IN SILICO STUDY OF BLOOD FLOW AS BIOMECHANICAL DETERMINANT OF PLAQUE FORMATION AND LOCALIZATION

Προσομοίωση αιματικής ροής για τον προσδιορισμό σημείων αθηρωμάτωσης με τη βοήθεια δεικτών αιμοδυναμικής φύσης

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Abstract

Atherosclerosis is a chronic inflammatory disease characterized by the accumulation of lipids and inflammatory cells along the inner walls of arteries, and is an underlying cause of cardiovascular disease. Atherosclerotic lesions develop predominantly at branches, bends, and bifurcations in the arterial tree because these sites are exposed to low or disturbed blood flow, which exerts low/oscillatory shear stress on the vessel wall. This mechanical environment alters endothelial cell physiology by enhancing inflammatory activation. In contrast, regions of the arterial tree that are exposed to uniform, unidirectional blood flow and experience high shear stress are protected from inflammation and lesion development. Wall Shear stress (WSS) is sensed by the endothelium via mechanoreceptors and is subsequently transduced into biochemical signals resulting in modulation of proinflammatory signaling pathways.

Our study was designed to test the hypothesis that flowfield properties such as WSS are closely related to cardiovascular disease. The spatial distribution patterns of several hemodynamic indices (gradient of WSS) were examined and compared with the (known) locations of plaque formation in human aorta. The part of the aorta on which we focused is ascending, aortic arch and descending aorta. Blood flow is influenced by vessel wall motion. Fluid Structure Interaction (FSI) is also investigated and discussed during the description of hemodynamic environment that leads to plaque formation in human aorta.

Our Data were DICOM files from Computed Tomography (CT) scans. Using Vascular Modeling Toolkit (VMTK) and these scans as the input, we choose level set segmentation method to extract the geometry of the vessel needed for the simulation. ANSYS CFX Solver was used for the simulation of blood flow.

The present numerical study revealed a direct correlation between low WSS values and atherosclerotic plaque localization. The results indicate also that Oscillating Shear Index (OSI) shows clearly points where the possibility of atherogenesis is high enough to be ignored. FSI provides unimportant details when we focused on plaque formation. In contrast, FSI can provide more comprehensive insight into plaque
disruption events such as rupture or erosion that may be due in large part to mechanical failure of plaque materials.
Περίληψη
Η Αθηροσκλήρωση είναι μια χρόνια, φλεγμονώδης νόσος κατά την οποία λιπίδια και φλεγμονώδη κύτταρα συσσωρεύονται στο εσωτερικό τοίχωμα των αρτηριών (ενδοθήλιο). Πρόκειται για μια βασική αιτία που οδηγεί σε καρδιαγγειακές παθήσεις, όπως είναι η στεφανιαία νόσος, η αρτηριακή υπέρταση και η καρδιακή ανεπάρκεια. Τα πιο πιθανά σημεία αθηρωμάτωσης αναπτύσσονται κυρίως σε διακλαδώσεις και κυρτά τμήματα αγγείων, γεγονός που δικαιολογείται επειδή οι περιοχές αυτές είναι συχνά εκτεθειμένες σε τυρβώδεις και χαμηλής ταχύτητας αιματικές ροές. Πράγματι, τέτοιου είδους ροές προκαλούν την ανάπτυξη διατμητικών τάσεων στα αγγειακά τοιχώματα που ευνοούν τη συγκέντρωση λιπιδίων και άλλων αθηρογενετικών λιποπροτεϊνών. Αυτό το περιβάλλον ροής μεταβάλλει τη φυσιολογική λειτουργία των επιθηλιακών κυττάρων που ενεργοποιούνται διαδικασίες σχηματισμού αθηρωματικών πλακών. Σε αντίθεση με τις περιοχές αυτές, υπάρχουν τμήματα του αρτηριακού δέντρου που εκτίθενται σε ομοιόμορφη και στρωτή ροή. Τα σημεία αυτά, στα οποία αναπτύσσονται υψηλές διατμητικές τάσεις, είναι περισσότερο προστατευμένα από φλεγμονές και, επομένως, είναι μικρότερη η πιθανότητα σχηματισμού αθηρωματικής πλάκας. Οι διατμητικές τάσεις στα τοιχώματα (Wall Shear stress, WSS) γίνονται αντιληπτές από τους υποδοχείς που βρίσκονται στις ενδοθηλιακές κυτταρικές μεμβράνες, καθώς και τους υποδοχείς που βρίσκονται στις ενδοθηλιακές κυτταρικές μεμβράνες μεμβράνες. Οι περιοχές αυτές στα τοιχώματα (Wall Shear stress, WSS) γίνονται αντιληπτές από τους υποδοχείς που βρίσκονται στις ενδοθηλιακές κυτταρικές μεμβράνες μεμβράνες. Οι διατμητικές τάσεις στα τοιχώματα (Wall Shear stress, WSS) γίνονται αντιληπτές από τους υποδοχείς που βρίσκονται στις ενδοθηλιακές κυτταρικές μεμβράνες μεμβράνες. Οι διατμητικές τάσεις στα τοιχώματα (Wall Shear stress, WSS) γίνονται αντιληπτές από τους υποδοχείς που βρίσκονται στις ενδοθηλιακές κυτταρικές μεμβράνες μεμβράνες. Οι διατμητικές τάσεις στα τοιχώματα (Wall Shear stress, WSS) γίνονται αντιληπτές από τους υποδοχείς που βρίσκονται στις ενδοθηλιακές κυτταρικές μεμβράνες μεμβράνες.
μελετήθηκαν και συζητήθηκαν κατά την περιγραφή του αιμοδυναμικού
περιβάλλοντος που ευθύνεται για γεγονότα αθηροσκλήρωσης.
Τα δεδομένα μας ήταν αρχεία DICOM από σαρώσεις Υπολογιστικής Τομογραφίας.
Χρησιμοποιώντας ένα εργαλείο για την ψηφιακή μοντελοποίηση των αγγείων, το
VMTK (Vascular Modeling Toolkit) και αυτές τις σαρώσεις σαν είσοδο, επιλέξαμε
τμηματοποίηση μέσω της μεθόδου level set για την εξαγωγή της επιθυμητής
γεωμετρίας που ήταν απαραίτητη για την προσομοίωση της αιματικής ροής.
Η επίλυση του προβλήματος έγινε μέσω του ANSYS CFX Solver v.14.
Η παρούσα αριθμητική μελέτη απέδειξε μια άμεση συσχέτιση ανάμεσα στις
χαμηλές τιμές των διατμητικών τάσεων και σε γεγονότα αθηρογένεσης.
Τα αποτελέσματα έδειξαν ακόμα ότι ο διατμητικός δείκτης ταλάντωσης της ροής
(Oscillating Shear Index, OSI) μπορεί με σαφήνεια να επισημάνει σημεία όπου η
πιθανότητα σχηματισμού τέτοιων πλακών είναι πολύ υψηλή για να αγνοηθεί.
Από την άλλη μεριά, το μοντέλο αλληλεπίδρασης ρευστού στερεού μας παρέχει
πληροφορίες ελάσσονος σημασίας όταν επικεντρώνουμε στη μελέτη σημείων
αθηρωμάτωσης. Ωστόσο, το μοντέλο αυτό (FSI) είναι χρήσιμο και μπορεί να δώσει
μια πιο ολική εικόνα για γεγονότα όπως η φθορά, ή η ρήξη μιας
αθηρωματικής πλάκας, κάτι που ενδέχεται να επιφέρει σημαντικές βλάβες όχι μόνο
στην ίδια την περιοχή αθηρωμάτωσης αλλά και σε ολόκληρο το κυκλοφορικό
σύστημα (κίνδυνος απόφραξης αγγείου, θρόμβωση).
Introduction

Each year almost 795,000 people experience a new or recurrent stroke, and mortality data from 2007 indicate that stroke accounted for 1 of every 18 deaths in the US [33]. The following figure (1.1) shows the number of deaths from 10 leading causes in USA during 2010, according to the National Vital Statistics System. In 2010, a total of 2,468,435 deaths occurred in the United States [34]. The first two leading causes of death, heart diseases (597,689 deaths) and cancer (574,743), accounted for nearly 50% of all deaths. In contrast, the other leading causes accounted for much smaller percentages. Therefore, cardiovascular diseases appear very often, lead to severe morbidity and their treatment needs to be urgent.

Fig. 1.1 Morbidity and Mortality Weekly Report. U.S. Department of Health and Human Services Centers for Disease Control and Prevention. [34]
In 2009, estimated direct and indirect costs for clinical care of cardiovascular disease in the United States alone are $475.3 billion [36]. Hospital statistics for atherosclerosis in England 2002-03 (1.2) showed that 8,480 hospital consultant episodes were for atherosclerosis. 85% of them required hospital admission and 11.7 days was the mean length of stay in hospitals for those patients, which means cost to the national health system. [35] The extent and severity of atherosclerosis is too important to be ignored. Atherosclerosis is associated with more than 12 million deaths worldwide each year.

Fig. 1.2 Hospital statistics for atherosclerosis in England 2002-03

1.1 Aim

Blood flow into human vessels carries various substances for each tissue and cell. As blood flows, temperature and pressure conditions form the hemodynamic environment next to vessel walls. Stresses and strains on these walls can vary as a result of blood flow type. Blood flow can be laminar or turbulent and vessel walls are compliant to this behavior. This means that walls can extent or shrink. Therefore, elastic properties of vessel walls control wall motion, but their endurance is not infinite.

Our study was designed to test the hypothesis that flowfield properties (like WSS) are closely related to cardiovascular disease (like atherosclerosis, aneurysm). The spatial distribution patterns of several hemodynamic indices (gradient of WSS) were examined and compared with the known locations of plaque formation in
human aorta. For example, atherosclerotic plaques in vessels of high curvature are usually formed and regions suffering from oscillating blood flow seem to be at risk.

The part of the aorta on which we focused is ascending, aortic arch and descending aorta. We are going to look in more detail the procedure followed and the obtained results.

1.2 Thesis Outline

Clinical problem of Atherogenesis is described and to some extent analyzed in mathematical terms without a very-detailed medical insight. Thesis is focused on the hemodynamic part of the problem through mathematical formulations of conservation laws. Clinical problem is presented through the relative Literature and then basic anatomy and physiology principles are cited. Heart anatomy, blood circulation and blood composition, arterial tree and cardiac cycle are studied. Mathematical expressions of mass, momentum and energy conservation laws are analyzed. Viscous stresses, types of flow and blood flow characteristics are described before the chapter of image processing methods. Medical imaging modalities used for blood flow simulations are presented and image segmentation methods follow.

Our method is outlined through the processing steps followed for results extraction. The vessel of interest is isolated from the whole geometry data file through image segmentation method of level set and then mesh construction takes place. Computational hemodynamic principles are implemented to form the final simulation of blood flow. A fluid-structure-interaction model is also built for another geometry and studied properly. Spatial and Temporal distribution patterns of several hemodynamic indices are calculated and presented. Final results are compared with previous studies and clinical practice. Conclusions are discussed and limitations that lead to future work are explained.
The Clinical Problem of Atherogenesis

Atherosclerosis, a vascular disease that appears widely in western societies, has been studied several times in order to identify its main causes. It appears to be a multifaceted medical problem with many parameters and factors that affect the frequency of its development. Being one of the major causes of mortality, atherosclerosis is the leading cause of heart attacks, stroke and peripheral vascular disease. As of 2006, cardiovascular disease was responsible for at least one in every 2.9 deaths in the United States (American Heart Association: Heart Disease and Stroke Statistics 2010).

Atherosclerosis is a fibro proliferative disease primarily of large- and medium-sized conduit arteries [1]. The arterial wall thickens due to the accumulation of fatty materials such as cholesterol and triglyceride and then an atherosclerotic plaque is formed. It is caused by high concentration of macrophage white blood cells along the endothelium, promoted by low-density lipoproteins (LDL) and inadequate removal of fats and cholesterol from the macrophages by functional high-density lipoproteins (HDL).

Various anatomic and physiological risk factors for atherosclerosis are known. According to R. A. Vogel [2] the traditional risk factors for coronary heart disease include hypercholesterolemia, hypertension, cigarette smoking, diabetes mellitus, and high-fat diet. Glass et al. [3] also consider factors responsible for the development of atherosclerosis with a significant genetic component such as elevated levels of very low-density lipoproteins (VLDL), LDL, homocysteine and hemostatic factors. Furthermore, the atherogenic effects of diabetes Mellitus,
Insuline resistance, obesity and family history are mentioned. All the above together with low level of HDL and male gender represent the most important risk factors for atherosclerosis. There are still some environmental factors such as lack of exercise, high fat diet and infectious agents that promote that disease. Because of the variety of the risk factors, atherosclerosis cannot be prevented by simple maintenance of one’s cholesterol, lipid levels, and blood pressure. Moreover, it has been observed that each atherosclerotic plaque exhibits an individual natural history of progression, regression, or stabilization, which is dependent not only on the formation and progression of atherosclerosis but also on the vascular remodeling response [1].

Atherosclerosis can be asymptomatic for decades. It may begins in childhood, but morbidity and mortality typically occurs in adulthood [4]. Chronically expanding lesions are often asymptomatic until lumen stenosis is so severe that blood supply to downstream tissue(s) is insufficient resulting in ischemia. Significant stenoses from advanced plaques are extremely dangerous in coronary arteries, where intersection of each lumen is small, and myocardial infarction can take place and cause scar formation and heart failure leading to cardiac death. Compared to nonstenotic vessels, an important drop in blood pressure changes the whole hemodynamic environment in lumen where plaques greatly hinder the blood flow [5].

According to pathobiology if arterial wall, known as fibrous cap, which covers the atherosclerotic plaque ruptures, thrombogenic material, such as collagen will be exposed to the circulation and eventually induce thrombus formation in the lumen [6]. Intraluminal thrombi can completely occlude arteries (i.e. coronary occlusion), but more often they detach, move into the circulation and eventually occlude smaller downstream branches causing thromboembolism (i.e. Stroke is often caused by thrombus formation in the carotid arteries).

This pathological formation of fibrous and lipid-rich plaque can be detected wherever in the vascular tree, as a result of most commonly-cited atherogenic effects of the systemic risk factors. However, numerous studies have noted that atherosclerotic plaques form preferentially in specific locations, such as in the vicinity of branch points, the outer wall of bifurcations, and the inner wall of curvatures, where disturbed flow occurs [7,8]. Therefore, the mechanics of flowing blood affects significantly the localization of atherosclerosis.
Treatment of atherosclerosis is usually achieved through several interventional methods. Thrombolysis, angioplasty, stent implantation and bypass grafting are some examples. The progression of atherosclerotic lesions can be controlled through statin therapy (drug therapy) which also reduce serum cholesterol [9]. Less severe cases diet and dietary supplements are suggested combined with practicing regular exercise.

**Fig. 2.1** The progression of atherosclerosis. Brief descriptions (left column) of tissue state are given and matched with the corresponding clinical behavior (right column). Almost each stage has different growth mechanism (second from right column) and its earliest onset appears at a specific time (third form right column). [6]
2.1 Biological Description of Atherosclerosis

The exact mechanism for lesion initiation is not clearly understood yet. According to Chatzizisis et al. [1] atherosclerotic process begins when the pro-atherogenic genes are upregulated and atheroprotective genes are suppressed due to low wall shear stress (WSS) occurring in regions with low and disturbed flow. Normally these genes are expressed and lead eventually to stability in that region. When wall shear stress decreases mechanoreceptors located on the surface of endothelial cell are activated and a process known as mechanotransduction is triggered. As a result several intracellular pathways are activated and lead to phosphorylation of some transcription factors (TFs). Cellular function and morphology is then modulated because phosphorylation of TFs suppresses the expression of numerous genes including those who provide protection to the cell from atherosclerosis.

2.2 Localization of Atherosclerosis

Atherosclerotic plaques in humans form preferentially in specific locations in the human vascular tree. While no artery is immune from the possibility of plaque formation, regions experiencing relatively lower levels of wall shear stress and regions experiencing oscillatory flow reversal tend to be most at risk to form lesions. The inner edges of curving vessels and branching vessels immediately distal to bifurcation are most prone to lesion formation. [24, 25] At certain eccentrically located sites shear stress control is modified to let it remain at near-zero levels. As explained in next section, low wall shear stress is a forerunner of lesions formation.

Nearly all lesions occur in four primary regions in the body (Fig. 4). The coronary arteries, major branches of the aortic arch such as the carotid arteries, the visceral branches of the abdominal aorta such as the renal arteries, and the terminal branches of the abdominal aorta such as the femoral arteries are the principal regions where plaques form in humans. [26] The coronary arteries, which supply blood to the myocardium, branch frequently and often form plaques immediately distal to divisions. [27] These arteries perfused primarily during diastole rather than during systole. In the abdominal aorta less branching occurs but lesions tend to form
immediately distal to branch locations. [28, 29] Other regions, such as the thoracic aorta where minimal branching occurs, tend not to form lesions. [5] The internal mammary artery, a long, straight vessel with few bifurcations and consequently minimal flow disturbance, rarely forms lesions, even in patients exhibiting advanced atherosclerosis in other vessels. [30]

Atherosclerosis appears preferentially at specific locations among the arterial tree due to different waveforms of flow across the cardiac cycle occurring in these areas. Tortuous and branching vascular geometry also facilitate the appearance of

![Diagrammatic representation of predominant anatomic sites (shown in black) and distribution of atherosclerotic occlusive disease in the four major arterial beds of body [26]](image)

*Fig. 2.2* Diagrammatic representation of predominant anatomic sites (shown in black) and distribution of atherosclerotic occlusive disease in the four major arterial beds of body [26]
For example, flow in carotid arteries, which supply blood to the brain and frequently form atherosclerotic plaques, will often reverse directions during the cardiac cycle. Size, shape and branching angles at the carotid bulb, a pouching on the internal carotid artery immediately distal to the carotid bifurcation, are responsible for the formation of secondary flows. Therefore, while plaques at the external carotid artery are rarely formed, in the internal carotid artery is a frequent phenomenon [31, 32]. Atherosclerosis in the abdominal aorta is caused by the low wall shear stress regions [28].

2.3 How low WSS causes Atherosclerosis

Arterial regions, where disturbed flow is developed and low WSS values occur, are exposed to atherogenic effect of local and systemic risk factors [10, 11, 12, 13, 14]. The fact comes through the decrease of endothelial nitric oxide synthase messenger ribonucleic acid and the limited production of the corresponding expressed protein. In addition to attenuation of nitric oxide dependent atheroprotection, low WSS causes subendothelial accumulation of LDL because it promotes activation of proteins that upregulate the expression of genes encoding LDL receptor. Moreover, inflammation and oxidative stress are promoted by low WSS [15, 16, 17, 18, 19]. During functional and structural alterations monocytes differentiate to macrophages under the endothelium and sustain the inflammation and oxidative stress promoting progression of atherosclerosis.

Furthermore, vascular smooth muscle cells migrate, differentiate and proliferate due to low WSS [15] while extracellular matrix degradation and attenuation in vascular wall and plaque fibrous cap is promoted. Progression of atherosclerotic plaques is also caused by angiogenesis in which the role of WSS is substantial [20]. It has been observed that plaque calcification and thrombogenicity are increased in low WSS conditions. Vascular remodeling is a common response of the wall to atherosclerosis formation. Mechanisms involved in the remodeling of atherosclerotic wall are influenced when WSS decreases. Important role has also WSS in the differential development of atherosclerotic wall into high-risk, quiescent, or stenotic plaque [1].
Blood-flow-induced shear stress acting on the arterial wall is of paramount importance in vascular biology. Endothelial cells sense shear stress and largely control its value in a feedback-control loop by adapting the arterial dimensions to blood flow. Nevertheless, to allow for variations in arterial geometry, such as bifurcations, shear stress control is modified at certain eccentrically located sites to let it remain at near-zero levels. In the presence of risk factors for atherosclerosis, low shear stress contributes to local endothelial dysfunction and eccentric plaque build up, but normal-to-high shear stress is atheroprotective. Initially, lumen narrowing is prevented by outward vessel remodeling. Maintenance of a normal lumen and, by consequence, a normal shear stress distribution, however, prolongs local unfavorable low shear stress conditions and aggravates eccentric plaque growth. While undergoing such growth, eccentric plaques at preserved lumen locations experience increased tensile stress at their shoulders making them prone to fissuring and thrombosis. Consequent loss of the plaque-free wall by coverage with thrombus and new tissue may bring shear-stress-controlled lumen preservation to an end. This change causes shear stress to increase, which as a new condition may transform the lesion into a rupture-prone vulnerable plaque. We present a discussion of the role of shear stress, in setting the stage for the generation of rupture-prone, vulnerable plaques, and how this may be prevented.
Principles of Anatomy and Physiology

The human heart pumps blood through the arteries, which connect to smaller arterioles and then even smaller capillaries. It is here that electrolytes, nutrients, dissolved gases and waste products are exchanged between the blood and surrounding tissues. The capillaries are thin-walled vessels interconnected with the smallest arteries and smallest veins. The structural part of the human circulatory system is comprised of two circuits; the pulmonary circulation which loops blood through the lungs for gas exchange, and the systemic circulation which provides oxygenated blood to the remainder of the body (Fig 3.1). The coronary circulation is, by definition, a part of the systemic circulatory system. Every day approximately 7.000 lt of blood is pumped by the heart. In an average person’s life, the heart will contract about 22.5 billion times.

Blood flow throughout the body begins its return to the heart when the capillaries return blood to the venules and then to the larger veins. The cardiovascular system, therefore, consists of a closed circuit: the heart, arteries, arterioles, capillaries, venules, and veins. The venules and veins are part of the pulmonary circuit because they send deoxygenated blood to the lungs to receive oxygen and unload carbon dioxide. The arteries and arterioles are part of the systemic circuit because they send oxygenated blood and nutrients to the body cells while removing wastes. All body tissues require circulation to survive [39].
3.1 Heart and Circulation

The heart is one of the most efficient organs in the human body and heart disease is one of the commonest causes of morbidity and mortality in both developing and developed countries. It is a muscular organ containing four chambers that is situated just to the left of the midline of the thoracic cavity. It is approximately the size of a man’s closed fist. The upper two chambers (atria) are divided by a wall-like structure called the interatrial septum. The lower two chambers (ventricles) are divided by a similar structure called interventricular septum. Between each atrium and ventricle, valves allow blood to flow in one direction, preventing backflow.

Blood that is low in oxygen flows into the right atrium from the veins known as the superior vena cava and inferior vena cava. The superior vena cava carries blood from the head, the neck, chest, and arms. The inferior vena cava carries blood from the remainder of the trunk and the legs. Blood in the right atrium flows through the right atrioventricular (tricuspid) valve into the right ventricle. From here pulmonary
circuit begins, with deoxygenated blood flowing into the right and left pulmonary arteries and their smaller branches. The blood becomes oxygenated while moving through the lungs’ capillary beds. Also in this part of the system, carbon dioxide is released. This newly oxygen-rich blood returns from the lungs to the left atrium through the pulmonary veins. Then the blood flows through the left atrium into the left ventricle. Finally, the left ventricle pumps the oxygen-rich blood out through the aorta and from there to all parts of the body. The human body has about 5.6 liters of blood, all of which circulates through the body three times every minute.

The movement of blood from the venules, which drain deoxygenated blood from the capillaries, through the veins to the vena cava, and from there through the right atrium and ventricle to the pulmonary circulation of the lungs, where the blood is oxygenated for return to the systemic circulation is called venous circulation.

### 3.2 Blood Vessels

The blood vessels of the human body carry blood to every type of tissue and organ. Vessels decrease in size as they move away from the heart (arteries and arterioles), ending in the capillaries, and then increase in size as they move toward the heart (venules and veins). The largest artery in the body is the aorta, with the largest veins being the venae cavae.

There are five general classes of blood vessels in the cardiovascular system: arteries, arterioles, capillaries, venules, and veins. Arteries are elastic vessels that are very strong, able to carry blood away from the heart under high pressure. They subdivide into thinner tubes that give rise to branched, finer arterioles. An artery’s wall consists of three distinct layers. The inner most tunica intima is made up of a layer of simple squamous epithelium known as endothelium. It rests on a connective tissue membrane with many elastic, collagenous fibers (Fig 3.3). The endothelium helps prevent blood clotting and may also help in regulating blood flow. It releases nitric oxide to relax the smooth muscle of the vessel. Vein walls are similar but not identical to artery walls.
The middle tunica media makes up most of an arterial wall, including smooth muscle fibers and a thick elastic connective tissue layer. The outer tunica externa (tunica adventitia) is thinner, mostly made up of connective tissue with irregular fibers—it is attached to the surrounding tissues. Smooth artery and arteriole muscles are innervated by the sympathetic nervous system. Vasomotor fibers receive impulses to contract and reduce blood vessel diameter (vasoconstriction). When inhibited, the muscle fibers relax and the vessel’s diameter increases (vasodilation). Changes in artery and arteriole diameters greatly affect blood flow and pressure.

Fig 3.3 General structure of the blood vessel [40]

Larger arterioles also have three layers in their walls, which get thinner as arterioles lead to capillaries. Very small arteriole wall only have an endothelial lining and some smooth muscle fibers, with a small amount of surrounding connective tissue.

The smallest-diameter blood vessels are capillaries, which connect the smallest arterioles to the smallest venules. The walls of capillaries are also composed of endothelium and form the semipermeable layer through which substances in blood are exchanged with substances in tissue fluids surrounding cells of the body. Blood pressure is highest in the arteries, less so in the arterioles, and lowest in the capillaries. Filtration occurs mostly at the arteriolar ends of capillaries because the
pressure is higher than at the venular ends. Plasma proteins trapped in capillaries create an osmotic pressure that pulls water into the capillaries (colloid osmotic pressure).

Venules are microscopic vessels that link capillaries to veins, which carry blood back to the atria. Vein walls are similar to arteries but have poorly developed middle layers. Because they have thinner walls that are less elastic than arteries, their lumens have a greater diameter. Many veins have flaplike valves projecting inward from their linings. These valves often have two structures that close if blood begins to back up in the vein. They aid in returning blood to the heart, opening if blood flow is toward the heart, but closing if it reverses. Unlike the arteries, veins do not have sufficient pressure from the contractions of the heart to keep blood moving through them. To keep blood flowing, the veins rely on the movement of nearby skeletal muscles, as well as the opening and closing of the valves within them. Therefore, a major structural difference between veins and arteries is that arteries do not have valves. Veins also act as reservoirs for blood in certain conditions, such as during arterial hemorrhage. Resulting venous constrictions help to maintain blood pressure by returning more blood to the heart, ensuring an almost normal blood flow even when up to one quarter of the blood volume is lost.

The largest-diameter artery in the body is the aorta, extending upward from the left ventricle to arch over the heart to the left, descending anterior and to the left of the vertebral column. The first portion of the aorta is called the ascending aorta. It begins at the aortic valve of the left ventricle. The left and right coronary arteries originate in the aortic sinus. This origination occurs at the base of the ascending, slightly superior to the aortic valve.

The aortic arch curves across the superior surface of the heart. It connects the ascending aorta with the descending aorta. Three arteries originate along the aortic arch. They deliver blood to the head, neck, shoulders, and upper limbs. These arteries are the brachiocephalic trunk, the left common carotid artery, and the left subclavian artery. The brachiocephalic trunk ascends only for a short distance before it branches to form the right subclavian and right common carotid arteries. The descending aorta is continuous with the aortic arch. The diaphragm divides the descending aorta into a superior thoracic aorta and an inferior abdominal aorta. The
branches of the thoracic aorta include the bronchial, pericardial, esophageal, mediastinal, and intercostals arteries.
The abdominal aorta, beginning immediately inferior to the diaphragm, is a continuation of the thoracic aorta. It delivers blood to the abdominopelvic organs and structures. The abdominopelvic branches of the aorta include the following: celiac, phrenic, superior mesenteric, suprarenal, renal, gonadal, inferior mesenteric, lumbar, middle sacral, and common iliac arteries. The subclavian and common carotid arteries supply blood to the neck, head, and brain. The main divisions of these arteries are the vertebral and thyrocervical arteries. The vertebral arteries run upward through the cervical vertebrae into the skull and supply blood to the vertebrae and to their ligaments and muscles. They unite in the cranial cavity to form the basilar artery, which branches to the pons, midbrain, and cerebellum. It ultimately divides into the two posterior cerebral arteries.

The thyrocervical arteries give off branches to the thyroid and parathyroid glands, larynx, trachea, esophagus, pharynx, and muscles of the neck, shoulder, and back. The left and right common carotid arteries separate into the internal and external carotid arteries. Near the base of the carotid arteries are enlargements (carotid sinuses) that contain baroreceptors and help to control blood pressure.

The subclavian artery, which is a branch of the brachiocephalic artery, continues into the arm, passing between the clavicle and first rib to become the axillary artery. It becomes the brachial artery and gives rise to a deep brachial artery. The ulnar artery leads down to the lower arm, on the ulnar side of the forearm to the wrist. Some of its branches supply the elbow joint, while others supply the muscles of the forearm. The radial artery provides blood to the wrist and hand, traveling along the radial side of the forearm to the wrist. It also supplies the lateral muscles of the forearm. Near the wrist, it approaches the surface, providing a point where the radial pulse may easily be taken.

The internal thoracic artery branches into two anterior intercostal arteries supplying the intercostal muscles and mammary glands. The posterior intercostal arteries supply other intercostal muscles as well as the vertebrae, spinal cord, and deeper back muscles. The internal thoracic artery and external iliac artery provide blood to the anterior abdominal wall while the phrenic artery and lumbar artery
supply blood to posterior and lateral abdominal wall structures. The major vessels of the arterial system include the common iliac arteries, internal iliac artery, femoral artery, popliteal artery, anterior tibial artery, and posterior tibial artery.

### 3.3 Blood and Blood Pressure

The circulatory system is the route by which the cells in human body get the oxygen and nutrients they need, but blood is the actual carrier of the oxygen and nutrients. Blood is made mostly of plasma, which is a yellowish liquid that is 90% water. But in addition to the water, plasma contains salts, glucose, and proteins that carry important nutrients to the body’s cells and strengthen the body’s immune system so it can fight off infection. Blood is actually a tissue. It is thick because it is made up of a variety of cells, each having a different job. In fact, blood is actually about 80% water and 20% solid. We know that blood is made mostly of plasma. But there are 3 main types of blood cells that circulate with the plasma:

- **Platelets**, which help the blood to clot. Clotting stops the blood from flowing out of the body when a vein or artery is broken. Platelets are also called thrombocytes.

- **Red blood cells**, which carry oxygen. Of the 3 types of blood cells, red blood cells are the most plentiful. In fact, a healthy adult has about 35 trillion of them. The body creates these cells at a rate of about 2.4 million a second, and they each have a life span of about 120 days. Red blood cells are also called erythrocytes.

- **White blood cells**, which ward off infection. These cells, which come in many shapes and sizes, are vital to the immune system. When the body is fighting off infection, it makes them in ever-increasing numbers. Still, compared to the number of red blood cells in the body, the number of white blood cells is low. Most healthy adults have about 700 times as many red blood cells as white ones. White blood cells are also called leukocytes.

Blood also contains hormones, fats, carbohydrates, proteins, and gases.

Blood carries oxygen from the lungs and nutrients from the digestive tract to the body’s cells. It also carries away carbon dioxide and all of the waste products that the body does
not need. The kidneys filter and clean the blood. Blood also helps keep the body at the right temperature, carries hormones to the body’s cells, sends antibodies to fight infection and contains clotting factors to help the blood to clot and the body’s tissues to heal.

Blood pressure is defined as the force that blood exerts against the inner walls of blood vessels. It most commonly refers to pressure in arteries supplied by the aortic branches, even though it actually occurs throughout the vascular system. Arterial blood pressure rises and falls according to cardiac cycle phases. The maximum pressure during ventricular contraction is called the systolic pressure.

The lowest pressure that remains in the arteries before the next ventricular contraction is called the diastolic pressure. Arterial blood pressure is measured with a device called a sphygmomanometer. Its results are reported as a fraction of the systolic pressure over the diastolic pressure, such as 120/80. The upper (first) number indicates the arterial systolic pressure in millimeters of mercury (mm Hg), and the lower (second) number indicates the arterial diastolic pressure, also in millimeters of mercury. A millimeter of mercury is a unit of pressure that is equal to 0.001316 of normal atmospheric pressure. This means that a blood pressure of 120/80 displaces 120 mm Hg on a sphygmomanometer, showing the systolic pressure, and also displaces 80 mm Hg on the same device, showing diastolic pressure.

3.4 Cardiac Cycle

The period between the start of one heartbeat and the beginning of the next is a single cardiac cycle. The cardiac cycle therefore includes alternate periods of contraction and relaxation. For any one chamber in the heart, the cardiac cycle can be divided into two phases. During contraction, or systole, a chamber ejects blood either into another heart chamber or into an arterial trunk. Systole is followed by the second phase, one of relaxation, or diastole. During diastole a chamber fills with blood and prepares for the start of the next cardiac cycle.
Fluids move due to the pressure gradient. Pressure within each chamber rises during systole and falls during diastole. Valves between adjacent chambers help ensure that blood flows in the desired direction, but blood will flow from one chamber to another only if the pressure in the first chamber exceeds that in the second. The basic principle governs the movement of blood between atria and ventricles, between ventricles and arterial trunks, and between major veins and atria. Blood could not move in the desired direction if an atrium and its attached ventricle contracted at precisely the same moment. At a representative heart rate of

![Cardiac Cycle Diagram](image)

**Fig. 3.5 Phases of Cardiac cycle. Blood flow and contractions are indicated by arrows. [42]**
75 bpm, a sequence of systole and diastole in either the atria or the ventricles lasts 800 msec.

The phases of atrial systole, atrial diastole, ventricular systole, and ventricular diastole are diagrammed in the Figure 3.5 for a heart rate of 75 bpm. As this cardiac cycle begins, all four chambers are relaxed and the ventricles are partially filled with blood. During atrial systole, the atria contract, filling the ventricles completely with blood. Atrial systole lasts 100msec. Over this period, blood cannot flow into the atria because atrial pressure exceeds venous pressure. Yet there is very little backflow into the veins, even though the connections with the venous system lack valves, because blood takes the path of least resistance. The atria next enter atrial diastole, which continues until the start of the next cardiac cycle. Atrial diastole and ventricular systole begin at the same time. During this period, blood is pushed through the systemic and pulmonary circuits and toward the atria. The heart then enters ventricular diastole. For the rest of this cycle, filling occurs passively and both the atria and the ventricles are relaxed. When the heart rate increases, all the phases of the cardiac cycle are shortened.
Computational Fluid Dynamics – Principles

This Chapter gives a brief account of the basic principles of fluid mechanics that describe the flow behavior. In fact, fluid behavior is derived from the interactive motion of a large number of individual particles. The medium, whose behavior is studied, is supposed to be continuum. That means, the density of the particles that compose the fluid is high enough and even an infinitesimally small element of the fluid still contains a sufficient number of particles, for which we can specify mean velocity and mean kinetic energy. This assumption allows the definition of quantities such as velocity, pressure, temperature, density at each point of the fluid.

The dynamical behavior of a fluid is determined by the following conservation laws:

1. Conservation of mass
2. Conservation of momentum
3. Conservation of energy

The conservation of a certain flow quantity means that its total variation inside an arbitrary volume can be expressed as the net effect of the amount of the quantity being transported across the boundary, taking into account any internal or external forces and sources acting on the volume. The amount of the quantity crossing the boundary is called flux.

The discussion of the conservation laws leads us to the idea of dividing the flow field into a number of volumes and to concentrate on the modeling of the behavior of the fluid in one such finite region. For this purpose, we define the so-called finite control volume (FCV) [Blazek].
4.1 Conservation laws

4.1.a The Continuity Equation (Conservation Law of Mass)

Our attention is restricted to single-phase fluids and we assume that mass cannot be created in such a fluid system, nor can disappear from it. There is also no diffusive flux contribution to the continuity equation, since for a fluid at rest, any variation of mass would imply a displacement of fluid particles.

In order to derive the continuity equation, consider the model of a FCV fixed in space $\Omega$. At a point on the surface that controls the FCV and is fixed in space (the so-called control surface), the flow velocity is $\vec{v}$, the unit normal vector is $\vec{n}$ and denotes $dS$ an elemental surface area. The conserved quantity in this case is the density $\rho$. There are no volume or surface sources present.

The integral form of the continuity equation - the conservation law of mass is:

$$\frac{\partial}{\partial t} \int_{\Omega} \rho \, d\Omega + \oint_{\partial \Omega} \rho (\vec{v} \cdot \vec{n}) dS = 0$$

The differential form of the continuity equation - the conservation law of mass is:

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \vec{v}) = 0$$

4.1.b The Momentum Equation (Conservation of Momentum)

The Momentum Equation is based on the particular form of Newton’s second law which states that the variation of momentum is caused by the net force acting on a mass element. The conserved quantity is here the product of density times the velocity $(\rho \vec{v} d\Omega)$.

The contribution of the convective flux tensor to the conservation of momentum is then given by: $-\oint_{\partial \Omega} \rho \vec{v} (\vec{v} \cdot \vec{n}) dS$. The diffusive flux is zero, since there is no diffusion of momentum possible for a fluid at rest.

There are two kinds of forces acting on the FCV:

1. External volume or body forces, which act directly on the mass of the volume.
   These are for example gravitational, buoyancy, Coriolis or centrifugal forces.

In some cases, there can be electromagnetic forces present as well.
2. Surface forces, which act directly on the surface of the control volume. They result from only two sources: (a) the pressure distribution, imposed by the outside fluid surrounding the volume (b) the shear and normal stresses, resulting from the friction between the fluid and the surface of the volume.

The contribution of the body (external) force per unit volume, denoted as $\vec{f}_e$, to the momentum conservation is:

$$\int_\Omega \rho \vec{f}_e d\Omega$$

The surface sources consist of two parts - an isotropic pressure component $p$ and a viscous stress tensor $\vec{\tau}$:

$$\overline{Q_S} = -p\vec{I} + \vec{\tau}$$

with $\vec{I}$ being the unit tensor.

Taking into account all the above contributions we finally obtain the expression for the momentum conservation inside an arbitrary control volume $\Omega$ which is fixed in space.

Integral form:

$$\frac{\partial}{\partial t} \int_\Omega \rho \vec{v} d\Omega + \oint_{\partial \Omega} \rho \vec{v} (\vec{v} \cdot \vec{n}) dS = \int_\Omega \rho \vec{f}_e d\Omega - \oint_{\partial \Omega} p \vec{n} dS + \oint_{\partial \Omega} (\vec{\tau} \cdot \vec{n}) dS$$

Differential form:

$$\rho \left( \frac{\partial \vec{v}}{\partial t} + \vec{v} \cdot \nabla \vec{v} \right) = \rho \vec{f}_e - \nabla p + \nabla \vec{\tau}$$
4.1.c The Energy Equation (Conservation of Energy)

According to the first law of thermodynamics any changes in time of the total energy inside the FCV are caused by the rate of work of forces acting on the volume and by the net heat flux into it. The total energy per unit mass $E$ of a fluid is equal to the sum of its internal energy per unit mass, $e$, to its kinetic energy per unit mass, $\frac{|\vec{v}|^2}{2}$.

$$E = e + \frac{|\vec{v}|^2}{2} = e + \frac{u^2 + v^2 + w^2}{2}$$

where $u, v, w$ are velocity components in the directions $x, y, z$ respectively.

The conserved quantity is in this case the total energy per unit volume $\rho E$. Its variation in time within the FCV $\Omega$ is:

$$\frac{\partial}{\partial t} \int_{\Omega} \rho Ed\Omega .$$

The contribution of the convective flux can be expressed as:

$$- \vec{\phi}_{\partial \Omega} \rho E (\vec{v} \cdot \vec{n})dS .$$

Since the diffusive flux $\vec{F}_D$ is defined for fluid at rest, only the internal energy becomes effective, as kinetic energy is considered negligible.

$$\vec{F}_D = -\gamma \rho \kappa \nabla e$$

$\gamma = \frac{C_p}{C_V}$ is the ratio of specific heat coefficients, and $\kappa$ denotes the thermal diffusivity coefficient. The diffusion flux represents one part of the heat flux into the control volume, namely the diffusion of heat due to molecular thermal conduction - heat transfer due to temperature gradients. Hence, $\vec{F}_D$ is obtained from the form of Fourier’s law of heat conduction.

$$\vec{F}_D = -k \nabla T$$

with $k$ standing for the thermal conductivity coefficient and $T$ for the absolute static temperature.

The other part of the net heat flux into the FCV consists of volumetric heating due to absorption or emission of radiation, or due to chemical reactions. We will denote the heat sources - the time rate of heat transfer per unit mass – as $\dot{q}_h$. 

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Taking into account the rate of work done by the body forces \( \overrightarrow{f_e} \), volume forces can be expressed as:

\[
Q_V = \rho \overrightarrow{f_e} \cdot \overrightarrow{v} + q_h
\]

The surface sources \( Q_S \) correspond to the time rate of work done by the pressure as well as the shear and normal stresses on the fluid element.

\[
Q_S = -p \overrightarrow{v} + \overrightarrow{t} \cdot \overrightarrow{v}
\]

We will also utilize the following general relation between the total enthalpy \( H \), the total energy and the pressure:

\[
H = E + \frac{p}{\rho}
\]

Finally, we can write the energy equation in the form:

**Integral form:**

\[
\frac{\partial}{\partial t} \int_\Omega \rho E d\Omega + \oint_{\partial\Omega} \rho H (\overrightarrow{v} \cdot \overrightarrow{n}) dS
\]

\[
= \oint_{\partial\Omega} k (\nabla T \cdot \overrightarrow{n}) dS + \int_\Omega (\rho \overrightarrow{f_e} \cdot \overrightarrow{v} + q_h) d\Omega + \oint_{\partial\Omega} (\overrightarrow{t} \cdot \overrightarrow{v}) \cdot \overrightarrow{n} dS
\]

**Differential form:**

\[
\frac{\partial}{\partial t} \left[ \rho \left( e + \frac{|\overrightarrow{v}|^2}{2} \right) \right] + \nabla \cdot \left[ \rho \left( e + \frac{|\overrightarrow{v}|^2}{2} \right) \overrightarrow{v} \right]
\]

\[
= \rho q_h + \frac{\partial}{\partial x} \left(k \frac{\partial T}{\partial x} \right) + \frac{\partial}{\partial y} \left(k \frac{\partial T}{\partial y} \right) + \frac{\partial}{\partial z} \left(k \frac{\partial T}{\partial z} \right) - \frac{\partial (up)}{\partial x} - \frac{\partial (vp)}{\partial y}
\]

\[
- \frac{\partial (wp)}{\partial z} + \frac{\partial (ut_{xx})}{\partial x} + \frac{\partial (ut_{yy})}{\partial y} + \frac{\partial (ut_{zz})}{\partial z} + \frac{\partial (vt_{xy})}{\partial x} + \frac{\partial (vt_{yy})}{\partial y}
\]

\[
+ \frac{\partial (vt_{xz})}{\partial z} + \frac{\partial (wt_{xx})}{\partial x} + \frac{\partial (wt_{yz})}{\partial y} + \frac{\partial (wt_{zz})}{\partial z} + \rho \overrightarrow{f_e} \cdot \overrightarrow{v}
\]

**4.2 Viscous Stresses**

In the above equations that describe the three conservation laws, the stress tensor \( \overrightarrow{t} \) is involved. This tensor denotes the viscous stresses, which originate from
the friction between the fluid and the surface of an element. In Cartesian coordinates the general form is given by:

$$\bar{\tau} = \begin{bmatrix} \tau_{xx} & \tau_{xy} & \tau_{xz} \\ \tau_{yx} & \tau_{yy} & \tau_{yz} \\ \tau_{zx} & \tau_{zy} & \tau_{zz} \end{bmatrix}$$

The notation $\tau_{ij}$ means by convention that the particular stress component affects a plane perpendicular to the $i$-axis, in the direction of the $j$-axis. The components $\tau_{xx}, \tau_{yy}, \tau_{zz}$ represent the normal stresses and the other components of $\bar{\tau}$ stand for the shear stresses, respectively.

![Fig. 4.2 Normal (left) and shear stresses (right) acting on a fluid element](image)

The viscous stresses depend on the dynamical properties of the medium. For fluids like air or water, Isaac Newton stated that the shear stress is proportional to the velocity gradient. Therefore, medium of such a type is designated as Newtonian fluid. On the other hand, fluids like for example melted plastic or blood behave in a different manner - they are non-Newtonian fluids. But, for the vast majority of practical problems, where the fluid can be assumed to be Newtonian, the components of the viscous stress tensor are defined:

$$\tau_{xx} = \lambda \left( \frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} + \frac{\partial w}{\partial z} \right) + 2\mu \frac{\partial u}{\partial x}$$

$$\tau_{yy} = \lambda \left( \frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} + \frac{\partial w}{\partial z} \right) + 2\mu \frac{\partial v}{\partial y}$$

$$\tau_{zz} = \lambda \left( \frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} + \frac{\partial w}{\partial z} \right) + 2\mu \frac{\partial w}{\partial z}$$
in which $\lambda$ represents the second viscosity coefficient, and $\mu$ denotes the dynamic viscosity coefficient. The expressions were derived by the Englishman George Stokes in the middle of the 19th century. The terms $\mu \frac{\partial u}{\partial x}$, etc. in the normal stresses represent the rate of linear dilatation - a change in shape. On the other hand, the term $(\lambda \text{ div } \vec{v})$ represents volumetric dilatation - rate of change in volume, which is in essence a change in density.

Another frequently used quantity is kinematic viscosity coefficient:

$$\nu = \frac{\mu}{\rho}$$

A term that must be defined is bulk viscosity. Bulk viscosity represents that property, which is responsible for energy dissipation in a fluid of uniform temperature during a change in volume at finite rate and refers to second viscosity coefficient $\lambda$.

$$\lambda + \frac{2}{3} \mu = 0$$

With the exception of extremely high temperatures or pressures, there is so far no experimental evidence that this hypothesis does not hold. Therefore, the expressions are:

$$\tau_{xx} = 2\mu \left( \frac{\partial u}{\partial x} - \frac{1}{3} \text{ div } \vec{v} \right)$$
$$\tau_{yy} = 2\mu \left( \frac{\partial v}{\partial y} - \frac{1}{3} \text{ div } \vec{v} \right)$$
$$\tau_{zz} = 2\mu \left( \frac{\partial w}{\partial z} - \frac{1}{3} \text{ div } \vec{v} \right)$$

The above equations simplify for an incompressible fluid (constant density) because of $\text{div } \vec{v} = 0$ (continuity equation).
4.3 Types of Flow

While studying the motion of a rigid body we do not have to bother about the relative motion of the particles of the rigid body as they are very firmly fixed to each other and move as a whole. But for the study of the motion of fluids, things are not so simple because the fluid particles are attached with each other with very weak forces. There are various relative motions and a lot of possibilities for relative motion between the fluid particles.

**Compressible vs incompressible flow**

All fluids are compressible to some extent, that is, changes in pressure or temperature will result in changes in density. However, in many situations the changes in pressure and temperature are sufficiently small that the changes in density are negligible. In this case the flow can be modelled as an incompressible flow. Otherwise the more general compressible flow equations must be used. Mathematically, incompressibility is expressed by saying that the density $\rho$ of a fluid parcel does not change as it moves in the flow field. [43]

**Viscous vs inviscid flow**

Viscous problems are those in which fluid friction has significant effects on the fluid motion. When two fluid layers move relative to each other, a friction force develops between them and the slower layer tries to slow down the faster layer. This internal resistance to flow is quantified by the fluid property viscosity, which is a measure of internal stickiness of the fluid. Viscosity is caused by cohesive forces between the molecules in...
liquids and by molecular collisions in gases. There is no fluid with zero viscosity, and thus all fluid flows involve viscous effects to some degree. However, in many flows of practical interest, there are regions (typically regions not close to solid surfaces) where viscous forces are negligibly small compared to inertial or pressure forces. Neglecting the viscous terms in such inviscid flow regions greatly simplifies the analysis without much loss in accuracy.

The development of viscous and inviscid regions of flow as a result of inserting a flat plate parallel into a fluid stream of uniform velocity is shown. The fluid sticks to the plate on both sides because of the no-slip condition, and the thin boundary layer in which the viscous effects are significant near the plate surface is the viscous flow region. The region of flow on both sides away from the plate and unaffected by the presence of the plate is the inviscid flow region.

The Reynolds number, which is a ratio between inertial and viscous forces, can be used to evaluate whether viscous or inviscid equations are appropriate to the problem. Stokes flow is flow at very low Reynolds numbers, $Re<<1$, such that inertial forces can be neglected compared to viscous forces. On the contrary, high Reynolds numbers indicate that the inertial forces are more significant than the viscous (friction) forces. Therefore, we may assume the flow to be an inviscid flow, an approximation in which we neglect viscosity completely, compared to inertial terms.

This idea can work fairly well when the Reynolds number is high. However, certain problems such as those involving solid boundaries, may require that the viscosity be included. Viscosity often cannot be neglected near solid boundaries because the no-slip condition can generate a thin region of large strain rate (known as Boundary layer) which enhances the effect of even a small amount of viscosity, and thus generating vorticity.

The standard equations of inviscid flow are the Euler equations. One often used model, especially in computational fluid dynamics, is to use the Euler equations away from the body and the boundary layer equations, which incorporates viscosity, in a region close to the body. The Euler equations can be integrated along a streamline to get Bernoulli's equation. When the flow is everywhere irrotational and inviscid, Bernoulli's equation can be used throughout the flow field. Such flows are called potential flows.
Steady vs unsteady flow

For steady flow, all fluid flow properties (e.g., velocity, temperature, pressure, and density) are independent of time. The properties, however, may vary from point to point, which means that they could be a function of space. In the study of fluid mechanics it is often assumed that the flow is steady to simplify the analysis but yet give a realistic representation of the real flow field. On the other hand, most flows encountered in real world applications are unsteady flows. It should be noted, steady flow does not mean the velocity and accelerations are constant. Flow in a curved pipe may be steady, but the velocity and/or acceleration is not constant. This is a common misconception based in part on particle dynamics for rigid bodies.

For unsteady flow, the fluid properties are function of time. Unsteady flows can be further divided into periodic flow, nonperiodic flow and random flow. For periodic flow, the property change is repeated in a predictable manner whereas the fluid motion and properties are difficult to predict in random flow.

Steady flows are often more tractable than otherwise similar unsteady flows. The governing equations of a steady problem have one dimension fewer (time) than the governing equations of the same problem without taking advantage of the steadiness of the flow field.

Laminar vs turbulence flow

Turbulence is flow characterized by recirculation, eddies, and apparent randomness. Flow in which turbulence is not exhibited is called laminar. It should be noted, however, that the presence of eddies or recirculation alone does not necessarily indicate turbulent flow—these phenomena may be present in laminar flow as well.

![Fig. 4.4 Laminar vs Turbulent Flow](image-url)
Mathematically, turbulent flow is often represented via a Reynolds decomposition, in which the flow is broken down into the sum of an average component and a perturbation component.

It is believed that turbulent flows can be described well through the use of the Navier–Stokes equations. Direct numerical simulation (DNS), based on the Navier–Stokes equations, make it possible to simulate turbulent flows at moderate Reynolds numbers. Restrictions depend on the power of the computer used and the efficiency of the solution algorithm. The results of DNS have been found to agree well with experimental data for some flows.

Laminar and Turbulent flows can be characterized and quantified using Reynolds Number (Re).

\[
Re = \frac{\rho \cdot u \cdot d}{\mu} = \frac{\text{inertial forces}}{\text{viscous forces}}
\]

where \(\rho = \text{density}, u = \text{mean velocity}, d = \text{diameter of flow profile} \) and \(\mu = \text{viscosity}\).

It can be interpreted that when the inertial forces dominate over the viscous forces (when the fluid is flowing faster and Re is larger) then the flow is turbulent. When the viscous forces are dominant (slow flow, low Re) they are sufficient enough to keep all the fluid particles in line, then the flow is laminar.

In summary:

**Laminar flow**

- \(\text{Re} < 2000\)
- 'low' velocity
- Dye does not mix with water
- Fluid particles move in straight lines
- Rare in practice in water systems.

**Transitional flow**

- \(2000 > \text{Re} < 4000\)
- 'medium' velocity
- Dye stream wavers in water - mixes slightly.
Turbulent flow

- $\text{Re} > 4000$
- 'high' velocity
- Dye mixes rapidly and completely
- Particle paths completely irregular
- Average motion is in the direction of the flow
- Changes/fluctuations are very difficult to detect. Must use laser.
- Mathematical analysis very difficult - so experimental measures are used
- Most common type of flow.

4.4 Properties of Blood Flow

Blood is not a Newtonian fluid, and blood vessels are not rigid tubes, so classic hydrodynamics is not capable to explain hemodynamics. Blood is composed of plasma and formed elements. The presence of these formed elements and their interaction with plasma molecules are the main reasons, why blood differs so much from ideal Newtonian fluids.

Blood moves in the blood vessels, while the heart serves as the pump for the blood. The vessel walls of the heart are elastic and are movable, therefore causing

Fig. 4.5 Qualitative representation of blood pressure and velocity distribution among human vessels
the blood and the wall to exert forces on each other which in turn influence their respective motion. Therefore to understand the mechanics of circulation of the heart, it will be worth the while to go through a review of basic mechanics of fluid, and elastic solids (momentum) and the nature of the forces exerted between two moving substances in contact.

The velocity of blood flow is often expressed in cm/s, this value is inversely related to the total cross-sectional area of the blood vessels, and also differs per cross-sections, because in normal condition the blood flow has laminar characteristic. Due to this fact the blood flow velocity is the fastest in the middle of the vessel and the slowest at the vessel wall. In most cases the mean velocity is in use [44]. Blood velocities in arteries are higher during systole than during diastole. One parameter to quantify this difference is pulsatility index (PI), which is equal to the difference between the peak systolic velocity and the minimum diastolic velocity divided by the mean velocity during the cardiac cycle. This value decreases with distance from the heart [45].

Normal plasma behaves like a Newtonian fluid at rates of shear. Typical values for the viscosity of normal human plasma at 37 °C is 1.2 N·s/m2. The viscosity of normal plasma varies with temperature in just the same way as does that of its solvent water, a 5 °C increase of temperature in the physiological range reduces plasma viscosity by about 10%.
5

Medical Imaging - Image Processing

Medical imaging, especially X-ray based examinations and ultrasonography, is crucial in every medical setting and at all levels of health care. In public health and preventive medicine as well as in curative medicine, effective decisions depend on correct diagnosis. Though medical/clinical judgment maybe sufficient in treatment of many conditions, the use of diagnostic imaging services is paramount in confirming, correctly assessing and documenting course of the disease as well as in assessing response to treatment.

5.1 Medical Imaging Modalities

Medical imaging comprises different imaging modalities and processes to image human body for diagnostic and treatment purposes and therefore has an important role in the improvement of public health in all population groups. Furthermore, medical imaging is justified also to follow the course of a disease already diagnosed and/or treated. Area of medical imaging is very complex and, depending on a context, requires supplementary activities of medical doctors, medical physicists, biomedical engineers as well as technicians.

With improved health care policy and increasing number of available medical equipment, the number of radiological medical procedures are increasing considerably. Effective and of good quality imaging is important for further medical decision making and can reduce unnecessary procedures. Reports from some countries indicate that a significant portion of all abdominal surgical interventions (explorative laparotomy) may have been avoided if simple diagnostic imaging services such as ultrasound had been available (World Health Organization, WHO).
Computed Tomography (CT)

X-ray computed tomography uses ionizing radiation that comes out from the source, which is external to the body. In some cases contrast agents are injected. Anatomical images are taken. Conventional x-ray radiography projects a 3-D object onto a 2-D detector plane.

Since 3-D information is diagnostically important, a 3-D object is considered to be a stack of 2-D images. The system beam source and detector is rotated obtaining projections at multiple angles (level x and y) and at different slices (axis z).

The intensity of X-rays passing through the imaged body is attenuated according to the density of tissues encountered, so that the line integral of tissue density is measured. For each angle the source and the detector rotate around the subject and collect a row of X-ray measurements. The reconstructed image, Fig. 5.1 X-ray tube (beam source) is rotated and detectors obtain radiation absorption images

<table>
<thead>
<tr>
<th>Tissue</th>
<th>CT Number (HU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone</td>
<td>+1000</td>
</tr>
<tr>
<td>Liver</td>
<td>40-60</td>
</tr>
<tr>
<td>White matter</td>
<td>-20 to -30</td>
</tr>
<tr>
<td>Grey matter</td>
<td>-37 to -45</td>
</tr>
<tr>
<td>Blood</td>
<td>40</td>
</tr>
<tr>
<td>Muscle</td>
<td>10-40</td>
</tr>
<tr>
<td>Kidney</td>
<td>30</td>
</tr>
<tr>
<td>CSF</td>
<td>15</td>
</tr>
<tr>
<td>Water</td>
<td>0</td>
</tr>
<tr>
<td>Fat</td>
<td>-50 to -100</td>
</tr>
<tr>
<td>Air</td>
<td>-1000</td>
</tr>
</tbody>
</table>

Table 5.1 Various CT numbers (Hounsfield Units, HU) calculated for different tissues
contains attenuation values, called CT numbers and expressed by Hounsfield units (HU). Water is conventionally represented by zero (0) CT number.

\[ CT = K \frac{\mu - \mu_w}{\mu_w} \]

where \( \mu \) is the linear attenuation coefficient of the voxel, \( \mu_w \) the linear attenuation coefficient of water and \( K \) a numerical constant quantity called magnifying or contrast factor. It usually has the value 1000.

For vascular imaging contrast is used via intravenous injection. The HU values of the contrast enhanced images are positive values between that of connective tissue and that of calcium. For this reason an artery affected by atherosclerosis will be surrounded by connective tissue values and low contrast (lipid pools) and high contrast (calcified plaques).

![Fig 5.2 Abdominal aorta with atherosclerosis](image)

3-dimensional images of the abdominal aorta reconstructed from CT images (WHO)

**Magnetic Resonance Imaging (MRI)**

MRI uses magnetic fields and radiofrequency pulses to produce anatomical images. In some cases contrast agents are injected. Powerful magnets are used to polarise and excite hydrogen nuclei (single proton) in water molecules in human
tissue, producing a detectable signal which is spatially encoded, resulting in images of the body. The MRI machine emits an RF (radio frequency) pulse that specifically binds only to hydrogen. The system sends the pulse to the area of the body to be examined. The pulse makes the protons in that area absorb the energy needed to make them spin in a different direction. This is the "resonance" part of MRI. The RF pulse makes them (only the one or two extra unmatched protons per million) spin at a specific frequency, in a specific direction. The particular frequency of resonance is called the Larmour frequency and is calculated based on the particular tissue being imaged and the strength of the main magnetic field. MRI uses three electromagnetic fields: a very strong (on the order of units of teslas) static magnetic field to polarize the hydrogen nuclei, called the static field; a weaker time-varying (on the order of 1 kHz) field(s) for spatial encoding, called the gradient field(s); and a weak radio-frequency (RF) field for manipulation of the hydrogen nuclei to produce measurable signals, collected through an RF antenna.

Like CT, MRI traditionally creates a 2-D image of a thin "slice" of the body and is therefore considered a tomographic imaging technique. Unlike CT, MRI does not involve the use of ionizing radiation and is therefore not associated with the same health hazards. For example, because MRI has only been in use since the early 1980s, there are no known long-term effects of exposure to strong static fields and therefore there is no limit to the number of scans to which an individual can be subjected, in contrast with X-ray and CT. However, there are well-identified health risks associated with tissue heating from exposure to the RF field.

Fig. 5.3 Magnetic Resonance Angiography (MRA) of the carotids, the subclavian arteries and aorta. Arrows show points of stenoses. [47]
and the presence of implanted devices in the body, such as pace makers. These risks are strictly controlled as part of the design of the instrument and the scanning protocols used.

Because CT and MRI are sensitive to different tissue properties, the appearance of the images obtained with the two techniques differ markedly. In CT, X-rays must be blocked by some form of dense tissue to create an image, so the image quality when looking at soft tissues will be poor. In MRI, while any nucleus with a net nuclear spin can be used, the proton of the hydrogen atom remains the most widely used, especially in the clinical setting, because it is so ubiquitous and returns a large signal. This nucleus, present in water molecules, allows the excellent soft-tissue contrast achievable with MRI. [46]

**Ultrasound**

Ultrasound Imaging uses high frequency sound waves and the pulse echo effect (which is the basis of radar) to give anatomical information. The range of frequency used in ultrasound imaging starts from 3 to 10 MHz, while human hears sounds only from 20 to 20000Hz.

![Ultrasound image of a 16 week fetus](image)

**Fig. 5.4 Ultrasound image of a 16 week fetus**
A Piezoelectric transducer is a crystalline material that changes shape when an electric current is applied creating sound waves and, on the other hand, when struck by sound waves creates electrical currents. Ultrasonic waves are emitted by the transducer and travel through human tissues at a velocity of 1540 m/s. When the wave reaches an object or surface with a different texture or acoustic nature, a wave is reflected back. These echoes are received by the apparatus, changed into electric current and a 2-D image is produced. More than 20 frames can be generated per second, giving a smooth, real-time image. The stronger the returning signal, the more white it will be on the grey scale image. Pure fluid (e.g. urinary bladder) gives no echoes, appearing black (anechoic) leading to acoustic enhancement of distal tissues. Acoustic shadow is the opposite effect where tissues distal to gas containing areas receive little sound and thus appear as black.

Ultrasound imaging is an interactive modality which does not depend on the operator. Also, ultrasound waves are greatly reflected by air soft tissue and bone soft tissue interfaces, thus limiting its use in the head, chest and musculoskeletal system.

**Nuclear Medical Imaging**

Nuclear medicine encompasses both diagnostic imaging and treatment of disease. Certain properties of isotopes and the energetic particles emitted from radioactive material to diagnose or treat pathology are used. Different from the typical concept of anatomic radiology, nuclear medicine enables assessment of physiology.

There are three types of emissions from radioactive isotopes: α particles, β particles and γ-rays (also some associated X-rays). Only γ-rays and their high energy photons are useful for radioisotope imaging. In radioisotope imaging, source is inside the body after injection.

Gamma cameras are used in e.g. scintigraphy, SPECT and PET to detect regions of biologic activity that may be associated with disease. Relatively short lived isotope, such as $^{123}$I is administered to the patient. Isotopes are often preferentially absorbed by biologically active tissue in the body, and can be used to identify tumors
or fracture points in bone. Images are acquired after collimated photons are detected by a crystal that gives off a light signal, which is in turn amplified and converted into count data.

- **Scintigraphy** is a form of diagnostic test wherein radioisotopes are taken internally, for example intravenously or orally. Then, gamma cameras capture and form two-dimensional images from the radiation emitted by the radiopharmaceuticals.

- **SPECT** is a 3D tomographic technique that uses gamma camera data from many projections and can be reconstructed in different planes. A dual detector head gamma camera combined with a CT scanner, which provides localization of functional SPECT data, is termed a SPECT/CT camera, and has shown utility in advancing the field of molecular imaging. In most other medical imaging modalities, energy is passed through the body and the reaction or result is read by detectors. In SPECT imaging, the patient is injected with a radioisotope, most commonly Thallium 201TI, Technetium 99mTC, Iodine 123I, and Gallium 67Ga. The radioactive gamma rays are emitted through the body as the natural decaying process of these isotopes takes place. The emissions of the gamma rays are captured by detectors that surround the body. This essentially means that the human is now the source of the radioactivity, rather than the medical imaging
devices such as X-Ray or CT.

- Positron emission tomography (PET) uses coincidence detection to image functional processes. Short-lived positron emitting isotope, such as 18F, is incorporated with an organic substance such as glucose, creating F18-fluorodeoxyglucose, which can be used as a marker of metabolic utilization. Images of activity distribution throughout the body can show rapidly growing tissue, like tumor, metastasis, or infection. PET images can be viewed in comparison to computed tomography scans to determine an anatomic correlate. Modern scanners may integrate PET, allowing PET-CT, or PET/MRI to optimize the image reconstruction involved with positron imaging. This is performed on the same equipment without physically moving the patient off of the gantry. The resultant hybrid of functional and anatomic imaging information is a useful tool in non-invasive diagnosis and patient management. [48]

5.2 Image Processing

Image processing covers four main areas: image formation, visualization, analysis, and management. The algorithms of image enhancement can be assigned as pre- and post-processing in all areas.

![Fig. 5.6 Modules of Image Processing](image)
1. **Image formation** includes all the steps from capturing the image to forming a digital image matrix.

2. **Image visualization** refers to all types of manipulation of this matrix, resulting in an optimized output of the image.

3. **Image analysis** includes all the steps of processing, which are used for quantitative measurements as well as abstract interpretations of biomedical images. These steps require a priori knowledge on the nature and content of the images, which must be integrated into the algorithms on a high level of abstraction.

4. **Image management** sums up all techniques that provide the efficient storage, communication, transmission, archiving, and access (retrieval) of image data. Thus, the methods of telemedicine are also a part of the image management.

Deserno et al. [49] and Angenent et al. [50] analyze each step of Image Processing separately and define in detail the corresponding terminology. The purpose of this work is to focus on image segmentation algorithms that are useful for vessel extraction during hemodynamic analysis. Segmentation is one of the four key problems we have in medical imaging:

- **Segmentation**: automated methods that create patient-specific models of relevant anatomy from images
- **Registration**: automated methods that align multiple data sets with each other
- **Visualization**: the technological environment in which image-guided procedures can be displayed
- **Simulation**: softwares that can be used to rehearse and plan procedures, evaluate access strategies, and simulate planned treatment.

### 5.3 Image Segmentation

Segmentation is the process of creating a structured visual representation from an unstructured one. In its modern formulation, image segmentation is the problem of partitioning an image into homogeneous regions that are semantically
meaningful, i.e., that correspond to objects we can identify. It also allows for quantitative shape analysis, and provides an indispensable anatomical framework for virtually any subsequent automatic analysis.

Many segmentation filters are used to isolate the region of interest (ROI). There are three categories:

1. **Intensity-based** segmentation filters use the intensity values of the pixels to segment an image. Usually, spatial contiguity is not considered in intensity based segmentation filters. These segmentation filters are often used to detect structure boundaries. The following submodules exist:
   - Pixel classification filters
   - Supervised classification filters
   - Unsupervised classification filters
   - Watershed-based segmentation filters

2. **Region-based** segmentation filters segment an image based on similarity of intensity values between spatially adjacent pixels. These filters are often used to detect object regions. There are the following submodules:
   - Fuzzy connectedness-based segmentation filters
   - Region growing filters
   - Markov random field-based filters

3. **Model-based** segmentation filters segment an image by starting with a model and then updating the model based on image features. The updates are typically constrained by a priori knowledge about the models. The following submodules exist:
   - Mesh-based segmentation filters
   - Level set-based segmentation filters

In the table below brief descriptions of several segmentation algorithms for vessels are presented with a detailed list of their benefits and drawbacks.
<table>
<thead>
<tr>
<th>Segmentation Algorithms</th>
<th>Brief Description</th>
<th>Steps</th>
<th>Benefits</th>
<th>Drawbacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Watershed (3D lumen Segmentation) [51]</td>
<td>It segments regions into catchment basins (homogeneous graylevel regions). Appropriate choice of height function is needed. Calculation of gradient magnitude is often used.</td>
<td>1. initial classification of all points into catchment basin regions 2. production of a tree of merges among adjacent regions (different maximum saliency values) 3. the flood level rises and boundaries between adjacent segments will merge</td>
<td>works best when the region to segment is composed of voxels which are very close to each other in intensity</td>
<td>• complexity in the computation of the merge tree • segmented image is divided into too many regions • very sensitive to the choice of parameters</td>
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</table>

II. Fuzzy Connectedness (3D lumen Segmentation) [51] | Segmentation via thresholding of a fuzzy connectedness scene. Based on statistical measures of gray level similarity. | 1. A seed point (or a set) is first specified within the region of interest 2. Fuzzy affinity is then computed between neighboring pixels 3. The strongest path strength between them is the fuzzy connectedness 4. A threshold is applied to the fuzzy scene, and a binary segmented object may be extracted | ✓ segmentation despite variable intensity levels ✓ overcome the fundamental problem of the watershed algorithm (complexity) | • too few restrictions imposed on the development of the front of the expanding region • no regards to the shape or boundary characteristics of the segmented region • easily tend to “leak” into parts of other structures • the threshold parameters, used by the algorithm, has to be adjusted for every individual data set |
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<tr>
<td>III. Level sets (3D and 2D Lumen segmentation) [51]</td>
<td>They are techniques created to follow the evolution of N-dimensional curves (interfaces), by observing their curvature.</td>
<td>1. embed the evolving surface in a function in one higher dimension 2. adjust this higher dimensional function corresponding to motion of the interface 3. compute the zero level set to find the position of the propagating interface 4. operate only on a surrounding band around the region of the level set being tracked</td>
<td>applied even where no a priori assumptions about the object’s topology are made</td>
<td></td>
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<tr>
<td>IV. Deformable Models [51]</td>
<td>They attempt to follow boundaries by placing a set of discrete marker points on the evolving front and then changing the position of these markers to correspond to the front as it moves.</td>
<td>1. place a set of discrete marker points 2. The discrete markers are updated in time using a set of finite difference approximations to the equations of motion</td>
<td>produces a segmentation with a smaller error (compared with level sets)</td>
<td>• unstable as the curvature increases around a cusp (entropy condition must be observed) • tendency of small errors in the position to produce large errors in the determination of the curvature • difficulties coping with topological changes • requires extensive manual initialization and user intervention</td>
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<td><strong>V. Discrete Deformable Model-based segmentation based on simplex meshes [52]</strong></td>
<td>An initial boundary is deformed under internal (shape-based) and external (image-based) forces until an equilibrium is achieved. The object boundary is represented by a polygonal mesh with particular topology (2-simplex). The deformation process, with discrete time steps $t$, is determined by the evolution equation. <strong>For lumen:</strong> the image-derived deformation term is based on a simple grey level appearance model (threshold-based force), <strong>For thrombus:</strong> appearance is modelled with a non-parametric pattern classification technique (k-nearest neighbours).</td>
<td>1. define the VOI and create a tube roughly located inside the <em>lumen</em> 2. the tube is used to initialize the deformable model for lumen segmentation 3. the segmented lumen is used to initialize another deformable model that automatically determines the <em>thrombus</em> boundary</td>
<td>✓ deformation (for thrombus segmentation) is driven by <em>three classes of intensity patterns</em> used not only during training, but also to steer deformation more efficiently</td>
<td>The method has difficulty to place the thrombus surface at the correct position where there is no intensity contrast at the boundary. They require large training sets. [53] Full retraining when adjustments are made. [53]</td>
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<tr>
<td><strong>VI. 2-simplex based deformable model Approach [53]</strong></td>
<td>Simplex meshes: simply connected meshes that are topologically dual of triangulations</td>
<td>✓ it allows control over smoothness and topology ✓ it can be transformed to high quality surface triangulations quite easily</td>
<td></td>
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<tr>
<td>Segmentation Algorithms</td>
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<td>Benefits</td>
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<tr>
<td>VII. active shape models (ASM) [52]</td>
<td>a simple grey value model is used image features are measured along the normal direction to the deforming boundary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VIII. Level set based implementation of geometric deformable models [54]</td>
<td>the front of the model follows a time evolution in the normal direction depending on a potential field (or speed function) signed distance function convolution with Gaussian filter</td>
<td>1. initialize the active contour by tubes of large diameters and apply it to the image at a large scale 2. add tubes of decreasing diameter by applying the evolution at lower scales, new distance functions 3. The standard deviation of the Gaussian smoothing kernel is computed in dependence of the current radius</td>
<td>✓ ability of the level set method to handle topological changes in a natural way ✓ a tube-detection filter takes the symmetry of the object into account so as a high degree of automation is achieved ✓ the reconnection procedure successfully rejects pieces of centerlines not belonging to the main trunk ✓ the evolution of deformable contour is carried out at different scales</td>
<td>• difficulties for data sets with high noise and low contrast between tubes and background • selectivity of the tube-detection filter</td>
</tr>
<tr>
<td>Segmentation Algorithms</td>
<td>Brief Description</td>
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| IX. statistical shape modelling approach [53] | The basic idea is to establish, from a training set, the pattern of ‘legal’ variation in the shapes and spatial relationships of structures in a given class of Images. | 1. smooth the volume in the preprocessing step  
2. generate a region map that is fed into the following steps  
3. calculate an initial boundary for the level set segmentation  
4. local feature analysis: calculate the likelihood that the given point belongs to the aneurysm (through SVM)  
5. level set segmentation: evolves a boundary to give the final results | ✓ better generalization ability than manual parameterized models | based on a set of 2D geometrical primitives and not on a true surface description implying that further processing steps will be necessary to come to a finite element mesh, which is a prerequisite for the simulations  
a set of dense correspondences across a training set of segmented shapes need to be established |
| X. Level set with region and statistical information [55] | It combines global region analysis, local feature analysis, and a level set boundary evolution method. | 1. smooth the volume in the preprocessing step  
2. global region analysis: generate a region map that is fed into the following steps  
3. surface initialization: calculate an initial boundary for the level set segmentation  
4. local feature analysis: calculate the likelihood that the given point belongs to the aneurysm (through SVM)  
5. level set segmentation: evolves a boundary to give the final results | ✓ demonstrated insensitivity to parameter settings within a reasonable range  
✓ user interaction is not required beyond identifying the most proximal and distal slices containing the aneurysm  
✓ good demonstrated accuracy | •there is no independent means of determining truth, (which voxels are indeed part of the aneurysm and which are not)  
•it is not a fully 3D method, (the region analyzer in the global region analysis step use only single 2D slices at a time)  
•assume that the aneurysm is roughly circular  
•some parameters were determined experimentally |
<table>
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<tbody>
<tr>
<td>XI. Standard deformable model approach with non-linear appearance model [53]</td>
<td>It reconstructs the dynamic lumen and vessel surface with 3D active objects. Leads to an object representation that allows robust and accurate translation to a Finite Element Model.</td>
<td>1. images are locally anisotropically filtered to reduce noise 2. To delineate the AAA ROI a wave-front propagation is performed on the in-slice gradient magnitude of the image intensity 3. the lumen centre line is constructed 4. from the centre line an initial 3DAO is created 5. The surface can be iteratively deformed based on forces computed from the image features and shape regularization forces</td>
<td>✓ The propagation method that we developed allows automatic computation of the dynamic volume of the vessel. ✓ The combination of the patient's blood pressure and the dynamic volume may be used to estimate the vessel wall compliance.</td>
<td>The deformable model has an extra, highly desirable, smoothness constriction which can cause the segmentation to deviate from the contours, even when the image features are very good. Orientations of the normals of the contours at the sample points are not taken into account when computing the distance between the contours and the 3DAO surface. Therefore, this 3D distance measure may give a too optimistic impression of the segmentation performance</td>
</tr>
<tr>
<td>XII. Level set segmentation with gradient-based, weighted expansion and mean curvature dependent regularizers [56]</td>
<td>1. User-defined initial curve from which several spheres are automatically generated 2. final detected vessel surface after the evolution guided by the partial differential equation 3. 2D evaluation of the detected surface by superimposition of the anatomical data and the corresponding detected contour</td>
<td>quantitatively highlight the well known differences in morphology and function of the ascending and descending aorta</td>
<td>a small number of patients tested</td>
<td></td>
</tr>
<tr>
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</table>
| XIII. edge-based level set segmentation approach [57] | It extracts the surface between two or more user-supplied end-points for tubular- or vessel-like structures | 1. The user picks two-end points and launches the path searching algorithm that detects the minimal path between these points  
2. An image is builted containing only the voxels that are within a distance R (depending on the geometry of ROI) around the extracted path  
3. Level set segmentation step is applied to a small portion of the image around the object of interest  
4. A freezing mechanism is designed to prevent the moving front to leak into undesired areas. | ✓ This method exploits the advantages of minimal path techniques (e.g., global minima, fast computation, and ease of incorporating user input)  
✓ Segmentation step is rendered very fast because only a portion of the image along the path and within a radius R is considered | • Better if start and end points could be determined automatically  
• Maximum diameter is unknown. It could be derived from the image data. |
| XIV. tracking-based segmentation based on 3D cylindrical intensity model and particle filter tracking [58] | It relies on a 3D cylindrical intensity model as the measurement model of the particle filter in conjunction with a model fitting scheme. A model fitting approach is used based on least-squares fitting of the 3D cylindrical model to the image intensities within a spherical 3D ROI. | 1. use a 3D parametric intensity model which represents the shape as well as the image intensities of a tubular structure within a 3D ROI (ideal sharp 3D cylinder convolved with a 3D Gaussian)  
2. particle filter approach and development of two different tracking schemes (state and dynamic model) | ✓ a segmentation step or computation of image gradients is not required  
✓ directly quantify 3D tubular structures based on the included model fitting scheme  
✓ use of 3D intensity model  
✓ it is possible to include a strategy for the detection of bifurcations | for a relatively high noise level, it turned out that the first tracking scheme terminates in the third winding due to the poor contrast |
<table>
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</table>
| XV. Segmentation using a Radial Model Approach [59] | Segmentation of the lumen is based on a 3D region growing algorithm starting from two or more manually selected seed points. The thrombus contour is modeled as a radial function which defines the target segmented region. | 1. image is preprocessed to reduce noise  
2. VOI is defined  
3. At each iteration: all neighborhood voxels are visited and the confidence criterion is evaluated and statistics are recomputed before the next iteration begins  
4. The resulting segmentation is smoothed by morphological closing  
The centerline extraction is performed on a slice-by-slice basis using 2D image Moments.  
The thrombus segmentation procedure consists of calculating the internal and external radii. | ✓ The thrombus segmentation shows promising results in defining the external contour, whose density is very similar to adjacent structures, and very prone to segmentation leaks in those areas.  
✓ Computational speed. | • underestimation of the radius in some places which were identified as leaks  
• improvement of thrombus model is needed  
• fine-tune the parameters of the process for a large number of datasets  
• no validation of the method by comparison with manual segmentations and other methods  
• some Radial Connected Components that are not part of the thrombus still remain |
<table>
<thead>
<tr>
<th>Segmentation Algorithms</th>
<th>Brief Description</th>
<th>Steps</th>
<th>Benefits</th>
<th>Drawbacks</th>
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<tbody>
<tr>
<td>XVI.</td>
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<tr>
<td>o Automatic lumen and outer wall segmentation through thresholding</td>
<td>image segmentation code (VESSEG v. 1.0.2, Carnegie Mellon University, PA)</td>
<td>Lumen Segmentation: 1. the user manually selects only a single sample point inside the lumen 2. a routine proceeds to identify the boundary of the lumen by detecting a sufficient gradient for each image in the data set. 3. a default threshold level is initialized to determine areas where the gradient image is greater than the threshold 4. The largest connected region containing the sample point is then labeled as the lumen region</td>
<td>The automatic lumen segmentation method produced better results than commercially available segmentation software when compared to the reference standard.</td>
<td>• user intervention is needed to correct the contours of the outer and inner walls • Accuracy and speed can be improved by replacing the 2D lumen segmentation algorithm with a 3D-based algorithm. • The number of subjects in the present study is small • There was variability in the slice spacing used to acquire the images.</td>
</tr>
<tr>
<td>o Wall thickness detection and quantification through segmentation routine that uses intensity histograms and a neural network trained on features of the image set itself [60]</td>
<td></td>
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<tr>
<td>XVII. 2D and 3D Deformable Models (active contours: snake models) [61]</td>
<td>DMs are based on elastic components. Frame and shell models are employed. External loadings are thought to arise</td>
<td>1. 2D DMs (snake-models) are used for luminal pre-segmentation 2. good initialization for the final segmentation of the lumen by a 3D DM (balloon-)</td>
<td>3D DMs provide an accurate segmentation without discriminating the out-of-plane direction 3D DMs facilitate the sever mesh distortions for large aneurysms with a thick eccentric intraluminal thrombus</td>
<td></td>
</tr>
</tbody>
</table>
from image data and internal pressure acting on the model.

This model does not consider inertia effects and viscosity.

The proposed FE representation of the DMs render a nonlinear system solved iteratively.

| XVIII. Tubular Surface Evolution for Segmentation [62] | The CB is modeled as a tubular surface. A general class of energies defined on these tubular surfaces is constructed. Energy functionals for segmentation whose optimum represents the structure of interest:
- Fixed Endpoint Implementation (for CB)
- Moving Endpoint Implementation (for CB and blood vessel segmentation) | 1. the cingulum bundle is modeled as a tubular surface determined by its center-line and the radius function of the discs along the center-line
2. a general class of energies is formulated directly on curves living in \( \mathbb{R}^4 \)
3. special consideration of the metric structure on curves is needed to optimize the energy | ✓ tubular surfaces provide a natural and accurate shape prior for the cingulum bundle (such a shape prior is necessary due to the noisy nature of the imagery and the fact that data is not very visible or highly corrupted in certain slices) ✓ representation as a 4D curve significantly reduce the computational cost of the algorithm compared to extracting an arbitrary surface. | • smoothness terms for the tubes in the energy needs to be studied • different choices of potential may facilitate the process • implementation of evolution of endpoints and the initialization will have to only be a single seed point |
<table>
<thead>
<tr>
<th>Segmentations Algorithms</th>
<th>Brief Description</th>
<th>Steps</th>
<th>Benefits</th>
<th>Drawbacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>XIX. thrombus segmentation method:</td>
<td>(1) approximate segmentation of the aortic lumen (2) simultaneous segmentation of the luminal and thrombotic surfaces (3) user-guided re-segmentation (if needed)</td>
<td>Aortic lumen segmentation 1. a triangular mesh of the approximate luminal surface for graph construction 2. a noise-reducing step (an anisotropic diffusion filter) 3. identification of approximate luminal region (region growing to the smoothed data set) 4. triangular mesh through marching cube isosurface algorithm 5. smoothed by averaging adjacent vertices (vertex smoothing)</td>
<td>✓ accuracy of this approach in estimating the area and the diameter of the aorta ✓ objective basis for pulse-wave velocity and distensibility estimations</td>
<td>• More objective validation would be possible using the reference standard acquired from multiple experts. • incorporating an intensity and/or texture-based cost terms may be useful to further reduce the user interaction and obtain even better segmentation results</td>
</tr>
<tr>
<td><strong>Segmenation Algorithms</strong></td>
<td><strong>Brief Description</strong></td>
<td><strong>Steps</strong></td>
<td><strong>Benefits</strong></td>
<td><strong>Drawbacks</strong></td>
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</tr>
<tr>
<td>XX. Automated segmentation technique, based on a 2D+t deformable surface model 2010 [64]</td>
<td>The intensity was automatically scaled to reduce variations in intensity within the aortic lumen during the cardiac cycle. To consider the coherence of the aortic wall motion the aortic contour was modeled by a 2D+t deformable surface ((x, y, t)). A two-step estimation to avoid attraction by a neighboring “white” structure or a narrowing...</td>
<td>1. ROI was manually defined around the aorta. 2. The dynamic sequence was averaged over time (single mean image). 3. Then a circle was automatically dilated from aorta’s center. 4. The modulus of the gradient of the mean image was summed along the circumference for each radius. 5. The circle providing the highest summed value was retained for initialization and was therefore duplicated over the cardiac cycle, resulting in an initial cylindrical surface. 6. Surface automated rescaling to reduce the variations induced by the inflow effect during the cardiac cycle. 7. 2D+t Deformable Surface Model</td>
<td>In addition to the classic methodological features of the deformable surfaces techniques: 1. consideration of the temporal dimension by using a 3D formulation of the deformable surface model. 2. the introduction of a specific attraction potential driving the contour toward the black rim surrounding the ascending aorta. 3. the normalization of the aortic lumen intensity. 4. the two-step strategy, which has proven to be very useful to avoid any unwanted attraction of the contour by the surrounding structures or by flow-related artifacts</td>
<td>Relatively high number of parameters used for optimizing the segmentation technique.</td>
</tr>
<tr>
<td><strong>Segmentation Algorithms</strong></td>
<td><strong>Brief Description</strong></td>
<td><strong>Steps</strong></td>
<td><strong>Benefits</strong></td>
<td><strong>Drawbacks</strong></td>
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</tr>
<tr>
<td>XXI. an automated, model-based segmentation: Hough transformation and 3D elastically deformable mass-spring model [65]</td>
<td>The method uses Hough transformations to detect the approximately circular shape of the aorta on the individual slices orthogonal to the vessel. To tract the aorta correctly prior knowledge about the shape of the aortic arch and a Kalman filter-like linear estimator is used. A 3D elastically deformable mass-spring model is used to adjust the detected contour more accurately to the aortic lumen.</td>
<td>Noise reduction filter as the preprocessing step Two seed points have to be determined (in descending and ascending aorta) Generation of the rough aortic mesh. Figure 3.2, p.39</td>
<td>✓ This method is faster than manual segmentation is fully automatic ✓ It segments the entire aorta, starting superior to the valve down to the iliac bifurcation ✓ the developed method has a high reproducibility, clinically acceptable accuracy</td>
<td>The largest increase in computational speed can be expected (detection of the center of the ascending as well as the descending aorta through two-level thresholding procedure). The involvement of the collateral branches of the aorta. Dissection can also propagate into carotid, renal, or iliac arteries.</td>
</tr>
<tr>
<td>XXII. Marginal space learning method for aortic root and aortic arch. 2D circle detector using Haar wavelet features and the boosting learning algorithm to detect aortic circles for asc and desc aortas. [66]</td>
<td>Combination of both approaches: MSL to detect the aortic root and arch, and use bottom-up tracking to detect ascending/descending aortas that have large variations in length. MSL detects and segments a 3D anatomical structure</td>
<td>1. the aortic root is detected first 2. detection of the aortic arch 3. train a 2D circle detector using Haar wavelet features and the boosting learning algorithm to detect aortic circles as primitive structures for tracking of asc and desc aorta 4. initial surface mesh of the aorta: assembling</td>
<td>✓ accuracy is comparable to (or better than) the state-of-the-art ✓ a fully automatic aorta segmentation and valve landmark detection system</td>
<td>MSL cannot deal with structural variations.</td>
</tr>
</tbody>
</table>
in medical images based on a discriminative machine learning technique.

A tracking technique is used to deal with variation of length of asc and desc aorta.

all the aortic parts together (the tracked aortic circles, aortic root, and aortic arch if it is present)

5. A learning based boundary detector is applied for final boundary delineation (a two-step iterative approach).

<table>
<thead>
<tr>
<th>XXIII. iteratively coupling intensity-based graph min-cut segmentation and geometric parametric model fitting [67]</th>
</tr>
</thead>
<tbody>
<tr>
<td>It uses a hybrid model that combines intensity information with global geometric parametric model constraint.</td>
</tr>
<tr>
<td>An iterative approach is used to estimate the latent model and to perform the segmentation. This coupling iteratively constrains the final global shape of the segmented surface.</td>
</tr>
<tr>
<td>1. Separate the AAA thrombus (object) from the surrounding structures with a hybrid model that consists of both intensity and global geometric shape constraint in a probabilistic framework that combines both model estimation and object segmentation.</td>
</tr>
<tr>
<td>2. A geometric parametric model is required, which describes the global shape of the required object (minimized using a two-step iterative approach)</td>
</tr>
<tr>
<td>3. Fit the geometric parametric model to initial segmentation. For each axial slice, we fit an ellipsoid using the Iterative Closest Point approach.</td>
</tr>
</tbody>
</table>

- The fitted model constrains the graph min-cut segmentation from leaking to the thrombus nearby structures such as the veins and muscles.
- The tool is:
  - accurate
  - easy to use
  - robust to varying thrombus locations and sizes for datasets with and without stents.
<table>
<thead>
<tr>
<th>Segmentation Algorithms</th>
<th>Brief Description</th>
<th>Steps</th>
<th>Benefits</th>
<th>Drawbacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>XXIV. implicit representation of a generalized cylinder and optimized a local region-based criterion under dedicated anatomical constraints [68]</td>
<td>Optimal two-phase separation problem, in which foreground (tubular representation) and background correspond to the IVC lumen and the surrounding structures.</td>
<td>1. An objective criterion is defined as the sum of some regularization term and image-dependent homogeneity measures integrated over the foreground and background regions. 2. The vessel representation is obtained by integrating a smooth decreasing radial function centered all over the medial curve. 3. Euler-Lagrange equations result in gradient-descent evolution equations for both the centerline and the scales. 4. A local likelihood criterion is defined at every $x$ from a weighted combination of local probability densities along the centerline. 5. Localization of the vertebral column is obtained by a simple thresholding.</td>
<td>✓ The promising results of this preliminary evaluation validate our choice of a model-based variational approach with local region homogeneity criteria under specific anatomical constraints. ✓ Model smooth complex objects with only simple explicit geometrical primitives, here a single curve. ✓ This is also the first use of implicit convolution surfaces for image segmentation.</td>
<td>Fully automatic and robust segmentation of the IVC requires significant additional effort. Future extensions to smooth branching structures, vascular trees and other medial representations.</td>
</tr>
<tr>
<td>XXV. minimal path techniques (centerline of coronary segments) and region-growing (for lumen boundaries of vessel segments) [69]</td>
<td>The iterative method first detects centerline of coronary segments and then extracts the corresponding lumen boundaries by using the centerlines and their associated scale information.</td>
<td>1. heart isolation (MSL and boundary evolution under the active shape model (ASM) framework) 2. Medialness Filter capture circular/elliptic shapes in cross-sectional views 3. Minimal-Cost Paths as Vessel Centerlines from Medialness Maps 4. A front propagation</td>
<td>✓ Computational efficiency of the approach ✓ Fully automatic centerline extraction including heart isolation and ostia detection ✓ Framework provides the user with</td>
<td>Longer propagations to locate the branch endpoints may yield anatomically incorrect centerlines as well as unnecessarily increased</td>
</tr>
</tbody>
</table>
starting from an ostia point is stopped after the medialness measure of fronts drops below a threshold value

5. Re-start the propagation from the fronts that are in the center of vessels and avoid propagation from fronts that are propagating towards vessel walls. In a breadth-first type, propagation starts from the most proximal front (active surface point).

Local Segmentation of Vessel Lumen

6. A tubular discrete graph is constructed around the local centerline segment using the estimated diameters as geometrical constraint.

7. An upper bound for the threshold is estimated from the intensity mean along the centerline points.

8. Graph nodes are partitioned into two parts

9. Step 3 is repeated by gradually decreasing the threshold (mean cut measure as our energy criterion)

10. Energy function measures the averaged cut between the two parts of the graph which is determined by the threshold-based region growing

simple tools for correcting and extending automatic results

computation times due to the accumulative nature of the method.

Traditional algorithms may not extract some of the vessel branches.

Increasing the computation times also results in leakages.
<table>
<thead>
<tr>
<th>Segmentation Algorithms</th>
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<th>Benefits</th>
<th>Drawbacks</th>
</tr>
</thead>
</table>
| XXVI. alpha-expansion approach of graph cut theory (cost function) [70] | Graph-cut is a two-class segmentation method which divides (or cuts) the graph in two sets of nodes. The goal of graph cut is to find the minimum cut. | 1. Building the graph  
2. An initialization (select ROI) at every 2 cm is enough, that is one contour every 8–20 images for a CT scan volume.  
3. The volume is divided into 3 regions: the “inside”, the “neutral” and the outside.  
4. Classification of nodes based on their edge capacity, which contains gradient information.  
5. The method ends up cutting the volume in areas of strong gradient, i.e. on the nearest edges  
6. Once the graph is built, the minimum cut optimizer is launched.  
7. The user can correct local deviations with a simple touch up tool which changes the region index of badly segmented nodes. This tool forces the selected nodes to be part of the inside, outside, or neutral regions. | ✓ This method does not leak  
✓ It also recovers a smooth 3D surface without a shape prior  
✓ The method does not leak when the aorta is pressed against another organ  
✓ It measures the maximum diameter of the aneurysm as well as the volume, position and eccentricity of the thrombus.  
✓ The average distance between our method and manual drawings is similar to the inter-observer variation. Therefore the automatic segmentation is as precise as an expert. | It sometimes overestimates the aortic wall in the vicinity of the collateral arteries. |
| XXVII. Combination of 3D model-based segmentation with elastic image Registration [71] | It combines 3D fitting of a parametric intensity model with intensity-based elastic image registration by a single energy-minimizing functional. Two different approaches, a 3D | 1. For segmentation of an entire vessel such as the aortic arch, we determine initial parameters with a fully automatic approach for vessel detection and incrementally minimize an energy-minimizing functional along the vessel centerline using a tracking approach based on a Kalman filter assuming a linear motion model | ✓ The joint approach can cope with a larger spectrum of vessel shapes.  
✓ The approach directly exploits the image intensities both for segmentation and registration. (full intensity information)  
✓ It does not require a prior atlas or | • Assumption that the foreground and background intensities are homogeneous is made. Thus, in the case of inhomogeneous intensities which are visible, the segmentation
and a 2D are developed. The first variant performs model fitting within a 3D ROI as well as uses 3D elastic image registration of the 3D ROI. The second variant uses 3D model fitting only for estimating the initial 3D orientation while image registration is performed on 2D image cross-sections orthogonal to the vessel centerline.

3. 3D parametric intensity model for tubular structures is constructed which represents an ideal sharp 3D cylinder convolved with a 3D Gaussian

4. To improve the agreement between the model and an imaged vessel in this case, elastic registration of an image generated from the 3D intensity model with a ROI of the original image is used

5. The result of elastic registration is a deformation field which can be used to compute, for example, a refined vessel contour and refined centerline positions. the deformations are computed using Gaussian elastic body splines.

6. The functional is optimized by an iterative scheme.

7. The result of elastic registration is used to improve the result of model fitting by re-estimating the model parameters including

8. The radius, the orientation, as well as the translation (centerline position).

9. Exploiting 2D and 3D image information.

10. A branch detection scheme that evaluates the image intensities within spherical ROIs is used to identify bifurcations.

template. the parametric intensity model is automatically generated by incremental 3D model-based segmentation.

- It does not require training, and does not depend on trained values representing the vessel shape or contrast.

- It simultaneously determines a segmentation and a quantification (e.g., estimation of the radius and centerline position)

- The approach is constrained to smooth shapes by employing a physically-based deformation model for registration

- An advantage of the approach is its flexibility: the choice of the parametric intensity model and the elastic registration scheme. Instead of sum-of-squared intensity differences, other intensity similarity measures, such as cross-correlation can be used for an intensity-based registration approach.
<table>
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<tr>
<th>Segmentation Algorithms</th>
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<th>Benefits</th>
<th>Drawbacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>XXVIII. Filtering algorithm (Frangi’s filtration, neighborhood analysis filter) [72]</td>
<td>The algorithm incorporate Frangi’s filtration with additional neighborhood analysis filter that eliminates local noises that often remains after that algorithm. The sensitivity of the method is steered by two algorithm’s parameters that might be visualized in 3D plot.</td>
<td>1. Consider its Taylor expansion in the neighborhood of a point. 2. Tubular structures enhancement filtering is based on eigenvalues of discrete hessian matrix 3. Define differentiation as a convolution with derivatives of Gaussians. 4. Filter generates vesselness measure for each pixel of 3D image. 5. The vesselness measure is analyzed at different scales. 6. The Frangi’s method operates under constraints that there are no large continues regions with higher density then contrasted tissues. (additional treshholding based on tissue density) 7. Another filter for noises and scanning artifacts. 8. The final response of the filter is a common part of Frangi’s and neighbor filter at the given threshold values.</td>
<td>✓ The filter has capability of finding the solid regions containing voxels in given density range ✓ The method can be use for adjusting the position of vascular tissues in volumetric and MIP visualization of 3D data. ✓ It can also be used in the preprocessing step before semantic classification of visualized symptoms.</td>
<td>• Filter cannot differ between tubular structures and surfaces. • Frangi’s filter eliminates surfaces. • Elimination of all thick-lines artifact by increasing the parameter of filtering thresholds might also damage the continuity of rightly detected thick vessels. • The Frangi’s neighbor filtering alone cannot detect all potential vascular structures.</td>
</tr>
</tbody>
</table>

From the numerous of studied methods DRLSE was found to be more effective for vessel segmentation. DRLSE stands for Distance Regularized Level Set Evolution and is proposed by Li et al. [73] In particular reinitialization is typically applied to periodically replace the degraded level set function with a signed distance
function. A new variational level set formulation in which the regularity of the level set function is intrinsically maintained during the level set evolution. Below the benefits of this method are presented.

Benefits:

- The distance regularization effect eliminates the need for reinitialization and thereby avoids its induced numerical errors.
- A simpler and more efficient finite difference scheme can be used to implement the DRLSE formulation.
- More general and efficient initialization of the level set function is allowed.
- Relatively large time steps can be used in the finite difference scheme to reduce the number of iterations, while ensuring sufficient numerical accuracy.
- It greatly reduces the computational cost.
- DRLSE formulation has an intrinsic capability of maintaining regularity of the level set function, particularly the desirable signed distance property in a vicinity of the zero level set, which ensures accurate computation and stable level set evolution.

For level set methods generally:

- These methods are able to handle topological changes, such as splitting and merging, in a natural and efficient way, which is not allowed in parametric active contour models without extra indirect procedures.
- Numerical computations can be performed on a fixed Cartesian grid without having to parameterize the points on a contour as in parametric active contour models.
Simulation Study – Basic Steps

The process by which the simulation is performed has to be defined precisely regardless of the problem type. The following briefly describes the basic steps in our simulation process:

1. **Problem Definition**

The goal of the study is to simulate the blood flow in aorta and particularly in ascending, descending aorta and aortic arch. Blood flow in human body needs to be simulated since it is the most noninvasive way to investigate the problem.

2. **Project Planning, System Definition, Model Formulation**

Our data for the first model were taken from CT scans after the appropriate image processing. The second simulated model was sketched in a simple way and was used as a primary Fluid Structure Interaction geometry model. [74] Next step was Mesh Construction and Definition of Boundary and Initial Conditions. The commercial package of ANSYS v.14 was our simulation program.

3. **Analysis**

Our analysis is based on studies of Stevens et al. [75], Mortazavinia et al. [74]. Initial and Boundary Conditions are in agreement with those proposed by Stevens and Mortazavinia. After results were exported, several hemodynamic indices were calculated. Velocity and Wall Shear Stress Contours were presented and conclusions were obtained.

4. **Verification and Validation**

Our models are compared with experimental surgery and results were confirmed. Comparison with recent studies proved that our model is close to reality.
5. Experimentations and Analysis, Documentation and Implementation

The results and implications of the study are discussed. The written report describes the procedure and possible differences with other studies are justified.

Solving the real problem of blood flow conditions, we come up with conclusions related to plaque formation in human vessels. Wall Shear stresses developed in arterial walls are responsible for cardiovascular diseases such as atherosclerosis and thrombosis.

6.1 Blood Flow Simulation in human aorta (1st Model)

Real geometry was segmented from CT scans and used for our simulations. The parts of ascending, aortic arch and descending aorta were chosen to be studied. The application of simulation involves the following specific steps.

6.1.a Geometry Extraction

Our data were DICOM files from CT scans. Using Vascular Modeling Toolkit (VMTK) and these scans as the input, we choose level set segmentation method to extract the geometry of the vessel needed for the simulation. Below you can see the commands we used on VMTK.

Commands in VMTK:

- vmtkimagereader -f dicom -d dicom_directory_path --pipe vmtkimagewriter -ofile name1.vti
- vmtk vmtklevelsetsegmentation --ifile name1.vti -ofile name2.vti
- vmtk vmtkmarchingcubes -ifile vti_directory_path -l 300.0 --ofile name3.vtp --pipe vmtksurfaceviewer
- vmtksurfacereader -ifile name3.vtp --pipe vmtksurfaceviewer -ofile name4.stl

The resulting contours after image segmentation can be used to create 3D reconstructions with the help of interpolation algorithms (like Marching cubes). Smoothing of the segmented geometry is also required to leave out noise or other
fine scale structures. The output of this process was an .stl geometry file. (STereoLithography)

Figure 6.1 shows the interface of the two software programs used for geometry extraction, VMTK and Geomagic studio. Where the three levels intersect in VMTK, the vessel of interest is visible. The output of VMTK is imported into Geomagic Studio, where final modifications, like smoothing and edge effect correction in our geometry take place.

6.1.b Mesh Construction

Our Geometry is imported in Ansys Workbench, where simulation takes place.

We continue with the construction of Mesh. Many trials of different types of Mesh prove that tetrahedral elements are the best choice. These trials helped to check the independency of our mesh. In other words, the solution should not depend on the grid to be used. Furthermore, mesh density has to change with
geometry abnormalities. Locally finer Mesh in curving vessels was implemented in order to achieve more accurate solution on those regions. (Fig.6.2)

Boundary surfaces need to be defined while mesh is constructed. Inlet, Outlet and Vessel wall are the three boundary surfaces. ANSYS Model Setup in Workbench is used in this step.

Fig. 6.2 Mesh Construction. Mesh Density has to change with model abnormalities

The figure above shows the mesh details in these points of inlet where geometry seems to have abnormalities. There are many other points in the entire geometry where mesh is locally denser.

6.1.c Computational Hemodynamics

ANSYS CFX Solver was used for our simulation. The problem is isothermal. Therefore, there are no differences in heat transfer. Judging from the value of blood velocity in this region, we assume that the flow is laminar. Cardiac output is constant with time. Blood flow is pulsatile. Incompressible, Newtonian Fluid flow into Rigid Vessel Walls was simulated.
The pulsatile flow model applied to the inlet was taken by a model flow function described by Stevens et al. [75] The main expression of this function appears here, and below there are all parameters that take part in this expression. It is a Fourier series.

\[
\text{velocity} = \frac{Q}{2\pi \text{radius} \lambda}
\]

\[
Q = A_0 + (A_1 \cos(2\omega t)) + (B_1 \sin(2\omega t)) + (A_2 \cos(4\omega t)) + (B_2 \sin(4\omega t)) + (A_3 \cos(6\omega t)) + (B_3 \sin(6\omega t)) + (A_4 \cos(8\omega t)) + (B_4 \sin(8\omega t)) + (A_5 \cos(10\omega t)) + (B_5 \sin(10\omega t)) + (A_6 \cos(12\omega t)) + (B_6 \sin(12\omega t))
\]

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<table>
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<th>Value</th>
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<tr>
<td>ω</td>
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</tr>
</tbody>
</table>

**Table 6.1 Model Flow Function Parameters**
Here is the diagram (Fig. 6.4) of the model flow function applied at the inlet. It represents through Fourier series the pulsatile cardiac output based on heart rate and stroke volume.

**Table 6.2 Boundary Conditions**

<table>
<thead>
<tr>
<th>Boundary Type</th>
<th>Boundary Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>INLET</td>
<td>• Inlet</td>
</tr>
<tr>
<td></td>
<td>• Flow Regime &gt; Subsonic</td>
</tr>
<tr>
<td></td>
<td>• Mass and Momentum &gt; Normal Speed &gt; velocity *</td>
</tr>
<tr>
<td>OUTLET</td>
<td>• Opening</td>
</tr>
<tr>
<td></td>
<td>• Flow Regime &gt; Subsonic</td>
</tr>
<tr>
<td></td>
<td>• Mass and Momentum &gt; Opening Pressure&gt; 0 [Pa]</td>
</tr>
<tr>
<td></td>
<td>• Flow Direction &gt; Normal to Boundary Condition</td>
</tr>
<tr>
<td>WALL</td>
<td>Wall</td>
</tr>
<tr>
<td></td>
<td>Mass and Momentum &gt; No Slip Wall</td>
</tr>
</tbody>
</table>

**Fig. 6.4 Boundary Conditions (Inlet)**
Pressure 0 [Pa] was applied at the outlet, where the flow direction was set normally to boundary. Blood velocity very close to the arterial wall has zero value. So, we choose no slip wall.

6.1.d Spatial and Temporal Distribution patterns of Several Hemodynamic Indices

Four Hemodynamic Indices were calculated. Wall Shear Stress (WSS), Gradient of WSS (WSSG), Time Averaged Wall Shear Stress (TAWSS) and Oscillating Shear Index (OSI). The expression for OSI includes one more variable. Time Averaged Wall Shear Stress Vector (TAWSSV).

For these calculations we used the following expressions where T stands for the period (T=2,5sec).

\[
WSSG = \sqrt{\left(\frac{\partial WSS}{\partial x}\right)^2 + \left(\frac{\partial WSS}{\partial y}\right)^2 + \left(\frac{\partial WSS}{\partial z}\right)^2}
\]

\[
TAWSS = \frac{1}{T} \int_{0}^{T} |WSS| dt
\]

\[
OSI = 0.5 \times \left(1.0 - \frac{TAWSSV}{TAWSS}\right)
\]

\[
TAWSSV = \frac{1}{T} \int_{0}^{T} WSS dt
\]

WSS comes from the product of dynamic viscosity and shear strain rate next to the vessel wall. Shear strain rate is calculated automatically in ANSYS CFD-Post. Spatial gradient (WSSG) and temporal mean value of WSS (TAWSS) can also provide a useful aspect of the problem, which is the localization of atherosclerosis.

OSI is a measure of how much flow changes direction over the cardiac cycle. In other words, OSI measures the percent of the cardiac cycle when flow is going a different direction than the mean flow direction. OSI could be especially important in locating regions of oscillatory flow, which are known to be atherogenic.
Hemodynamic indices are analyzed in many studies and contribute in order to understand the environment that is formed across blood flow. [32, 76, 77]

The role of low WSS and high Oscillating Shear Index (OSI) in atherosclerosis are proved extremely important. Our results (Chapter 7) indicate possible regions of atherosclerotic plaque formation.

6.2 Fluid Structure Interaction Model, FSI (2\textsuperscript{nd} Model – Stenosed Artery)

The interaction between the blood and the vessel wall is of great clinical interest in studying cardiovascular diseases, the major causes of death in developed countries. Therefore, understanding the effects of incorporating fluid-structure interaction into the simulation of blood flow through an anatomically realistic model is of great interest. [74]

An anatomically realistic model of abdominal aorta is shown in Figure 6.5. As discussed above, the main objective of this study was to simulate blood flow through our vessel geometry.

![Vertical Section of Geometry](image)

\textbf{Fig. 6.5 Vertical Section of Geometry}
Geometry Dimensions are given in the table below:

<table>
<thead>
<tr>
<th>Dimension</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diam</td>
<td>5mm</td>
</tr>
<tr>
<td>L</td>
<td>1.5mm</td>
</tr>
<tr>
<td>φ2</td>
<td>30°</td>
</tr>
<tr>
<td>z1</td>
<td>1mm</td>
</tr>
<tr>
<td>Lout</td>
<td>50mm</td>
</tr>
<tr>
<td>z</td>
<td>1mm</td>
</tr>
<tr>
<td>x</td>
<td>1.4mm</td>
</tr>
<tr>
<td>z2</td>
<td>1.7mm</td>
</tr>
<tr>
<td>Lin</td>
<td>15mm</td>
</tr>
<tr>
<td>φ1</td>
<td>45°</td>
</tr>
<tr>
<td>y</td>
<td>2mm</td>
</tr>
</tbody>
</table>

Total Length = Lout + z1 + L + z2 + Lin = 69.2mm

Table 6.3 Geometry Parameters

Fig. 6.6 Cylindrical Shell represents arterial wall with stenosis

Fig. 6.7 Cylinder with stenosis – Final Geometry
After sketching the desired geometry, mesh construction is the next step. For an FSI analysis it is of great importance to distinguish the problem in two parts, one for the solid and the other for fluid motion. Table 6.4 presents our analysis separately for the two parts.

<table>
<thead>
<tr>
<th>Mesh</th>
<th>Solid</th>
<th>Fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial wall</td>
<td>Mesh → Tetrahedrons</td>
<td>Blood flow → Mesh → Tetrahedrons</td>
</tr>
<tr>
<td>→ Body Sizing</td>
<td>→ Element Size 0.001m</td>
<td>→ Sizing → 0.001m</td>
</tr>
</tbody>
</table>

| Boundary / Initial Conditions | 1. both ends of the cylindrical shell → Fixed support | Inlet: flow rate=4.3[ml/s]+2.6·sin(2·π·T/t) [ml/s] |
|                               | 2. inside the cylindrical shell → Fluid Solid Interface | Period: T=0.345[s] |
|                               | 3. outer wall of the cylindrical shell → Displacement: x=0, y=free, z=free | Outlet: Static Pressure=4140Pa |

| Properties | Young Modulus: 4.66 MPa | Density → 1050 kg/m3 |
|            | Poisson’s ratio: 0.45 | Dynamic Viscosity → 0.0035 Pa·s for Newtonian Fluid |
|            | Density: 1062 kg/m3 | |

**Problem set up**

- Total Time: 1 s
- Timestep: 0.1 sec
- Initialization:
  - Static Pressure: 1 atm
  - Cartesian Velocity Components: v=30cm/s (in the direction of flow), the other components are zero.
- Transient → Trn Results

**Table 6.4 FSI Problem Parameters**

It should be noted that only movement in the radial-tangential plane was allowed and solution is calculated with tolerance of 0.1% of the diameter. Convergence criteria for all the fluid variables were $10^{-5}$.

Similar simulation steps were applied to a real vessel geometry constructed from CT images of abdominal aorta. In this case lumen and external arterial wall separately were obtained after image segmentation process. Subtracting the first
from the second we acquire the arterial wall alone and simulation steps for solid and fluid parts are easily distinguished.

Fig. 6.8 Complete Geometry (Arterial wall with Lumen inside)

Fig. 6.9 Arterial Wall

Fig. 6.10 Mesh of arterial wall (solid part)
Fig. 6.11 Mesh of Lumen (fluid part)
Results – Analysis

The results obtained from the simulation of the 1st Model predict a marked dependency on both WSS and WSSG on the geometry. The biological aspects of the links between hemodynamic factors in general and WSSG in particular as well as the location and severity of arterial diseases have already presented in Chapter 2. Model for FSI (2nd) essentially verified the study of Mortazavinia et al. [74]

7.1 Results

1st Model

**WSS and WSSG distribution.** Spatial distribution for the values of WSS and WSSG during one period are given in following Figures. Our simulation lasts 10 seconds. The Period from 4,5sec to 7sec, where the flow has been fully developed, is
here presented. It should be noted that the scale is different every time. The maximum and minimum values increase and decrease periodically. We must notice that there is a small region in the curved part of the geometry where WSS is permanently increased compared to the environment. The same goes for WSSG on a more limited scale. Probably it is a possible sign of atherosclerosis.
The magnitude and distribution of WSS and WSSG prove that arterial wall receives many different shear stresses along the flow of blood. The differences generated by blood rheology are most notable for the curved part of the vessel. Peaks and troughs of WSS appear when geometry changes (here in curvature) occur. The peak of WSSG is mainly located in the part of ascending aorta. The majority of vessel wall is subjected to WSS values between $10^{-3}$ Pa and 0.36 Pa.

Areas of increased values for both WSS and WSSG near the output is next to the edge of our geometry. So, they cannot be taken into account and lead to reliable conclusions, since the flow condition over there is influenced by the flow below, in abdominal aorta.

**Velocity Field.** Figures that follow show velocity streamlines across the whole geometry. During acceleration the development of the flow is clearly presented. Velocity of the flow is shown at six different times that include a complete period of 2.5 sec.
Notable local increase of blood flow velocity is observed at the curved part of the geometry, especially when $t=4.5s$ and $t=5.5s$. This is another indication that this region is more likely to be pathogenic comparing with the rest of the regions in our geometry.

**Time Averaged WSS.** TAWSS distribution is shown in the following Figures. These color maps depict the spatial distribution of mean temporal value for WSS calculated in matlab. It comes out that after a fully developed flow higher values are developed in the part of descending aorta. However we observe that there is no area that stands out for its values as there is a uniform distribution to a large piece of geometry.

The area that we found previously as possible for the formation of atherosclerotic plaque is included within areas with high TAWSS. Therefore, there is no clear indication through this hemodynamic parameter.
**Oscillatory Shear Index.** Figures below show quantitatively and qualitatively how OSI is distributed. Two regions stand out clearly in the color maps. The first one is next to the inlet boundary and the second at the curved part of our geometry. For the last one we have reasonable suspicion that plaque can be formed. Perhaps here comes the confirmation. For the first one, there seems to be oscillatory flow in this specific area. Geometry complexity may justify that behavior, because locally abrupt changes in geometry can cause high values for OSI.
**2\textsuperscript{nd Model}**

For the FSI model axial velocity profile was calculated and compared with the study of Mortazavinia et al. [74]. According to these figures, there is acceptable agreement between the results obtained by the two compared studies.

FSI analysis reveals that compliance of the arterial wall influences wall shear stresses developed among the arterial tree. WSS is directly related to the rate of velocity change near the wall. Therefore, wall deformability has notable effect on WSS, which is of great clinical interest. Blood flow characteristics will also change if
we incorporate and consider arterial wall compliance in studying blood flow through vessels.

### 7.2 Comparison with recent studies

Other relative studies show that actually high values of OSI are detected in areas next to inlet boundary and in regions with high curvature. The same goes for WSS. The observed differences are due to different geometry and flow conditions (In the first study, Figure 7.1, the flow is not pulsatile.)

![Fig 7.1 Color Maps of WSS (Pa) [78]](image1)

![Fig 7.2 Color Maps of OSI (M²-N⁻¹) [79]](image2)
There are plenty of studies which claim that Low and Oscillatory Wall Shear Stress promote atherosclerotic plaque formation. Localization of Atherosclerosis is of great clinical interest and there is enough work remained to be done. Color maps give only a qualitative distribution of the possibility for plaque formation. We need more specific results for the exact point of pathogenesis.
Atherosclerosis tends to develop in preferred sites, such as the bifurcations and flow divisions of the arteries [81]. The development and progression of the atherosclerosis are related to the complex flow field occurring in the inner wall of curvatures and bifurcations of the arteries. It is widely known that there is the correlation between atherosclerosis lesion location and low or oscillating wall shear stress.

The objective of this study was to simulate blood flow in order to calculate hemodynamic indices that help in localization of atherosclerosis. Wall Shear Stress values and their spatial distribution among human aorta were presented and analyzed. Furthermore, a typical FSI model of a stenosed artery was studied. Our conclusions are summarized below.

- Atherosclerosis is present in the majority of the population in the modern world and often causes episodes that required medical care.
- CFD provide a powerful approach to the investigation of vascular blood flow phenomena.
- Our study detects potential indicators for therapeutic intervention and prognostic criteria.
- Attention should be put in curving vessels which experience different WSS magnitudes on the inner edge and outer edge of curvature.
- Accurate calculations of hemodynamic parameters such as WSSG and OSI can significantly contribute to prevention of atherosclerosis-related morbidity and mortality.
The effects of FSI models on the stenosis can cause changes to WSS values and influence blood flow simulation. The model with fluid-structure interaction is introduced to investigate the wall shear stresses, blood flow field and recirculation zone in the stenotic vessels. However, it should be noted that according to Buriev et al [80] FSI models at 25% stenosed rate case did not change the fluid and solid behavior significantly. In case of 50% and 75% stenosed rate, the effects of FSI model on the stenosis were high which means blood flow could be closure or vessel wall could be collapsing due to high stenosed rate and high shear stress. Therefore, when vessel is highly narrowed, compliance of the wall must be taken into account.

8.1 Limitations and Future Work

It is proved that a relationship between WSS and atherogenesis may exist. Identification of WSSG, OSI and correlated indices conditions, that “facilitate” plaque formation, can significantly contribute to prevention of atherosclerosis-related morbidity and mortality. Therefore, accurate calculations of these hemodynamic parameters are required.

Atherogenesis is a heavily researched disease. However, more work remains since clinicians require better tools to identify and treat plaques. In future work the exact evaluation of the impact that wall motion and compliance have on bulk flow patterns in the human aorta (FSI) can be studied. Furthermore, in order to gain insight into the aetiology of plaque formation and aneurysm inception, in addition to sophisticated CFD simulations, improved understanding and modelling of the mechanobiology of the arterial wall is needed. Another problem that still exists is the time-consuming process that is required in order to export useful results. More rapid processing steps could produce immediate and clinical useful conclusions. Method improvement should be designed to automate the process and make it attractive to clinicians.
Heart diseases in Western societies, such as atherosclerosis, are too important to be ignored. One must always consider the effects of flow and biomechanical properties of vessel wall when studying problems in cardiology.
References


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49. T.M. Deserno. (2011) Biomedical Image Processing, Biological and Medical Physics, Biomedical Engineering, DOI: 10.1007/978-3-642-15816-2 1, Springer-Verlag Berlin Heidelberg

50. Angenent S, Pichon E, Tannenbaum A. Mathematical Methods in Medical Image Processing. Bulletin (New Series) of the American Mathematical Society. Volume 00, Number 0, Pages 000-000, S 0273-0979(X)0000-0


