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ABSTRACT

Cardiovascular diseases are one of the major causes of mortality in the modern world. A possible method of treating such conditions is the replacement of a blood vessel's pathological segment with an artificial one. Dacron and ePTFE are the main materials currently used in the manufacturing of artificial vessels. A great disadvantage of theirs is their low compliance in relation to biological vessels, which may lead to additional pathologies. State-of-the-art research focuses on the production of artificial vessels with increased compliance. The manufacturing of artificial vases from PCL using the electrospinning method is a potential solution.

In this Master Thesis we performed a biomechanical study of blood vessels, covering the various theoretical aspects involved in cardiovascular problems. Then, a combined experimental and FEM computational study was carried out. A PCL/PVA carotid caliber vessel was produced by the method of electrospinning and tested under various operating conditions using a physiological flow apparatus. A finite element FSI model was developed in order to simulate and assess the experimental results, as well as to predict the vascular compliance and other mechanical properties. The simulations were performed at pressure intervals between 0 to 150 mmHg. For the modeling of the PCL vessel wall, various elastic and hyperelastic material models were examined.

All material models showed errors less than 16% when comparing the calculated vascular compliance to the experimentally measured one and less than 7% compared with bibliographic values at the physiological 80-125 mmHg pressure interval. In this interval, the FEM calculated compliance ranged from 4.7 to 5.1 %/100 mmHg $\times 10^4$, while the experimental one had a mean value of 4.4%/100 mmHg $\times 10^4$ with the corresponding bibliographic value being 5 %/100 mmHg $\times 10^4$. Moreover, at least one material model had an error less than 12% for operating pressures up to 150 mmHg. In addition, the maximum values of the 1st principal stress at 100 kPa and fluid velocity at 0.93 m/s were validated by relevant studies for carotid caliber arteries. The importance of deformable wall analysis provided by the FSI methods was highlighted by the rigid model's wall shear stress overestimation up to 45% compared to compliant models.

In conclusion, the FEM simulations showed that the FSI modelling can yield more realistic results than rigid wall simulations. Although no wall material model can fully describe the PCL vessel's response for every pressure interval, a hyperelastic

constitutive model such as an Ogden material is more appropriate for the modelling of arterial walls, compared to elastic materials. On the other hand, a linear elastic material model is better suited for less compliant artificial vessels. Overall, the FEM model developed in this study was validated by both experimental and bibliographic data and has the potential to be used in predictive models in the future.

Key words:

biomechanics, artificial vessels, electrospinning, compliance, FSI

ΠΕΡΙΛΗΨΗ

Τα καρδιαγγειακά νοσήματα αποτελούν μία από τις σημαντικότερες αιτίες θνησιμότητας στον σύγχρονο κόσμο. Η εμβιομηχανική μελέτη και ανάλυση της συμπεριφοράς των αιμοφόρων αγγείων αποτελεί βασικό βήμα της κατανόησης των μηχανισμών που οδηγούν στην ανάπτυξη παθολογιών και των συνεπειών τους.

Μια πιθανή μέθοδος αντιμετώπισης τέτοιων παθήσεων αποτελεί η αντικατάσταση ενός παθολογικού τμήματος αγγείου με τεχνητό αιμοφόρο αγγείο. Το Dacron και το ePTFE αποτελούν τα κυριότερα συνθετικά υλικά που χρησιμοποιούνται σήμερα στην κατασκευή τεχνητών αγγείων. Ένα μεγάλο μειονέκτημα που παρουσιάζουν είναι η μικρή τιμή ενδοτικότητάς τους σε σχέση με τα βιολογικά αγγεία, που μπορεί να οδηγήσει σε επιπλέον παθολογίες. Σήμερα, αποτελεί αντικείμενο έρευνας η κατασκευή τεχνητών αγγείων με αυξημένη ενδοτικότητα, συγκρίσιμη με αυτήν των βιολογικών αγγείων. Η κατασκευή τεχνητών αγγείων από PCL, με τη μέθοδο του electrospinning μπορεί να αποτελέσει μία πιθανή λύση.

Η ανάπτυξη των πακέτων πεπερασμένων στοιχείων και υπολογιστικής ρευστοδυναμικής μας επιτρέπει να μοντελοποιήσουμε σύνθετα προβλήματα αιμοδυναμικής που δεν μπορούν να προσεγγιστούν με κλασσικές, αναλυτικές μεθόδους ρευστομηχανικής. Ένα τέτοιο πρόβλημα είναι η Αλληλεπίδραση Ροής-Τοιχώματος (FSI) στα αιμοφόρα αγγεία.

Σκοπός της παρούσας Διπλωματικής Εργασίας είναι η εμβιομηχανική μελέτη των αιμοφόρων αγγείων. Για τον λόγο αυτό διενεργήθηκε μια συνδυαστική πειραματική και υπολογιστική μελέτη ροής τεχνητών αγγείων σε διάφορες πιέσεις λειτουργίας. Μια ειδική πειραματική διάταξη κλειστού κυκλώματος παλμικής κυκλοφορίας χρησιμοποιήθηκε για την διεκπεραίωση των πειραμάτων. Η υπολογιστική μελέτη πραγματοποιήθηκε με την δημιουργία ενός μοντέλου Αλληλεπίδρασης Ροής-Τοιχώματος πεπερασμένων στοιχείων ανοιχτού κώδικα για την προσομοίωση τεστ φυσιολογικής κυκλοφορίας ρευστού σε τεχνητά αγγεία και την πρόβλεψη της ενδοτικότητάς τους.

Το Κεφάλαιο 2 ξεκινάει με μία σύντομη περιγραφή του καρδιακού κύκλου. Στη συνέχεια, γίνεται αναφορά στην ανατομία των βιολογικών αρτηριών και πώς αυτή καθορίζει τη συμπεριφορά, τις μηχανικές ιδιότητες και τη λειτουργικότητά τους, ενώ δίνεται και ο ορισμός της αγγειακής ενδοτικότητας. Στην Ενότητα 2.3 γίνεται μια

σύγκριση μεταξύ βιολογικών και τεχνητών αιμοφόρων αγγείων, με χρήση του μοντέλου του Windkessel. Τέλος, στην Ενότητα 2.4 παρουσιάζονται οι κυριότερες παθογένειες που προσβάλλουν τα αιμοφόρα αγγεία και η επίδρασή τους στις ιδιότητες αυτών, αλλά και στην υγεία του ασθενή.

Το Κεφάλαιο 3 αφιερώνεται αποκλειστικά στις ιδιότητες της ροής του αίματος. Η φυσιολογία και η σύσταση του αίματος εξετάζεται στις επιμέρους ενότητες. Αρχικά, παρατίθενται οι βασικές σχέσεις της κλασικής ρευστομηχανικής, στις οποίες στηρίζεται η αιμοδυναμική. Στην Ενότητα 3.2, με τη βοήθεια του πεδίου της ρεολογίας, παρουσιάζονται τα μοντέλα περιγραφής της μη-Νευτώνειας συμπεριφοράς του αίματος και οι συνθήκες στις οποίες μπορούμε να προσδιορίσουμε το φαινόμενο ιξώδους του. Ακολούθως, παρουσιάζεται το πρόβλημα της παλμικότητας της ροής και μέθοδοι για μοντελοποίηση της κυματικής διάδοσης του παλμού πίεσης. Το κεφάλαιο κλείνει με την περιγραφή των κυριότερων ροϊκών φαινομένων στις αρτηριακές διακλαδώσεις, περιοχές που συχνά αποτελούν σημεία έναρξης παθογενειών.

Αντίστοιχα, στο Κεφάλαιο 4 ασχολούμαστε με τη μηχανική του αγγειακού τοιχώματος. Γίνεται ανασκόπηση βασικών εννοιών του πεδίου της μηχανικής στερεού σώματος και προσέγγιση της συμπεριφοράς των αγγείων βάσει της θεωρίας των λεπτότοιχων κυλινδρικών δοχείων. Επιπρόσθετα, παρουσιάζονται τα βασικά μοντέλα ιξωδοελαστικότητας και η απόκριση τους σε δυναμική καταπόνηση. Στη συνέχεια, γίνεται μελέτη της μηχανικής συμπεριφοράς βιολογικών και τεχνητών αγγείων, ενώ προσδιορίζονται και οι μηχανικές τους ιδιότητες. Τέλος, αναφέρονται μέθοδοι υπολογισμού της αγγειακής ενδοτικότητας.

Στο Κεφάλαιο 5 περιγράφεται η διαδικασία μοντελοποίησης και σύζευξης των δύο παραπάνω συστημάτων με χρήση υπολογιστικού προγράμματος πεπερασμένων στοιχείων: το ρευστομηχανικό σύστημα προσομοίωσης της συμπεριφοράς του αίματος συνδέεται με το σύστημα μηχανικής στερεού σώματος του αγγείου. Η διαδικασία αυτή, γνωστή και ως Αλληλεπίδραση Ροής-Δομής (FSI), επιτρέπει την αμφίδρομη ανταλλαγή δεδομένων μεταξύ των δύο συστημάτων, δίνοντας αποτελέσματα πιο συμβατά με την πραγματικότητα.

Τέλος, το Κεφάλαιο 6 περιγράφει τις μεθόδους διεκπεραίωσης των πειραμάτων, μοντελοποίησης τεχνητών αγγείων και προσομοίωσης μηχανικών δοκιμών. Μέσω αυτής της προσομοίωσης, η αγγειακή συμμόρφωση των τεχνητών αγγείων υπολογίζεται και συγκρίνεται με τα αντίστοιχα πειραματικά αποτελέσματα, που εκτελούνται εκ των προτέρων. Το πειραματικό μέρος περιλαμβάνει τη δημιουργία των

τεχνητών αγγείων από PCL/PVA με τη μέθοδο του electrospinning, την πειραματική διαδικασία και την επεξεργασία δεδομένων. Στο τμήμα της μοντελοποίησης γίνεται η προσομοίωση του πειράματος χρησιμοποιώντας μεθόδους πεπερασμένων στοιχείων FSI. Η προσομοίωση πραγματοποιήθηκε σε διαστήματα πιέσεων από 0 έως 1500 mmHg και η τιμή της αγγειακής ενδοτικότητας συγκρίθηκε τόσο με πειραματικά αποτελέσματα, όσο και με βιβλιογραφικά δεδομένα. Για την μοντελοποίηση του αγγείου PCL χρησιμοποιήθηκαν τρεις τύποι υλικού: ένα γραμμικά ελαστικό και δύο υπερελαστικά (Neo-Hookean και Ogden 1^{ης} τάξης). Τα μέγιστα σφάλματα υπολογισμού της ενδοτικότητας σε διαστήματα έως 150 mmHg ήταν μικρότερα από 12% συγκριτικά με τα πειραματικά και βιβλιογραφικά δεδομένα, τουλάχιστον για ένα τύπο υλικού. Επιπλέον, όλα τα μοντέλα υλικών είχαν σφάλμα μικρότερο από 16% για το διάστημα φυσιολογικής πίεσης 80-120 mmHg. Τα σφάλματα αυτά ήταν μικρότερα από μοντέλα αντίστοιχων ερευνών.

Εν κατακλείδι, το μοντέλο πεπερασμένων στοιχείων που αναπτύχθηκε μπορεί να χρησιμοποιηθεί για ορισμένους τύπους υλικών και σε συγκεκριμένα διαστήματα πιέσεων για την διερεύνηση και τον υπολογισμό της αγγειακής ενδοτικότητας τεχνητών αγγείων, αλλά και ρευστομηχανικές ιδιότητες όπως ταχύτητα ρευστού, πιέσεις και διατμητική τάση τοιχώματος.

Τέλος, υποβάλλονται προτάσεις για μελλοντική επέκταση της εργασίας, με την περίπτωση μιας διακλάδωσης καρωτιδικής αρτηρίας να συζητείται σύντομα.

Λέξεις κλειδιά:

εμβιομηχανική, τεχνητά αγγεία, ηλεκτροστατική ινοποίηση, ενδοτικότητα, FSI

CONTENTS

ACKNOWLEDGEMENTS.....	iii
ABSTRACT.....	v
ΠΕΡΙΛΗΨΗ.....	vii
FIGURES.....	xiii
TABLES	xvii
1 INTRODUCTION	1
1.1 THEORETICAL BACKGROUND	2
1.2 THESIS LAYOUT.....	2
2 ARTERIAL SYSTEM PHYSIOLOGY	5
2.1 ANATOMY OF ARTERIES	5
2.2 PRESSURE, FLOW AND RESISTANCE OF THE ARTERIAL SYSTEM	7
2.3 BIOLOGICAL – ARTIFICIAL VESSELS	8
2.4 VASCULAR DISEASES.....	10
3 HAEMODYNAMICS	13
3.1 FUNDAMENTAL FLUID DYNAMICS EQUATIONS	13
3.1.1 CONTINUITY EQUATIONS	14
3.1.2 SHEAR STRESS	14
3.2 BLOOD RHEOLOGY AND VISCOSITY	15
3.3 FLOW PULSATILITY	18
3.4 REALISTIC FLOW MODELLING	21
3.4.1 WAVE PROPAGATION	21
3.4.2 FOURIER ANALYSIS.....	23
3.5 FLOW IN BIFURCATIONS	25
4 ARTERIAL WALL MECHANICS	29
4.1 THIN-WALLED CYLINDRICAL VESSELS	30
4.2 VISCOELASTICITY – DYNAMIC LOADING	31
4.3 MECHANICAL BEHAVIOUR OF BLOOD VESSELS	33
4.4 VASCULAR COMPLIANCE COMPUTATION	36
4.5 HYPERELASTIC MATERIALS	37
4.5.1 OGDEN MATERIAL	37
4.5.2 MOONEY-RIVLIN MATERIAL	38
5 COMPUTATIONAL MODELLING AND SIMULATION	39

5.1	COMPUTATIONAL FLUID DYNAMICS	39
5.2	COMPUTATIONAL STRUCTURAL MECHANICS.....	40
5.3	FLUID – STRUCTURE INTERACTION	41
5.4	FSI TYPES OF APPROACH.....	42
5.4.1	MONOLITHIC APPROACH.....	43
5.4.2	PARTITIONED APPROACH.....	43
6	A COMBINED EXPERIMENTAL AND COMPUTATIONAL STUDY ON TUBULAR ARTIFICIAL VESSELS.....	45
6.1	EXPERIMENTAL PART	46
6.1.1	VESSEL PRODUCTION	46
6.1.2	TESTING APPARATUS DESCRIPTION	48
6.1.3	EXPERIMENTAL PROCEDURE	51
6.1.4	EXPERIMENTAL RESULTS.....	52
6.2	FINITE ELEMENT MODELLING AND SIMULATION	56
6.2.1	MODEL DESCRIPTION AND GEOMETRY	56
6.2.2	FSI FORMULATION.....	57
6.2.3	DISCRETIZATION.....	58
6.2.4	MATERIAL PROPERTIES	59
6.2.5	BOUNDARY CONDITIONS AND LOADS	61
6.2.6	ANALYSIS.....	63
6.2.7	RESULTS AND DISCUSSION	64
6.2.8	CONVERGENCE STUDY	75
6.2.9	FUTURE WORK.....	76
7	CONCLUSIONS	81
	BIBLIOGRAPHY	85

FIGURES

Figure 2.1 Cross-section of a medium sized artery	5
Figure 2.2 Pressure-volume curves in the arterial and venous systems	6
Figure 2.3 Representation of the Windkessel model	8
Figure 2.4 Windkessel model: pressure-time curves	9
Figure 2.5 Artificial vessels from woven polyester and PTFE	9
Figure 2.6 Basic structure of atherosclerotic plaque	10
Figure 2.7 Schematic representation of an aneurysm-stenosis	11
Figure 3.1 Red blood cell schematic	13
Figure 3.2 Blood viscosity dependency on strain rate, haematocrit and temperature	16
Figure 3.3 Stress-strain relationship for Newtonian and non-Newtonian fluids.....	16
Figure 3.4 Theoretical blood velocity profile according to Casson's model	17
Figure 3.5 Newtonian and non-Newtonian fluid velocity profiles, for constant flow	18
Figure 3.6 Blood supply waveform in a large artery	19
Figure 3.7 Pressure change in systemic circulation	19
Figure 3.8 Schematic of wave propagation in a thin-walled, elastic tube.	21
Figure 3.9 Modulus and phase difference of Womersley model as a function of α . ..	22
Figure 3.10 Artery pressure gradient and the first harmonics of it and the computed fluid supply	23
Figure 3.11 Velocity pulse analysis in Fourier series	24
Figure 3.12 Geometry and flow development at a bifurcation	26
Figure 3.13 Pressure gradient effect on velocity profile near the wall	27
Figure 4.1 Stress-strain curve for a biological, soft tissue	29
Figure 4.2 Diameter and wall thickness for various types of arteries	30
Figure 4.3 Development of forces on a thin-walled vessel's cross-sections	31
Figure 4.4 The Maxwell and Kelvin-Voight models. Modeling of viscoelastic material with spring and viscosity damping in series and in parallel	32
Figure 4.5 Response of a viscoelastic material under static and dynamic loading.	32
Figure 4.6 Stress-strain curves of biological tissue for a combination of elastin and collagen fibers	34
Figure 4.7 Tangential stress-strain curves of biological arteries and polymeric arterial grafts	35
Figure 4.8 Compliance- mean pressure curves for biological and artificial vessels...	35
Figure 5.1 Flow-structure interaction (FSI): Coupling process.	41
Figure 5.2 Monolithic approach to FSI problems	43
Figure 5.3 Partitioned approach to FSI problems	44
Figure 6.1 Presentation of the electrospinning procedure.....	46
Figure 6.2 Electrospinning system used for the production of the PCL/PVA vessels.	47
Figure 6.3 Photo of a produced tubular vessel	48
Figure 6.4 Experimental apparatus schematic	48
Figure 6.5 The Left Ventricle element.....	49
Figure 6.6 Systematic circulation tubing system schematic	50
Figure 6.7 Vessel test section.....	50

Figure 6.8 Acquiring and digitization of the signals.....	51
Figure 6.9 Vessel's diameter trend due to viscoelastic effects	52
Figure 6.10 Fourier analysis of acquired signals	53
Figure 6.11 IIR low-pass filter characteristics	53
Figure 6.12 Pressure, diameter and flow rate of tested vessel. Pressure range of 0-40 mmHg.	54
Figure 6.13 Pressure, diameter and flow rate of tested vessel. Pressure range of 50-90 mmHg.	54
Figure 6.14 Pressure, diameter and flow rate of tested vessel. Pressure range of 80-130 mmHg.	55
Figure 6.15 PCL tubular vessel compliance. Comparison between experimental results and bibliographic values.....	56
Figure 6.16 FEM vessel model schematic	57
Figure 6.17 Meshed model used in the simulations.....	59
Figure 6.18 Fluid domain properties.....	59
Figure 6.19 Solid domain properties, linear elastic material	60
Figure 6.20 Solid domain properties, Mooney-Rivlin (Neo-Hookean) material.....	60
Figure 6.21 Solid domain properties, Ogden material	61
Figure 6.22 FSI traction load and zero displacement boundary condition application elements/nodes.....	61
Figure 6.23 No-slip condition applied on the wall's internal nodes	62
Figure 6.24 Application of velocity/fluid dilatation loads on Inlet/outlet surface nodes	62
Figure 6.25 Velocity inlet/ Dilatation outlet load curves.....	63
Figure 6.26 Analysis parameters.....	64
Figure 6.27 Vessel's internal radius measurement	65
Figure 6.28 Calculated internal radius for each pressure interval of the simulation.	66
Figure 6.29 Pressure – radius relationship of the vessel and stress-strain curve of the simulation materials.....	67
Figure 6.30 Distribution of first principal stress in the vessel wall at peak systole....	67
Figure 6.31 Dynamic vascular compliance. Comparison between experimental results, simulation results and bibliographic values.	68
Figure 6.32 Vascular compliance yielded by the simulations, compared to our experimental results and bibliographic values.	69
Figure 6.33 Fluid velocity contours at start of pulse, peak systole and flow deceleration.	71
Figure 6.34 Mid-vessel velocity for the 80-125 pressure interval.	71
Figure 6.35 Comparison of fluid velocity between deformable (linear elastic, FSI) and rigid (CFD) wall models	72
Figure 6.36 Pressure propagation in a deformable and rigid vessel	73
Figure 6.37 Wall shear stress calculated in the middle of the vessel	74
Figure 6.38 Global maximum wall shear stress for the rigid and deformable vessel models	75
Figure 6.39 Different meshes used in displacement convergence study	76
Figure 6.40 Displacement convergence study: Element displacement and relative errors.	76

Figure 6.41 Processed carotid bifurcation geometry and final mesh.	77
Figure 6.42 Flow velocity in a bifurcating carotid. Absolute velocity magnitude and z-velocity component	77
Figure 6.43 Wall shear stress distribution in a carotid bifurcation.	78

TABLES

Table 6-1 Electrospinning parameters.....	47
Table 6-2 Dimensions of FEM vessel model	57

1 INTRODUCTION

Cardiovascular diseases are presently the most common cause of death in the world. According to the World Health Organization, in 2019 15 million people worldwide died from ischemic heart disease-related incidents [1]. This number represents 27% of global total deaths, a proportion that increases if we examine the western world alone.

The main cause of this type of disease is atherosclerosis. The formation of atherosclerotic plaque can lead to narrowing or severe obstruction of peripheral or coronary arteries.

Possible methods of treating such diseases may include, depending on the severity, medication, angioplasty (balloon and stent), arterial bypass or replacement of a vessel segment. For the latter two in particular, it is possible to use superficial veins of the patient's lower extremities or thoracic arteries as an autograft. However, in case the patient does not have vessels with desirable properties, artificial blood vessels are used.

Various synthetic polymers are used as biomaterials today in prosthetic implants for vascular surgery. Although they function well as large diameter and high blood supply vessels, their use has many disadvantages compared to biological vessels. In recent years, efforts have also been made to develop tissue-engineered blood vessels that will provide solutions to problems such as repeat surgeries in children.

The need to determine the mechanical and fluid dynamics properties of blood vessels is thus easily understood. This way an initial prediction of vessels' pathogenic regions, such as a stenosis or bifurcation, can be made and their impending consequences may be evaluated. Finite Element Modelling (FEM) methods are employed as a simulation and predictive tool in cardiovascular applications. The accuracy of these predictions is heavily dependent on the modeling assumptions. So, in order to increase the fidelity of such models, realistic modelling parameters instead of synthetic ones are essential.

The purpose of this Thesis is the biomechanical study of blood vessels and the development of a fluid - solid interaction (FSI) finite elements (FE) model for the simulation of mechanical tests in arteries. As a result, the arterial compliance of the vessel, as well as other important flow and mechanical properties may be estimated in various pressure intervals. A PVA/PCL tubular vessel was produced by the method of

electrospinning following the steps of a novel approach [66]. An experimental simulation of blood flow through the vessel was performed, using a physiological flow experimental apparatus. The results were compared to the ones provided by the FE model developed, as well as relevant literature.

1.1 THEORETICAL BACKGROUND

The object of Vascular Mechanics is the study of the mechanics of solids (for example the wall of a vessel) and fluids (eg blood) that participate in the structure and function of the circulatory system, as well as the interaction between them. The biomechanical study of blood vessels, like any biological system, is a multifactorial problem and requires an interdisciplinary approach. The main scientific fields employed are that of Medicine (anatomy, physiology, pathology and histology of blood vessels) and various branches of Engineering (Solid Engineering, Fluid Mechanics, Computational Engineering).

The field of Solid Engineering, in addition to Classical Engineering, includes the branches of Bio-solid Mechanics, Theory of Viscoelasticity, Materials Science and Biomechanics. Respectively, the field of Fluid Mechanics, based on Classical Fluid Mechanics, uses the branches of Bio-fluid Mechanics, Hemodynamics and Rheology¹. The existence of modern imaging methods (CT, MRI, ultrasound, 3D imaging) allows the reconstruction of patients' vascular geometry, which, introduced in Computer Engineering software, allows the creation of appropriate, personalized models simulating vascular function.

All the above fields of knowledge are combined, in order to study the response of the cardiovascular system under physiological and pathological conditions.

1.2 THESIS LAYOUT

Chapter 2 begins with a brief description of the heart cycle. Next, reference is made to the anatomy of the biological arteries and how it determines their behavior, mechanical properties and functionality, while the definition of vascular compliance is given. In Section 2.3 a comparison is made between biological and artificial blood vessels, using

¹ Rheology is the study of the flow of matter, mainly in the liquid state, but also as "soft solids" or solids under plastic flow conditions instead of elastic deformation, in response to an applied force, such as e.g. sludges, polymers, sauces, blood, etc. [14]

the Windkessel model. Finally, Section 2.4 presents the main pathogens that affect the blood vessels and their effect on their properties, but also on the patient's overall health.

Chapter 3 is devoted exclusively to the properties of blood flow. The physiology and composition of the blood are examined in the individual sections. First, the basic relationships of classical fluid mechanics, on which hemodynamics is based are presented. In Section 3.2, with the help of the field of rheology, we present the models describing the non-Newtonian behavior of the blood and the conditions under which we can determine its apparent viscosity. Next, the problem of pulsatile flow and methods for modeling the wave propagation of the pressure pulse are presented. The chapter ends with a description of the main flow phenomena in the arterial branches, regions that are often the initiating points of pathogens.

Respectively, in Chapter 4 we consider the mechanics of the vascular wall. We review basic concepts of the field of solid body mechanics and the behavior of the vessels is approached based on the theory of thin-walled cylindrical vessels. In addition, the basic models of viscoelasticity and their response to dynamic stress are presented. Then, the mechanical behavior of biological and artificial vessels is studied, while their mechanical properties are determined. Next, some methods for calculating vascular compliance are reported. Finally, we present some of the most common material models used in research.

Chapter 5 describes the process of modeling and coupling the above two systems using a finite element computer program: the fluid mechanical system simulating the behavior of the blood is connected to the mechanical solid body system of the vessel. This process, also known as Flow-Structure Interaction (FSI), allows two-way data exchange between the two systems, giving results more compatible with reality. Two types of approaches are highlighted: Monolithic and Partitioned.

Finally, Chapter 6 describes the method of modeling artificial vessels and simulating mechanical tests. Through this simulation, the vascular compliance of artificial vessels is calculated and compared with corresponding experimental results, performed a priori. The experimental part consists of the creation of the artificial vessels by electrospinning, the experimental procedure and data processing. In the modelling part we attempt to simulate the experiment using an FSI Finite Element simulation approach. Then, an analysis of the results regarding the vessel's mechanical behavior is carried out, conclusions are drawn and suggestions are made for future expansion of the work, with the case of a bifurcating carotid artery being briefly discussed.

2 ARTERIAL SYSTEM PHYSIOLOGY

Systemic circulation includes blood flow from the left ventricle to the aorta, the peripheral body regions through the arteries and its return to the right atrium, through the venous system. Arterial circulation is conducted under high pressures, compared to the venous. This high pressure is the result of the cardiac muscle contraction during the systolic phase of the left ventricle. Pressure waves generated this way cause the arteries to undertake additional load, apart from the pressure acting as the blood's flow driving force. Thus, in order to withstand the high stresses developed, arteries are composed of relatively thick and muscular walls.

2.1 ANATOMY OF ARTERIES

The arterial wall consists of three discrete layers: the tunica intima, tunica media and tunica adventitia (Figure 2.1). The tunica intima surrounds the vessel lumen, meaning the region through which blood is transferred. It consists of a thin layer of endothelial cells, coating the vessel's internal surface, and limited connective tissue from elastic fibers that assist the endothelial wall's structural integrity. It is separated from the tunica media by a thick internal elastic membrane.

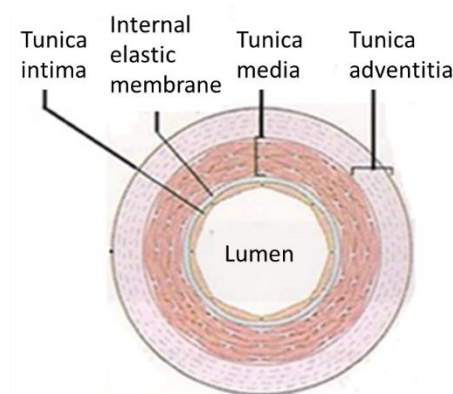


Figure 2.1 Cross-section of a medium sized artery [23].

The tunica media is usually the thickest of the three layers. It consists of circularly arranged smooth muscle cells and elastic connective tissue. These cells are responsible for the vessel's diameter variations, as well as its integrity. Due to this mechanism, arteries can be allowed to have sufficient mechanical properties, in order to withstand the high pressure generated by the heart. The tunica adventitia is made of connective

tissue, mainly collagen and elastin fibers, and its function is to stabilize and connect the blood vessel to the neighboring tissues.

A vessel's ability to change its diameter, and thus its volume, as a response to a pressure alteration in its interior is called distensibility, D_{dist} [m³Pa⁻¹]. The ratio of a vessel's volume change over its initial volume is defined as the volumetric deformation of the vessel. The property that connects the volumetric deformation with the vessel's internal pressure p , is called arterial compliance, C [Pa⁻¹] and is defined as [2]:

$$C = \frac{\Delta V / V}{\Delta p} \quad (2.1)$$

, where ΔV is the volumetric change, V is the initial volume and Δp the change of pressure. Figure 2.2 shows the pressure – volume relation in the arterial and venous systems of a human.

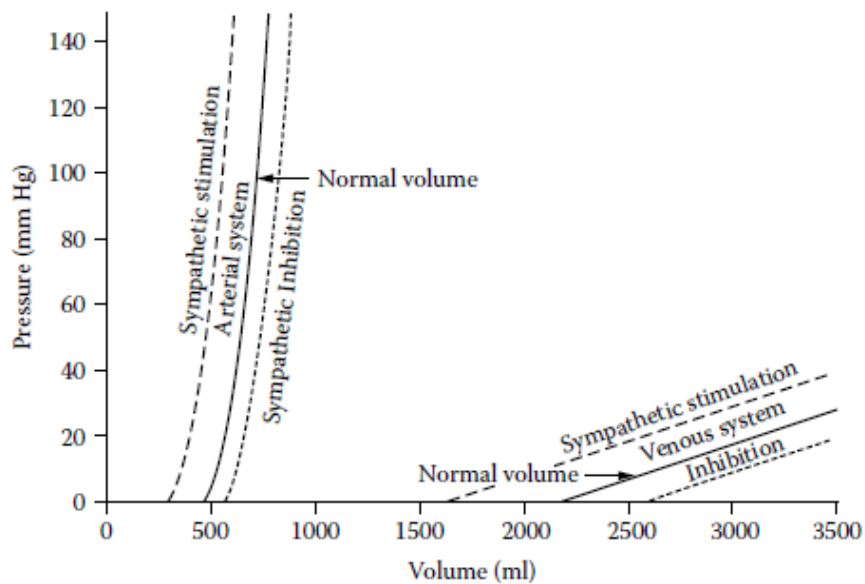


Figure 2.2 Pressure-volume curves in the arterial (left) and venous (right) systems [28].

One can observe that a slight increase in the arterial volume leads to a large increase in pressure, in contrast to the venous case. It is obvious that the arterial walls demonstrate a lower compliance than the venous ones. Thus, systemic veins operate as the circulatory system's pressure depot, as described by the Windkessel model (Section 2.3).

2.2 PRESSURE, FLOW AND RESISTANCE OF THE ARTERIAL SYSTEM

The simplest case for modelling the blood flow through a vessel, that regardless allows us to comprehend some basic principles, is the Ohm's law formulation. According to it, the volumetric flow rate Q [m³/s] depends on the pressure change ΔP between two regions along the vessel and the flow resistance R_{res} of the vessel, according to Equation [29]:

$$Q = \frac{\Delta P}{R_{res}} \quad (2.2)$$

Under normal circumstances, blood flow during rest is approximately 5 L/min [29], while pressure can be easily measured. On the contrary, resistance can only be approximated by computation. That being said, there are several properties affecting blood flow and resistance, meaning that Eq. (2.2) is oversimplified. A few of the hypotheses being made are that the fluid properties and flow are time invariable and that the vessel is rigid with a uniform cross-section. The latter can be considered valid only in the case of artificial vessels.

A more useful approach is Haegen-Poiseuille law. The volumetric flow can be calculated by integration of the velocity profile at the cross section of the vessel [11]:

$$Q = \int_0^R 2\pi r u(r) dr \quad (2.3)$$

The velocity profile is given by the solution of the Navier-Stokes equation (Section 3.3.1) for a cylindrical vessel, under constant fluid properties, time-invariable, laminar, uncompressed flow and zero velocity boundary conditions on the walls:

$$u(r) = \frac{R^2}{4\mu} \frac{\partial P}{\partial x} \left[\left(\frac{r}{R} \right)^2 - 1 \right] \quad (2.4)$$

Using Eq. (2.4) and (2.3), we can calculate the blood flow [29]:

$$Q = \frac{\pi \Delta P R^4}{8\mu L} \quad (2.5)$$

, where $\Delta P / L$ is the pressure gradient along a vessel of length L and of constant cross-section, with radius R . The assumptions made to arrive at this relationship are that the blood viscosity is constant and the vessel has a constant and uniform surface, along the entirety of its length L . In addition, all the properties of blood must be constant over time. Albeit, it can be used for a distinct period of time when the properties are considered to be temporarily constant.

Using Eq. (2.2), (2.5) we can define flow resistance as:

$$R_{res} = \frac{8\mu L}{\pi R^4} \quad (2.6)$$

It is interesting to note that small changes in the radius of the vessel cause a very large change in the blood supply, significantly affecting the resistance. This is important, as less energy is required from the muscle tissue of the vessel in order to be able to meet potential future energy needs.

2.3 BIOLOGICAL – ARTIFICIAL VESSELS

The distensibility of biological vessels plays an important role in blood circulation. First of all, when the muscles of the intima media are relaxed, the arterial diameter increases, significantly reducing arterial flow resistance (Figure 2.6). This allows increased blood flow where and when needed, such as in the aorta during the systolic phase.

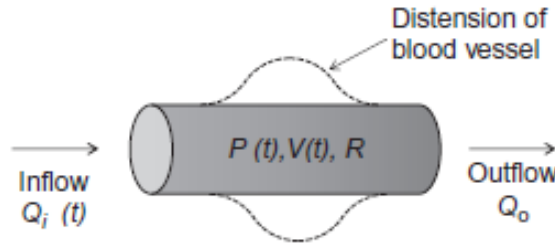


Figure 2.3 Representation of the Windkessel model. The artery dilates, allowing changes in the rate of blood accumulation and acting as a pressure depot. Time variables: Inflow $Q_i(t)$, Inlet-outlet pressure difference $p(t)$, vessel volume $V(t)$. Fixed values: Flow resistance R , outflow Q_o .

A second, significant consequence of vascular dilatation is perceived if we consider the Windkessel model (Figure 2.3). According to this, fluid (blood) is channeled into the chamber from the inlet, after the ventricular outflow and the supply at the outlet (Q_o) is constant and depends on the pressure gradient and the flow resistance of the Hagen-Poiseuille model (Equation 2.6). The storage capability of the elastic blood vessels is given by the distensibility D , according to the relation:

$$D = \frac{dV}{dp} \quad (2.7)$$

, where V is the volume and p is the pressure inside the vessel-chamber. The principle of mass conservation for the fluid in the elastic chamber is formulated as:

$$\text{Inflow} - \text{Outflow} = \text{Fluid storage rate}$$

or else:

$$Q(t) - \frac{p(t)}{R} = \frac{dV}{dt} = D \frac{dp}{dt} \quad \left(\frac{m^3}{s} \right) \quad (2.5)$$

In the case where we consider a sinus flow during contraction and zero during expansion, the graph of pressure for a cardiac cycle is shown in Figure 2.4.

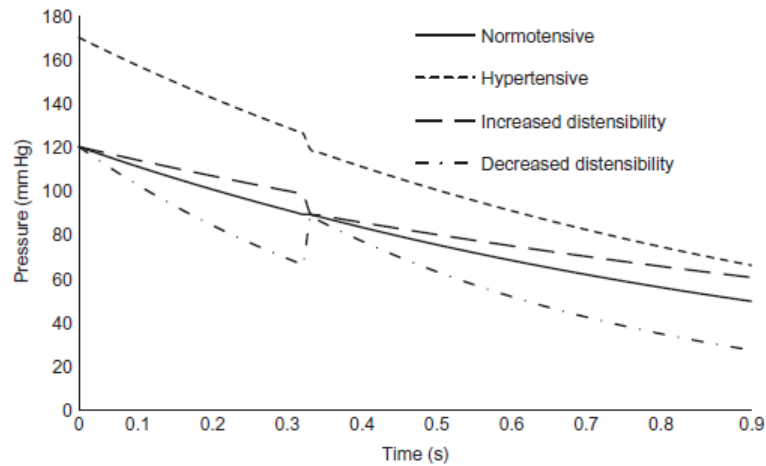


Figure 2.4 Windkessel model: pressure-time curves. Vessels of different dilatation: The pressure gradient of a physiological vessel drops smoothly, ensuring a constant supply at the outlet and smoothing the flow [3].

Taking everything into consideration, we see that the dilatation of the vessels allows them to function as a storehouse of pressure, so that a pressure gradient is maintained and the flow is not interrupted during the systolic phase of the heart. With this mechanism, in essence, the flow is gradually converted from pulsed to continuous, distal to the heart.

Here lies the main difference between biological and artificial vessels, which is a serious disadvantage of the latter. Artificial vessels are usually made of synthetic biopolymers (Figure 2.5), whose compliance is not close to that of biological ones.

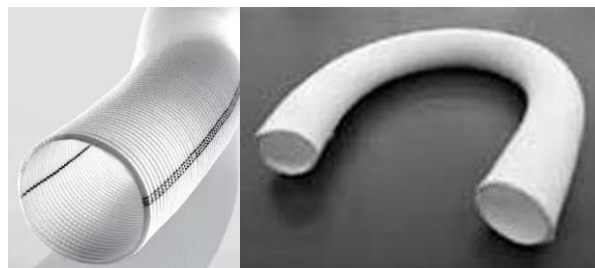


Figure 2.5 Artificial vessels from woven polyester (left) and PTFE (right).

As a result, artificial vessels generally develop very small changes in their diameter [6]. They can therefore be considered to remain undeformed in their radial direction. As shown in Equation (2.6), this leads to an increased flow resistance, compared to a biological vessel. At the same time, the pressure pulse is not smoothed, a function which

is consequently undertaken by the biological vessels downstream. This leads to an additional strain applied, due to the higher loads they receive, with a risk of pathogenesis. The case of the ascending aortic replacement is typical, which results in greater pressure on the aortic arch and carotid arteries, and may potentially increase the risk of stroke.

2.4 VASCULAR DISEASES

Vascular diseases are associated with changes in the properties of the arterial wall. The main ones are arteriosclerosis, thromboembolism and aneurysm.

In general, arteriosclerosis is characterized by an increase in the thickness and stiffness of the arterial wall. The reduction of the blood vessels' lumen cross section has significant effects. The flow is accelerated in the area of the stenosis, causing increased shear stresses and affecting the pressure gradient in the fluid. In addition, stagnant blood regions may be formed near the stenosis if the pressure gradient is not sufficient to overcome the increased flow resistance. Furthermore, the flow can be separated from the wall, as in the case of wide-angle branches, a phenomenon which, in combination with the possible narrowing of the lumen, reduces the average velocity and can cause the formation of recirculation zones [22] (Figure 3.12). When the average flow rate decreases, there is a possibility of reduced tissue oxygenation. Moreover, the increase in the stiffness of the arterial wall causes a decrease in the compliance of the vessel, leading to an inability to withstand the high pressures exerted on it.

Arteriosclerosis manifests itself mainly in two forms: calcification of the arterial wall or atheromatosis. Calcification is associated with the deposition of calcium salts between the tunica intima and media and the rupture of smooth muscle cells. Atheromatosis is the deposition of lipids inside the arterial wall, resulting in the formation of atherosclerotic plaque (Figure 2.6).

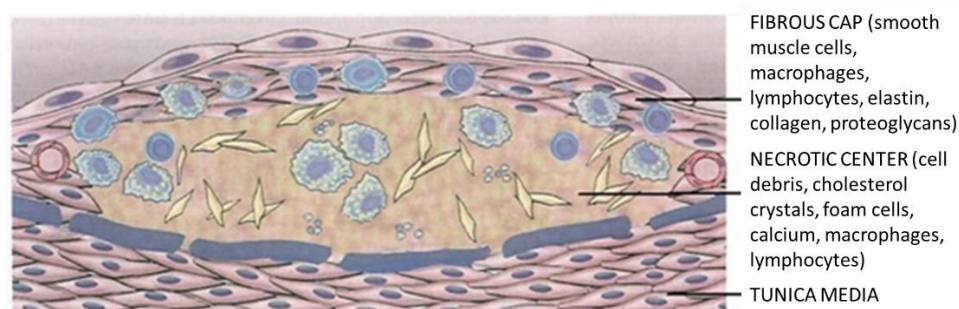


Figure 2.6 Basic structure of atherosclerotic plaque [23].

Atherosclerosis is an inflammatory disease and occurs due to disturbances of fluid dynamic forces, which can cause injury to the tunica intima of the vascular wall (for example in a branch). When this happens, lipid deposition in the subendothelial space and proliferation of vascular muscle cells is observed, resulting in an increase in the thickness of the tunica intima and the development of stenosis. Simultaneous adhesion of white blood cells and platelets to the area is often observed, leading to further deterioration of the condition.

This platelet adhesion on the vascular walls is likely to trigger platelet activation, initiating a chain reaction that results in the proliferation of extra platelets, fibrinogen, and the formation of agglomerates in the endothelial wall. Platelet aggregates are called clots and their effects are similar to those of atherosclerotic plaques, in the sense that they block blood flow and reduce the cross-section of the blood vessel. When the clot becomes large enough, the shear stresses acting on it also increase (due to the increase in the speed of the blood flow around it). If the shear stresses exceed the strength of the intercellular bonds, the clot may detach from the endothelial wall and enter the circulation, causing thromboembolism. If the clot clogs a smaller diameter blood vessel, the blood supply to the area can be completely interrupted, as is the case with myocardial infarction, by coronary artery embolism.

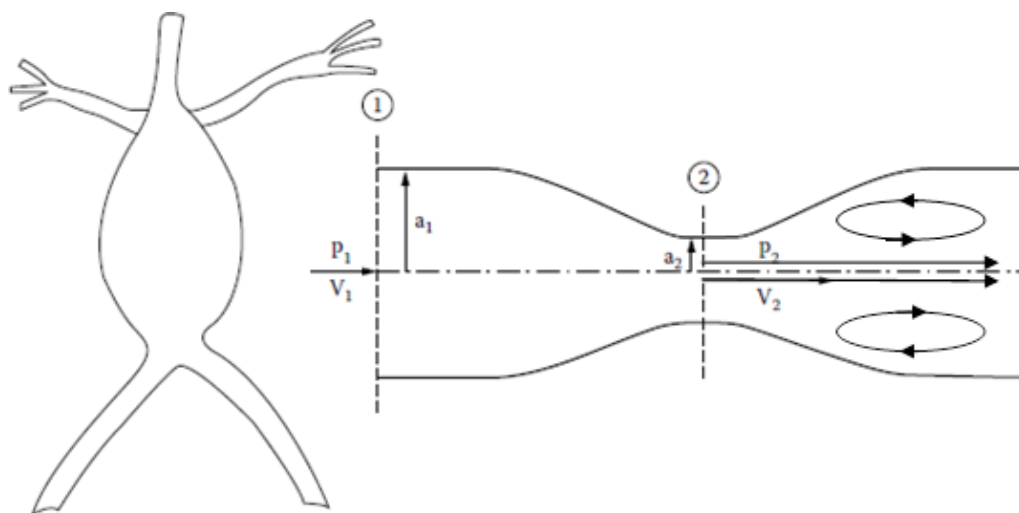


Figure 2.7 Schematic representation of an aneurysm-stenosis [3].

An aneurysm is the dilatation of an artery wall due to an increase in inner diameter, usually caused by a weakening of muscle tissue. This is due to the high and pulsating pressures that the vessel walls receive when they exceed their viscoelastic strength properties. The result of the swelling is an increase in the internal transverse surface (cross section) of the vessel (Figure 2.7).

According to the conservation of mass, for constant fluid density, between the aneurysmal region (1) and after it (2) we get [11]:

$$A_1 u_1 = A_2 u_2 \left(\frac{m^3}{s} \right) \quad (2.9)$$

We observe that the increase of the cross-section causes a reduce in blood velocity.

Taking Bernoulli's law, we also get [32]:

$$\frac{p}{\rho} + \frac{u^2}{2} + gz = \text{const.} \left(\frac{J}{kg} \right) \quad (2.10)$$

, where:

- $\frac{p}{\rho}$ corresponds to the hydrostatic pressure energy
- $\frac{u^2}{2}$ corresponds to the kinetic energy
- gz corresponds to the dynamic energy.

If we assume a steady flow and ignore height difference, we can see that a drop in mean blood velocity results in an increase of vessel pressure. This increase may lead to further deterioration and inflation of the vessel wall, until the point when it cannot bear further loads and is led to rupture, causing severe hemorrhage and leading to death.

3 HAEMODYNAMICS

Blood consists of two main components: plasma at about 55%, while the rest is cell matter. Of the cellular components, more than 99% consists of red blood cells. The percentage of red blood cells in the blood is called hematocrit (Ht) and under normal conditions ranges from 39% to 50% in men and 35% to 45% in women. The red blood cells are flattened disc-shaped, with an excess of cell membrane (Figure 3.1) that allows them to deform, depending on the flow conditions. The cellular content of the blood is supplemented by white blood cells and platelets.

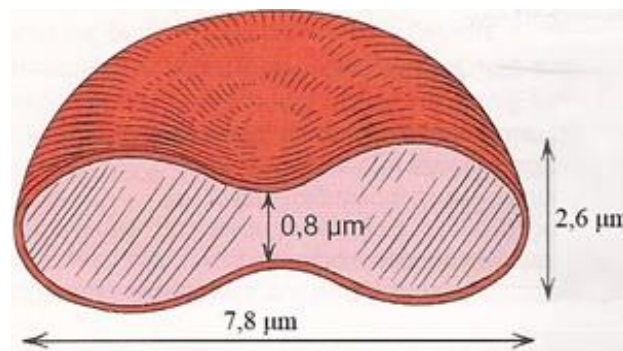


Figure 3.1 Red blood cell schematic [24].

It is easily understood that when studying and analyzing of hemodynamic problems, the models and relationships of classical fluid mechanics are not sufficient. This is due to the complexity of the nature of the fluid (blood), but also the boundary conditions, such as pulsatile flow and wall distensibility (vessels). It is therefore necessary to use appropriate hemodynamic models, which will approach the problem to a greater extent.

3.1 FUNDAMENTAL FLUID DYNAMICS EQUATIONS

The development of hemodynamic models is based on the principles of classical fluid mechanics. In this section the main relationships will be briefly developed, from which the analysis of the problems begins.

3.1.1 CONTINUITY EQUATIONS

The two basic equations upon which the solution of fluid dynamics problems is based, are the equations of mass and momentum conservation. Mass conservation is expressed, per volume unit, as:

Net mass flow rate through the surface of a control volume, constant in space, enclosed by surface A + Rate of change of mass inside this volume = Zero

Or else, per volume unit [11]:

$$\nabla \cdot (\rho \vec{V}) + \frac{\partial \rho}{\partial t} = 0 \quad \left(\frac{kg}{m^3s} \right) \quad (3.1)$$

In the case of an incompressible fluid ($\frac{\partial \rho}{\partial t} = 0$), the above equation transforms into:

$$\nabla \cdot \vec{V} = \frac{\partial u}{\partial x} \hat{i} + \frac{\partial v}{\partial y} \hat{j} + \frac{\partial w}{\partial z} \hat{k} = 0 \quad (3.2)$$

Momentum conservation is expressed as:

Sum of all external forces acting on the control volume = Net rate of momentum flow in the control volume + Rate of change of the momentum of the fluid contained in the control volume.

In the case of incompressible flow, the above equation can be expressed, per mass unit, as:

$$\frac{\partial \vec{V}}{\partial t} + (\vec{V} \cdot \nabla) \vec{V} = -\frac{1}{\rho} \nabla p + \vec{g} + \nu (\nabla^2 \vec{V}) \quad \left(\frac{m}{s^2} \right) \quad (3.3)$$

, where:

- $\frac{\partial \vec{V}}{\partial t}$ expresses the moments rate of change
- $(\vec{V} \cdot \nabla) \vec{V}$ expresses the moment convection
- $-\frac{1}{\rho} \nabla p$ is the pressure gradient (from an internal source)
- $\nu (\nabla^2 \vec{V})$ is the stress gradient that causes moment diffusion, due to viscosity
- $\vec{g}$ is an external force source.

Equation (3.3) is called **Navier-Stokes equation**.

3.1.2 SHEAR STRESS

Viscosity is a property of fluids that correlates the shear stress acting on them to the resulting shear strain rate. It basically allows fluids to deform continuously, as a

response to a constant shear load. In fluid mechanics, the stress-strain constitutive equation is expressed as:

$$\tau_{xy} = \mu \dot{\gamma} \quad (3.4)$$

, where τ_{xy} [Pa] is the shear stress on the x-y plane, μ [Pa.s] is the dynamic viscosity and $\dot{\gamma}$ [s⁻¹] is the strain rate.

Based on theory of elasticity, the strain tensor² is expressed as:

$$\varepsilon_{ij} = \frac{1}{2} \left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right) \quad (3.5)$$

, where $\partial u_{i,j}$ is the translation in the i, j directions.

On the x-y plane, mechanical stress is calculated as:

$$\gamma_{xy} = 2\varepsilon_{xy} = \left(\frac{\partial u_x}{\partial y} + \frac{\partial u_y}{\partial x} \right) \quad (3.6)$$

Using Equations (3.4), (3.5) shear stress constitutive equation can be expressed as:

$$\tau_{xy} = \mu \dot{\gamma} = \mu \left(\frac{\partial u}{\partial y} + \frac{\partial v}{\partial x} \right) \quad (3.7)$$

, where u, v are the velocity compounds in x, y directions.

By solving Navier-Stokes equation for steady, unidirectional flow of an incompressible fluid, inside a cylindrical pipe, wall shear stress (WSS) is finally computed as [2, 29]:

$$\tau_w = \frac{R}{2} \frac{\partial p}{\partial x} = \frac{4\mu Q}{\pi R^3} \quad (3.8)$$

3.2 BLOOD RHEOLOGY AND VISCOSITY

Blood consists mainly of two components: plasma (55%) and cells (45%). Out of the cellular components, 99% are red blood cells. Plasma consists mainly of water at about 92%, with the rest being electrolytes, sugars, phospholipids, cholesterol and proteins [23]. Under normal circumstances, plasma can be considered as a Newtonian fluid, meaning it has a constant viscosity, regardless of its shear strain rate, with a value of $\mu = 1.1 - 1.3$ mPa.s at 37 °C [4]. However, in total blood is a multiphasic fluid and has a non-Newtonian behavior, as well as an initial yield stress [5]. Blood viscosity depends on the strain rate, haematocrit and temperature (Figure 3.2).

² Tensors are defined as quantities independent of the reference system, through polylinear, gradient vector functions. They are essentially generalized vectors. In continuous medium mechanics the Cauchy σ tensor is a 2nd order symmetric tensor with 9 σ_{ij} components, which accurately determines the load state at a point in the material, in the deformed state. Accordingly, the strain tensor ε_{ij} determines the state of strain at a given position, according to the tensile relationship $\varepsilon_{ij} = S_{ijkl} \times \sigma_{kl}$, where S_{ijkl} is the tensile compliance [30].

The main categories of non-Newtonian fluids are Power Law fluids (pseudoplastic or shear thinning and dilatant or shear thickening), Bingham plastics and Casson fluids (Figure 3.3).

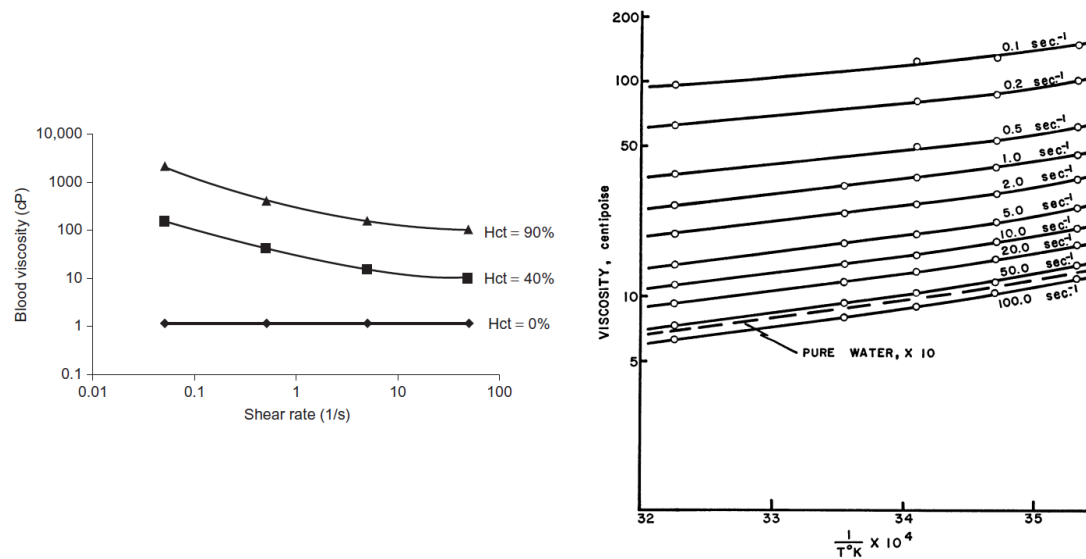


Figure 3.2 Blood viscosity dependency on strain rate, haematocrit [3] and temperature [7].

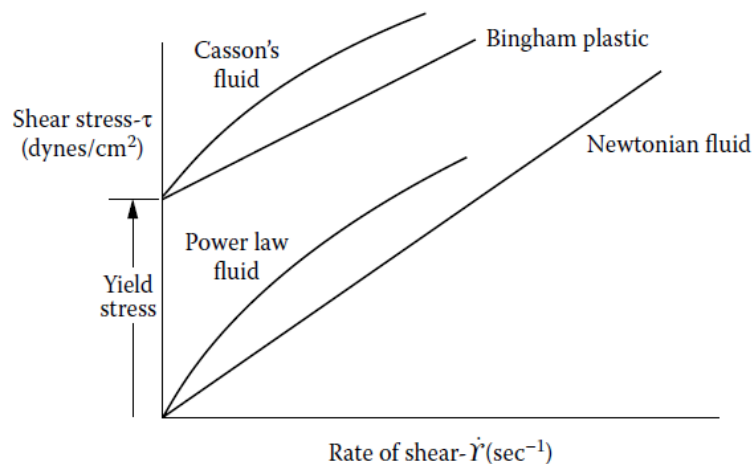


Figure 3.3 Stress-strain relationship for Newtonian and non-Newtonian fluids [2].

Pseudoplastic or shear-thinning fluids are a subcategory of fluids that obey the law of force. Their viscosity potential decreases as their deformation rate increases. In the blood, red blood cells tend to form agglomerates, resulting in flow resistance (increased viscosity). As the speeds increase, the agglomerates separate, making the blood thinner. Gradually, the red blood cells deform and become oriented along the flow, reducing the viscosity further. This behavior of viscosity over time is called thixotropic.

The law of force for fluids is expressed as:

$$\tau_{xy} = k \left(\frac{\partial u}{\partial y} + \frac{\partial v}{\partial x} \right)^n \quad (3.9)$$

, where k is called the flow consistency index and n is the behavior index. Pseudoplastic fluids, such as blood, have a behavior index of less than one, which indicates a decrease in viscosity.

The second category are **Bingham** plastics. These do not flow when subjected to small stress and a yield limit τ_y must be exceeded in order for there to be flow. In blood, this limit corresponds to the cohesive forces between the red blood cells. The behavior of this type of fluid is described as follows:

$$\tau_{xy} = \tau_y + \mu \left(\frac{\partial u}{\partial y} + \frac{\partial v}{\partial x} \right) \quad (3.10)$$

Blood is a combination of a pseudoplastic and Bingham plastic fluid. As a result, it is best modeled using the **Casson's model**:

$$\sqrt{\tau_{xy}} = \sqrt{\tau_y} + \sqrt{\eta} \sqrt{\left(\frac{\partial u}{\partial y} + \frac{\partial v}{\partial x} \right)} \quad (3.11)$$

, where n is the apparent viscosity, which is an experimental constant approaching blood viscosity. According to Merrill E. W. et al. [7], the yield stress of a healthy person is between 0.015 and 0.05 dynes/cm². In case of a steady and laminar flow, the shear stress at the center of the vessel is zero (parabolic velocity profile). Therefore, the blood in the center area will move like a solid body, since the leakage limit has not been exceeded, up to a radius r_y (Figure 3.4). Figure 3.5 compares the velocity profiles for all four types of fluids under constant flow conditions.

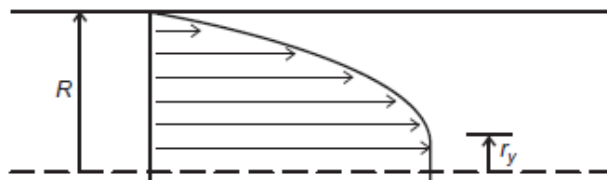


Figure 3.4 Theoretical blood velocity profile according to Casson's model.

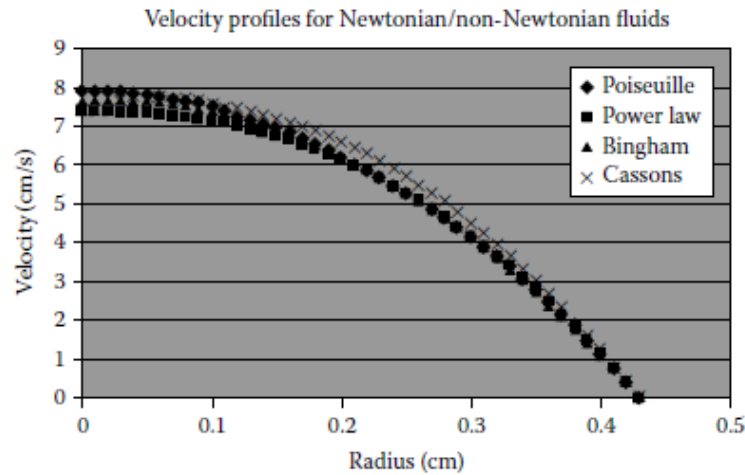


Figure 3.5 Newtonian and non-Newtonian fluid velocity profiles, for constant flow. In large arteries with high shear rates the deviations are small and the blood can be thought of as a Newtonian fluid.

According to Figure 3.2, for strain rates of $\dot{\gamma} > 100 \text{ s}^{-1}$ blood viscosity is expected to be constant. This happens to be the case, when studying blood vessels other than capillaries, where strain rates are sufficiently high, so that blood can be treated as a Newtonian fluid with a dynamic viscosity of $\mu = 3.5 \text{ mPa.s}$ [2,25]. Even with this simplification, deviations in flow properties observed are generally small, for example $< 10\%$ difference in WSS calculation in medium and large vessels [2].

3.3 FLOW PULSATILITY

Although constant flow models help us to approach the flow in the arteries, if we want a more accurate analysis we must take into account the pulsating nature of the flow in the circulatory system. Unstable flow models include the phenomenon of wave propagation of the pressure pulse through the arterial walls, the inertial accelerating forces of the blood and the dilatation of the arteries.

Due to the cardiac cycle, the blood supply profile to the vascular system is similar to that of the left ventricular pressure pulse (Figure 3.6). This pulsation weakens in the smaller vessels. In the large arteries there is a significant change in pressure with a range of about 40 mmHg and values of maximum and minimum pressure of 120 mmHg and 80 mmHg respectively (Figure 3.7).

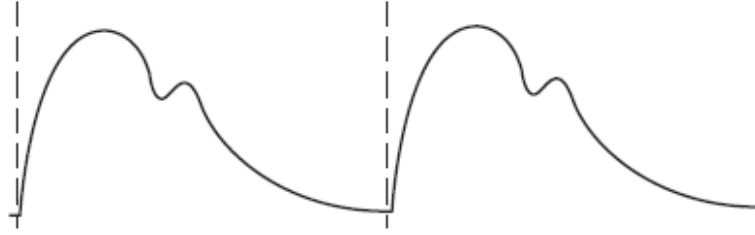


Figure 3.6 Blood supply waveform in a large artery.

The nature of the flow can be described by the Renolds number:

$$Re = \frac{\rho u d}{\mu} \quad (3.12)$$

, where d [m] is the vessel diameter, u [m/s] the blood velocity, ρ [kg/m³] is the blood density and μ [Pa·s] its dynamic viscosity. Reynolds number is the ratio of inertial to viscous forces of the flow. For values of $Re < 2320$ [11], the flow can be considered as laminar in a cylindrical vessel. For $2320 < Re < 10000$ flow can be regarded as transitional. For higher Re values, blood flow is fully turbulent. According to Stein et al. [8], in people with normal aortic valve Re ranges from 5700 to 8900, while in rare cases it approaches 10000. On the contrary, in patients with aortic insufficiency or stenosis the flow during the systolic phase is purely turbulent, with Re ranging 10000-20000.

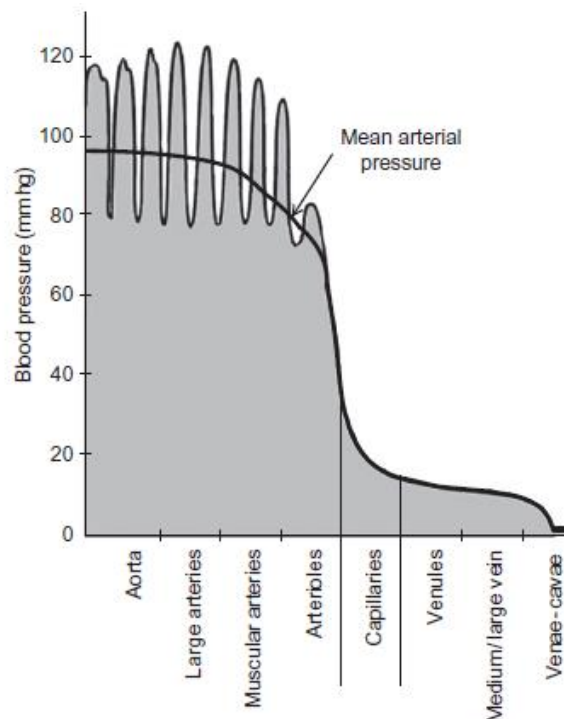


Figure 3.7 Pressure change in systemic circulation.

Several models for turbulent flow have been developed. A widely used one is the k - ω SST model, which uses two parameters³. The turbulent energy, k , can be computed as:

$$k = \frac{3}{2} (U I)^2 \quad (3.13)$$

, where U is the mean flow velocity and I is the turbulence intensity.

The specific turbulent dissipation rate, ω , is calculated as:

$$\omega = \frac{\sqrt{k}}{l} \quad (3.14)$$

, where l is the turbulent length scale. For a fully developed pipe flow it can be calculated as:

$$l = 0.038 d_h \quad (3.15)$$

, where d_h is the hydraulic diameter.

Despite the high Reynolds values (> 2300), in non-pathological conditions the flow does not become highly turbulent. This is due to the very short period of time, during which the systolic phase is at its peak, that does not allow the full development and maintenance of turbulent flow. At the end of the contraction, expansion occurs, during which the flow decelerates abruptly and transits to laminar.

Womersley number is used to characterize pulsatile flow and is the ratio of transient inertial forces of the flow over the viscous forces:

$$\alpha = R \sqrt{\frac{\omega \rho}{\mu}} \quad (3.16)$$

, where R [m] is the vessel radius, ω [rad/s] is the cyclic frequency of cardiac pulse, ρ [kg/m³] is the blood density and μ [Pa·s] the dynamic viscosity of blood. Womersley number ranges from 0.001 at the capillaries to 20 at the ascending aorta. For $\alpha > 1$ we can assume the blood to have a Newtonian behavior.

For all the above reasons, when examining flow in medium sized to large arteries we can assume the blood to be a Newtonian fluid and assume laminar flow.

³ Definitions available at https://www.cfd-online.com/Wiki/Turbulence_free-stream_boundary_conditions

3.4 REALISTIC FLOW MODELLING

3.4.1 WAVE PROPAGATION

Wave propagation in the arteries is related to the displacement of the arterial wall, in response to the propagation of pressure / velocity waves in the blood vessel. Pressure pulses are created by the contraction of the left ventricle of the heart. The displacement of the wall is possible due to the compliance of the vessels. To develop such a model, we assume a cylindrical blood vessel, which is thin-walled, homogeneous and elastic. The assumption that blood is incompressible remains, while we consider non-viscous flow.

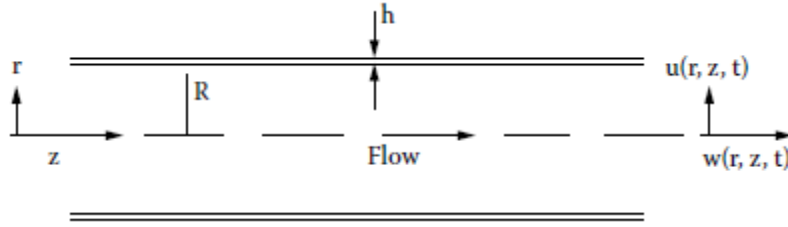


Figure 3.8 Schematic of wave propagation in a thin-walled, elastic tube.

Under these conditions and using the Navier-Stokes equation in the axial direction, as well as the balance of forces in the radial direction, one arrives at the pressure wave equation [2]:

$$\frac{\partial^2 p}{\partial z^2} = \frac{1}{c_0^2} \frac{\partial^2 p}{\partial t^2}$$

, with C_0 described by the Moens-Korteweg equation:

$$c_0^2(\omega) = \frac{hE}{2R\rho} \left(1 - \frac{\omega^2 \rho_t R^2}{E} \right) \quad (3.17)$$

, where $C_0(\omega)$ is the pressure pulse propagation velocity, h is the wall thickness, E the wall's Young modulus, R the radius, ρ the blood density, ω the cyclic frequency of the pulse and ρ_t the density of the wall material.

In Equation (3.17), although the frequency is included, the order of magnitude of the second term in parentheses is much smaller than one. Therefore, the speed of wave propagation will be substantially constant over a wide range of frequencies.

A second approach can be made with the Womersley model. The assumptions that differ are that the viscosity terms are taken into account in the constitutive equations, but we consider rigid walls. This means that the propagation speed is virtually infinite.

If we assume a sinusoidal change for the pressure gradient $\frac{dp}{dz} = |A|e^{i\omega t}$, as well as the velocity, the Navier-Stokes equation takes the form of a first type Bessel differential equation, in terms of axial velocity [12]. The solution of this equation, for the real part of the pressure step is calculated as:

$$u_z(r) = -\frac{|A|R^2}{\mu} \frac{M'_0}{a^2} \sin(\omega t - \varphi + \varepsilon_0) \quad (3.18)$$

and

$$Q = \int_0^R 2\pi r u_z(r) dr = \frac{|A|R^4}{\mu} \frac{M'_{10}}{a^2} \cos(\omega t - \varphi + [90^\circ - \varepsilon_{10}]) \quad (3.19)$$

, where $|A|$ is the pulse amplitude of the pressure gradient, μ is the dynamic viscosity, M'_{10} , ε_{10} the modulus and the phase difference, which are functions of the J functions of the Bessel equation and α the Womersley number.

As an example, if α becomes zero, meaning we have a constant flow, the ratio $\frac{M'_{10}}{a^2}$ and ε_{10} become 1/8 and 90° respectively (Figure 3.9). Under these conditions, the volumetric flow Q takes the form of the Haegen-Poiseuille relation (Equation 2.5). As the pulse frequency increases, the flow tends to decrease and the phase difference between pressure and flow increases.

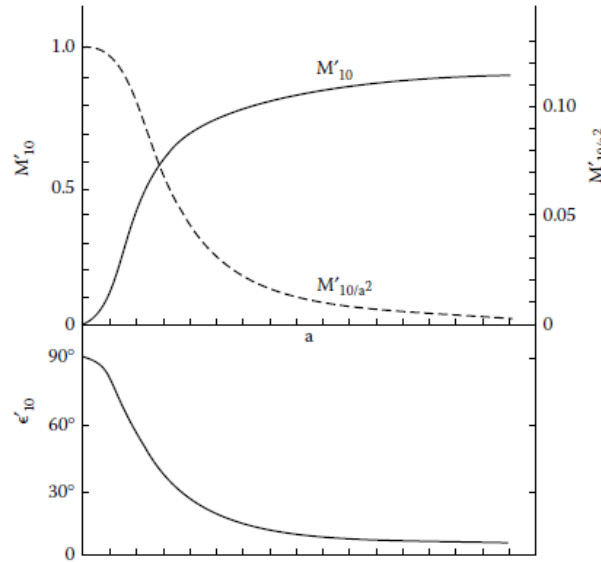


Figure 3.9 Modulus and phase difference of Womersley model as a function of α .

Figure 3.10 shows the real pulse of an artery. This pulse can be analyzed in Fourier series, as the sum of harmonics. The middle panel depicts the first harmonic of the pressure pulse and the last depicts the calculated flow. Also shows the phase difference, as predicted by the Womersley model.

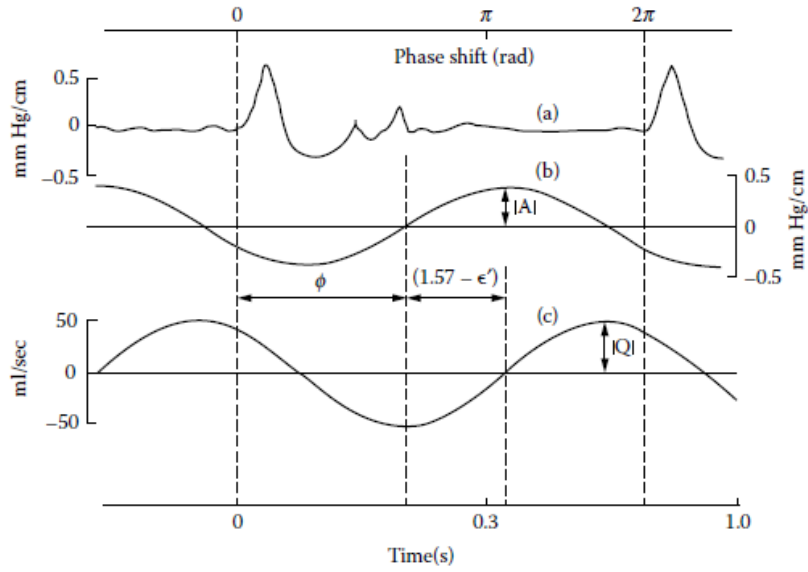


Figure 3.10 Artery pressure gradient and the first harmonics of it and the computed fluid supply. We can see the pressure gradient amplitude $|A|$, the volumetric flow rate $|Q|$ (function of $|A|$, $\frac{M'_{10}}{a^2}$) and the phase difference ϵ_{10} .

3.4.2 FOURIER ANALYSIS

The basic principle of Fourier analysis is that any complex waveform, such as an arterial pressure wave, can be broken down into a set of sine waves and then be recomposed from them. Each of these waves (called harmonics) will have a different amplitude and frequency, and will be out of phase with the others. Thus, for a single sinusoidal pressure wave, we can calculate the corresponding blood flow rate wave. Then, the complex flow waveform can be constructed by adding all the sine waves. Such an analysis, however, will only be valid if the system under study is linear. Otherwise, the different harmonics interact, and the behavior of the composite wave cannot be predicted by superimposing the individual sines.

A possible source of non-linearity is due to the fact that the pressure changes, which occur in the vessel due to the pressure pulse, cause deformation in its cross section. From Equation (2.4), this means that the velocity of the blood changes along the vessel, and therefore there will be convection accelerations, but also local accelerations, which will compensate for the varying pressure gradient. From Bernoulli's law (Equation (2.10)) we observe that the nonlinear term is that of the convection acceleration, $\frac{u^2}{2}$. To eliminate this source of nonlinearity, the time scale of local velocity changes, i.e. the

wave period, must be much less than the time required for an element to be transported to a position with a different velocity (wavelength/fluid velocity u). For this to be valid:

$$\frac{\bar{u}}{c_0} \ll 1 \quad (3.20)$$

, where $\bar{u}$ is the average velocity of the fluid and c_0 the pulse propagation velocity. In large arteries this ratio has a value of about 0.2 [32], which roughly satisfies the condition of linearity.

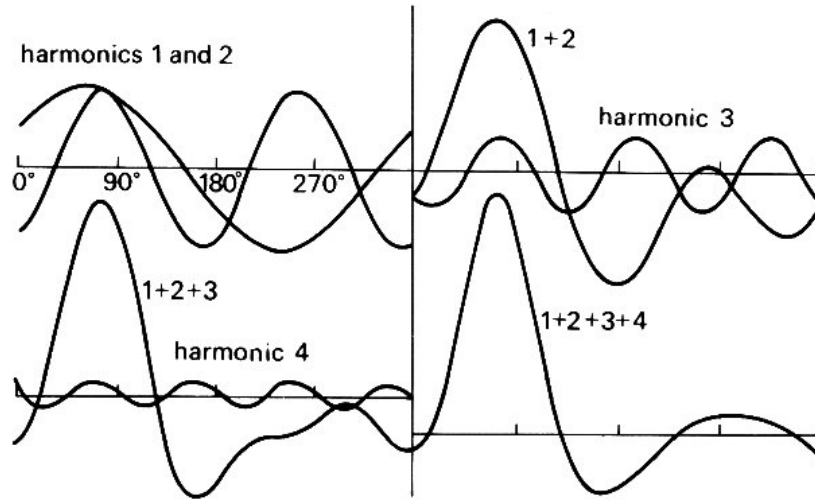


Figure 3.11 Velocity pulse analysis in Fourier series. Superposition of the first four harmonics of the pulse in an artery.

The velocity waveform in an artery can be adequately approximated using four harmonics (Figure 3.11). Its equation is:

$$u = u_0 + u_1 \cos(\omega t + \theta_1) + u_2 \cos(2\omega t + \theta_2) + u_3 \cos(3\omega t + \theta_3) + u_4 \cos(4\omega t + \theta_4) \quad (3.21)$$

, where $u_2/u_1=0.97$, $u_3/u_1=0.47$, $u_4/u_1=0.14$, $\theta_1 = -1.01$ rad, $\theta_2 = -2.64$ rad, $\theta_3 = 2.16$ rad, $\theta_4 = 1.5$ rad. The pressure gradient analysis in Fourier series, as a sum of sines, will have a zero mean value. To achieve a positive net flow, we must add, a constant flow u_0 to the pulsatile flow.

If we consider that the pressure and velocity waves change spatially, their harmonics will take the form $B\cos[\omega(t - x/c_0) - \theta]$. From Navier-Stokes Equation (3.3), if we ignore the external field force term and assume non-viscous flow, we get the expression:

$$\rho \frac{du}{dt} = -\frac{dp}{dx} \quad (3.22)$$

Deriving the term of a harmonic to find the acceleration and the pressure gradient we get:

$$\begin{cases} \rho \frac{du}{dt} = -\omega u_0 \rho \sin[\omega(t - x/c_0) - \theta] \\ -\frac{dp}{dx} = -\frac{\omega p_0}{c_0} \sin[\omega(t - x/c_0) - \theta] \end{cases} \quad (3.23)$$

Therefore, for the equality of Equation (3.23) to apply, the following must hold true:

$$u_0 = \frac{p_0}{\rho \cdot c_0}. \quad (3.24)$$

For the above Fourier analysis, the following must be taken into account:

- i. The vessel is considered to be of infinite length. In fact, wave reflections occur at the end of the arteries. Typically, the length of the aorta is about 0.5 m, while the wavelength of the first harmonic is 4 m, for a frequency of 1.2 Hz and a propagation speed of 5 m / s.
- ii. Arteries do not have a fixed cross-section along their length, such as a narrowing aorta.
- iii. The non-linear behavior of biological systems.
- iv. The fact that we consider non-viscous flow, thus ignoring the viscous diffusion of energy, which leads to the damping of the wave. In theory, viscosity damping can be approached through the relation:

$$\tilde{p} = p_0 e^{-kx/\lambda} \cos[\omega(t - x/c_0) - \theta] \quad (3.25)$$

3.5 FLOW IN BIFURCATIONS

The vascular system includes a complex network of vessels, interconnected at various angles and branches. These complex geometries impose major changes in the form of the flow in them, which affect the circulation dynamics and the forces exerted on the inner wall of the vessels.

As the blood reaches the branch area (Figure 3.12), the flow divides into two daughter vessels (i.e. the iliac arteries). On the walls, near the beginning of the branch, the boundary layer⁴ is relatively thin and the maximum velocity is outside of it. When blood enters the daughter vessel, the fluid with the highest velocity is on the side of the

⁴ The boundary layer is defined as the area near the wall, where the velocity of the fluid changes from zero to the velocity of the free flow [11].

flow separator, resulting in an asymmetric velocity profile. On this side of the walls, due to the small boundary layer and the large slope of velocity, high shear stresses are observed, which are responsible for the destruction of the endothelial wall (see Chapter 2.4). On the outer wall boundaries, the phenomenon of flow separation may occur.

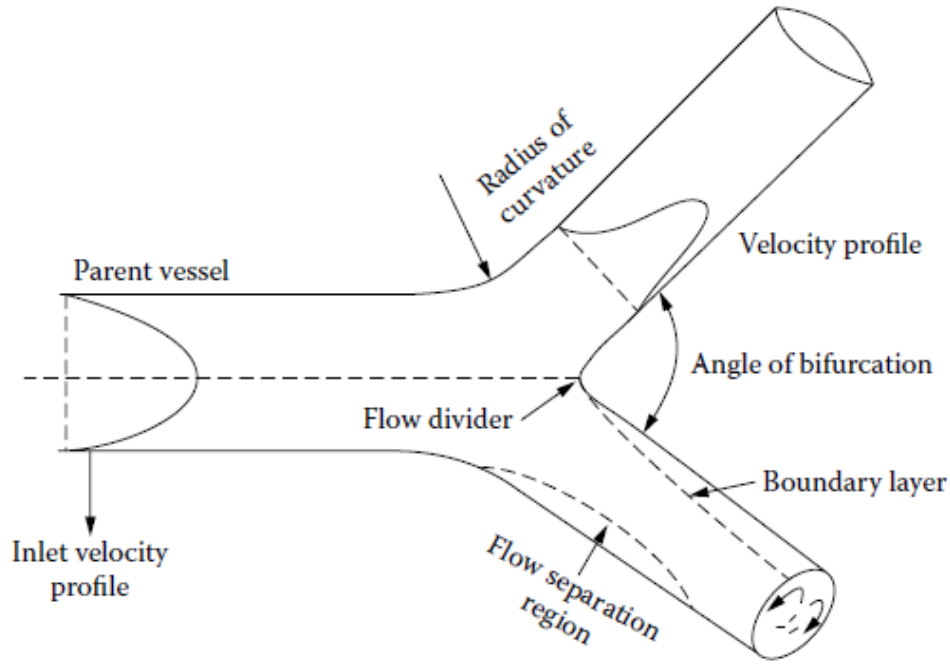


Figure 3.12 Geometry and flow development at a bifurcation.

Flow separation happens when the fluid diverges from the wall, forming a very low flow velocity region. In this area recirculation zones are usually created, in which the fluid is trapped, as it cannot overcome the pressure of the moving fluid in order to return to the main flow. Recirculation zones may occur at a fork following a significant 50% narrowing in the main branch. They can also be formed after 90% stenosis with or without the presence of a branching [22]. A common way to create separation is to have a reverse pressure gradient. In a simplified, constant, pressure-driven flow, the Navier-Stokes equation (Equation 3.3) near the wall becomes:

$$\left. \frac{\partial^2 u}{\partial y^2} \right|_{y=0} = \frac{1}{\mu} \frac{\partial p}{\partial x} \left(\frac{1}{m \cdot s} \right) \quad (3.26)$$

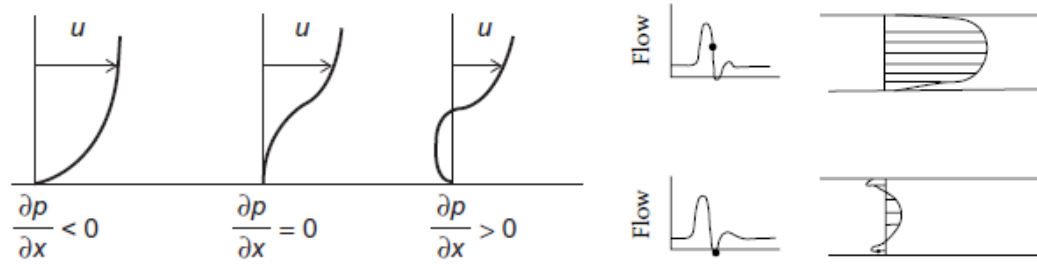


Figure 3.13 Pressure gradient effect on velocity profile near the wall.

To maintain a flow without recirculation zones the curvature should have the same sign as the pressure gradient. In general, the pressure gradient is negative, so the parabolic profile near the wall matches the sign. When the pressure gradient approaches zero or becomes positive, the flow begins to separate from the walls (Figure 3.13). This can happen during the diastolic phase of the left ventricle, when the flow slows down sharply.

4 ARTERIAL WALL MECHANICS

As blood flows through the arterial system, there is a constant interaction between the fluid and the wall of the arteries. To study the unstable blood flow, it is necessary to approach the mechanical behavior of the vascular wall as a biological solid.

The interaction between stress and strain for an elastic material is a constitutive equation that describes the behavior of the material when it is under external load. The most typical constitutive equation is Hooke's law [30]:

$$\varepsilon_{ij} = C_{ijkl}\sigma_{kl} \quad (4.1.1)$$

, where σ_{ij} , ε_{kl} are the stress and strain tensors and C_{ijkl} is the compliance tensor.

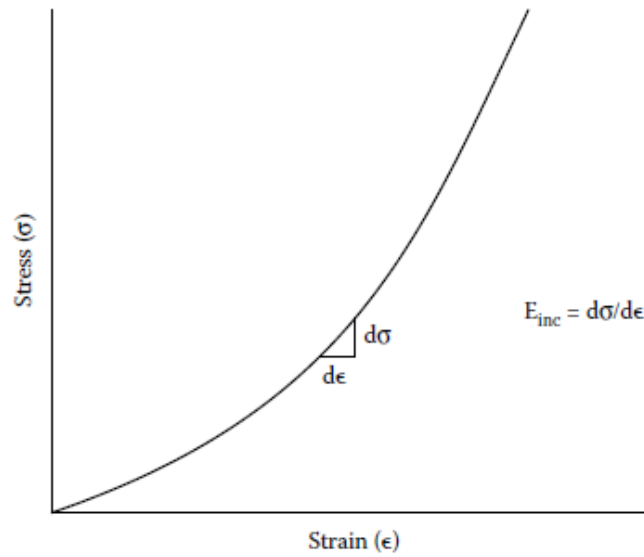


Figure 4.1 Stress-strain curve for a biological, soft tissue.

If we consider a homogeneous, isotropic and linearly elastic material, in a generalized intensive state, Hook's law can be expressed as a matrix [31]:

$$\begin{Bmatrix} \varepsilon_x \\ \varepsilon_y \\ \varepsilon_z \\ \gamma_{yz} \\ \gamma_{xz} \\ \gamma_{xy} \end{Bmatrix} = \begin{bmatrix} 1/E & -\nu/E & -\nu/E & 0 & 0 & 0 \\ & 1/E & -\nu/E & 0 & 0 & 0 \\ & & 1/E & 0 & 0 & 0 \\ & & & 1/G & 0 & 0 \\ & & & & 1/G & 0 \\ & & & & & 1/G \end{bmatrix} \begin{Bmatrix} \sigma_x \\ \sigma_y \\ \sigma_z \\ \tau_{yz} \\ \tau_{xz} \\ \tau_{xy} \end{Bmatrix} \quad (4.1.2)$$

, where ν is Poisson's ratio. For incompressible materials, a category in which biological materials are classified, we consider $\nu \approx 0.5$ [32], which is the maximum possible value it can get. The shear modulus is calculated as $G = \frac{E}{2(1+\nu)}$ [13]. Young's modulus of elasticity is approached in Section 4.3.

The above relations describe the behavior of a linear material. To describe mathematically and more accurately the mechanical behavior of a nonlinear material (Figure 4.1), such as a blood vessel, alternative stress-strain relations are used. Those are mainly exponential, polynomial or logarithmic.

The motion of an elastic solid is mathematically described as [44]:

$$\rho_w \frac{\partial^2 d_i}{\partial t^2} = \frac{\partial \sigma_{ij}}{\partial x_j} + F_i \left(\frac{N}{m^3} \right), \quad i = 1, 2, 3 \quad (4.2)$$

, where d_i, σ_{ij} are the elements of the displacement and stress tensors, ρ_w is the arterial wall density and F_i are the elements of the field force vector per volume unit acting on the solid. The elements of the stress tensor can be calculated from the constitutive equation of the material, which for a Hookean elastic solid can be represented as:

$$\sigma_{ij} = \lambda e_{kk} \delta_{ij} + 2\mu e_{ij} \quad (4.3)$$

, where λ, μ are the Lamé coefficients, δ_{ij} is Kronecker's delta ($=1$ για $i=j$ και $=0$ για $i \neq j$) and e_{ij} are the strain tensor elements.

4.1 THIN-WALLED CYLINDRICAL VESSELS

As a first approach, large arteries can be thought of as thin-walled, elastic, cylindrical vessels. To apply the thin-walled vessel theory, the thickness ratio to the radius of the vessel cross-section must be less than 1/10. This condition is met for the large and medium-sized arteries (Figure 4.2).

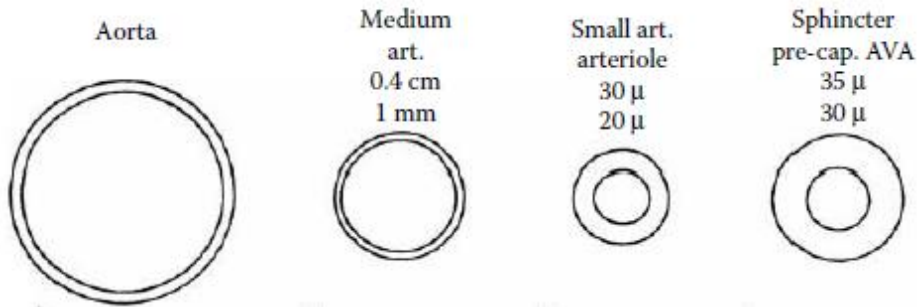


Figure 4.2 Diameter and wall thickness for various types of arteries [2].

By applying the equilibrium condition on a longitudinal and a transverse section of the cylindrical vessel (Figure 4.3), we can calculate the tangential σ_θ and axial σ_z stresses, as follows [13]:

$$\begin{cases} \sigma_\theta = \frac{pR}{t} \\ \sigma_z = \frac{pR}{2t} \end{cases} \quad (4.4)$$

, where p is the internal pressure, R the radius and t the wall thickness of the vessel.

The initial perimeter of the cross section has a value of $2\pi R$. As the radius increases by an amount of ΔR , due to the existing internal pressure, the tangential deformation is calculated as:

$$\varepsilon_{\theta} = [2\pi(R + \Delta R) - 2\pi R] / 2\pi R = \Delta R / R \quad (4.5)$$

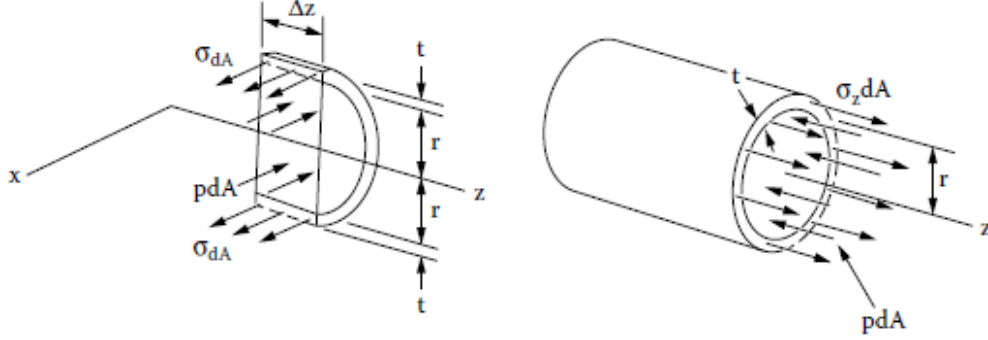


Figure 4.3 Development of forces on a thin-walled vessel's cross-sections.

Therefore, from Equations (4.4), (4.5) the vessel Young modulus is calculated as:

$$E = \frac{\sigma_{\theta}}{\varepsilon_{\theta}} = \frac{pR^2}{t\Delta R} \quad (4.6)$$

When the thin-walled vessel condition is not met, as is the case with arterioles ($t / R > 0.1$), a thick-walled vessel model should be used.

4.2 VISCOELASTICITY – DYNAMIC LOADING

The previous analysis applies to purely elastic materials, in which the application of load, leads to an instantaneous deformation. When the load is removed, the material instantly returns to its original dimensions. In a viscous material, the deformation does not occur directly, due to the fact that the applied stress is a function of the shear rate (Equation (3.4)). A material that exhibits both elastic and viscous behavior is called viscoelastic. The elastic element of such a material obeys Equation (4.1), while the viscous one Equation (3.4).

The behavior of a viscoelastic material can be modeled with a spring and a viscous damping either in series (Maxwell Model), parallel (Kelvin-Voight Model) (Figure 4.4) or in any other combination of those.

In the case of Maxwell's model, the constitutive equation is [26]:

$$\frac{\dot{\sigma}}{E_s} + \frac{\sigma}{\mu} = \dot{\varepsilon} \quad (4.7)$$

, while in Kelvin-Voight's model it is given by:

$$\sigma = E_s \varepsilon + \mu \dot{\varepsilon} \quad (4.8)$$

, where E_s is the elastic element's Young's modulus and μ is the dynamic viscosity of the viscous element.

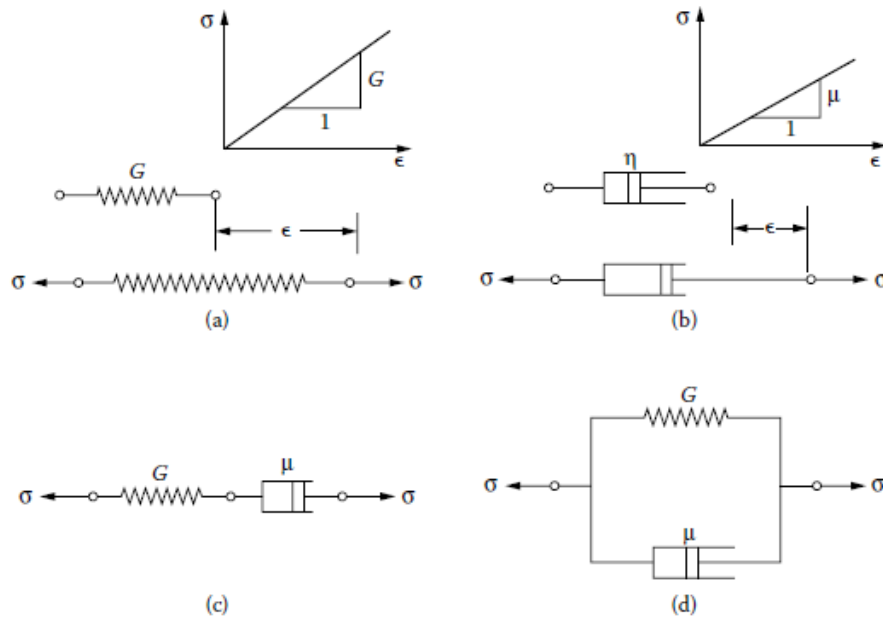


Figure 4.4 The Maxwell and Kelvin-Voigt models. Modeling of viscoelastic material with spring and viscosity damping in series (Maxwell model, left) and in parallel (Kelvin-Voigt model, right) [2].

In general, two-element models are not sufficient to describe the viscoelastic behavior, under various loading conditions, so models with three or more elements are used to describe the behavior of real materials. The properties of these materials are determined by creep experiments (measurement of strain under constant voltage) and relaxation of stress (measurement of stress under constant strain. From these experiments it is shown that a finite time period must pass from the application of the stimulus to the finalization of the response, in the case of static loading.

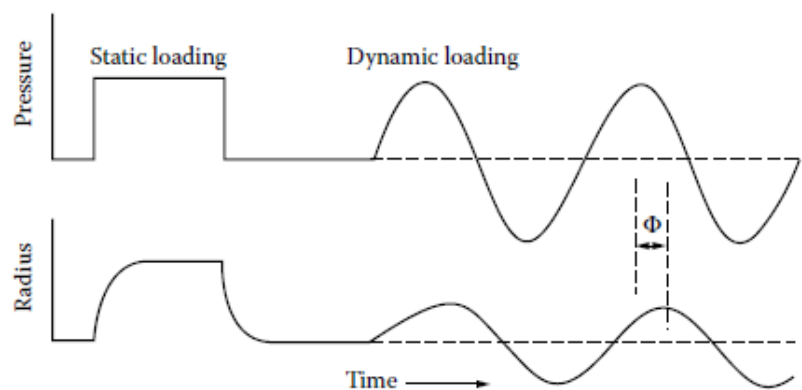


Figure 4.5 Response of a viscoelastic material under static and dynamic loading [2].

In the case of dynamic loading of a vessel, we consider that the pressure changes sinusoidally (as is the case with the pressure pulse from Fourier series analysis). The response is shown in Figure 4.5. The two oscillations have the same frequency, but due to the viscosity, there is a phase difference ϕ . In addition, we observe that the maximum value of the deformation under sinusoidal load is less than the static deformation. This is because before the response reaches its maximum value, the load has already started to decrease.

Due to the phase difference between the applied flow pressure and the change in the radius of the vessel, the dynamic measure of elasticity is a complex quantity and is described by the relation [26]:

$$E^* = |E^*|e^{i\phi} = |E^*|\cos\phi + i|E^*|\sin\phi \quad (4.9)$$

, where the real part corresponds to the storage modulus, while the complex part expresses the loss modulus. As the frequency of the dynamic loading increases, for the same applied mean stress, the deformation of the material decreases, as it does not manage to fully respond to the load in time, due to inertia. Based on this and according to Equation (4.1), the dynamic modulus of elasticity is expected to be higher than the corresponding static one.

In the case of a thin-walled vessel (Figure 4.6), the complex elastic measure is modified as:

$$E^* = \frac{pR^2}{t\Delta R} e^{i\phi} \quad (4.10)$$

4.3 MECHANICAL BEHAVIOUR OF BLOOD VESSELS

As we discussed in Section 2.1, the artery wall is largely made of elastic tissue. This tissue is mainly composed of elastin and collagen fibers. Elastin fibers have a low degree of elasticity and are easily deformed. Collagen, on the other hand, is much stiffer. Albeit, because its fibers are initially in a state of relaxation, their complete rigidity does not become apparent until they are fully stretched. For this reason, the walls of the arteries can be characterized in the simplest case as a bilinear material (Figure 4.6) with a measure of elasticity of the elastin phase $E_{el} \approx 0.6 - 1$ MPa and a measure of elasticity of the collagen phase $E_{col} \approx 1000$ MPa [20], [21].

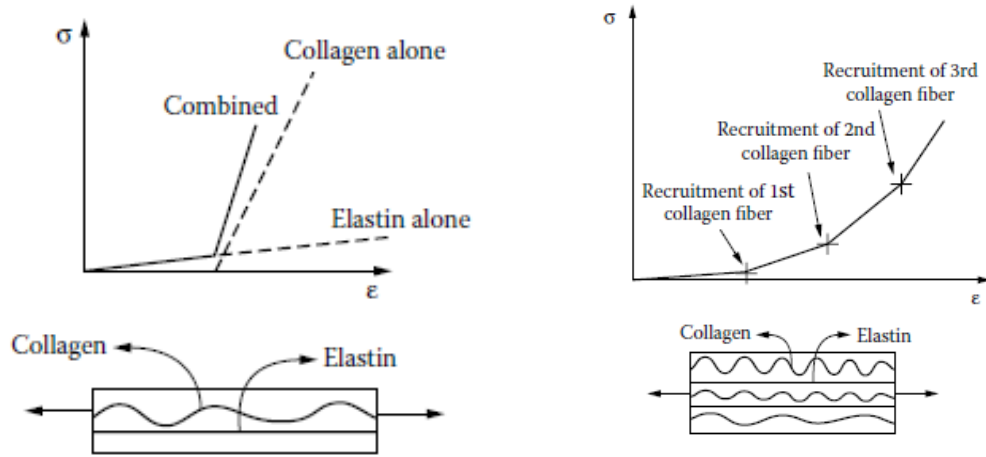


Figure 4.6 Stress-strain curves of biological tissue for a combination of elastin and collagen fibers. As the deformation increases, more and more collagen fibers align, resulting in an increase in the incremental modulus of elasticity. In the simplest case of bilinear material, two phases are distinguished: the elastin phase and the collagen phase [2].

The mechanical properties of the vessels were determined in vivo by Peterson et al. [15], following a study in animal arteries. Considering the arteries as thin-walled and incompressible pressure vessels, their viscoelastic behavior is described by Equation (4.6). The study showed that the viscosity component is small compared to the elastic one. The values of Young's modulus ranged from 1.9×10^5 to 34.3×10^5 Pa. Bergel et al. [16,17] calculated the measure of elasticity of different types of arteries, based on the theory of a thick-walled container for homogeneous and isotropic material, by performing in vitro experiments on canine arteries. The findings showed that the dynamic modulus of elasticity may range between 1 and 20×10^5 Pa, depending on the pressure amplitude, frequency and type of artery examined.

The main synthetic materials used in the manufacturing of artificial vessels are polyethylene terephthalate (PET or Dacron®), polytetrafluoroethylene (PTFE or Teflon®) and polyurethane (compliant poly(carbonate)polyurethane or CPU) [2,27]. Dacron is commonly used in large diameter vessels, while PTFE is used in smaller diameters. The disadvantage of these materials is their high elastic modulus (Figure 4.7).

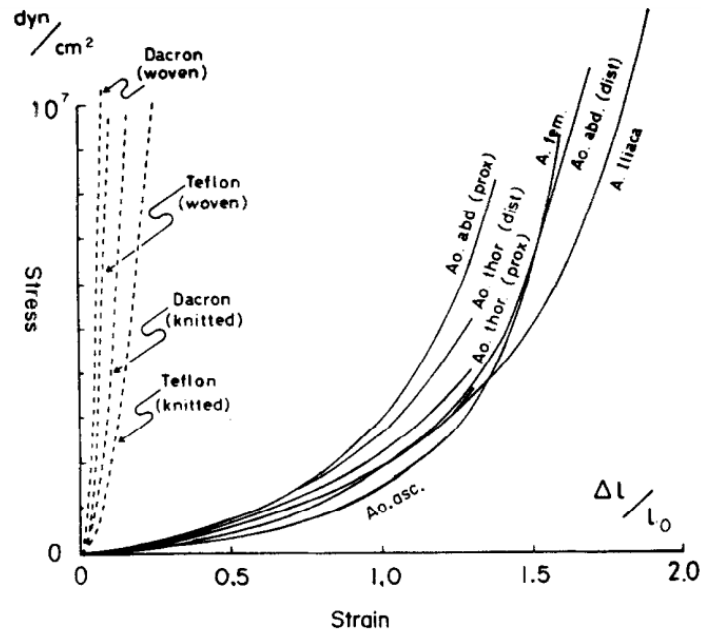


Figure 4.7 Tangential stress-strain curves of biological arteries (continuous lines) and polymeric arterial grafts (dashed lines). The slope of each curve gives the incremental modulus of elasticity of the corresponding material. Ao. thor. (prox) and Ao. thor. (dist): Proximal and distal thoracic aorta, Ao. abd. (prox) and Ao. abd. (dist): Proximal and distal abdominal aorta, Ao. Asc.: Ascending aorta, A. fem.: Femoral artery, A. iliaca: Iliac artery [19].

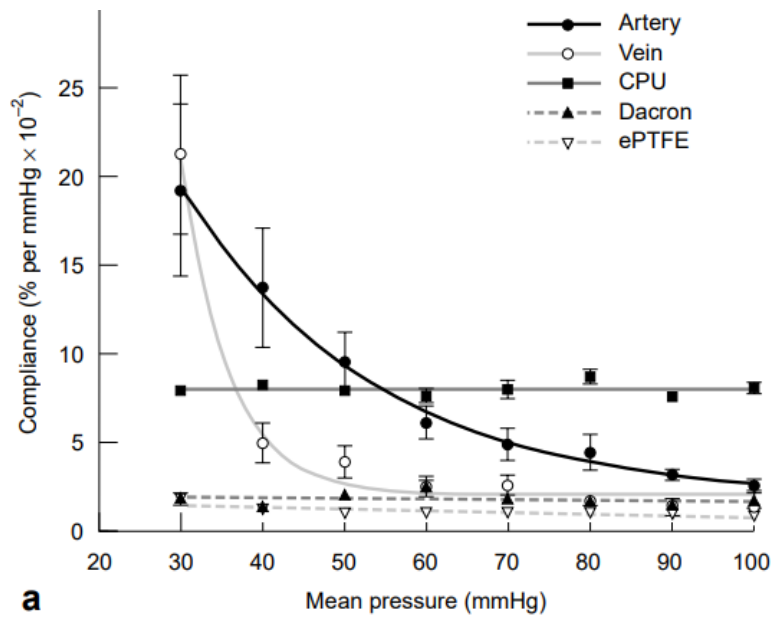


Figure 4.8 Compliance- mean pressure curves for biological and artificial vessels. CPU: compliant polyurethane, Dacron: polyethylene terephthalate, ePTFE: expanded polytetrafluoroethylene [27].

The module of elasticity of a Dacron® graft is 2.1 MPa [8]. Sugie et al. [18] observed that the dispensability of Teflon grafts was 1/10 of the corresponding value of the biological thoracic aorta. For this reason, a more compliant version of PTFE, the (expanded) ePTFE, is used in many applications, but it does not have adequate blood

compatibility and resistance to thrombogenesis. The much lower compliance of artificial compared to biological vessels (Figure 4.8) remains a problem to be solved. A novel approach by Dimopoulos, Markatos et al. (2021) [66] of the university of Patras is a promising step in developing artificial grafts with a compliance similar to biological arteries.

4.4 VASCULAR COMPLIANCE COMPUTATION

The concept of vascular flexibility is defined in Section 2.1. Here, we will define some ways to calculate it

Theoretically, the compliance of the vessel can be calculated from Equation (4.11) [47]:

$$C_R = \frac{\Delta R/R}{\Delta p} \quad (4.11)$$

, while the volumetric compliance is calculated as:

$$C_V = \frac{\Delta V/V}{\Delta p} \quad (4.12)$$

In case we assume R to be the internal radius of the vessel and V its internal (lumen) volume, the following relation must hold true:

$$C_V = 2C_R \quad (4.13)$$

Alternatively, vascular compliance in an operating pressure range can be computed based on ISO 7198:2016 “Cardiovascular implants and extracorporeal systems – Vascular prostheses – Tubular vascular grafts and vascular patches”. Radial compliance is expressed as the percentage of diameter change per 100 mmHg.

$$\% \text{ compliance} = \frac{(R_{p_2} - R_{p_1}) / R_{p_1}}{(p_2 - p_1)} \times 10^4 \quad (4.14)$$

, where:

$$R_p = (D_p/2) - t$$

p2	Lowest operating pressure (mmHg)
p1	Highest operating pressure (mmHg)
Rp	Internal radius under pressure
Dp	Measured external diameter under pressure
t	Wall thickness

4.5 HYPERELASTIC MATERIALS

For many materials, linear elastic models do not accurately describe their behavior. Hyperelastic materials is a type of constitutive model of elastic materials, for which the stress-strain relationship derives from a strain energy density function [33]. Hyperelastic materials are generally non-linear elastic, isotropic, incompressible and their stress-strain ratio is independent of the strain rate. Elastomers are classified in this category, as well as biological tissues [34]. Some of the most popular super-elastic models are the Mooney-Rivlin, the Neo-Hookean [53,55,57,61,62] and the Ogden material [54,57,62].

4.5.1 OGDEN MATERIAL

In the Ogden model, the density function of the strain energy is expressed as a function of the main "stretches", λ_j , $j = 1,2,3$. Assuming incompressible material, the function takes the form [67]:

$$W(\lambda_1, \lambda_2, \lambda_3) = \sum_{i=1}^N \frac{c_i}{m_i^2} (\lambda_1^{m_i} + \lambda_2^{m_i} + \lambda_3^{m_i} - 3) + U(J) \quad (4.15)$$

, where c_i, m_i are material parameters, and N is the model order. The $U(J)$ term expresses the compressibility of the material and can be neglected for high values of bulk moduli K . The Initial shear modulus is calculated as:

$$\mu = \frac{1}{4} \sum_{i=1}^N c_i m_i \quad (4.16)$$

The three principal Cauchy stresses can be calculated from the relation:

$$\sigma_j = -p + \lambda_j \frac{\partial W}{\partial \lambda_j} = p + \sum_{p=1}^N \mu_p \lambda_j^{\alpha_p} \quad (4.17)$$

The values of the Ogden model coefficients can be calculated experimentally with uniaxial tensile, biaxial tensile and shear experiments. In finite element packages the parameters can be calculated by fitting theoretical curves in a swarm of experimental points from the above experiments.

4.5.2 MOONEY-RIVLIN MATERIAL

The 2-parameter Mooney-Rivlin strain energy function given as:

$$W = C_1(I_1 - 3) + C_2(I_2 - 3) + \frac{K}{2}(\ln(J))^2 \quad (4.17)$$

Where:

C_1 , C_2 : Mooney-Rivlin constants (MPa)

K : Bulk modulus like, penalty parameter (MPa)

I_1 : first invariant of the deviatoric right Cauchy-Green deformation tensor

I_2 : second invariant of the deviatoric right Cauchy-Green deformation tensor

J : determinant of the deformation gradient tensor (volume ratio)

In case that we set $C_2 = 0$, we get the constitutive equation of a Neo-Hookean material. Both Neo-Hookean and mooney-Rivlin models (usually of 3 or 5 more parameters) are widely used in FEM simulations of biological systems [53,55,57,61,62].

5 COMPUTATIONAL MODELLING AND SIMULATION

The rapid development of computer technology and the field of Computational Fluid Dynamics (CFD) has allowed computational analysis to gradually become the main method of studying and simulating hemodynamic problems in recent decades [36]. However, there are still problems to be solved. The pulsating nature of blood flow representing a true heart waveform has not been adequately studied [37]. Also, in many studies the vessels are modeled as simple cylindrical tubes, like in [38,39], where blood flow in vascular branches was studied, considering a fixed cross section, i.e. rigid vessels. All of these assumptions lead to approximate solutions. Arterial stenosis has also been studied without taking into account the arterial compliance [40]. An early approach was attempted by Mortazavinia et al. [41], in order to simulate pulsatile blood flow and investigated its effect on the vascular wall. Some of the computer programs used extensively for flow simulation are Ansys Fluent, ICEM CFD, COMSOL Multiphysics, openFoam and Febio, following the same basic principles.

Traditional computational fluid dynamics simulations, albeit being able to provide important information about flow conditions, in some cases make assumptions about them, which overall reduce the reliability of the numerical solution. One such assumption is the view of the walls as undeformable (rigid). A modern approach to artery modeling employs a different technique, in addition to the classical fluid dynamics simulations, called Fluid-Structure Interaction and is described in Section 5.3.

5.1 COMPUTATIONAL FLUID DYNAMICS

Most CFD packages use the finite volume method (FVM)⁵ to discretize the fluid volume. The equations governing the problem are integrated in a control volume and their integrated form is discretized [45]. This method calculates conservative quantities

⁵ The finite volume method is used for solving partial differential equations, in the form of algebraic equations. The values are calculated at discrete points of a grid. In this method, volume integrals containing terms of deviation are converted to surface integrals, according to Gauss' theorem. These terms are calculated as outflows through the surfaces of each finite volume. The inflow to each volume element is equal to the outflow of its adjacent element.

such as mass, pressure and energy. The fluid volume grid can be created using prismatic, tetrahedral or hexagonal elements, as well as combinations of them.

The basic parameters characterizing blood flow are velocity u and pressure p . Through these, the stresses that develop in the arterial wall can be calculated. The mathematical equations that govern the fluid domain are the continuity Equation (3.2), as well as the Navier-Stokes Equation (3.3), which for incompressible, Newtonian fluid take the form:

$$\frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} + \frac{\partial w}{\partial z} = 0 \quad (5.1)$$

and

$$\begin{cases} \rho \left(\frac{\partial u}{\partial t} + u \frac{\partial u}{\partial x} + v \frac{\partial u}{\partial y} + w \frac{\partial u}{\partial z} \right) = -\frac{\partial p}{\partial x} + \mu \left(\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} + \frac{\partial^2 u}{\partial z^2} \right) + F_x \\ \rho \left(\frac{\partial v}{\partial t} + u \frac{\partial v}{\partial x} + v \frac{\partial v}{\partial y} + w \frac{\partial v}{\partial z} \right) = -\frac{\partial p}{\partial y} + \mu \left(\frac{\partial^2 v}{\partial x^2} + \frac{\partial^2 v}{\partial y^2} + \frac{\partial^2 v}{\partial z^2} \right) + F_y \\ \rho \left(\frac{\partial w}{\partial t} + u \frac{\partial w}{\partial x} + v \frac{\partial w}{\partial y} + w \frac{\partial w}{\partial z} \right) = -\frac{\partial p}{\partial z} + \mu \left(\frac{\partial^2 w}{\partial x^2} + \frac{\partial^2 w}{\partial y^2} + \frac{\partial^2 w}{\partial z^2} \right) + F_z \end{cases} \quad (5.2)$$

, where u , v , w are the components of the velocity of the fluid on the three axes, p is the pressure, μ the dynamic viscosity and F the external force, which are generally omitted.

In most studies, Arbitrary Lagrangian-Eulerian (ALE) methods are used for solving these equations and computational blood flow determination in models such as tubes and bifurcations [55].

5.2 COMPUTATIONAL STRUCTURAL MECHANICS

The structural problem of the vascular wall can be solved by the finite element analysis (FEA) method, based on displacement fields. The values of the quantities of the field are calculated at the nodes, i.e. the points of the mesh where elements are joined, loads are imposed and boundary conditions are introduced. The vascular wall can be discretized using either shell elements, if it meets the requirement of a thin-walled vessel, or with solid elements. The meshes of the solid and fluid domains may be distinct, or shared, as explained in Section 5.3.

The motion of the solid domain (vascular wall) is described by Equations (4.2) and (4.3), which are solved at each node of the mesh. From these, we can calculate the deformation of the wall and the displacement of the mesh at the fluid-structure boundary.

5.3 FLUID – STRUCTURE INTERACTION

Fluid-Structure Interaction (FSI) is a modeling approach that helps us to design more realist models in the process of using fluid mechanics in the cardiovascular system [3]. For example, the blood flow in a vessel is affected by its permeability and conversely, the diameter of the vessel changes due to the pressure exerted by the heartbeat on its walls. In the case of pathologies such as an aneurysm, vascular dilatation increases and the need for FSI modeling is greater. In order to make this fluid flow – wall motion correlation, all their constant mechanical properties must be known.

The direct coupling of fluid properties with solid boundary properties is the challenge of FSI modeling. For each time step, during the computational solution, the flow characteristics must be calculated in relation to the boundary motion, and at the same time, the changes in the boundary position caused by the fluid motion must be taken into account. The procedure, its flow chart shown in Figure 5.1, is as follows:

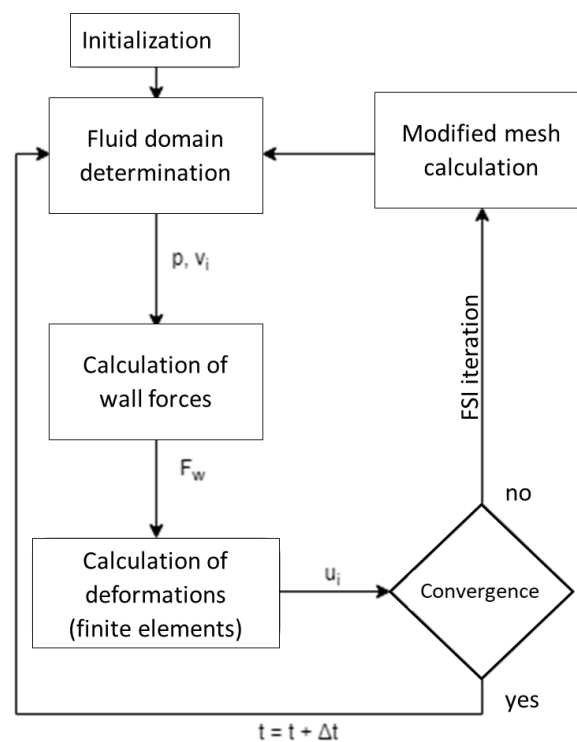


Figure 5.1 Flow-structure interaction (FSI): Coupling process. There are two nested loops. In the inner loop the convergence of the FSI model takes place and in the outer the time progresses.

Initially, a mechanical model is used to describe the properties of the boundary (fluid-induced motion, elasticity, viscosity, other mechanical properties). Along with this movement, the flow characteristics (pressure, velocity, viscosity) must be recalculated to take into account changes in geometry (increase or decrease in surface

area). These two models are repetitively coupled, allowing the grid displacements and forces to be shared between the two domains. Once all these parameters are resolved for a single time step, they are used as initial conditions for the next. The complexity of the method lies in the fact that after each time step, the domain grid will have to be re-defined to account for changes in geometry, and nodes may need to be removed or added. With this calculation of the wall mechanics and fluid mesh reconstruction, the simulation may become quite complex and the computational cost increases, especially in the case of a dense mesh.

The following kinematic-dynamic equations must be satisfied at the fluid-structure interface in order to achieve equilibrium [46]:

$$\mathbf{v}_f = \mathbf{v}_s = \frac{d\mathbf{u}_s}{dt} \quad (5.3)$$

and

$$\boldsymbol{\sigma}_f \cdot \mathbf{n}_f = -\boldsymbol{\sigma}_s \cdot \mathbf{n}_s \quad (5.4)$$

, where $\mathbf{v}_{f,s}$ is the velocity vector at the border of the fluid-solid domain, $\mathbf{u}_s$ is the boundary's displacement vector, $\boldsymbol{\sigma}_{f,s}$ is the stress tensor at the boundary for both domains and $\mathbf{n}$ is the local normal unit vector.

The development of a fluid-structure interaction model can greatly improve the physiological realism of vessel simulations and help to better understand the mechanical stresses-deformations imposed on the endothelial cells of its wall. This makes it easier to predict their behavior and biological response, in different mechanical environments, with greater accuracy.

5.4 FSI TYPES OF APPROACH

Logically, problems involving multiple fields of physics are very difficult to approach with analytical methods. Therefore, they must be solved either by using numerical simulations or by conducting experiments. The advanced techniques offered by the commercial packages in the fields of Computational Fluid Dynamics and Computational Structural Engineering, as well as the availability of open source software make it possible to perform reliable numerical simulations. There are two different approaches to solving FSI problems: the monolithic approach and the partitioned approach. Both approaches have advantages and disadvantages, that will be discussed next.

5.4.1 MONOLITHIC APPROACH

In this approach both sub-problems (fluid and structure) are formulated as a combined problem. The system of algebraic equations resulting from the discretization of the governing equations is solved as a whole [48,49]. The interaction of fluid and structure at the interface is performed synchronously and by applying an implicit⁶ method. This leads to the preservation of the physical properties at the interface, thereby increasing the stability of the solution. Figure 5.2 shows the flow chart of the monolithic approach.

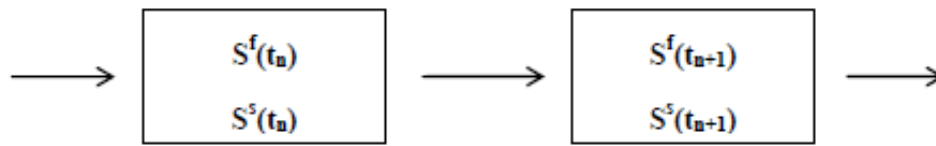


Figure 5.2 Monolithic approach to FSI problems. S^f is the solution of the flow problem and S^s is the solution of the structural problem for successive time steps t_n, t_{n+1} , where n is the step of the numerical method.

The monolithic approach, although considered more robust than the split one, has a higher computational cost and cannot benefit from the autonomy of the various modules offered commercial packages. Most modern studies are choosing this approach, as it is applied by open source FEM packages specialized in biological systems modeling, such as FEBIO [64].

5.4.2 PARTITIONED APPROACH

The second option for solving FSI problems is the partitioned method. Here, the two sub-problems are solved separately, which means that the flow properties do not change simultaneously, during the calculation of the structure solution. The equations of the mathematical models that describe the properties of the flow and the displacement of the structure are solved alternately and iteratively at each time step, by two separate solvers. The iterative determination of the solution of the fluid-structure sub-problems makes this approach strongly coupled. The flow intermediate solution is introduced as a boundary condition for the structure and vice versa, as the iterative process continues

⁶ In implicit methods, the parameters to be calculated depend on each other in both the same and the previous time step. This makes these approaches more complex to apply, but at the same time more stable and robust compared to explicit methods.

until a convergence criterion is met. At the interface (boundary between fluid and structure domains), data exchange takes place according to the type of coupling technique applied [6,7]. In the partitioned approach, the interface boundary conditions are introduced explicitly⁷ in the data exchange process between fluid and structure. For this reason, stability problems can arise, so it is necessary to choose an adequately small time step. Figure 5.3 illustrates the process of the separated method.

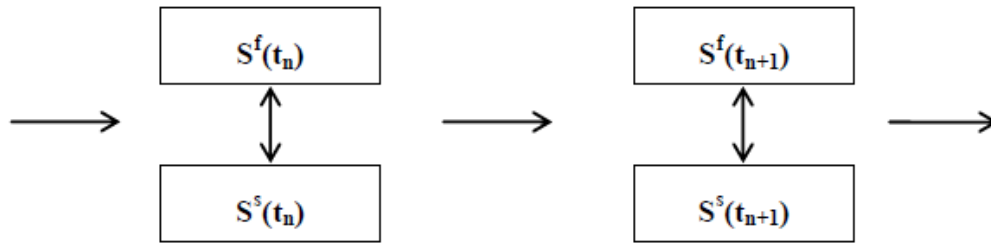


Figure 5.3 Partitioned approach to FSI problems. S^f is the solution of the flow problem and S^s is the solution of the structural problem for successive time steps t_n, t_{n+1} , where n is the step of the numerical method.

Due to the time lag between the integration of the flow and structure domains, the boundary interface conditions are applied asynchronously, which implies the possibility of losing the preservation of the properties during their transfer. This problem can be solved using mapping algorithms of the target source nodes.

The partitioned approach allows the autonomy of autonomous modules to be utilized, enabling the simulation of more complex problems, in a grand scale. One of the most characteristic examples of programs applying the partitioned approach for FSI problems is Ansys [61].

⁷ In explicit methods, the parameters are calculated based only on the previous time step. Explicit methods are less stable than implicit and require a shorter time step.

6 A COMBINED EXPERIMENTAL AND COMPUTATIONAL STUDY ON TUBULAR ARTIFICIAL VESSELS

The experimental testing of blood vessels is a quite common practice among the biomedical community and has been studied for years. An early approach was performed by Yearwood and Chandras in 1982 [68], who performed physiological pulsatile flow experiments in a rigid model of the human aortic arch to determine its flow properties. In 2003, Eguchi et al. [69] used an experimental system like the one in this study, as well as a numerical approach to investigate the flow of simple rigid/elastic tubes. In the next years, Huo and Kassab (2006) [70] performed experiments on living animals, to investigate the blood flow in the entire coronary tree, though without numerical modelling. Relevant work continued in more recent years. In 2017, Geoghegan and Jermy [71] performed a comparison of the flow field and wall shear stress in both rigid and compliant models of carotid arteries. However, numerical simulations were absent from their study and phantom vessels were used instead of biological or artificial ones. Sharzeehee et al. (2018) [72] developed an FSI model to simulate arteries under steady-state and pulsatile flow, though without experimental validation. Mi et al. [52] performed tests on PU/PCL vessels fabricated by electrospinning, though without numerical simulation. A combination of FSI numerical and experimental study was performed by Siguenza et al. (2018) [73], in an application of an aortic valve model. Many relevant works do not include both experimentation and simulation. Moreover, there is oftentimes a lack of realistic applicable vessels involved in the experiments. A study by Bouchet et al. [51] tried to overcome these shortcomings, by developing a predictive analytical model and experiments on PU/PCL electrospun vessels. Still, analytical models can't be completely trusted when examining biological systems, due to the complexity of the latter. For this reason, attempts have been made in recent years to provide a framework for the FEM simulation of blood vessels using FSI [64] and CFD [65] techniques in the modelling of carotid bifurcations.

In this thesis, we performed a combined study of mechanical tests and FEM simulations on artificial vessels, to assess their flow behavior and compliance under simulated physiological conditions. Tubular compliant polymeric vessels were firstly produced by the method of electrospinning, following the steps of a novel approach by

Dimopoulos, Markatos, Mitropoulou et al. (2021) [66]. The vessel diameter was selected accordingly as to approach the size of a carotid artery. Experiments were conducted using a physiological flow apparatus where the tubular scaffolds were installed and various flow conditions were monitored. These parameters were used as an input to a predictive FEM model that we developed. In the end, the numerical results were compared to the experimental ones, as well as bibliographic values for the purpose of validation.

6.1 EXPERIMENTAL PART

6.1.1 VESSEL PRODUCTION

The tested vessel segments were created by electrospinning. Electrospinning is a method applied for the production of fiber structured materials, which uses the electric force created between the metallic needle of a computer controlled syringe pump filled with polymeric solution fluid extruder and a metallic collector to attract nanofibers from one to the other (Figure 6.1). This is possible, as electrostatic repulsion counteracts the liquid's surface tension, due to the high voltage applied. The resulting scaffold depends on multiple parameters, such as the voltage applied, the fluid feed rate and the solution parameters that affect the fibers diameter, distribution and alignment [74]. The system used is presented in Figure 6.2. It consists of an in house cylindrical rotating aluminum collector and a syringe pump filled with a solution that ends up in a metallic needle, through plastic tubing. Two different solutions were used: a PCL and a PVA one, in order to create a multilayered structure. The study of [66] showed that the PCL vessel had biomimicking characteristics comparable to physiological blood vessels regarding its mechanical behavior. The PVA layers were superimposed to PCL to improve the proliferation of cells in its interior and have no significant effect on the mechanical properties of the vessel.

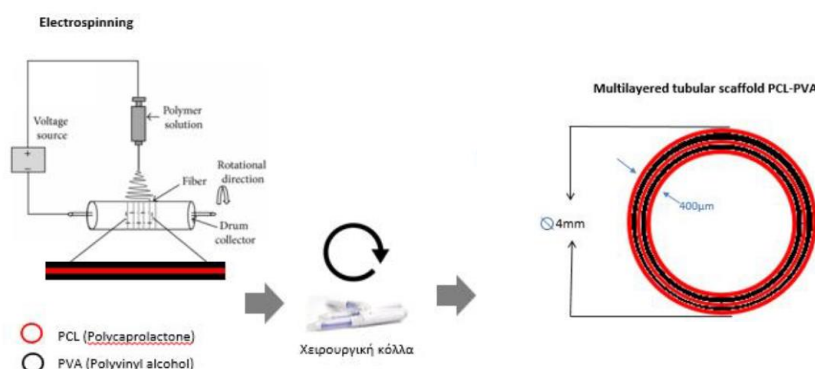


Figure 6.1 Presentation of the electrospinning procedure.



Figure 6.2 Electrospinning system used for the productions of the PCL/PVA vessels.

For the creation of the PCL solution, 20% w/v PCL pellets were dissolved in acetic acid and stirred in a laboratory mixer under 40 °C for 24h prior to the electrospinning process. For the PVA solution, 10% PVA was dissolved in distilled water. The electrospinning parameters are presented in Table 6-1. A 10 ml syringe containing the solution was mounted on the syringe infusion pump, whose feeding rate was set separately for each solution. Through plastic tubing, the syringe ended up at a 0.6 mm (20G) metallic needle. A high voltage (20-24 kV) was applied between the metallic needle and the rotating metallic cylindrical drum collector that was covered with aluminum foil in order to collect the electrospun scaffold. The distance between the needle and the collector was set at 20 cm. The rotating speed of the collector was set accordingly for each solution in use, with the help of an Arduino driven motor. The rotational speed was monitored throughout the electrospinning process with the use of a digital tachometer to ensure constant operating conditions. The rotation speed was set at 1280 rpm for the PCL and at 2100 rpm for the PVA solution. For the PCL solution, electrospinning was performed for 2 hours, with an infusion flow rate of 2 ml/h. The same parameters for each PVA layer were 3.5 hours and 0.25 ml/h.

Table 6-1 Electrospinning parameters.

Temperature (°C)	20	
Needle size (G)	20	
	PCL/CH₃COOH	PVA/dH₂O
Collector rotational speed (rpm)	1200-1280	2100-2150
Kilovolt (kV)	24	20
Needle-Collector distance (cm)	22	22
Flow rate (ml/h)	2	0.25
Time (h)	2	3.5

Following the electrospinning process, multiple strips were cut off of the aluminum collection foil and were intertwined to create the tubular scaffold. The direction of the

membrane strips was chosen so that the alignment of the fibers to be longitudinal to the vessel axis. By this fiber orientation we achieved to mimic the physiological mechanical behavior of blood vessels; their axial Young modulus is higher than the circumferential about an order of magnitude. A surgical glue was used to fix the ends of the membrane strips of the vessels. An image of a produced tubular vessel is presented in Figure 6.3. An internal diameter of 4.1 mm, with a wall thickness of about 550 μm was chosen to represent a carotid artery segment.

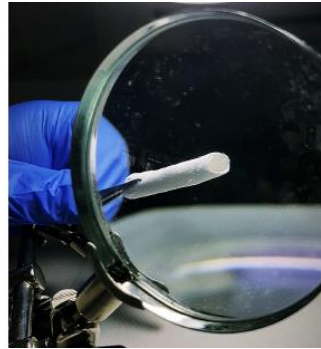


Figure 6.3 Photo of a produced tubular vessel [66].

6.1.2 TESTING APPARATUS DESCRIPTION

A schematic of the closed loop mock circulation experimental apparatus is shown in Figure 6.4. The whole apparatus can be broken down into three parts: The Left Ventricle (L.V.) Element, the systemic circulation tubing and the test section. The fluid flow is denoted by the arrows.

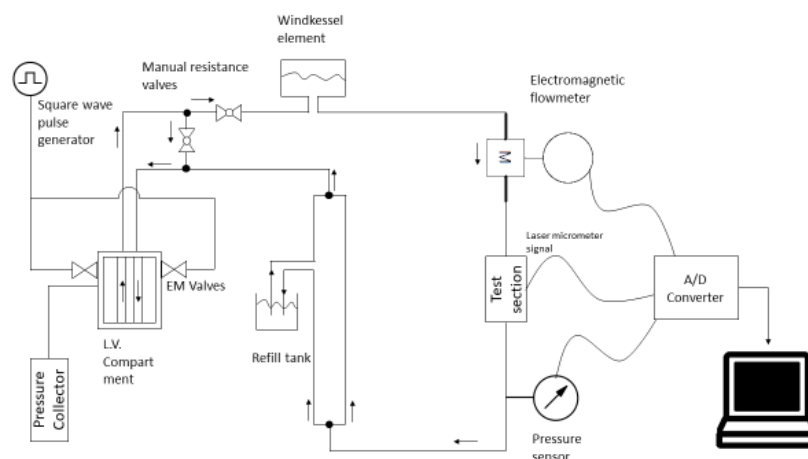


Figure 6.4 Experimental apparatus schematic

The L.V. element consists of the L.V. compartment, a square wave pulse generator that controls two electric valves and a pressurized air collector providing air into the compartment (Figure 6.5). During the systolic phase, a pulse from the generator opens the input electric valves, allowing air from the pressure vessel to enter the compartment. As a result, the flexible tubes inside the compartment compress, ejecting fluid towards the systemic circulation (backflow is prevented by the direction of the artificial valves). During the diastolic phase, the input valve closed, while the exit electric valve opened, releasing the pressure inside the compartment. Thus, the flexible tubes decompress and are refilled by fluid entering through the now open inlet artificial valve. The fluid flow exiting the left ventricle element decelerates.

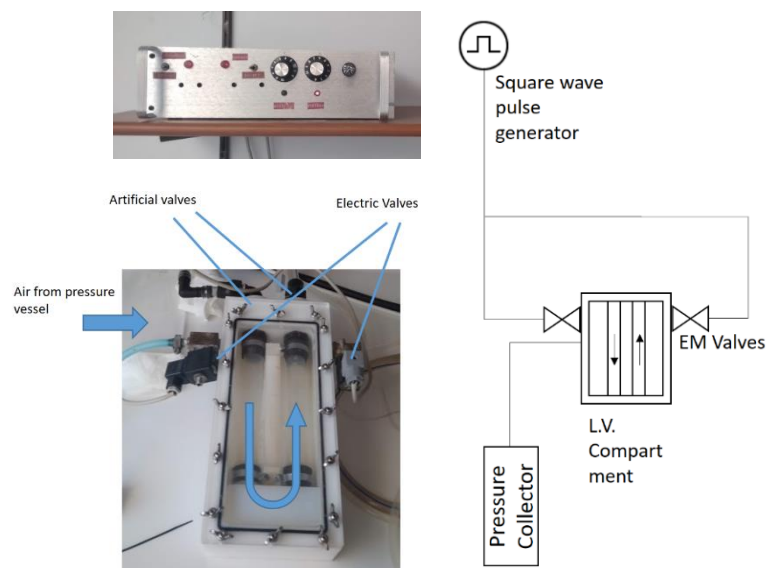


Figure 6.5 The Left Ventricle element.

The systemic circulation vessels correspond to the tubing system between the L.V. element and the test section (Figure 6.6). This tubing system also includes a number of control mechanical valves, a Windkessel element, a refill tank and a magnetic flowmeter. The control valves can be tuned to simulate the arterial resistance. The resistance increases by opening the return valve and closing the outflow valve. The Windkessel element compensates for the low flexibility of the tubing system; as the tubes are almost rigid, the compliance of the system is determined by this element. The Windkessel element acts as a pressure reservoir (or a capacitor), that is charged during systole and discharged during diastole, allowing for a smoother flow. Finally, the electromagnetic flowmeter utilizes a probe in series with the circulation, that detects

alterations in its magnetic field translated into inductive voltage. It is used to measure the instant volumetric flow rate of the fluid entering the test section.

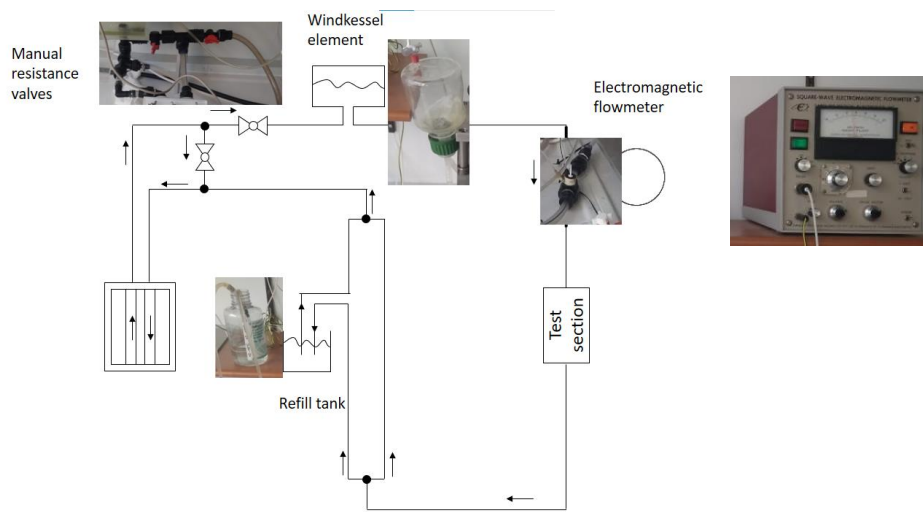


Figure 6.6 Systematic circulation tubing system schematic.

The test section consists of the vessel segment under examination, a laser micrometer and a pressure transducer at its outlet portion (Figure 6.7). The vessel segment (tubular scaffold) is installed in series with the circulation. The scaffold is cannulated by inserting quick connector fittings at both ends and connecting it with the apparatus tubing system. A laser micrometer is used to monitor the vessel's real time diameter change, during the circulation. The pressure transducer at the end of the test section measures the pressure fluctuation.

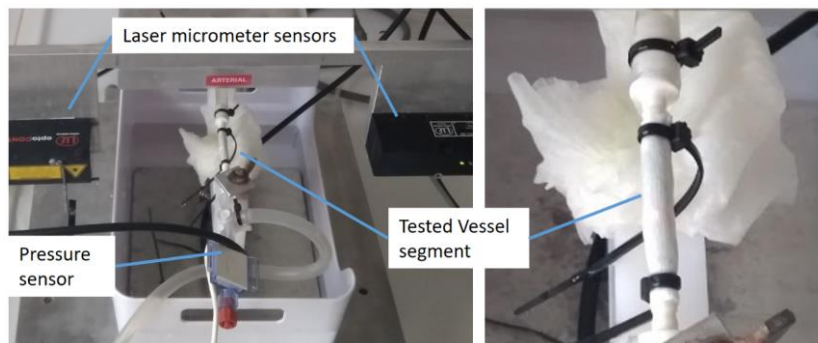


Figure 6.7 Vessel test section.

During the experiment, we measured three parameters of the test vessel: the inlet instantaneous volumetric fluid rate, the outlet pressure and the diameter fluctuation, using the electromagnetic flowmeter, the pressure transducer and the laser micrometer respectively. These three signals were digitized through an A/D converter and transmitted to a lab pc in real time (Figure 6.8).

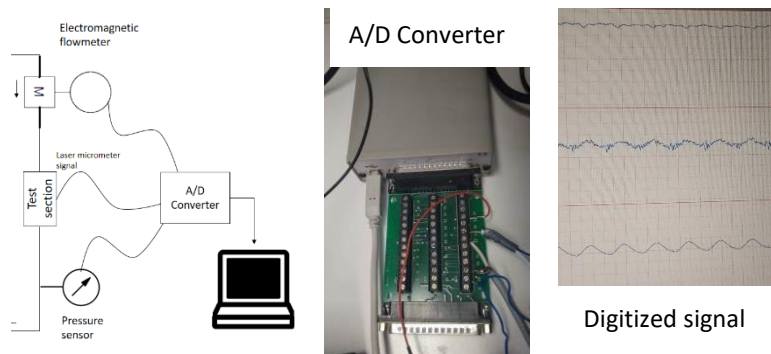


Figure 6.8 Acquiring and digitization of the signals.

6.1.3 EXPERIMENTAL PROCEDURE

The fluid that we used as a substitute for blood in the circulation was a saline solution. The square wave pulse generator controlling the electric valves of the left ventricle chamber was modified properly to allow 80 contractions of the elastic tubes per minute, representing a normal cardiac rate. Moreover, the time lag between the opening and closing of the electric valves was set accordingly in order for the time period of the systole to be approximately the 1/3 of a whole cardiac cycle, while the rest 2/3 of the circle was occupied by the diastolic phase.

We performed a set of test in three different pressure ranges. These ranges were 0 - 40, 50 - 90 and 80 - 125 mmHg. For each of these ranges, the lower value represents the diastolic pressure and the higher value corresponds to the peak systolic pressure. The 40 mmHg range was chosen as a standard practice when measuring the arterial compliance. In each of the above cases, the circulation resistance valves and air supply from the pressure collector had to be manually adjusted, with feedback from the output, in order to achieve the desirable pressure values.

For each test, we monitored the real time values of the volumetric fluid flow at the inlet, the pressure at the outlet and the diameter at the midpoint of the vessel. For the measurements to be more precise, we waited an adequate number of cardiac cycles for the mean diameter to be stabilized after its original increasing trend due to viscoelastic effects (Figure 6.9). After stabilization, up to 10 cycles were monitored for each vessel. The measured parameters were used to calculate the vascular compliance for each pressure range.

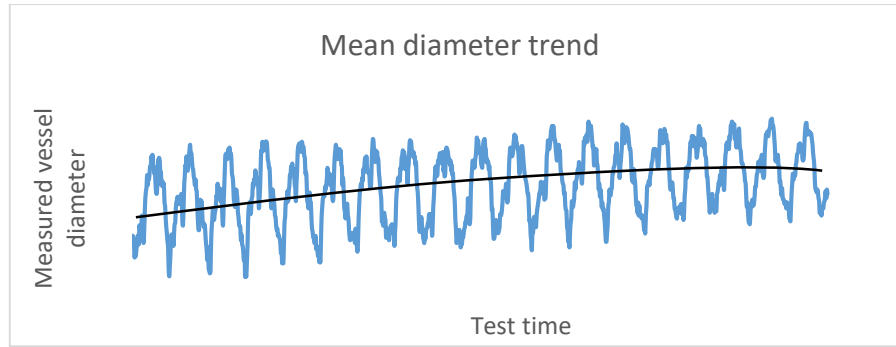


Figure 6.9 Vessel's diameter trend due to viscoelastic effects.

The magnetic flowmeter's probe was located at some distance before the vessel's inlet in the test section. This means that the fluid volumetric flow measured should not be the same as at the vessel's inflow section. However, as the plastic tubes accommodating the circulation were almost rigid (meaning no compliance), we assumed that the value measured by the flowmeter was equal to the one of the tested vessel.

A challenge we faced during measurements was that of a fluid leakage through the tested vessel walls. This leakage originated from the porous nature of the PCL scaffold that makes its walls permeable. This caused a fluid film to be created around the vessel, due to surface tension. This effect was more prominent the higher the pressure conditions were. To overcome this problem, we padded the ends of the tested vessel with absorbing material, while leaving its center intact so as to not disturb the laser measurement. Albeit this helped reduce the thickness of the leakage film, it did not eliminate it completely. As a result, the measured diameter and compliance are expected to be lower than their true value.

6.1.4 EXPERIMENTAL RESULTS

The goal of the experimental measurements was to use them for the FEM simulations both as an input (Boundary Conditions) as well as a comparison and validation measure of the simulations results regarding the arterial compliance. For those measurements to be meaningful and applicable for our FSI simulations, digital filtering was a prerequisite. We first performed a Fourier analysis to determine the frequency components of our obtained signals (Figure 6.10). As we can see, there is some high frequency noise, above the expected up to 3.5 Hz frequencies existing in a physiological cardiac output signal [75]. In order to eliminate this noise, we used an Infinite Impulse Response (IIR) Butterworth Low-Pass filter that was materialized using Matlab code.

The filter characteristics are presented in Figure 6.11. The cutoff frequency was selected between 3.5 and 5 Hz for each case. Backwards and forward filtering was implemented to allow zero phase distortion of the signal. The resulted signals before and after filtering are shown in Figures 6.12-6.14. We can see the need for appropriate digital filtering, as there are a lot of artefacts and noise, especially in the pressure and diameter measurements.

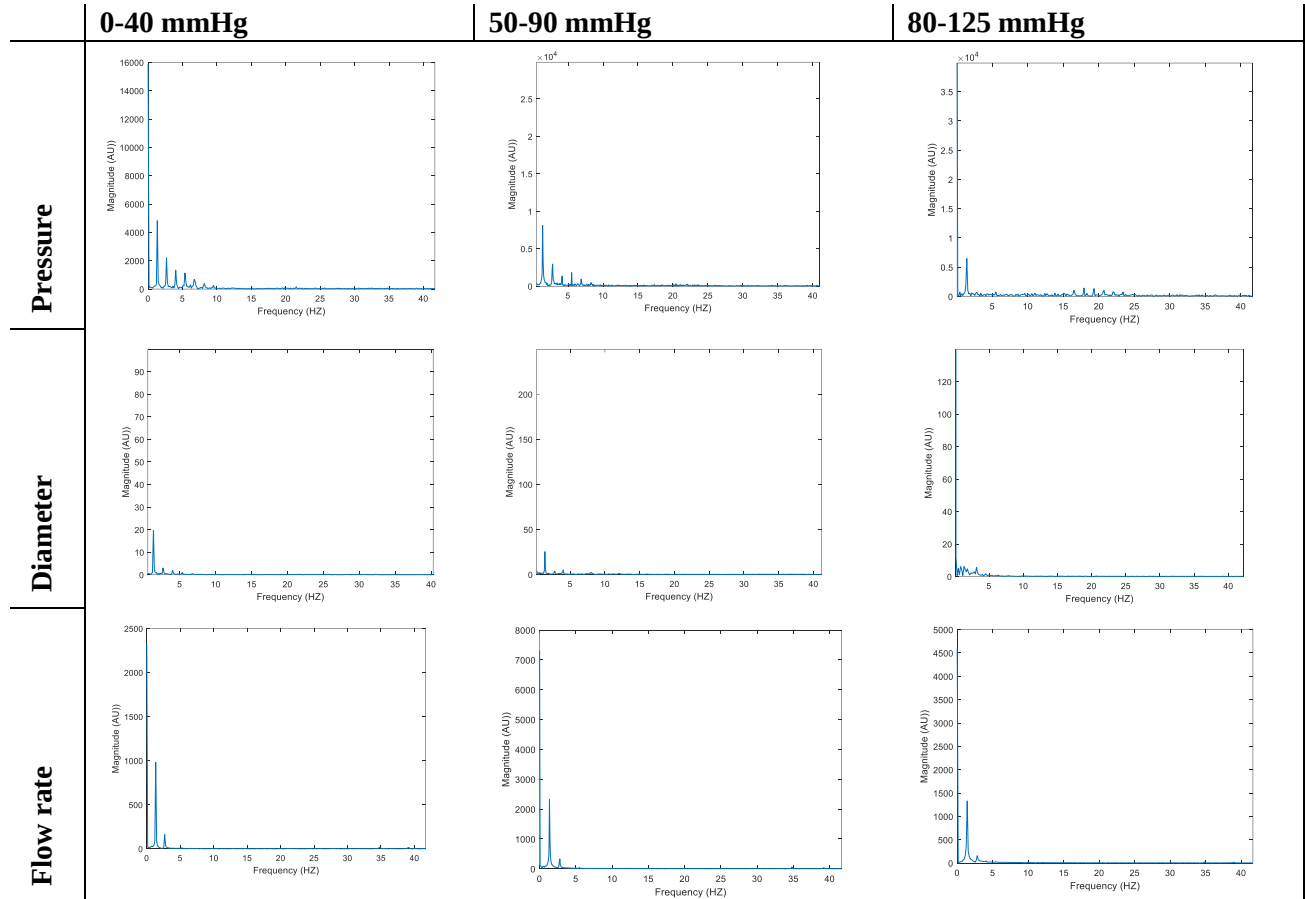


Figure 6.10 Fourier analysis of acquired signals.

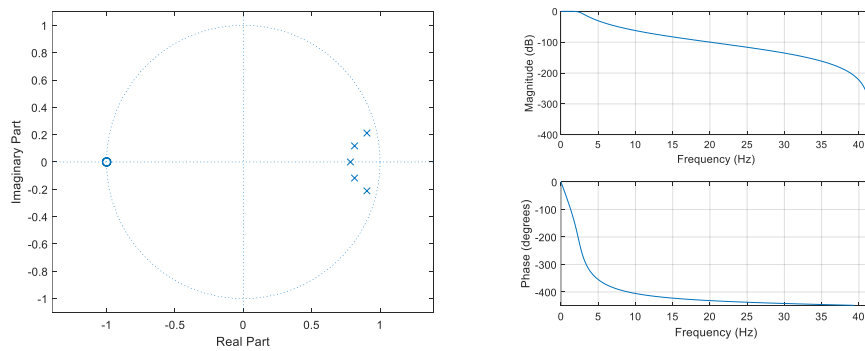


Figure 6.11 IIR low-pass filter characteristics.

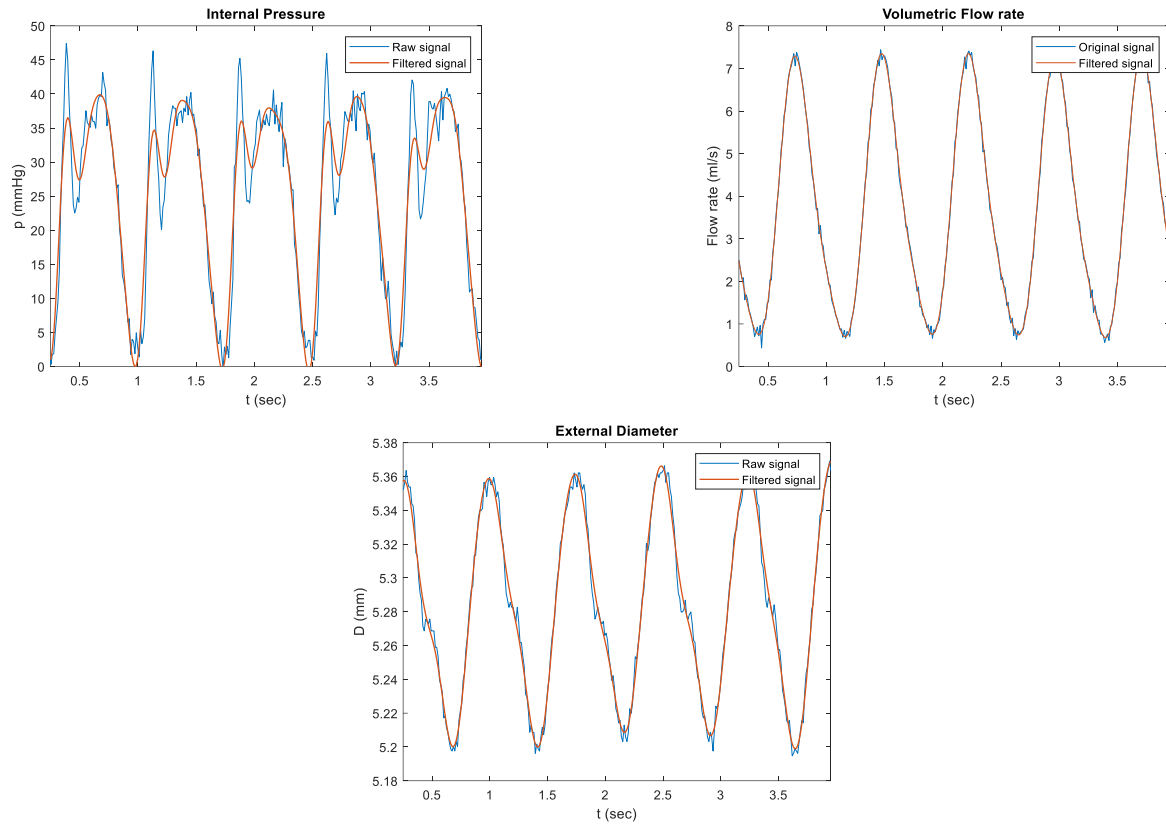


Figure 6.12 Pressure, diameter and flow rate of tested vessel. Pressure range of 0-40 mmHg.

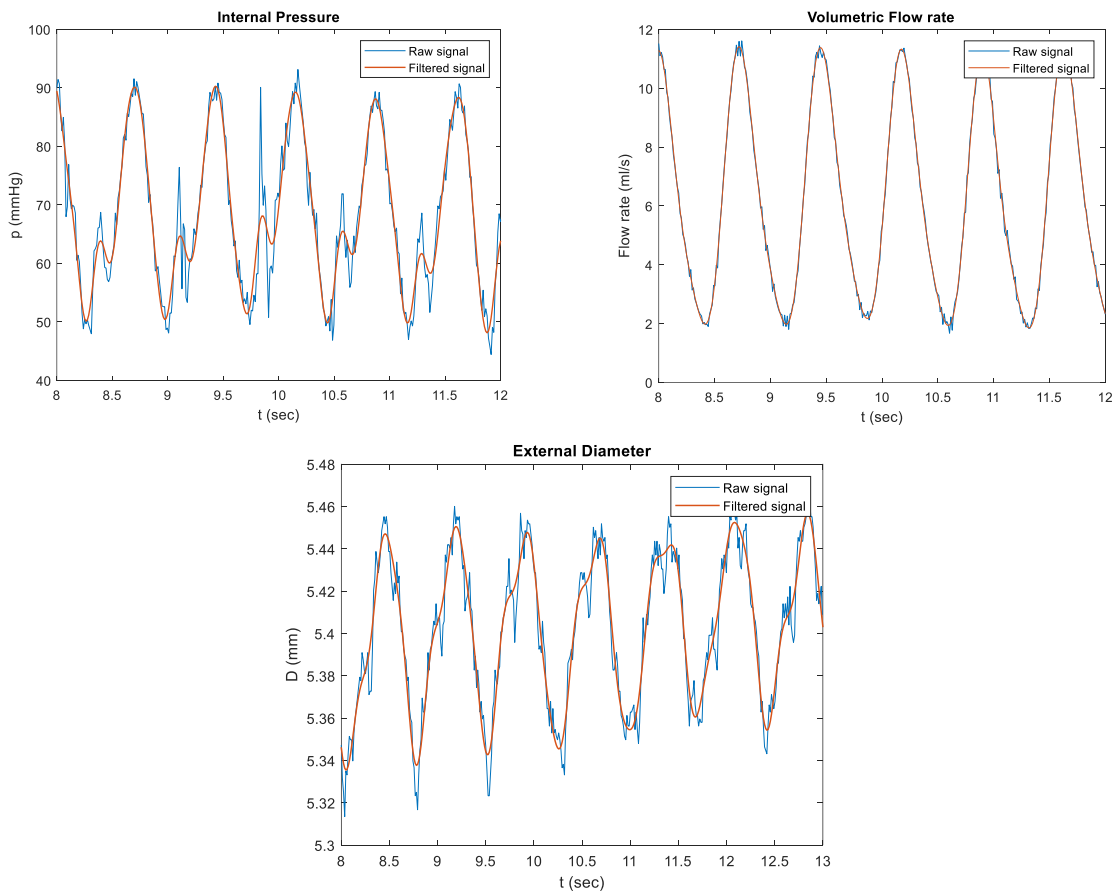


Figure 6.13 Pressure, diameter and flow rate of tested vessel. Pressure range of 50-90 mmHg.

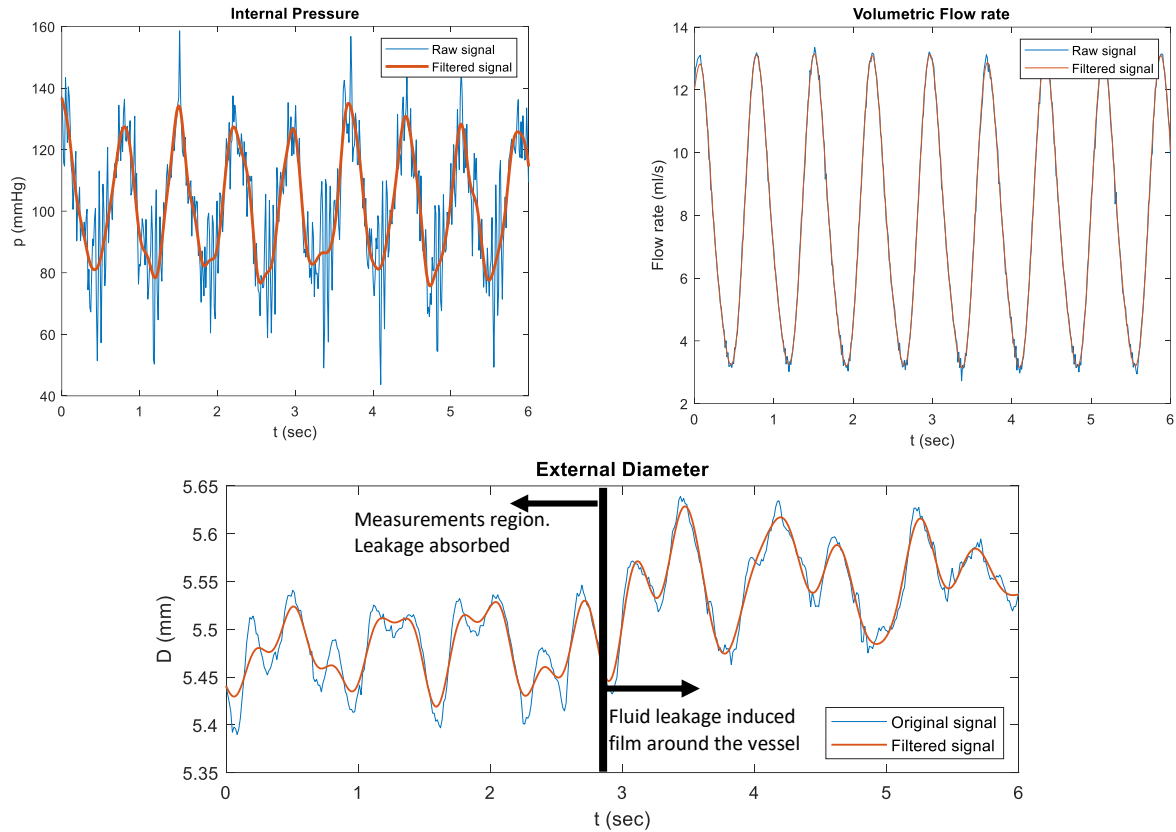


Figure 6.14 Pressure, diameter and flow rate of tested vessel. Pressure range of 80-130 mmHg.

The peak flow rate was measured at 7.3, 10.83 and 13.1 ml/s for each pressure interval of 0-40, 50-90 and 80-130 mmHg. According to Kaazempur et al. [56], the peak volumetric flow rates in the common and external carotid arteries can range between 9 to 16 ml/s under physiological operating conditions. This is important, as our vessel is of a similar caliber to a common carotid artery (CCA) or an external carotid artery (ECA), meaning that our results can be partially validated. Using Equation (4.14), we were then able to calculate the arterial compliance of the vessel for each pressure interval. The upper and lower pressure values used were those of the interval's limits, while the external diameters were taken by the highest and lowest measured diameters for each interval. An average value of the pressures and diameters was taken for each case, using a time window of about 3-4 seconds with stable operating conditions. The calculated compliance, alongside with the bibliographic value is shown in Figure 6.15. There, we can see that there is a convergence between our results and the bibliographic values, their error being less than 13% for the common cases of intervals. Moreover, both studies follow the same declining trend. However, in our study the compliance is systematically underestimated. There could be a plethora of reasons for this phenomenon. First of all, compliance in the bibliographic study [66]

was performed under static conditions. Our approach used pulsatile flow, which in theory should yield a reduced compliance due to inertial effects, as the vessel doesn't have infinite time to fully expand in each loading cycle. In addition, as we discussed in Section 6.1.3 there was a fluid film formed around our vessel during the measurements that led to higher diameters measured by the laser micrometer. Despite our effort, it could not be eliminated. Furthermore, the vessel we used was slightly bigger (4 - 4.2 mm internal diameter instead of the 4 mm used in [66]), which could lead to a lower compliance according to [51]. As our vessel consisted of additional PVA layers, both internal and external, its true internal diameter would be even greater under testing conditions (PVA is transformed into gel when interacting with water). Under these considerations, our experimental results seemed appropriate to be used for our following FEM simulations.

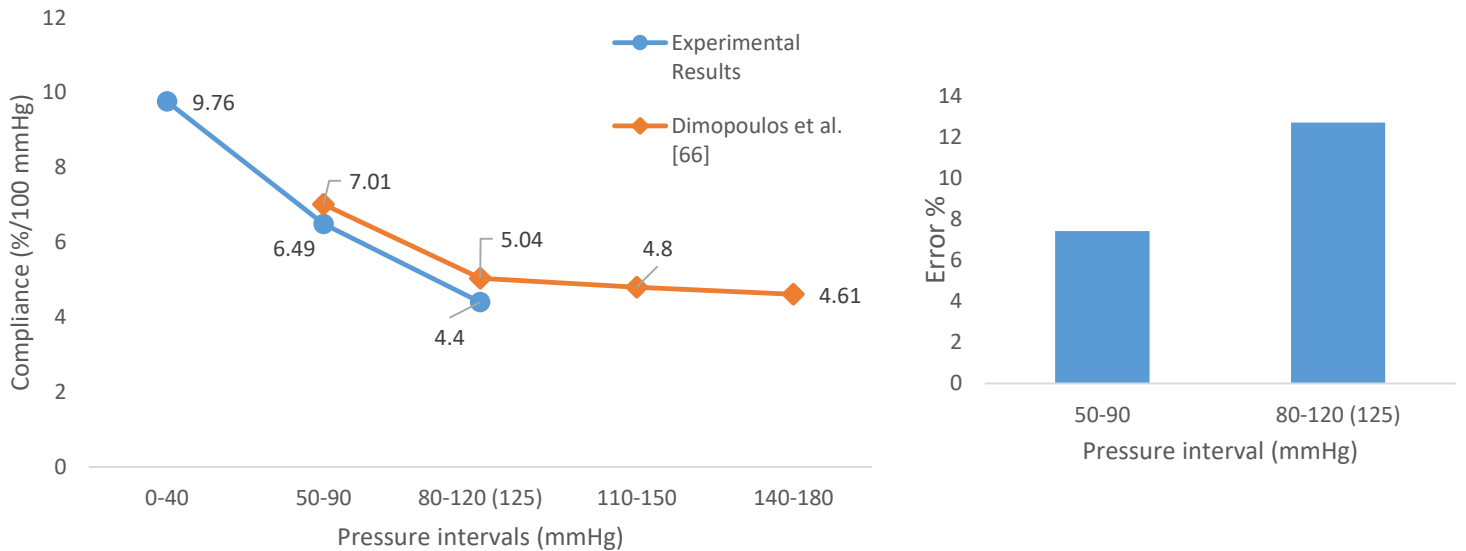


Figure 6.15 PCL tubular vessel compliance. Comparison between experimental results and bibliographic values [66].

6.2 FINITE ELEMENT MODELLING AND SIMULATION

6.2.1 MODEL DESCRIPTION AND GEOMETRY

For the FEM simulations, we considered a cylindrical vessel, fixed at both ends, with a known free length, initial diameter and wall thickness. Its mechanical properties for each case studied were either known by bibliographic sources or approximated by simulations. At one end of the vessel we applied the fluid flow measured by the previous experiment. This end acted as the vessel's input. At the other end, which is the output, we applied the experimentally measured pressure. The geometry of the model

is shown in Figure 6.16. and its dimensions in Table 6-2. During the simulation, the vessel deformed and we calculated the change in its diameter in the midpoint between both ends. At the same time, we calculated other quantities, such as the velocity of the fluid, first principal and effective stress-strain, wall shear stress (WSS) and the change in wall thickness. From the above results we proceeded to calculate the compliance of the vessel, alongside with other operating characteristics, and compared it with the experimental results. This procedure was repeated for all three pressure intervals (0-50, 40-90 and 80-125 mmHg) examined in the experiments, as well as for different elastic and hyperelastic materials.

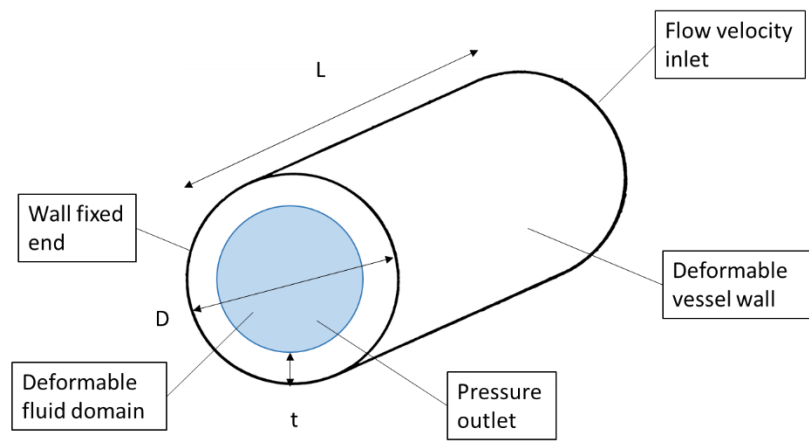


Figure 6.16 FEM vessel model schematic.

Table 6-2 Dimensions of FEM vessel model.

Vessel dimensions (mm)	
External Diameter (D):	5.2
Wall thickness (t):	0.55
Length (L):	24.6

6.2.2 FSI FORMULATION

FEBIO uses a monolithic approach to solve FSI problems (see Chapter 5), in the sense that both solid and fluid domains are modelled and solved simultaneously by the same solver, without the need of an external coupling tool for two different systems. The FSI formulation in FEBIO adapts methods from widely used ALE (Section 5.1) formulations to achieve temporal discretization of the problem, while avoiding the requirement of special stabilization schemes, thus providing a simpler set of equations [64]. This is achieved by the introduction of mixture theory to the modelling approach

that helps to simplify the formulation, while in the same time conserving the robustness of the solution.

In FEBIO's FSI formulation, the fluid domain Ω_f is defined by a biphasic material that consists of a fluid-solid mixture. In this mixture, the solid material acts as a matrix that is considered to be porous, deformable, with zero mass and a negligible stiffness. Also, there is zero viscous friction with the fluid component, allowing the fluid to flow inside the matrix. The sole purpose of the fluid domain's solid porous component is to define the deformable mesh through which the fluid flows and to transfer the deformations and tractions introduced to the adjacent solid domains through the fluid-solid boundary Γ_{fs} . The solid part of the biphasic fluid is characterized as a material and the fluid part in a spatial frame. This means that the fluid domain's mesh follows the motion and deformation of its solid part, while its velocity is given by the relative velocity of its fluid part. The solid matrix's nodes in the fluid domain are shared with the nodes of the neighboring solid domain Ω_s , or can be enforced with tied contact conditions, in order to achieve continuity in the fluid-solid boundary. The solid domain can also be deformed or transfer tractions that are imposed on it in the biphasic fluid domain.

6.2.3 DISCRETIZATION

The discretization for both solid and fluid domains was performed by FEBIO's built in meshing tool. For the fluid domain we created a cylinder with 40 elements along its length, 40 slices in the circumferential direction and 12 segments along its radial direction. The result was a mesh with 17600 8-node hexahedral elements and 1600 6-node pentahedral elements, for a total of 19200 elements and 21361 nodes. In addition, an inflation modification of the mesh was applied, in order to bias the mesh near the vessel's wall, where the velocity gradient in the radial direction is more abrupt. The mean aspect ratio of the fluid domain elements was 6.5, with a maximum value of 27.8 at the vessel's wall due to the inflation. In general, an aspect ratio less than 5 is considered to be ideal; however larger aspect ratios can be used, depending on the case.

The solid wall domain was derived by extruding the element faces of the fluid domain's outer layer towards their respective local normal by a length equal to the vessel's wall thickness. This was done in order to assure that the solid-fluid interface nodes were common for both domains, as described earlier. A three segment partition

along its radial direction was chosen for better computational results and intra-thickness stress-strain calculations. The solid wall mesh consisted of 4800 8-node hexahedral solid elements, with an average volume of 4.1 e-11 m^3 , and 6560 nodes. The use of shell elements could be examined, however, due to high deformations and high thickness/radius ratio ($t/R > 0.1$), the thin-vessel hypothesis could not be satisfied, so solid elements were used. The average aspect ratio was 3.36 (an aspect ratio bellow 5 is generally considered to be ideal). The resulting mesh is presented in Figure 6.17.

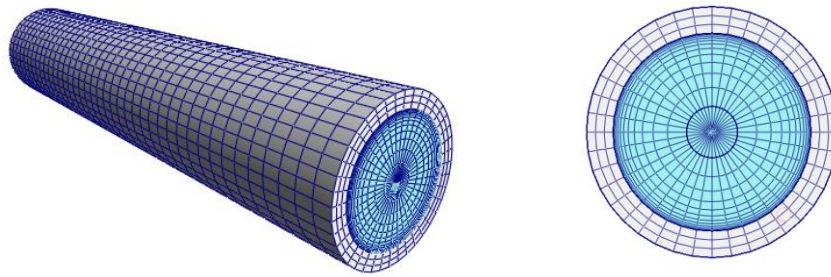


Figure 6.17 Meshed model used in the simulations. The fluid domain is colored in blue, while the solid domain (wall) is white.

6.2.4 MATERIAL PROPERTIES

6.2.4.1 FLUID DOMAIN

As explained in Section 6.2.2, the fluid domain was defined as a biphasic fluid-solid FSI material in FEBIO. The fluid component was considered to be a Newtonian fluid, with a density of 997 kg/m^3 , a bulk modulus of $2.2\text{e}9 \text{ Pa}$ to assure incompressibility and a constant dynamic viscosity of $1.003 \text{ mPa}\cdot\text{s}$, which are common known values of water at 20°C . For the solid porous part of the fluid domain, an elastic material with a negligible Young's modulus of $1\text{e-}9 \text{ Pa}$ was used, which is known to work well in FEBIO's FSI simulations [76].

Property	Value
▼ fluid	fluid
density	997
bulk modulus	$2.2\text{e}+09$
▼ viscous	Newtonian fluid
shear viscosity	0.001003
bulk viscosity	0
▼ solid	neo-Hookean
Young's modulus	$1\text{e-}09$
Poisson's ratio	0

Figure 6.18 Fluid domain properties.

6.2.4.2 SOLID DOMAIN

The solid domain of the FSI problem corresponds to the tested vessel wall. As our PCL tubular scaffold was produced by a novel approach, its material properties are not fully defined. For this reason, three different material had to be implemented separately in our model, in order to find out their response: an isotropic linear elastic, and two hyperelastic models: A Neo-Hookean and an Ogden material (see Section 4.5). All of the above material models are commonly used in relevant blood vessel simulation studies [54-57, 61-62].

For the linear elastic material, its Young Modulus was taken from [66], by the stress-strain diagram's slope at 10 % strain produced by a uniaxial tensile experiment and was found to be 1 MPa. Poisson's ratio was assumed to be 0.49, which is a characteristic value for incompressible materials, such as PCL [51].

Property	Value
density	960
Young's modulus	1e+06
Poisson's ratio	0.49

Figure 6.19 Solid domain properties, linear elastic material.

For the Neo-Hookean material, we used the uncoupled elastic, two-parameter Mooney-Rivlin hyperelastic material model described in Section 4.5.2. The Mooney-Rivlin Constants were set according to relevant studies in carotid artery FEM simulations; C1 was set as 210.986 kPa [62], while C2 was set to 0 in order to reduce the material model to Neo-Hookean. The bulk modulus K, was defined as 2.2e8 Pa in order to assure incompressibility.

Property	Value
density	960
c1	210986
c2	0
bulk modulus	2e+08

Figure 6.20 Solid domain properties, Mooney-Rivlin (Neo-Hookean) material.

In order to calculate the material coefficients for the Ogden hyperelastic material, we used various sources [54, 57,62], as well as iterative estimations. This was necessary because specific uniaxial and biaxial experiments are normally required in order to

approach these coefficients accurately. The final values used in our simulations were $c = 0.3$ MPa and $m = 24$, for a 1st order material (Eq. 4.15).

```
<material id="4" name="Material5" type="Ogden">
  <density>960</density>
  <k>2.2e+08</k>
  <c1>300000</c1>
  <m1>24</m1>
</material>
```

Figure 6.21 Solid domain properties, Ogden material.

For all of the material models, the vessel's wall density was set at 960 kg/m³, according to the value in [55] for carotid arteries.

6.2.5 BOUNDARY CONDITIONS AND LOADS

Both ends of the vessel's wall were set as fixed, by prescribing a zero displacement boundary condition on their respective nodes, following the practice of [36] (Figure 6.22). Albeit, this use of boundary condition seems unintuitive at first, it is shown that there is no notable difference between that and a more realistic restrictive boundary condition, such as contact with adjacent connective, adipose tissue [64]. An FSI traction load was applied on the element facets in the fluid-solid domain interface, to allow the interaction and exchange of loads.

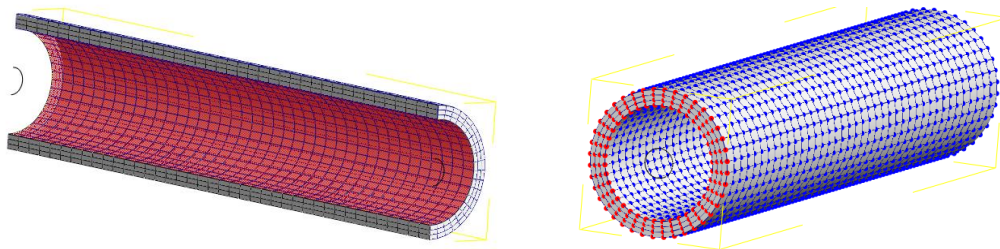


Figure 6.22 FSI traction load (left) and zero displacement boundary condition application elements/nodes.

A no-slip condition was enforced on the fluid-solid interface's nodes to ensure that the fluid cannot move through the wall and “sticks” on it, due to its viscosity (figure 2.23). This means that the fluid velocity on the wall would be:

$$u = 0; v = 0 \text{ and } w = 0$$

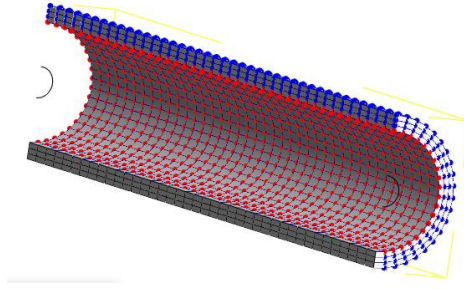


Figure 6.23 No-slip condition applied on the wall's internal nodes.

The previously calculated pressure and flow rate was used as an outlet and inlet boundary condition respectively, at the vessel's ends. As a substitute of pressure, FEBIO uses fluid dilatation $e^f = -\frac{p}{K}$ as a nodal boundary condition, where K is the fluid's bulk modulus. The reason behind this is that the dilatation is a kinematic measure, like velocity, while pressure needs to be formulated as a function of deformation. The fluid dilatation boundary condition was applied on the nodes at the fluid's outlet surface, as well as at the fluid-solid interface inlet curve. The latter was done for better solutions stabilization, as recommended.

The experimentally measured fluid flow rate was applied at the vessel's inlet nodes, as a normal velocity load. The velocity magnitude v had to be properly scaled according to Eq. (2.9) to correspond to the flow rate Q of the inlet surface. A parabolic profile was chosen, as the flow was fully developed at that point.

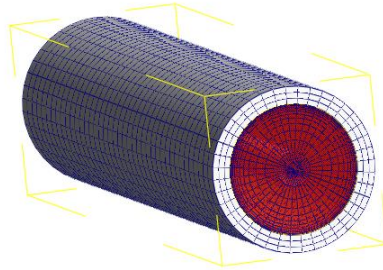


Figure 6.24 Application of velocity/fluid dilatation loads on Inlet/outlet surface nodes.

Both velocity and dilatation values were steadily increased in the first steps of the analysis for stability, before being applied normally. The load curves used as boundary conditions are shown in Figure 6.25. All of these curves were exported in XML by a custom MATLAB code in order to be embedded in FEBIO's format.

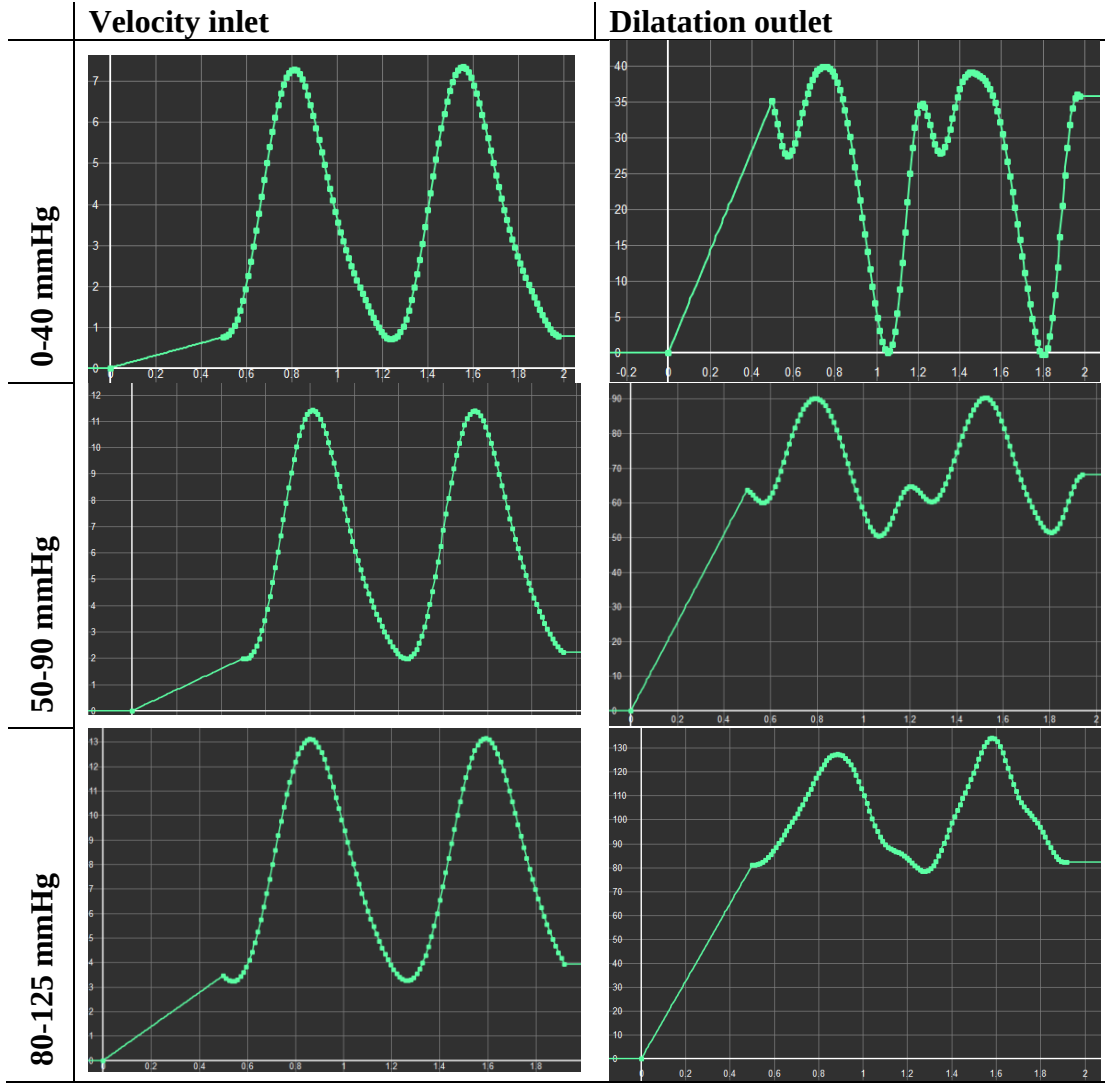


Figure 6.25 Velocity inlet/ Dilatation outlet load curves.

In some cases, vortices being shed inside the finite element domain try to cross the outlet boundary, which may lead to instabilities. For this reason, a fluid backflow stabilization and a fluid tangential stabilization surface load were applied at the fluid's outlet surface facets. These loads prescribe a velocity-dependent viscous traction t_τ , resolving the above issue.

6.2.6 ANALYSIS

In order to reduce the computational cost and make debugging easier, the time window of the simulations was set accordingly to include two cardiac cycles. The total physical time simulated was 2 seconds, the first 0.5 of them being dedicated to ramp the flow rate and pressure loads to their initial conditions, as well as to stabilize the solution. In total, 14 simulations were run: 9 of them for each of the three wall materials and for

each of the three pressure intervals (0-40, 50-90, 80-125 mmHg as measured by the previous experiment); 3 additional were performed using synthetic boundary conditions in order to include the 110-150 mmHg pressure interval not included in the experiments; one extra case was run using only a CFD approach (assuming a rigid vessel wall) in order to compare with the FSI approach; finally, a convergence study was performed, by running a simulations with a coarser and a finer meshed model.

One hundred to two hundred time steps with an initial step size of 0.02 s to 0.01 s were initially defined, with an enabled autostepper in order to adjust the time step according to the convergence facility. Model analysis parameters are shown in Figure 6.26.

Figure 6.26 Analysis parameters.

All simulations were performed on a computer with an Intel ® Core™ i5-5200U CPU @ 2.20 GHz 2.20 GHz processor and 8 GB of Ram, using Febio Studio version 1.0.0. The total elapsed time for each simulation ranged from 1 to 2 hours, depending on the case. The peak memory consumed was 5873.3 MB.

6.2.7 RESULTS AND DISCUSSION

6.2.7.1 COMPLIANCE CALCULATION

First of all, the internal radius of the vessel was measured for each material and pressure interval case. The ability to direct measure the internal radius is an advantage of the simulation as compared to the experimental laser micrometer, which can only account for the external diameter. The internal radius measurement was possible by selecting an element midway the vessel's length which was closer to the fluid-solid domain interface and calculating its center radial xy position. The biased (inflated) fluid mesh towards the wall helped in selecting an element that almost coincided with the interior of the wall. The element chosen is shown in Figure 6.27.

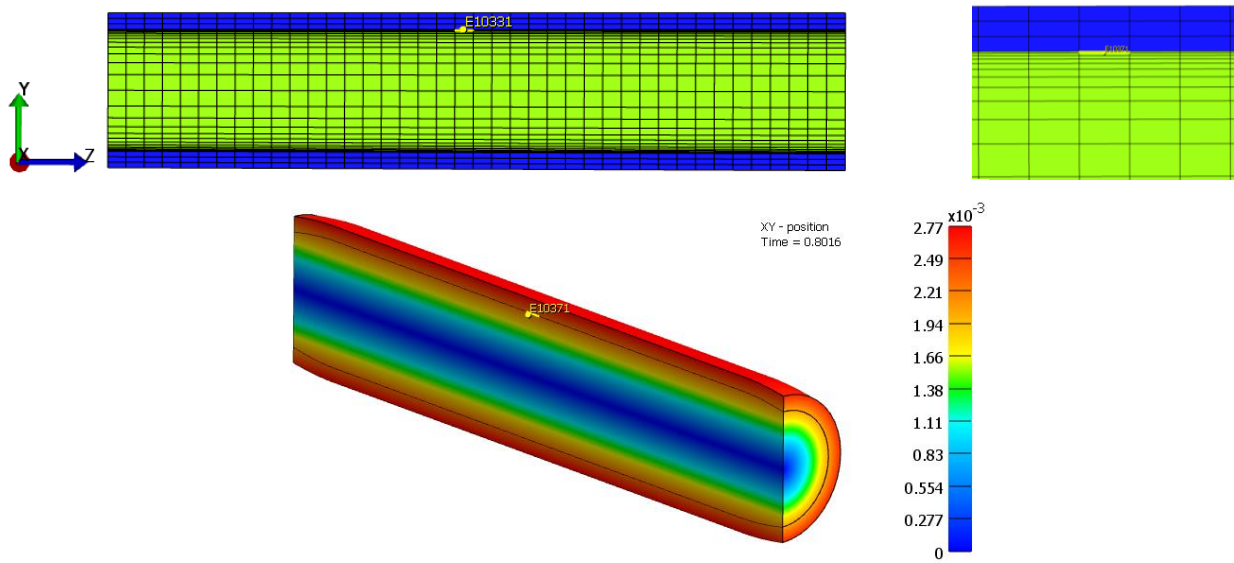


Figure 6.27 *Vessel's internal radius measurement. The element of the fluid domain closest to the fluid-solid interface was selected.*

The calculated internal radii are shown in Figure 6.28. For each case the radius was monitored for at least a full cardiac cycle. The first 0.5 s correspond to the ramping of the initial conditions. We can observe that in the cases where the vessel wall is modeled as the Ogden material, the measured radii are larger compared to the Mooney-Rivlin and Linear elastic cases. The maximum internal radius is 2.13, 2.21 and 2.25 mm for each pressure interval ([0-40], [50-90], [80-125] mmHg) for the Ogden material. The corresponding values for the Mooney Rivlin material are 2.07, 2.12 and 2.16 mm. We can see that the wall material has a significant impact on the radius calculation.

Having calculated the vessel's inner diameter changes under various operating pressure ranges, we were able to identify the radius – pressure relation. This was done by calculating the change of the inner radius over the initial radius dr/r for the above pressure ranges. The graph was completed by making static simulations for the unknown pressure ranges. The results are shown in Figure 6.29 (top). The difference in the response of the materials is obvious. The Linear elastic model follows a constant relation between pressure and radius change, as one would expect. The Mooney-Rivlin (reduced to Neo- Hookean) model has a different behavior, its slope being higher for low pressures and declining for higher ones. This means that a Neo-Hookean material has an opposite response than most elastin-collagen, natural fibrous tissues. Normally, these kind of tissue structures experience a lower elastic modulus for low pressures, which constantly rises as the collagen fibers stretch and align with the load's direction

(see Section 4.3). This behavior can only be predicted by the Ogden hyperelastic material.

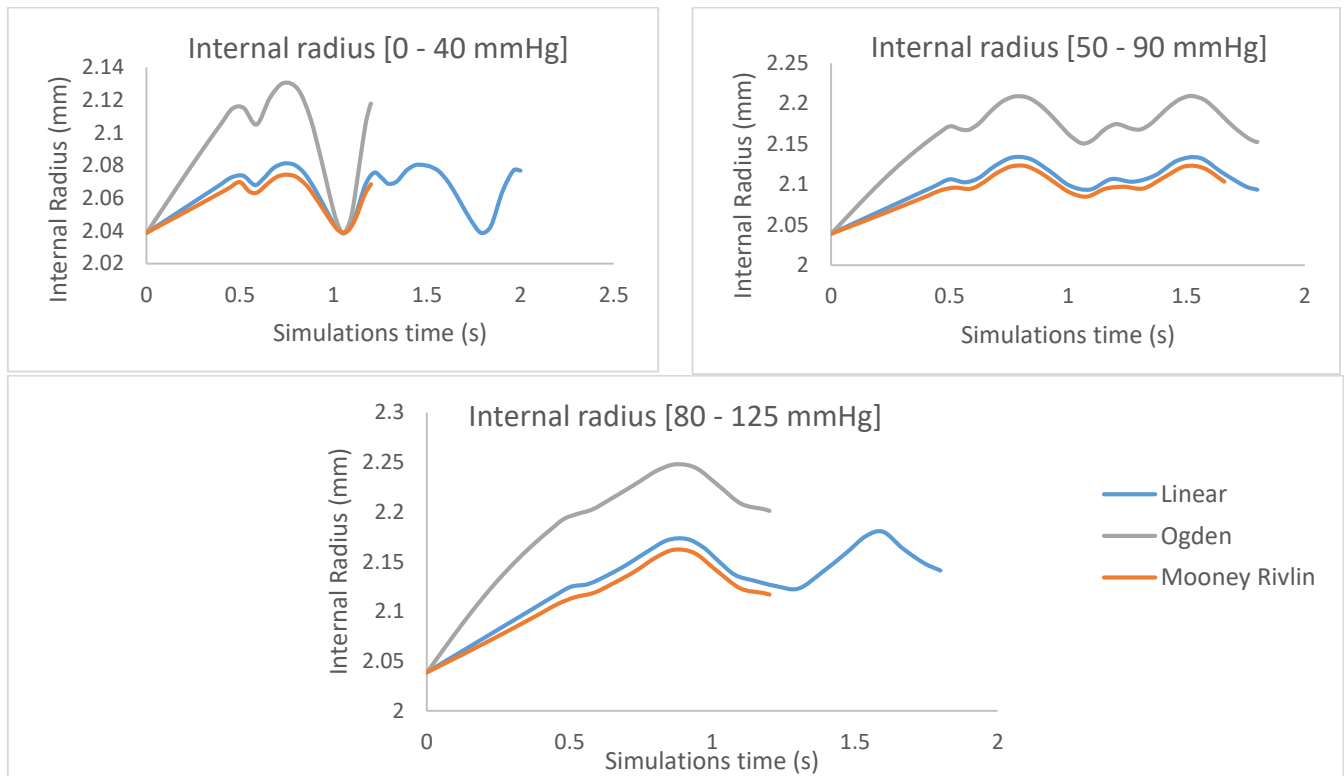


Figure 6.28 Calculated internal radius for each pressure interval of the simulation.

In order to reinforce the above assessment, the stress-strain relationship of the arterial wall was calculated and is presented in Figure 6.29 (bottom). We can see that the Ogden material model follows the response of a biological vessel, while the Linear model would be more suitable to model a stiffer polymeric material, like Dacron or Teflon (see Figure 4.7).

The 1st Principal wall stress for the Ogden model is shown in Figure 6.30., under 80, 120 and 150 mmHg internal vessel pressure. We can see that, under physiological operating pressures, the maximum 1st Principal stress developed is about 100 kPa. Our result is in accordance with the stress analysis of a carotid wall, performed by Gao et al. [77], where stresses larger than 100 kPa were only observed locally on non-circular cross sections.

Having measured the vessel's internal radius, we were able to calculate its dynamic compliance for each pressure interval (Figure 6.31). The calculations were performed according to the theoretical Equation 4.11, substituting R with the lowest radius measured for every pressure interval; ΔR is the difference between the highest and the lowest measured value for the diameter and Δp is the pressure interval length.

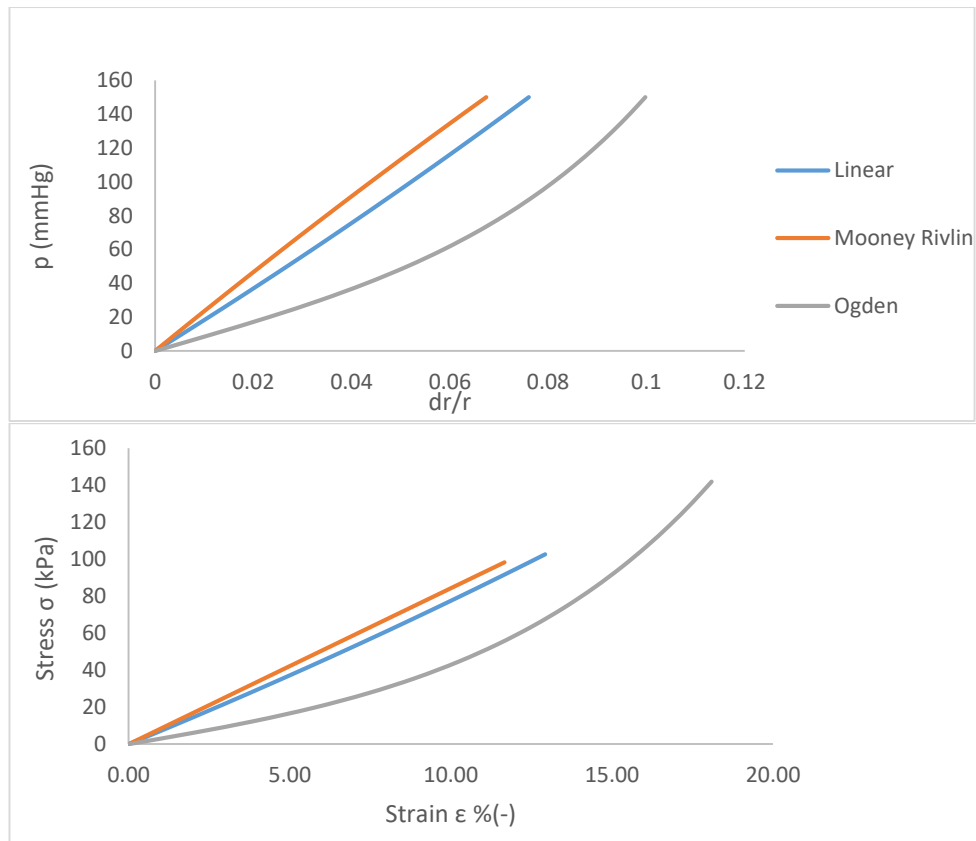


Figure 6.29 Pressure – radius relationship of the vessel (top) and stress-strain curve of the simulation materials (bottom).

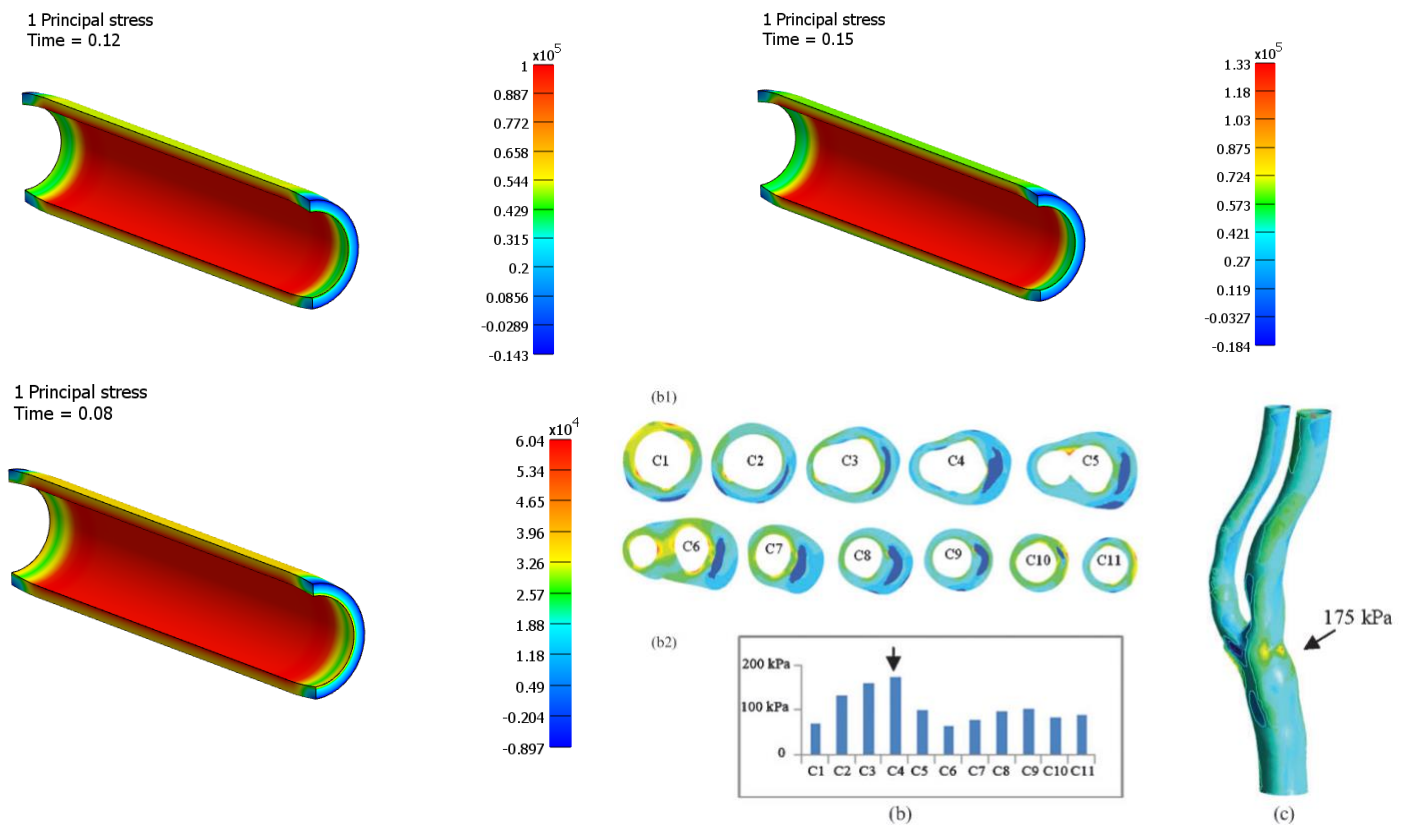


Figure 6.30 Distribution of first principal stress in the vessel wall at peak systole. Top, bottom left: this study's results. Bottom right: study in [77].

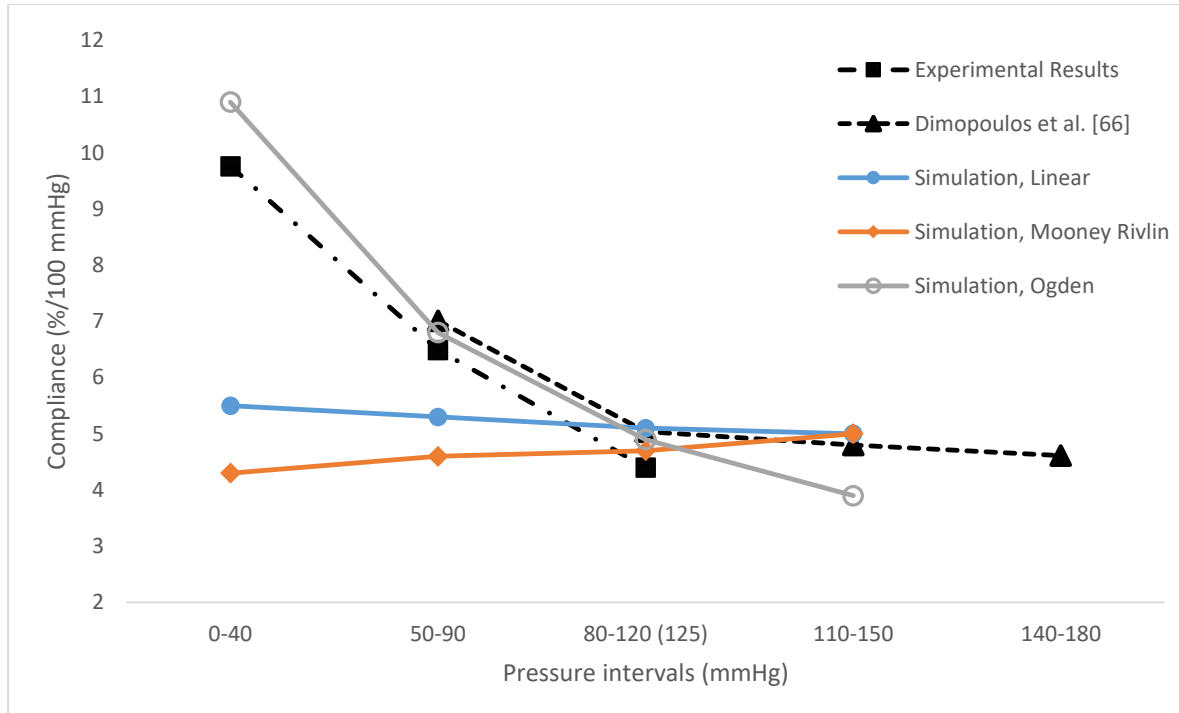


Figure 6.31 Dynamic vascular compliance. Comparison between experimental results, simulation results and bibliographic values.

We can firstly observe that none material model used in the simulations approaches the vessel's true compliance perfectly for every pressure range. This phenomenon is quite understandable, as an artery wall has a complex structure that cannot be fully modeled using a simple constitutive equation, as is the case with the material models used in our simulations. One can also see that different material models may approach the true vessel's behavior better, for different operating conditions. For example, the Ogden material model approaches the vessel's compliance more faithfully up to the 80-125 mmHg pressure interval, having a compliance that ranges from 10.8 to 6.8 and 4.9 %/100 mmHg $\times 10^4$. Beyond that range it falls short, while the linear isotropic and Mooney-Rivlin materials are more reliable for higher pressures. One common point for all of the simulation materials is that they have a very good approximation of the arterial compliance under physiologic pressure range (80-125 mmHg), which is to be expected, as they all have been used in relevant studies [54-57, 61-62]. The linear isotropic material model showcases an almost constant compliance. This is confirmed by relevant studies in modelling electrospun small caliber vessels with the use of isotropic linear elastic materials [51,52]. In our results the linear material model compliance ranges between 5.5-5 %/100 mmHg $\times 10^4$, while the value it yields depends on the vessel's diameter and wall thickness. Finally, the Mooney-Rivlin material has a behavior that contrasts the one of a physiological vessel, as its compliance increases for

higher pressures, ranging from 4.3 to 5 %/100 mmHg $\times 10^4$ for pressures of 40 to 150 mmHg.

Figure 6.32 shows the error of the vascular compliance calculated by the simulations, in comparison to our experimental results and bibliographic values. Specifically, for the physiological pressure range of 80-120 mmHg, the simulation error was less than 16% for all material models compared to our experimental results and less than 7% compared to bibliographic values for the material [66]. In addition, there was at least one material model for each pressure interval with an error of less than 12%. This shows that a careful selection of a material can vastly increase the fidelity of a vascular FEM simulation. For the same pressure ranges, relevant studies showed errors as high as 34%, when comparing vascular compliance calculated by analytical models with an experimentally measured one [51].

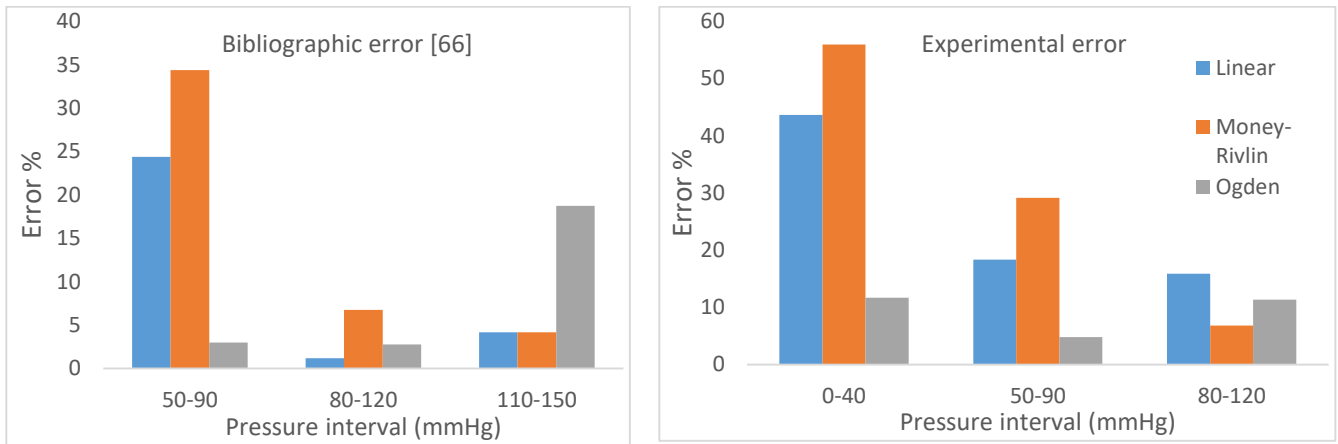


Figure 6.32 Vascular compliance yielded by the simulations, compared to our experimental results and bibliographic values.

All things considered, the Ogden material model can be assumed to have the best general response, as far as the vascular compliance is concerned, as it follows the declining trend of the vessel's real compliance. The Ogden material could be more precise for every pressure interval, by using a higher order model rather than the 1st order model used here. However, in order for such a model to be implemented, its material parameters must be approached by fitting an optimized curve over various point clouds obtained by different experiments. These experiments are common for hyperelastic materials and require uniaxial, biaxial and shear curves to be produced, which were not performed in this study due to limited resources.

6.2.7.2 FLOW VELOCITY

An approach regarding the flow properties in a vascular simulation could be a completely separate field of study. Albeit not being the main scope of this thesis, some indicative results regarding the fluid velocity are presented, in order to make a more complete assessment. For this reason, we chose to investigate the Linear and Ogden material models, which represent two different types of behaviors as we saw in the compliance calculations: Linear for stiffer vessels like Dacron and Ogden for biological arteries, or in this case PCL compliant vessels.

At first, we can see the velocity contours for the three main stages of a full cardiac cycle: The start of a pulse, peak flow and flow deceleration (Figure 6.33.). The maximum fluid velocity in the centerline of the vessel is almost identical for both materials at 0.958 m/s for the linear and 0.953 for the 80-125 mmHg interval and happens during the systolic phase, at peak systole. As these velocities are biased due to the imposition of the inlet boundary condition, a more suitable location to measure the fluid velocity would be downstream, at the vessel's mid-point or at the outlet (Figure 6.34.). There, the maximum velocities range about 0.93 m/s for the linear and 0.91 - 0.92 m/s for the Ogden case. Those velocities are in the range of what has been measured in experimental and computational studies on carotid artery flow [78,79].

Another point to be noticed is that there is almost no fluid backflow and flow separation near the walls during the deceleration phase of the cycle. As we saw in Section 3.2 this could happen due to an inverse pressure gradient when the blood flow approaches zero. The maximum negative velocity during deceleration happens for the Ogden model, for a small time window and is approximately -6 mm/s. This practically means that the flow is smoothed by the compliance of the system, which compensates for when the input flow decreases and makes the flow constant. In our simulations, this effect is represented by the boundary conditions and loads that prescribe the inlet flow rate to always be net positive. The latter would not be the case for example when simulating the aortic arch, where the flow would range from its maximum to almost zero and backflow would be expected near the wall. This is demonstrated by the velocity contours for the 0-40 mmHg pressure interval (Figure 6.33.), where the inlet flow rate B.C. during the diastolic rate approaches zero. The maximum negative velocity in this case is approximately -9 mm/s. Also, in the case of realistic geometries more backflow and recirculation zones are to be expected (Figure 6.42.).

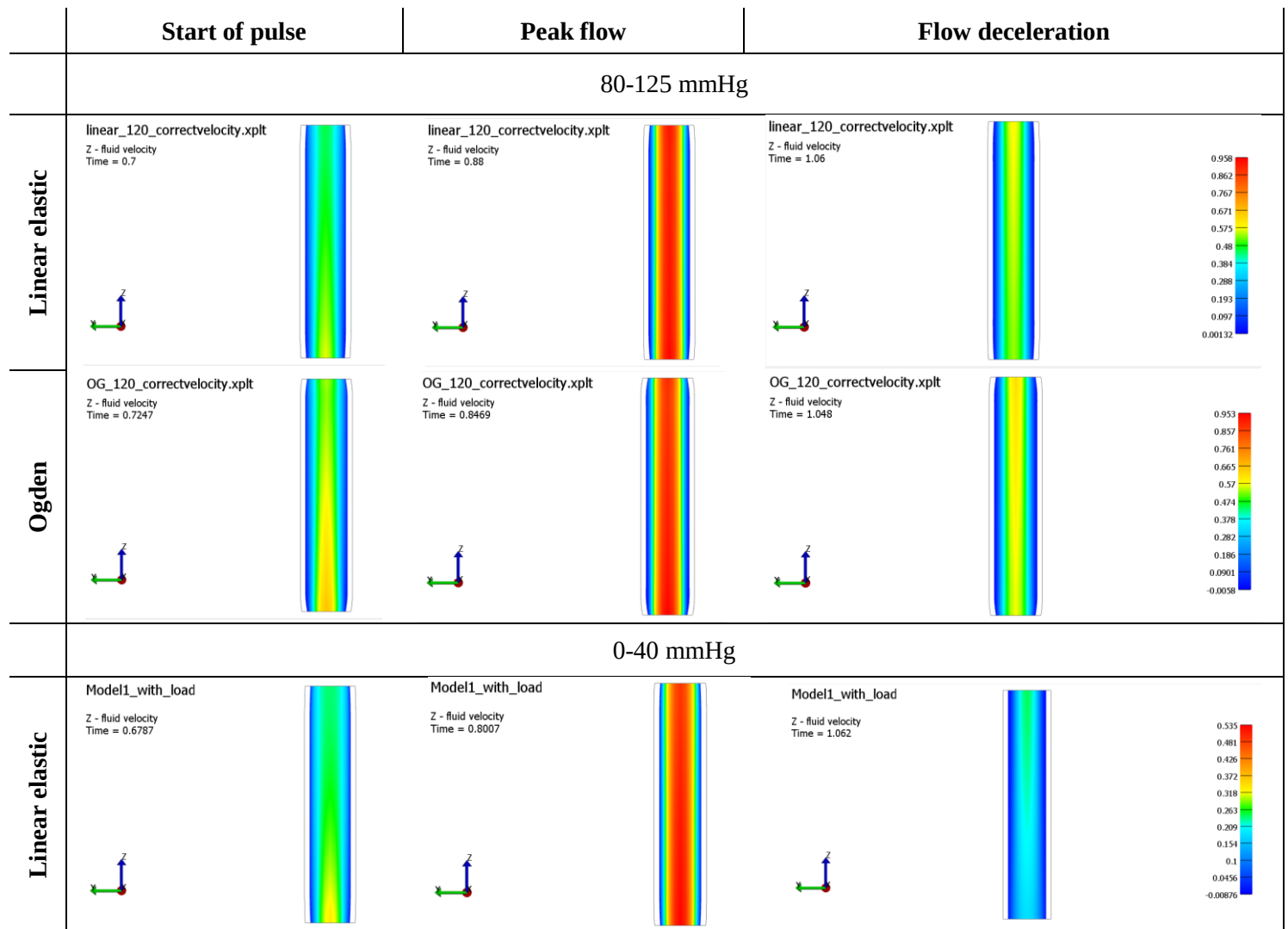


Figure 6.33 Fluid velocity contours at start of pulse, peak systole and flow deceleration.

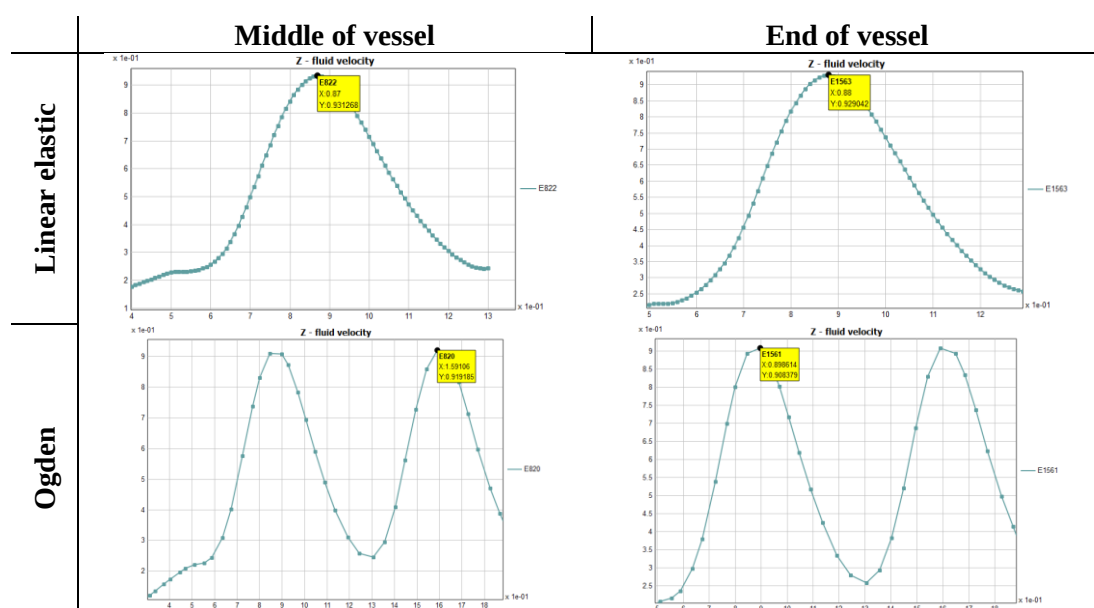


Figure 6.34 Mid-vessel velocity for the 80-125 pressure interval.

6.2.7.3 COMPLIANT VS RIGID WALL ANALYSIS

Finally, we made a comparison between rigid (CFD) and deformable (FSI) wall models. In this study, the importance of the arterial compliance has been well highlighted multiple times. As our simulation process relied heavily on the FSI aspect of the models, it was important to investigate how such an approach could yield different and hopefully more reliable results than a more traditional CFD study. The above comparison was made using the velocity and pressure propagation, as well as the wall shear stress (WSS) as indices.

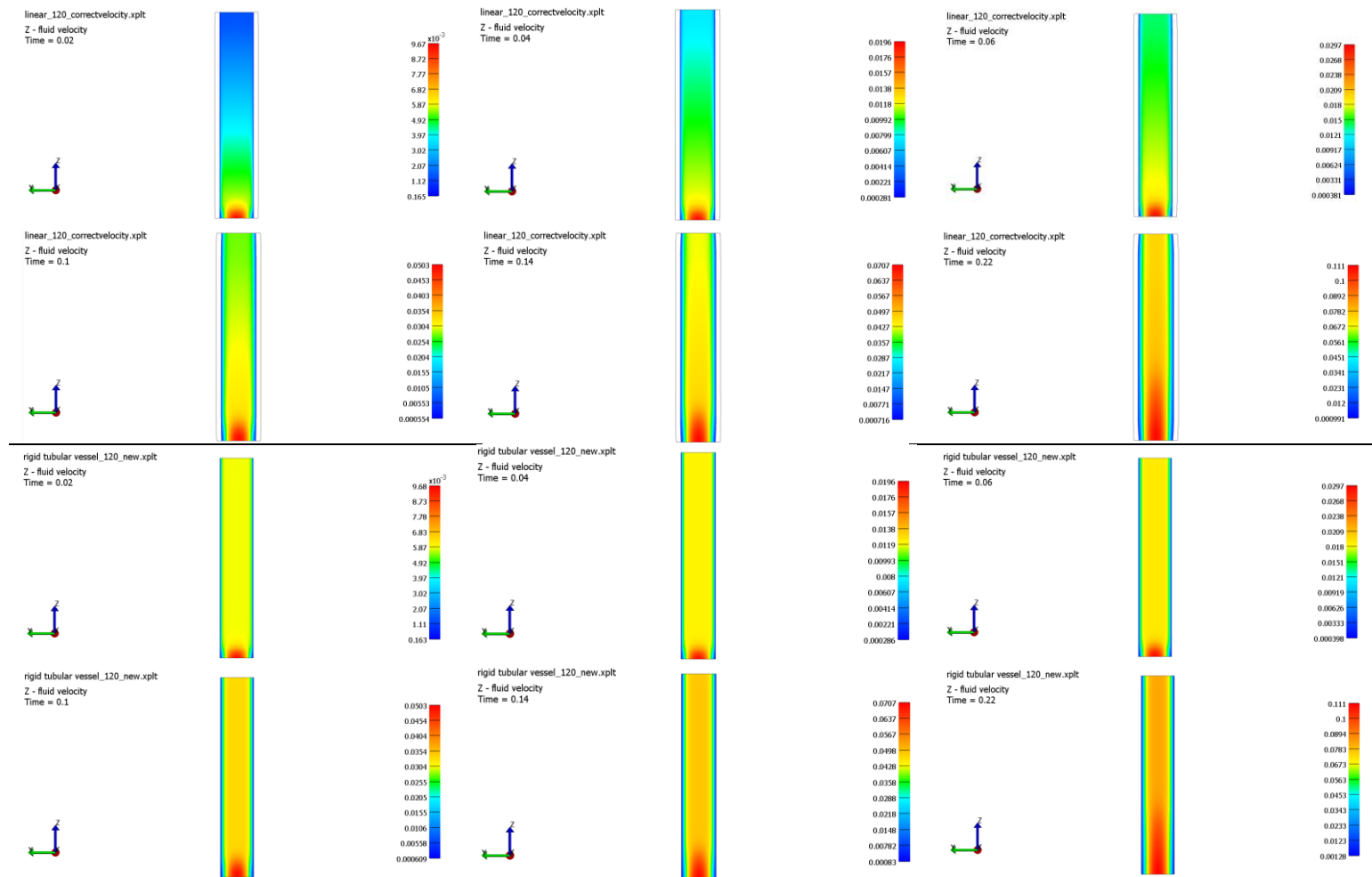


Figure 6.35 Comparison of fluid velocity between deformable (linear elastic, FSI) (top) and rigid (CFD) (bottom) wall models

We first applied a ramping velocity boundary load at the entrance of the vessel and compared the response of an FSI, deformable wall model (the Linear material model was used) and a CFD rigid one (Figure 6.35.). We can see that, even from the first steps, the fluid velocity in the rigid wall model is applied instantly on the whole length of the vessel. On the other hand, the fluid velocity of the deformable wall vessel has to

propagate for some time until it reaches the end of the vessel. Moreover, the fluid velocity in the middle of the vessel is lower in the case of the deformable vessel. This is in agreement with our previous findings when, by comparing the Ogden and Linear material models, we found that the higher the compliance of the vessel the lower its maximum fluid velocity.

The same pattern in pressure propagation can be observed in Figure 6.36. In the rigid model, the pressure is applied instantly on the whole length of the vessel. In contrast, on the deformable model the pressure propagates with a certain velocity, as explained in Section 3.4.1. According to Eq. 3.17, this velocity is proportional to the wall's Young modulus, which means that the higher the compliance, the lower the pressure pulse propagation speed. For a rigid wall, an infinite Young's modulus is assumed, explaining the instant pressure pulse propagation.

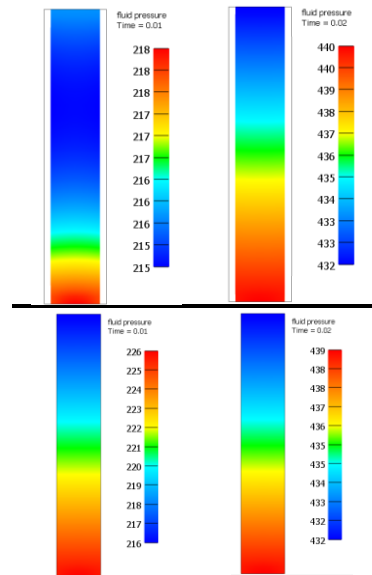


Figure 6.36 Pressure propagation in a deformable (top) and rigid (bottom) vessel.

After establishing that the fluid velocity changed according to the vessel compliance, we decided to assess its effect on the WSS. To this end, we examined the fluid domain element nearest to the fluid-solid domain interface (Figure 6.27.) and calculated its fluid shear stress. This was done for at least a full cardiac cycle with the boundary conditions of the 80-125 mmHg pressure interval. In addition to the Rigid and Linear material deformable models, the Ogden one was also examined in order to find out the correlation between the arterial compliance magnitude and maximum WSS. As shown in Figure 6.37., the maximum WSS at the center of the vessel is recorded for the rigid vessel and has a magnitude of 1.04 Pa, during peak systole. The deformable wall models have a lower WSS as expected: 0.69 Pa for the Linear (34% reduction) and 0.57 Pa for

the Ogden model (45% reduction). Thus, our assumption that the WSS is lower for higher vascular compliance can be validated. We can also see how a rigid wall model overestimates the WSS. This is an important finding, as according to Geoghegan et al. [51] a 40% reduction in peak WSS would help avoid cell damage. In the same study, the peak WSS was calculated as 2.3 and 1.4 Pa for a rigid and compliant vessel respectively. These values for the WSS may seem low, but they refer to a straight tube with constant diameter. A more realistic geometry with bendings, bifurcations and narrowings should yield higher WSS values (Figure 6.43.).

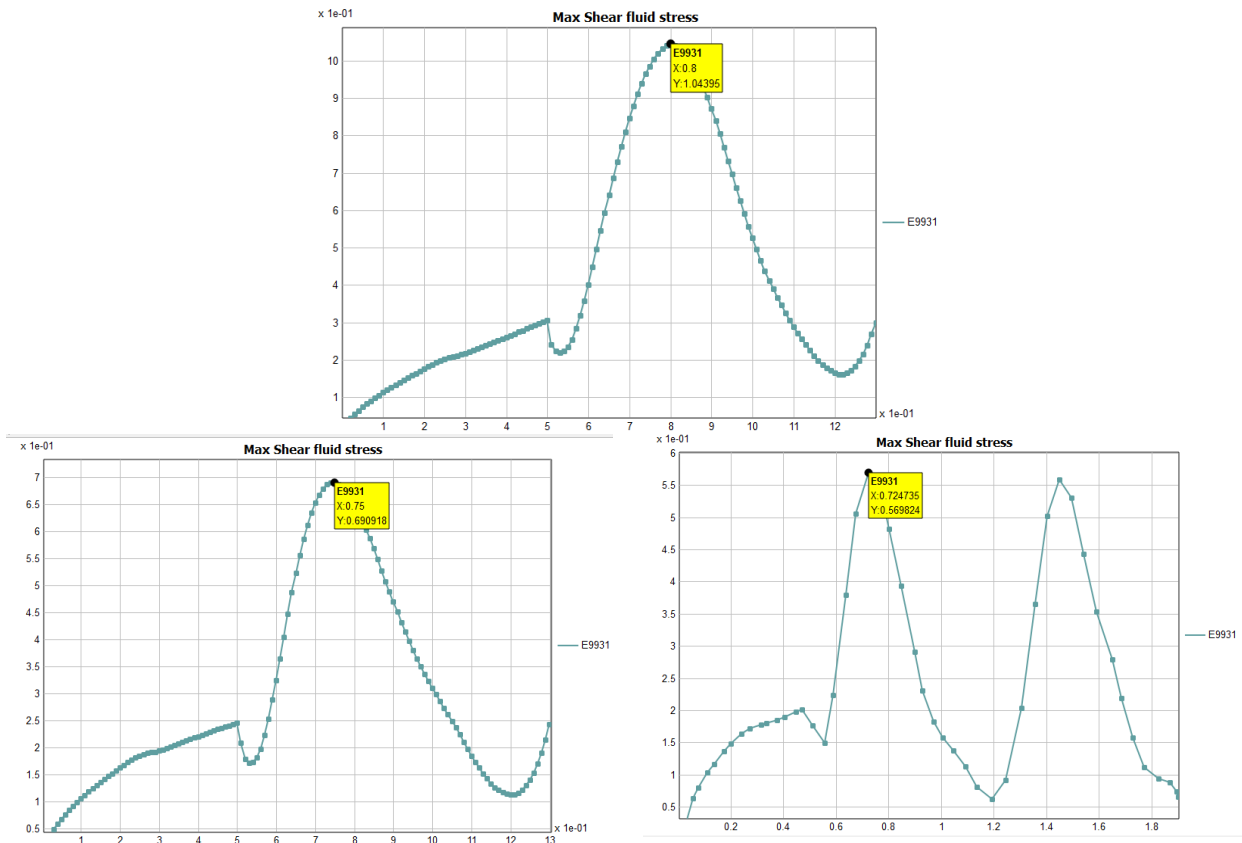


Figure 6.37 Wall shear stress calculated in the middle of the vessel. Top: Rigid vessel, Bottom left: Deformable (Linear elastic) model, Bottom right: Deformable (Ogden) model.

Finally, a comparison of the global maximum WSS is made between the rigid and Ogden deformable models in Figure 6.38. At first glance, the WSS seems to be double in the deformable model (2.28 vs 1.14 Pa). However, by looking carefully it can be seen that this high WSS is located at the outlet region of the vessel, where there is an artificial stenosis due to the fixed ends boundary condition. In a physiological setup, this increased WSS could further deteriorate the condition of a stenosis or lead to thromboembolism, as we discussed in Section 2.4. This means that the ends of the

tubular vessel should be carefully joined with the adjacent biological vessels to avoid properties mismatch.

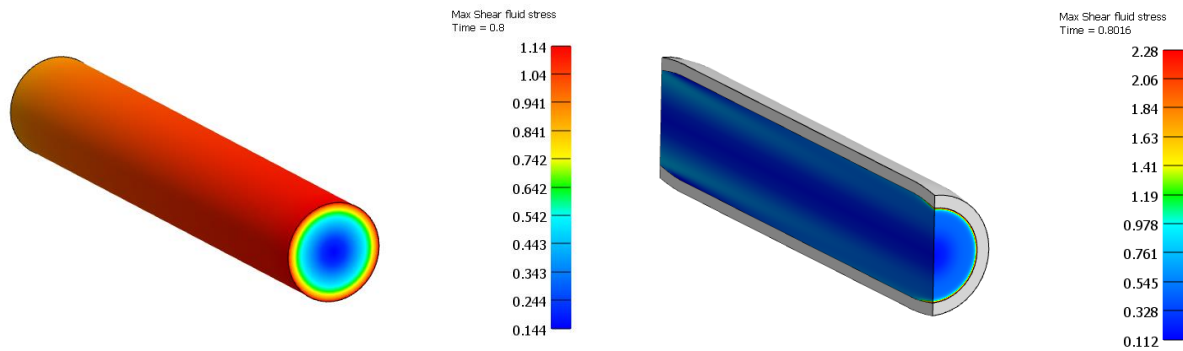


Figure 6.38 Global maximum wall shear stress for the rigid (left) and deformable (right) vessel models.

One should note that it is challenging to make a proper comparison of rigid vs deformable vessels via simulation, as the boundary conditions may depend on the nature of the vessel itself. In our analysis, we used the same outlet pressure boundary condition, despite the fact that it should be influenced by the vessel itself. Although some significant observations were made, a more extensive study of boundary conditions could be examined in future work.

6.2.8 CONVERGENCE STUDY

In order to further assess the reliability of our FEM model, a convergence study was performed, in which three different meshes with varying density and element size were used. The meshes used are shown in Figure 6.39. The middle mesh corresponds to the same one used in our simulations. The left one is a coarse mesh, with half the number of elements, while the right one is a fine mesh with about 4.5 times the base number of elements. A simulation was run for each mesh, where the outlet pressure was incremented up to 120 mmHg and the radial displacement of the element closest to the wall was measured. Then, the relative error when moving from one mesh to the next in density was calculated. The results are shown in Figure 6.40. We can see that the error is about 1% between the coarser and the base mesh, as well as for the finer mesh. These relative differences are quite insignificant and do not compensate for the high computational cost of the finer mesh. For these reasons, we can assume that the mesh used is sufficient for the displacement calculations. Note that the stress convergence may slightly differ, as is generally considered to be slower; However, identifying the stress convergence more precisely is outside the scope of this thesis.

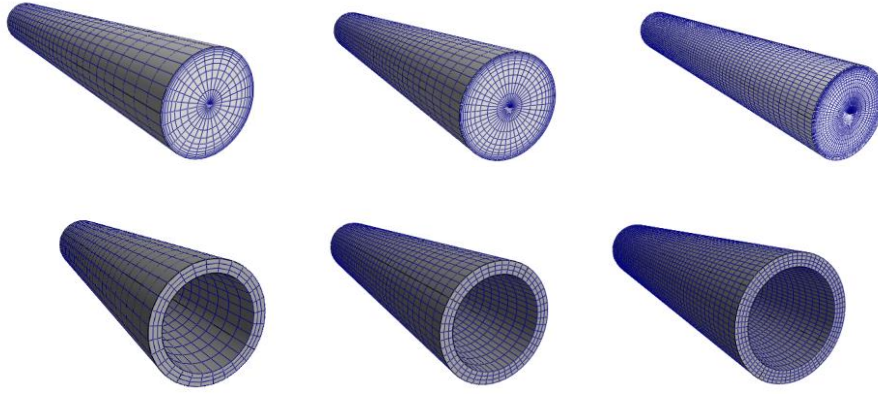


Figure 6.39 Different meshes used in displacement convergence study. From left to right: Coarse, base and fine fluid-wall mesh.

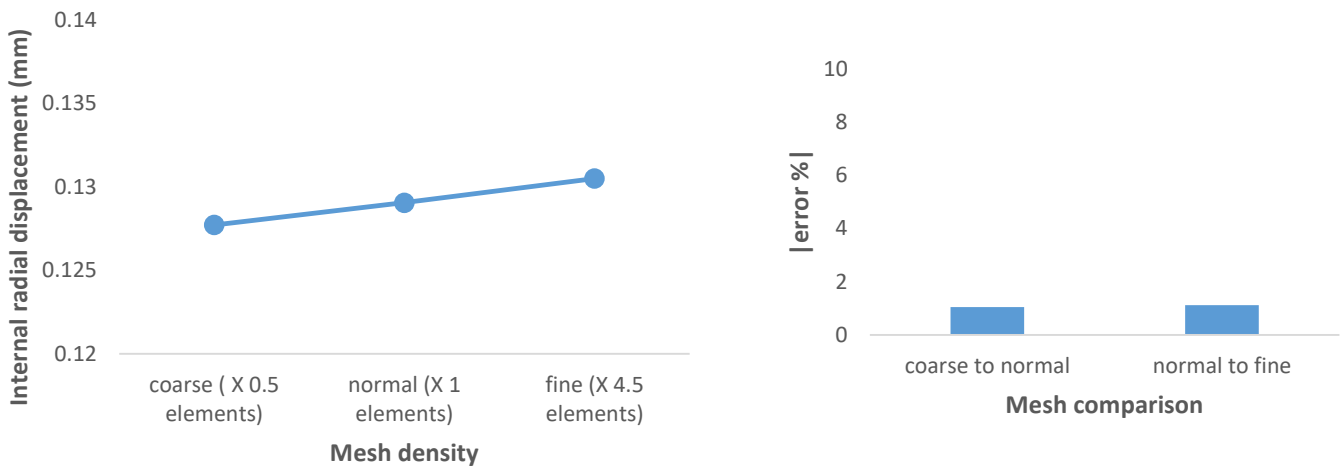


Figure 6.40 Displacement convergence study: Element displacement and relative errors.

6.2.9 FUTURE WORK

A direct expansion and continuation of this study could include the FEM simulation of realistic carotid arteries. Some preliminary work has already been done and will be briefly presented.

The model used was taken from the Grabcad community⁸, where it is freely shared. A geometry preprocessing was performed using Blender and Meshlab in order to scale the model accordingly and create the .stl geometry files for Febio. Then, the final geometry was meshed using Febio's built-in TetGen routine, in order to discretize the volume enclosed by the .stl surfaces of the wall, input and outputs. The final geometry used is shown in Figure 6.41. We can use this geometry in the future to perform an

⁸ <https://grabcad.com/library/carotid-bifurcation>

analysis using similar boundary conditions with the ones in our study. This way we can evaluate the simulation results based on more realistic conditions. For example, we can properly simulate the recirculation and stagnant flow zones (Figure 6.42), which could not be examined in a straight vessel. Furthermore, the WSS can be calculated in certain regions of interest, like a bifurcation (Figure ..). The next step would be to perform an FSI simulation of the carotid bifurcation, using the material models that were examined in our study. This way, the response of the PCL vessel could be estimated under conditions with higher physiological affinity.

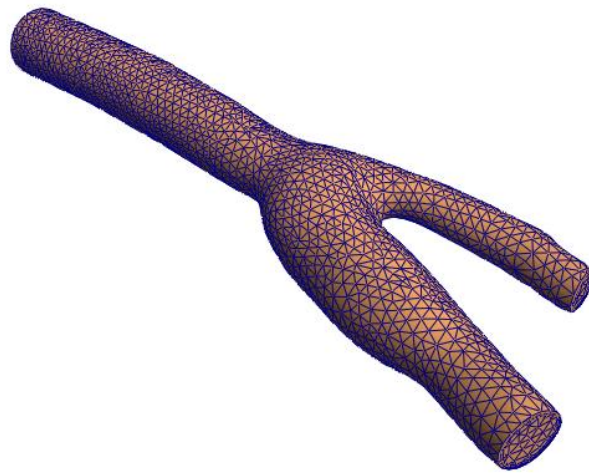


Figure 6.41 Processed carotid bifurcation geometry and final mesh.

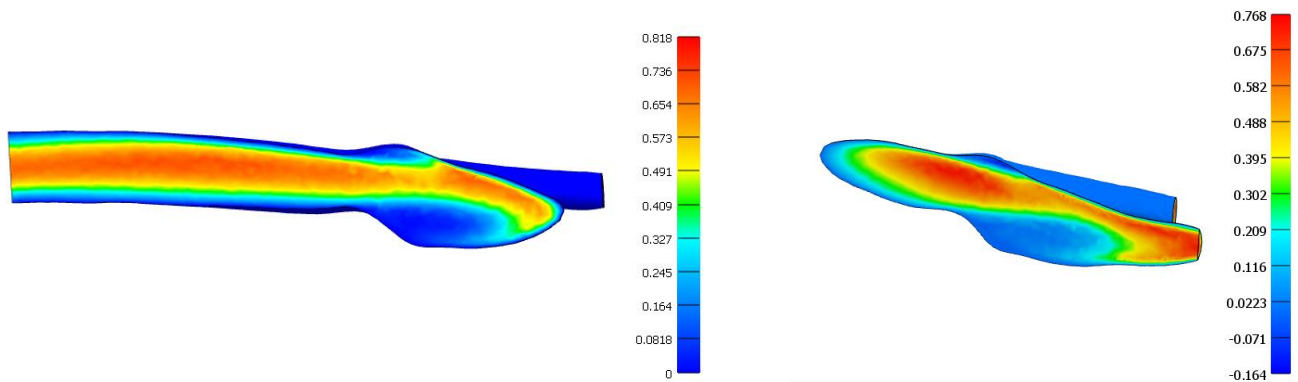


Figure 6.42 Flow velocity in a bifurcating carotid. Absolute velocity magnitude (left) and z-velocity component (right). Flow separation and recirculating zones can be observed.

Besides the geometrical model, there is a number of modelling parameters that could be improved. First of all, the mechanical behavior of a vascular wall can be better defined with the implementation of an anisotropic material model. This aligns with the physiological structure of both biological as well as PCL electrospun vessels, where the scaffold fibers are biased to certain directions in order to create a higher longitudinal

than radial Young's modulus. A way to achieve such a complex, anisotropic material structure is with the use of a Holzapfel-Gasser-Ogden material [80]. This material model features two fiber bundles with different circumferential orientation and a hyperelastic (i.e. Neo-Hookean) ground matrix and is considered to be suitable for artery simulations. Another approach would be to model the three different arterial wall layers separately, with different material properties, and make a comparison with our one-layer resultant wall model. There is also still room for improvement even for the simpler isotropic hyperelastic Ogden material model used in this study. A potential improvement would be to characterize the PCL tubular vessel of our study by performing appropriate uniaxial, biaxial and shear mechanical tests that can be used to extract the material model parameters by a curve fitting optimization process, through the experimental stress-strain points scatter. A higher order model could also be used for better consistency with the experimental results.

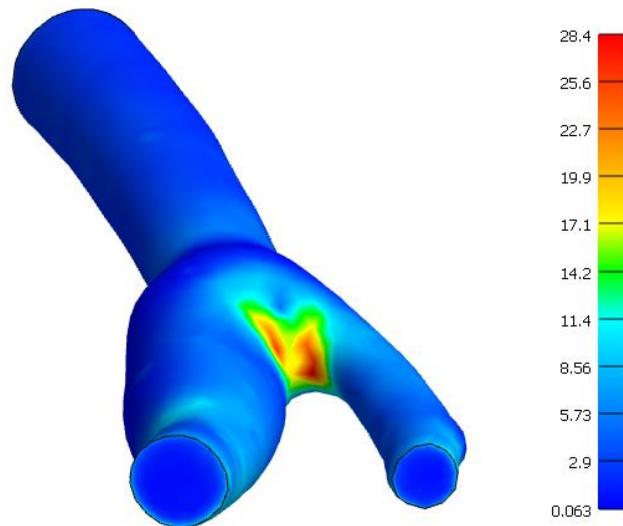


Figure 6.43 Wall shear stress distribution in a carotid bifurcation.

Finally, different boundary conditions could be implemented in our model, in order to investigate a more generalized behavior of the vessel under conditions other than the experimental ones. This can be done by modelling the adjacent tissue that surrounds the carotid artery and include it in our simulations. This approach was followed by Shim et al. [64] who proposed using a block of adipose material, created by a Boolean operation subtracting the carotid geometry from the block. This adipose block can be modeled using a Neo-Hookean solid. Then the carotid can be embedded into the block, with a tied contact condition between their interface's nodes. Different inlet and outlet boundary conditions can also be investigated, like a resistance outlet condition. This

way we can mitigate the need to experimentally measure both flow and pressure, and we can perform simulations under a wider range of operating conditions.

7 CONCLUSIONS

The biomechanical study of blood vessels is a key step in understanding and addressing the mechanisms that lead to the development of cardiovascular diseases. A crucial function of the blood vessels is their distensibility, which is expressed by their compliance. Through this mechanism, the vessels function as a pressure storage, converting the flow from pulsating to continuous along the arterial tree and smoothing the changes in pressure.

Blood flow modeling allows us to predict signs of increased likelihood of pathogenesis. Blood separation, stagnant flow, backflow and increased wall shear stress regions can be determined by CFD simulations. In addition, cardiovascular modelling and simulation, allows experts to predict the behavior of vascular grafts, stents and artificial valves in the human body, reducing the risk of complications. However, the classical approach of computational fluid dynamics problems is not always sufficient to model biological systems, as it cannot account for the change of the fluid's geometric space and the wall's deformation. For this reason, the Flow-Structure Interaction (FSI) approach is oftentimes employed. Although commercial FEM suites are commonly used in such applications, they are not designed to handle large deformation problems. A monolithic approach provided by open source FEM solvers like Febio is more suitable for cardiovascular modelling.

In this thesis, we performed a combined experimental and FEM simulation study on the response of artificial blood vessels under physiological simulated conditions. This comparison seems to be absent from many relevant studies. A PCL/PVA tubular vessel was produced, according to [66], by the method of electrospinning and was tested under conditions imposed by a physiological flow apparatus. The test was then simulated in Febio's studio FEM suite, using an FSI approach.

The PCL/PVA tubular vessel produced exhibits behavior similar to that of biological arteries, as its compliance is higher at low pressures and drops for higher pressure intervals. This happens due to the fibrous morphology of its wall. As is the case with collagen fibers in biological vessels, PCL fibers align with the application direction of the loads, resulting in a gradual increase in the incremental wall Young's modulus (non-linear behavior).

The compliance of the vessel was calculated by both the experimental and FEM simulation approach. The calculated compliance showed low errors between both, as well as compared with respective bibliographic values for the tubular vessel. The FEM simulations showed that no wall material model can fully describe the PCL's response for all pressure intervals. However, it can be concluded that a hyperelastic constitutive model, such as an Ogden material, is more appropriate for the modelling of arterial walls and elastin-collagen tissue structures in general, compared to other elastic materials. On the other hand, a linear elastic material model is better suited for less compliant artificial vessels made of Dacron or Teflon. That being said, both linear elastic, Neo-Hookean and Ogden material models had a vascular compliance almost equal to the experimentally calculated one and its bibliographic value at the physiological 80-125 mmHg pressure interval. In addition, all models showcased low errors for operating pressures up to 150 mmHg and can be used in future predictive models under certain circumstances.

The volumetric flow rate measurements of our experiment confirmed the corresponding bibliographic values for carotid caliber arteries like the produced vessel of this thesis. The same holds true for the fluid velocity calculated by the simulations. A correlation was found between higher compliance wall material models, lower peak fluid velocity and a significant drop in the maximum wall shear stress (WSS) in the middle of the vessel. Moreover, it was shown that traditional CFD simulations which assume vessel wall rigidity greatly underestimate the WSS. Furthermore, the maximum WSS at the narrowing of the fixed vessel ends was calculated to be four times greater than the one midway of the vessel. In a physiological setup, this increased WSS could further deteriorate the condition of a stenosis or lead to thromboembolism. This means that the ends of the tubular vessel should be carefully joined with the adjacent biological vessels in order to avoid properties mismatch.

Even though FSI simulation approaches are maturing, it can be seen that there is still room for improvement in cardiovascular problem applications. Experimental validation is still required and further investigation of the boundary conditions that are applied to the geometries under examination is important. These boundary conditions are crucial in order to obtain the correct response of the simulated vascular segment to the applied loads.

Taking all of the above into consideration, one could say that the possible improvements of any biological finite element model are numerous. In our case many

factors like neighboring tissues cannot be modeled properly and the wall materials need further testing for their properties to be fully defined. The number of improvements we can potentially include to our FEM model is increasing relative to our requirements on the model's fidelity and its targeted application.

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