MATHEMATICAL MODELLING OF BLOOD FLOW IN A CATHETERIZED ARTERY WITH TIME VARIANT MULTIPLE STENOSES

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DEDICATION

This thesis is dedicated to my loving Abba Father in heaven, for the favors granted me throughout the course of my studies. It is also dedicated to my parents and siblings, for their blessing and my dearest friends, Angeline, Husna, Jing Jing, Khiy Wei for supporting me throughout this journey.

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ABSTRACT

Mathematical modelling of Newtonian blood flow in a catheterized stenosed artery is considered. A catheter which is a long, and hollow thin tube is a clinical device to diagnose and treat certain diseases. However, the insertion of a catheter into the blood vessel will alter and disturb the hemodynamic characteristics of blood flow. In this research, the effect of physical parameters of the catheter in an eccentric position is investigated in a tapered artery with multiple stenoses taking the cosine shape varying with time. The governing equations which consist of a system of non-linear partial differential equations are analytically solved using the perturbation technique under the assumption of axisymmetric, unsteady, fully developed laminar flow. A Mathematica software package is developed to assist in the solution procedure which is complicated and tedious. The results for axial velocity have been compared and validated in the case of a single stenosis. In a multiple stenosed artery, it is found that with the increase of eccentricity parameter and radius of catheter, the axial velocities across the three stenoses decrease drastically. If the velocity of catheter is increased, the wall shear stress has the highest value in the case of diverging tapered multiple stenosed artery. The increase of catheter radius has significant effect on the impedance at the location of the first and third stenosis. In both single and multiple stenosed artery, the streamline patterns show that the trapping bolus is formed near the wall of stenosis and in between stenosis when the physical parameters of eccentric catheter increases. It is found that the ratio of the catheter's size to the artery should be less than 0.2 and must be placed at an eccentric position of 0.1 to avoid artery's rupture.

ABSTRAK

Permodelan matematik bagi aliran darah Newtonan di dalam arteri yang berkateter dipertimbangkan. Kateter adalah peranti klinikal yang merupakan suatu tiub panjang, nipis dan berongga digunakan untuk mendiagnosis atau merawat penyakit tertentu. Walau bagaimanapun, sisipan kateter ke dalam saluran darah akan mengubah dan mengganggu ciri hemodinamik aliran darah. Kajian ini adalah mengenai kesan parameter fizikal kateter pada kedudukan eksentrik di dalam arteri tirus dengan beberapa stenosis berbentuk kosinus yang berubah terhadap masa. Persamaan menakluk terdiri daripada suatu sistem persamaan terbitan separa tak linear telah diselesaikan secara analisis menggunakan kaedah usikan dengan andaian bahawa aliran lamina terbentuk penuh, simetri sepaksi dan tak mantap. Pakej perisian Matematica dibina untuk membantu prosedur penyelesaian yang rumit dan memerlukan ketelitian. Keputusan berkaitan dengan halaju aksial telah dibandingkan dan disahkan bagi kes stenosis tunggal. Bagi arteri stenosis berganda, didapati peningkatan parameter eksentrik dan radius kateter menurun dengan drastik bagi halaju aksial untuk ketiga-tiga stenosis. Sekiranya halaju kateter meningkat, tegasan ricih dinding arteri mencapai nilai maksimum bagi kes arteri stenosis berganda tirus mencapah. Peningkatan radius kateter memberi kesan ketara terhadap rintangan di lokasi stenosis pertama dan ketiga. Bagi kedua-dua arteri stenosis tunggal dan berganda, corak garis arus menunjukkan bahawa bolus pemerangkap terbentuk berhampiran dengan dinding stenosis serta di antara dua stenosis apabila parameter fizikal kateter eksentrik meningkat. Kajian mendapati nisbah saiz kateter kepada arteri perlu kurang daripada 0.2 dan diletak pada kedudukan eksentrik 0.1 untuk mengelakkan kemungkinan arteri mengalami ruptur.

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LIST OF ABBREVIATIONS

PCI	-	Percutaneous Coronary Intervention
FFR	-	Fractional Flow Reserve

LIST OF SYMBOLS

d	-	Location of stenosis
R_e	-	Reynolds number
$R_1(z,t)$	-	Geometry of Single Cosine Stenosis
$R_2(z,t)$	-	Geometry of Multiple Cosine Stenosis
R_0	-	Constant radius of normal artery
p	-	Fluid pressure
t	-	Time
ρ	-	Density of fluid
ω	-	Angular frequency of forced oscillation
ϕ	-	Angle of tapering
μ	-	Dynamic viscosity
τ_w	-	Wall shear stress
σ	-	Radius of catheter
θ	-	Angle of circumferential direction
v_z	-	Axial velocity
dp/dz	-	Pressure gradient
l_0	-	Stenosis length of single cosine stenosis
L_0	-	Length of artery
ψ	-	Stream function
ϵ	-	Eccentricity parameter
δ	-	Maximum height of stenosis

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CHAPTER 1

INTRODUCTION

1.1 Research Background

According to the statistics published by Ministry of Health Malaysia (2017), the principal cause of death in government and private hospital is the disease of circulatory system, which is 24.38% of the overall cause of death. Besides that, according to Department of Statistics Malaysia (2017), the principal cause of death in 2016 is coronary heart diseases, which stand for 13.2% of the overall cause of death in Malaysia. Coronary heart disease or coronary artery disease, is a disease which the blood flow is restricted or reduced when the arteries are narrowed, less blood and oxygen reaches the heart muscles thus ultimately leads to heart attack. Most coronary heart diseases are caused by atherosclerosis or stenosis, which is the coronary arteries become narrowed by a gradually build up fatty material within the artery lumen (Philip *et al*., 2013).

There are several ways to treat patients who are at high risk of developing coronary heart disease such as injection of an anticoagulant, thrombolysis, embolectomy, amputation or revascularization. All such treatment requires the use of catheter to direct the drug or treatment towards targeted location. A catheter is made of a long, skinny, flexible plastic tube that generally inserted or injected into a body cavity, duct or vessel, which allow drainage or injection of fluids or to treat diseases and perform a surgical procedure under X-ray guidance. The procedure of inserting a catheter is called catheterization. According to Arman *et al.* (2011), Percutaneous Coronary Intervention (PCI), also known as coronary angioplasty, first used in 1977, is a procedure where a guiding catheter is introduced via femoral, brachial or radial artery, and is positioned near the target stenosis or atherosclerosis. A balloon catheter is then advanced over and then inflated at the site of the stenosis to increase the luminal diameter as referred as Figure 1.1.

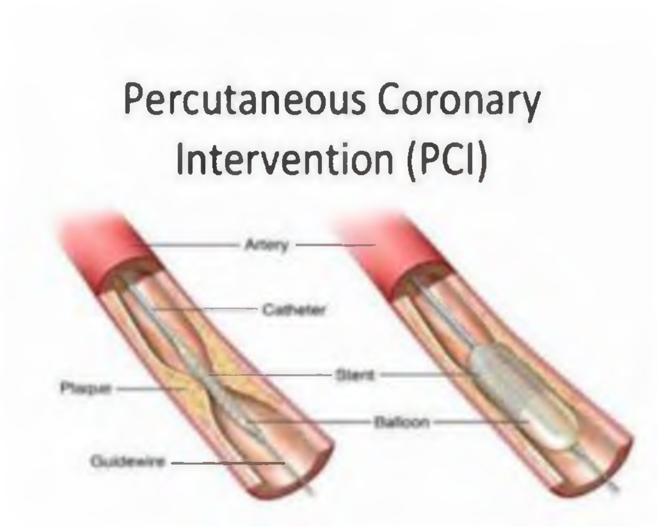

Figure 1.1 Percutaneous Coronary Intervention (PCI)
(https://speciality.medicaldialogues.in/does-robotically-assisted-pci-in-complex-cases-work-study-finds-out/)

Furthermore, cardiac catheterization is a general term of the insertion of a catheter into a chamber or vessel of the heart for a group of procedures such as coronary angioplasty, balloon septostomy, electrophysiology study, catheter ablation or Fractional Flow Reserve (FFR). Due to the evolution of coronary balloon angioplasty, there has been extensive increase in the use of catheter of various sizes. These includes the guiding catheter mentioned above, whose tip is positioned in the coronary ostium. Other than that, doppler catheter is used in the procedure with the tip positioned proximal to the coronary lesion. Thus, catheter is a very important medical device used for medical diagnosis and it has many clinical applications.

Moreover, in catheterization laboratory, the extensive usage of FFR has become nowadays gold standard for invasive assessment of physiological stenosis significance and is an indispensable tool for decision making in coronary revascularization as compared with coronary angiography due to its accuracy and lesion-specific index to indicate whether a particular stenosis or coronary segment can be held responsible for ischemia (Pijls *et al.*, 1993; De Bruyne *et al.*, 1994). FFR value is defined as the ratio of maximal blood flow achievable in a stenotic coronary artery relative to the maximal blood flow in the same vessel if it were normal. The measurement of the two flows requires the usage of a guiding catheter and a pressure wire. A pressure sensory tipped coronary angioplasty guide catheter is introduced through the neck artery into coronary artery to measure the coronary pressure within the artery. It has been observed that due to the injection of catheter into the blood vessel or artery, the blood flow is altered results in the formation of annular region between the wall of the catheter and artery. Hence, the presence of catheter disturbs the hemodynamic factors such as pressure distribution, wall shear stress and resistance in the artery. Any size of the guiding catheter can be used yet it is important to realize that, depending on the relative size of guiding catheter and the coronary ostium, the presence of the catheter can impede coronary flow (Gabor *et al.*, 2016).

In many cases of previous study, most of the assumptions made neglected the importance of physiological effects such as the flexible vessel wall of artery, the flow is time dependent and the geometry of the stenosis. In reality, artery is tapered. Additionally, when the arteries become severely diseased, the arterial lumen become locally restricted by the stenosis that builds up. Thus and so, it is importance to define the geometry of stenosis according to time variant.

No attempts have been made yet to discuss the effect of eccentric catheter characteristics on blood flow through an artery with time variant multiple cosine stenoses. Thus, an appropriate model of blood flow is designed to discuss the mathematical representation for the effect of eccentric catheter characteristics on blood flow through a catheterized stenosed artery.

1.2 Problem Statement and Research Questions

When performing cardiac catheterization procedure, the catheter that inserted into a blood vessel would cause blood clots at the tips of the arterial guiding catheter and thus blood flow is blocked. Aside from that, the insertion of a guiding catheter into a blood vessel would also alter the flow field in the blood vessel and disturbs the hemodynamic conditions. The presence of time variant stenosis with different geometry could also affects the flow of blood through the catheterized artery.

Hence, the research questions are:

i. How does the insertion of an eccentric catheter affect the blood flow characteristics in the presence of time variant single cosine stenosis?

ii. How does the eccentric catheter affect the hemodynamic condition such as axial velocity, wall shear stress, impedance of blood flow through time variant multiple cosine stenosed artery?

1.3 Objectives of the Study

The objectives of this research are

i. To determine the effect of physical parameters of an eccentric catheter on the characteristics of Newtonian blood flow through a time variant single cosine stenosed artery

ii. To determine the effect of specific physical parameter of an eccentric catheter on blood flow characteristics through a time variant multiple cosine stenosed artery

iii. To develop a *Mathematica* package based on the mathematical model that can simulate the behavior of the blood flow characteristics through time variant cosine single stenosis and multiple stenoses

1.4 Scope of the Study

The scope of the study is limited to a mathematical modeling of blood flow through two different time variant geometry of stenosed arteries in the presence of an eccentric catheter. The geometry of the stenosis is a time variant single cosine stenosis, which is considered by Zaman *et al.* (2015). The geometry of stenosis for multiple stenoses is modified from single cosine stenosis of Zaman *et al.* (2015) to become time variant multiple cosine stenoses. The blood flow is assumed to be incompressible, Newtonian, axisymmetric and laminar. The arterial wall is considered as a cylindrical tube with cosine stenosis developed in its lumen. The Newtonian model of blood viscosity is considered.

1.5 Research Methodology

The flow of research methodology undertaken in this study is

i. Literature review of blood flow in catheterized artery, the geometry of stenosis, the usage of catheter in clinical technologies and Newtonian rheology of blood flow

ii. Identify the problem statement

iii. Development of a mathematical model governing the physical situation of a catheterized artery with time variant multiple stenoses

iv. Non-dimensionalization of the governing equations and solved using perturbation method to find the analytical solution

v. Develop a Mathematica package that help in obtaining the analytical solution

vi. Analysis and interpretation of results obtained for axial velocity, wall shear stress, impedance and streamline

1.6 Significance of the Study

The significance of the study is the behaviour of blood flow through a catheterized artery with time variant multiple stenoses can be determined. Besides that, the understanding of the flow through blood vessel with the presence of single and multiple stenoses can provide the possibility of diagnosing the effect of the eccentric catheter towards blood flow and hence an early treatment can be provided.

In addition, the presence of stenosis that builds up on the arterial lumen can cause turbulence and reduce flows. Very high shear stresses near the throat of the stenosis can activate platelet and thereby induce thrombosis, which can totally block blood flow to the heart muscle. Thus, detection and quantification of stenosis while performing catheterization in FFR serves as the basis for surgical intervention. Moreover, knowledge about the domain of biomechanics associated with the blood flow through catheterized artery with time variant multiple stenoses is achieved. This configuration and the related results could be very useful in the development of various clinical related technologies and equipment especially in the usage of FFR.

1.7 Outline of Thesis

This thesis is divided into seven chapters including this introductory chapter. Chapter 1 presents the general introduction, research background, the research questions and objectives, the scope of the study, research methodology and the significance of the study. In this research, the effect of different physical parameters of eccentric catheter on unsteady Newtonian blood flow through time variant multiple stenosed artery is investigated.

In Chapter 2, the literature review is presented. This chapter begins by discussing the previous works on the blood flow through a catheterized artery. There will be a brief discussion of the study of the geometry of the stenosis in the next section. The practical usage of guiding catheter in various clinical related technologies is also studied. In addition, the literature on the boundary conditions and the Newtonian rheology of blood flow properties is included.

Chapter 3 disclosed the derivation of governing equations for the mathematical model. Mathematical model for unsteady blood flow through catheterized artery with two different geometry of stenosis associated with boundary conditions is presented. Besides that, the solution procedure in solving the unsteady blood flow through catheterized stenosed artery is discussed. The solution procedure begins with the conversion of the governing equations into non-dimensional governing equations. The process is then continued with the determination of the analytical solution of the non-dimensionalized governing equations using perturbation method. A Mathematica package is developed and attached in Appendix B.

Chapter 4 accounts for the unsteady blood flow through a time variant single cosine stenosed artery under the effect of eccentric catheter. The effect of physical parameter of eccentric catheter on blood flow characteristics such as axial velocity, wall shear stress, streamlines and impedance are studied and discussed.

In Chapter 5, the mathematical model of blood flow through time variant multiple cosine stenosed artery with specific physical parameter of eccentric catheter obtained from Chapter 4 is considered. The effects of specific values of catheter radius, catheter's velocity and eccentricity parameter on axial velocity, impedances and streamline are discussed. The consideration of angle of tapering of the stenosed artery is studied along with the effects of specific values of catheter radius, catheter's velocity and eccentricity parameter on variation of wall shear stress distribution.

Finally, in Chapter 6, the summary of the work on blood flow through catheterized artery with time variant multiple stenoses is presented and conclusion is addressed. Some useful recommendations to overcome this study and the suggestions on possible extension of this research are also given.

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