

**COMPUTATIONAL ANALYSIS ON STENT GEOMETRIES IN CAROTID
ARTERY**

MUHAMMAD SUFYAN AMIR BIN PAISAL

A thesis submitted in fulfillment of the requirement for the award of the
Degree of Master of Mechanical Engineering by Research



PTTA UTHM
PERPUSTAKAAN TUNKU TUN AMINAH

**Faculty of Mechanical and Manufacturing Engineering
Universiti Tun Hussein Onn Malaysia**

AUGUST 2018

I dedicate this thesis to my beloved Umi, Abah, Angah, Acik, Haikal and Damia. Not to be forgotten, this thesis is also dedicated to my handsome supervisors, Dr Ishkrizat Taib, Assoc Prof Ts Dr Al Emran Ismail and Dr Ahmad Mubarak Tajul Ariffin.



PTTA UTHM
PERPUSTAKAAN TUNKU TUN AMINAH

ACKNOWLEDGEMENT

In the name of Allah, the Most Merciful and the Most Beneficent,

Alhamdulillah and praise to Allah who gave me the strength to finish this thesis. I am heartily thankful and express my sincere gratitude to my parent, Che Hasmah Binti Mat Hassan and Paisal Bin Salim, and also to my siblings for the continuous support and motivation.

I also would like to express my gratitude to my supervisor, Dr. Ishkrizat Bin Taib, co-supervisors, Assoc. Prof. Ts. Dr. Al Emran Bin Ismail, Dr. Ahmad Mubarak Bin Tajul Ariffin and not to be forgotten, Assoc. Prof. Dr. Norzelawati Binti Asmuin, for their encouragement, advices, guidance, constructive suggestions, ideas, knowledge and sharing their expertise to me for developing full understanding of this research.

I also would like to express an appreciation to my families, housemates of Taman Siswa Jaya, laboratory technicians, faculty members, research group members especially Dr. Mohd Hafizal bin Hanipah, Riyadhusollehan Bin Khairulfuaad, Muhammad Faqhrurrazi Bin Abd Rahman and all my friends for their untiring prayer, inspiration, encouragement and support.

Lastly, I would like to offer my regard and blessings to all of those support me in any respect during the completion of this thesis. May Allah bless all of us with success and guidance whether in this world and the here's after.

ABSTRACT

Stent implantation is an alternative invasive technique for treating the narrowed artery or stenosis in carotid artery to restore blood to the brain. However, the restenosis process is usually observed after a few weeks of carotid stenting due to abnormal progression of atherosclerosis and thrombosis. Many studies reported that the activity of atherosclerosis and thrombosis is majorly influenced by the geometrical strut configuration. Thus, this study was carried out to determine the haemodynamic performance on different geometrical stent strut configurations based on numerical modelling and statistical analyses. Six different stent strut configurations were 3-D modelled and simulated in different physiological conditions; normal blood pressure (NBP), pre-hypertension (PH) and hypertension stage one (HS1) through computational fluid dynamic (CFD) method. The haemodynamic performance of stent was analysed based on parameters namely time averaged wall shear stress (TAWSS), time averaged wall shear stress gradient (TAWSSG), oscillatory shear index (OSI), relative residence time (RRT) and flow separation parameter (FSP). Meanwhile, Pictorial Selection Method was used to evaluate the best haemodynamic stent performance based on a scoring system. From observation, stent Type VI was seen to show the highest score for TAWSS, which was 2.98 in overall physiological condition. For TAWSSG, the lowest score was observed for Type V stent with 0.51. Furthermore, Type VI stent displayed the highest score for OSI while Type IV has the lowest score for FSP with 2.08 and 0.28, respectively. On the other hand, RRT was seen varying according to the physiological condition where the highest score in NBP and PH conditions were achieved by Type I while HS1 condition was achieved by Type V. In conclusion, Type VI has the best stent performance, whereas Type IV has the worst stent performance according to the scoring system based on haemodynamic parameters. Further, Type I, Type II, Type III and Type V stents showed moderate hemodynamic performances for all physiological conditions.

ABSTRAK

Implantasi *stent* adalah teknik invasif alternatif untuk merawat *stenosis* atau arteri ter sempit pada arteri karotid untuk mengembalikan aliran darah ke otak. Walau bagaimanapun, proses *restenosis* diperhatikan berlaku setelah beberapa minggu menjalani angioplasti karotid dan *stenting* disebabkan oleh perkembangan aterosklerosis dan trombosis yang tidak normal. Banyak kajian melaporkan aktiviti aterosklerosis dan trombosis adalah sangat dipengaruhi oleh konfigurasi geometri *strut*. Jadi, kajian ini dijalankan bagi menentukan prestasi hemodinamik pada geometri konfigurasi *strut stent* yang berbeza berdasarkan pemodelan berangka dan analisis statistik. Enam konfigurasi *strut stent* yang berbeza dimodelkan secara tiga dimensi dan disimulasikan dalam keadaan fisiologi yang berbeza; tekanan darah normal (*NBP*), pra-hipertensi (*PH*) dan peringkat hipertensi satu (*HS1*) melalui kaedah pengkomputeran dinamik bendalir (*CFD*). Prestasi hemodinamik *stent* dianalisis berdasarkan parameter-parameter iaitu tegasan ricih dinding purata masa (*TAWSS*), kecerunan tekanan geseran dinding purata masa (*TAWSSG*), indeks osilasi ricih (*OSI*), masa kediaman relatif (*RRT*) dan parameter pemisahan aliran (*FSP*). Kaedah Piktorial Pemilihan *Stent* digunakan bagi menilai prestasi *stent* hemodinamik terbaik berdasarkan sistem pemarkahan tertentu. Daripada pemerhatian, *stent* Type VI menunjukkan skor *TAWSS* tertinggi secara purata iaitu 2.98 dalam keseluruhan keadaan fisiologi. Bagi *TAWSSG*, skor terendah diperhatikan pada *stent* Type V adalah 0.51. *Stent* Type VI mempunyai skor *OSI* tertinggi manakala Type IV mempunyai skor *FSP* terendah, masing-masingnya adalah 2.08 dan 0.28. *RRT* berbeza-beza mengikut keadaan fisiologi yang mana skor tertinggi dalam keadaan *NBP* dan *PH* dicapai oleh Type I manakala keadaan *HS1* dicapai oleh Type V. Kesimpulannya, Type VI mempunyai prestasi *stent* terbaik manakala Type IV mempunyai prestasi *stent* terburuk berkenaan sistem pemarkahan berdasarkan parameter hemodinamik. Seterusnya, *stent* Type I, Type II, Type III dan Type V menunjukkan prestasi hemodinamik sederhana untuk semua keadaan fisiologi.

CONTENTS

TITLE	i
DECLARATION	ii
DEDICATION	iii
ACKNOWLEDGEMENT	iv
ABSTRACT	v
ABSTRAK	vi
CONTENTS	vii
LIST OF TABLES	xi
LIST OF FIGURES	xiv
LIST OF SYMBOLS AND ABBREVIATIONS	xviii
LIST OF APPENDICES	xxii
CHAPTER 1 INTRODUCTION	1
1.1 Background of Study	1
1.2 Problem Statement	3
1.3 Objective	3
1.4 Scope of Study	3
1.5 Significance of Study	4
CHAPTER 2 LITERATURE REVIEW	5
2.1 Introduction	5
2.2 Stenosis in Normotensive and Hypertensive Carotid Artery	5
2.3 Stent Implantation in Stenosed Carotid Artery	9
2.4 Induced Arterial Restenosis by Implanted Stent	13
2.5 Effects of Stent Strut Configuration on Blood Flow	15
2.5.1 Single Stent Strut	16
2.5.2 Repetitive Strut Pattern of Stent	17

2.6	<i>In Silico</i> Studies of Haemodynamic Parameters of Stented Artery	19
2.7	Evaluation Method of Stent Performance	26
2.8	Design Selection method on the Medical Device of Cannula	28
2.9	Incompatibility of using Rubric Scoring for Determining Weights of Haemodynamic Parameters	29
2.10	Decision Making Process on Allocating Weights of Criteria	31
2.8	Summary	32
CHAPTER 3 METHODOLOGY		33
3.1	Introduction	33
3.2	Flow Chart of the Study	34
3.3	Simplified Geometry of Carotid Artery	36
3.4	Stent Strut Geometrical Configuration	37
3.5	Parameter Assumptions and Boundary Conditions	39
3.6	Meshing of Stented Carotid Artery Models	43
3.7	Computational Fluid Dynamics Governing Equations	45
3.8	Validation Data of Numerical Simulation for the Present Study	45
3.9	Haemodynamic Parameters of Stented Carotid Artery	46
3.9.1	Time Averaged Wall Shear Stress (TAWSS)	47
3.9.2	Time Averaged Wall Shear Stress Gradient (TAWSSG)	47
3.9.3	Oscillatory Shear Index (OSI)	48
3.9.4	Relative Residence Time (RRT)	49
3.9.5	Flow Separation Parameter (FSP)	49
3.10	Percentage Change of Haemodynamic Performance	49
3.11	Statistical Properties for Stent Performance Evaluation	50
3.12	Decision Making Process on the Weight Allocation	51
3.13	Stent Pictorial Selection Method	53
3.12	Evaluation of Haemodynamic Parameters and	55

Statistical Properties on Stent Performance Through
MATLAB

**CHAPTER 4 COMPARISON OF HAEMODYNAMIC
CHARACTERISTICS AMONG THE STENTED**

CAROTID ARTERY **58**

4.1	Introduction	58
4.2	Validation of Numerical Simulation	58
4.2.1	Pulsatile Velocity Waveform of Computational Model Inlet	58
4.2.2	Mean Velocity Profile in Common Carotid Artery	60
4.3	Grid Independent Test (GIT) of Computational Model	60
4.4	Y+ Distribution Near Wall of the Present Computational Model	62
4.5	Difference Between Non-Newtonian and Newtonian Blood	63
4.6	Wall Shear Stress (WSS) Development on Stented Artery	64
4.7	Time Averaged Wall Shear Stress (TAWSS)	67
4.8	Time Averaged Wall Shear Stress Gradient (TAWSSG)	73
4.9	Oscillatory Shear Index (OSI)	77
4.10	Relative Residence Time (RRT)	81
4.11	Flow Separation Parameter (FSP)	85
4.12	Haemodynamic Parameters Due to Different Stent Strut Configurations	89

CHAPTER 5 EVALUATION OF STENTED CAROTID ARTERY

USING STENT PICTORIAL SELECTION METHOD **91**

5.1	Introduction	91
5.2	Performance of Statistical Properties on Haemodynamic Parameters	91
5.2.1	Statistical Distribution of TAWSS	91
5.2.2	Statistical Distribution of TAWSSG	96

5.2.3 Statistical Distribution of OSI	99
5.2.4 Statistical Distribution of RRT	102
5.2.5 Statistical Distribution of FSP	105
5.3 Evaluation of Stent Geometrical Performance Through Stent Pictorial Selection Method	108
5.3.1 Screening Process	108
5.3.2 Rating Process	109
5.3.2.1 Rating of TAWSS	110
5.3.2.2 Rating of TAWSSG	113
5.3.2.3 Rating of OSI	114
5.3.2.4 Rating of RRT	115
5.3.2.5 Rating of FSP	117
5.3.3 Scoring Process	119
5.3.3.1 Scoring of TAWSS	120
5.3.3.2 Scoring of TAWSSG	121
5.3.3.3 Scoring of OSI	122
5.3.3.4 Scoring of RRT	123
5.3.3.5 Scoring of FSP	125
5.3.3.6 Rank of Stent for Specific Physiological Condition	126
CHAPTER 6 CONCLUSION	129
6.1 Conclusion	129
6.2 Recommendations for Future Work	130
REFERENCES	132
APPENDIX A–H	149
VITA	

LIST OF TABLES

2.1	Correlation of blood pressure against thickness of carotid artery as atherosclerotic plaque progression	7
2.2	Classification of high blood pressure	7
2.3	Blood pressure of specific velocity waveform	9
2.4	Geometrical stent designs	10
2.5	Detailed information of the selected commercial stents	11
2.6	Post-procedural event rates and restenosis hazard ratios at increasing free cell area	13
2.7	Post-procedural event rates after 30 days for patients stented with opened and closed type cell	14
2.8	Post-procedural event rates for each carotid stent	15
2.9	Chronological criteria of hemodynamic parameter for stented artery	20
2.10	Justification of the haemodynamic parameters for stented artery part 1	21
2.11	Justification of the haemodynamic parameters for stented artery part 2	22
2.12	Chronological justification on turbulent blood flow	23
2.13	Chronological justification on blood as non-Newtonian fluid	24
2.14	Chronological study on blood using SST viscous model	25
2.15	Statistical properties of PS, GR-II and Bx stent	28
3.1	Dynamic viscosity at each cardiac phase for all physiological conditions	40
3.2	Velocity at each cardiac phase for all physiological	

conditons	40
3.3 Empirical parameters of Fourier series for each blood condition	42
3.4 Weight consideration matrix	52
3.5 Weight considered for each haemodynamic parameter	52
3.6 Reference data of luminal surface area covered by haemodynamic specific parameter	53
3.7 Screening stage matrix	54
3.8 Rate of relative stent performance	54
3.9 Rating stage matrix	54
3.10 Scoring stage matrix	55
4.1 Maximum y^+ at peak-systolic phase for all study cases	63
4.2 TAWSS _{low} ($TAWSS < 0.5 \text{ Pa}$) distribution exposure to luminal surface area	71
4.3 TAWSS _{norm} ($1.0 \text{ Pa} \geq TAWSS \geq 7.0 \text{ Pa}$) distribution exposure to luminal surface area	72
4.4 TAWSS _{high} ($TAWSS > 7.0 \text{ Pa}$) distribution exposure to luminal surface area	73
4.5 TAWSSG $\leq 5000 \text{ Pa/m}$ distribution exposure to luminal surface area	77
4.6 OSI ≤ 0.2 distribution exposure to luminal surface area	81
4.7 RRT $\leq 10 \text{ Pa}^{-1}$ distribution exposure to luminal surface area	85
4.8 FSP _{low} ($FSP < 0.1$) distribution exposure to luminal surface area	89
4.9 FSP _{high} ($FSP > 0.5$) distribution exposure to luminal surface area	89
4.10 Discrepancy of luminal surface area of stent strut configurations for different haemodynamic parameter	91
5.1 Statistical properties of TAWSS	95
5.2 Statistical properties of TAWSSG	98
5.3 Statistical properties of OSI	101

5.4	Statistical properties of RRT	104
5.5	Statistical properties of FSP	107
5.6	Screening of stent performance in NBP condition	109
5.7	Screening of stent performance in PH condition	109
5.8	Screening of stent performance in HS1 condition	109
5.9	Statistical properties rating for TAWSS distribution	111
5.10	Rating of TAWSS _{low} distribution exposure to luminal surface area	112
5.11	Rating of TAWSS _{norm} distribution exposure to luminal surface area	112
5.12	Rating of TAWSS _{high} distribution exposure to luminal surface area	112
5.13	Rating for statistical properties and percentage of luminal surface area exposed to TAWSSG $\leq 5000 \text{ Pa/m}$	113
5.14	Rating for statistical properties and percentage of luminal surface area exposed to OSI ≤ 0.2	115
5.15	Rating for statistical properties and percentage of luminal surface area exposed to RRT $\leq 10 \text{ Pa}^{-1}$	116
5.16	Statistical properties rating for FSP distribution	118
5.17	Rating of FSP _{low} distribution exposure to luminal surface area	119
5.18	Rating of FSP _{high} distribution exposure to luminal surface area	119
5.19	Scoring of TAWSS performance	120
5.20	Scoring of TAWSSG performance	122
5.21	Scoring of OSI performance	123
5.22	Scoring of RRT performance	124
5.23	Scoring of FSP performance	125
5.24	Ranking of stent performance	126

LIST OF FIGURES

2.1 (a) Angiography of CCA shaded with pink colour in red circle and (b) illustration of stenosis in CCA	6
2.2 Velocity waveform in CCA for (A) normal, (B) pre-hypertension and (C) hypertension stage 1 for both male and female	9
2.3 Difference of self-expandable and balloon-expandable stent	12
2.4 Illustration of closed and opened type cell	12
2.5 Parameter on single strut which θ is angle, l_a is length of amplitude and l_c is width of curvature	16
2.6 Varying parametric strut design (a), (b), (c) and (d) using axial strut pitch h , strut amplitude f and curvature radius r	17
2.7 CFD analysis of (a) WSS and (b) WSSG for four different design of stent configurations	18
2.8 Normalised TAWSS for stent BX Velocity, Driver, Integrity and Vision	19
2.9 WSS distribution for (a) Newtonian and (b) non-Newtonian flow	25
2.10 Distribution of viscosity that correspond around the stent struts	26
2.11 (a) PS, (b) GR-II and (c) Bx stent	26
2.12 WSS distribution of blood in artery stented with (a) PS, (b) GR-II and (c) Bx stent	27
2.13 Example of concept-scoring matrix	28
2.14 The screening matrix by Darlis in 2016	29

2.15	The weighted scoring matrix by Darlis in 2016	29
2.16	Example of rubric scoring; Rohwedder's welding rubric	30
2.17	A decision making processes by Robbins <i>et al.</i> in 2012 which is focusing on weights allocation as bounded by red dashed line	31
3.1	Process of stent haemodynamic performance evaluation part 1	34
3.2	Process of stent haemodynamic performance evaluation part 2	35
3.3	The simplified model of carotid artery, where CCA (green) is common carotid artery, ECA (yellow) is external carotid artery, CS (blue) is carotid sinus and ICA (red) is internal carotid artery	37
3.4	Geometrical shape of Type I, Type II, Type III, Type IV, Type V and Type VI that resembled to the existing stent strut configurations	38
3.5	Geometrical shape of each stent strut configuration (dark grey region shows stent and light grey region shows artery model)	39
3.6	Boundary conditions of carotid artery model	41
3.7	Meshing of stented carotid artery model with the effect of (a) 'body sizing' and (b) inflation	43
3.8	Computational model with centerline MN	44
3.9	CCA velocity waveform	46
3.10	Mean velocity profile	46
3.11	Linear distribution of weight consideration	52
3.12	Algorithm of haemodynamic parameters computation	55
3.13	Algorithm of Stent Pictorial Selection Method	56
4.1	Velocity waveform in common carotid artery of present study as compared to experimental data for different physiological condition of (a) NBP, (b) PH	59

and (c) HS1	
4.2 Mean velocity profile of blood in CCA for both present study and previous experimental data	60
4.3 Velocity profile along carotid artery for different number of nodes	61
4.4 Normalised relative error percentage (Ne) on sampled nodes of specific GIT setting	62
4.5 Y+ distribution on stented arterial wall produced by Type II in PH condition	62
4.6 Blood rheological test on (a) straight line MN with (b) resulting TAWSS	64
4.7 Velocity waveform categorised into cardiac phases for all blood conditions	64
4.8 Distribution of area covered by WSS ranging from 1.0 to 7.0 Pa at each cardiac phase for (a) NBP, (b) PH and (c) HS1 blood condition	66
4.9 Different result on varying geometrical perspectives for haemodynamic model with (a) non-visible and (b) visible stent	67
4.10 TAWSS distribution at stent strut configuration for NBP condition	68
4.11 TAWSS distribution at stent strut configuration for PH condition	69
4.12 TAWSS distribution at stent strut configuration for HS1 condition	70
4.13 TAWSSG distribution at stent strut configuration for NBP condition	74
4.14 TAWSSG distribution at stent strut configuration for PH condition	75
4.15 TAWSSG distribution at stent strut configuration for HS1 condition	76
4.16 OSI distribution at stent strut configuration for NBP	78

condition	
4.17 OSI distribution at stent strut configuration for PH condition	79
4.18 OSI distribution at stent strut configuration for HS1 condition	80
4.19 RRT distribution at stent strut configuration for NBP condition	82
4.20 RRT distribution at stent strut configuration for PH condition	83
4.21 RRT distribution at stent strut configuration for HS1 condition	84
4.22 FSP distribution at stent strut configuration for NBP condition	86
4.23 FSP distribution at stent strut configuration for PH condition	87
4.24 FSP distribution at stent strut configuration for HS1 condition	88
5.1 TAWSS statistical distribution for NBP condition	93
5.2 TAWSS statistical distribution for PH condition	94
5.3 TAWSS statistical distribution for HS1 condition	95
5.4 TAWSSG statistical distribution for NBP condition	96
5.5 TAWSSG statistical distribution for PH condition	97
5.6 TAWSSG statistical distribution for HS1 condition	98
5.7 OSI statistical distribution for NBP condition	99
5.8 OSI statistical distribution for PH condition	100
5.9 OSI statistical distribution for HS1 condition	101
5.10 RRT statistical distribution for NBP condition	102
5.11 RRT statistical distribution for PH condition	103
5.12 RRT statistical distribution for HS1 condition	104
5.13 FSP statistical distribution for NBP condition	105
5.14 FSP statistical distribution for PH condition	106
5.15 FSP statistical distribution for HS1 condition	107

LIST OF SYMBOLS AND ABBREVIATIONS

a_0	-	Initial empirical parameter a
a_n	-	Empirical parameter a at n th number
A_i	-	Surface area of face i
b_n	-	Empirical parameter b at n th number
d_P	-	End-diastolic
D	-	Diameter
D_P	-	Peak-diastolic
f	-	Strut amplitude
F	-	Fourier function
\vec{g}	-	Gravitational acceleration vector
h	-	Axial strut pitch
h_S	-	Thickness of stent
Hct	-	Hematocrit index
i_1	-	First incisura
i_2	-	Second incisura
K	-	Kurtosis
l_a	-	length of amplitude
l_c	-	Width of curvature
l_s	-	Length of stent
n	-	Number
\vec{n}	-	Normal vector
n_A	-	Normal to surface area
N_∞	-	Consistency index
Ne	-	Normalised relative error
Q, \dot{V}	-	Flow rate
r	-	Curvature radius

r_o	-	Stent outer radius
r_{ij}	-	Raw rating of stent j for stent performance i
Re	-	Reynolds number
Rt	-	Rating
S_j	-	Weighted score summation
S_I	-	Peak-systolic
S_2	-	Second systolic
t, T	-	Time
ν	-	Kinematic viscosity
V	-	Velocity magnitude
\vec{V}	-	Velocity vector
w	-	Weightage
α	-	Blood flow direction
β	-	Normal to blood flow direction
$\dot{\gamma}$	-	Shear rate
μ_d	-	Dynamic viscosity
μ_p	-	Plasma viscosity
μ_∞^2	-	Yield stress
ω	-	Angular frequency
ρ	-	Density
τ	-	Shear stress
$\vec{\tau}_{ij}$	-	Fluid viscous stress tensor
ψ	-	Flow separation parameter
μ	-	Mean
σ	-	Standard deviation
φ_i	-	Haemodynamic characteristics at face i
φ_{perc}	-	Area distribution percentage of haemodynamic parameter
φ_{ref}	-	Reference area distribution percentage of haemodynamic parameter
φ_{PC}	-	Percentage change
$\varphi_{highest}$	-	The highest variable performance

φ_{lowest}	-	The lowest variable performance
∇	-	Vector differential operator
θ	-	Angle
3-D	-	Three dimensional
AAA	-	Abdominal aortic aneurysm
AWSS	-	Axial wall shear stress
CAD	-	Computer-aided design
CCA	-	Common carotid artery
CFD	-	Computational Fluid Dynamic
CS	-	Carotid sinus
DBP	-	Diastolic Blood Pressure
ECA	-	External carotid artery
FEA	-	Finite element analysis
FSP	-	Flow separation parameter
FSP_{low}	-	Low flow separation parameter
FSP_{high}	-	High flow separation parameter
FSI	-	Fluid-structure interaction
FVM	-	Finite volume method
GIT	-	Grid Independent Test
HS1	-	Hypertension stage one
ICA	-	Internal carotid artery
IMT	-	Intimal-Medial Thickening
MR	-	Magnetic resonance
NBP	-	Normal blood pressure
OSI	-	Oscillatory shear index
PH	-	Pre-hypertension
PIV	-	Particle Image Velocimetry
RRT	-	Relative residence time
SBP	-	Systolic Blood Pressure
SST	-	Shear stress transport
TAWSS	-	Time averaged wall shear stress
$TAWSS_{low}$	-	Low time averaged wall shear stress

TAWSS _{norm}	– Normal time averaged wall shear stress
TAWSS _{high}	– High time averaged wall shear stress
TAWSSG	– Time averaged wall shear stress gradient
TIA	– Transient ischemic attack
WSS	– Wall shear stress
WSSG	– Wall shear stress gradient
WSSAD	– Wall shear stress angle deviation
WSSAG	– Wall shear stress angle gradient



PTTA UTHM
PERPUSTAKAAN TUNKU TUN AMINAH

LIST OF APPENDICES

A	Gantt Chart	149
B	Outflow Calculation for FLUENT Setup	150
C	User Defined Function for Inlet Velocity Waveform FLUENT Setup	151
D	CFD Post Processing Script for AWSS Multi-Results Extraction	153
E	Main Algorithm for Stent Analysis	156
F	Algorithm of Haemodynamic Parameters Computation	158
G	Algorithm of Statistical Properties	161
H	Algorithm of Stent Pictorial Selection Method	163

CHAPTER 1

INTRODUCTION

1.1 Background of Study

Moderate restenosis with 50% of an arterial diameter reduced is reported to have an occurrence rate about 40.7% while severe restenosis with 70% of the arterial diameter reduced has an occurrence rate about 10.6% within five years after stent implantation [1]. Meanwhile in the first month after stent implantation, the restenosis or re-blockage in the artery is already occurs due to atherosclerosis and growth of thrombosis [2]. Atherosclerosis is the hardening of arterial wall caused by a plaque build-up of fatty material while thrombosis is the formation of blood clot within the lining of an artery especially in stented artery. The thrombogenic process is accelerated due to the effect of misalignment of blood flow direction near the stent strut that gives tiny injury on the arterial wall [3]. This abnormality of blood movement makes the fatty materials to be deposited near the stent strut configuration. The arterial injury causes the arterial wall to undergo an episodic process of thrombus formation, arterial inflammation, neointimal hyperplasia and stent remodelling [2].

Previous study reported a different strut configuration that have a significant progress of an atherosclerosis and thrombosis formation [4]. The significant progress is due to each of the stent has its own strut configuration presenting different flow characteristic near to the strut. Thus, the significant progress allows the haemodynamic performance of the stent to be predicted. However, different vascular region has presented different flow characteristic that highly depends on the vascular

morphologies. Since this study focuses on carotid artery, the vertical direction of blood flow was highly concerned. Many studies reported that the suitable stent strut configuration has been suggested to have an opened type cell, self-expandable with material made up of nitinol [5, 6]. Even though the conventional stent strut configurations are carefully chosen, the post-procedural event rates after 30 days of stent implantation due to restenosis are still random [7]. Hence, this study aimed at determining the flow phenomenon near geometrical pattern of the stent strut configuration, which plays the main role in predicting the process of restenosis.

The restenosis development of carotid artery implanted with different geometrical stent strut configuration can be invasively analysed and predicted with the current numerical simulation technology via computational fluid dynamic (CFD) method. The use of CFD method has emerged as a powerful tool to predict blood flow patterns in stented artery with the development of electronic computers before undergoing the *in vivo* study. Thus, the restenosis due to misalignment of blood flow direction causing recirculation and vortex near the stent strut can be numerically detected [8]. Additionally, several haemodynamic variables are very useful in predicting the restenosis of blood flow consist of time averaged wall shear stress (TAWSS), time averaged wall shear stress gradient (TAWSSG), oscillatory shear index (OSI), relative residence time (RRT) and flow separation parameter (FSP) [2]. Based on previous studies, these haemodynamic parameters have specific threshold or range of values to indicate the activity of atherosclerosis and thrombosis that reflect the restenosis development [9–14].

From each haemodynamic variables, a statistical distribution is obtained to evaluate the best stent performance based on the threshold of acceptable values determined by previous studies [15, 16]. The stent performance evaluation known as Stent Pictorial Selection Method was used in this study adapted from the Concept Selection Method by Ulrich *et al.*, which originally evaluates the concept design of a product [17]. The evaluation method is able to detect the best stent strut configuration with the lowest score of restenosis development. Thus, this study is aimed at statistically evaluating the haemodynamic performance of different stent geometrical designs in different physiological conditions especially normotensive and hypertensive blood flow.

1.2 Problem Statement

Different stent strut configurations influence the progress of restenosis formation especially in bifurcated carotid artery [4]. Restenosis is caused by the development of atherosclerosis at the stent strut and episodic process of thrombosis consisting of thrombus formation, arterial inflammation, neointimal hyperplasia and stent remodelling.

The progress of atherosclerosis and thrombosis formation is highly dependent on the haemodynamic effect at carotid wall, which is presented as a flow recirculation at the stent strut configuration. This phenomenon occurs due to misaligned blood flow direction in an artery especially in common carotid artery to external and internal carotid artery. Furthermore, many studies reported that the stent geometrical design has resulted in a random value of post-procedural event rate due to restenosis development within 30 days after stent implantation [7, 18, 19].

Thus, restenosis development that induced by the flow recirculation due to the misaligned direction of blood flow, is identified as the main issue in the present study. In addition, different geometries of stent strut configuration have different behaviour of blood flow recirculation.

1.3 Objective

- i. To determine the haemodynamic effect on different stent strut configurations in carotid artery during the specific physiological conditions.
- ii. To analyse critical haemodynamic parameters affecting the flow characteristic due to different stent strut configurations in carotid artery.
- iii. To evaluate the stent performance due to haemodynamic effect on different strut configurations in the carotid artery.

1.4 Scope of Study

- i. Physiological conditions consist of normal blood pressure (NBP), pre-hypertension (PH) and hypertension stage one (HS1).
- ii. Opened type cell stent for six different strut configurations were considered.
- iii. Simplified model of carotid artery for normal morphology was considered.
- iv. Stent strut configuration was implanted at the luminal region of common carotid artery.

REFERENCES

- [1] Bonati, L. H., Gregson, J., Dobson, J., McCabe, D. J. H., Nederkoorn, P. J., van der Worp, H. B., de Borst, G. J., Richards, T., Cleveland, T., Müller, M. D., Wolff, T., Engelter, S. T., Lyrer, P. A. and Brown, M. M. Restenosis and risk of stroke after stenting or endarterectomy for symptomatic carotid stenosis in the International Carotid Stenting Study (ICSS): secondary analysis of a randomised trial. *Lancet Neurol.*, 2018, 17: 587–596.
- [2] Murphy, J. and Boyle, F. Predicting Neointimal Hyperplasia in Stented Arteries Using Time-Dependant Computational Fluid Dynamics: A Review. *Comput. Biol. Med.*, 2010, 40(4): 408–418.
- [3] Cohen, B. J. and DePetris, A. *Medical Terminology: An Illustrated Guide*. Philadelphia: Lippincott Williams & Wilkins. 2013.
- [4] Paraskevas, K. I. and Veith, F. J. Techniques and Innovations to Improve Carotid Artery Stenting Outcomes. *Int. J. Cardiol.*, 2016, 222(2016): 986–987.
- [5] Rabe, K., Franke, J. and Sievert, H. *Practical Handbook of Advanced Interventional Cardiology: Tips and Tricks*. 3rd edition. Massachusetts: Blackwell Publishing. 2009.
- [6] Lin, P. H., Poi, M. J., Matos, J., Kougias, P., Bechara, C. and Changyi, C. *Schwartz's Principles of Surgery*. 10th edition. New York City: McGraw-Hill Education. 2015.
- [7] Bosiers, M., De Donato, G., Deloose, K., Verbist, J., Peeters, P., Castriota, F., Cremonesi, A. and Setacci, C. Does Free Cell Area Influence the Outcome in Carotid Artery Stenting?. *Eur. J. Vasc. Endovasc. Surg.*, 2007, 33(2): 135–141.
- [8] Guccione, J. M., Kassab, G. S. and Ratcliffe, M. B. *Computational Cardiovascular Mechanics Modelling and Applications in Heart Failure*. 1st

- edition. New York: Springer. 2010.
- [9] Malek, A. M., Alper, S. L. and Izumo, S. Hemodynamic Shear Stress and Its Role in Atherosclerosis. *Jama*, 1999, 282(21): 2035–2042.
 - [10] Murphy, J. and Boyle, F. Comparing Stent Design Using Computational Fluid Dynamics to Predict Wall Shear Stress Based Parameters. *Bioengineering in Ireland 15 Conference*. January 30–31, 2009.
 - [11] LaDisa, J. F., Guler, I., Olson, L. E., Hettrick, D. A., Kersten, J. R., Warltier, D. C. and Pagel, P. S. Three-Dimensional Computational Fluid Dynamics Modeling of Alterations in Coronary Wall Shear Stress Produced by Stent Implantation. *Ann. Biomed. Eng.*, 2003, 31(8): 972–980.
 - [12] Nandini, D., Schoephoerster, R. T. and Moore Jr, J. E. Comparison of Near-wall Hemodynamic Parameters in Stented Artery Models. *J. Biomech. Eng.*, 2009, 131(6): 1–22.
 - [13] Balossino, R., Gervaso, F., Migliavacca, F. and Dubini, G. Effects of Different Stent Designs on Local Hemodynamics in Stented Arteries. *J. Biomech.*, 2008, 41(5): 1053–1061.
 - [14] He, Y., Duraiswamy, N., Frank, A. O. and Moore, J. E. Blood Flow in Stented Arteries: A Parametric Comparison of Strut Design Patterns in Three Dimensions. *J. Biomech. Eng.*, 2005, 127(4): 637–647.
 - [15] Murphy, J. B. and Boyle, F. J. A Numerical Methodology to Fully Elucidate the Altered Wall Shear Stress in a Stented Coronary Artery. *Cardiovasc. Eng. Technol.*, 2010, 1(4): 256–268.
 - [16] Taib, I. *Improvement of Haemodynamic Stent Strut Configuration for Patent Ductus Arteriosus through Computational Modelling*. Ph.D. Universiti Teknologi Malaysia; 2016.
 - [17] Ulrich, K. T. and Eppinger, S. D. *Product Design and Development*. 5th edition. Singapore: McGraw-Hill. 2012.
 - [18] Schillinger, M., Gschwendtner, M., Reimers, B., Tremkler, J., Stockx, L., Mair, J., Macdonald, S., Karnel, F., Huber, K. and Minar, E. Does Carotid Stent Cell Design Matter?. *Stroke*, 2008, 39(3): 905–909.
 - [19] De Donato, G., Setacci, C., Deloose, K., Peeters, P., Cremonesi, A. and Bosiers, M. Long-Term Results of Carotid Artery Stenting. *J. Vasc. Surg.*, 2008, 48(6): 1431–1441.
 - [20] Himburg, H. A., Grzybowski, D. M., Hazel, A. L., LaMack, J. A., Li, X. M.

- and Friedman, M. H. Spatial comparison between wall shear stress measures and porcine arterial endothelial permeability. *Am J Physiol Hear. Circ Physiol*, 2004, 286: H1916–H1922.
- [21] Robbins S. P. and Coulter, M. *Management*, 11th edition. Upper Saddle River: Prentice Hall, 2012.
 - [22] Darlis, N. *Improvement of spiral flow aortic cannula for cardiopulmonary bypass operation*. Ph.D. Universiti Teknologi Malaysia; 2016.
 - [23] Hoya, K., Morikawa, E. and Tamura, A. Common Carotid Artery Stenosis and Amaurosis Fugax. *J. Stroke Cerebrovasc. Dis.*, 2008, 17(1): 1–4.
 - [24] Berg, M., Vanninen, R. and Manninen, H. *Imaging of Carotid Artery Stenosis*. St. Stefan: Springer Wien New York. 2007.
 - [25] Dudley, S. R. *Mastering Catering Science*. Basingstoke: Macmillan Education. 1988.
 - [26] Woo, S. Y., Joh, J. H., Han, S. and Park, H. Prevalence and risk factors for atherosclerotic carotid stenosis and plaque. *Medicine (Baltimore)*., 2017, 96(4): e5999.
 - [27] Chobanian, A. V., Bakris, G. L., Black, H. R., Cushman, W. C., Green, L. A., Izzo, J. L., Jones, D. W., Materson, B. J., Oparil, S., Wright, J. T. and Roccella, E. J. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*, 2003, 42(6): 1206–1252.
 - [28] National Heart Foundation of Australia. *Guideline for the diagnosis and management of hypertension in adults*. Melbourne: National Heart Foundation of Australia. 2016.
 - [29] Whelton, P. K., Carey, R. M., Aronow, W. S., Casey, D. E., Collins, K. J., Himmelfarb, C. D., DePalma, S. M., Gidding, S., Jamerson, K. A., Jones, D. W., MacLaughlin, E. J., Muntner, P., Ovbiagele, B., Smith, S. C., Spencer, C. C., Stafford, R. S., Taler, S. J., Thomas, R. J., Williams, K. A., Williamson, J. D. and Wright, J. T. Guideline for the Prevention , Detection , Evaluation , and Management of High Blood Pressure in Adults. *Hypertension*, 2017.
 - [30] Ghiadoni, L., Taddei, S., Virfis, A., Sudano, I., Legge, V. D., Meola, M., Venanzio, L. D. and Salvetti, A. Endothelial Function and Common Carotid Artery Wall Thickening in Patients with Essential Hypertension. *Hypertension*, 1998, 32(1): 25–32.

- [31] Su, T., Jeng, J., Chien, K., Sung, F., Hsu, H. and Lee, Y. Hypertension Status Is the Major Determinant of Carotid Atherosclerosis. *Stroke*, 2001, 32: 2265–2271.
- [32] Litwin, M., Trelewicki, J., Wawer, Z., Antoiewicz, J., Wierzbicka, A., Rajszys, P. and Grenda, R. Intima-Media Thickness and Arterial Elasticity in Hypertensive Children: Controlled Study. *Pediatr. Nephrol.*, 2004, 19(7): 767–774.
- [33] Lábrová, R., Honzíková, N., Maderová, E., Vysocanová, P., Nováková, Z., Závodná, E., Fišer, B. and Semrád, B. Age-Dependent Relationship Between the Carotid Intima-Media Thickness, Baroreflex Sensitivity, and the Inter-Beat Interval in Normotensive and Hypertensive Subjects. *Physiol. Res.*, 2005, 54(6): 593–600.
- [34] Zakopoulos, N. A., Tsivgoulis, G., Barlas, G., Papamichael, C., Spengos, K., Manios, E., Ikonomidis, I., Kotsis, V., Spiliopoulou, I., Vemmos, K., Mavrikakis, M., Moulopoulos, S. D. Time Rate of Blood Pressure Variation Is Associated with Increased Common Carotid Artery Intima-Media Thickness. *Hypertension*, 2005, 45(4): 505–512.
- [35] Azhim, A., Sakagami, K., Ueno, A., Kinouchi, Y. and Fukui, Y. Independent factors of Flow Velocity Indices in Common Carotid Artery. *World Congress on Medical Physics and Biomedical Engineering*. 2013. 39: 445–448.
- [36] Klabunde, R. E. *Cardiovascular Physiology Concepts*. 2nd edition. Baltimore: Lippincott Williams & Wilkins. 2004.
- [37] Wilkinson, I. B., Fuchs, S. A., Jansen, I. M., Spratt, J. C., Murray, G. D., Cockcroft, J. K. and Webb, D. J. Reproducibility of pulse wave velocity and augmentation index measured by pulse wave analysis. *J. Hypertens.*, 1998, 16: 2079–2084.
- [38] Takeuchi, S. and Karino, T. Flow Patterns and Distributions of Fluid Velocity and Wall Shear Stress in The Human Internal Carotid and Middle Cerebral Arteries. *World Neurosurg.*, 2010, 73(3): 174–185.
- [39] Deplano, V. and Siouffi, M. Experimental and Numerical Study of Pulsatile Flows Through Stenosis: Wall Shear Stress Analysis. *J. Biomech.*, 1999, 32(10): 1081–1090.
- [40] Hart, J. P., Peeters, P., Verbist, J. and Deloose, K. Do Device Characteristics Impact Outcome in Carotid Artery Stenting?. *J. Vasc. Surg.*, 2006, 44: 725–

- 730.
- [41] Albertini, J.-N., Muller, L., Fouilhé, L. and Clément, C. Techniques Endoluminales de Traitement Des Lesions de la Bifurcation Carotidienne. *EMC - Chir.*, 2005, 2(6): 659–685.
 - [42] Wissgott, C., Schmidt, W., Behrens, P., Brandt, C., Schmitz, K. P. and Andresen, R. Experimental Investigation of Modern and Established Carotid Stents. *RoFo Fortschritte auf dem Gebiet der Rontgenstrahlen und der Bildgeb. Verfahren*, 2014, 186(2): 157–165.
 - [43] Jung, T. and Kim, J. Y. Finite Element Structural Analysis of Self-Expandable Stent Deployment in a Curved Stenotic Artery. *J. Mech. Sci. Technol.*, 2016, 30(7): 3143–3149.
 - [44] Dake, M. D., Alstine, W. G. V., Zhou, Q. and Ragheb, A. O. Polymer-Free Paclitaxel-Coated Zilver PTX Stents - Evaluation of Pharmacokinetics and Comparative Safety in Porcine Arteries. *J. Vasc. Interv. Radiol.*, 2011, 22(5): 603–610.
 - [45] García, A., Peña, E. and Martínez, M. A. Influence of Geometrical Parameters on Radial Force During Self-Expanding Stent Deployment. Application for a Variable Radial Stiffness Stent. *J. Mech. Behav. Biomed. Mater.*, 2012, 10: 166–175.
 - [46] Voûte, M. T., Hendriks, J. M., Laanen, J. H. H. V., Pattynama, P. M. T., Muhs, B. E., Poldermans, D. and Verhagen H. J. M. Radial Force Measurements in Carotid Stents: Influence of Stent Design and Length of the Lesion. *J. Vasc. Interv. Radiol.*, 2011, 22(5): 661–666.
 - [47] Stoeckel, D., Pelton, A. and Duerig, T. Self Expanding Nitinol Stents - Material and Design Considerations. *Eur Radiol.*, 2003, 14(2): 292–301.
 - [48] Fanous, A. A. and Siddiqui, A. H. Mechanical Thrombectomy: Stent Retrievers Vs. Aspiration Catheters. *Cor Vasa*, 2016, 58(2): e193–e203.
 - [49] Fortier, A., Gullapalli, V. and Mirshams, R. A. Review of Biomechanical Studies of Arteries and Their Effect on Stent Performance. *IJC Hear. Vessel.*, 2014, 4(1): 12–18.
 - [50] Gundert, T. J., Marsden, A. L., Yang, W. and LaDisa, J. F. Optimization of Cardiovascular Stent Design Using Computational Fluid Dynamics. *J Biomech Eng*, 2012, 134(1): 11002–10.
 - [51] Kastrati, A., Mehilli, J., Dirschinger, J., Seyfarth, M. and Schmitt, C.

- Restenosis After Coronary Placement of Various Stent Types. *Am. J. Cardiol.*, 2001, 87(1): 34–39.
- [52] LaDisa, J. F., Olson, L. E., Guler, I., Hetrick, D. A., Kersten, J. R., Warltier, D. C. and Pagel, P. S. Circumferential Vascular Deformation after Stent Implantation Alters Wall Stress Evaluated with Time-Dependent 3D Computational Fluid Dynamics Models. *J Appl Physiol*, 2005, 98: 947–957.
- [53] Mejia, J., Ruzzeh, B., Mongrain, R., Leask, R. and Bertrand, O. F. Evaluation of the Effect of Stent Strut Profile on Shear Stress Distribution Using Statistical Moments. *Biomed. Eng. Online*, 2009, 8: 8.
- [54] Gundert T. J., Dholakia, R., McMahon, J. D. and LaDisa, J. F. Computational Fluid Dynamics Evaluation of Equivalency in Hemodynamic Alterations Between Driver, Integrity, and Similar Stents Implanted into an Idealized Coronary Artery. *J. Med. Device.*, 2013, 7(1): 11004.
- [55] Suess, T., Anderson, J., Danielson, L., Pohlson, K., Remund, T., Blears, E., Gent, S. and Kelly, P. Examination of Near-Wall Hemodynamic Parameters in The Renal Bridging Stent of Various Stent Graft Configurations for Repairing Visceral Branched Aortic Aneurysms. *J. Vasc. Surg.*, 2016, 64(3): 788–796.
- [56] Youssefi, P., Gomez, A., He, T., Anderson, L., Bunce, N., Sharma, R., Figueira, C. A. and Jahangiri, M. Patient-Specific Computational Fluid Dynamics – Assessment of Aortic Hemodynamics in a Spectrum of Aortic Valve Pathologies. *J. Thorac. Cardiovasc. Surg.*, 2016, 153(1): 8–20.
- [57] Hsiao, H. M., Lee, K. H., Liao, Y. C. and Cheng, Y. C. Hemodynamic Simulation of Intra-Stent Blood Flow. *Procedia Eng.*, 2012, 36: 128–136.
- [58] Frydrychowicz, A., Stalder, A. F., Russe, M. F., Bock, J., Bauer, S., Harloff, A., Langer, M., Hennig, J. and Markl, M. Three-dimensional analysis of segmental wall shear stress in the aorta by flow-sensitive four-dimensional-MRI. *J. Magn. Reson. Imaging*, 2009, 30(1): 77–84.
- [59] Chaichana, T., Sun, Z. and Jewkes, J. Computation of hemodynamics in the left coronary artery with variable angulations. *J. Biomech.*, 2011, 44(10): 1869–1878.
- [60] Samuelson, R., Nair, P., Snyder, K., Frakes, D., Preul, M. C., Nakaji, P. and Spetzler, R. F. Fluid dynamic characterization of a novel branching anastomosis design. *Int. Biomech.*, 2015, 2(1): 73–78.
- [61] Lu, Y., Li, W., Oraifige, I. and Wang, W. Converging Parallel Plate Flow

- Chambers for Studies on the Effect of the Spatial Gradient of Wall Shear Stress on Endothelial Cells. *J. Biosci. Med.*, 2014, 2(2): 50–56.
- [62] LaDisa, J. F., Olson, L. E., Guler, I., Hettrick, D. A., Audi, S. H., Kersten, J. R., Warltier, D. C. and Pagel, P. S. Stent design properties and deployment ratio influence indexes of wall shear stress: a three-dimensional computational fluid dynamics investigation within a normal artery. *J Appl Physiol*, 2004, 97: 424–430.
- [63] Ahsaas, S. and Tiwari, S. Numerical Simulation of Blood Flow through Asymmetric and Symmetric Occlusion in Carotid Artery. *Proceedings of the 3rd International Conference on Fluid Flow, Heat and Mass Transfer (FFHMT'16)*. May 2–3, 2016.
- [64] Soulis, J. V., Lampri, O. P., Fytanidis, D. K. and Giannoglou, G. D. Relative residence time and oscillatory shear index of non-Newtonian flow models in aorta. *10th International Workshop on Biomedical Engineering*. October 5–7, 2011.
- [65] Mahmoud, M. M., Serbanovic-Cavic, J., Feng, S., Souilhol, C., Xing, R., Hsiao, S., Mammoto, A., Chen, J., Ariaans, M., Francis, S. E., Van der Heiden, K., Ridger, V. and Evans, P. C. Shear stress induces endothelial- to-mesenchymal transition via the transcription factor Snail. *Sci. Rep.*, 2017, 7(1): 3375.
- [66] Miura, Y., Ishida, F., Umeda, Y., Tanemura, H., Suzuki, H., Matsushima, S., Shimosaka, S. and Taki, W. Low wall shear stress is independently associated with the rupture status of middle cerebral artery aneurysms. *Stroke*, 2013, 44(2): 519–521.
- [67] Eshtehardi, P., Brown, A. J., Bhargava, A., Costopoulos, C., Hung, O. Y., Corban, M. T., Hosseini, H., Gogas, B. D., Giddens, D. P. and Samady, H. High wall shear stress and high-risk plaque: an emerging concept. *Int. J. Cardiovasc. Imaging*, 2017, 33(7): 1089–1099.
- [68] Chistiakov, D. A., Orekhov, A. N. and Bobryshev, Y. V. Effects of shear stress on endothelial cells: go with the flow. *Acta Physiol*, 2016, 219(2): 382–408.
- [69] Geoghegan, P. H., Jermy, M. C. and Nobes, D. S. A PIV Comparison of the Flow Field and Wall Shear Stress in Rigid and Compliant Models of Healthy Carotid Arteries. *J. Mech. Med. Biol.*, 2017, 17(4): 1–16.

- [70] Timmins, L. H., Molony, D. S., Eshtehardi, P., McDaniel, M. C., Oshinski, J. N., Giddens, D. P. and Samady, H. Oscillatory wall shear stress is a dominant flow characteristic affecting lesion progression patterns and plaque vulnerability in patients with coronary artery disease. *J. R. Soc. Interface*, 2017, 14: 20160972.
- [71] Saw, S. N., Dawn, C., Biswas, A., Mattar, C. N. Z. and Yap, C. H. Characterization of the in vivo wall shear stress environment of human fetus umbilical arteries and veins. *Biomech. Model. Mechanobiol.*, 2016, 16(1): 197–211.
- [72] John, L., Pustějovská, P. and Steinbach, O. On the influence of the wall shear stress vector form on hemodynamic indicators. *Comput Vis. Sci.*, 2017, 18(4–5): 113–122.
- [73] McCormick, M. E., Manduchi, E., Witschey, W. R. T., Gorman, R. C., Gorman, J. H., Jiang, Y. Z., Stoeckert, C. J., Barker, A. J., Yoon, S., arkl, M. and Davies, P. F. Spatial phenotyping of the endocardial endothelium as a function of intracardiac hemodynamic shear stress. *J. Biomech.*, 2016, 50: 11–19.
- [74] Kanokjaruvijit, K., Donprai-on, T., Phanthura, N., Noidet, P. and Siripokharattana, J. Wall shear stress and velocity distributions in different types of stenotic bifurcations. *J. Mech. Sci. Technol.*, 2017, 31(5): 2339–2349.
- [75] Sano, T., Ishida, F., Tsuji, M., Furukawa, K., Shimosaka, S. and Suzuki, H. Hemodynamic differences between ruptured and unruptured cerebral aneurysms simultaneously existing in the same location: two case reports and proposal of a novel parameter oscillatory velocity index. *World Neurosurg.*, 2017, 98: 868.e5-868.e10.
- [76] Geers, A. J., Morales, H. G., Larrabide, I., Butakoff, C., Bijlenga, P. and Frangi, A. F. Wall shear stress at the initiation site of cerebral aneurysms *Biomech. Model. Mechanobiol.*, 2017, 16(1): 97–115.
- [77] Bergersen, A. W. *Investigating the Link Between Patient-specific Morphology and Hemodynamics : Implications for Aneurism Initiation?* University of Oslo; 2016.
- [78] Soulis, J. V., Fytanidis, D. K., Seralidou, K. V. and Giannoglou, G. D. Wall shear stress oscillation and its gradient in the normal left coronary artery tree bifurcations. *Hippokratia*, 2014, 18(1): 12–16.

- [79] Mut, F., Löhner, R., Chien, A., Tateshima, S., Viñuela, F., Putman, C. and Cebral, J. Computational Hemodynamics Framework for the Analysis of Cerebral Aneurysms. *Int j Numer method biomed eng*, 2011 27(6): 822–839.
- [80] Suzuki, D., Funamoto, K., Sugiyama, S., Hayase, T., Miyauchi, S. and Tominaga, T. Effects of upstream bifurcation and bend on the blood flow in a cerebral aneurysm. *J. Biomech. Sci. Eng.*, 2017, 12(4): 1–11.
- [81] Gayathri, K. and Shailendhra, K. Mathematical investigation of aetiology and pathogenesis of atherosclerosis in human arteries. *Int. J. Bioinforma. Res. Appl.*, 2018, 14(1/2): 3–28.
- [82] Chen, Y. Zhang, P., Deng, X., Fan, Y., Xing, Y. and Xing, N. Improvement of hemodynamic performance using novel helical flow vena cava filter design. *Scientific Reports*, 2017.
- [83] Asiruwa, J. J., Propst, A. M. and Gent, S. P. Hemodynamics Study of Different Take-off Angles of the Left Coronary Artery. *Design of Medical Devices Conference*. April 10–13, 2017.
- [84] Tran, J. S., Schiavazzi, D. E., Ramachandra, A. B., Kahn, A. M. and Marsden, A. L. Automated Tuning for Parameter Identification and Uncertainty Quantification in Multi-scale Coronary Simulations. *Comput. Fluids*, 2016, 142: 128–138.
- [85] Xu, H., Piccinelli, M., Leshnower, B. G., Lefieux, A., Taylor, W. R. and Veneziani, A. Coupled Morphological – Hemodynamic Computational Analysis of Type B Aortic Dissection : A Longitudinal Study. *Ann. Biomed. Eng.*, 2018, 46(7): 927–939.
- [86] Riccardello, G. J., Shastri, D. N., Changa, A. R., Thomas, K. G., Roman, M. Prestigiacomo, C. J. and Gandhi C. D. Influence of Relative Residence Time on Side-Wall Aneurysm Inception,” *Neurosurgery*, 2017.
- [87] Berg, P. and Beuing, O. Multiple intracranial aneurysms : a direct hemodynamic comparison between ruptured and unruptured vessel malformations. *Int. J. Comput. Assist. Radiol. Surg.*, 2017, 13(1): 83–93.
- [88] Van de Velde, L., Donselaar, E. J., Groot Jebbink, E., Boersen, J. T., Lajoinie, G. P. R., de Vries, J. P. M., Zeebregts, C. J., Versluis, M. and Reijnen, M. M. P. J. Partial renal coverage in endovascular aneurysm repair causes unfavorable renal flow patterns in an infrarenal aneurysm model. *J. Vasc. Surg.*, 2018, 67(5): 1585–1594.

- [89] Bit, A. and Chattopadhyay, H. Acute Aneurysm is more Critical than Acute Stenoses in Blood Vessels : a Numerical Investigation Using Stress Markers. *BioNanoSci.*, 2018, 8(1): 329–336.
- [90] Asiruwa, J. J., Propst, A. M. and Gent, S. P. Assessing Near-Wall Hemodynamics of Blood Flow in the Left Anterior Descending Segment of the left Coronary Artery using Computational Fluid Dynamics. *ASME 2017 International Mechanical Engineering Congress and Exposition*. November 3–9, 2017.
- [91] Himeno, M., Noda, S., Fukasaku, K., Himeno, R. and Tadano, S. A method to evaluate relevance of hemodynamic factors to artery bifurcation shapes using computational fluid dynamics and genetic algorithms. *Mech. Eng. J.*, 2017, 4(3): 1–15.
- [92] Terashima, M., Miura, Y., Ishida, F., Toma, N., Araki, T., Shimodaka, S., Kanamaru, K. and Suzuki, H. One-stage Stent-assisted Coil Embolization for Rupture-side-unknown Bilateral Vertebral Artery Dissecting Aneurysms in an Acute Stage : A Case Report. *NMC Case Rep. J.*, 2018, 5: 45–49.
- [93] DePaola, N., Gimbrone, M. A. J., Davies, P. F. and Dewey, C. F. J. Vascular Endothelium Responds to Fluid Shear Stress Gradients. *Arterioscler. Thromb.*, 1992, 12: 1254–1257.
- [94] Filipović, N., Nikolić, D., Saveljić, I., Exarchos, T. and Parodi, O. Experimental Testing and Numerical Modelling of Stents in the Coronary Arteries. *Contemp. Mater.*, 2016, 2(7): 99–108.
- [95] Tanaka, K., Ishida, F., Kawamura, K., Yamamoto, H., Horikawa, D. D., Kishimoto, T., Tsuji, M., Tanemura, H. and Shimosaka, S. Hemodynamic Assessment of Cerebral Aneurysms using Computational Fluid Dynamics (CFD) Involving the Establishment of Non-Newtonian Fluid Properties. *J. Neuroendovascular Ther.*, 2018, 12(6): 1–10.
- [96] Asiruwa, J. J. *Assessing the Near-Wall Hemodynamics in the Left Coronary Artery Using CFD*. South Dakota State University; 2017.
- [97] Zhao, J.-L., Jia, L., Wang, X.-B., Zhang, L.-L., Rong, W.-L., Jiang, J.-W. and Li, M.-H. Effects of adjustable impinging flow on the vascular endothelial cell layer in a modified T chamber. *Int J Clin Exp Med*, 2017, 10(3): 5068–5074.
- [98] Machi, P., Ouared, R., Brina, O., Bouillot, P., Yilmaz, H., Vargas, M. I., Bijlenga, P., Lovblad, K. O. and Kulesár, Z. Hemodynamics of Focal Versus

- Global Growth of Small Cerebral Aneurysms. *Clin Neuroradiol*, 2017.
- [99] Liu, Z., Cai, Y., Chen, G., Lu, G. and Li, Z. Anatomical Variations in Circle of Willis and Intracranial Aneurysm Formation. *MCN*, 2017, 15(1): 19–31.
- [100] Dai, Y., Lv, P., Javadzadegan, A., Tang, X., Qian, Y. and Lin, J. Hemodynamic analysis of carotid artery after endarterectomy: a preliminary and quantitative imaging study based on computational fluid dynamics and magnetic resonance angiography resonance angiography. *Quant Imaging Med Surg*, 2018, 8(4): 399–409.
- [101] Avery, M. *Can Mesenchymal Stem Cells Inhibit the Formation of Saccular Aneurysms?* University of Calgary; 2017.
- [102] Lauric, A., Greim-Kuczewski, K., Antonov, A., Dardik, G., Magida, J. K., Hippelheuser, J. E., Kono, K. and Malek, A. M. Proximal Parent Vessel Tapering is Associated With Aneurysm at the Middle Cerebral Artery Bifurcation. *Neurosurgery*, 2018.
- [103] Tsukui, H., Shinke, M., Park, Y. K. and Yamazaki, K. Longer coronary anastomosis provides lower energy loss in coronary artery bypass grafting. *Heart Vessels*, 2017, 32(1): 83–89.
- [104] Pike, D., Shiu, Y.-T., Somarathna, M., Guo, L., Isayeva, T., Totenhagen, J. and Lee, T. High resolution hemodynamic profiling of murine arteriovenous fistula using magnetic resonance imaging and computational fluid dynamics. *Theor. Biol. Med. Model.*, 2017, 14(5): 1–17.
- [105] Yang, L., Yin, A. and Liu, W. Variation of flow rate and angle of injected venous needle on influencing intimal hyperplasia at the venous anastomosis of the hemodialysis graft. *Australas. Phys. Eng. Sci. Med.*, 2017, 40(1): 239–248.
- [106] Shamloo, A., Nejad, M. A. and Saeedi, M. Fluid–structure interaction simulation of a cerebral aneurysm: effects of endovascular coiling treatment and aneurysm wall thickening. *J. Mech. Behav. Biomed. Mater.*, 2017, 74: 72–83.
- [107] Barber, T. Wall shear stress and near-wall flows in the stenosed femoral artery. *Comput. Methods Biomech. Biomed. Engin.*, 2017, 20(10): 1048–1055.
- [108] Brindise, M. C., Chiastra, C., Burzotta, F., Migliavacca, F. and Vlachos, P. P. Hemodynamics of Stent Implantation Procedures in Coronary Bifurcations: an In Vitro study. *Ann Biomed Eng.*, 2017, 45(3): 542–553.
- [109] Pinto, S. I. S., Castro, C. F., Sousa, L. C. and Campos, J. B. L. M. Numerical

- Study of Atherogenesis Risk Associated to Different Stenotic Arteries. *7th International Conference on Mechanics and MAterials in Design*. June 11–15 2017.
- [110] Varble, N., Rajabzadeh-Oghaz, H., Wang, J., Siddiqui, A., Meng, H. and Mowla, A. Differences in Morphologic and Hemodynamic Characteristics for ‘PHASES-Based’ Intracranial Aneurysm Locations. *Am. J. Neuroradiol.*, 2017, 38(11): 2105–2110.
 - [111] Zhang, X., Lv, N., Wang, C., Cao, W., Liu, J. and Huang, Q. Late recurrence of a completely occluded large intracranial aneurysm treated with a Tubridge flow diverter. *Journal of NeuroInterventional Surgery*, 2016, 9(2).
 - [112] Arzani, A., Shadden, S. C., Gambaruto, A. M. and Chen, G. Wall shear stress exposure time: a Lagrangian measure of near-wall stagnation and concentration in cardiovascular flows. *Biomech. Model. Mechanobiol.*, 2017, 16(3): 787–803.
 - [113] Xiong, J., Hu, Z., Zhang, H., Xu, H., Chen, D. and Guo, W. Successful use of retrograde branched extension limb assembling technique in endovascular repair of pararenal abdominal aortic aneurysm. *J. Vasc. Surg. Cases Innov. Tech.*, 2017, 3(2): 90–94.
 - [114] Chen, Z., Yu, H., Shi, Y., Zhu, M., Wang, Y., Hu, X., Zhang, Y., Chang, Y., Xu, M. and Gao, W. Vascular Remodelling Relates to an Elevated Oscillatory Shear Index and Relative Residence Time in Spontaneously Hypertensive Rats. *Sci. Rep.*, 2017, 7(1): 2007.
 - [115] Tzirakis, K., Kamarianakis, Y., Metaxa, E., Kontopidis, N., Ioannou, C. V. and Papaharilaou, Y. A robust approach for exploring hemodynamics and thrombus growth associations in abdominal aortic aneurysms. *Med. Biol. Eng. Comput.*, 2017, 55(8): 1493–1506.
 - [116] Carrascal, P. G., Garcia, J. G., Pallares, Ruiz, F. C. and Martin, F. J. M. Numerical Study of Blood Clots Influence on the Flow Pattern and Platelet Activation on a Stented Bifurcation Model. *Ann. Biomed. Eng.*, 2016, 45(5): 1279–1291.
 - [117] Duraiswamy, N., Cesar, J. M., Schoephoerster, R. T. and Moore, J. E. Effects of stent geometry on local flow dynamics and resulting platelet deposition in an in vitro model. *Biorheology*, 2008, 45: 547–561.
 - [118] Bradley, W. G., Waluch, V., Fernandez, E. J. and Spalter, C. The Appearance

- of Rapidly Flowing Blood on Magnetic Resonance Images. *AJR*, 1984, 143: 1167–1174.
- [119] Houston, J. G., Gandy, S. J., Sheppard, D. G., Dick, J. B., Belch, J. J. F. and Stonebridge, P. A. Two-Dimensional Flow Quantitative MRI of Aortic Arch Blood Flow Patterns: Effect of Age, Sex, and Presence of Carotid Atheromatous Disease on Prevalence of Spiral Blood Flow. *J. Magn. Reson. Imaging*, 2003, 18(2): 169–174.
- [120] Grigioni, M., Daniele, C., Morbiducci, U., Del Gaudio, C., D'Avenio, G., Balducci, A. and Barbaro, V. A Mathematical Description of Blood Spiral Flow in Vessels: Application to a Numerical Study of Flow in Arterial Bending. *J. Biomech.*, 2005, 38(7): 1375–1386.
- [121] Nakamura, M., Wada, S. and Yamaguchi, T. Computational Analysis of Blood Flow in an Integrated Model of the Left Ventricle and the Aorta. *J. Biomech. Eng.*, 2006, 128(6): 837–843.
- [122] Tanaka, M., Sakamoto, T., Suqawara, S., Nakajima, H., Kameyama, T., Katahira, Y., Ohtsuki, S. and Kanai, H. Spiral Systolic Blood Flow in the Ascending Aorta and Aortic Arch Analyzed by Echo-Dynamography. *J. Cardiol.*, 2010, 56(1): 97–110.
- [123] Liu, X., Fan, Y. and Deng, X. Effect of Spiral Flow on the Transport of Oxygen in the Aorta: A Numerical Study. *Ann. Biomed. Eng.*, 2010, 38(3): 917–926.
- [124] Yukhnev, A. D., Smirnov, E. M., Chumakov, Y. S., Gataulin, Y. A., Kulikov, V. P. and Kirsanov, R. I. Swirling Flow Visualization in Blood Vessels and Its Hydrodynamic Models. *15 th Int. Symp. Flow Vis. ISFV15*, 2012, 1–10.
- [125] Javadzadegan, A., Fakhim, B., Behnia, M. and Behnia, M. Fluid-Structure Interaction Investigation of Spiral Flow in a Model of Abdominal Aortic Aneurysm. *Eur. J. Mech. B/Fluids*, 2014, 46: 109–117.
- [126] Perktold, K., Resch, M. and Florian, H. Pulsatile Non-Newtonian Flow Characteristics in a Three-Dimensional Human Carotid Bifurcation Model. *J. Biomech. Eng.*, 1991, 113(4): 464–75.
- [127] Lou, Z. and Yang, W. J. A Computer Simulation of the Non-Newtonian Blood Flow at the Aortic Bifurcation. *J. Biomech.*, 1993, 26(1): 37–49.
- [128] Gijsen, F. J. H., van de Vosse, F. N. and Janssen, J. D. The Influence of the Non-Newtonian Properties of Blood on the Flow in Large Arteries: Steady

- Flow in A Carotid Bifurcation Model. *J Biomech*, 1999, 32(6): 601–608.
- [129] Johnston, B. M., Johnston, P. R., Corney, S. and Kilpatrick, D. Non-Newtonian Blood Flow in Human Right Coronary Arteries: Transient Simulations. *J Biomech*, 2006, 39(6): 1116–1128.
- [130] Benard, N., Perrault, R. and Coisne, D. Computational Approach to Estimating the Effects of Blood Properties on Changes in Intra-Stent Flow. *Ann. Biomed. Eng.*, 2006, 34(8): 1259–1271.
- [131] Valencia, A., Zarate, A., Galvez, M. and Badilla, L. Non-Newtonian Blood Flow Dynamics in a Right Internal Carotid Artery with a Saccular Aneurysm. *Int. J. Numer. Methods Fluids*, 2006, 50(6): 751–764.
- [132] Bodnár, T., Sequeira, A. and Prosi, M. On the Shear-Thinning and Viscoelastic Effects of Blood Flow under Various Flow Rates. *Appl. Math. Comput.*, 2011, 217(11): 5055–5067.
- [133] Walker, A.M., Johnston, C. R. and Rival, D. E. On The Characterization of a Non-Newtonian Blood Analog and Its Response to Pulsatile Flow Downstream of a Simplified Stenosis. *Ann. Biomed. Eng.*, 2014, 42(1): 97–109.
- [134] Thomas, B. and Sumam, K. S. Blood Flow in Human Arterial System-A Review. *Procedia Technol.*, 2016, 24: 339–346.
- [135] Kagadis, G. C., Skouras, E. D., Bourantas, G. C., Paraskeva, C. A., Katsanos, K., Karnabatidis, D. and Nikiforidis, C. Computational Representation and Hemodynamic Characterization of In Vivo Acquired Severe Stenotic Renal Artery Geometries Using Turbulence Modeling. *Med. Eng. Phys.*, 2008, 30(5): 647–660.
- [136] Jozwik, K. and Obidowski, D. Numerical Simulations of the Blood Flow Through Vertebral Arteries. *J. Biomech.*, 2010, 43(2): 177–185.
- [137] Benim, A. C., Nahavandi, A., Assmann, A., Schubert, D., Feindt, P. and Suh, S. H. Simulation of Blood Flow in Human Aorta with Emphasis on Outlet Boundary Conditions. *Appl. Math. Model.*, 2011, 35(7): 3175–3188.
- [138] Mustafa, I., Ishtiaque,S., Xu, X. Y. and Wood, N. B. Turbulence Modeling in Stenosed Carotid Arteries Using CFD. *Yanbu J. Eng. Sci.*, 2011, 2: 83–90.
- [139] Cheng, Z., Wood, N. B., Gibbs, R. G. J. and Xu, X. Y. Geometric and Flow Features of Type B Aortic Dissection: Initial Findings and Comparison of Medically Treated and Stented Cases. *Ann. Biomed. Eng.*, 2014, 43(1): 177–

- 189.
- [140] Pal, P. Computational Modeling of the Effects of Transient Blood Flow Characteristics and Wall Thickness on the Rupture of Abdominal Aortic Aneurysm. *ASME Int. Mech. Eng. Congr. Expo. Proc.*, January, 2014, 9: 1–8.
 - [141] Catarino, C. R. F. C. *Computational Blood Flow Simulations and Geometric Uncertainty Quantification in Patient-Specific Aorta-Insight*. Master. Technico Lisboa; 2015.
 - [142] Alimohammadi, M., Sherwood, J. M., Karimpour, M., Agu, O., Balabani, S. and Díaz-Zuccarini, V. Aortic Dissection Simulation Models for Clinical Support: Fluid-Structure Interaction Vs. Rigid Wall Models. *Biomed. Eng. Online*, 2015, 14: 34.
 - [143] Gataulin, Y. A., Zaitsev, D. K., Smirnov, E. M., Fedorova, E. A. and Yukhnev, A. D. Weakly Swirling Flow in A Model of Blood Vessel with Stenosis: Numerical and Experimental Study. *St. Petersbg. Polytech. Univ. J. Phys. Math.*, 2015, 1(4): 364–371.
 - [144] Pugh, S. *Concept Selection*. New York: Xerox Corporation. 1987.
 - [145] Brookhart, S. M. *How to Create and Use Rubrics for Formative Assessment and Grading*. Alexandria: ASCD. 2013.
 - [146] Perktold, K., Resch, M. and Peter, R. O. Three-Dimensional Numerical Analysis of Pulsatile Flow and Wall Shear Stress in the Carotid Artery Bifurcation. *J. Biomech.*, 1991, 24(6): 409–420.
 - [147] Datta, A. and Rakesh, V. *An Introduction to Modelling Transport Processes: Applications to Biomedical Systems*. Cambridge: Cambridge University Press. 2010.
 - [148] Pant, S., Bressloff, N. W., Forrester, A. I. J. and Curzen, N. The influence of strut-connectors in stented vessels: A comparison of pulsatile flow through five coronary stents. *Ann. Biomed. Eng.*, 2010, 38(5): 1893–1907.
 - [149] Zhao, H. Q., Nikanorov, A., Virmani, R., Jones, R., Pacheco, E. and Schwartz, L. B. Late Stent Expansion and Neointimal Proliferation of Oversized Nitinol Stents in Peripheral Arteries. *Cardiovasc. Intervent. Radiol.*, 2009, 32(4): 720–726.
 - [150] Chandran, K. B., Yoganathan, A. P. and Rittgers, S. E. *Biofluid Mechanics The Human Circulation*. Boca Raton: Taylor & Francis. 2007.
 - [151] Waite, L. and Fine, J. *Applied Biofluid Mechanics*. New York: McGraw-Hill.

- 2007.
- [152] Walawender, W. P., Chen, T. Y. and Cala, D. F. An Approximate Casson Fluid Model for Tube Flow of Blood. *Biorheology*, 1975, 12(2): 111–119.
 - [153] Cengel, Y. A. and Cimbala, J. M. *Fluid Mechanics Fundamentals and Applications*. 3rd edition. New York: McGraw-Hill. 2006.
 - [154] Ghalichi, F., Deng, X., De Champlain, A., Douville, Y., King, M. and Guidoin, R. Low Reynolds number turbulence modeling of blood flow in arterial stenoses. *Biorheology*, 1998, 35(4, 5): 281–294.
 - [155] Aldoori, M. I. and Lee, R. E. *Cardiac Output and Regional Flow in Health and Disease*. 1st edition. Dordrecht: Springer Science+Business Media. 1993.
 - [156] Salim, S. M. and Cheah, S. C. Wall y^+ Strategy for Dealing with Wall-bounded Turbulent Flows. *International MultiConference of Engineers and Computer Scientists (IMECS)*. March 18–20, 2009.
 - [157] Molina-Aiz, F. D., Fatnassi, H., Boulard, T., Roy, J. C. and Valera, D. L. Comparison of Finite Element and Finite Volume Methods for Simulation of Natural Ventilation in Greenhouses. *Comput. Electron. Agric.*, 2010, 72(2): 69–86.
 - [158] Kim, G. B., Je, J. H. and Lee, S. J. Synchrotron X-Ray PIV Technique for Measurement of Blood Flow Velocity in CP879, *Synchrotron Radiation Instrumentation: Ninth International Conference*. 2007, 1891–1894.
 - [159] Samijo, S. K., Willigers, J. M., Barkhuysen, R., Kitslaar, P. J., Reneman, R. S., Brands, P. J. and Hoeks A. P. Wall Shear Stress in the Human Common Carotid Artery as Function of Age and Gender. *Cardiovasc. Res.*, 1998, 39(2): 515–522.
 - [160] Ku, D. N., Giddens, D. P., Zarins, C. K. and Glagov, S. Pulsatile Flow and Atherosclerosis in the Human Carotid Bifurcation Positive Correlation between Plaque Location and Low Oscillating Shear Stress. *Arter. Thromb Vasc Biol*, 1985, 5(3): 293–302.
 - [161] Bennet, J. and Briggs, W. *Using and Understanding Mathematics A Quantitative Reasoning Approach*. 6th edition. Boston: Pearson. 2015.
 - [162] Tu, J., Yeoh, G. H. and Liu, C. *Computational Fluid Dynamics a Practical Approach*. 1st edition. Burlington: Elsevier. 2008.
 - [163] Martin, D., Murphy, E. and Boyle, F. Computational Fluid Dynamics Analysis of Balloon-Expandable Coronary Stents: Influence of Stent and Vessel

- Deformation coronary stents : Influence of stent and vessel deformation. *Med Eng Phys*, 2014, 36(8): 1047–1056.
- [164] De Santis, G., Trachet, B., Conti, M., De Beule, M., Morbiducci, U., Mortier, P., Segers, P., Verdonck, P. and Verhegghe, B. A Computational Study of the Hemodynamic Impact of Open- Versus Closed-Cell Stent Design in Carotid Artery Stenting. *Artif. Organs*, 2013, 37(7): E96–E106.



PTTA UTHM
PERPUSTAKAAN TUNKU TUN AMINAH