technique for the registration, based on the epipolar geometry. The disadvantages of this technique are that it requires at least two views of coronary angiography, and approximation is used in determining the correspondence points. In this research, the registration proposes to use a single-plane Angiography, which is the medical imaging technology that is still relevant and used in many catheterization labs around the world to reconstruct the 3D artery based on the registration with IVUS modality. Firstly, the IVUS modality; the catheter shape, the lumen and the media-adventitia are completely segmented using labeling and a parametric deformable model. Next, the trajectory of the artery is reconstructed based on the catheter path of IVUS and the biological landmarks found on the coronary angiography image. A new method for reconstructing 3D coronary artery based on the circle trigonometry

equation for the registration of single-plane coronary angiography and IVUS was introduced in this research. To help the CAD diagnostic process, this research offers an accurate measurement of the lumen cross-sectional area, minimum lumen diameter, and maximum lumen diameter. In IVUS segmentation, the result shows that 100% of the catheter shape on IVUS image is detected correctly using the labelling approach. The accuracy of the lumen segmentation increases with a percentage of area difference (PAD) 0.07, and the media-adventitia segmentation could be done without manual initialization process. It is also proven that the trajectory of the artery could be generated using only one view of Angiography that contains the catheter path of IVUS. Furthermore, the accuracy of the equation used in the registration experiment is acceptable, where it is shown by P is 0.9999 more than the significant value. As a result, the new approach of the registration of the single-plane Angiography and IVUS to produce a 3D coronary artery is accepted by the medical practitioners. The 3D model shows the precise location of the catheter in the artery and the coronary artery is measured through the cross-sectional area of the lumen and the minimum and maximum diameters. The result of this study may help us to understand the longitudinal view of the coronary artery and the morphology of the arterial wall. It could be used by cardiologists to make decisions in diagnosing coronary artery disease.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

PEMBINAAN SEMULA KORONARI ARTERI TIGA DIMENSI BERDASARKAN KEPADA PENDAFTARAN ANGIOGRAFI TUNGGAL DAN ULTRABUNYI INTRAVASKULAR

Oleh

SUHAILI BINTI BEERAN KUTTY

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Kadar kematian akibat kegagalan jantung atau penyakit jantung telah meningkat di seluruh dunia. Penyakit arteri koronari (CAD) adalah salah satu jenis penyakit jantung yang disebabkan oleh proses aterosklerosis. Prosesnya dimulakan dengan penumpukan plak di sepanjang dinding dalaman arteri koronari. Penyumbatan arteri akan mengurangkan aliran darah yang beredar melalui jantung. Pengurangan aliran darah ke jantung boleh menyebabkan sakit angina atau dada dan serangan jantung. Angiografi koronari sinar-X adalah ujian berpiawaian emas untuk menyiasat arteri yang terjejas, namun, modaliti ini hanya menggambarkan saluran arteri. Untuk membantu proses diagnosis, Ultrasound Intravaskular (IVUS) yang berdasarkan teknologi ultrabunyi digunakan untuk menunjukkan struktur dalaman arteri. Angiografi koronari dan IVUS saling melengkapi. Walau bagaimanapun, untuk menggunakan angiografi koronari dan IVUS pada masa serentak, pakar kardiologi melihat kedua-dua kaedah pada skrin yang sama tetapi dalam tetingkap yang berbeza dan menggabungkan kedua-dua modality secara mental menggunakan mercu tanda biologi dan juga berdasarkan pengetahuan dan pengalaman mereka. Pendaftaran mental boleh menyebabkan kesilapan dalam penafsiran plak dan memakan masa. Oleh kerana itu, kajian mengenai pendaftaran Angiografi dan IVUS telah diketengahkan sehingga hari ini. Sebilangan besar pendekatan pendaftaran sebelumnya berdasarkan Angiografi dwi-satah yang memerlukan dos radiasi yang lebih besar dan teknik umum untuk pendaftaran adalah berdasarkan geometri epipolar. Kelemahan teknik ini ialah sekurang-kurangnya dua pandangan angiografi koronari diperlukan dan pendekatan penganggaran digunakan dalam menentukan titik-titik yang terlibat. Dalam penyelidikan ini, pendaftaran dicadangkan untuk menggunakan Angiografi satah tunggal, yang merupakan teknologi pengimejan perubatan yang masih relevan dan digunakan di banyak makmal kateterisasi di seluruh dunia, untuk membina semula arteri 3D berdasarkan pendaftaran dengan modaliti IVUS. Pertama, modaliti IVUS; bentuk kateter, lumen dan media-Adventitia disegmen sepenuhnya menggunakan pelabelan dan model ubah bentuk parametrik. Seterusnya, lintasan arteri disusun semula berdasarkan jalur kateter IVUS

dan mercu tanda biologi yang terdapat pada gambar angiografi koronari. Kaedah baru untuk membina semula arteri koronari 3D berdasarkan persamaan trigonometri lingkaran untuk pendaftaran angiografi koronari satah tunggal dan IVUS diperkenalkan dalam penyelidikan ini. Untuk membantu proses diagnosis CAD, penyelidikan ini menawarkan pengukuran tepat dari luas keratan rentas lumen, diameter lumen minimum, dan diameter lumen maksimum. Dalam segmentasi IVUS, hasilnya menunjukkan bahawa 100% bentuk kateter pada gambar IVUS dikesan dengan betul menggunakan pendekatan pelabelan. Ketepatan segmentasi lumen meningkat dengan peratusan perbezaan kawasan (PAD) 0.07, dan segmentasi media-Adventitia dapat dilakukan tanpa proses inisialisasi manual. Hal ini juga membuktikan bahawa lintasan arteri dapat dihasilkan hanya menggunakan satu pandangan Angiografi yang mengandungi jalur kateter IVUS. Seterusnya, ketepatan persamaan yang digunakan dalam eksperimen pendaftaran dapat diterima di mana ditunjukkan oleh P adalah 0.9999 lebih tinggi daripada nilai signifikan. Hasilnya, pendekatan baru pendaftaran Angiografi satah tunggal dan IVUS untuk menghasilkan arteri koronari 3D diterima oleh pengamal perubatan. Model 3D menunjukkan lokasi kateter di arteri tepat dan arteri koronari diukur melalui luas keratan rentas lumen dan diameter minimum dan maksimum. Hasil kajian ini dapat membantu kita memahami pandangan membujur arteri koronari dan morfologi dinding arteri. Ini dapat digunakan oleh ahli kardiologi untuk membuat keputusan dalam mendiagnosis penyakit arteri koronari.

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With the name of Allah, the Most Compassionate and Most Merciful;

Peace and blessings of Allah be upon our Prophet Muhammad (S.A.W);

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The most beautiful dua' for my lovely parents,

"My Lord, have mercy upon them as they brought me up [when I was] small." (Qur'an 17:24)

This thesis was submitted to the Senate of the Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Doctor of Philosophy. The members of the Supervisory Committee were as follows:

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Date: 08 July 2021

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LIST OF ABBREVIATIONS

3D	Three dimensional
AHA	American Heart Association
ANN	Artificial Neural Network
BNM	Bank Negara Malaysia
CAD	Coronary Artery Disease
CHD	Coronary Heart Disease
CSA	Cross Sectional Area
CT	Computed Tomography
CTA	Computed Tomography Angiography
CTC	Clinical Training Centre
CVD	Cardiovascular Disease
DICOM	Digital Imaging and Communications in Medicine
ECG	Electrocardiogram
EEM	External Elastic Membrane
ESS	Endothelial Shear Stress
GVF	Gradient Vector Flow
ICP	Iterative Closest Point
IEM	Internal Elastic Membrane
IVUS	Intravascular Ultrasound
JPEG	Joint Photographic Experts Group
LAD	Left Anterior Descending Artery
LCA	Left Coronary Artery
MRI	Magnetic Resonance Imaging
OCT	Optical Coherence Tomography
PACS	Picture Archiving and Communication Systems
PAD	Percentage of Area Difference

PCI	Percutaneous Coronary Intervention
PET	Positron Emission Tomography
PDE	Partial Differential Equations
QCA	Quantitative Coronary Analysis
RCA	Right Coronary Artery
ROI	Region of Interest
SIFT	Scale-invariant Feature Transform
SPECT	Single Photon Emission Computed
SSD	Sum of Squared intensity Differences
SURF	Speeded Up Robust Features

CHAPTER 1

INTRODUCTION

1.1 Research Background

The distribution of mortality rates caused by heart diseases is widespread all over the world. In Malaysia, ischaemic heart diseases were the principal cause of death in 2018 (Department of Statistics Malaysia, 2019). Heart diseases, including Coronary Artery Disease (CAD), remains the number one cause of death in the US in 2017 and 2018 (J. Xu et al., 2020). Recently, the American Heart Association (AHA) reported that CAD is the most common type of heart disease, killing 365,914 people in 2017 (Benjamin et al., 2019). This is a global issue because the number of CAD cases increases steadily for both genders, men and women (Pathak et al., 2017).

CAD is a disease which happens due to the atherosclerosis process. The process starts by plaque buildup inside the inner walls of the coronary arteries. The process occurs over many years and the obstruction of the coronary artery limits the blood flow circulating through the heart. When the plaque hardens, it blocks the artery, hence reducing blood flow and oxygen to the heart, which causes angina or chest pain and can possibly lead to a heart attack.

CAD can be diagnosed by using an electrocardiogram, blood tests, cardiac stress testing, and cardiovascular imaging techniques, such as echocardiography, coronary angiography, Intravascular Ultrasound (IVUS), Magnetic Resonance Imaging (MRI), and Computed Tomography Angiography (CTA). Coronary angiography has remained the gold standard of the cardiovascular imaging technique to define the presence of vulnerable plaque in the coronary artery (Kočka, 2015; Lim & White, 2013). The cardiologist will inject a contrast dye into one of the patient's veins to highlight the arteries on the x-ray images. This can help guide the cardiologist to diagnose CAD using a visual inspection of the images (Ho et al., 1999).

The main limitation of the coronary angiography is this modality only shows the lumen of the arteries and not the arterial wall (Kočka, 2015). Furthermore, this modality leads to the interobserver variability. Interobserver variability could be defined as a variance of results that were obtained by two or more observers examining the same modality. This is justified by Zir et al. (1976), where they stated that variability in determining the stenosis could lead to variability in the recommendation of the treatment. This issue was also discussed by Venermo et al. (2017).

To eliminate the limitation of coronary angiography, Intravascular Ultrasound (IVUS) technology is used to demonstrate the inner structure of the artery. Both modalities complement each other. The use of IVUS with other modalities serves as an advantage to medical specialists and confirms their understanding of the arterial structure observed (Marrocco et al., 2012).

However, in clinical practice, cardiologists combine these modalities mentally, based on the biological landmarks in the coronary artery, knowledge, and experiences (Mäkelä et al., 2002). This mental integration is very subjective, time-consuming, and can cause an error in the interpretation of the vulnerable plaque (Tu et al., 2011).

To solve this problem, a computation for medical image registration is proposed, where two or more medical images, either from the same modality or different modalities, are combined to help the diagnostic process. The registration will also help solve the limitation of the acquired IVUS images that are not correlated with their exact locations on the angiography modality (Frimerman et al., 2016). In addition, the effect of the use of IVUS technology, as suggested by (Maresca et al., 2014).

From the registration, a three-dimensional (3D) model of the coronary artery can be developed. This model will accurately show the structure of the inner wall and path of the artery. Thus, it eliminates the limitation of the 3D coronary artery by stacking the 2D sequential IVUS, with the assumption that the catheter pullback is straight (Shi et al., 2017).

1.2 Problem Statement

The limitation in the previous proposed registration method is in the IVUS segmentation phase. Ma et al. (2013) stated that the result of the IVUS segmentation will affect the output of the registration. The utmost finding shows that previous works only segmented the lumen before proceeding to the registration phase. They did not emphasize the visualization of the outer wall, which is very important to guide the cardiologist in the diagnostic process. The correlation between wall thickness and CAD had been stated in the study by Gradus-Pizlo et al. (2001), where the coronary artery wall thickness and external diameter are significantly common among patients with CAD.

The previous IVUS segmentation phase also eliminates the catheter area on the IVUS images. This area was assumed to be undesirable and should be removed in the segmentation process (Moraes et al., 2013). Some of the approaches and commercial IVUS viewer software also assume that the position of the catheter be straight in order to display the longitudinal view of the artery, as depicted in Figure 1.1. However, the actual position of the catheter is in accordance with the artery position on the coronary angiography image, as illustrated in Figure 1.2. When the catheter shape is eliminated, the registration for both modalities is not accurate because only the catheter shape is visibly clear in both images.

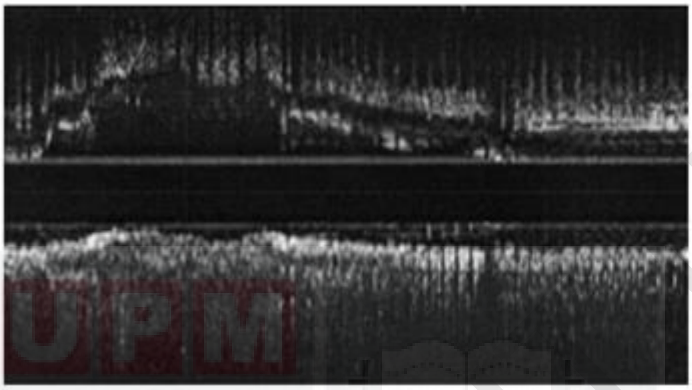

Figure 1.1 : Longitudinal view (L-mode) of IVUS. From "Quantitative Measurements in IVUS Images." By J. Dijkstra, G. Koning & J.H.C. Reiber, 1999, International Journal of Cardiac Imaging, p. 518 (doi: 10.1023/A:1006334517720.). Copyright 1999 by Springer Nature

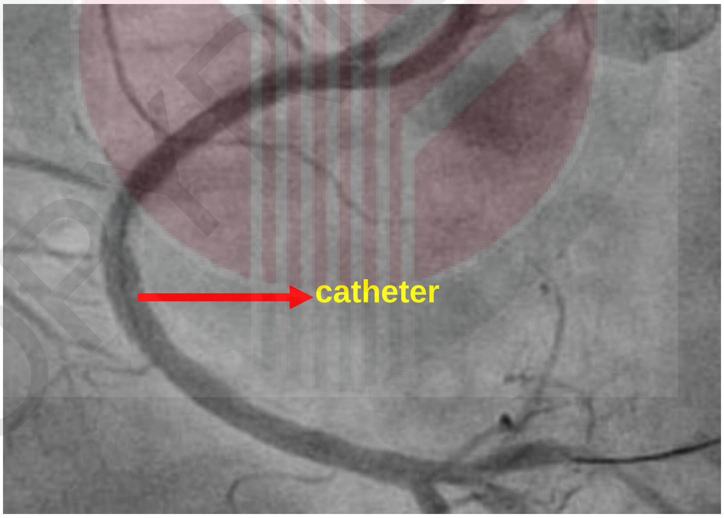

Figure 1.2 : Shape and location of the catheter on coronary angiography image.

Most of the previous studies that proposed the registration between angiography and IVUS, preferred the use of a bi-plane coronary angiography rather than a single-plane angiography. Recently, Takeda et al. (2017) investigated the comparison of radiation dose used for both imaging types. This investigation agreed with the previous experiment conducted by Sadick et al. (2010), where bi-plane technology needs more radiation dose and fluoroscopy time. It also delivered an insignificant reduction in contrast load than single-plane imaging. In addition to that, not all catheterization labs are available with the technology (Guedes et al., 2015), but instead, they still use a single-plane coronary angiography for the diagnostic process.

In terms of the method used in solving the registration between the coronary angiography and IVUS, most of the previous studies used the epipolar technique to construct the trajectory and fused the modalities. The main drawback of this method is at least two views of the coronary angiography are needed, even when single-plane technology is used (Guedes et al., 2015). Moreover, if this technique is used, it is tough to determine the correspondence points in the views (Cong et al., 2015). This is caused by a few factors, such as the heart's beating motion, the variation of positioning the equipment to have the best visualization, and the noises that x-ray pictures produce. Therefore, an approximation is used to determine the correspondence points of two or more views (Bourantas et al., 2005).

From the previous works of IVUS and angiography registration, the measurement of the artery was only provided by researchers, Cornelis J Slager et al. (2000), and Doulaverakis et al. (2013). The measurement of the artery is crucial because it will lead to the diagnosis interpretation. Rentoukas & Lazaros (1999) have outlined the guidelines for implementing IVUS measurements via lumen cross-sectional area (CSA), maximum and minimum lumen diameter. Based on these three important measurements, other measurements could be defined, such as the lumen eccentricity and atheroma cross-sectional area, which is vital to help with the CAD diagnosis.

As a summary, the problems that need to be solved are as follows:

1. Limitations in the current IVUS segmentation process include only detecting the lumen area without emphasizing the outer layer and eliminating the catheter shape, the most important region that can be used as correspondence points in the registration process.
2. In the registration process, most of the previous studies focused on the use of the Bi-plane Angiography modality and used the epipolar technique. This technique requires more than two views of images and an approximation of correspondence points. Bi-plane angiography needs a greater radiation dose and longer procedural time. Furthermore, single-plane coronary angiography is still used in many catheterization labs.
3. The insufficiency in providing the size or measurement of the coronary artery after the registration process.

1.3 Objective

Ultimately, the main goal of this research project is to propose a new framework for 3D coronary artery reconstruction. The framework is based on the registration of single-plane coronary angiography and IVUS. It will assist medical specialists to perform diagnosis and treatments by providing them with the relationship between these two modalities. The following are the objectives of the study:

i. To improve the segmentation of IVUS modality by detecting the catheter shape area, lumen, and media adventitia layer using thresholding and deformable model method.
ii. To register the single-plane coronary angiography and IVUS, using circle trigonometry equation to reconstruct the 3D coronary artery.
iii. To compute measurement of lumen cross sectional area, minimum lumen diameter, and maximum lumen diameter, based on image-based solution for coronary artery analysis.

1.4 Significance of the Study

This research project explores how the 3D coronary artery model could be developed by merging two imaging technologies. Both technologies have their advantages and disadvantages yet registering them makes the output complement each other. Hopefully, this research project could be used to reconstruct a 3D artery model that can be used as a tool to diagnose CAD accurately. The model could also be printed using a 3D printer, used as an augmented reality application for education purposes, as well as to better explain and describe the problem to the patient or their kin, rather than sketching it on paper or giving a verbal description.

The positive impacts of this research project are as follows:

i. The IVUS completely segmented and detected catheter shape could be used in correcting the longitudinal view of the IVUS.
ii. Accurate quantitative measurement of the lumen CSA, minimum lumen diameter, and maximum lumen diameter can be used to define another measurement that can help the CAD diagnostic process.
iii. Eliminates subjectivity in terms of merging coronary angiography and IVUS to have a complete structure of the coronary artery.
iv. New technique in image registration process.

1.5 Scope of the Study

This research project deals with the two modalities images taken by single C-arm x-ray coronary angiography devices and intravascular ultrasound machines. The input data for this research are taken from the available repository in the catheterization lab.

1.6 Thesis Structure

The thesis is organized as per the following:

i. Chapter 1 designates the introduction of this thesis. It starts with the research background that describes what motivates the initiation of this exploration. The research objectives are then described, following the explanation on the limitations of the existing approaches carried out by various researchers. Later in this chapter, the significance and scope of this research project are also stated for clarification.
ii. Chapter 2 presents the literature review for this research project, which starts with an introduction and the description of the human heart and coronary artery disease. Detailed descriptions of the modalities used in this research are also stated. Following that, the role of the 3D coronary artery is explained and the methods that can be used to reconstruct the artery model based on the registration technique is then described for further understanding. After that, reviews on the previous studies including IVUS segmentation, IVUS measurement, and the registration technique are presented.
iii. Chapter 3 presents the research methodology conducted throughout this research project. The chapter thoroughly discusses all the steps that were used to make this research project possible, including the project framework, preliminary research carried out prior to the preparation and implementation, and finally the validation phases.
iv. Chapter 4 to Chapter 6 cover the contributions of this research to the field, which includes the IVUS segmentation, IVUS measurement, and the newly proposed technique for the registration process. These chapters extensively describe the proposed methodology and its implementation, the experimental results with relevant and important discussions, along with detailed explanations on the advantages and limitations of the proposed method and its summary.
v. Chapter 7 is the last chapter of this thesis and it concludes the overall achievements and discoveries made in this research project. It also sums up the advantages and limitations of this work and proposes for some potential improvements or advancement that can be carried out in the future.

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